Self-management of oral anticoagulant therapy: A systematic review and meta-analysis

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Abstract

Background: A number of randomized controlled trials have compared self-management of oral anticoagulant therapy with conventional management. However, the results have not appeared consistent and a systematic review and meta-analysis are therefore needed in order to evaluate self-management of oral anticoagulant therapy. The aim of this study was to evaluate the efficacy and safety of self-management of oral anticoagulant therapy for patients on long-term oral anticoagulant therapy.
Methods: A systematic review and meta-analysis including randomized controlled trials with highly selected patients comparing self-management of oral anticoagulant therapy with conventional treatment. Data were extracted in terms of study characteristics, quality of trials and outcome (death, minor and major complications (thromboembolic and bleeding events), and time within therapeutic INR target range).
Results: Ten trials with a total of 2724 patients were included. Two of the trials could be classified as high quality trials. Considering all trials, self-management was associated with a reduced risk of death (relative risk (RR)=0.48, 95% confidence interval (CI) 0.29–0.79, $p=0.004$), major complications (RR=0.58, 95% CI 0.42–0.81, $p=0.001$) and with increasing time within therapeutic INR target range (weighted mean difference=6.53, 95% CI 2.24–10.82, $p=0.003$). No clear effect was found regarding minor complications (RR=0.98, 95% CI 0.49–1.99, $p=0.96$).
Conclusions: A majority of the existing trials have various methodological problems. However, self-management of oral anticoagulant therapy appeared at least as good and possible better than conventional management in highly selected patients.
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Keywords: Coumarin; Anticoagulant; Blood coagulation; International normalized ratio

1. Introduction

Oral anticoagulant therapy with coumarin derivates is prescribed as prevention and treatment to patients with an increased risk of thromboembolism [1]. Since oral anticoagulant therapy increases the risk of bleeding, the therapy requires a careful attention to the balance between the risks of these two outcomes.

Oral anticoagulant therapy is conventionally monitored by laboratory analysis of the international normalized ratio (INR) on plasma obtained by venipuncture. Based on the INR value, health care providers determine the appropriate dosage of coumarin.

Self-management of oral anticoagulant therapy in which highly selected patients analyzes a drop of blood using a portable coagulometer and uses the displayed INR-value for coumarin dosage has over the last years gained interest and is now widely used in routine settings. However, findings from randomized controlled trials that have evaluated the efficacy of self-management compared to conventional management

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have been inconsistent and the scientific basis for implementing self-management has therefore been debated.

A systematic review [2] and a meta-analysis [3] on the efficacy of self-management of oral anticoagulant therapy are available. However, these papers did not include the most recent trials and did not assess the methodological quality of the included trials [4]. An updated systematic review and a subsequent meta-analysis are needed in order to further evaluate the efficacy and safety of self-management.

2. Materials and methods

2.1. Study identification

We searched The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2005, issue 4) and PubMed (start 1951 to December 2005). The search was supplemented by a review of personal files and hand search of published reviews. No language restriction was applied. The following strategy was used to search the CENTRAL and adapted appropriately for the PubMed: (((("4-hydroxycoumarins" [MeSH]) OR (acenocoumar* OR sinkumar OR sinthrome OR sintrom OR mini-sintrom OR syncoumar OR syncumar OR synthrom) OR (bishydroxycoumarin OR dicoumarin OR dicoumarol) OR (phenprocoumarol OR phenylpropylhydroxycumarine OR phenprocoumon OR falithrom OR liquamar OR marcoumar OR marcumar) OR (biscoumacetate ethyl OR ethyldicoumarol OR carbethoxy dicoumarol OR pelentan OR tromexan) OR (warfarin potassium OR warfarin sodium OR coumadin)) OR ("anticoagulants" [MeSH])) AND ("administration, oral" [MeSH] OR oral*)) AND ("self administration" [MeSH] OR "self medication" [MeSH] OR home based OR self monitoring OR self monitored OR self administ* OR self medication* OR self manag* OR self care).
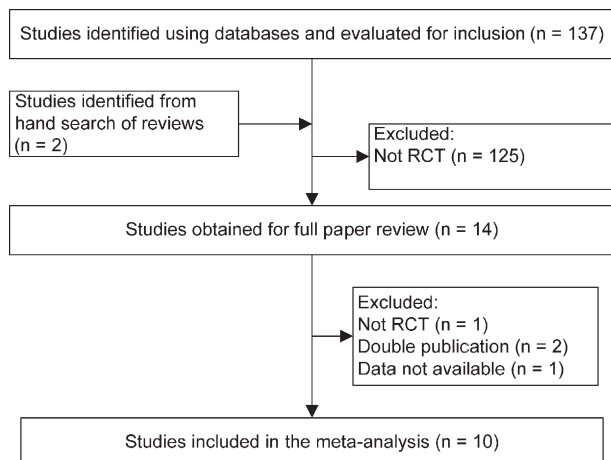

