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## Original Research

# Clinical pharmacist implementation of a medication assessment tool for long-term management of atrial fibrillation in older persons

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### Abstract

**Background:** Optimisation of drug therapy is important in the older population and may be facilitated by medication assessment tools (MATs).

**Objective:** The purpose of the study was to evaluate whether appropriateness of drug therapy and clinical pharmacist intervention documentation improved following implementation of a previously developed MAT for the long-term management of atrial fibrillation (MAT-AF).

**Methods:** Adherence to MAT-AF review criteria and clinical pharmacist intervention documentation was assessed by the researcher pre-MAT implementation in 150 patients aged  $\geq 60$  years admitted to a rehabilitation hospital with a diagnosis of atrial fibrillation. MAT-AF was introduced as a clinical tool in the hospital for identification of pharmaceutical care issues in atrial fibrillation patients. Adherence to MAT-AF and pharmacist intervention documentation were assessed by the researcher post-MAT implementation for a further 150 patients with the same inclusion criteria. Logistic regression analysis and measurement of odds ratio was used to identify differences in adherence to MAT-AF pre- and post-MAT implementation. The differences between two population proportions z-test was used to compare pharmacist intervention documentation pre- and post-MAT implementation.

**Results:** Adherence to MAT-AF criteria increased from 70.9% pre-implementation to 89.6% post-implementation. MAT-AF implementation resulted in a significant improvement in prescription of anticoagulant therapy (OR 4.07,  $p < 0.001$ ) and monitoring of laboratory parameters for digoxin (OR 10.40,  $p < 0.001$ ). Clinical pharmacist intervention documentation improved significantly post-implementation of MAT-AF (z-score 20.249,  $p < 0.001$ ).

**Conclusions:** Implementation of MAT-AF within an interdisciplinary health care team significantly improved the appropriateness of drug therapy and pharmacist intervention documentation in older patients with atrial fibrillation.

### Keywords

Atrial Fibrillation; Disease Management; Drug Utilization Review; Medication Therapy Management; Inappropriate Prescribing; Pharmaceutical Services; Pharmacists; Aged; Clinical Audit; Malta

## INTRODUCTION

Extensive literature has confirmed the value of clinical pharmacist intervention in improving the appropriateness of drug treatment in older patients.<sup>1-5</sup> As the proportion of older persons continues to increase, the role of the clinical pharmacist as a member of a multi-professional team is becoming more crucial for optimisation of drug therapy in this patient population.<sup>4</sup> Documentation of pharmacist interventions provides a record which is important for continuity of care, accountability of pharmacist services and quality assurance.<sup>6,7</sup>

Several medication review tools have been designed to enhance appropriate prescribing in older patients.<sup>8</sup> The medication assessment tool MAT-AF is an innovative and

validated tool, previously developed by this research group, for the long-term management of atrial fibrillation (AF) in older persons.<sup>9</sup> MAT-AF incorporates criteria for assessing appropriateness of drug therapy whilst applying the clinical considerations required in managing drug therapy for AF (refer to supplementary material). Review criteria in MAT-AF are composed of a qualifying statement and a standard, sectioned into antithrombotic, rate control and rhythm control therapy. Content validity was tested by an expert group using a Delphi technique and consensus obtained for all final criteria. Inter- and intra-observer reliability and feasibility was demonstrated. An application guide for consistent interpretation and application of the MAT was compiled.<sup>9</sup>

MAT-AF was developed on the basis that AF is associated with substantial morbidity and mortality and requires consideration of management recommendations focusing on thromboembolic risk reduction, rate control and rhythm control.<sup>10-13</sup> MAT-AF considers guidelines on the use of antithrombotic agents endorsed for the prevention of thromboembolism namely warfarin and direct oral anticoagulants (DOACs).<sup>10-13</sup> Recent guidelines recommend that a DOAC be used preferentially to warfarin on the basis of strong evidence of a lower risk of intracranial haemorrhage, although cost effectiveness remains a debatable issue considering the high cost of DOACs.<sup>12-14</sup> Rate control is a key component in the management of AF

