

A Prospective Observational Study on Evaluating the Appropriateness and Prescription Pattern of Restricted Antibiotics in a Quaternary Care Hospital

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ABSTRACT

Aim: To evaluate the appropriateness of Restricted Antibiotics in accordance with Indian Council of Medical Research (ICMR) guidelines and Prescription Pattern of Restricted Antibiotics in a quaternary care hospital.

Methodology: This prospective observational study included the in-patients of different wards in a quaternary care hospital who have been prescribed Restricted Antibiotics in the drug chart. The appropriateness of Restricted antibiotic use is assessed on the basis of the ICMR guidelines. The appropriateness of Restricted Antibiotics was verified, according to three main criteria: choice of antibiotic, dose, and frequency.

Results: A total of 110 patients who had been prescribed with Restricted Antibiotics were included in the study. The most prescribed Restricted Antibiotic was Meropenem (59.6 %) followed by Linezolid (18.5%). The overall appropriateness of Restricted Antibiotics was found to be 72.7%.

Conclusion: On evaluating the Prescription pattern of the Restricted Antibiotics, we concluded that Meropenem was the highly prescribed Restricted antibiotic in our hospital, followed by Linezolid, Levofloxacin, and Tigecycline. Even Though we conclude that most of the Antibiotics are prescribed appropriately, few patients were administered with inappropriate choice of Restricted Antibiotics. The findings also emphasized the significance of evaluating prescribing practices on a regular basis.

Keywords: ICMR, Restricted Antibiotics, Prescription pattern

INTRODUCTION

Antibiotics are medicines that fight infections caused by bacteria in humans and animals by either killing the bacteria or making it difficult for the bacteria to grow and multiply.⁽¹⁾ Antibiotics may be

classified as bacteriostatic or bactericidal based on their action. They have negative side effects and can lead to antibiotic resistance. Common risks associated with the overuse of antibiotics include increased antimicrobial resistance (AMR) and more

severe diseases. Restricted antimicrobials are those that adhere to the hospital's regulations for limiting their usage, as specified by the Drug and Therapeutics Committee (DTC) in cooperation with the antimicrobial stewardship (AMS) committee. These Restricted Antimicrobials require rigorous monitoring and adherence to the hospital's antimicrobial prescribing policy. They can only be prescribed with the approval of an infectious disease specialist, a clinical microbiologist, or the AMS team. Additionally, these antimicrobials must be recommended and supplied with permission from a consultant microbiologist before administration.⁽²⁾ The pharmacist must verify microbiology approval or formulary indication. Certain medications may be subject to restrictions based on factors such as antimicrobial activity spectrum, cost, and potential for toxicity.

The list of Restricted Antibiotics in our hospital includes Colistimethate sodium, Vancomycin, Fosfomycin, Minocycline, Levofloxacin, Tigecycline, Teicoplanin, Linezolid, Daptomycin, Imipenem, Meropenem, Doripenem and Ceftazidime / Avibactam.

According to the World Health Organization (WHO), antimicrobial resistance (AMR) occurs when bacteria, viruses, fungi, and parasites change over time and no longer respond to treatment, increasing the risk of disease spread, severe illness, and death. As a result of drug resistance, antibiotics and antimicrobial medicines become ineffective, and infections become increasingly difficult or impossible to treat.⁽³⁾ These organisms that cause antimicrobial resistance are called 'superbugs'. The four basic mechanisms of antimicrobial resistance include limiting drug uptake, modifying drug targets, and inactivating drugs. The latest 'surveillance of Antimicrobial Resistance' report published by the European Centre for Disease Prevention and Control (ECDC) shows a high percentage of resistance to last-line antibiotics, such as carbapenems, in several countries of the WHO European

region. Examples of AMR include Methicillin-Resistant Staphylococcus Aureus, Clostridium difficile, and active drug efflux.⁽⁴⁾ The increasing antibiotic resistance has led to serious infections, complications, extended hospital stays, and higher mortality rates. Community-acquired AMR is of particular concern due to the prevalence and easy transmission of these infections.⁽⁵⁾ Individual resistance to antibiotics may persist for up to 12 months after treatment. The European Centre for Disease Prevention and Control estimates that 25,000 people in Europe die directly as a result of resistant infections each year.