Fig. 1. Study selection flow diagram. Abbreviations: RCT: randomized controlled trial.

References found in the studies were scanned for additional studies.

2.2. Assessment of study eligibility

The titles (and abstracts when available) identified through the search were reviewed. Any article that might met the eligibility criteria was included (please see below). The final assessment of trial quality of each included study was assessed by two reviewers (TDC and JMH) using predefined criteria's [5]. Disagreement was solved using consensus.

2.3. Eligibility criteria

Type of studies: randomized controlled trials assessing the efficacy of self-management.

Type of participants: patients >18 years on long-term oral anticoagulant therapy (expected treatment time >6 months) irrespective of the indication for treatment, e.g., valve replacement, coagulopathies and atrial fibrillation.

Types of intervention: self-management of oral anticoagulant therapy (self-testing and self-dosing of oral anticoagulant therapy) as compared to either:

- Routine care (provided by the general practitioner)
- Care provided by hospital outpatient clinics (provided by physicians working at a hospital, but not specialized in oral anticoagulant therapy)
- Care provided by highly specialized anticoagulation clinics (provided by a dedicated, specialized clinic where physicians, nurses and pharmacists are trained in the speciality of oral anticoagulant therapy)
- Shared care (a collaboration of conducting the oral anticoagulant therapy between the general practitioner and a hospital outpatient clinic)
- Use of computer assessed dosage (the dosaging of the coumarin is performed by a computer)
- Patient self-testing (the patients takes the blood sample using a coagulometer, but the dosaging is done by a physician/health care provider)

All the displayed methods (except self-management) were defined as conventional treatment.

Type of outcome measures:

- Death, all causes
- Major complications:
  ○ Major thromboembolic event (defined as: death due to thromboembolism, valve-related/prosthetic thrombosis, residual neurological deficit (symptoms lasting >24 h), peripheral ischemia requiring surgery, events requiring inpatient treatment)
  ○ Major bleeding events (defined as: death due to bleeding, intracranial bleeding, requiring transfusion, events requiring inpatient treatment)
- Minor complications

Table 1
Summary of trials regarding self-management of oral anticoagulant therapy

Trial	Patients[a] (PSM/control)	Follow-up (months)	Indication for OAT	OAT in the control group	INR-interval	Concealment of allocation	Intention-to-treat analysis
Cromheecke et al. [7]	24/25	6	All indications	HSAC	Target ±0.5	A	No
Fitzmaurice et al. [8]	23/26	6	All indications	GP	Target ±0.5	A	No
Fitzmaurice et al. [15]	337/280	12	All indications	GP	2.0–3.0 and 3.0–4.0	A	Yes
Gadisseur et al. [9]	47/60	6.5	All indications	HSAC	Target ±0.5	A	No
Körtke and Körfer [10]	280/295	24	MV	GP	2.5–4.5	B	No
Menendez-Jandula et al. [11]	289/360	11.8	All indications	HSAC	2.0–3.0, 2.5–3.5 and 3.0–4.5	A	Yes
Sawicki [12]	83/82	6	All indications	GP, HOC	2.0–3.0, 3.0–4.0, 3.0–4.5 and 2.5–3.5	A	No
Sidhu and O'Kane [13]	35/49	24	MV	GP, HOC	2.0–3.0	B	No
Sunderji et al. [14]	69/70	8	All indications	GP	Target ±0.5	A	No
Völler et al. [16]	101/101	4.6	Afib	GP	2.0–3.0	B	No

