Trombemboolia riski hindamise meetod

Kliiniline küsimus

Kas trombemboolia riski hindamiseks tuleks KVA patsientidel kasutada CHA2DS2-VASc skoori vs kliiniline hinnang vs teised teadaolevad skoorid?

Olulised tulemusnäitajad

Surm, ajuinfarkt, trombemboolia, oluline verejooks, elukvaliteet, koljusisene verejooks, südame löögisageduse eesmärkväärtuse (nt ≤100 x/min) saavutamine, tõsine kõrvaltoime.

Mõõdukalt olulised: hospitaliseerimine, KVA taasteke (sek preventsioonil), ravi katkestama sundiv kõrvaltoime, südamepuudulikkus, aeg KVA esimese taastekkeni, siinusrütmi taastumine (kardioversioonil), siinusrütmi püsimine 12 kuud.

Kliinilise tõenduse kokkuvõte

Kodade virvendusarütmiaga käib kaasas trombemboolia (peamiselt ajuinfarkti) riski keskmiselt 5 kordne tõus. Risk on heterogeenne ja sõltub mitmetest riskifaktoritest (vanus, sugu, varasem insult või TIA, müokardiinfarkt, hüpertensioon, süstoolne düsfunktsioon, perifeersete arterite ateroskleroos, diabeet, neerufunktsioon jt).

Riski kvantifitseerimine on oluline, et otsustada, millised patsiendid saavad kasu antikoagulantravist ning millistel on trombemboolia risk nii madal, et ei õigusta antikoagulatsiooni võimalikke kõrvaltoimeid. Kaasajal ongi kõige olulisem aru saada, millised on trombemboolia väga madala riskiga patsiendid.

Riski kvantifitseerimiseks on loodud mitmesuguseid töövahendeid (riskiskoore), mida on valideeritud ja võrreldud kohortuuringuis ja omavahel võrreldud ka süstemaatilistes ülevaadetes.

2014. aasta NICE juhendi tarvis on tehtud süsteemne ülevaade. Tegime ka kirjanduse otsingu, kuna on teada, jätkuvalt püütakse et uusi riskihindamisvahendeid välja töötada. Leidsime ühe uuema analüüsi, mis kinnitas NICE ülevaate järeldusi (Stroke. 2014;45:426-431), ühe ATRIA skoorimissüsteemi hindava uuringu Ühendkuningriigist[1], mille tulemus oli vastuolus kahe varasemaga ning publikatsiooni uue, biomarkereid kaasava ABC insuldiskoori valideerimisest, mille kohta on andmeid seni vähe ning mis võib olla marginaalselt täpsem senistest[2].

Leiti 11 kohortuuringut, kaasati need, kus esines üle 100 ajuinfarkti.

1 Van den Ham jt. J Am Coll Cardiol 2015;66:1851–9

[2] Oldgren J jt. Performance and Validation of a Novel Biomarker-Based Stroke Risk Score for Atrial Fibrillation. Circulation. 2016 Nov 29;134(22):1697-1707. Epub 2016 Aug 28.