According to CDC antimicrobial stewardship is the effort to measure and improve how antibiotics are prescribed by clinicians and used by patients. Improving antibiotic prescribing and use is critical to effectively treat infections, protect patients from harm caused by unnecessary antibiotic use, and combat antibiotic resistance, AMS is one of the three pillars of an integrated strategy for strengthening the health system other two are Medicine and patient safety and infection prevention and control by maximizing the use of antibiotics. The aim of the AMS program is to:

- To optimize the use of antibiotics, to promote behaviour change in antibiotic prescribing and dispensing practice.
- To improve the quality of care and patient outcome.
- To save on unnecessary healthcare cost.
- To reduce further emergence selection and spread of AMR.⁽⁶⁾

"The Chennai Declaration" is the outcome of India's first-ever joint assembly of medical associations to discuss antibiotic resistance. The declaration is a national policy. They examined all main facets of the antimicrobial resistance problem, proposed practical remedies, and detailed each stakeholder's responsibilities. The region's vast population, sanitation concerns, lack of a working antibiotic policy, and inadequate infection control facilities in many hospitals make it an epicenter of the growth of multi-drug-resistant microorganisms, such as

Carbapenem-Resistant Enterobacteriales. The country's high antibiotic resistance rate, as well as inspiration from ongoing worldwide efforts, encouraged Indian doctors to organize the Chennai summit. The efforts resulted in an Indian medical society and policymakers developing a strategy to address the major threat of antibiotic resistance in the country. Pharmacist involved in the AMS promote optimal antimicrobial use, to reduce the transmission of infection, and to educate other health care professionals, patients, and the public. Pharmacist participating in AMS has duties to encourage appropriate antibiotic usage and reduce the spread of illness, and educate other healthcare professionals ⁽⁷⁾, patients and the general public. Prescription auditing is an important method for improving prescription quality, Regular and timely antibiotic prescription audits can help to prevent irrational antibiotic use. ⁽⁸⁾

MATERIALS & METHODS

A prospective observational study on evaluating the appropriateness and prescription pattern of Restricted Antibiotics in a quaternary care hospital was conducted by drug chart review. This study was carried out in quaternary care hospital-Chennai. This study was carried out for a 6 months period from February to July 2023. The estimated sample size for the total study population was 110 patients, who were prescribed Restricted Antibiotics during the study period, with a 95% confidence interval (CI) and a margin of error of 5%.

Eligibility criteria:

- **Inclusion criteria:** Inpatients prescribed with Restricted Antibiotics in their drug chart, aged above 18 years, and of all genders.
- **Exclusion criteria:** Pregnant and lactating women, and patients who passed away during treatment.

A literature survey was conducted to evaluate the appropriateness and prescription pattern of Restricted Antibiotics

in patients admitted to different wards/departments across the hospital. Most studies indicated a remarkable rate of inappropriateness, which may contribute to antimicrobial resistance (AMR). This, in turn, raised the risk posed by resistant bacteria, leading to prolonged hospitalization and increased mortality. AMR was also influenced by the overuse of Antibiotics. Antimicrobial audit and measuring antibiotic consumption remained fundamental aspects of an antimicrobial stewardship program. Restricted Antibiotics justification forms helped control the use of Antibiotics. Recognizing the importance of Restricted Antibiotics and their association with antimicrobial resistance, we decided to conduct a study evaluating their appropriateness and prescription patterns in a quaternary care hospital located in Chennai, Tamil Nadu. The study protocol was prepared and submitted to the Medical Superintendent of our study site for approval. We collected individual patient data through patient chart review, including age, indication, length of hospital stays, type of surgery, required lab parameters, culture reports, sensitivity of Antibiotics, and prescribed Antibiotics. We assessed the compliance of Restricted Antibiotics based on the following criteria: choice, dose, and frequency, with reference to the Indian Council of Medical Research (ICMR) guidelines.

STATISTICAL ANALYSIS

For statistical analysis, we used the Statistical Package for the Social Sciences (SPSS). After data collection, we compiled and tabulated it in Microsoft Excel, and descriptive analysis was performed using mean and standard deviation for quantitative variables, as well as frequency and proportion for categorical variables. Additionally, we represented the data using appropriate diagrams such as bar charts.

