

## Improving the prescription of oral anticoagulants in atrial fibrillation

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## Supplementary Figure 1: Sample search strategy

Database: Ovid MEDLINE

- 1 Atrial Fibrillation/ or "atrial fibrillation".mp.
- 2 Atrial Flutter/ or "atrial flutter".mp.
- 3 ("auricular fibrillation" or "heart fibrillation" or "heart atrium fibrillation").ti,ab.
- 4 1 or 2 or 3
- 5 exp Anticoagulants/tu, th [Therapeutic Use, Therapy]
- 6 ((anticoagula\$ or antithrombotic\$1) adj2 (therapy or treatment or under-treatment or uptake or underus\$ or prescri\$ or prophylaxis or management or assessment or clinic\$1)).ti,ab.
- 7 exp Factor Xa Inhibitors/tu [Therapeutic Use]
- 8 exp Antithrombins/tu [Therapeutic Use]
- 9 ("direct thrombin inhibitor\$1" or DTI\$1 or "factor Xa inhibitor\$1" or "fxa inhibitor\$1" or NOAC\$1 or "novel oral anticoagulant\$1" or "new oral anticoagulant\$1" or "non-vitamin K antagonist\$1").ti,ab.
- 10 Dabigatran/ or ("dabigatran etexilate" or dabigatran or Pradaxa).ti,ab.
- 11 Rivaroxaban/ or (rivaroxaban or Xarelto).ti,ab.
- 12 (apixaban or Eliquis).ti,ab.
- 13 (edoxaban or Lixiana or Savaysa).ti,ab.
- 14 exp Coumarins/tu, th [Therapeutic Use, Therapy]
- 15 (4-hydroxyc?umarin\$1 or "Vitamin K antagonist" or VKA\$1).mp.
- 16 Warfarin/ or (warfarin or C?umadin or Jantoven or Marevan).ti,ab.
- 17 Dicumarol/ or (dic?umarol\$ or dic?umarin or Bis-Hydroxyc?umarin or bishydroxyc?umarin or Acadyl or Acavyl or Barac?umin or Cuma or Cumid or Dic?uma\$ or Dicumol or Dikumol or Dufalone or Kumoran or Melitoxi or Temparin or Trombosan).ti,ab.
- 18 Phenprocoumon/ or (phenproc?umon\$ or fenproc?umon or phenproc?umarol or Marc?umar or Falithrom).ti,ab.
- 19 Acenocoumarol/ or (acenoc?umarol or nic?umalon\$ or Sintrom or Ascumar or Acitrom or Mini-sintrom or Neo-sintrom or Sinkumar or Sinthrome or Sync?umar or Synthrom or Trombostop).ti,ab.
- 20 (tiocloamarol\$ or Apegmone).ti,ab.
- 21 Ethyl Biscoumacetate/ or ("ethyl bisc?umacetate" or carbethoxydic?umarol or ethyldic?umarol or dic?umacyl or Pelentan or Tromexan or Thrombolysan or Thrombarin or Neodic?umari\$).ti,ab.

- 22 ("indandione derivative\$1" or "non-c?umarin VKA\$1").ti,ab.
- 23 Phenindione/ or (phenindion\$ or fenindion\$ or Dindevan or Fenilin or Phenyline or Soluthrombine).ti,ab.
- 24 (clorindion\$ or chlorphenindone or Indaliton or Cumachlor).ti,ab.
- 25 (diphenadion\$ or difenadion\$ or diphenacin or Dipaxin or Diphac\$).ti,ab.
- 26 (fluindion\$ or Previscan).ti,ab.
- 27 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
- 28 Health Education/ or Health Promotion/ or "Outcome and Process Assessment (Health Care)"/ or Primary Health Care/ or Health Knowledge, Attitudes, Practice/ or "Outcome Assessment (Health Care)"/ or Program Evaluation/
- 29 Education, Professional/ or Education, Professional, Retraining/
- 30 Practice Patterns, Physicians'/ or Practice Guideline/ or Practice Patterns, Nurses'/ or Practice Guidelines as Topic/ or Practice Management/ or General Practice/ or Family Practice/
- 31 Medical Audit/ or Nursing Audit/
- 32 Reminder Systems/
- 33 exp Drug Therapy, Computer-Assisted/ed, mt, nu, td, ut [Education, Methods, Nursing, Trends, Utilization]
- 34 "Marketing of Health Services"/
- 35 Guideline Adherence/
- 36 Information Dissemination/ or "dissemination tool\$1".ti,ab.
- 37 Decision Support Techniques/ or Decision Support Systems, Clinical/
- 38 exp Decision Making/de [Drug Effects]
- 39 ("decision aid\$" or "decision support" or "decision making").ti,ab.
- 40 (intervention\$ or "local consensus process" or "education\$ material" or "education\$ outreach" or "education\$ meeting\$1" or "behavior?r\$ change\$1" or "perception change\$1" or "practice change\$1" or reminder\$1 or alert\$1 or "guideline\$1 implementation" or "guideline\$1 adherence" or "practice guideline\$1" or "practice pattern\$1" or audit or feedback or "evaluation feedback" or "information dissemination" or "software enhancement" or "software tool\$1" or "medical practice management software" or "stroke prevention" or "action and monitoring").ti,ab.
- 41 ((education\$ or behavior?r\$ or prescri\$ or persuasive or informational or marketing or professional\$ or physician\$1 or clinician\$1 or doctor\$1 or practitioner\$1 or GP\$1 or pharmacist\$1 or