Study	Stroke risk score	Population	Outcomes
Baruch 200737 Prospective cohort (based on randomised parallel-group trials) N = 7329 This study is the same as Lip 2010, but at 1.5 year mean follow up, rather than up to 9 years.	CHADS2 CHA2DS2-VASc ACC/AHA/ESC NICE 2006	Patients with AF enrolled in SPORTIF III and SPORTIF V trials. Received anticoagulation (warfarin or ximelagatran)	Stroke (c statistics and hazard ratios based on continuous scores and 3 strata risk scores)
Coppens 2013104 Prospective cohort N = 4670	CHADS2 CHA2DS2-VASc	Patients with AF and a CHADS2 score of 1 enrolled in AVERROES, ACTIVE-W and ACTIVE-A trials, treated with aspirin or clopidogrel.	Thromboembolism (c statistics and hazard ratios based on dichotomised risk scores)
Fang 2008142 Prospective cohort N = 13559 (5588 not on warfarin).	CHADS2 ACCP 2004	Patients with AF enrolled in ATRIA study.	Thromboembolism (c statistics based on continuous scores and 3 strata risk scores)
Friberg 2012B154 Retrospective cohort N = 170291 (90490 not on warfarin)	CHADS2 CHA2DS2-VASc ACC/AHA/ESC NICE 2006	Patients with AF	Stroke and thromboembolism (c statistics based on continuous and 3 strata risk scores) NRI for CHADS2, ref = CHA2DS2-VASc
Gage 2004161 Data from 6 trials (AFASAK-I, PATAF, EAFT, low risk SPAF III, AFASAK -2 and high risk SPAF III. N = 2580 (2/6 trials included warfarin)	CHADS2 ACCP 2001	Patients with non valvular AF - all received aspirin.	Stroke (c statistic based on 3 strata risk scores).
Larsen 2012262 Prospective cohort N = 1603 (not on warfarin)	CHADS2 CHA2DS2-VASc	Patients with AF	Stroke and mortality (continuous data).
Li 2012275 Prospective cohort N = 1297 (1112 without anticoagulants)	CHADS2 CHA2DS2-VASc	Patients hospitalised with acute stroke and non valvular AF.	Stroke recurrence and mortality (c statistic).
Lip 2010A287 Prospective cohort (SPORTIF III and V trials) N = 7329	CHADS2 CHA2DS2-VASc 8th ACCP NICE 2006	Patients with non-valvular AF. Received anticoagulation (warfarin or ximelagatran)	Thromboembolism (c statistics and hazard ratios based on 3 strata risk scores)
Olesen 2011336 Retrospective cohort N=73538	CHADS2 CHA2DS2-VASc	Patients with AF not treated with vitamin K antagonists	C-statistics for thromboembolism

Olesen 2012B340 Retrospective cohort N = 47576 (without anticoagulants)	CHADS2 CHA2DS2-VASc	Patients with non-valvular AF or atrial flutter.	Thromboembolism (hazard ratio by dichotomised scores, c statistic and NRI)
Vanstaa 2011444 Prospective cohort N = 79844 (20% received anticoagulants)	ACCP (2001, 2004, 2008) CHADS2 CHA2DS2-VASc NICE 2006 ACC/AHA/ESC	AF patients identified in general practice.	Stroke and mortality (c statistics for continuous and 3 strata risk factors).

NICE viis läbi ka kulutõhususe analüüsi, mille fookuseks oli kahe Ühendkuningriigis kasutatava skoori (CHADS2 ja CHA2DS2-VASc) võrdlus.

Selgituseks metoodikast:

Tulemusi riskisuhtena (hazard ratio, HR) väljendades hinnati, kui palju erineb insuldirisk selle meetodiga tekitatud riskikategooriate vahel.

C-statistik näitab keskmist tõenäosust, et skooringusüsteem teeb vahet madala ja kõrge riskiga indiviidide vahel. Aitab hinnata, kas meetod on üldse parem, kui juhus (c statistik sel juhul 0,5), ent ei ole eriti informatiivne testi kliinilise kasulikkuse kirjeldamisel.

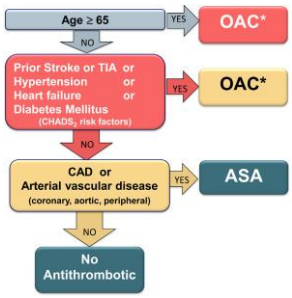
Kokkuvõttes leiti:

- mõõduka kvaliteediga tõendus, et
  - trombemboolia riskisuhe (hazard ratio, HR) CHA2DS2-VASc kasutades oli 2,2 – 2,69 patsientidel, kellel CHADS2 skoor oli 1.
- kõrge kvaliteediga tõendus, et
  - insuldi riskisuhe CHADS2 skoori kasutades oli 1,48 (pideva tunnusena) ja 2,44 (kui kasutati 3 riskigruppi);
  - trombemboolia riskisuhe oli 2,59 ACCP skooril, 2,59 ACC/AHA/ESC skooril, 2,27-2,51 CHADS2 skooril ja 3,74 CHA2DS2-VASc skooril;
- mõõduka kvaliteediga tõendus, et
  - trombemboolia c-statistik antikoaguleerimata patsientidel oli ACCP (8th) puhul 0,60 (st kehv);
- madala kuni mõõduka kvaliteediga tõendus, et
  - trombemboolia c-statistik oli CHA2DS2-VASc skooril 0,56 kuni 0,85 (kehv kuni hea, 7 uuringut)
  - trombemboolia c-statistik oli CHA2DS2 skooril 0,61 kuni 0,72 (kehv kuni rahuldav, 9 uuringut.
- Ravijuhendi käigus koostatud kulutõhususanalüüs (üldine antikoagulatsiooni kulutõhususe mudel) näitas, et CHA2DS2-VASc skoori kasutamine antikoagulatsioonivajaduse hindamisel on marginaalselt parem (rahaliselt soodsam) kui CHADS2 skoori kasutamine.

Teiste ravijuhendite soovitused samal teemal

AHA 2014 juhend soovitab kodade virvendusarütmia patsientidel insuldiriski hindamiseks kasutada CHA2DS2-VASc skoori (I B).

Kanada ravijuhend (2014) soovitab kasutada oma algoritmi (CCS algoritm), mis kaasab CHADS2 ja mõned CHA2DS2-VASc riskitegurid (v.a naissugu ja vaskulaarhaigus).



ESC 2016 ravijuhend soovitab kodade virvendusarütmia patsientidel insuldiriski hindamiseks kasutada CHA2DS2-VASc skoori (I A).

2016. juhend ei aruta tõendust, kuna skoori kasutamise soovitus viidi sisse juba 2010. Ega sealgi süsteemset ülevaadet ole, aga on viidatud 2008 analüüsile, mis võrdles 12 erinevat skoori.

NICE ravijuhend soovitab kodade virvendus- ja laperdusarütmiaga patsientidel (sh kardioversiooni järel) insuldiriski hindamiseks kasutada CHA2DS2-VASc skoori.

Soome ravijuhend soovitab kodade virvendusarütmia patsientidel kohe diagnoosimise järel insuldiriski hindamiseks kasutada CHA2DS2-VASc skoori.

Viited

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6. *Nielsen PB, Skjøth F, Rasmussen LH, Larsen TB, Lip GY. Using the CHA2DS2-VASc score for stroke prevention in atrial fibrillation: a focus on vascular disease, women, and simple practical application. Can J Cardiol. 2015;31:820.e9–820.10.*
7. *Olesen JB, Torp-Pedersen C, Hansen ML, Lip GY. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0-1: a nationwide cohort study. Thromb Haemost. 2012;107:1172–1179. doi: 10.1160/TH12-03-0175.*

Uuringud tabelina:

Table 22: Clinical evidence profile: Stroke risk scores

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
Hazard ratio for stroke (categorical variables) – CHA_2DS_2-VASc[340] -No anticoagulant										
CHA_2DS_2-VASc 1 versus 0										
1	Cohort studies	serious limitations (a)	no serious inconsistency	no serious indirectness	no serious imprecision	none	1: 159/8880 (1.79%) 0: 58/6919 (0.83%)	9 more per 1000 (from 5 more to 15 more)	2.10 [1.56 - 2.81	MODERATE
CHA_2DS_2-VASc 2 versus 0										
1	Cohort studies	serious limitations (a)	no serious inconsistency	no serious indirectness	no serious imprecision	none	2: 435/11863 (3.67%) 0: 58/6919 (0.83%)	27 more per 1000 (from 20 more to 35 more	4.22 [3.40 - 5.24]	MODERATE
CHA_2DS_2-VASc 3 versus 0										
1	Cohort studies	serious limitations (a)	no serious inconsistency	no serious indirectness	no serious imprecision	none	3: 660/11473 (5.75%) 0: 58/6919 (0.83%)	46 more per 1000 (from 32 more to 64 more)	6.49 [4.84 - 8.71]	MODERATE
CHA_2DS_2-VASc 4 versus 0										