RESULT

In our study, Among the total of 110 patients many male patients were prescribed

Restricted Antibiotics compared to female patients. The mean age of the patients was found to be 64.2 ± 16.5 years. The majority of the study population was above 50 years. Nearly half of the patients received Restricted Antibiotics empirically and half

of the patients received Restricted Antibiotics based on antimicrobial susceptibility reports. The results of our study were depicted below in tables and bar charts.

Table 1: Gender categorization (n=110)

GENDER	NUMBER OF PATIENTS	PERCENTAGE
MALE	68	61.82
FEMALE	42	38.18
TOTAL	110	100.0

Table 2: Categorization based on type of therapy

TYPE OF THERAPY	NUMBER OF PRESCRIPTIONS	PERCENTAGE
DEFINITIVE	57	51.8
EMPIRICAL	53	48.2
TOTAL	110	100.0

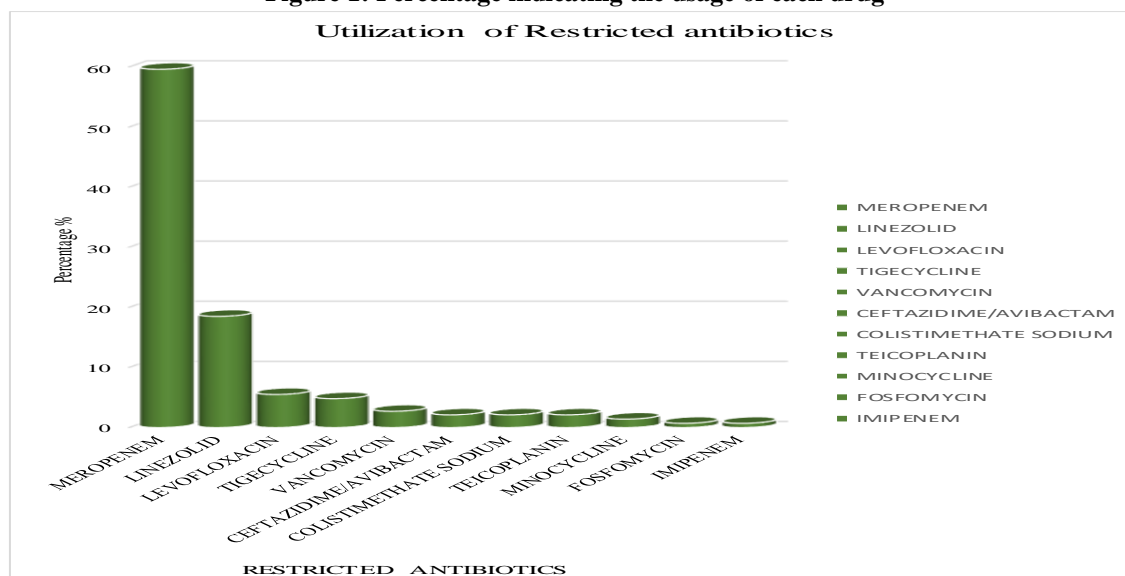
Table 3: Age distribution of patients (n=110)

AGE (YEARS)	NUMBER OF PATIENTS	PERCENTAGE
18-20	2	1.8
21-30	2	1.8
31-40	3	2.7
41-50	8	7.3
51-60	22	20.0
61-70	32	29.1
71-80	26	23.6
81-90	11	10.0
91-100	4	3.6
Total	110	100.0

Table 4: Number of Restricted Antibiotics prescribed per patient

NUMBER OF RESTRICTED ANTIBIOTICS PRESCRIBED PER PATIENT	NUMBER OF PATIENTS	PERCENTAGE
1 Restricted Antibiotic	81	73.6
2 Restricted Antibiotics	26	23.6
≥ 3 Restricted Antibiotics	3	2.8
Total	110	100.0

Figure 1: Percentage indicating the usage of each drug



Among the total of 149 Restricted Antibiotics prescribed, the most frequently prescribed Restricted Antibiotic was Meropenem (59.6%), followed by Linezolid (18.5%) and Levofloxacin (5.5%). The least prescribed were Fosfomycin and Imipenem. Meropenem was most commonly prescribed for sepsis, recurrent UTI and urosepsis.