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patients. Beta-blockers, nondihydropyridine calcium channel blockers or digoxin are recommended as suitable first-line options.<sup>13</sup> When monotherapy is insufficient to achieve rate control, digoxin is recommended in combination with a beta-blocker or with a nondihydropyridine calcium channel blocker.<sup>10-13</sup> Amiodarone should be considered when other agents are unsuccessful or contraindicated.<sup>10,12,13</sup> Monitoring of serum digoxin levels, renal function, thyroid function and electrolytes is recommended for safe use of digoxin.<sup>15</sup> Liver, thyroid, ophthalmic and pulmonary monitoring is recommended with amiodarone treatment.<sup>16</sup> Restoring and maintaining sinus rhythm is another aspect of AF management.<sup>10-13</sup> Clinical evidence has demonstrated that both rhythm and rate control strategies have resulted in similar outcomes.<sup>17,18</sup> Long-term antiarrhythmic agents should be commenced judiciously after consideration of the extent of symptoms and potential for adverse drug reactions. A rate control strategy is often preferred in older persons.<sup>10,13</sup>

The purpose of the study was to evaluate whether implementation of MAT-AF in clinical practice contributes to improving the appropriateness of drug therapy and clinical pharmacist intervention documentation. Adherence to MAT-AF review criteria was used to measure appropriateness of drug therapy and to determine whether a pharmacist intervention was generated.

## METHODS

The study setting was Karin Grech Hospital in Malta, a 280-bed hospital specialising in rehabilitation of older patients. Clinical pharmacists complete a paper-based pharmacy patient profile for each patient at the hospital. Pharmaceutical care issues, interventions and outcomes are documented by the pharmacist on the profile in daily clinical practice.

Adherence to MAT-AF criteria was assessed by the researcher prior to MAT implementation by application of the tool to 150 patients admitted for rehabilitation.<sup>9</sup> Inclusion criteria were a diagnosis of AF and age  $\geq 60$  years while transfer of the patient to acute care and death were considered as exclusion criteria. The MAT was applied by the researcher to patients consecutively at discharge from March to September 2016. The pharmacy patient profile of each patient was reviewed to determine whether care issues generated by MAT application resulted in a documented intervention by the clinical pharmacist. The pharmaceutical care issues were classified in terms of a set of care issue types defined in the hospital standard operating procedure for patient profiling.<sup>19</sup>

The use of MAT-AF as a clinical tool was introduced by the researcher to the nine clinical pharmacists at the hospital. Following a training period of two weeks, the pharmacists used the tool in practice by applying the MAT criteria to patients admitted with AF for identification of pharmaceutical care issues which were to be followed by intervention and documentation.

Adherence to MAT-AF and clinical pharmacist intervention documentation were assessed post-MAT implementation for a further 150 patients admitted to the hospital with the same inclusion criteria. MAT-AF was applied by the researcher to audit patients consecutively at discharge from November 2016 to May 2017.

The study protocol was approved by the Karin Grech Hospital Research Committee and the University of Malta Research Ethics Committee.

## Statistical analysis

Data analysis was conducted using IBM SPSS® Statistics version 24. Descriptive statistics were generated for the study population in the pre- and post-implementation

(n=150)		Pre-implementation		Post-implementation	
Gender (n)	male	54	(36.0%)	44	(29.3%)
	female	96	(64.0%)	106	(70.7%)
Age (years)	mean (SD)	81.7	(7.6)	82.7	(6.4)
	min, max	60	97	63	97
	$\geq 75$ years (n)	127	(84.7%)	134	(89.3%)
Atrial fibrillation (n)	paroxysmal	54	(36.0%)	67	(44.7%)
	persistent	12	(8.0%)	11	(7.3%)
	permanent	84	(56.0%)	72	(48.0%)
Comorbidities (n)	heart failure	93	(62.0%)	92	(61.3%)
	hypertension	108	(72.0%)	112	(74.7%)
	diabetes	48	(32.0%)	59	(39.3%)
	stroke/TIA/thromboembolism	51	(34.0%)	50	(33.3%)
	vascular disease*	52	(34.7%)	53	(35.3%)
	anaemia	68	(45.3%)	82	(54.7%)
	chronic kidney disease**	103	(68.7%)	116	(77.3%)
CHA <sub>2</sub> DS <sub>2</sub> VASc score $\geq 1$ (n)***		149	(99.3%)	150	(100.0%)
HAS-BLED score (0-9)	mean (SD)	2.0	(0.8)	2.1	(0.8)
	min, max	1	4	0	4

