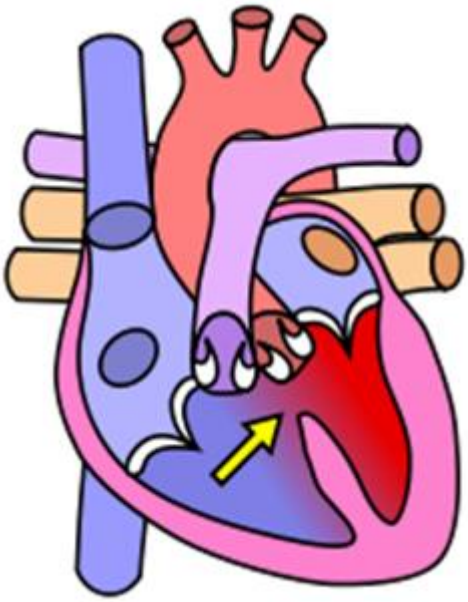
University Hospitals Bristol NHS
NHS Foundation Trust

# Cardiac Nurses
# Current Awareness Bulletin



## May 2017

Respecting everyone
Embracing change
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# Lunchtime Drop-in Sessions

*All sessions last one hour*

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|---|---|
| **May (13.00)** | |
| Fri 26th | **Interpreting Statistics** |
| Weds 31st | **Critical Appraisal** |
| **June (12.00)** | |
| Thurs 1st | **Literature Searching** |
| Thurs 8th | **Interpreting Statistics** |
| Tues 13th | **Critical Appraisal** |
| Thurs 29th | **Literature Searching** |
| **July (13.00)** | |
| Mon 3rd | **Interpreting Statistics** |
| Wed 12th | **Critical Appraisal** |
| Fri 21st | **Literature Searching** |
| Wed 26th | **Interpreting Statistics** |

## Your Outreach Librarian – Sarah Barrett

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# Contents

# New Additions to NICE, the Cochrane Library, and UpToDate®

NICE National Institute for Health and Care Excellence

Prescribing dronedarone for paroxysmal atrial fibrillation: how is it done across the UK and is it safe?

12 May 2017 - Publisher: European Journal of Hospital Pharmacy
This short report (n=181) describes an audit of a shared care protocol between primary and secondary care on the use of dronedarone for paroxysmal atrial fibrillation. There were no deaths or serious adverse events and 88% stopped dronedarone within 6 months.

Cochrane Library

Clarkesmith DE, Pattison HM, Khaing PH, Lane DA. Educational and behavioural interventions for anticoagulant therapy in patients with atrial fibrillation. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD008600. DOI: 10.1002/14651858.CD008600.pub3.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008600.pub3/full

UpToDate®

*OpenAthens login required. Register here: https://openathens.nice.org.uk/*

**Cardiac resynchronization therapy in heart failure: Indications**
Authors: Leslie A Saxon, MD; Teresa DeMarco, MD; Section Editor: Wilson S Colucci, MD; Deputy Editor: Susan B Yeon, MD, JD, FACC
All topics are updated as new evidence becomes available and our peer review process is complete.
**Literature review current through:** Apr 2017. | **This topic last updated:** Mar 31, 2017.

**INTRODUCTION** — Ventricular dyssynchrony can impair ventricular pump function. Cardiac resynchronization therapy (CRT) involves simultaneous pacing of both ventricles (biventricular or BiV pacing) (figure 1) or of one ventricle in patients with bundle branch block to reduce dyssynchrony [1-6]. Resynchronization may improve pump performance, reduce functional mitral regurgitation, and reverse the deleterious process of ventricular remodeling in patients with heart failure (HF). (See "Rationale for and mechanisms of benefit of cardiac resynchronization therapy".)

CRT is recommended in selected patients with HF, systolic dysfunction, and prolonged QRS interval since it has been shown to reduce mortality, HF symptoms, and HF hospitalizations in randomized controlled trials. CRT is recommended in addition to guideline-directed medical therapy, such as angiotensin converting enzyme inhibitors, beta blockers, aldosterone antagonist therapy (see "Overview of the therapy of heart failure with

reduced ejection fraction"), and implantable cardioverter-defibrillators (ICDs) when indicated for primary or secondary prevention of sudden cardiac death. (See "Primary prevention of sudden cardiac death in heart failure and cardiomyopathy", section on 'Use of an ICD'.) After initiation of treatment with CRT, some patients may be better able to tolerate optimal doses of guideline-directed medical therapy [7]. CRT can be achieved with a device designed only for pacing or can be incorporated into a combination device with an ICD.

The clinical trials and indications for CRT in the management of patients with HF will be reviewed here. The rationale for CRT, implantation and other considerations for CRT therapy, studies evaluating standard dual-chamber pacing in HF, and the possible role of CRT in patients with atrial fibrillation are discussed separately. (See "Rationale for and mechanisms of benefit of cardiac resynchronization therapy" and "Cardiac resynchronization therapy in heart failure: Implantation and other considerations" and "Overview of cardiac pacing in heart failure" and "Cardiac resynchronization therapy in atrial fibrillation".)

https://www.uptodate.com/contents/cardiac-resynchronization-therapy-in-heart-failure-indications?source=related_link

# Current Awareness Database

**Below is a selection of articles recently added to the healthcare databases.**

**If you would like any of the following articles in full text, or if you would like a more focused search on your own topic, then get in touch: library@uhbristol.nhs.uk**

**Atrial fibrillation, inherited channelopathies, cardiac resynchronisation therapy**

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1. Patient characteristics associated with false arrhythmia alarms in intensive care.
2. Sleep-Disordered Breathing and Arrhythmia in Heart Failure Patients.
3. Arrhythmia Surgery for Adults with Congenital Heart Disease.
4. Unnecessary overuse. Study of "inadvisable practices" for patients with atrial fibrillation.
5. Screening for Atrial Fibrillation: A Report of the AF-SCREEN International Collaboration.
6. Autoimmune channelopathies as a novel mechanism in cardiac arrhythmias.
7. Prediction of New-Onset and Recurrent Atrial Fibrillation by Complete Blood Count Tests: A Comprehensive Systematic Review with Meta-Analysis.
8. Integrated care in atrial fibrillation: a systematic review and meta-analysis.
9. Thromboembolic risk and effect of oral anticoagulation according to atrial fibrillation patterns: A systematic review and meta-analysis.
10. Are cardiovascular risk factors also associated with the incidence of atrial fibrillation? A systematic review and field synopsis of 23 factors in 32 population-based cohorts of 20 million participants.
11. Clinical significance of nutritional status in patients with atrial fibrillation: An overview of current evidence.
12. Revisiting pulmonary vein isolation alone for persistent atrial fibrillation: A systematic review and meta-analysis.
13. Conventional acupuncture for cardiac arrhythmia: A systematic review of randomized controlled trials.
14. The Global Burden of Atrial Fibrillation and Stroke: A Systematic Review of the Clinical Epidemiology of Atrial Fibrillation in Asia.
15. Bleeding risk of antiplatelet drugs compared with oral anticoagulants in older patients with atrial fibrillation: a systematic review and meta-analysis.
16. Is echocardiography valid and reproducible in patients with atrial fibrillation? A systematic review.
17. Link Between Non-Alcoholic Fatty Liver Disease and Atrial Fibrillation: A Systematic Review and Meta-Analysis.
18. Digoxin versus placebo, no intervention, or other medical interventions for atrial fibrillation and atrial flutter: a protocol for a systematic review with meta-analysis and Trial Sequential Analysis.
19. Predictive performance of the CHA2DS2-VASc rule in atrial fibrillation: a systematic review and meta-analysis.
20. Rivaroxaban Versus Dabigatran or Warfarin in Real-World Studies of Stroke Prevention in Atrial Fibrillation: Systematic Review and Meta-Analysis.
21. Is There an Obesity Paradox for Outcomes in Atrial Fibrillation? A Systematic Review and Meta-Analysis of Non-Vitamin K Antagonist Oral Anticoagulant Trials.
22. Comparison of catheter ablation for paroxysmal atrial fibrillation between cryoballoon and radiofrequency: a meta-analysis.
23. Predictive Role of Coagulation, Fibrinolytic, and Endothelial Markers in Patients with Atrial Fibrillation, Stroke, and Thromboembolism: A Meta-Analysis, Meta-Regression, and Systematic Review.
24. Systematic review and meta-analysis on the impact of pre-operative atrial fibrillation on short- and long-term outcomes after aortic valve replacement.
25. Platelets Cellular and Functional Characteristics in Patients with Atrial Fibrillation: A Comprehensive Meta-Analysis and Systematic Review.
26. Bleeding events associated with a low dose (110 mg) versus a high dose (150 mg) of dabigatran in patients treated for atrial fibrillation: a systematic review and meta-analysis.
27. Patient values and preferences for antithrombotic therapy in atrial fibrillation. A Narrative Systematic Review.
28. The effects of rhythm control strategies versus rate control strategies for atrial fibrillation and atrial flutter: a protocol for a systematic review with meta-analysis and Trial Sequential Analysis.