Table 5: Categorization based on Indications

INDICATION	NUMBER OF PATIENTS	PERCENTAGE
Acute Febrile Illness	3	2.7
Bone infections	3	2.7
Candidemia	1	0.9
Cardiovascular diseases	8	7.3
Casualty	1	0.9
Cellulitis	5	4.5
CNS Diseases	2	1.8
Liver disease	1	0.9
Lung Diseases	7	6.4
Lung Infection	1	0.9
Meningitis	2	1.8
Pneumonia	5	4.5
Renal diseases	6	5.5
Seizure	1	0.9
Sepsis	21	19.1
SSI	2	1.8
Urosepsis	10	9.1
Recurrent UTI	19	17.3
Others	12	10.9
Total	110	100.0

Restricted Antibiotics were most frequently prescribed for sepsis (19.1%), followed by recurrent UTI (17.3%), and urosepsis (9.1%). In our study, approximately 73.6% of patients received one Restricted Antibiotic therapy, either alone or in combination with other unrestricted antibiotics.

Table 6: Categorization based on the bacterial species detected

Gram negative Organism	Number of Isolates	% of Isolates
Acinetobacter species	3	1.9
Escherichia species	21	13.5
Pseudomonas species	12	7.1
Enterobacter species	1	0.6
Klebsiella species	20	12.9
Morganella species	1	0.6
Achromobacter species	2	1.3
Burkholderia species	1	0.6
Proteus species	2	1.3
Stenotrophomonas species	1	0.6
Elizabeth kingia species	2	1.3
Citrobacter species	2	1.3
Gram positive Organism	Number of Isolates	% of Isolates
Staphylococcus species	2	1.3
MRSA	2	1.3
Enterococcus species	6	3.9
Streptococcus species	4	2.6
NO GROWTH	73	47.1

Escherichia species were the most detected gram-negative organisms, accounting for about 13.5%, followed by Klebsiella species at about 12.9%, and Pseudomonas species at

about 7.1%. Enterococcus species were the most detected among Gram-positive organisms (3.9%), followed by Streptococcus species (2.6%).

Figure 2: Percentage of the appropriateness of Restricted Antibiotics usage

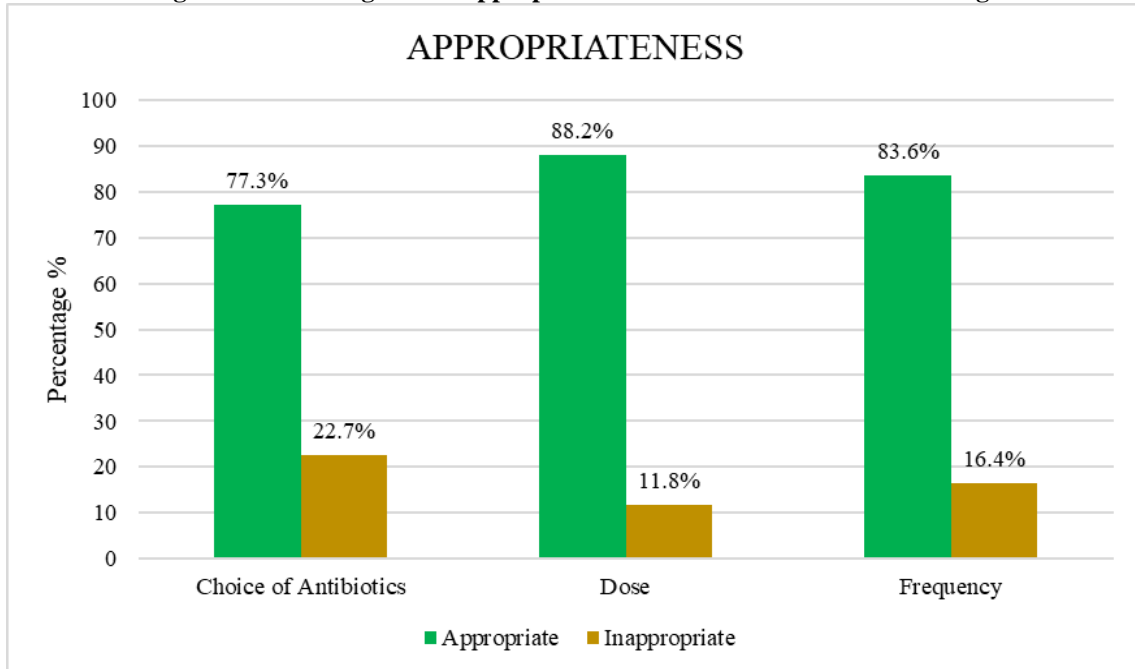


Table 7: Overall appropriate use of Restricted Antibiotics

OVERALL APPROPRIATENESS	NUMBER OF PATIENTS	PERCENTAGE
Appropriate	80	72.7
Inappropriate	30	27.3
Total	110	100.0