multifaceted or multidisciplinary or "patient-mediated" or "patient-driven") adj2 (intervention\$1 or strateg\$ or program\$ or initiative\$1 or incentive\$1 or improv\$)).ti,ab.

42 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41

43 4 and 27 and 42

44 limit 43 to humans

Supplementary Figure 2: Risk of bias in RCTs using the Cochrane Risk of Bias Tool.

	Random sequence generation	Allocation concealment	Blinding of study participants	Blinding of investigators	Blinding of outcome assessment	Incomplete Primary outcome data	Incomplete Secondary outcome data	Handling missing data	Selective reporting
Bajorek, 2016 <sup>1</sup>	●	●	●	●	●	●	●	●	●
Arts, 2017 <sup>2</sup>	●	●	●	●	●	●	●	●	●
Holt, 2017 <sup>3</sup>	●	●	●	●	●	●	●	●	●

● = Low risk of bias; ● = Unclear; ● = Risk of bias

**Supplementary Figure 3: Risk of bias in controlled studies using an adjusted Cochrane Risk of Bias Tool.**

	1	2	3	4	5	6	7	8	9	10	11	12	13
Jackson, 2004 <sup>4</sup>	●	NA	NA	●	●	●	●	●	●	●	NA	●	●
Touchette, 2008 <sup>5</sup>	●	●	●	●	●	●	●	●	●	NA	NA	●	●
Hendriks, 2010 <sup>6</sup>	●	●	●	●	●	●	●	●	NA	●	NA	●	●
Boriani, 2012 <sup>7</sup>	●	NA	NA	●	●	●	●	●	●	NA	●	●	●
Cook, 2015 <sup>8</sup>	●	●	●	●	●	●	●	●	●	NA	NA	●	●

● = Low risk of bias; ● = Unclear; ● = Risk of bias; NA = not applicable

Criteria used:

1. How were different groups selected (e.g. from the same source, at the same time).
2. For historical controlled studies also consider if the two sets of patients are comparable.
3. For historical controlled studies also consider: 1. changes in the diagnostic criteria; 2. differences in concomitant standards of care over time (e.g. new guidelines).
4. Were different groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?
5. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?
6. Blinding of outcome assessment.
7. Was blinding of outcome assessment the same for all groups?
8. Incomplete primary outcome data.
9. Incomplete secondary outcome data.
10. Handling missing data (e.g. intention to treat).
11. Was follow-up time and method of follow-up the same in both groups?
12. Selective reporting (e.g. only certain outcomes, no adverse events).
13. Other sources of bias.

