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 ≥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.1,2 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.3 Documentation of pharmacist interventions provides a record which is important for continuity of care, accountability of pharmacist services and quality assurance.4,5

Several medication review tools have been designed to enhance appropriate prescribing in older patients.6 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.9 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.5

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.10-13 MAT-AF considers guidelines on the use of antithrombotic agents endorsed for the prevention of thromboembolism namely warfarin and direct oral anticoagulants (DOACs).10-13 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.12-14 Rate control is a key component in the management of AF.
patients. Beta-blockers, nondihydropyridine calcium channel blockers or digoxin are recommended as suitable first-line options.\textsuperscript{13} When monotherapy is insufficient to achieve rate control, digoxin is recommended in combination with a beta-blocker or with a nondihydropyridine calcium channel blocker.\textsuperscript{10-13} Amiodarone should be considered when other agents are unsuccessful or contraindicated.\textsuperscript{10,12,13} Monitoring of serum digoxin levels, renal function, thyroid function and electrolytes is recommended for safe use of digoxin.\textsuperscript{15} Liver, thyroid, ophthalmic and pulmonary monitoring is recommended with amiodarone treatment.\textsuperscript{16} Restoring and maintaining sinus rhythm is another aspect of AF management.\textsuperscript{10-13} Clinical evidence has demonstrated that both rhythm and rate control strategies have resulted in similar outcomes.\textsuperscript{17,18} 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.\textsuperscript{10,11}

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.\textsuperscript{9} Inclusion criteria were a diagnosis of AF and age ≥260 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.\textsuperscript{29}

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 phases of the study. Continuous data were tested for normality with the Shapiro-Wilk test. Data for pre-implementation phase reported by Gauci et al.\textsuperscript{7}
### 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** |
| Antithrombotic therapy | | | | |
| 1 | No antithrombotic therapy if CHA2DS2-VASc score 0* | 1 (0.7) | 1 (100) | 0 (0) | 0 (0) | - | - |
| 2 | Prescription of oral anticoagulant if CHA2DS2-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 [0.97 – 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, nondihydropyridine 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 nondihydropyridine calcium channel blocker and contraindicated/not tolerated | 1 (0.7) | 1 (00) | 1 (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) | 1 (00) | 1 (0) | 0 (0) | - | - |
| 12a | Monitoring of liver and thyroid function with amiodarone and within range | 21 (14.0) | 21 (100) | 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) | 21 (100) | 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 [1.53 – 95.57] | 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 |
| Total criteria | 458 (19.1) | 325 (70.9) | 454 (18.9) | 407 (89.6) | | |

*CHA2DS2-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.©

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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.© 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 CHA2DS2-VASc score.©

**RESULTS**

Patient population characteristics in the pre- and post-implementation phases of MAT-AF application are
Adherence to the 458 applicable criteria was 70.9% before MAT-AF implementation. 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.

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 | Unnecessary drug if CHA2DS2-VASc score 0* | 11 | 0 (0) | 0 | 0 (0) | >0.407 |
| 1 Prescripion of oral anticoagulant if CHA2DS2-VASc score 1* | Need for additional drug | 60 | 12 (20.0) | 51 | 48 (94.1) | <0.001 |
| 2 Prescription of direct oral anticoagulant at recommended dose if creatinine clearance ≥50ml/min | Monitoring need/Dose too low | 5 | 1 (20.0) | 2 | 1 (50.0) | 0.430 |
| 3 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 |
| 4 Prescription of warfarin if creatinine clearance <15ml/min | Monitoring need/Improper drug selection | 0 | 0 (0) | 0 | 0 (0) | >0.407 |
| Rate control therapy | Monitoring need                  | 150 | 0 (0) | 150 | 143 (95.3) | <0.001 |
| 5b 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 |
| 6 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) | >0.407 |
| 7 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 |
| 8 Monitoring of renal function, thyroid function, serum electrolytes with digoxin and within range | Monitoring need | 53 | 0 (0) | 59 | 50 (84.7) | <0.001 |
| 9 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 |
| 10 Prescription of amiodarone for additional rate control or contraindication/intolerance to other agents | Improper drug selection | 1 | 0 (0) | 0 | 0 (0) | >0.407 |
| 11 Monitoring of liver and thyroid function with amiodarone and within range | Monitoring need | 21 | 10 (47.6) | 16 | 13 (81.3) | 0.037 |
| 12 Monitoring of liver and thyroid function with amiodarone after discharge | Seamless care need | 21 | 1 (4.8) | 16 | 5 (31.3) | 0.030 |
| 13 Monitoring of ophthalmic and pulmonary function with amiodarone | Monitoring need/Counselling need | 21 | 0 (0) | 16 | 8 (50.0) | <0.001 |
| Rhythm control therapy | Need for additional drug/Dose too low | 0 | 0 (0) | 1 | 0 (0) | >0.407 |
| 14 Cardiology referral/follow up if maintained in sinus rhythm with antiarrhythmic agent and well tolerated | Risk for adverse drug reaction | 0 | 0 (0) | 2 | 0 (0) | >0.407 |
| 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 |

