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Original Article

Cardiovascular Medication Saving Activity during Dispensing Process at Specialist Clinic Pharmacy in Malaysia

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Abstract

Background: Medication saving activity via reduction of medication supply due to medication refusal by patients during dispensing process is a vital activity that can be led by the pharmacists. However, there is a lack of evidence on how to conduct this activity especially at specialist or outpatient pharmacy for those patients diagnosed with cardiovascular disease (CVD). Thus, this study aimed to determine prevalence, factors and cost associated with patients' refusal to the CVD medication supply during dispensing process by pharmacist at specialist clinic pharmacy. Methods: Patients prescribed with CVD medications were invited to participate in this cross-sectional survey after medication dispensing process was completed. This process involved assessing participants' refusal to the dispensed CVD medication and issues related to their treatment. Data regarding cost was obtained from Pharmacy Information System (PhIS) at the current facility. Results: A total of 270 patients participated in this survey. Prevalence of participants refusing medication prescribed was 33.7%. Participants receiving care from primary and secondary healthcare simultaneously, experiencing side effects and self-modified treatment were 4.88 (P = 0.027), 5.01 (P < 0.05) and 2.98 (P = 0.018) times more likely to refuse medications dispensed. Those who participated in 'Medication' Therapy Adherence and Counselling' (MTAC) program however were 0.43 times less likely to refuse medication during dispensing process, (P = 0.012). A saving of 4.8% was achieved from this activity. Conclusion: Cost-saved achieved during this study was minimal and factors associated with medication refusal was rather concerning.

Keywords: Adherence; Healthcare System; Medication Saving; Specialist Pharmacy

Introduction

Dispensing is the process of preparing, packing, and giving prescribed medication to patients. In order to ensure safe and effective pharmacological intervention during the dispensing process, pharmacists will provide necessary information regarding the medications prescribed, such as indications, dosing, and possible side effects of those medications, to the patients (Ferreira *et al.*, 2016). Other activities include assessment of both medications' side effects and adherence (Payne *et al.*, 2019), and medication-saving activities such as discussion regarding the quantities of medications needed by the patients (Bekker *et al.*, 2018). Patients are an ideal target for medication-saving activity since interventions are highest during interactions between pharmacists and patients compared to interactions between pharmacists and doctors, which are reported to be around 86.65% and 11.80%, respectively (Payne *et al.*, 2019). The practice of discussing the medication at home and, in turn, affect the patient's health, the economy, and the environment (Azad *et al.*, 2016), especially for those

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experiencing adverse effects or receiving the same medications from multiple pharmacies. The United States Food and Drug Administration (US FDA) has also advised that patients are allowed to partially fill their prescriptions so that waste will not occur due to overstocking of medication (Makki *et al.*, 2019).

A reduction in the quantity of medications supplied to patients during the dispensing process is a key element of medication-saving activity (Oh et al., 2022; Lim et al., 2021; Van Herpen-Meeuwissen et al., 2019). The advantage of reducing the amount of medication supplies has been reported in inpatient and outpatient settings internationally and locally via programs such as the use of 'patient's own medicines' (POMs). to educate patients about good pharmacology, to follow up in a structured manner, to identify clinical recurrence in patients with heart failure, and to create medicines in advance of acute exacerbations (Amalia, Said & Nambiar, 2024). However, those studies focused mainly on the costsaving aspect of POMs, while factors associated with the excessiveness of POMs were rarely reported (Oh et al., 2022; Lim et al., 2021; Van Herpen-Meeuwissen et al., 2019; Nugraha et al., 2023). On the other hand, reductions in medication supply in outpatient or specialist pharmacy settings are rarely practiced by pharmacists (Bekker et al., 2018). Hence, there is a lack of evidence regarding the factors and benefits supporting medication-saving activities in outpatient or specialist pharmacy settings obtained via reduction of medication supply during the dispensing process. The types of medications suitable for medication-saving activities might also vary depending on the type of facility. The current facility is a secondary healthcare provider and cater treatment for various disorders for patients under specialists' care, such as cardiologists and nephrologists, and the majority of the medications served revolve around cardiovascular disease (CVD) medicines.