**Supplementary Figure 4: Risk of bias in cross-sectional studies using the NIH National Heart, Lung and Blood Institute Quality Assessment Tool for observational cohort and cross-sectional studies.**

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
<b>Falces, 2011<sup>9</sup></b>	✓	✓	CD	✓	x	NA	✓	✓	✓	x	✓	NR	✓	✓

✓ = YES; x = NO; CD = cannot determine; NA = not applicable; NR = not reported

Criteria used:

1. Was the study question or objective clearly stated?
2. Were eligibility/selection criteria for the study population pre-specified and clearly described?
3. Was the participation rate of eligible persons at least 50%?
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants?
5. Was a sample size justification, power description, or variance and effect estimates provided?
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
10. Was the exposure(s) assessed more than once over time?
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
12. Were the outcome assessors blinded to the exposure status of participants?
13. Was loss to follow-up after baseline 20% or less?
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

**Supplementary Figure 5: Risk of bias in before-after studies using an adapted form of the NIH National Heart, Lung and Blood Institute Quality Assessment Tool for before-after studies with no control group.**

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
<b>Sobreques, 2002</b> <sup>10</sup>	✓	x	✓	CD	NR	x	CD	✓	NR	✓	CD	✓	x	✓
<b>Lowdon, 2004</b> <sup>11</sup>	✓	CD	✓	CD	CD	✓	✓	x	CD	CD	NA	CD	x	✓
<b>Bajorek, 2005</b> <sup>12</sup>	✓	✓	x	x	✓	✓	✓	✓	CD	✓	✓	✓	x	✓
<b>Bo, 2007</b> <sup>13</sup>	✓	✓	x	✓	✓	✓	✓	✓	CD	✓	✓	✓	x	✓
<b>Coll-Vinent, 2007</b> <sup>14</sup>	✓	✓	✓	CD	CD	✓	✓	✓	CD	✓	✓	✓	x	✓
<b>Jackson, 2011</b> <sup>15</sup>	✓	✓	x	x	CD	✓	✓	✓	✓	✓	CD	✓	x	✓
<b>Robson, 2014</b> <sup>16</sup>	✓	✓	x	✓	CD	✓	✓	✓	CD	✓	NA	✓	✓	✓
<b>Oliveira, 2014</b> <sup>17</sup>	✓	✓	x	CD	CD	✓	CD	✓	NR	CD	x	x	x	✓
<b>Das, 2015</b> <sup>18</sup>	✓	✓	✓	x	CD	✓	✓	✓	NA	✓	✓	✓	x	✓
<b>Hsieh, 2016</b> <sup>19</sup>	✓	x	x	CD	CD	✓	✓	✓	CD	✓	CD	✓	✓	✓
<b>Wang, 2017</b> <sup>20</sup>	✓	✓	x	CD	CD	✓	✓	✓	CD	✓	✓	✓	x	NA

✓ = YES; x = NO; CD = cannot determine; NA = not applicable; NR = not reported

Criteria used:

1. Was the study question or objective clearly stated?
2. Were eligibility/selection criteria for the study population pre-specified and clearly described?
3. Were the participants in the study representative of those who would be eligible for the service/intervention in the general or clinical population of interest?
4. Were all eligible participants that met the pre-specified entry criteria enrolled?
5. Was the sample size sufficiently large to provide confidence in the findings?



6. Was the service/intervention clearly described and delivered consistently across the study population?
7. Was the duration of the intervention sufficient so that one could reasonably expect to see any changes in practice and/or behaviour?
8. Were the outcome measures pre-specified, clearly defined, valid, reliable, and assessed consistently across all study participants?
9. Were the people assessing the outcomes blinded to the participants' interventions?
10. Was the length of follow-up sufficient so that one could reasonably expect to capture any changes in practice and/or behaviour?
11. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?
12. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?
13. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?
14. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?

**Supplementary Table 1: Excluded studies**

<b>Study</b>	<b>Reason for exclusion</b>
Makowski 1994 <sup>21</sup>	Full text unavailable
Steffensen, 1997 <sup>22</sup>	Ineligible outcome
Gaughan, 2000 <sup>23</sup>	Not original data
Valeti, 2000 <sup>24</sup>	Full text unavailable
Batty, 2001 <sup>25</sup>	Ineligible outcome
O'Rourke 2001 <sup>26</sup>	Ineligible study design
Elliot, 2002 <sup>27</sup>	Ineligible outcome
Jackson, 2003 <sup>28</sup>	Not original data
Batty, 2004 <sup>29</sup>	Ineligible outcome
Alberts, 2004 <sup>30</sup>	Ineligible study design
Kiechl, 2004 <sup>31</sup>	Ineligible study design
Claes, 2005 <sup>32</sup>	Ineligible outcome
Wright, 2007 <sup>33</sup>	Ineligible outcome
Schwarz, 2009 <sup>34</sup>	Ineligible outcome
Albert, 2010 <sup>35</sup>	Ineligible outcome
Bishop, 2011 <sup>36</sup>	Ineligible outcome
Szabo, 2011 <sup>37</sup>	Ineligible population
Boriani, 2011 <sup>38</sup>	Not original data
Healicon, 2011 <sup>39</sup>	Full text unavailable
Hendriks, 2012 <sup>40</sup>	Ineligible population
Boriani, 2012 <sup>41</sup>	Not original data
Larsen, 2012 <sup>42</sup>	Full text unavailable
Skanes, 2013 <sup>43</sup>	Ineligible intervention
Samani, 2013 <sup>44</sup>	Ineligible outcome
Gadzhanova, 2013 <sup>45</sup>	Ineligible outcome