\*acute coronary syndrome or peripheral arterial disease (including revascularisation), \*\*creatinine clearance  $< 60$  ml/min, \*\*\*excluding gender, TIA – transient ischaemic attack  
Data for pre-implementation phase reported by Gauci *et al.*<sup>9</sup>

Table 2. Adherence to applicable criteria of MAT-AF pre- and post-implementation

Criterion focus		Pre-implementation		Post-implementation		Odds Ratio [95% CI]	p-value
		Applicable cases	Adherence	Applicable cases	Adherence		
		n (%)	n (%)	n (%)	n (%)		
Antithrombotic therapy							
1	No antithrombotic therapy if CHA <sub>2</sub> DS <sub>2</sub> VASc score 0*	1 (0.7)	1 (100)	0 (0)	0 (0)	-	-
2	Prescription of oral anticoagulant if CHA <sub>2</sub> DS <sub>2</sub> VASc score ≥1*	149 (99.3)	105 (70.5)	150 (100)	136 (90.7)	4.07 [2.12 – 7.82]	<0.001
3	Prescription of direct oral anticoagulant at recommended dose if creatinine clearance ≥50mL/min	5 (3.3)	4 (80.0)	7 (4.7)	6 (85.7)	1.50 [0.07 – 31.58]	0.794
4	Prescription of direct oral anticoagulant at lower dose or warfarin if creatinine clearance between 15-49mL/min	47 (31.3)	47 (100)	58 (38.7)	55 (94.8)	-	-
5	Prescription of warfarin if creatinine clearance <15mL/min	1 (0.7)	1 (100)	1 (0.7)	1 (100)	-	-
Rate control therapy							
6	Prescription of beta-blocker, non-dihydropyridine calcium channel blocker and/or digoxin	97 (64.7)	82 (84.5)	95 (63.3)	92 (96.8)	3.92 [1.06 – 14.54]	0.041
7	Cardiology referral/follow up if non-dihydropyridine calcium channel blocker and contraindicated/not tolerated	1 (0.7)	0 (0)	0 (0)	0 (0)	-	-
8	Prescription of beta-blocker and/or digoxin if heart failure with left ventricular ejection fraction <40%	12 (8.0)	12 (100)	7 (4.7)	7 (100)	-	-
9	Monitoring of renal and thyroid function, serum electrolytes with digoxin and within range	53 (35.3)	27 (50.9)	59 (39.3)	54 (91.5)	10.40 [3.59 – 30.10]	<0.001
10	Monitoring of serum digoxin level if at risk of high serum concentration and within range	23 (15.3)	17 (73.9)	23 (15.3)	20 (87.0)	2.35 [0.51 – 10.86]	0.273
11	Prescription of amiodarone for additional rate control or contraindication/intolerance to other agents	1 (0.7)	0 (0)	0 (0)	0 (0)	-	-
12a	Monitoring of liver and thyroid function with amiodarone and within range	21 (14.0)	17 (81.0)	16 (10.7)	15 (93.8)	3.53 [0.35 – 35.16]	0.282
12b	Monitoring of ophthalmic and pulmonary function with amiodarone	21 (14.0)	0 (0)	16 (10.7)	4 (25.1)	-	-
Rhythm control therapy							
13	Continuation at prescribed dose if maintained in sinus rhythm with antiarrhythmic agent and well tolerated	10 (6.7)	7 (70.0)	10 (6.7)	9 (90.0)	3.86 [0.33 – 45.57]	0.284
14	Cardiology referral/follow-up if maintained in sinus rhythm with antiarrhythmic agent and contraindicated/not well tolerated	3 (2.0)	0 (0.0)	2 (1.3)	0 (0)	-	-
15	Cardiology referral/follow-up if prescribed antiarrhythmic agent and not maintained in sinus rhythm	13 (8.7)	5 (38.5)	10 (6.7)	8 (80.0)	8.00 [1.13 – 56.79]	0.038
<b>Total criteria</b>		<b>458 (19.1)</b>	<b>325 (70.9)</b>	<b>454 (18.9)</b>	<b>407 (89.6)</b>		