Total care issues: 386 37 (9.6) 361 301 (83.4) <0.001

*CHA2DS2-VASc score excluding gender

presented in Table 1. No significant variation between the two study populations was evident (p>0.05).
MAT-AF implementation resulted in a significant improvement in prescription of anticoagulants (OR 4.07, p<0.001). The CHADS2-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 CHADS2-VASc score, possibly indicating that stroke risk was not being given due consideration. In contrast, in a study by Lefebre 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. 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 anemia, which was most commonly mild and would merit monitoring rather than exclusion of anticoagulation. Age is a strong predictor for ischaemic stroke in AF patients and robust evidence exists to support the use of anticoagulation in older persons. 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. 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. 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. 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. 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. 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. 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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References

1. Kaboli PJ, Hoth AB, Mcclimom BJ, Schnipper JL. Clinical pharmacists and inpatient medical care. Arch Intern Med. 2006;166(9):955-964. doi: 10.1001/archinte.166.9.955
2. Castelino RL, Bajorek BV, Chen TF. Targeting suboptimal prescribing in the elderly: A review of the impact of pharmacy services. Ann Pharmacother. 2009;43(6):1096-1106. doi: 10.1346/aph.1L700
3. Kaut S, Mitchell G, Vilella L, Roberts MS. Interventions that can reduce inappropriate prescribing in the elderly. Drugs Aging. 2009;26(12):1013-1028. doi: 10.2165/11318890-000000000-00000
4. Spinnewood A, Fialova D, Byrne S. The role of the pharmacist in optimizing pharmacotherapy in older people. Drugs Aging. 2012;29(6):495-510. doi: 10.1165/11631720-000000000-00000
5. Cooper JA, Cadogan CA, Patterson SM, Kense N, Bradley MC, Ryan C, Hughes CM. Interventions to improve the appropriate use of polypharmacy in older people: A Cochrane systematic review. BMJ Open. 2015;5(12):e009235. doi: 10.1136/bmjopen-2015-009235
6. American Society of Health-System Pharmacists (ASHP). ASHP guidelines on documenting pharmaceutical care in patient medical records. Am J Health-Syst Pharm. 2003;60(7):705-707. doi: 10.1093/ajhp/60.7.705
7. Royal Pharmaceutical Society. Guidance on recording of interventions. Pharm J. 2006;276:517-518.
8. Page RL, Linnebur SA, Bryant LL, Ruscín JM. Inappropriate prescribing in the hospitalized elderly patient: defining the problem, evaluation tools, and possible solutions. Clin Interv Aging. 2010;5:75-87. doi: 10.2147/Clia.S9564
9. Gaucì M, Wirth F, Camilleri L, Azzopardi LM, Serracino-Inglott A. Assessing appropriateness of drug therapy in older persons: Development and application of a medication assessment tool for long-term management of atrial fibrillation. Pharm Pract (Granada). 2017;15(4):1021-1025. doi: 10.18549/pharmpract.2017.04.1021
10. January CT, Wann LS, Alpert JS, Calkins H, Cleveland JC, Cigarroa JE, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW. AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2014;130(23):2071-2104. doi: 10.1161/cir.0000000000000041
11. National Institute for Health and Care Excellence (NICE). Atrial fibrillation: The management of atrial fibrillation. Clinical guideline 180. UK: NICE; 2014.
12. Macle L, Cairns J, Leblanc K, Tsang T, Skanes A, Cox JL, Healey JS, Bell A, Piloté L, Andrade JG, Mitchell LB, Atzema C, Gladstone D, Sharma M, Verma S, Connolly S, Dorian P, Parkash R, Talajic M, Nattel S, Verma A. 2016 Focused update of the Canadian Cardiovascular Society guidelines for the management of atrial fibrillation. Can J Cardiol. 2016;30(10):1114-1130. doi: 10.1016/j.cjca.2016.07.591
13. Kirchhoff P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hindricks J, Hindricks G, Manolis AS, Oldjen G, Popescu BA, Schotten U, Van Putte B, Vardas P. 2016 ESC guidelines for the management of atrial fibrillation: The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37(38):2893-2962. doi: 10.1093/eurheartj/ehw210
14. Ziff OJ, Camm AJ. Individualized approaches to thromboprophylaxis in atrial fibrillation. Am Heart J. 2016;173:143-158. doi: 10.1016/j.ahj.2015.10.021
15. Electronic Medicines Compendium (eMC). Summary of product characteristics of digoxin 0.0625mg tablets. UK: eMC; January 2018. https://www.medicines.org.uk/emc/product/6018 (accessed Jul 5, 2018).

16. Electronic Medicines Compendium (eMC). Summary of product characteristics of amiodarone 200mg tablets. UK: eMC; May 2017. https://www.medicines.org.uk/emc/product/6018 (accessed Jul 5, 2018).