Abbreviations: Afib: atrial fibrillation, GP: general practitioner, HOC: hospital outpatient clinic, HSAC: highly specialized anticoagulation clinic, INR: international normalized ratio, MV: mechanical heart valve, OAT: oral anticagulation therapy, PSM: patient self-management
The study by Cromheecke is a cross-over study.
Concealment of the group allocation was used as the primary quality measurements according to the method described by the Cochrane collaboration. It was rated A (adequate), B (unclear) and C (inadequate).
All studies used the CoaguCheck® coagulometer (Roche Diagnostics, Switzerland), except for the study by Sunderji, who used the Pro-Time® coagulometer (International Technidyne Corporation, USA).
  [a] The figure is the number of patients included in the analysis.

○ Minor thromboembolic events (defined as: all other events than major)
○ Minor bleeding events (defined as: all other events than major)
• Time (in percent) within therapeutic INR target range.

2.4. Quality assessment

We assessed the methodological quality of the included trials according to the use of adequate concealment of treatment group allocation and the use of the intention-to-treat principle.

Concealment of the group allocation was assessed according to the method described by The Cochrane Collaboration [5]. It was rated A (adequate), B (unclear) and C (inadequate). Adequate concealment was central randomization; either computerized or using serial numbered, opaque, sealed envelopes or otherwise convincing concealment of allocation. Inadequate was all other methods (e.g., references to case numbers, using date of inclusion or birth). Unclear was when no clear or no description was used. The intention-to-treat principle is followed when participants are analyzed according to the group they were randomized to and when all randomized participants are included in the analysis.

2.5. Data extraction and statistical analysis

Data was extracted by two reviewers (TDC and JMH) and consisted of the number of patients in each group, length of follow-up, indication for oral anticoagulant therapy, type of

conventional management, INR-interval, method of measuring INR, type of used coagulometer and outcomes.

Cross-over studies were included and analyzed while ignoring the cross-over design [6].

The statistical analysis was performed by the package provided by The Cochrane Collaboration (RevMan software, version 1.0.3, available from http://www.cochrane.org). For continuous variables (time within therapeutic INR target range), the effect of self-management was defined as a weighted mean difference between the self-management group and the conventional managed group. For dichomatous variables (death and complication events), relative risk (RR) was used and a RR higher than 1 indicated a beneficial effect of self-management and a RR lower than 1 indicated a harmful effect.

The fixed effects model was used, assuming that each study estimates the same effect of the treatment ("what is the average treatment effect") and that the difference between the studies are due to sampling error. Variation between studies, which were not due sampling error, was considered to be heterogeneity. A heterogeneity test (I^2) was performed in order to determine if the included studies were statistically heterogeneous. If the I^2 test was positive ($>50\%$), a random effect model was applied, which assumes that the true effect varies around an overall average treatment effect ("what is the best estimate of the treatment effect").