\*CHA<sub>2</sub>DS<sub>2</sub>VASc score excluding gender; Adherence to MAT criteria was calculated by the sum of the 'adherence' and 'justified non-adherence' responses expressed as a percentage of the applicable criteria; Odds ratio not reported for percentage adherence 0 and 100.  
Data for pre-implementation phase reported by Gauci *et al.*<sup>9</sup>

phases. Characteristics of the patient populations were compared by the independent samples t-test for quantitative variables and the differences between two population proportions z-test for qualitative variables. Adherence to MAT criteria was computed by the sum of the 'adherence' and 'justified non-adherence' responses expressed as a percentage of the applicable criteria. Criterion responses which were not applicable or which had insufficient data for the qualifying statement were excluded.<sup>9</sup> Logistic regression analysis and measurement of odds ratio was used to identify differences in adherence to MAT-AF pre- and post-MAT implementation. The

differences between two population proportions z-test was used to compare pharmacist intervention documentation pre- and post-MAT implementation. The Pearson chi-square test was used to assess the relationship between prescription of anticoagulation with patient age and CHA<sub>2</sub>DS<sub>2</sub>VASc score.<sup>20</sup>

## RESULTS

Patient population characteristics in the pre- and post-implementation phases of MAT-AF application are

Table 3. Documented pharmacist interventions for care issues generated by MAT-AF application pre- and post-implementation

Criterion focus		Care issue type	Pre-implementation		Post-implementation		p-value
			Care issue generated	Intervention documented	Care issue generated	Intervention documented	
			n	n (%)	n	n (%)	
Antithrombotic therapy							
1	No antithrombotic therapy if CHA <sub>2</sub> DS <sub>2</sub> VASc score 0*	Unnecessary drug	0	0 (0)	0	0 (0)	-
2	Prescription of oral anticoagulant if CHA <sub>2</sub> DS <sub>2</sub> VASc score $\geq 1$ *	Need for additional drug	60	12 (20.0)	51	48 (94.1)	<0.001
3	Prescription of direct oral anticoagulant at recommended dose if creatinine clearance $\geq 50$ ml/min	Monitoring need/Dose too low	5	1 (20.0)	2	1 (50.0)	0.430
4	Prescription of direct oral anticoagulant at lower dose or warfarin if creatinine clearance between 15-49ml/min	Monitoring need/Dose too high	1	1 (100)	7	4 (57.1)	0.407
5	Prescription of warfarin if creatinine clearance <15ml/min	Monitoring need/Improper drug selection	0	0 (0)	0	0 (0)	-
Rate control therapy							
6a	Monitoring of pulse	Monitoring need	150	0 (0)	150	143 (95.3)	<0.001
6b	Prescription of beta-blocker, non-dihydropyridine calcium channel blocker and/or digoxin	Improper drug selection	13	1 (7.7)	7	3 (42.9)	0.060
7	Cardiology referral/follow up if non-dihydropyridine calcium channel blocker and contraindicated/not tolerated	Risk for adverse drug reaction	1	0 (0)	0	0 (0)	-
8	Prescription of beta-blocker and/or digoxin if heart failure with left ventricular ejection fraction <40%	Improper drug selection	5	0 (0)	3	1 (33.3)	0.503
9	Monitoring of renal function, thyroid function, serum electrolytes with digoxin and within range	Monitoring need	53	0 (0)	59	50 (84.7)	<0.001
10	Monitoring of serum digoxin level if at risk of high serum concentration and within range	Monitoring need	23	11 (47.8)	23	19 (82.6)	0.013
11	Prescription of amiodarone for additional rate control or contraindication/intolerance to other agents	Improper drug selection	1	0 (0)	0	0 (0)	-
12a	Monitoring of liver and thyroid function with amiodarone and within range	Monitoring need	21	10 (47.6)	16	13 (81.3)	0.037
12b	Monitoring of liver and thyroid function with amiodarone after discharge	Seamless care need	21	1 (4.8)	16	5 (31.3)	0.030
12c	Monitoring of ophthalmic and pulmonary function with amiodarone	Monitoring need/Counselling need	21	0 (0)	16	8 (50.0)	<0.001
Rhythm control therapy							
13	Continuation at prescribed dose if maintained in sinus rhythm with antiarrhythmic agent and well tolerated	Need for additional drug/Dose too low	0	0 (0)	1	0 (0)	-
14	Cardiology referral/follow-up if maintained in sinus rhythm with antiarrhythmic agent and contraindicated/not well tolerated	Risk for adverse drug reaction	0	0 (0)	2	0 (0)	-
15	Cardiology referral/follow-up if prescribed antiarrhythmic agent and not maintained in sinus rhythm	Improper drug selection	11	0 (0)	8	6 (75.0)	<0.001
<b>Total care issues</b>			<b>386</b>	<b>37 (9.6)</b>	<b>361</b>	<b>301 (83.4)</b>	<b>&lt;0.001</b>