In 2020, CVD medicines constituted 19.65% and 20.21%, respectively, in terms of the number and cost of medicines issued to the specialist dispensary from the current facility's pharmacy's medical store. Nationally, 5 out of 10 most commonly used therapeutic groups during 2016 were from the CVD group, namely calcium channel blockers (CCB), renin-angiotensin agents (RAS), lipid-modifying agents, and diuretics such as amlodipine, perindopril, simvastatin, atorvastatin, acetyl salicylic acid, and hydrochlorothiazide (Chok & Ahmad Shanizza, 2020). Due to their frequent use, CVD medicines contributed 17.7% of the spending costs between 2010 and 2014, ranking third among 14 other anatomical therapeutic chemicals (ATC) (Hamzah *et al.*, 2020). However, they also ranked first at 32.5% in terms of quantity returned to the outpatient pharmacy in Malaysia in 2021 (Jamalud-din *et al.*, 2022), risking medication wastage since excess medications returned to the pharmacy in Malaysia were inevitably disposed of instead of being reused (Yang *et al.*, 2018). Considering the large impact CVD has on our economy coupled with its high medication wastage potential, medication saving activities between pharmacists and patients during the CVD medicine dispensing process are necessary.

Recently, research conducted in Malaysia's tertiary public hospital found that CVD medicines ranked second in terms of cost savings after the implementation of POM for patients discharged from the wards (Oh *et al.*, 2022). However, for outpatient settings, previously reported studies have only investigated cost savings obtained from reduction of medication supplied during the dispensing process for non-CVD medications such as analgesics, antihypertensive, and benzodiazepines due to medication refusal by patients during dispensing process (Koya et al, 2021; MV Mohamed Koya *et al.*, 2022). Medication refusal refers to the act of patients refusing the dispensed medication by the pharmacists during dispensing process after discussion with the pharmacists (Koya *et al.*, 2021; MV Mohamed Koya *et al.*, 2022). However, to our knowledge, there is no study regarding the reduction of CVD medications between pharmacists and patients during the dispensing process. Determining factors associated with patients' refusal to the dispensed medication that leads to the reduction can be conducted effectively and safely. Thus, current study aimed to determine 1) the prevalence of patients prescribed with CVD medications refusing the dispensed medications and 2) factors and costs -saving associated with a refusal to the dispensed CVD medication during the dispensing process.

Methodology

Research Population

This study was conducted during the dispensing process using the convenience sampling method at the Specialist Pharmacy Department of Jerantut Hospital from October 1st to December 31st, 2020, involving patients prescribed medications for cardiovascular disorders (CVDs). Sample size of 377 participants were required using Raosoft software calculator with margin error of 5% and a confidence interval of 95%.

Data Collection

The dispensing process was conducted according to the current facility standard operating procedure. At the end of the dispensing process, patients were invited to participate in the survey. After signing the consent form, participants' demographic and medication details were entered into the data collection form.

After that, participants were asked if there were any medications they wished to refuse. Participants were also asked questions regarding medication side effects, forgetfulness, belief in medication effectiveness that includes use of traditional medicines, overconfidence that includes belief that their illness is under control, self-modification of the treatment and fear of medication shortage. These are 'household factors' that lead to medication wastage. For 'health system cause' that leads to medication wastage, participants were asked if they are attending multiple medical appointments at other facilities for the same treatment (repeat treatment prescribing). Insufficient professional support for proper medicine uses such as participation in medication therapy and adherence counselling (MTAC) were determined from the PhIS record. In cases where medication refusals were due to side effects, participants were advised to seek their doctors.

Medications refused and returned to the pharmacist by the participants were grouped accordingly for data analysis. CVD medications referred to combinations of any type of antihypertensive, anti-anginal drugs such as glyceryl trinitrate, trimetazidine, and isosorbide dinitrate, as well as antiplatelet and anti-hypercholesterolemia drugs (Koya *et al.*, 2021). The total cost for every prescription and price for every item refused were extracted from the PhIS that stored patients' medication details and price for each medication. Inclusion criteria for this study were: all patients collecting CVD drugs at the specialist's pharmacy of Jerantut Hospital and adults aged more than 18 years old who collected medication by themselves. Those newly started on CVD medicines on the day of the data collection were excluded.