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
1	Cohort studies	serious limitations (a)	no serious inconsistency	no serious indirectness	no serious imprecision	none	4: 93/1137 (8.18%) 0: 58/6919 (0.83%)	67 more per 1000 (from 46 more to 97 more)	9.12 [6.53 - 12.72]	MODERATE
Hazard ratio for stroke (continuous variables) – $CHADS_2$[37]										
$CHADS_2$ 1	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Low: 0/238 (0%) Moderate: 72/7286 (1.0%) High: 87/3721 (2.3%)	-	1.48 [1.31 - 1.66]	HIGH
Hazard ratio for stroke (3 strata continuous variables) – $CHADS_2$[37]										
1	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Low: 0/238 (0%) Moderate: 72/7286 (1.0%) High: 87/3721 (2.3%)	-	2.44 [1.78 - 3.33]	HIGH
Hazard ratio for thromboembolism (categorical variables) – CHA_2DS_2-VASc[104]										
CHA_2DS_2-VASc 2 versus 1										
1	Cohort studies	no serious limitations	no serious inconsistency	Serious indirectness (b)	no serious imprecision	none	1: 27/1224 (2.20%) 2: 92/1984 (4.64%)	26 more per 1000 (from 9 more to 53 more)	2.2 [1.43 - 3.39]	MODERATE

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
CHA_2DS_2-VASc 2-4 versus 1										
1	Cohort studies	no serious limitation	no serious inconsistency	serious indirectness (b)	no serious imprecision	none	1: 27/1224 (2.20%) 2 - 4: 178/3446 (5.16%)	37 more per 1000 (from 16 more to 69 more)	2.69 [1.75 - 4.14]	MODERATE
CHA_2DS_2-VASc 3-4 versus 1										
1	Cohort studies	no serious limitation	no serious inconsistency	serious indirectness (b)	no serious imprecision	none	1: 27/1224 (2.20%) 3 - 4: 86/1462 (5.88)	33 more per 1000 (from 15 more to 61 more)	2.51 [1.66 - 3.79]	MODERATE
Hazard ratio for thromboembolism (3 strata continuous variables) – $CHADS_2$[287]										
$CHADS_2$ (1 = moderate)										
1	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Low: 0/238 (0 %) Moderate: 87/7276 (1.19%) High: 97/3716 (2.61%)	-	2.51 [1.73 - 3.64]	HIGH
$CHADS_2$ (1-2 = moderate)										

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
1	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Low: 0/238 (0 %) Moderate: 31/3563 (0.87%) High: 153/7431 (2.05%)	-	2.27 [1.73 - 2.99]	HIGH
NICE 2006										
1	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Low: 0/238 (0 %) Moderate: 32/3651 (0.87%) High: 152/7580 (2.00%)	-	2.27 [1.56 - 3.29]	HIGH
ACC/AHA/ESC 2006										
1	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Low: 0/212 (0 %) Moderate: 29/3469 (0.83%) High: 155/7551 (2.05%)	-	2.59 [1.75 - 3.83]	HIGH
ACCP 2008										
Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
1	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Low: 0/212 (0%) Moderate: 29/3479 (0.83%) High: 155/7541 (2.05%)	-	2.59 [1.75 - 3.83]	HIGH
CHA_2DS_2-VASc										
1	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	serious imprecision[f]	none	Low: 0/2 (0%) Moderate: 3/65 (4.61%) High: 181/10578 (1.71%)	-	3.75 [1.20, 11.73]	MODERATE
C statistic for stroke (3 strata continuous variables) NICE 2006[154] No anticoagulants										
1	Cohort studies	serious limitations [(a)]	no serious inconsistency	no serious indirectness	no serious imprecision	none	Event rate/100 years Low:0.2 Intermediate: 2.2 High: 6.4	-	C statistic: 0.61 [0.60 - 0.62]	MODERATE
C statistic for stroke (3 strata continuous variables) – CHA_2DS_2-VASc[154] No anticoagulants										
1	Cohort studies	serious limitations [(a)]	no serious inconsistency	no serious indirectness	no serious imprecision	none	Event rate/100 years Low:0.2 Intermediate: 0.6 High: 6.2	-	C statistic: 0.56 [0.56 - 0.57]	MODERATE
C statistic for stroke (3 strata continuous variables) – $CHADS_2$ [154] No anticoagulants										