On evaluating the appropriateness based on choice of antibiotics, dose and frequency, 77.3% were administered with appropriate Restricted Antibiotic choice. 88.2% were administered with appropriate dose. 83.6%

were administered with appropriate frequency when compared with the ICMR guidelines. About 72.7 % of patients have met all three criteria appropriately.

Table 8: Type of therapy affecting the appropriateness

Variable	Categories	Appropriateness		Fisher's exact Test
		Appropriate	Inappropriate	P Value
Type of therapy	Definitive	51	6	<0.001*
	Empirical	29	24	

*P<0.05 is considered significant

The Fisher's exact Test is performed to find whether the type of therapy affects the overall appropriateness of restricted antibiotics prescribed. The result shows that there is a statistically significant difference which concludes that the type of therapy

affects the overall appropriateness of prescribed Restricted Antibiotics.

DISCUSSION

In this study, the appropriateness of Restricted Antibiotic use for inpatients is assessed on the basis of the International

Council of Medical Research (ICMR) guidelines. The appropriateness of Restricted Antibiotics was verified, according to three main criteria: choice of antibiotic, dose, and frequency. The prescription pattern of Restricted Antibiotics is evaluated to identify problem areas in which further information and education may be needed by healthcare providers.

In a similar study conducted by Shiv Kumar et al., with a total of 350 patients, 54% were male and 46% were female. ⁽⁹⁾ The patients included in our study also showed an increase in the ratio of male patients when compared with female patients.

In this study most of the patients were between the age group of 61-70 years, followed by 71 -80 years. A similar study was conducted to evaluate the utilization in a tertiary care hospital by Dhakchinamoorthi Krishna Kumar et al., However, both studies conclude that patients above the age of 50 are mostly prescribed with these Restricted Antibiotics. ⁽¹⁰⁾

In this study the most commonly detected gram-negative organism is Escherichia species which accounts for 13.5% followed by Klebsiella species which is about 12.9%, and most commonly detected gram-positive organism is Enterococcus species 3.9% and Streptococcus species 2.6%. While comparing our study results with other studies there exist a difference in commonly isolated organisms. In other studies staphylococcus is the most detected gram-positive organism and pseudomonas and Acinetobacter species were most commonly detected gram-negative organisms. From this, we can say that Escherichia and Klebsiella species were mostly prescribed Restricted Antibiotics due to resistance developed by these organisms to other Antibiotics which gives a hint that there is an increase in resistance pattern of these organisms.

On evaluating the prescription pattern of Restricted Antibiotics in this study, found that Meropenem was the highly prescribed Restricted antibiotic in this hospital (59.6

%). Ceftazidime/Avibactam, Teicoplanin, Colistimethate sodium are least used which found similar with the results of other studies. A study conducted by Dhakchinamoorthi Krishna Kumar et al., in Chennai reveals that Meropenem (29.8%) was most commonly prescribed 29.8% followed by Imipenem (28.8%) and the least prescribed was Linezolid and Vancomycin. ⁽¹⁰⁾

In the case of carbapenems, the adaptation of dosage regimens to the creatinine clearance is very important, because their elimination is mainly renal and can be severely affected by a decreased renal function.

Although the formularies for Restricted Antibiotics were designed and introduced in order to control and optimize their use, the lack of infectious diseases specialists and local antimicrobial guidelines maintained the number of inappropriate prescriptions at a high level. ⁽¹¹⁾ Studies showed that the interventions compulsory order forms, expert approval (clinical pharmacist and infectious disease specialist), guidelines implementation, rapid laboratory testing, removal or restriction of drugs, reviewing and prescription changing by the clinical pharmacist, as well as therapeutic drug monitoring. ⁽¹²⁾

Another measure that may be taken into consideration to improve the prescribing of antibiotics is computerized physician order entry which allows the detection of mistakes in prescribing in real time. ⁽¹³⁾ In Romania, hospitals have a program which allows online prescribing, but the existing information is insufficient for the pharmacist to evaluate the treatment. A combination of both restrictive and educational measures appears to be necessary to improve overall antibiotic usage in hospitals.