Arts, 2013 <sup>46</sup>	Ineligible study design
Jeng, 2013 <sup>47</sup>	Not original data
Beadles, 2014 <sup>48</sup>	Ineligible intervention
Po, 2014 <sup>49</sup>	Ineligible outcome
Grant, 2014 <sup>50</sup>	Ineligible outcome
Alkhalil, 2014 <sup>51</sup>	Full text unavailable
Skolarus, 2014 <sup>52</sup>	Ineligible outcome
Sibai, 2014 <sup>53</sup>	Ineligible study design
Das, 2014 <sup>54</sup>	Not original data
Fuenzalida, 2015 <sup>55</sup>	Ineligible outcome
Daacke, 2015 <sup>56</sup>	Full text unavailable
Akhavein, 2015 <sup>57</sup>	Full text unavailable
Garber, 2015 <sup>58</sup>	Ineligible study design
Zheng, 2016 <sup>59</sup>	Ineligible intervention
Eckman, 2016 <sup>60</sup>	Ineligible outcome
Eckman, 2016 <sup>61</sup>	Ineligible outcome
Abidi, 2016 <sup>62</sup>	Ineligible outcome
Lee, 2016 <sup>63</sup>	Ineligible study design
Rao, 2016 <sup>64</sup>	Ineligible study design
Willis, 2016 <sup>65</sup>	Ineligible study design
Czernik, 2016 <sup>66</sup>	Full text unavailable
Cloutier, 2016 <sup>67</sup>	Full text unavailable
Amiri, 2017 <sup>68</sup>	Ineligible outcome
Barmano, 2017 <sup>69</sup>	Ineligible outcome
Rose, 2017 <sup>70</sup>	Ineligible outcome
Karlsson, 2017 <sup>71</sup>	Ineligible study design
Virdee, 2017 <sup>72</sup>	Ineligible study design

**Supplementary Table 2: Outcome measures and results**

Author	Outcome measure	Baseline or pre-intervention % (n)	Follow-up or post-intervention % (n)	Group comparison	P-value
<b>RCTs</b>					
Bajorek et al. <sup>1</sup> Australia, 2016	a. Use of anticoagulants b. Proportion of patients recommended a different type of therapy c. Proportion of GPs agreeing with recommendations	<u>January-June 2013</u> <i>Control</i> a. (total n=187): 94.7% (177) <i>Intervention</i> a. (total n=206): 89.3% (184)	<u>12 month follow-up</u> <i>Control</i> a. Not reported <i>Intervention</i> a. (total n=206): 92.2% (190) b. 36.4% c. 75.2%	a. OACs in the intervention arm at baseline and follow-up	a. 0.02
Arts et al. <sup>2</sup> The Netherlands, 2017	a. Proportion of patients treated according to the Dutch guidelines. b. Proportion of patients on OACs at baseline and follow-up	<u>01/10/2013</u> <i>Control</i> a. (total n=235): 42% (99) b. 40% (94) <i>Intervention</i> a. (total n=496): 50% (248) b. 48% (238)	<u>01/09/2014</u> <i>Control</i> a. (Total n=259): 50% (130) b. 51% (132) <i>Intervention</i> a. (Total n=522): 55% (287) b. 60% (313)	a. between group difference at baseline: 8% between group difference at follow-up: 5% b. between group difference at baseline: 8% between group difference at follow-up: 9%	a. Chi sq. between group difference at baseline: 0.04 Chi sq. between group difference at follow-up: 0.23 a. Cluster analysis between groups: 0.21 b. Chi sq. between group difference at baseline: 0.05 Chi sq. between group difference at follow-up: 0.02