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
$CHADS_2$ (1-2 = moderate)										
1	Cohort studies	serious limitations (a)	no serious inconsistency	no serious indirectness	no serious imprecision	none	Event rate/100 years Low:0.6 Intermediate: 3.0 High: 6.6	-	C statistic: 0.62 [0.61 - 0.62]	MODERATE
$CHADS_2$ (1 = moderate)										
1	Cohort studies	serious limitations (a)	no serious inconsistency	no serious indirectness	no serious imprecision	none	Event rate/100 years Low:0.6 Intermediate: 3.6 High: 9	-	C statistic: 0.65 [0.64 - 0.65]	MODERATE
C statistic for stroke (3 strata continuous variables) – $CHADS_2$[37,161] All patients										
1	Cohort studies	serious limitations (c)	no serious inconsistency	no serious indirectness	not assessed	none	Event rate/100 years Low:0.8 Intermediate: 2.7 High: 5.3	-	C statistic: 0.7 (CI not reported)	MODERATE
C statistic for stroke (3 strata continuous variables) – ACCP 2001[161]										
1	Cohort studies	serious limitations (c)	no serious inconsistency	no serious indirectness	not assessed	none	N/R	-	C-statistic: 0.58 (CI not reported)	MODERATE
Quality assessment							**No of events/patients**		**Effect**	
Number of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Number of events/people (%) with and without risk factor**	**Absolute risk difference**	**Hazard ratios [95% CI] c**	**Quality**
C statistic for stroke (3 strata continuous variables) – ACC/AHA/ESC[154]										
1	Cohort studies	serious limitations (a)	no serious inconsistency	Serious indirectness (b)	no serious imprecision	none	Event rate/100 years Low:0.6 Intermediate: 2.8 High: 6.6	-	C statistic: 0.62 [0.61 - 0.62]	MODERATE
C statistic for stroke (continuous) – ACCP[37]										
1	Cohort studies	serious limitations (c)	no serious inconsistency	no serious indirectness	not assessed	none	ACCP 2001: Low: 2/173 (1.2 %) Moderate: 1/271 (0.4%%) High: 156/10800 (1.4%) ACCP 2004: Low: 0/29 (0%) Moderate: 0/250 (0%) High: 159/10965 (1.5%)	-	C statistic: 0.51 (CI not reported)	MODERATE
C statistic for stroke (continuous) – $CHADS_2$, all patients[37,161,275]										

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
2	Cohort studies	serious limitations [c]	no serious inconsistency	no serious indirectness	not assessed	none	Baruch 2007 Low: 0/238 (0 %) Moderate: 72/7286 (0.99%) High: 87/3721 (2.34%) Li: N/R	-	Median c-statistic [95% CI]: 0.53 0.65 Range: 0.53-0.65	MODERATE
C statistic for stroke (continuous) – $CHADS_2$, no anticoagulation[154,262]										
2	Cohort studies	serious limitations [a]	no serious inconsistency	no serious indirectness	Serious imprecision[d]	none	Friberg 2012: Event rate/100 years Low:0.6 Intermediate: 3.6 High: 9.0 Larsen 2012: N/R	-	Median c-statistic [95% CI]: 0.64 [0.56-0.71] 0.66 [0.66-0.67] Range0.64 - 0.66	LOW
C statistic for stroke (continuous) – CHA_2DS_2-VASc, all patients[275]										
1	Cohort studies	serious limitations [c]	no serious inconsistency	no serious indirectness	not assessed	none	N/R	-	C statistic: 0.53 (CI not reported)	MODERATE