Data analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) version 21.0. Categorical variables were described as frequencies and percentages (%), while continuous variables were reported as mean and standard deviation (SD). Binary logistic regression was used to determine possible independent variables associated with a reduction in the amount of CVD medication supplied. Numerical variables were analysed using the *T*-Test. Independent variables with a P-value of less than 0.05 were considered significant.

Ethical Consideration

This study was approved by Medical Research and Ethics Committee (MREC), Malaysia with registration number: NMRR-20-1068-55189(IIR) on June 29th, 2020.

Results

Overall, 325 individuals were approached to participate in the study. However, 16 refused to participate due to language barrier, 39 were excluded since they were collecting on behalf of the patients. Overall, 270 patients participated in the survey. Mean age of the participants was 56.2 ± 12.2 The majority of the participants were male (69.6%, n = 188) and of Malay race (83.0%, n = 224). The prevalence of patients who refused their medication and having unused medicines at home was 33.7% (n = 91) and 85.1% (n = 232), respectively. Around 14.4% (n = 39) of the participants reported extra follow-ups at

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primary health clinics, and 8.9% (n = 24) received treatment for the same condition from other facilities (or 24/39 = 61.5%). Side effects and self-dose modification were reported by 13% (n = 35) and 10.0% (n = 27) of the participants, respectively. Forgetfulness to take medicines, believe that illness was under control and consuming traditional medicines were common, (49.3%, n = 133) followed by 13% (n = 35) and 10% (n = 27) respectively. About 30.4% (n = 82) were from the MTAC program at the current facility. The data are shown in Table 1.

Parameters	Value	
Age* (years)	56.2 ± 12.2	
Gender		
Male	188 (69.6)	
Female	82 (30.4)	
Race		
Malay	224 (83.0)	
Others	46 (17.0)	
Diabetic		
Yes	97 (35.9)	
No	173 (64.1)	
Education		
Secondary or lower	146 (54.1)	
Diploma or higher	122 (45.2)	
Employment status		
Working	75 (27.8)	
Not working	195 (72.2)	
Refusal status		
Refused	91 (33.7)	
Accepted	179 (66.3)	
Have unused medicines		
Yes	232 (85.9)	
No	38 (14.1)	
Primary health clinic follow up	·	
Yes	39 (14.4)	
No	231 (85.6)	
Received treatment from primary health clinic	·	
Yes	24 (8.9)	
No	246 (91.1)	
Side effects	·	
Yes	35 (13.0)	
No	235 (87.0)	
Self-dose modification		
Yes	27 (10.0)	
No	243 (90.0)	
Forget to take medicines		
Yes	133 (49.3)	
No	137 (50.7)	
Illness under control		
Yes	35 (13.0)	
No	235 87.0)	
Traditional medicines	· · · · · · · · · · · · · · · · · · ·	
Yes	27 (10.0)	
No	243 (90.0)	
MTAC participants		
Yes	82 (30.4)	
No	188 (69.6)	
*Data are presented as n(0/) event where indicated		

Table 1: Par	rticipant	Characteristics
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*Data are presented as n(%) except where indicated

**Data are expressed as mean± standard deviation (SD)

The total number of items dispensed throughout the study period was 1726, accounting for a total of Ringgit Malaysia (RM) 24987.38. Total items refused and returned to the pharmacy were 116, equivalent to 6.7% of total items dispensed. The cost of items refused and returned to the pharmacy was RM 1189.20, or equivalent to 4.8% of the total cost prescribed for overall prescriptions. Anti-cholesterols were the most commonly refused CVD drugs by participants, (26.7%, n = 31), followed by calcium channel blockers (21.6%, n = 25), sublingual GTN (16.4%, n = 19), angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin II receptor blockers (ARBs) (11.2%, n = 13), beta blockers (9.5%, n = 11), acetylsalicylic acid (6%, n = 7), antianginal (5.2%, n = 6), diuretics (2.6%, n = 3), and alpha blockers (0.9%, n = 18), followed by hypotension (13.5%, n = 5). The data are shown in Table 2.