Author	Outcome measure	Baseline or pre-intervention % (n)	Follow-up or post-intervention % (n)	Group comparison	P-value
Holt et al. <sup>3</sup> UK, 2017	Proportion of patients eligible for OAC who were currently prescribed an OAC (CHADS <sub>2</sub> ≥ 2)	<u>20/02/2014</u> <i>Control</i> 61.9% (9.89) <i>Intervention</i> 63.5% (8.85)	<u>a. 6 month follow-up</u> <i>Control</i> 63.9% (SD 9.46) <i>Intervention</i> 66.3% (SD 9.25)  <u>b. 12 month follow-up</u> <i>Control: 67.8%</i> <i>Intervention: 65.9%</i>	<u>a. baseline to 6 months</u> adjusted for baseline prescribing mean difference [95% confidence interval]: 1.21% [-0.72 to 3.13]  <u>b. baseline to 12 month</u> adjusted for baseline prescribing mean difference [95% confidence interval]: 1.79% [-0.82 to 4.41]	<u>a. 0.213</u>  <u>b. 0.173</u>
<b>Controlled studies</b>					
Jackson et al. <sup>4</sup> Australia, 2004	a. Percentage of eligible patients receiving warfarin upon hospital admission b. Percentage of eligible patients receiving warfarin upon hospital discharge c. All prescriptions dispensed in area (DDDs per 1000 of population)	<i>Pre-intervention (01/02/2001 - 31/01/2002)</i> <i>Receiving warfarin:</i> <i>Intervention</i> <i>a. On admission</i> total 33% (n=81/245); high risk 33% (n=64/192); high risk without contraindications 39% (n=50/127); intermediate risk 30% (n=11/37) <i>b. On discharge</i> total 39% high risk 40% high risk without contraindications: 49% <i>c. Prescriptions dispensed</i> <i>Control region: 1127</i> <i>Intervention region: 1124</i>	<i>Post-intervention (01/02/2002 - 31/01/2003)</i> <i>Receiving warfarin:</i> <i>Intervention</i> <i>a. On admission</i> total 43% (n=67/157); high risk 46% (n=58/125); high risk without contraindications 53% (n=46/87); intermediate risk 36% (n=9/25) <i>b. On discharge</i> total 51% high risk 56% high risk interventions 64% <i>c. Prescriptions dispensed</i> <i>Control region: 1149</i> <i>Intervention region: 1191</i>	Performed comparisons between all different group combinations	<i>a. On admission (pre- to post-intervention)</i> total 0.05; high risk 0.02; high risk without contraindications 0.05; intermediate risk 0.60 <i>b. On discharge (pre- to post-intervention)</i> total <0.05; high risk <0.01; high risk without contraindications <0.05; <i>c. Dispensed prescriptions</i> Intervention region: pre- vs. post <0.001 Control region: pre- vs. post <0.001 Intervention vs control region pre-intervention: 0.34 Intervention vs control region post-intervention: <0.001

Author	Outcome measure	Baseline or pre-intervention % (n)	Follow-up or post-intervention % (n)	Group comparison	P-value
Touchette et al. <sup>5</sup> USA, 2008	a. Percentage of patients receiving warfarin in-hospital at discharge b. Percentage of patients with a discharge plan for warfarin use c. Percentage of patients in planned or actual warfarin use at discharge (high risk according to Chest 2004 guidelines <sup>73</sup> )	Not reported	<i>Control</i> <u>(01/05/2001- 25/07/2001)</u> a. 41.8% (n=41/98) b. 56.1% (n=55/98) c. 57.1% (n=56/98) <i>Intervention</i> <u>(20/09/2001 – 28/02/2002)</u> a. 45.5% (n=70/154) b. 77.9% (n=120/154) c. 78.6% (n=121/154)	<i>Between group difference</i> a. 3.7% b. 21.8% c. 21.5%; OR 2.46 [95% CI, 1.63-3.74]	a. 0.60 b. <0.01 c. <0.01
Hendriks et al. <sup>6</sup> Netherlands, 2010	The percentage of patients receiving VKA treatment (according to the ACC/AHA/ESC AF guidelines <sup>74</sup> :- control group: 2001; intervention group: 2006)	Not reported	<i>Control</i> <u>2003-2004</u> CHADS <sub>2</sub> =0 39% (n=7/18) CHADS <sub>2</sub> =1 93% (n=28/30) CHADS <sub>2</sub> >1 80% (n=42/52) In high -risk patients appropriate treatment was given to 79% (41/52) <i>Intervention</i> <u>06/2006-04/2007</u> CHADS <sub>2</sub> =0 18% (n=6/34) CHADS <sub>2</sub> =1 64% (n=25/39) CHADS <sub>2</sub> >1 90% (n=34/38) In high -risk patients appropriate treatment was given to 97% (n=37/38)	<i>Between group difference</i> CHADS <sub>2</sub> =0 21% CHADS <sub>2</sub> =1 29% CHADS <sub>2</sub> >1 10% In high -risk patients 18%	<i>Difference in therapy per CHADS<sub>2</sub> score</i> <0.001 <i>Difference in high-risk patients</i> <0.05