For all types of variables, Mantel–Haenszel statistics was applied in the fixed effect model, and the DerSimonian and Laird method was used in the random effect model. 95% confidence intervals (CI) were used.
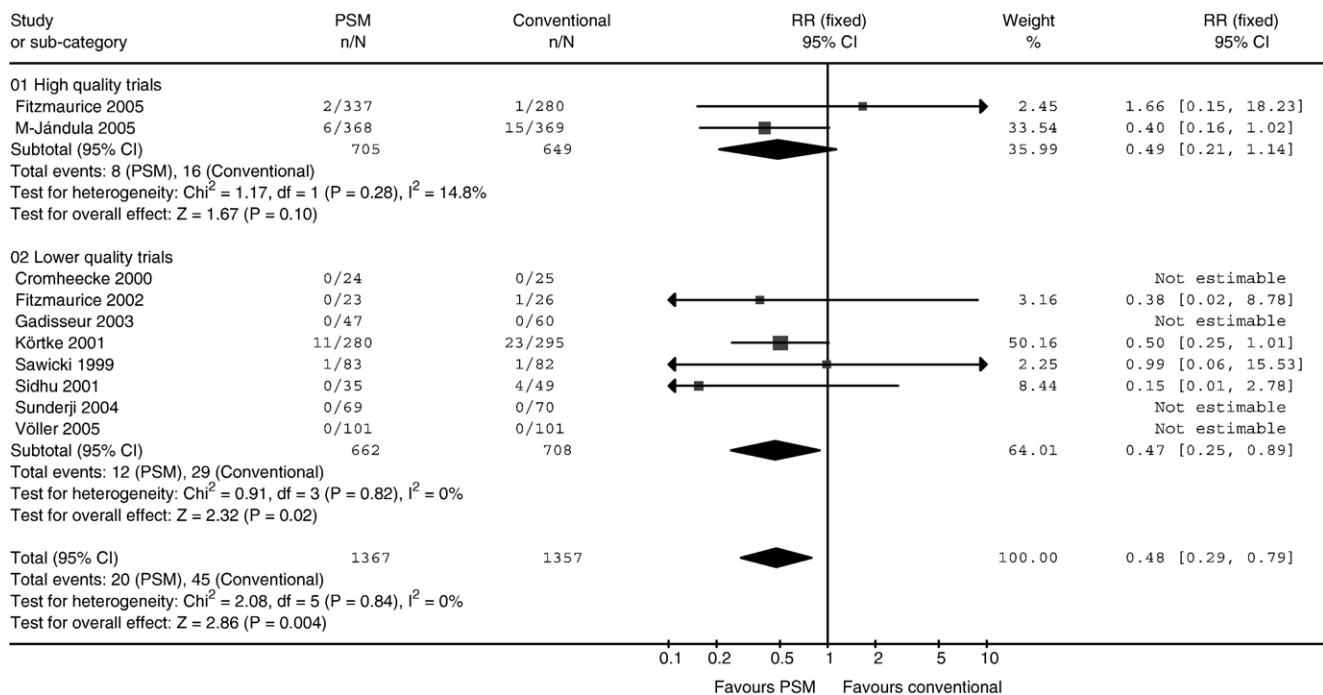
Fig. 2. Death, all causes of self-management of oral anticoagulant therapy compared to conventional treatment. Abbreviations: CI: confidence interval, *n*: number of deaths, *N*: number of patients, PSM: patient self-management, RR: relative risk. Subtotals designate the subgroup analysis of trials of high quality and lower quality. A fixed effect model is applied. I^2 quantifies the percentage of variation between study results that is not due to sampling error.

The analyses were performed both including all studies and subsequently separately for high and lower quality studies.

Funnel plot was performed to elucidate the presence of publication bias, a systematic difference between smaller and larger studies or the use of an inappropriate effect measure.

3. Results

3.1. Data extraction

Disagreement was present between the two reviewers regarding 32% of the extracted data, but consensus was reached in all cases.

3.2. Description of studies

Ten trials comparing self-management to conventional management with a total of 2724 patients were included (Fig. 1 and Table 1) [7–16]. A description of the included studies is displayed in Table 1.

The included studies had a substantial inter-study variation, e.g., in terms of follow-up, number of patients, INR-interval and type of treatment management offered in the control arm (Table 1).

Three authors (Horstkotte, Körtke and Sidhu) were contacted for additional information regarding the results of their trial. Körtke responded adequately regarding the number of minor complications. None of the other authors responded. The study by Horstkotte [17] was excluded, since it was merely published as an abstract with inadequate data.

For the studies by Körtke and Körfer [10] and Sidhu and O'Kane [13], the *p*-value regarding time within therapeutic INR target range was given as $p < 0.001$ and $p < 0.0001$, respectively. Since the exact *p*-value was not available for calculating the standard deviation, it was set to $p = 0.001$ and $p = 0.0001$, respectively.