**1. Patient characteristics associated with false arrhythmia alarms in intensive care.**

**Author(s):** Harris, Patricia R; Zègre-Hemsey, Jessica K; Schindler, Daniel; Bai, Yong; Pelter, Michele M; Hu, Xiao

**Source:** Therapeutics and clinical risk management; 2017; vol. 13 ; p. 499-513

**Publication Type(s):** Journal Article

Available in full text at Therapeutics and Clinical Risk Management - from National Library of Medicine

**Abstract:**INTRODUCTIONA high rate of false arrhythmia alarms in the intensive care unit (ICU) leads to alarm fatigue, the condition of desensitization and potentially inappropriate silencing of alarms due to frequent invalid and nonactionable alarms, often referred to as false alarms.OBJECTIVEThe aim of this study was to identify patient characteristics, such as gender, age, body mass index, and diagnosis associated with frequent false arrhythmia alarms in the ICU.METHODSThis descriptive, observational study prospectively enrolled patients who were consecutively admitted to one of five adult ICUs (77 beds) at an urban medical center over a period of 31 days in 2013. All monitor alarms and continuous waveforms were stored on a secure server. Nurse scientists with expertise in cardiac monitoring used a standardized protocol to annotate six clinically important types of arrhythmia alarms (asystole, pause, ventricular fibrillation, ventricular tachycardia, accelerated ventricular rhythm, and ventricular bradycardia) as true or false. Total monitoring time for each patient was measured, and the number of false alarms per hour was calculated for these six alarm types. Medical records were examined to acquire data on patient characteristics.RESULTSA total of 461 unique patients (mean age =60±17 years) were enrolled, generating a total of 2,558,760 alarms, including all levels of arrhythmia, parameter, and technical alarms. There were 48,404 hours of patient monitoring time, and an average overall alarm rate of 52 alarms/hour. Investigators annotated 12,671 arrhythmia alarms; 11,345 (89.5%) were determined to be false. Two hundred and fifty patients (54%) generated at least one of the six annotated alarm types. Two patients generated 6,940 arrhythmia alarms (55%). The number of false alarms per monitored hour for patients' annotated arrhythmia alarms ranged from 0.0 to 7.7, and the duration of these false alarms per hour ranged from 0.0 to 158.8 seconds. Patient characteristics were compared in relation to 1) the number and 2) the duration of false arrhythmia alarms per 24-hour period, using nonparametric statistics to minimize the influence of outliers. Among the significant associations were the following: age ≥60 years (P=0.013; P=0.034), confused mental status (P<0.001 for both comparisons), cardiovascular diagnoses (P<0.001 for both comparisons), electrocardiographic (ECG) features, such as wide ECG waveforms that correspond to ventricular depolarization known as QRS complex due to bundle branch block (BBB) (P=0.003; P=0.004) or ventricular paced rhythm (P=0.002 for both comparisons), respiratory diagnoses (P=0.004 for both comparisons), and support with mechanical ventilation, including those with primary diagnoses other than respiratory ones (P<0.001 for both comparisons).CONCLUSIONPatients likely to trigger a higher number of false arrhythmia alarms may be those with older age, confusion, cardiovascular diagnoses, and ECG features that indicate BBB or ventricular pacing, respiratory diagnoses, and mechanical ventilatory support. Algorithm improvements could focus on better noise reduction (eg, motion artifact with confused state) and distinguishing BBB and paced rhythms from ventricular arrhythmias. Increasing awareness of patient conditions that apparently trigger a higher rate of false arrhythmia alarms may be useful for reducing unnecessary noise and improving alarm management.

**2. Sleep-Disordered Breathing and Arrhythmia in Heart Failure Patients.**

**Author(s):** Fox, Henrik; Bitter, Thomas; Horstkotte, Dieter; Oldenburg, Olaf

**Source:** Sleep medicine clinics; Jun 2017; vol. 12 (no. 2); p. 229-241

**Publication Type(s):** Journal Article Review

**Abstract:**Heart failure (HF) treatment remains complex and challenging, with current recommendations aiming at consideration and treatment of comorbidities in patients with HF. Sleep-disordered breathing (SDB) and arrhythmia come into play, as both are associated with quality of life deterioration, and morbidity and mortality increase in patients with HF. Interactions of these diseases are versatile and may appear intransparent in daily practice. Nevertheless, because of their importance for patients' condition and prognosis, SDB and arrhythmia

individually, but also through interaction on one another, necessitate attention, following the fact that treatment is requested and desired considering latest research findings and outcomes.

**3. Arrhythmia Surgery for Adults with Congenital Heart Disease.**

**Author(s):** Deal, Barbara J; Mavroudis, Constantine

**Source:** Cardiac electrophysiology clinics; Jun 2017; vol. 9 (no. 2); p. 329-340

**Publication Type(s):** Journal Article Review

**Abstract:**Patients with repaired or unrepaired congenital heart anomalies are at increased risk for arrhythmia development throughout their lives, often paralleling the need for reoperations for hemodynamic residua. The ability to incorporate arrhythmia surgery into reoperations can result in improvement in functional class and decreased need for antiarrhythmic medications. Every reoperation for congenital heart disease can be viewed as an opportunity to assess the electrical and arrhythmia substrates and to intervene to improve the arrhythmias and the hemodynamic condition of the patient. The authors review and summarize the operative techniques for arrhythmia surgery that are based on the arrhythmia mechanisms.

**4. Unnecessary overuse. Study of "inadvisable practices" for patients with atrial fibrillation.**

**Author(s):** Ortiz, M M; Llamas, P; Sanmartín, M; Egido, J A; Del Toro, J; Egocheaga, M I; Estévez, M S; Navarro, I M; Mira, J J

**Source:** Revista clinica espanola; May 2017; vol. 217 (no. 4); p. 181-187

**Publication Type(s):** Journal Article

**Abstract:**OBJECTIVETo identify overuse (diagnostic, therapeutic and self-care practices that represent risks that outweigh the potential benefits) in patients with atrial fibrillation.METHODThe study was based on qualitative research techniques. Using the "Metaplan" technique, we identified and ordered potentially inappropriate, ineffective and inefficient practices. By means of a consensus conference, we then established a number of "inadvisable practice" measures (relatively common practices that should be eliminated based on the scientific evidence or clinical experience). Professionals from the specialties of cardiology, haematology, neurology, internal medicine, family medicine and nursing participated in the consensus.RESULTSWe developed a catalogue of 19 "inadvisable practices" related to the diagnosis, treatment and care of anticoagulated patients that were inappropriate, had questionable effectiveness or were ineffective, as well as 13 beliefs or behaviours for anticoagulated patients that could result in injury or were useless or inefficient.CONCLUSIONThe "inadvisable practices" approach helps identify practices that represent greater risks than benefits for patients. It seems appropriate to include algorithms in the clinical decision-making support systems that consider this information for the diagnosis, treatment and for home care. For this last case, recommendations have also been prepared that define specific contents for the healthcare education of these patients.

**5. Screening for Atrial Fibrillation: A Report of the AF-SCREEN International Collaboration.**

**Author(s):** Freedman, Ben; Camm, John; Calkins, Hugh; Healey, Jeffrey S; Rosenqvist, Mårten; Wang, Jiguang; Albert, Christine M; Anderson, Craig S; Antoniou, Sotiris; Benjamin, Emelia J; Boriani, Giuseppe; Brachmann, Johannes; Brandes, Axel; Chao, Tze-Fan; Conen, David; Engdahl, Johan; Fauchier, Laurent; Fitzmaurice, David A; Friberg, Leif; Gersh, Bernard J; Gladstone, David J; Glotzer, Taya V; Gwynne, Kylie; Hankey, Graeme J; Harbison, Joseph; Hillis, Graham S; Hills, Mellanie T; Kamel, Hooman; Kirchhof, Paulus; Kowey, Peter R; Krieger, Derk; Lee, Vivian W Y; Levin, Lars-Åke; Lip, Gregory Y H; Lobban, Trudie; Lowres, Nicole; Mairesse, Georges H; Martinez, Carlos; Neubeck, Lis; Orchard, Jessica; Piccini, Jonathan P; Poppe, Katrina; Potpara, Tatjana S; Puererfellner, Helmut; Rienstra, Michiel; Sandhu, Roopinder K; Schnabel, Renate B; Siu, Chung-Wah; Steinhubl, Steven; Svendsen, Jesper H; Svennberg, Emma; Themistoclakis, Sakis; Tieleman, Robert G; Turakhia, Mintu P; Tveit, Arnljot; Uittenbogaart, Steven B; Van Gelder, Isabelle C; Verma, Atul; Wachter, Rolf; Yan, Bryan P

**Source:** Circulation; May 2017; vol. 135 (no. 19); p. 1851-1867

**Publication Type(s):** Journal Article Review

Available in full text at Circulation - from Highwire Press

**Abstract:**Approximately 10% of ischemic strokes are associated with atrial fibrillation (AF) first diagnosed at the time of stroke. Detecting asymptomatic AF would provide an opportunity to prevent these strokes by instituting appropriate anticoagulation. The AF-SCREEN international collaboration was formed in September 2015 to promote discussion and research about AF screening as a strategy to reduce stroke and death and to

provide advocacy for implementation of country-specific AF screening programs. During 2016, 60 expert members of AF-SCREEN, including physicians, nurses, allied health professionals, health economists, and patient advocates, were invited to prepare sections of a draft document. In August 2016, 51 members met in Rome to discuss the draft document and consider the key points arising from it using a Delphi process. These key points emphasize that screen-detected AF found at a single timepoint or by intermittent ECG recordings over 2 weeks is not a benign condition and, with additional stroke factors, carries sufficient risk of stroke to justify consideration of anticoagulation. With regard to the methods of mass screening, handheld ECG devices have the advantage of providing a verifiable ECG trace that guidelines require for AF diagnosis and would therefore be preferred as screening tools. Certain patient groups, such as those with recent embolic stroke of uncertain source (ESUS), require more intensive monitoring for AF. Settings for screening include various venues in both the community and the clinic, but they must be linked to a pathway for appropriate diagnosis and management for screening to be effective. It is recognized that health resources vary widely between countries and health systems, so the setting for AF screening should be both country- and health system-specific. Based on current knowledge, this white paper provides a strong case for AF screening now while recognizing that large randomized outcomes studies would be helpful to strengthen the evidence base.

**6. Autoimmune channelopathies as a novel mechanism in cardiac arrhythmias.**

**Author(s):** Lazzerini, Pietro Enea; Capecchi, Pier Leopoldo; Laghi-Pasini, Franco; Boutjdir, Mohamed

**Source:** Nature reviews. Cardiology; May 2017

**Publication Type(s):** Journal Article Review

**Abstract:**Cardiac arrhythmias confer a considerable burden of morbidity and mortality in industrialized countries. Although coronary artery disease and heart failure are the prevalent causes of cardiac arrest, in 5-15% of patients, structural abnormalities at autopsy are absent. In a proportion of these patients, mutations in genes encoding cardiac ion channels are documented (inherited channelopathies), but, to date, the molecular autopsy is negative in nearly 70% of patients. Emerging evidence indicates that autoimmunity is involved in the pathogenesis of cardiac arrhythmias. In particular, several arrhythmogenic autoantibodies targeting specific calcium, potassium, or sodium channels in the heart have been identified. Experimental and clinical studies demonstrate that these autoantibodies can promote conduction disturbances and life-threatening tachyarrhythmias by inducing substantial electrophysiological changes. In this Review, we propose the term 'autoimmune cardiac channelopathies' to define this novel pathogenic mechanism of cardiac arrhythmias, which could be more frequent and clinically relevant than previously appreciated. Indeed, pathogenic autoantibodies against ion channels are detectable not only in patients with manifest autoimmune disease, but also in apparently healthy individuals, which suggests a causal role in some cases of unexplained arrhythmias and cardiac arrest. Considering this possibility and performing specific testing in patients with 'idiopathic' rhythm disturbances could create novel treatment opportunities.