Author	Outcome measure	Baseline or pre-intervention % (n)	Follow-up or post-intervention % (n)	Group comparison	P-value
Boriani et al. <sup>7</sup> Italy, 2012	Percentage of patients on OAC therapy at the end of the observational period ( $\leq 48$ months) (CHADS <sub>2</sub> $\geq 1$ )	<i>Control</i> 46.9% (n=693/1477) <i>Intervention</i> 46.1% (n=904/1961)	<i>Control</i> 56.8% (n=258/454) <u>(Intervention during the stroke risk evaluation phase 69.4% (n=474/683))</u> <i>Intervention: final follow-up</i> 72.6% (n=496/683)	<i>Between group difference</i> 15.8%	<0.001
Cook et al. <sup>8</sup> USA, 2015	a. Prescription of warfarin in high-risk eligible patients within 30 days of AF diagnosis (CHADS <sub>2</sub> $\geq 2$ ) b. Prescription of warfarin in all eligible patients within 30 days of AF diagnosis (CHADS <sub>2</sub> $\geq 2$ ) c. Frequency of an appropriate medication prescription (warfarin for any warfarin-eligible patient, or aspirin for warfarin-eligible low-risk patients [CHADS <sub>2</sub> <2]).	<i>Control:</i> <u>(12/2008 – 02/2009)</u> a. High risk (CHADS <sub>2</sub> $\geq 2$ ) 36% (n=34/94)  b. Not provided  c. 43% (n=85/196)	<i>Intervention:</i> <u>(12/2009 – 02/2010)</u> a. High risk (CHADS <sub>2</sub> $\geq 2$ ) 27% (n=34/125)  b. Not provided  c. 45% (n=109/244)	<i>a. Between group difference in high-risk patients</i> OR 0.66 [95% CI, 0.37-1.17]  <i>b. Between group difference in all warfarin-eligible patients</i> Adjusted OR 0.91 [95% CI, 0.60 -1.38]  <i>c. Between group difference in appropriate prescription</i> OR 1.05 [95% CI, 0.72–1.54]; adjusted OR 1.12 [95% CI, 0.76–1.66]	<i>a. Difference in high-risk patients</i> 0.16  <i>b. Difference in all warfarin-eligible patients</i> 0.65  <i>c. Between group difference in appropriate prescription</i> 0.78 adjusted: 0.57
<b>Cross-sectional studies</b>					
Falces et al. <sup>9</sup> Spain, 2011	Percentage prescription of anticoagulation therapy (ACC/AHA/ESC AF guidelines <sup>74</sup> )	<i>Usual care:</i> <u>(Specialist units 01/2008 – 12/2008)</u> 69.3% (n=201/290) (Univariate analysis)	<i>Integrated care:</i> <u>Primary care 01/2008 – 12/2009; specialist units 01/2009 - 12/2009)</u> 94.6% (n=211/223) (Univariate analysis)	<i>Logistic regression model:</i> adjusted OR 7.1 [95% CI, 3.8-13.5]	<0.001 for univariate analysis and logistic regression