3.3. Quality assessment of included studies

The concealment of allocation was adequate in seven studies and unclear in the remaining three studies. Further, two of the studies were analyzed applying the intention-to-treat analysis, eight using a per-protocol analysis. Thus, only two studies [11,15] were rated as high-quality studies.

3.4. Death, all causes

Including all trials in a fixed effect model the RR was 0.48 (95% CI 0.29–0.79, $p = 0.004$). The heterogeneity test was found non-significant ($I^2 = 0\%$). When restricting the analyses to the high quality studies, we found that RR was 0.49 (95% CI 0.21–1.14, $p = 0.10$).

3.5. Major complications

Including all trials in a fixed effect model the RR was 0.58 (95% CI 0.42–0.81, $p = 0.001$). The heterogeneity test was non-significant ($I^2 = 0\%$). When restricting the analyses to the high quality studies, we found that RR was 0.47 (95% CI 0.26–0.84, $p = 0.01$).

Study or sub-category	PSM n/N	Conventional n/N	RR (fixed) 95% CI	Weight %	RR (fixed) 95% CI
01 High quality trials					
Fitzmaurice 2005	9/337	7/280		8.46	1.07 [0.40, 2.83]
M-Jándula 2005	8/368	27/369		29.84	0.30 [0.14, 0.65]
Subtotal (95% CI)	705	649		38.30	0.47 [0.26, 0.84]
Total events: 17 (PSM), 34 (Conventional)					
Test for heterogeneity: Chi² = 4.07, df = 1 (P = 0.04), I² = 75.4%					
Test for overall effect: Z = 2.56 (P = 0.01)					
02 Lower quality trials					
Cromheecke 2000	0/24	0/25			Not estimable
Fitzmaurice 2002	0/23	1/26		1.56	0.38 [0.02, 8.78]
Gadisseur 2003	2/47	2/60		1.94	1.28 [0.19, 8.73]
Körtke 2001	29/280	45/295		48.50	0.68 [0.44, 1.05]
Sawicki 1999	1/83	3/82		3.34	0.33 [0.03, 3.10]
Sidhu 2001	0/35	1/49		1.39	0.46 [0.02, 11.04]
Sunderji 2004	0/69	3/70		3.85	0.14 [0.01, 2.75]
Völler 2005	2/101	1/101		1.11	2.00 [0.18, 21.71]
Subtotal (95% CI)	662	708		61.70	0.66 [0.44, 0.98]
Total events: 34 (PSM), 56 (Conventional)					
Test for heterogeneity: Chi² = 2.86, df = 6 (P = 0.83), I² = 0%					
Test for overall effect: Z = 2.08 (P = 0.04)					
Total (95% CI)	1367	1357		100.00	0.58 [0.42, 0.81]
Total events: 51 (PSM), 90 (Conventional)					
Test for heterogeneity: Chi² = 7.71, df = 8 (P = 0.46), I² = 0%					
Test for overall effect: Z = 3.22 (P = 0.001)					