**7. Prediction of New-Onset and Recurrent Atrial Fibrillation by Complete Blood Count Tests: A Comprehensive Systematic Review with Meta-Analysis.**

**Author(s):** Weymann, Alexander; Ali-Hasan-Al-Saegh, Sadeq; Sabashnikov, Anton; Popov, Aron-Frederik; Mirhosseini, Seyed Jalil; Liu, Tong; Lotfaliani, Mohammadreza; Sá, Michel Pompeu Barros de Oliveira; Baker, William L L; Yavuz, Senol; Zeriouh, Mohamed; Jang, Jae-Sik; Dehghan, Hamidreza; Meng, Lei; Testa, Luca; D'Ascenzo, Fabrizio; Benedetto, Umberto; Tse, Gary; Nombela-Franco, Luis; Dohmen, Pascal M; Deshmukh, Abhishek J; Linde, Cecilia; Biondi-Zoccai, Giuseppe; Stone, Gregg W; Calkins, Hugh; Surgery And Cardiology-Group Imcsc-Group, Integrated Meta-Analysis Of Cardiac

**Source:** Medical science monitor basic research; May 2017; vol. 23 ; p. 179-222

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUND Atrial fibrillation (AF) is one of the most critical and frequent arrhythmias precipitating morbidities and mortalities. The complete blood count (CBC) test is an important blood test in clinical practice and is routinely used in the workup of cardiovascular diseases. This systematic review with meta-analysis aimed to determine the strength of evidence for evaluating the association of hematological parameters in the CBC test with new-onset and recurrent AF. MATERIAL AND METHODS We conducted a meta-analysis of observational studies evaluating hematologic parameters in patients with new-onset AF and recurrent AF. A comprehensive subgroup analysis was performed to explore potential sources of heterogeneity. RESULTS The literature search of all major databases retrieved 2150 studies. After screening, 70 studies were analyzed in the meta-analysis on new-onset AF and 23 studies on recurrent AF. Pooled analysis on new-onset AF showed platelet count (PC) (weighted mean difference (WMD)=WMD of -26.39×10^9/L and p<0.001), mean platelet volume (MPV) (WMD=0.42 FL and p<0.001), white blood cell (WBC) (WMD=-0.005×10^9/L

and p=0.83), neutrophil to lymphocyte ratio (NLR) (WMD=0.89 and p<0.001), and red blood cell distribution width (RDW) (WMD=0.61% and p<0.001) as associated factors. Pooled analysis on recurrent AF revealed PC (WMD=-2.71×109/L and p=0.59), WBC (WMD=0.20×10^9/L (95% CI: 0.08 to 0.32; p=0.002), NLR (WMD=0.37 and p<0.001), and RDW (WMD=0.28% and p<0.001). CONCLUSIONS Hematological parameters have significant ability to predict occurrence and recurrence of AF. Therefore, emphasizing the potential predictive role of hematological parameters for new-onset and recurrent AF, we recommend adding the CBC test to the diagnostic modalities of AF in clinical practice.

**8. Integrated care in atrial fibrillation: a systematic review and meta-analysis.**

**Author(s):** Gallagher, Celine; Elliott, Adrian D; Wong, Christopher X; Rangnekar, Geetanjali; Middeldorp, Melissa E; Mahajan, Rajiv; Lau, Dennis H; Sanders, Prashanthan; Hendriks, Jeroen M L

**Source:** Heart (British Cardiac Society); May 2017

**Publication Type(s):** Journal Article

Available in full text at Heart - from Highwire Press

**Abstract:**OBJECTIVEAtrial fibrillation (AF) is an emerging global epidemic associated with significant morbidity and mortality. Whilst other chronic cardiovascular conditions have demonstrated enhanced patient outcomes from coordinated systems of care, the use of this approach in AF is a comparatively new concept. Recent evidence has suggested that the integrated care approach may be of benefit in the AF population, yet has not been widely implemented in routine clinical practice. We sought to undertake a systematic review and meta-analysis to evaluate the impact of integrated care approaches to care delivery in the AF population on outcomes including mortality, hospitalisations, emergency department visits, cerebrovascular events and patient-reported outcomes.METHODSPubMed, Embase and CINAHL databases were searched until February 2016 to identify papers addressing the impact of integrated care in the AF population. Three studies, with a total study population of 1383, were identified that compared integrated care approaches with usual care in AF populations.RESULTSUse of this approach was associated with a reduction in all-cause mortality (OR 0.51, 95% CI 0.32 to 0.80, p=0.003) and cardiovascular hospitalisations (OR 0.58, 95% CI 0.44 to 0.77, p=0.0002) but did not significantly impact on AF-related hospitalisations (OR 0.82, 95% CI 0.56 to 1.19, p=0.29) or cerebrovascular events (OR 1.00, 95% CI 0.48 to 2.09, p=1.00).CONCLUSIONSThe use of the integrated care approach in AF is associated with reduced cardiovascular hospitalisations and all-cause mortality. Further research is needed to identify optimal settings, methods and components of delivering integrated care to the burgeoning AF population.

**9. Thromboembolic risk and effect of oral anticoagulation according to atrial fibrillation patterns: A systematic review and meta-analysis.**

**Author(s):** Lilli, Alessio; Di Cori, Andrea; Zacà, Valerio

**Source:** Clinical cardiology; May 2017

**Publication Type(s):** Journal Article Review

**Abstract:**Oral anticoagulation (OAC) is recommended in both paroxysmal atrial fibrillation (pxAF) and nonparoxysmal AF (non-pxAF), but disagreement exists in classes of recommendation. Data on incidence/rate of stroke in pxAF are conflicting, and OAC is often underused in this population. The objectives of the meta-analysis were to investigate different impact on outcomes of pxAF and non-pxAF, with and without OAC. Two reviewers searched for prospective studies on risk of stroke and systemic embolism (SE) in pxAF and non-pxAF, with and without OAC. Quality of evidence was assessed according to GRADE approach. Stroke combined with SE was the main outcome. Meta-regression was performed to evaluate OAC effect on stroke and SE incidence rate. We identified 18 studies. For a total of 239 528 patient-years of follow-up. The incidence rate of stroke/SE was 1.6% (95% confidence interval [CI]: 1.3%-2.0%) in pxAF and 2.3% (95% CI: 2.0%-2.7%) in non-pxAF. Paroxysmal AF was associated with a lower risk of overall thromboembolic (TE) events (risk ratio: 0.72, 95% CI: 0.65-0.80, P < 0.00001) compared with non-pxAF. In both groups, the annual rate of TE events decreased as proportion of patients treated with OAC increased. Non-pxAF showed a reduction from 3.7% to 1.7% and pxAF from 2.5% to 1.2%. Major bleeding rates did not differ among groups. Stroke/SE risk is significantly lower, although clinically meaningful, in pxAF. OAC consistently reduces TE event rates across any AF pattern. As a whole, these data provide the evidence to warrant OAC irrespective of the AF pattern in most (virtually all) patients.

**10. Are cardiovascular risk factors also associated with the incidence of atrial fibrillation? A systematic review and field synopsis of 23 factors in 32 population-based cohorts of 20 million participants.**

**Author(s):** Allan, Victoria; Honarbakhsh, Shohreh; Casas, Juan-Pablo; Wallace, Joshua; Hunter, Ross; Schilling, Richard; Perel, Pablo; Morley, Katherine; Banerjee, Amitava; Hemingway, Harry

**Source:** Thrombosis and haemostasis; May 2017; vol. 117 (no. 5); p. 837-850

**Publication Type(s):** Journal Article

**Abstract:**Established primary prevention strategies of cardiovascular diseases are based on understanding of risk factors, but whether the same risk factors are associated with atrial fibrillation (AF) remains unclear. We conducted a systematic review and field synopsis of the associations of 23 cardiovascular risk factors and incident AF, which included 84 reports based on 28 consented and four electronic health record cohorts of 20,420,175 participants and 576,602 AF events. We identified 3-19 reports per risk factor and heterogeneity in AF definition, quality of reporting, and adjustment. We extracted relative risks (RR) and 95 % confidence intervals [CI] and visualised the number of reports with inverse (RR [CI]1.00) associations. For hypertension (13/17 reports) and obesity (19/19 reports), there were direct associations with incident AF, as there are for coronary heart disease (CHD). There were inverse associations for non-White ethnicity (5/5 reports, with RR from 0.35 to 0.84 [0.82-0.85]), total cholesterol (4/13 reports from 0.76 [0.59-0.98] to 0.94 [0.90-0.97]; 8/13 reports with non-significant inverse associations), and diastolic blood pressure (2/11 reports from 0.87 [0.78-0.96] to 0.92 [0.85-0.99]; 5/11 reports with non-significant inverse associations), and direct associations for taller height (7/10 reports from 1.03 [1.02-1.05] to 1.92 [1.38-2.67]), which are in the opposite direction of known associations with CHD. A systematic evaluation of the available evidence suggests similarities as well as important differences in the risk factors for incidence of AF as compared with other cardiovascular diseases, which has implications for the primary prevention strategies for atrial fibrillation.