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
C statistic for stroke (continuous) – CHA_2DS_2-VASc, no anticoagulation[154,262]										
2	Cohort studies	serious limitations [a]	no serious inconsistency	no serious indirectness	Serious imprecision[d]	none	Friberg 2012: Event rate/100 years Low:0.2 Intermediate: 0.6 High: 6.2 Larsen 2012 N/R	-	Median c-statistic [95% CI]: 0.66 [0.59-0.72] 0.67 [0.66-0.68] Range: 0.66-0.67	LOW
C statistic for thromboembolism (3 strata)– ACC/AHA/ESC[154,287]										
2	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Friberg 2012: Event rate/100 years Low:0.8 Intermediate: 3.9 High: 9.2 Lip 2010: Low: 0/212 (1.8%) Moderate: 29/3469 (30.3%) High: 155/7551 (67.9%)	-	Median c-statistic [95% CI]: 0.59 [0.56-0.61] 0.62 [0.61-0.62] Range: 0.59-0.62	HIGH

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
C statistic for thromboembolism (3 strata) – ACCP, all patients[142,287]										
2	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Fang 2008: Low: 11.7% Moderate: 7.9% High: 80.4% Lip 2010: Low: 0/212 (%) Moderate: 29/3479 (0.83%) High: 155/7541 (2.05%)	-	Median c-statistic [95% CI]: 0.56 0.59 [0.56-0.61] Range of HR: 0.56-0.59	HIGH
C statistic for thromboembolism (3 strata) – ACCP, no anticoagulation[142]										
1	Cohort studies	serious limitations (c)	no serious inconsistency	no serious indirectness	not assessed	none	N/R	-	C statistic 0.6 (CI not reported)	MODERATE
C statistic for thromboembolism (3 strata)– $CHADS_2$, all patients[142,287]										

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
2	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Fang 2008: Low: 18.8% Moderate: 61.2% High: 20.1% Lip2010: Low: 0/238 (0 %) Moderate (1): 31/3563 (0.87%) High: 153/7431 (2.05%) Lip2010: Low: 0/238 (0 %) Moderate (1 - 2) : 87/7276 (1.19%) High: 97/3716 (2.61%)	-	Median c-statistic [95% CI]: 0.58 0.64 [0.61-0.67] Range: 0.58-0.64	HIGH
C statistic for thromboembolism (3 strata) – $CHADS_2$, no anticoagulation[142,154,339,340]										

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
4	Cohort studies	serious limitations [a]	no serious inconsistency	no serious indirectness	no serious imprecision	none	Fang 2008: Event rate not given. Friberg 2012: Event rate/100 years Low:0.9 Intermediate: 5.2 High: 12.3 Olesen 2012: 1: 159/8880 (1.79%) 0: 58/6919 (0.83%) Olesen 2011: Event rate/100 person years Low: 1.67 Intermediate: 4.75 High: 12.27	-	Median c-statistic [95% CI]: 0.61 [0.61-0.62] 0.66 [0.65-0.68] 0.67 [CI not reported] 0.72 [0.69-0.75] Range: 0.61-0.72	MODERATE
C statistic for thromboembolism (continuous) – $CHADS_2$, all patients[142]										
1	Cohort studies	serious limitations [c]	no serious inconsistency	no serious indirectness	not assessed	none	Fang 2008: Event rate not given.	-	C statistic 0.6 (CI not reported)	MODERATE