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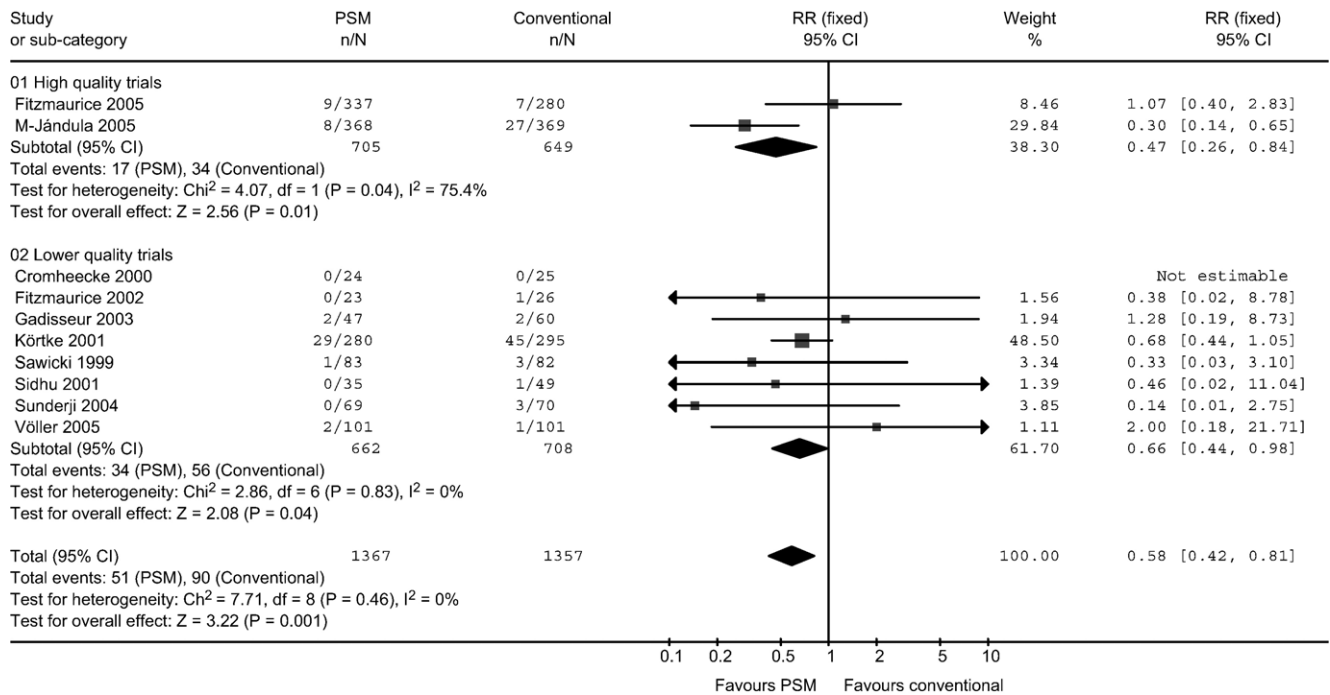Favours PSM   Favours conventional

Fig. 3. Major complications of self-management of oral anticoagulant therapy compared to conventional treatment. Abbreviations: CI: confidence interval, *n*: number of major complications, *N*: number of patients, PSM: patient self-management, RR: relative risk. Subtotals designate the subgroup analysis of trials of high quality and lower quality. A fixed effect model is applied. I^2 quantifies the percentage of variation between study results that is not due to sampling error.

3.6. Minor complications

Including all trials in a fixed effect model the RR was 0.76 (95% CI 0.63–0.91, $p=0.003$). The heterogeneity test was significant ($I^2=87.4\%$). A random effect model was therefore applied and a non-significant result was subsequently found; RR=0.98 (95% CI 0.49–1.99, $p=0.96$). When restricting the analyses to the high quality

Study or sub-category	PSM n/N	Conventional n/N	RR (random) 95% CI	Weight %	RR (random) 95% CI
01 High quality trials					
Fitzmaurice 2005	0/337	0/280			Not estimable
M-Jándula 2005	55/368	134/369		24.02	0.41 [0.31, 0.54]
Subtotal (95% CI)	705	649		24.02	0.41 [0.31, 0.54]
Total events: 55 (PSM), 134 (Conventional)					
Test for heterogeneity: not applicable					
Test for overall effect: Z = 6.24 (P < 0.00001)					
02 Lower quality trials					
Cromheecke 2000	1/24	4/25		7.68	0.26 [0.03, 2.17]
Fitzmaurice 2002	7/23	0/26		5.04	16.88 [1.02, 280.13]
Gadisseur 2003	0/47	0/60			Not estimable
Körtke 2001	72/280	59/295		23.86	1.29 [0.95, 1.74]
Sawicki 1999	13/83	10/82		19.29	1.28 [0.60, 2.76]
Sidhu 2001	11/35	12/49		20.11	1.28 [0.64, 2.57]
Sunderji 2004	0/69	0/70			Not estimable
Völler 2005	0/101	0/101			Not estimable
Subtotal (95% CI)	662	708		75.98	1.28 [0.86, 1.91]
Total events: 104 (PSM), 85 (Conventional)					
Test for heterogeneity: Chi² = 5.47, df = 4 (P = 0.24), I² = 26.9%					
Test for overall effect: Z = 1.21 (P = 0.23)					
Total (95% CI)	1367	1357		100.00	0.98 [0.49, 1.99]
Total events: 159 (PSM), 219 (Conventional)					
Test for heterogeneity: Chi² = 39.84, df = 5 (P < 0.00001), I² = 87.4%					
Test for overall effect: Z = 0.04 (P = 0.96)					