**11. Clinical significance of nutritional status in patients with atrial fibrillation: An overview of current evidence.**

**Author(s):** Anaszewicz, Marzena; Budzyński, Jacek

**Source:** Journal of cardiology; May 2017; vol. 69 (no. 5); p. 719-730

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUNDObesity is a well-known atherosclerosis risk factor; however, its role and the importance of undernutrition in atrial fibrillation (AF) pathogenesis are still not well understood. The aim of this study was to present the current state of knowledge on this issue in different groups of patients.METHODSSystematic review of papers published between 1980 and 2016.RESULTSThe literature shows contradicting views regarding the impact of nutritional status on the risk, course, and complications of AF. On the one hand, it has been revealed that overweight, obesity, and high birth mass increase the risk of AF, and that their reduction is linked to an improved course of AF and reduced all-cause and cardiovascular mortality. On the other hand, a so-called obesity paradox has been found, which shows lower all-cause mortality in overweight patients with AF compared to those of normal weight or who are underweight. It has also been shown, although based on a small number of studies, that the relationship between nutritional status and risk of AF and its complication may be U-shaped, which means that not only patients with obesity, but also individuals with underweight, cachexia, and low birth weight may have an increased risk and poor outcome of AF.CONCLUSIONSThe relationship between patients' nutritional status and the course of AF has become clearer but it requires further studies examining the importance of weight reduction on AF course.

**12. Revisiting pulmonary vein isolation alone for persistent atrial fibrillation: A systematic review and meta-analysis.**

**Author(s):** Voskoboinik, Aleksandr; Moskovitch, Jeremy T; Harel, Nadav; Sanders, Prashanthan; Kistler, Peter M; Kalman, Jonathan M

**Source:** Heart rhythm; May 2017; vol. 14 (no. 5); p. 661-667

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUNDEarly studies demonstrated relatively low success rates for pulmonary vein isolation (PVI) alone in patients with persistent atrial fibrillation (PeAF). However, the advent of new technologies and the observation that additional substrate ablation does not improve outcomes have created a new focus on PVI alone for treatment of PeAF.OBJECTIVEThe purpose of this study was to systematically review the recent medical literature to determine current medium-term outcomes when a PVI-only approach is used for PeAF.METHODSAn electronic database search (MEDLINE, Embase, Web of Science, PubMed, Cochrane) was performed in August 2016. Only studies of PeAF patients undergoing a "PVI only" ablation strategy using contemporary radiofrequency (RF) technology or second-generation cryoballoon (CB2) were included. A random-effects model was used to assess the primary outcome of pooled single-procedure 12-month arrhythmia-

free survival. Predictors of recurrence were also examined and a meta-analysis performed if ≥4 studies examined the parameter.RESULTSFourteen studies of 956 patients, of whom 45.2% underwent PVI only with RF and 54.8% with CB2, were included. Pooled single-procedure 12-month arrhythmia-free survival was 66.7% (95% confidence interval [CI] 60.8%-72.2%), with the majority of patients (80.5%) off antiarrhythmic drugs. Complication rates were very low, with cardiac tamponade occurring in 5 patients (0.6%) and persistent phrenic nerve palsy in 5 CB2 patients (0.9% of CB2). Blanking period recurrence (hazard ratio 4.68, 95% CI 1.70-12.9) was the only significant predictor of recurrence.CONCLUSIONA PVI-only strategy in PeAF patients with a low prevalence of structural heart disease using contemporary technology yields excellent outcomes comparable to those for paroxysmal AF ablation.

**13. Conventional acupuncture for cardiac arrhythmia: A systematic review of randomized controlled trials.**

**Author(s):** Liu, Jing; Li, Si-Nai; Liu, Lu; Zhou, Kun; Li, Yan; Cui, Xiao-Yun; Wan, Jie; Lu, Jin-Jin; Huang, Yan-Chao; Wang, Xu-Sheng; Lin, Qian

**Source:** Chinese journal of integrative medicine; Apr 2017

**Publication Type(s):** Journal Article

**Abstract:**OBJECTIVETo exam the effect and safety of conventional acupuncture (CA) on cardiac arrhythmia.METHODSNine medical databases were searched until February 2016 for randomized controlled trials. Heterogeneity was measured by Cochran Q test. Meta-analysis was conducted if I2 was less than 85% and the characteristics of included trials were similar.RESULTSNine qualified studies involving 638 patients were included. Only 1 study had definitely low risk of bias, while 7 trials were rated as unclear and 1 as high. Meta-analysis of CA alone did not have a significant benefit on response rate compared to amiodarone in patients with atrial fibrillation (Af) and atrial flutter (AF) [relative risk (RR): 1.09; 95% confidence interval (CI): 0.79-1.49; P=0.61; I2=61%, P=0.11]. However, 1 study with higher methodological quality detected a lower recurrence rate of Af in CA alone as compared with sham acupuncture plus no treatment, and benefits on ventricular rate and time of conversion to normal sinus rhythm were found in CA alone group by 1 study, as well as the response rate in CA plus deslanoside group by another study. Meta-analysis of CA plus anti-arrhythmia drug (AAD) was associated with a significant benefit on the response rate when compared with AAD alone in ventricular premature beat (VPB) patients (RR, 1.19, 95% CI: 1.05-1.34; P=0.005; I2=13%, P=0.32), and an improvement in quality-of-life score (QOLS) of VPB also showed in 1 individual study. Besides, a lower heart rate was detected in the CA alone group by 1 individual study when compared with no treatment in sinus tachycardia patients (MD-21.84 [-27.21,-16.47]) and lower adverse events of CA alone were reported than amiodarone.CONCLUSIONSCA may be a useful and safe alternative or additive approach to AADs for cardiac arrhythmia, especially in VPB and Af patients, which mainly based on a pooled estimate and result from 1 study with higher methodological quality. However, we could not reach a robust conclusion due to low quality of overall evidence.

**14. The Global Burden of Atrial Fibrillation and Stroke: A Systematic Review of the Clinical Epidemiology of Atrial Fibrillation in Asia.**

**Author(s):** Bai, Ying; Wang, Yan-Liang; Shantsila, Alena; Lip, Gregory Y H

**Source:** Chest; Apr 2017

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUNDOur previous review showed great variability on the incidence and prevalence of atrial fibrillation (AF) in non-Western cohorts, especially from Asian countries; in recent years, epidemiology studies on AF have been increasingly reported.METHODSWe therefore conducted an updated systematic review, to present the current knowledge base of AF epidemiology in Asian countries since our prior review. We also explored AF incidence and the risk of stroke in AF using meta-analysis, with I2 testing the heterogeneity. Third, 'real world' antithrombotic drug use for ischemic stroke (IS) prevention associated with AF was studied.RESULTS58 papers from 8 countries in Asia were finally included in our analysis. The summary annual incidence of AF was 5.38 (95% CI: 4.53-6.24, I2=99.5%, N=10) per 1000 person-years and the IS annual risk in AF was 3.0% (1.60%-4.95%, I2=99.8%, N=8) when meta-analysis was performed on hospital- and community-based studies. Hospital- and community- based AF prevalence ranged from 0.37% to 3.56% and 2.8% to 15.8%, respectively. IS prevalence in AF ranged 1.9-6.0% and 0.36-28.3% in community and hospital studies, respectively. Warfarin use in Chinese is relatively low (1.0-4.1%) when compared with Japanese (49.1-70.0%) in community-based studies. The rate of warfarin use was <50% in hospital-based studies.CONCLUSIONSAF incidence and prevalence has increased in recent years, though great variability still exists in Asian countries. Variability in annual IS risk in AF patients was apparent between hospital- and

community-based studies. However, the rate of warfarin use was less than 50% in hospital studies from Asian countries.

**15. Bleeding risk of antiplatelet drugs compared with oral anticoagulants in older patients with atrial fibrillation: a systematic review and meta-analysis.**

**Author(s):** Melkonian, M; Jarzebowski, W; Pautas, E; Siguret, V; Belmin, J; Lafuente-Lafuente, C

**Source:** Journal of thrombosis and haemostasis : JTH; Apr 2017

**Publication Type(s):** Journal Article

**Abstract:**Essentials Hemorrhagic risk of antiplatelet drugs is generally thought to be lower than anticoagulants. We systematically reviewed trials comparing antiplatelet and anticoagulant drugs in older patients. Overall, the risk of major bleeding was similar with antiplatelet and with anticoagulant drugs. In elderly patients, risks and benefits of antiplatelet drugs should be carefully weighted.SUMMARYBackground The hemorrhagic risk of antiplatelet drugs in older patients could be higher than is usually assumed. Objective To compare the bleeding risk of antiplatelet drugs and oral anticoagulants in elderly patients. Methods We carried out a systematic review and meta-analysis. We searched PubMed, EMBASE and the Cochrane Library up to January 2016 for randomized and non-randomized controlled trials (RCTs) and parallel cohorts comparing antiplatelet drugs and oral anticoagulants in patients aged 65 years or older. Two independent authors assessed studies for inclusion. The pooled relative risk (RR) of major bleeding was estimated using a random model. Results Seven RCTs (4550 patients) and four cohort studies (38 649 patients) met the inclusion criteria. The risk of major bleeding when on aspirin or clopidogrel was equal to that when on warfarin in RCTs (RR, 1.01; 95% confidence interval (95% CI), 0.69-1.48; moderate-quality evidence), lower than when on warfarin in non-randomized cohort studies (RR, 0.87; 95% CI, 0.77-0.99; low-quality evidence) and not different when all studies were combined (RR, 0.86; 95% CI, 0.73-1.01). Bleeding of any severity (RR, 0.70; 95% CI, 0.57-0.86) and intracranial bleeding (RR, 0.46; 95% CI, 0.30-0.73) were less frequent with antiplatelet drugs than with warfarin. All-cause mortality was similar (RR, 0.99). Subgroup analysis suggested that major bleeding might be higher with warfarin than with aspirin in patients over 80 years old. Conclusion Elderly patients treated with aspirin or clopidogrel suffer less any-severity bleeding but have a risk of major bleeding similar to that of oral anticoagulants, with the exception of intracranial bleeding.