Parameters	Value
Total items dispensed (n)	1726
Total items refused (n, %)	116 (6.7)
Total cost of items dispensed	RM 24987.38
Total cost of items refused (<i>n</i> ,%)	RM 1189.2 (4.8)
Names of items refused (n)	
Felodipine	19
Amlodipine	5
Diltiazem	1
Bisoprolol	6
Metoprolol	3
Atenolol	1
Propranolol	1
Prazosin	1
Perindopril	7
Enalapril	2
Telmisartan	3
Losartan	1
Frusemide	2
Spironolactone	1
Simvastatin	14
Atorvastatin	12
Fenofibrate	1
Gemfibrozil	4
Trimetazidine	4
Isosorbide mononitrate	2
Acetylsalicylic acid	7
Sublingual glyceryl trinitrate (GTN)	19
Groups of items refused (n %)	
Calcium channel blockers	25 (21.6)
Beta blockers	11 (9.5)
Alpha blockers	1 (0.9)
ACE inhibitors/ ARB	13 (11.2)
Diuretics	3 (2.6)
Anticholesterol	31 (26.7)
Antiangina	6 (5.2)
Blood thinning agent	7 (6.0)
GTN	19 (16.4)
Type of items refused (n %)	
Original	23 (19.8)
Generic	93 (80.2)
Type of side effects (n %)	· · · · · · · · · · · · · · · · · · ·

Table 2: Details of Medications Reduced and Side Effects Associated with Treatment

Bleeding stools	1 (2.7)
Bradycardia	1(2.7)
Sleep disturbance	1 (2.7)
Dizziness	18 (48.7)
Hypotension	5 (13.5)
Palpitation	1 (2.7)
Deranged liver function	1 (2.7)
Gastric	2 (5.4)
Hunger pang	2 (5.4)
Drowsiness	1(2.7)
Frequent urine	1 (2.7)
Nausea	1 (2.7)
Numbness	1 (2.7)
Itchiness	1 (2.7)

Four categorical variables were found to be significantly associated with refusal to medication supply during the dispensing process: receiving treatment from primary health clinics, experiencing side effects, self-dose modification, and MTAC program recruits. The odds for patients who received simultaneous treatment from both a hospital and a primary health clinic to refuse medications were 4.88 times higher compared to those receiving treatment from a single facility alone (P = 0.027, 95% Cl = 1.190 – 18.616). Those experiencing side effects were 5.01 times more likely to refuse the medication during the dispensing process compared to those who did not experience medication side effects (P < 0.05, 95% Cl = 2.213 – 11.660). Those who admitted to self-dose modification were 2.98 times more likely to refuse medication compared to those who maintained taking the prescribed dose (P = 0.018, 95% Cl = 1.211 – 7.334). MTAC recruits were 0.43 times less likely than non-MTAC patients to refuse the medication (P = 0.012, 95% Cl = 0.222 – 0.831). The data are shown in Table 3.

Table 3: Binomial Regression	n for Predictors Associated	with Medic	ation Reduction
Variables	Cotogory		Odda Datia (05% CI)

Variables	Category	Exp (B)	Odds Ratio (95% CI)	Ρ
Gender	Female	1.17	0.629-2.176	0.621
Race	Malay	0.065	0.225-1.045	0.065
Education	Secondary school and lower	1.044	0.581-1.878	0.884
Employment	Employed	1.109	0.497-2.476	0.801
Have unused medicines	Yes	1.57	0.664-3.693	0.305
Primary health clinic follow up	Yes	1.16	0.367-3.634	0.805
Receiving treatment from	Yes	4.88	1.190-18.616	0.027
primary health clinic				
Side effects	Yes	5.01	2.213-11.660	<0.05
Self-dose modification	Yes	2.98	1.211-7.334	0.018
Forget to take medicines	Yes	0.61	0.656-2.047	0.612
Illness under control	Yes	1.458	0.798-2.701	0.218
Traditional medicines	Yes	2.15	0.849-5.423	0.106
MTAC Patients	Yes	0.43	0.222-0.831	0.012

*Exp (B) (exponentiated coefficient) = Odd ratio

**CI=Confidence interval

Overall, in terms of cost, a saving of RM 13.22 \pm 11.79 per patient was produced among those who refused medication supplied compared to RM 0.05 \pm 0.67, *P* < 0.05 in those who did not refuse medication supplied. In terms of saving percentages, those who refused their medications supplied contributed toward 22.13 \pm 22.30% versus 0.06 \pm 0.86% in those who did not refuse their medication supply, *P* < 0.05. The data are shown in Table 4.