17. Kirchhof P, Curtis AB, Skanes AC, Gillis AM, Wann LS, Camm AJ. Atrial fibrillation guidelines across the Atlantic: A comparison of the current recommendations of the European Society of Cardiology/European Heart Rhythm Association/European Association of Cardiothoracic Surgeons, the American College of Cardiology Foundation/American Heart Association/Heart Rhythm Society, and the Canadian Cardiovascular Society. Eur Heart J. 2013;34(20):1471-1474. doi:10.1093/eurheartj/eht446

18. Al-Khabib SM, Allen LaPointe NM, Chatterjee R, Crowley MJ, Dupre ME, Lopes DF, Povsic TJ, Raju SS, Shah B, Kosinski AS, McBroom AJ, Sanders GD. Rate- and rhythm-control therapies in patients with atrial fibrillation: A systematic review. Ann Intern Med. 2014;160(11):760-773. doi:10.7326/m13-1467

19. Mamo M, Wirth F, Azzopardi LM, Serracino-Inglott A. Standardising pharmacist patient-profiling activities in a rehabilitation hospital in Malta. Eur J Hosp Pharm. 2014;21(1):49-53. doi:10.1136/ejhpharm-2013-000351

20. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijs HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: The Euro Heart Survey on atrial fibrillation. Chest. 2010;137(2):263-272. doi:10.1378/chest-09-1584

21. Lefebre MD, St-Onge M, Glazer-Cavanagh M, Bell L, Nam Kha Nguyen J, Viet-Quoc Nguyen P, Tannenbaum C. The effect of bleeding risk and frailty status on anticoagulation patterns in octogenarians with atrial fibrillation: The FRAIL-AF study. Can J Cardiol. 2016;32(2):169-176. doi:10.1016/j.cjca.2015.05.012

22. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijs HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess one-year risk of major bleeding in atrial fibrillation patients: The Euro Heart Survey. Chest. 2010;138(5):93-100. doi:10.1378/chest.10-0134

23. Suarez Fernandez CS, Formiga F, Camafort M, Cepeda Rodrigo JM, Diez-Manglano J, Pose Reino A, Tiberio G, Mostaza JM. Antithrombotic treatment in elderly patients with atrial fibrillation: A practical approach. BMC Cardiovascular Disorders. 2015;15:143. doi:10.1186/s12872-015-0137-7

24. Mant J, Hobbs FD, Fletcher K, Roallfe A, Fitzmaurice D, Lip GY, Murray E. Warfarin vs. aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): A randomised controlled trial. Lancet. 2007;370(9586):493-503. doi:10.1016/S0140-6736(07)61233-1

25. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, Camm AJ, Weitz JI, Lewis BS, Parkhomenko A, Yamashita T, Antman EM. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: A meta-analysis of randomised trials. Lancet. 2014;383(9921):955-962. doi:10.1016/S0140-6736(13)62343-0

26. Graham DJ, Reichman ME, Wernerche M, Zhang R, Southworth MR, Levenson M, Sheu TC, Mott K, Goulding MR, Houstoun M, McCurdy TE, Worrall C, Kelman JA. Cardiovascular, bleeding, and mortality risks in elderly medicare patients treated with dabigatran or warfarin for nonvalvular atrial fibrillation. Circulation. 2015;131(2):157-164. doi:10.1161/circulationaha.114.012061

27. Pugh D, Pugh J, Mead GE. Attitudes of physicians regarding anticoagulation for atrial fibrillation: A systematic review. Age Ageing. 2011;40(6):675-683. doi:10.1093/ageing/abr097

28. Sellers MB, Newby LK. Atrial fibrillation, anticoagulation, fall risk, and outcomes in elderly patients. Am Heart J. 2011;161(2):241-246. doi:10.1016/j.ahj.2010.11.002

29. Banerjee A, Clementy N, Huguenoer K, Fauchier L, Lip GY. Prior history of falls and risk of outcomes in atrial fibrillation: The Loire Valley Atrial Fibrillation Project. Am J Med. 2014;127(10):972-978. doi:10.1016/j.amjmed.2014.05.035

30. Bahri O, Roca F, Lechani T, Druesne L, Jouanny P, Serot JM, Boulanger E, Puisieux F, Chassagne P. Underuse of oral anticoagulation for individuals with atrial fibrillation in a nursing home setting in France: Comparisons of resident characteristics and physician attitude. J Am Geriatr Soc. 2015;63(1):71-76. doi:10.1111/jgs.13200

31. Man-Son-Hing M, Nichol G, Lau A, Laupacis A. Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk for falls. Arch Intern Med. 1999;159(7):677-685. doi:10.1001/archinte.159.7.677

32. Donze J, Clair C, Hug B, Rodondi N, Waebber G, Cornuz J, Aujesky D. Risk of falls and major bleeds in patients on oral anticoagulation therapy. Am J Med. 2012;125(8):773-778. doi:10.1016/j.amjmed.2012.01.033