**16. Is echocardiography valid and reproducible in patients with atrial fibrillation? A systematic review.**

**Author(s):** Kotecha, Dipak; Mohamed, Mohamed; Shantsila, Eduard; Popescu, Bogdan A; Steeds, Richard P

**Source:** Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology; Apr 2017

**Publication Type(s):** Journal Article

Available in full text at Europace - from Highwire Press

**Abstract:**AimsEchocardiography is vital in the routine assessment and management of atrial fibrillation (AF). We performed a systematic review of the validity and reproducibility of echocardiographic left ventricular systolic and diastolic function in AF, and optimal acquisition methods.Methods and resultsOnline databases were searched for studies in patients with AF at the time of echocardiography (1960 to August 2015), prospectively registered with PROSPERO (CRD42015025297). The systematic review included 32 studies from 3 066 search results (1 968 patients with AF). Average age was 67 years, 33% were women, mean LVEF 53% (±10%), and average E/e' 11.7 (±2.7). Data on the validity and reproducibility of systolic indices were extremely limited. In contrast, diastolic parameters demonstrated correlation with invasive filling pressure and adequate reproducibility: E/e' (n = 444) r = 0.47 to 0.79; IVRT (n = 177) r = -0.70 to -0.95; E/Vp` (n = 55) r = 0.63 and 0.65; pulmonary vein diastolic flow (n = 67) r = -0.80 and -0.91. Elevated E/e' (>15) was associated with functional capacity, quality of life, and impaired prognosis. For optimal acquisition in AF patients, cardiac cycles with controlled heart rate (<100 beats/min) and similar preceding and pre-preceding RR intervals are required. Cardiac cycle length and equivalence were more important than the number of beats averaged.ConclusionWith careful selection of appropriate cardiac cycles, echocardiography is a valid tool to identify diastolic dysfunction in AF, and E/e' is an independent marker of clinical status and adverse prognosis. However, data on systolic function was extremely limited and requires further prospective study and assessment of variability in clinical practice.

**17. Link Between Non-Alcoholic Fatty Liver Disease and Atrial Fibrillation: A Systematic Review and Meta-Analysis.**

**Author(s):** Minhas, Abdul M; Usman, Muhammad Shariq; Khan, Muhammad S; Fatima, Kaneez; Mangi, Muhammad A; Illovsky, Michael A

**Source:** Cureus; Apr 2017; vol. 9 (no. 4); p. e1142

**Publication Type(s):** Journal Article Review

**Abstract:**Association between non-alcoholic fatty liver disease (NAFLD) and various cardiovascular diseases has been demonstrated previously. Recent clinical studies have shown that increased circulating levels of γ glutamyl transpeptidase and liver transaminase, markers which are elevated in NAFLD, increase the risk of new-onset atrial fibrillation. We conducted a systematic review and meta-analysis of the available evidence to establish the possible association of increased chances of atrial fibrillation in patients with NAFLD. We extensively searched the PubMed, EMBASE, Cochrane Library, ISI Web of Science and Scopus databases to identify all possible studies that investigated the possible association of NAFLD with atrial fibrillation. Random effect models were used to pool the data between NAFLD and non-NAFLD group. I2 testing was done to assess the heterogeneity of the included studies. Our primary outcome was atrial fibrillation. A total of three studies including 1044 patients in the NAFLD arm and 1016 in the placebo arm were included. On pooled analysis, it was observed that patients with NAFLD had 2.5 times significantly higher chance (OR = 2.47, CI = 1.30-4.66, p = 0.005) of developing new-onset atrial fibrillation. Our meta-analysis identifies the paucity of high-quality evidence regarding the association between NAFLD and atrial fibrillation. More studies are needed to confirm the link between NAFLD and atrial fibrillation.

### 18. Digoxin versus placebo, no intervention, or other medical interventions for atrial fibrillation and atrial flutter: a protocol for a systematic review with meta-analysis and Trial Sequential Analysis.

**Author(s):** Sethi, Naqash J; Safi, Sanam; Feinberg, Joshua; Nielsen, Emil E; Gluud, Christian; Jakobsen, Janus C

**Source:** Systematic reviews; Apr 2017; vol. 6 (no. 1); p. 71

Available in full text at Systematic Reviews - from BioMed Central

**Abstract:**BACKGROUNDAtrial fibrillation is the most common arrhythmia of the heart with a prevalence of approximately 2% in the western world. Atrial flutter, another arrhythmia, occurs less often with an incidence of approximately 200,000 new patients per year in the USA. Patients with atrial fibrillation and atrial flutter have an increased risk of death and morbidities. In the management of atrial fibrillation and atrial flutter, it is often necessary to use medical interventions to lower the heart rate. Lowering the heart rate may theoretically prevent the development of heart failure and tachycardia-mediated cardiomyopathy. The evidence on the benefits and harms of digoxin compared with placebo or with other medical interventions is unclear. This protocol for a systematic review aims at identifying the beneficial and harmful effects of digoxin compared with placebo, no intervention, or with other medical interventions for atrial fibrillation and atrial flutter.METHODSThis protocol for a systematic review was conducted following the recommendations of Cochrane and the eight-step assessment procedure suggested by Jakobsen and colleagues. We plan to include all relevant randomised clinical trials comparing digoxin with placebo, no intervention, or with other medical interventions. We plan to search the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, LILACS, Science Citation Index Expanded on Web of Science, and BIOSIS to identify relevant trials. Any eligible trial will be assessed and classified as either at high risk of bias or low risk of bias, and our primary conclusions will be based on trials with low risk of bias. We will perform our meta-analyses of the extracted data using Review Manager 5.3 and Trial Sequential Analysis ver. 0.9.5.5 beta. For both our primary and secondary outcomes, we will create a 'Summary of Findings' table based on GRADE assessments of the quality of the evidence.DISCUSSIONThe results of this systematic review have the potential to benefit millions of patients worldwide as well as healthcare economy.SYSTEMATIC REVIEW REGISTRATIONPROSPERO CRD42016052935.

### 19. Predictive performance of the CHA2DS2-VASc rule in atrial fibrillation: a systematic review and meta-analysis.

**Author(s):** van Doorn, S; Debray, T P A; Kaasenbrood, F; Hoes, A W; Rutten, F H; Moons, K G M; Geersing, G J

**Source:** Journal of thrombosis and haemostasis : JTH; Apr 2017

**Publication Type(s):** Journal Article

**Abstract:**Essentials The widely recommended CHA2DS2-VASc shows conflicting results in contemporary validation studies. We performed a systematic review and meta-analysis of 19 studies validating CHA2DS2-VASc. There was high heterogeneity in stroke risks for different CHA2DS2-VASc scores. This was not

explained by differences between setting of care, or by performing meta-regression.SUMMARYBackground The CHA2DS2-VASc decision rule is widely recommended for estimating stroke risk in patients with atrial fibrillation (AF), although validation studies show ambiguous and conflicting results. Objectives To: (i) review existing studies validating CHA2DS2-VASc in AF patients who are not (yet) anticoagulated; (ii) meta-analyze estimates of stroke risk per score; and (iii) explore sources of heterogeneity across the validation studies. Methods We performed a systematic literature review and random effects meta-analysis of studies externally validating CHA2DS2-VASc in AF patients not receiving anticoagulants. To explore between-study heterogeneity in stroke risk, we stratified studies to the clinical setting in which patient enrollment started, and performed meta-regression. Results In total, 19 studies were evaluated, with over two million person-years of follow-up. In studies recruiting AF patients in hospitals, stroke risks for scores of 0, 1 and 2 were 0.4% (approximate 95% prediction interval [PI] 0.2-3.2%), 1.2% (95% PI 0.1-3.8%), and 2.2% (95% PI 0.03-7.8%), respectively. These were consistently higher than those in studies recruiting patients from the open general population, with risks of 0.2% (95% PI 0.0-0.9%), 0.7% (95% PI 0.3-1.2%) and 1.5% (95% PI 0.4-3.3%) for scores of 0, 1, and 2, respectively. Heterogeneity, as reflected by the wide PIs, could not be fully explained by meta-regression. Conclusions Studies validating CHA2DS2-VASc show high heterogeneity in predicted stroke risks for different scores.

**20. Rivaroxaban Versus Dabigatran or Warfarin in Real-World Studies of Stroke Prevention in Atrial Fibrillation: Systematic Review and Meta-Analysis.**

**Author(s):** Bai, Ying; Deng, Hai; Shantsila, Alena; Lip, Gregory Y H

**Source:** Stroke; Apr 2017; vol. 48 (no. 4); p. 970-976

**Abstract:**BACKGROUND AND PURPOSEThis study was designed to evaluate the effectiveness and safety of rivaroxaban in real-world practice compared with effectiveness and safety of dabigatran or warfarin for stroke prevention in atrial fibrillation through meta-analyzing observational studies.METHODSSeventeen studies were included after searching in PubMed for studies reporting the comparative effectiveness and safety of rivaroxaban versus dabigatran (n=3), rivaroxaban versus Warfarin (n=11), or both (n=3) for stroke prevention in atrial fibrillation.RESULTSOverall, the risks of stroke/systematic thromboembolism with rivaroxaban were similar when compared with those with dabigatran (stroke/thromboembolism: hazard ratio, 1.02; 95% confidence interval, 0.91-1.13; I2=70.2%, N=5), but were significantly reduced when compared with those with warfarin (hazard ratio, 0.75; 95% confidence interval, 0.64-0.85; I2=45.1%, N=9). Major bleeding risk was significantly higher with rivaroxaban than with dabigatran (hazard ratio, 1.38; 95% confidence interval, 1.27-1.49; I2=26.1%, N=5), but similar to that with warfarin (hazard ratio, 0.99; 95% confidence interval, 0.91-1.07; I2=0.0%, N=6). Rivaroxaban was associated with increased all-cause mortality and gastrointestinal bleeding, but similar risk of acute myocardial infarction and intracranial hemorrhage when compared with dabigatran. When compared with warfarin, rivaroxaban was associated with similar risk of any bleeding, mortality, and acute myocardial infarction, but a higher risk of gastrointestinal bleeding and lower risk of intracranial hemorrhage.CONCLUSIONSIn this systematic review and meta-analysis, rivaroxaban was as effective as dabigatran, but was more effective than warfarin for the prevention of stroke/thromboembolism in atrial fibrillation patients. Major bleeding risk was significantly higher with rivaroxaban than with dabigatran, as was all-cause mortality and gastrointestinal bleeding. Rivaroxaban was comparable to warfarin for major bleeding, with an increased risk in gastrointestinal bleeding and decreased risk of intracranial hemorrhage.