Variables	Medication Fully	Medication	df	Ρ
	Dispensed	Reduced		
Age* (years)	56.8 ±12.7	54.8 (11.2	268	0.209
Total daily medicines	6.30 ± 2.42	6.73 ± 2.36	266	0.164
Cost of treatment (RM)	94.42±102.78	125.15±227.10	268	0.127
Cost of treatment after refusal status assessment (RM)	94.26±102.72	112.10±228.02	268	0.376
Cost of refused medications (RM)	0.05 ± 0.67	13.22 ± 11.79	268	<0.05
Percentage of cost saving after refusal status	0.06 ±0.86	22.13 ± 22.30	268	<0.05
assessment				

Table 4: Numerical Factors Associated with Reduction in Medication Supplied

*Data are expressed as mean± standard deviation (SD)

Discussion

Prevalence

Previous studies reported that 86% of the pharmacists from 22 developed countries claimed they were allowed to reduce the amount of medication supplied during the dispensing process and considered this an important activity despite a lack of implementation due to time constraints (Bekker *et al.*, 2018). In addition, the current study provides a new finding that the prevalence of patients with CVD refusing some of the medications supplied during the dispensing process was 33.7%. This prevalence is similar to the prevalence of patients being late in collecting their CVD medication refill in the United States and Finland, which were reported to be 33% and 40%, respectively (Nabi *et al.*, 2008; Bailey *et al.*, 1996). This prevalence was also comparable to the refusal to take benzodiazepines, which was reported to be 38.7% among those diagnosed with depression or schizophrenia (MV Mohamed Koya *et al.*, 2022). Even though the prevalence of having excess CVD medicines at home in the current study was 85.9%, similar to 84% among the general population with or without chronic diseases in Malaysia (Wang *et al.*, 2021), it was not associated with refusal to medication supply during the dispensing process.

Receiving Treatment from Multiple Facilities: Medication Oversupply

Patients receiving CVD medicines tend to oscillate between primary and secondary care for various reasons, such as monitoring of blood pressure and glucose control. In the current study, 14.4% of patients receiving CVD medicines reported multiple medical appointments. However, only 9.8% received prescriptions for the same drugs (repeat treatment prescribing) from multiple facilities (interfacilities) from different doctors, which can lead to medication oversupply. This figure was similar to 8.9% of hypertensive patients that floated between clinics and hospitals and reported having excess medications as measured by the medication possession ratio (MPR) (Kim et al., 2017). Medication oversupply also occurred in 13.4% of hospital patients in our neighbouring country. Thailand (Dilokthornsakul et al., 2014), and 8.6% of diabetic patients in Saudi Arabia (Balkhi et al., 2019) who received treatment within the same facilities. Multiple medical appointments can lead to inappropriate prescribing and repeated dispensing involving both prescribers and pharmacists, respectively, which is considered a health system's or healthcare provider's failure (Makki et al., 2019), consequently resulting in increased healthcare costs such as USD 189,024 in financial loss per year due to medication wastage and hospitalization risk (Dilokthornsakul et al., 2014; Kim et al., 2017). However, discussion between pharmacists and patients might reduce the occurrence of these incidents since those with multiple medical appointments were five times more likely to agree on reducing the quantities of medication dispensed to them.

Side Effects

The incidence of side effects from CVD medicines in the current study was only 13.1%, which was similar to 18.1% reported in a study in Nigeria (Olowofela & Isah, 2017), but it led to more than half of our patients with side effects refusing their medications during the dispensing process. Side effects of antihypertensive medications have also reduced adherence in 42.3% (Ramli, Ahmad & Paraidathathu, 2012) of hypertensive patients. A current study found that those experiencing medication side effects

were five times more likely to refuse medication supply during the dispensing process. Similarly, hypertensive patients experiencing side effects were 4.84 times more likely to be nonadherent to their medication (Kretchy *et al.*, 2015). Similar to a previous report, the current study found that the commonest side effects of the therapy were dizziness and hypotension (Rossello *et al.*, 2015). Current findings indicate the importance of medication side effects' assessment during the dispensing process. If it remains unaddressed, it will lead to medication wastage (Wang *et al.*, 2021; Makki *et al.*, 2019), since 2.9% of Malaysians admitted to keeping unused medicines due to the occurrence of side effects.