Author	Outcome measure	Baseline or pre-intervention % (n)	Follow-up or post-intervention % (n)	Group comparison	P-value
<b>Before-after studies</b>					
Sobreques et al. <sup>10</sup> Spain, 2002	Percentage of eligible patients taking acenocumarol	Pre-intervention 70.5% (total n=53)	Post-intervention 88.6% (total n=53)	<i>Between group difference</i> 18.1%	<0.01
Lowdon et al. <sup>11</sup> UK, 2004	Percentage of eligible patients prescribed anticoagulants	<u>Pre-intervention (01/01 – 04/02)</u> total 31.4% (n=38/121); eligible patients only (no contraindications) 43.7% (n=38/87); total high risk 39.6% (n=36/91); eligible high risk 52.2% (n=36/69)	<u>Post-intervention (05/02 – 12/02)</u> total 54.5% (n=30/55); eligible patients only (no contraindications) 90.9% (n=30/33); total high risk 62.8% (n=27/43); eligible high risk 93.1% (n=27/29)	<i>Between group difference</i> total 23.1%; eligible patients only (no contraindications) 47.2%	only reported for total <0.01 and total eligible <0.001
Bajorek et al. <sup>12</sup> Australia, 2005	Percentage of patients receiving warfarin (± aspirin)	<i>Pre-intervention</i> <i>On admission</i> 20.7% (n=45/218)	<i>Post-intervention</i> <u>a. At discharge</u> 17.4% (n=38/218) <u>b. At 3 month follow-up</u> 16.1 (30/187) <u>c. At 6 month follow-up</u> 16.5 (30/184)	<i>Between group difference</i> <u>post-intervention</u> <u>a. 3.3%</u>	<u>a. 0.39</u>



Author	Outcome measure	Baseline or pre-intervention % (n)	Follow-up or post-intervention % (n)	Group comparison	P-value
Bo et al. <sup>13</sup>  Italy, 2007	Increase in appropriate OAC prescription at discharge	<i>Pre-intervention</i> <i>Year 2000</i> <i>On admission</i> OAC strongly recommended: 36.8% <i>Year 2000</i> <i>At discharge</i> OAC strongly recommended: 56.6% with OAC (n=60/106)	<i>Post-intervention</i> <i>Year 2004</i> <i>On admission</i> OAC strongly recommended: 58.1% <i>Year 2004</i> <i>At discharge</i> OAC strongly recommended: 81.9% (n=86/105)	<i>Between groups absolute difference at discharge in OAC strongly recommended group</i> 25.3% (95%CI: 15% 35%).  Adjusted OR for OAC prescription at discharge 2.11 [95% CI, 1.47 3.04]	no p values provided
Coll-Vinent et al. <sup>14</sup>  Spain, 2007	a. Percentage of patients receiving anticoagulation treatment b. No anticoagulation when this is indicated	<u><i>The pre-intervention period (June 2004)</i></u> <i>a. Before visit in the pre-intervention period: 53% (n=154/293)</i> <i>a. After visit in the pre-intervention period: 52% (n=151/293)</i> <i>b. Before visit in the pre-intervention period: 25% (n=74/293)</i> <i>b. After visit in the pre-intervention period: 24% (69/293)</i>	<u><i>The post-intervention period (June 2005)</i></u> <i>a. Before visit in the post-intervention period: 58% (n=155/267)</i> <i>a. After visit in the post-intervention period: 62% (n=163/267)</i> <i>b. Before visit in the post-intervention period: 13% (n=36/267)</i> <i>b. After visit in the post-intervention period: 10% (n=25/267)</i>	<i>a. Between group difference: After visit between pre- and post-intervention periods: 10%</i> <i>b. Between group difference: After visit between pre- and post-intervention periods: -14%</i>	a. Not reported  b. Not reported