**21. Is There an Obesity Paradox for Outcomes in Atrial Fibrillation? A Systematic Review and Meta-Analysis of Non-Vitamin K Antagonist Oral Anticoagulant Trials.**

**Author(s):** Proietti, Marco; Guiducci, Elisa; Cheli, Paola; Lip, Gregory Y H

**Source:** Stroke; Apr 2017; vol. 48 (no. 4); p. 857-866

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUND AND PURPOSEObesity is a risk factor for all-cause and cardiovascular death but, despite this, an inverse relationship between overweight or obesity and a better cardiovascular prognosis in long-term follow-up studies has been observed; this phenomenon, described as obesity paradox, has also been found evident in atrial fibrillation cohorts.METHODSWe performed a systematic review on the relationship between body mass index and major adverse outcomes in atrial fibrillation patients. Moreover, we provided a meta-analysis of non-vitamin K antagonist oral anticoagulants (NOACs) trials.RESULTSAn obesity paradox was found for cardiovascular death and all-cause death in the subgroup analyses of randomized trial cohorts; however, observational studies fail to show this relationship. From the meta-analysis of NOAC trials, a significant obesity paradox was found, with both overweight and obese patients reporting a lower risk for

stroke/systemic embolic event (odds ratio [OR], 0.75; 95% confidence interval [CI], 0.66-0.84 and OR, 0.62; 95% CI, 0.54-0.70, respectively). For major bleeding, only obese patients were at lower risk compared with normal weight patients (OR, 0.84; 95% CI, 0.72-0.98). A significant treatment effect of NOACs was found in normal weight patients, both for stroke/systemic embolic event (OR, 0.66; 95% CI, 0.56-0.78) and for major bleeding (OR, 0.72; 95% CI, 0.54-0.95). Major bleeding risk was lower in overweight patients treated with NOACs (OR, 0.84; 95% CI, 0.71-1.00).CONCLUSIONSThere may be an obesity paradox in atrial fibrillation patients, particularly for all-cause and cardiovascular death outcomes. An obesity paradox was also evident for stroke/systemic embolic event outcome in NOAC trials, with a treatment effect favoring NOACs over warfarin for both efficacy and safety that was significant only for normal weight patients.

**22. Comparison of catheter ablation for paroxysmal atrial fibrillation between cryoballoon and radiofrequency: a meta-analysis.**

**Author(s):** Chen, Chao-Feng; Gao, Xiao-Fei; Duan, Xu; Chen, Bin; Liu, Xiao-Hua; Xu, Yi-Zhou

**Source:** Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing; Apr 2017; vol. 48 (no. 3); p. 351-366

**Publication Type(s):** Journal Article Review

**Abstract:**PURPOSEThe present systematic review and meta-analysis aimed to assess and compare the safety and efficacy of radiofrequency (RF) and cryoballoon (CB) ablation for paroxysmal atrial fibrillation (PAF). RF and CB ablation are two frequently used methods for pulmonary vein isolation in PAF, but which is a better choice for PAF remains uncertain.METHODSA systematic review was conducted in Medline, PubMed, Embase, and Cochrane Library. All trials comparing RF and CB ablation were screened and included if the inclusion criteria were met.RESULTSA total of 38 eligible studies, 9 prospective randomized or randomized controlled trials (RCTs), and 29 non- RCTs were identified, adding up to 15,496 patients. Pool analyses indicated that CB ablation was more beneficial in terms of procedural time [standard mean difference = -0.58; 95% confidence interval (CI), -0.85 to -0.30], complications without phrenic nerve injury (PNI) [odds ratio (OR) = 0.79; 95% CI, 0.67-0.93; I 2 = 16%], and recrudescence (OR = 0.83; 95% CI, 0.70-0.97; I 2 = 63%) for PAF; however, the total complications of CB was higher than RF. The subgroup analysis found that, compared with non-contact force radiofrequency (non-CF-RF), both first-generation cryoballoon (CB1) and second-generation cryoballoon (CB2) ablation could reduce complications with PNI, procedural time, and recrudescence. However, the safety and efficacy of CB2 was similar to those of CF-RF.CONCLUSIONAvailable overall and subgroup data suggested that both CB1 and CB2 were more beneficial than RF ablation, and the main advantages were reflected in comparing them with non-CF-RF. However, CF-RF and CB2 showed similar clinical benefits.

**23. Predictive Role of Coagulation, Fibrinolytic, and Endothelial Markers in Patients with Atrial Fibrillation, Stroke, and Thromboembolism: A Meta-Analysis, Meta-Regression, and Systematic Review.**

**Author(s):** Weymann, Alexander; Sabashnikov, Anton; Ali-Hasan-Al-Saegh, Sadeq; Popov, Aron-Frederik; Jalil Mirhosseini, Seyed; Baker, William L; Lotfaliani, Mohammadreza; Liu, Tong; Dehghan, Hamidreza; Yavuz, Senol; de Oliveira Sá, Michel Pompeu Barros; Jang, Jae-Sik; Zeriouh, Mohamed; Meng, Lei; D'Ascenzo, Fabrizio; Deshmukh, Abhishek J; Biondi-Zoccai, Guiseppe; Dohmen, Pascal M; Calkins, Hugh; Cardiac Surgery And Cardiology-Group Imcsc-Group, Integrated Meta-Analysis Of Cardiac

**Source:** Medical science monitor basic research; Mar 2017; vol. 23 ; p. 97-140

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUND The pathophysiological mechanism associated with the higher prothrombotic tendency in atrial fibrillation (AF) is complex and multifactorial. However, the role of prothrombotic markers in AF remains inconclusive. MATERIAL AND METHODS We conducted a meta-analysis of observational studies evaluating the association of coagulation activation, fibrinolytic, and endothelial function with occurrence of AF and clinical adverse events. A comprehensive subgroup analysis and meta-regression was performed to explore potential sources of heterogeneity. RESULTS A literature search of major databases retrieved 1703 studies. After screening, a total of 71 studies were identified. Pooled analysis showed the association of coagulation markers (D-dimer (weighted mean difference (WMD) =197.67 and p<0.001), fibrinogen (WMD=0.43 and p<0.001), prothrombin fragment 1-2 (WMD=0.53 and p<0.001), antithrombin III (WMD=23.90 and p=0.004), thrombin-antithrombin (WMD=5.47 and p=0.004)); fibrinolytic markers (tissue-type plasminogen activator (t-PA) (WMD=2.13 and p<0.001), plasminogen activator inhibitor (WMD=11.44 and p<0.001), fibrinopeptide-A (WMD=4.13 and p=0.01)); and endothelial markers (von Willebrand factor (WMD=27.01 and p<0.001) and soluble thrombomodulin (WMD=3.92 and p<0.001)) with AF.

CONCLUSIONS The levels of coagulation, fibrinolytic, and endothelial markers have been reported to be significantly higher in AF patients than in SR patients.

**24. Systematic review and meta-analysis on the impact of pre-operative atrial fibrillation on short- and long-term outcomes after aortic valve replacement.**

**Author(s):** Saxena, Akshat; Virk, Sohaib A; Bowman, Sebastian; Bannon, Paul G

**Source:** The Journal of cardiovascular surgery; Mar 2017

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUNDThis systematic review and meta-analysis was performed to evaluate the impact of preoperative atrial fibrillation (preAF) on early and late outcomes after aortic valve replacement (AVR).METHODSMedline, EMBASE, and CENTRAL were systematically searched for studies that reported AVR outcomes according to the presence or absence of preAF. Data were independently extracted by two investigators; a meta-analysis was conducted according to predefined clinical endpoints. Studies including patients undergoing concomitant atrial fibrillation surgery were excluded.RESULTSSix observational studies with 8 distinct AVR cohorts (AVR ± concomitant surgery) met criteria for inclusion, including a total of 6693 patients. Of these, 1014 (15%) presented with preAF. Overall, peri-operative mortality was increased in patients with preAF (odds ratio [OR] 2.33; 95% CI, 1.48 - 3.67; p<0.001). Subgroup analysis of patients undergoing isolated AVR also demonstrated preAF as a risk factor for peri-operative mortality (OR 2.49; 95% CI, 1.57-3.95; p<0.001). PreAF was also associated with acute renal failure (OR 1.42; 95% CI, 1.07-1.89; p=0.02) but not stroke (OR 1.11; 95% CI, 0.59 - 2.12; p=0.74). Late mortality was significantly higher in patients with preAF (hazard ratio [HR] 1.75; 95% CI, 1.33-2.30; p<0.001). This relationship remained true when only patients who underwent isolated AVR were analyzed (HR 1.97; 95% CI, 1.11-3.51; p=0.02).CONCLUSIONSPreAF is associated with an increased risk of early- and late-mortality after AVR. These data support the more widespread utilization of concomitant AF ablation.