\*CHA<sub>2</sub>DS<sub>2</sub>VASc score excluding gender

presented in Table 1. No significant variation between the two study populations was evident ( $p > 0.05$ ).

Adherence to the 458 applicable criteria was 70.9% before MAT-AF implementation.<sup>9</sup> In the post-implementation phase, adherence to the 454 applicable criteria was 89.6%.

Application of MAT-AF post-implementation resulted in a significant increase in adherence from 70.9% to 89.6%. Adherence to MAT-AF criteria for antithrombotic, rate control and rhythm control therapy before and after implementation is presented in Table 2.

MAT-AF implementation resulted in a significant improvement in prescription of anticoagulants (OR 4.07,  $p < 0.001$ ). The CHA<sub>2</sub>DS<sub>2</sub>VASc score did not have a significant effect on the prescription of anticoagulation both before and after MAT-AF implementation. The prescription of anticoagulation according to age range indicated a significant decrease in anticoagulation with increasing age (chi-square(3)=11.57,  $p = 0.009$ ) pre-MAT implementation. Patient age did not have a significant effect on the prescription of anticoagulation (chi-square(3)=4.119,  $p = 0.249$ ) post-MAT implementation. Recurrent falls or a high risk for falls was the most frequent reason for omission of anticoagulant therapy in the study population.

Adherence to appropriate rate control therapy was 84.5% before implementation and 96.8% after MAT-implementation (OR 3.92,  $p = 0.041$ ) (Table 2). Monitoring of renal function, thyroid function and serum electrolytes in patients receiving digoxin was performed and within limits in 50.9% of patients pre-implementation and in 91.5% post-implementation (OR 10.40,  $p < 0.001$ ). The most common deficiency for this criterion was in the request for monitoring of serum magnesium. Monitoring of serum digoxin levels was indicated due to poor renal function, dose of more than 0.0625mg daily or signs and symptoms of toxicity. Monitoring was conducted and was within limits in 73.9% of patients in whom it was indicated pre-implementation and in 87.0% post-implementation (OR 2.35,  $p = 0.273$ ).

Rhythm control with antiarrhythmic agents was achieved in 8.3% of patients. Adherence to MAT-AF for cardiology referral in patients on antiarrhythmic agents but not maintained in sinus rhythm increased from 38.5% pre-implementation to 80.0% post-implementation (OR 8.00,  $p = 0.038$ ) (Table 2). Liver and thyroid function tests in patients receiving amiodarone therapy were performed and within limits in 81.0% of patients pre-implementation and in 93.8% post-implementation (OR 3.53,  $p = 0.282$ ).

Documented pharmacist interventions for care issues generated by MAT-AF application are shown in Table 3. MAT-AF application before implementation identified 386 care issues, 9.6% of which were documented. After MAT-AF implementation, 361 care issues were identified and 83.4% were documented. The increase in documented pharmacist interventions following MAT-AF implementation as a clinical tool was significant (z-score 20.249,  $p < 0.001$ ).

## DISCUSSION

Application of MAT-AF pre-implementation revealed suboptimal adherence to clinical practice guidelines incorporated in the tool. MAT-AF application after implementation denoted a significant increase in adherence from 70.9% to 89.6% principally in prescription of anticoagulation and monitoring of laboratory parameters for digoxin. Documentation of clinical pharmacist intervention improved significantly post-implementation of MAT-AF from 9.6% to 83.4%.