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
C statistic for thromboembolism (continuous) – $CHADS_2$, no anticoagulation[154,339]										
2	Cohort studies	serious limitations [a]	no serious inconsistency	no serious indirectness	serious imprecision [d]	none	Friberg 2012: Event rate/100 years Low:0.3 Intermediate: 1.0 High: 8.9 Olesen 2011: Event rate/100 person years Low: 1.67 Intermediate: 4.75 High: 12.27		Median c-statistic [95% CI]: 0.66 [0.65-0.66] 0.72 [0.69 - 0.75] Range: 0.66-0.72	LOW
C statistic for thromboembolism (3 strata) – CHA_2DS_2-VASc , all patients[104,287]										
2	Cohort studies	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	Low: 0/2 (%) Moderate: 3/65 (4.61%) High: 181/10578 (1.71%) Coppens 2013: 1: 27/1224 (2.20%) 2: 92/1984 (4.64%) 3 - 4: 86/1462 (5.88)	-	Median c-statistic [95% CI]: 0.57 [0.54-0.59] 0.65 [0.61-0.68] Range: 0.57-0.65	HIGH

Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
C statistic for thromboembolism (3 strata) – CHA_2DS_2-VASc , no anticoagulation[154,339,340]										
3	Cohort studies	serious limitations (a)	serious inconsistency (e)	no serious indirectness	no serious imprecision	none	Friberg 2012: Event rate/100 years Low:0.3 Intermediate: 1.0 High: 8.9 Olesen 2011 Event rate per 100 years Low: 0.78 Intermediate: 2.01 High: 8.82 Olesen 2012 Event rate/100 years 0= 0.84 1= 1.79 2= 3.67 3= 5.75 4= 8.18	-	Median c-statistic [95% CI]: 0.56 [0.56-0.57] 0.63 [0.62-0.65] 0.85 [0.83-0.87] Range: 0.56-0.85	LOW
C statistic for thromboembolism (continuous) – CHA_2DS_2-VASc , no anticoagulation[154,339]										
Quality assessment							No of events/patients		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of events/people (%) with and without risk factor	Absolute risk difference	Hazard ratios [95% CI] c	Quality
2	Cohort studies	serious limitations (a)	serious inconsistency (e)	no serious indirectness	no serious imprecision	none	Friberg 2012: Event rate/100 years Low:0.3 Intermediate: 1.0 High: 8.9 Olesen 2011 Event rate per 100 years Low: 0.78 Intermediate: 2.01 High: 8.82	-	Median c-statistic [95% CI]: 0.67 [0.67-0.68] 0.85 [0.83-0.87] Range: 0.67-0.85	LOW
C statistic for thromboembolism – NICE 2006, no anticoagulation and all patients[154,287]										
2	Cohort studies	serious limitations (a)	no serious inconsistency	no serious indirectness	no serious imprecision	none	Friberg 2012: Event rate/100 years Low:0.3 Intermediate: 0.5 High: 9.0 Lip 2010: Low: 0/238 (0 %) Moderate: 32/3651 (0.87%) High: 152/7580 (2.00%)	-	Median c-statistic [95% CI]: 0.58 [0.55-0.60] 0.61 [0.60-0.62] Range: 0.58-0.61	MODERATE

(a) Retrospective cohort. Data obtained through database searching. Unknown if patients were selected randomly or consecutively.

(b) Indirectness - selected patients with a $CHADS_2$ score of 1.
(c) Missing data, point estimate for c statistic given and no confidence intervals provided.
(d) Wide confidence intervals make it difficult to know the true effect size for this outcome.
(e) Inconsistency detected across studies
(f) Confidence interval crossed one MID

Quality assessment							No of patients/events		Effect	
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Number of people with an event reclassified to a higher risk	Number of people without an event were reclassified to a higher risk	Net reclassification index (95% CI)	Quality
Net reclassification index using CHA_2DS_2-VASc instead of $CHADS_2$[262,340]										
2	Cohort studies	serious limitations [(a)]	no serious inconsistency	no serious indirectness	no serious imprecision	none	Olesen: 1307/1405 (93%)	Olesen: 36410/46171 (78.9%)	Larsen: -3% (-6% to -1%) Olesen: 14.2%	MODERATE

(g) Retrospective cohort. Data obtained through database searching. Unknown if patients were selected randomly or consecutively.