**25. Platelets Cellular and Functional Characteristics in Patients with Atrial Fibrillation: A Comprehensive Meta-Analysis and Systematic Review.**

**Author(s):** Weymann, Alexander; Ali-Hasan-Al-Saegh, Sadeq; Sabashnikov, Anton; Popov, Aron-Frederik; Mirhosseini, Seyed Jalil; Nombela-Franco, Luis; Testa, Luca; Lotfaliani, Mohammadreza; Zeriouh, Mohamed; Liu, Tong; Dehghan, Hamidreza; Yavuz, Senol; de Oliveira Sá, Michel Pompeu Barros; Baker, William L; Jang, Jae-Sik; Gong, Mengqi; Benedetto, Umberto; Dohmen, Pascal M; D'Ascenzo, Fabrizio; Deshmukh, Abhishek J; Biondi-Zoccai, Giuseppe; Calkins, Hugh; Stone, Gregg W; Surgery And Cardiology-Group Imcsc-Group, Integrated Meta-Analysis Of Cardiac

**Source:** Medical science monitor basic research; Mar 2017; vol. 23 ; p. 58-86

**Publication Type(s):** Journal Article

**Abstract:**BACKGROUND This systematic review with meta-analysis aimed to determine the strength of evidence for evaluating the association of platelet cellular and functional characteristics including platelet count (PC), MPV, platelet distribution width (PDW), platelet factor 4, beta thromboglobulin (BTG), and p-selectin with the occurrence of atrial fibrillation (AF) and consequent stroke. MATERIAL AND METHODS We conducted a meta-analysis of observational studies evaluating platelet characteristics in patients with paroxysmal, persistent and permanent atrial fibrillations. A comprehensive subgroup analysis was performed to explore potential sources of heterogeneity. RESULTS Literature search of all major databases retrieved 1,676 studies. After screening, a total of 73 studies were identified. Pooled analysis showed significant differences in PC (weighted mean difference (WMD)=-26.93 and p<0.001), MPV (WMD=0.61 and p<0.001), PDW (WMD=-0.22 and p=0.002), BTG (WMD=24.69 and p<0.001), PF4 (WMD=4.59 and p<0.001), and p-selectin (WMD=4.90 and p<0.001). CONCLUSIONS Platelets play a critical and precipitating role in the occurrence of AF. Whereas distribution width of platelets as well as factors of platelet activity was significantly greater in AF patients compared to SR patients, platelet count was significantly lower in AF patients.

**26. Bleeding events associated with a low dose (110 mg) versus a high dose (150 mg) of dabigatran in patients treated for atrial fibrillation: a systematic review and meta-analysis.**

**Author(s):** Bundhun, Pravesh Kumar; Chaudhary, Nabin; Yuan, Jun

**Source:** BMC cardiovascular disorders; Mar 2017; vol. 17 (no. 1); p. 83

**Publication Type(s):** Journal Article

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**Abstract:**BACKGROUNDThe newer oral anticoagulant dabigatran is considered to be more beneficial in patients with non-valvular Atrial Fibrillation (AF) when compared to warfarin. However, because bleeding events which are associated with a low dose (110 mg) versus a high dose (150 mg) of dabigatran have seldom been compared, we aimed to systematically solve this important issue through this meta-analysis.METHODSEnglish publications comparing 110 mg with 150 mg dabigatran in patients who were treated for AF were electronically searched through medical databases. Bleeding outcomes were the major clinical endpoints to be assessed. Odds Ratios (OR) and 95% Confidence Intervals (CIs) for each subgroup were calculated and the main analysis was carried out by the latest version of the RevMan 5.3 software.RESULTSTwenty-nine thousand two hundred and sixty-four (29,264) patients were included in this meta-analysis. Fifteen thousand eight hundred and forty-eight (15,848) patients were treated with 110 mg dabigatran whereas 13,416 patients were treated with 150 mg dabigatran. 110 mg dabigatran was associated with a significantly lower rate of minor bleeding (OR: 1.19, 95% CI: 1.10-1.27; $P < 0.00001$). A similar rate of fatal and major bleeding was observed with both dosages (OR: 1.12, 95% CI: 0.69-1.82; $P = 0.65$) and (OR: 1.09, 95% CI: 0.86-1.37; $P = 0.49$) respectively. However, ischemic stroke insignificantly favored a higher dose of dabigatran, (OR: 0.77, 95% CI: 0.51-1.16; $P = 0.21$). In addition, this analysis showed mortality to significantly favor 150 mg of dabigatran (OR: 0.41, 95% CI: 0.34-0.50; $P < 0.00001$).CONCLUSIONNo significant differences in major and fatal bleedings were observed with 110 mg versus 150 mg dabigatran. However, 110 mg dabigatran was associated with a significantly lower risk of minor bleeding. These results should further be confirmed in future trials.

### 27. Patient values and preferences for antithrombotic therapy in atrial fibrillation. A Narrative Systematic Review.

**Author(s):** Loewen, Peter S; Ji, Angela Tianshu; Kapanen, Anita; McClean, Alison

**Source:** Thrombosis and haemostasis; Mar 2017

**Publication Type(s):** Journal Article

**Abstract:**Guidelines recommend that patients' values and preferences should be considered when selecting stroke prevention therapy for atrial fibrillation (SPAF). However, doing so is difficult, and tools to assist clinicians are sparse. We performed a narrative systematic review to provide clinicians with insights into the values and preferences of AF patients for SPAF antithrombotic therapy. Narrative systematic review of published literature from database inception.RESEARCH QUESTIONS1) What are patients' AF and SPAF therapy values and preferences? 2) How are SPAF therapy values and preferences affected by patient factors? 3) How does conveying risk information affect SPAF therapy preferences? and 4) What is known about patient values and preferences regarding novel oral anticoagulants (NOACs) for SPAF? Twenty-five studies were included. Overall study quality was moderate. Severe stroke was associated with the greatest disutility among AF outcomes and most patients value the stroke prevention efficacy of therapy more than other attributes. Utilities, values, and preferences about other outcomes and attributes of therapy are heterogeneous and unpredictable. Patients' therapy preferences usually align with their values when individualised risk information is presented, although divergence from this is common. Patients value the attributes of NOACs but frequently do not prefer NOACs over warfarin when all therapy-related attributes are considered. In conclusion, patients' values and preferences for SPAF antithrombotic therapy are heterogeneous and there is no substitute for directly clarifying patients' individual values and preferences. Research using choice modelling and tools to help clinicians and patients clarify their SPAF therapy values and preferences are needed.

### 28. The effects of rhythm control strategies versus rate control strategies for atrial fibrillation and atrial flutter: a protocol for a systematic review with meta-analysis and Trial Sequential Analysis.

**Author(s):** Sethi, Naqash J; Safi, Sanam; Nielsen, Emil E; Feinberg, Joshua; Gluud, Christian; Jakobsen, Janus C

**Source:** Systematic reviews; Mar 2017; vol. 6 (no. 1); p. 47

**Publication Type(s):** Journal Article

Available in full text at Systematic Reviews - from BioMed Central

**Abstract:**BACKGROUNDAtrial fibrillation is the most common arrhythmia of the heart with a prevalence of approximately 2% in the western world. Atrial flutter, another arrhythmia, occurs less often with an incidence of

approximately 200,000 new patients per year in the USA. Patients with atrial fibrillation and atrial flutter have an increased risk of death and morbidities. The management of atrial fibrillation and atrial flutter is often based on interventions aiming at either a rhythm control strategy or a rate control strategy. The evidence on the comparable effects of these strategies is unclear. This protocol for a systematic review aims at identifying the best overall treatment strategy for atrial fibrillation and atrial flutter.METHODSThis protocol for a systematic review was performed following the recommendations of the Cochrane Collaboration and the eight-step assessment procedure suggested by Jakobsen and colleagues. We plan to include all relevant randomised clinical trials assessing the effects of any rhythm control strategy versus any rate control strategy. We plan to search the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, LILACS, Science Citation Index Expanded on Web of Science, and BIOSIS to identify relevant trials. Any eligible trial will be assessed and classified as either high risk of bias or low risk of bias, and our conclusions will be based on trials with low risk of bias. The analyses of the extracted data will be performed using Review Manager 5 and Trial Sequential Analysis. For both our primary and secondary outcomes, we will create a 'Summary of Findings' table and use GRADE assessment to assess the quality of the evidence.DISCUSSIONThe results of this systematic review have the potential to benefit thousands of patients worldwide as well as healthcare systems and healthcare economy.SYSTEMATIC REVIEW REGISTRATIONPROSPERO CRD42016051433.

**29. Oral anticoagulants for primary prevention, treatment and secondary prevention of venous thromboembolic disease, and for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis and cost-effectiveness analysis.**

**Author(s):** Sterne, Jonathan Ac; Bodalia, Pritesh N; Bryden, Peter A; Davies, Philippa A; López-López, Jose A; Okoli, George N; Thom, Howard Hz; Caldwell, Deborah M; Dias, Sofia; Eaton, Diane; Higgins, Julian Pt; Hollingworth, Will; Salisbury, Chris; Savović, Jelena; Sofat, Reecha; Stephens-Boal, Annya; Welton, Nicky J; Hingorani, Aroon D

**Source:** Health technology assessment (Winchester, England); Mar 2017; vol. 21 (no. 9); p. 1-386

**Publication Type(s):** Meta-analysis

**Abstract:**BACKGROUNDWarfarin is effective for stroke prevention in atrial fibrillation (AF), but anticoagulation is underused in clinical care. The risk of venous thromboembolic disease during hospitalisation can be reduced by low-molecular-weight heparin (LMWH): warfarin is the most frequently prescribed anticoagulant for treatment and secondary prevention of venous thromboembolism (VTE). Warfarin-related bleeding is a major reason for hospitalisation for adverse drug effects. Warfarin is cheap but therapeutic monitoring increases treatment costs. Novel oral anticoagulants (NOACs) have more rapid onset and offset of action than warfarin, and more predictable dosing requirements.OBJECTIVETo determine the best oral anticoagulant/s for prevention of stroke in AF and for primary prevention, treatment and secondary prevention of VTE.DESIGNFour systematic reviews, network meta-analyses (NMAs) and cost-effectiveness analyses (CEAs) of randomised controlled trials.SETTINGHospital (VTE primary prevention and acute treatment) and primary care/anticoagulation clinics (AF and VTE secondary prevention).PARTICIPANTSPatients eligible for anticoagulation with warfarin (stroke prevention in AF, acute treatment or secondary prevention of VTE) or LMWH (primary prevention of VTE).INTERVENTIONSNOACs, warfarin and LMWH, together with other interventions (antiplatelet therapy, placebo) evaluated in the evidence network.MAIN OUTCOME MEASURESEfficacy  Stroke, symptomatic VTE, symptomatic deep-vein thrombosis and symptomatic pulmonary embolism. Safety  Major bleeding, clinically relevant bleeding and intracranial haemorrhage. We also considered myocardial infarction and all-cause mortality and evaluated cost-effectiveness.DATA SOURCESMEDLINE and PREMEDLINE In-Process & Other Non-Indexed Citations, EMBASE and The Cochrane Library, reference lists of published NMAs and trial registries. We searched MEDLINE and PREMEDLINE In-Process & Other Non-Indexed Citations, EMBASE and The Cochrane Library. The stroke prevention in AF review search was run on the 12 March 2014 and updated on 15 September 2014, and covered the period 2010 to September 2014. The search for the three reviews in VTE was run on the 19 March 2014, updated on 15 September 2014, and covered the period 2008 to September 2014.REVIEW METHODSTwo reviewers screened search results, extracted and checked data, and assessed risk of bias. For each outcome we conducted standard meta-analysis and NMA. We evaluated cost-effectiveness using discrete-time Markov models.RESULTSApixaban (Eliquis®, Bristol-Myers Squibb, USA; Pfizer, USA) [5 mg bd (twice daily)] was ranked as among the best interventions for stroke prevention in AF, and had the highest expected net benefit. Edoxaban (Lixiana®, Daiichi Sankyo, Japan) [60 mg od (once daily)] was ranked second for major bleeding and all-cause mortality. Neither the clinical effectiveness analysis nor the CEA provided strong evidence that NOACs should replace postoperative LMWH in primary prevention of VTE. For acute treatment and secondary prevention of VTE, we found little evidence that NOACs offer an efficacy advantage over warfarin, but the risk of bleeding complications was lower for some NOACs than for warfarin. For a willingness-to-pay threshold of