Author	Outcome measure	Baseline or pre-intervention % (n)	Follow-up or post-intervention % (n)	Group comparison	P-value
Jackson et al. <sup>15</sup> Australia, 2011	Proportion of eligible patients receiving warfarin	Pre-intervention <u>(02/2004 - 09/2004)</u> <i>On admission:</i> high risk 31% (n=76/248); moderate risk 30% (n=22/73); low risk 16% (n=3/19); total 30% (n=101/340) <i>At discharge:</i> high risk 30% (n=76/259); moderate risk 33% (n=26/80); low risk 16% (n=4/35); total 29% (n=106/364)	Post-intervention <u>(10/2004 - 02/2006)</u> <i>On admission:</i> high risk 44% (n=47/107); moderate risk 50% (n=6/12); low risk 0% (n=0/3); total 43% (n=53/122) <i>At discharge:</i> high risk 57% (n=65/115); moderate risk 80% (n=13/16); low risk 0% (n=0/3); total 58% (n=78/134)	Performed comparisons between all different group combinations	<i>Between study arms on admission:</i> high risk <0.01; moderate risk 0.15; low risk no p-value; total 0.004 <i>Between study arms at discharge:</i> high risk <0.0001; moderate risk 0.0004; low risk no p-value; total 0.0008 <i>Admission vs discharge:</i> Pre-intervention: no significant difference Post-intervention: total 0.05; high risk 0.04; moderate/low risk no p-value
Oliveira et al. <sup>17</sup> Portugal, 2014	a. Percentage of patients prescribed appropriate prophylactic therapy based on risk-scores (> 94% with CHA <sub>2</sub> DS <sub>2</sub> -VASc ≥2) a. antithrombotics b. OACs	<u>Pre-intervention (01/05/2012 – 04/05/2012)</u> a: 49.5% (n=52/105) b: 46.4% (n=45/97)	<u>Post-intervention (03/09/2012 – 07/09/2012)</u> a: 60% (n=57/95) b: 56.3% (n=49/87)	<i>Between group difference</i> a. "This means an increase of 21.2% in the number of patients receiving appropriate therapy compared to the first assessment" b. no comparison	Not reported
Robson et al. <sup>16</sup> UK, 2014	Percentage of patients with AF and CHA <sub>2</sub> DS <sub>2</sub> -VASc ≥1 on anticoagulants	<u>Pre-intervention: (04/2008)</u> 50.8% (n=1943/3825) <u>Pre-intervention: 04/2011</u> 52.6% (n=2085/3964) (Intervention commenced 04/2011)	<u>Post-intervention: (04/2013)</u> 59.8% (n=2492/4168)	<i>Between group difference:</i> <i>Pre-intervention to pre-intervention</i> 2008 vs. 2011: 2.2% <i>Immediately pre-intervention to post-intervention</i> 2011 vs. 2013: 7.2% <i>Difference in slope of the trends:</i> 1.63 [95% CI, 1.32 - 1.94] p=<0.001	<i>Pre-intervention to pre-intervention:</i> 2008 vs. 2011: 0.184 <i>Pre-intervention to post-intervention:</i> 2011 vs. 2013: <0.001

Author	Outcome measure	Baseline or pre-intervention % (n)	Follow-up or post-intervention % (n)	Group comparison	P-value
Das et al. <sup>18</sup> UK, 2015	Overall proportion of eligible patients receiving anticoagulation (CHADS <sub>2</sub> or CHA <sub>2</sub> DS <sub>2</sub> -VASc ≥1)	Pre-intervention 77% (n=4187/5471)	Post-intervention 95% (n=5207/5471)	<i>Between group difference</i> 18%	<0.0001
Hsieh et al. <sup>19</sup> Taiwan, 2016	Percentage of discharge prescription of oral anticoagulants for eligible AF	<u>Pre-intervention (05/2006 – 07/2008)</u> 32.1% (total n=9612)	<u>During- intervention (08/2010 – 07/2011)</u> 64.1% (total n=7492)	<i>Between group difference</i> 32%	<0.001
Wang et al. <sup>20</sup> Australia, 2017	a. Proportion of participants receiving OACs (Warfarin and NOACs) b. Level of HCP agreement with tools recommendations	Pre-intervention a. Total n=251 OAC 50.5% (126): Warfarin 30.3% (76) NOAC 20.0% (50)	Post-intervention a. Total n=251 OAC 70.0% (176): Warfarin 40.0% (76) NOAC 30.0% (54) (Interpreted from a graph) b. Agreed whether eligible for OACs:199 (79.3%) b. Agreed with recommended therapy 132 (52.6%)	Change in patient use of OACs (in eligible patients according to risk assessment tool)	a. Change in Warfarin use p<0.001 a. Change in NOAC use p<0.001 b. Agreement between HCPs and tool re use of anticoagulants vs other therapy p<0.001

Abbreviations: AF, atrial fibrillation; CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc, scoring schemes for stroke risk assessment; CI, confidence interval; OAC, oral anticoagulants; OR, odds ratio

; SD, standard deviation; VKA, Vitamin K antagonists; HCP, healthcare professional.

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