Self-Dose Modification

Self-dose modification is a common occurrence in those with health disorders to varying degrees. In the current study, 9.6% of our participants with CVD altered their dose, which is much lower compared to the 27% found in the previous study. One of the explanations for this finding is that the current study focused specifically on CVD medicines, while previous studies focused on those prescribed with either CVD medicines or analgesics. A previous study was also conducted in a primary health care setting where patients were attended by general practitioners (GPs) (Säfholm *et al.*, 2019) compared to this study, where patients received treatment from specialists. Another study also reported that 3.8% of those with atrial fibrillation (AF) admitted to taking smaller doses of medicines in order to reduce costs (Bamgbade *et al.*, 2023). However, dose modification in the current study could not result from cost since medications were subsidized by the government or obtained free of charge. Thus, even though dose modification can reduce the number of medications supplied, the main concern from this finding is that inappropriate and unmonitored self-dose adjustment can result in the occurrence of various health complications such as end-stage renal failure, coronary artery disease, cerebrovascular disease, and mortality.

Medication Therapy Adherence and Counselling (MTAC) Participation

Medication counselling was reported to affect medicine-taking behaviour differently. For instance, a previous study reported that patients who received standard medication review and counselling by community pharmacists after they were discharged from hospitals had significantly fewer numbers and quantities of medication dispensed compared to patients who did not receive medication counselling (Hugtenburg et al., 2009). In contrast, the current study showed that participation in MTAC, namely anticoagulation, nephrology, or diabetes mellitus discipline, was not associated with a reduction in the number of medications supplied. This finding is consistent with another study that reported medication counselling has significantly improved several outcomes in patients, such as medication adherence and guality of life (Mishra et al., 2017). Main activities in the MTAC program usually involve activities such as regular counselling sessions with patients and education regarding their illnesses on monthly basis. This might result in increased awareness and knowledge related to medication use and the importance of good medication adherence. In current setting, regular medication reviews by pharmacists were done by MTAC pharmacists and attending doctors were notified regarding issues faced by those in our MTAC programs. Due to this, common issues such as occurrence of side effects, unnecessary prescribing and repeat treatment prescribing are less likely to occur thus resulting in less refusal to the medication prescribed and supplied.

Cost Saving

Overall, reduction in the quantities of CVD medications during the dispensing process in the current study only produced a modest 4.8% direct medication cost saving, similar to the 4.3% produced at an inpatient nephrology ward in Iran during clinical pharmacist interventions (Gharekhani *et al.*, 2014). However, the percentage of cost savings after reduction in the quantities of the medications supplied was 22%, slightly low compared to the 38.96% produced in the POM study among diabetic patients conducted in an outpatient setting in Malaysia. One of the explanations for this finding was that 80.2% of the medicines refused in the current study were generic medicines, which were always considered cheaper. In contrast, 70% of the top 10 drugs by price used for POMs in the previous study were of original brand (Lim *et al.*, 2021).

Limitations

This study is subject to several considerations that highlight its specific context and scope. Participants' ability to accurately recall whether they have received similar medications from other facilities adds a nuanced layer to the data collection process. The study emphasizes the medication counselling history recorded at the current facility, providing a targeted and specific insight into the services rendered. By including patients who were able to collect their medication personally, the study ensures a focus on individuals actively engaged in their treatment process.

Conclusion

Medication-saving activity performed during the dispensing process between pharmacists and patients via assessment of refusal to medication prescribed during dispensing process has produced minimal cost savings. However, this activity has revealed several issues involving both the healthcare system and patient factors. While some aspects of the patient's treatment might support this activity, the refusal of medication due to factors such as self-dose modification and medication side effects needs further observation and investigation by pharmacists so that these issues will not compromise the patient's treatment and ultimately their health.

Conflict of Interest

The authors declare that they have no competing interests.

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