This study concludes that Restricted Antibiotics are highly prescribed for sepsis in this hospital (19.1%), followed by recurrent UTI, urosepsis and lung diseases. We also found that more than half of the Restricted Antibiotics are prescribed as

definitive therapy based on the culture reports and susceptibility tests.⁽¹⁴⁾ About 51.8 % patients have received definitive therapy while 48.2% of patients were prescribed empirically. Similar studies were conducted by Jaime Elizabeth et al., and Dr. Lakshmi Gayathri. M et al., concludes that most of the Restricted Antibiotics are prescribed empirically.⁽¹⁵⁾

In our study, appropriate choice of Restricted Antibiotic accounts for 77.3%, appropriate dose of Restricted Antibiotic accounts for 88.2% and appropriate frequency of Restricted Antibiotic accounts for 83.6% and overall, 72.7% of the Restricted Antibiotics were prescribed appropriately. Overall appropriateness of Restricted Antibiotics is 72.7%. A study conducted in Bhutan shows that overall 55.6% of the Restricted Antibiotics are prescribed inappropriately and 53% of the prescriptions had inappropriate choice of Restricted Antibiotics.⁽¹⁶⁾

While comparing our study results with other studies we concluded that inappropriateness of Restricted Antibiotics is higher in hospital with poor implementation of AMS programs and some studies included inappropriate duration of Restricted Antibiotics as a criterion which is the major cause of inappropriateness in that study.

Antibiotic resistance has evolved as a major public health issue and a concern. The reduction in the manufacturing of novel Antibiotics, along with the increasing prevalence of multi-drug resistant (MDR) bacteria, results in significant limitations in treatment options for various bacterial diseases. To reduce overall resistance and the emergence of bacteria that are resistant to all Antibiotics, certain medications are administered sparingly, after all other choices have been explored. Methods for reducing antibiotic resistance are becoming more crucial as antibiotic resistance rates rise in along with poor rates of new drug development. The purpose of such limits is to keep medication resistance to a minimum

and to avoid the development of antibiotic-resistant microorganisms.⁽¹⁷⁾

CONCLUSION

The overuse of Antibiotics globally has accelerated the global public health problem of antimicrobial resistance. The cause of serious infections, complications, extended hospital stays, and higher mortality has been increasing antibiotic resistance. Antibiotic overuse is linked to a higher risk of adverse effects, more frequent re-visits, and increased medicalization of self-limiting conditions.

Evaluating the appropriateness and prescription pattern of Restricted Antibiotics have been an important factor to minimise the antimicrobial resistance and to avoid the inappropriate dosing, frequency, and choice of the Antibiotics. However, now that many bacteria have become resistant to multiple antimicrobial agents which lead to significant cause of morbidity and mortality worldwide.

Considering the importance of usage of Restricted Antibiotics, our current study aimed to evaluate the appropriateness in compliance with ICMR guidelines and utilization of Restricted Antibiotics across various departments and wards in a quaternary care hospital.

We have analysed the appropriateness, prescription pattern of the Restricted Antibiotics and analyzed the drug utilization of these Antibiotics. Even though we conclude that most of the Antibiotics are prescribed appropriately, few patients were administered with inappropriate choice of Restricted Antibiotics. The problem behind this inappropriate selection of Restricted Antibiotics is that the hospital has not prepared a standard guideline for the usage of Restricted Antibiotics.

As a part of this study, we approached our hospital's Medical Superintendent and got approval for preparing an Antibiotics dilution protocol. We have covered 29 drugs in our dilution protocol to improve the appropriate dosing of Antibiotics.

Training and awareness programs regarding AMS and antimicrobial resistance at the institutional level may be beneficial in improving this situation. The findings also emphasized the significance of evaluating prescribing practices on a regular basis. The daily antimicrobial audits by clinical pharmacists can be a more active intervention.

Declaration by Authors

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Conflict of Interest: The authors declare no conflict of interest.

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