> £5000, apixaban (5 mg bd) had the highest expected net benefit for acute treatment of VTE. Aspirin or no pharmacotherapy were likely to be the most cost-effective interventions for secondary prevention of VTE: our results suggest that it is not cost-effective to prescribe NOACs or warfarin for this indication.CONCLUSIONSNOACs have advantages over warfarin in patients with AF, but we found no strong evidence that they should replace warfarin or LMWH in primary prevention, treatment or secondary prevention of VTE.LIMITATIONSThese relate mainly to shortfalls in the primary data: in particular, there were no head-to-head comparisons between different NOAC drugs.FUTURE WORKCalculating the expected value of sample information to clarify whether or not it would be justifiable to fund one or more head-to-head trials.STUDY REGISTRATIONThis study is registered as PROSPERO CRD42013005324, CRD42013005331 and CRD42013005330.FUNDINGThe National Institute for Health Research Health Technology Assessment programme.

**30. Adjunctive ablation strategies improve the efficacy of pulmonary vein isolation in non-paroxysmal atrial fibrillation: a systematic review and meta-analysis.**

**Author(s):** Afzal, Muhammad R; Samanta, Anweshan; Chatta, Jawaria; Ansari, Brihh; Atherton, Sam; Sabzwari, Syed; Turagam, Mohit; Lakkireddy, Dhanunjaya; Houmsse, Mahmoud

**Source:** Expert review of cardiovascular therapy; Mar 2017; vol. 15 (no. 3); p. 227-235

**Publication Type(s):** Meta-analysis Journal Article Review

**Abstract:**BACKGROUNDPulmonary vein (PV) isolation (PVI) has suboptimal outcomes in patients with non-paroxysmal atrial fibrillation (AF). Adjunctive strategies employed to ablate non-PV triggers have shown favorable outcomes.AIMSTo delineate the incremental benefit of adjunctive ablation in patients with non-paroxysmal AF through a meta-analysis.METHODS AND RESULTSDatabase searches through August 2016 identified five non-randomized and seven randomized controlled trials (enrolling 1694 patients). The adjunctive strategies employed for non-PV ablation included focal impulse and rotor modulation; empirical linear lines, ablation of complex fractionated atrial electrograms and ganglionated plexi. The risk ratio (RR) for AF recurrence, calculated with random effects meta-analysis showed a 36% reduction of AF recurrence at a median follow up of 12 months (RR: 0.64, 95% Confidence interval: 0.48 to 0.85; p = 0.003). The benefits persisted during longer follow up when assessed in subgroup analysis.CONCLUSIONSAddition of adjunctive ablation to PVI improves outcomes.

**31. Body mass index, abdominal fatness, fat mass and the risk of atrial fibrillation: a systematic review and dose-response meta-analysis of prospective studies.**

**Author(s):** Aune, Dagfinn; Sen, Abhijit; Schlesinger, Sabrina; Norat, Teresa; Janszky, Imre; Romundstad, Pål; Tonstad, Serena; Riboli, Elio; Vatten, Lars J

**Source:** European journal of epidemiology; Mar 2017; vol. 32 (no. 3); p. 181-192

**Publication Type(s):** Journal Article Review

**Abstract:**Different adiposity measures have been associated with increased risk of atrial fibrillation, however, results have previously only been summarized for BMI. We therefore conducted a systematic review and meta-analysis of prospective studies to clarify the association between different adiposity measures and risk of atrial fibrillation. PubMed and Embase databases were searched up to October 24th 2016. Summary relative risks (RRs) were calculated using random effects models. Twenty-nine unique prospective studies (32 publications) were included. Twenty-five studies (83,006 cases, 2,405,381 participants) were included in the analysis of BMI and atrial fibrillation. The summary RR was 1.28 (95% confidence interval: 1.20-1.38, I2 = 97%) per 5 unit increment in BMI, 1.18 (95% CI: 1.12-1.25, I2 = 73%, n = 5) and 1.32 (95% CI: 1.16-1.51, I2 = 91%, n = 3) per 10 cm increase in waist and hip circumference, respectively, 1.09 (95% CI: 1.02-1.16, I2 = 44%, n = 4) per 0.1 unit increase in waist-to-hip ratio, 1.09 (95% CI: 1.02-1.16, I2 = 94%, n = 4) per 5 kg increase in fat mass, 1.10 (95% CI: 0.92-1.33, I2 = 90%, n = 3) per 10% increase in fat percentage, 1.10 (95% CI: 1.08-1.13, I2 = 74%, n = 10) per 5 kg increase in weight, and 1.08 (95% CI: 0.97-1.19, I2 = 86%, n = 2) per 5% increase in weight gain. The association between BMI and atrial fibrillation was nonlinear, p nonlinearity < 0.0001, with a stronger association at higher BMI levels, however, increased risk was observed even at a BMI of 22-24 compared to 20. In conclusion, general and abdominal adiposity and higher body fat mass increase the risk of atrial fibrillation.

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**March 07 2017, Volume 135, Issue 10**

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**May 21 2017, Volume 38, Issue 20**

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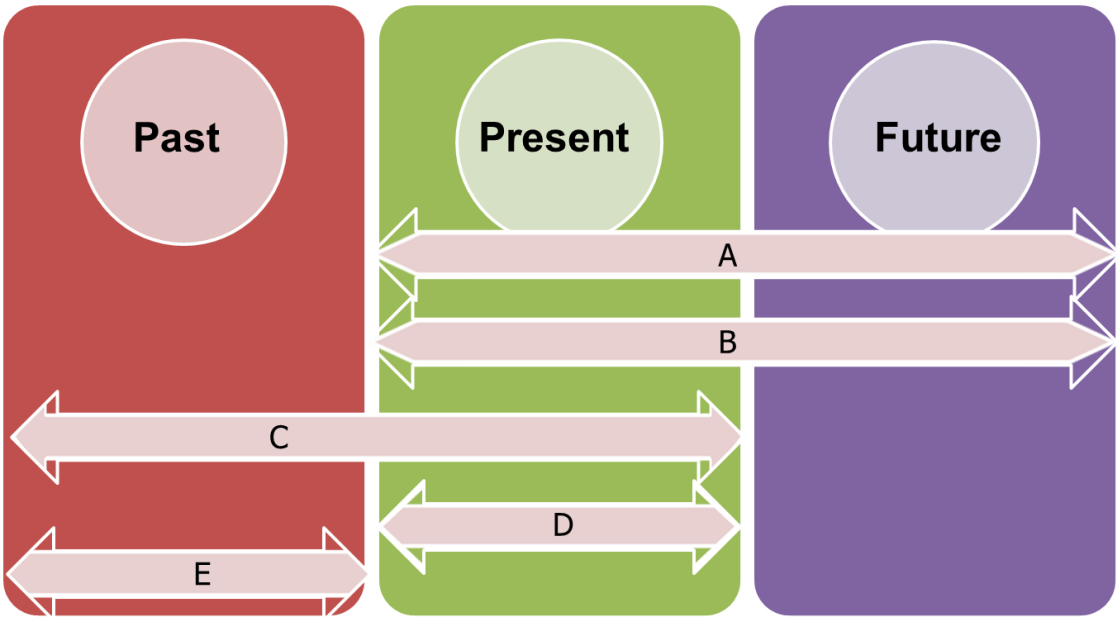


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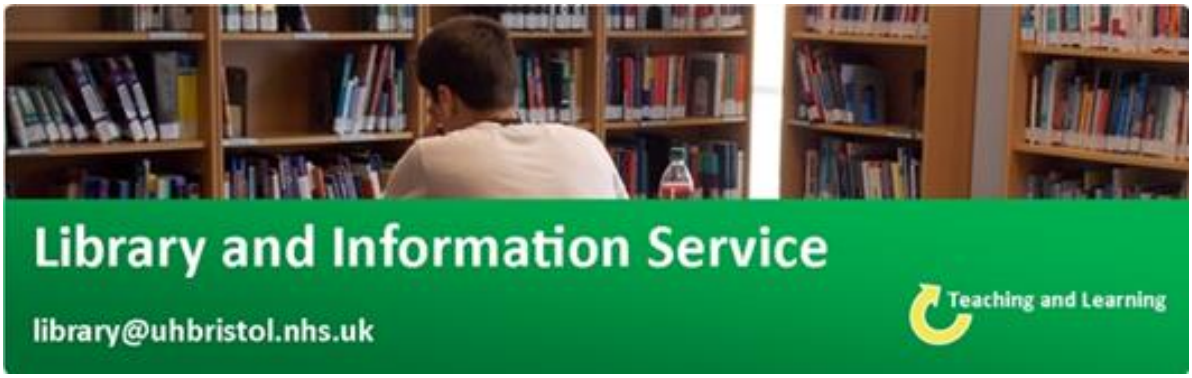


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