Prior to MAT-AF implementation, adherence to anticoagulation was 70.5% despite a high risk of stroke in the study population. Analysis of the results indicates that there was no correlation between prescription of

anticoagulation and CHA<sub>2</sub>DS<sub>2</sub>VASc score, possibly indicating that stroke risk was not being given due consideration. In contrast, in a study by Lefebvre *et al.* among octogenarians, anticoagulation was positively associated with stroke risk score. The HAS-BLED score was applied for assessment of bleeding risk to establish justifications for non-adherence.<sup>21,22</sup> The study population prior to MAT-AF implementation had a mean HAS-BLED score of 2. The principal contributor to the score was the presence of anaemia, which was most commonly mild and would merit monitoring rather than exclusion of anticoagulation.<sup>23</sup> Age is a strong predictor for ischaemic stroke in AF patients and robust evidence exists to support the use of anticoagulation in older persons.<sup>20,24-26</sup> In a systematic review of studies assessing attitudes of physicians regarding anticoagulation for AF, Pugh *et al.* concluded that physicians were reluctant to recommend warfarin for older persons in AF.<sup>27</sup> Implementation of MAT-AF resulted in oral anticoagulants being prescribed irrespective of age.

Recurrent falls or a high risk of falls were common reasons for omission of anticoagulation in the study population, as has been stated in other studies.<sup>28-30</sup> Although the use of anticoagulation in patients at risk of falls requires caution, AF guidelines stipulate that anticoagulants should only be excluded in patients with severe uncontrolled falls, such as epilepsy or advanced multi-system atrophy with backward falls.<sup>13</sup> Conversely, evidence indicates that stroke risk tends to exceed bleeding risk of anticoagulation, even in older persons, in patients with cognitive impairment, or in patients with frequent falls or frailty.<sup>31,32</sup> Documentation of clinical pharmacist interventions regarding the appropriate prescription of anticoagulation therapy was shown to significantly increase following MAT-AF implementation.

MAT-AF implementation significantly increased monitoring of laboratory parameters contributing to the safe use of digoxin therapy. A significant increase in clinical pharmacist documentation for the recommended monitoring to be performed was observed following MAT implementation.

Rhythm control therapy was only prescribed in a minor proportion of patients, which is coherent with evidence which has demonstrated that rhythm and rate control strategies have resulted in similar outcomes.<sup>17,18</sup> MAT-AF implementation significantly increased monitoring for ophthalmic and pulmonary adverse reactions with amiodarone therapy. Although adherence was suboptimal, even after MAT-AF implementation, there was increased awareness among the clinical pharmacists shown by an increase in documentation of the monitoring requirement. MAT-AF implementation significantly increased cardiology referral recommendable to avoid the use of antiarrhythmic agents when not indicated. A significant increase in the respective documentation of clinical pharmacist intervention was observed following MAT implementation.

The value of MAT-AF implementation was demonstrated in the highly significant improvement in documentation of interventions by clinical pharmacists in the rehabilitation hospital. Documentation is of particular importance in the care of the older patient. Multiple morbidities and medication are likely to result in numerous care issues which require prioritisation and resolution in a timely manner. Documentation is more likely to ascertain that all



issues are ultimately communicated with the healthcare team. MAT-AF provides a structured system with the purpose of guiding pharmacists and facilitating the documentation process.

MAT-AF can be implemented in other care settings for older persons including acute, ambulatory and long-term care after validation for adaptation to the setting and patient population. For a more comprehensive approach in the optimisation of drug therapy, it is recommended that MATs for other disease states prevalent in older patients are developed and implemented.

A limitation of the study is that MAT-AF criteria which incorporate aspects of treatment that are relevant to only a few patients resulted in a low applicability when considering the entire patient cohort.<sup>9</sup> Another limitation is that more emphasis may have been given to applying the MAT during the study period since the pharmacists were aware of the audit being conducted by the researcher (Hawthorne effect).

## CONCLUSIONS

Implementation of MAT-AF had a significant impact on underprescribing of anticoagulation recommended for the

prevention of thromboembolism in patients with AF and on parameter monitoring to ensure safe use of digoxin. Documentation of the care provided by clinical pharmacists at the rehabilitation hospital improved as a result of MAT-AF implementation.

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## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest to disclose.

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