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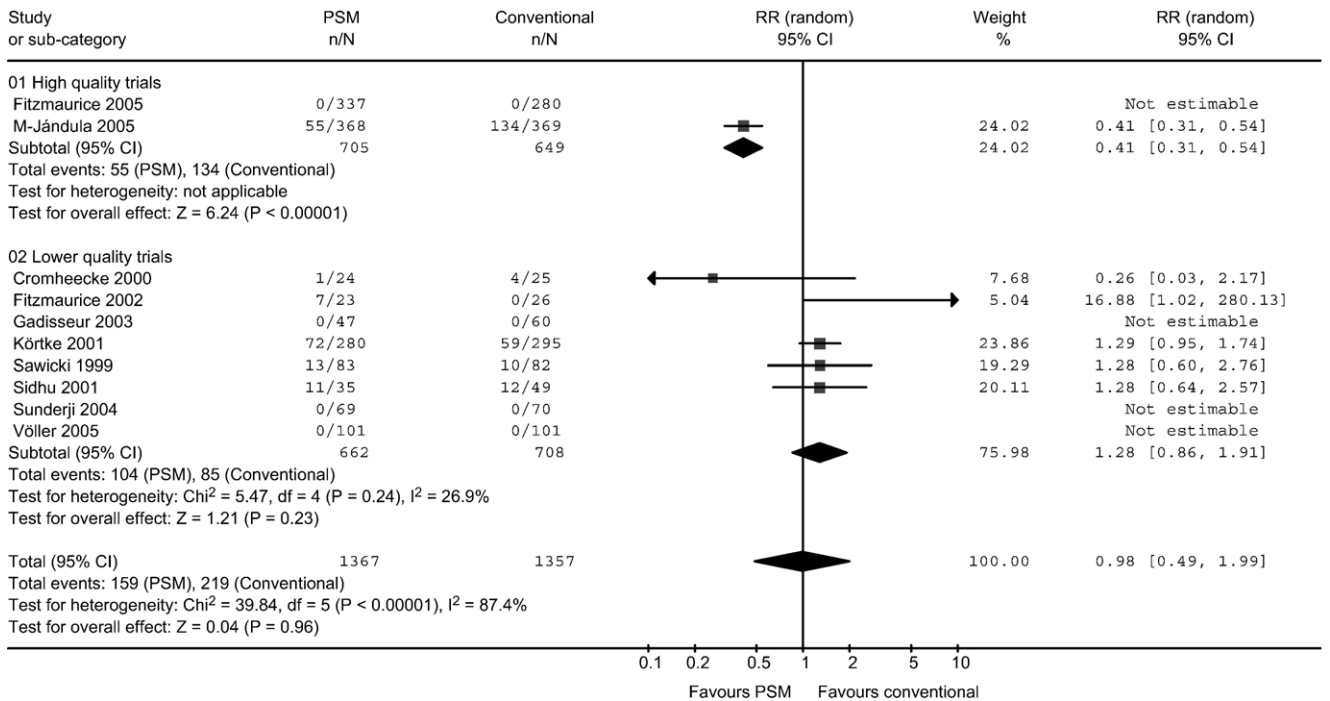Favours PSM   Favours conventional

Fig. 4. Minor complications of self-management of oral anticoagulant therapy compared to conventional treatment. Abbreviations: CI: confidence interval, *n*: number of minor complications, *N*: number of patients, PSM: patient self-management, RR: relative risk. Subtotals designate the subgroup analysis of trials of high quality and lower quality. A random effect model is applied. I^2 quantifies the percentage of variation between study results that is not due to sampling error.
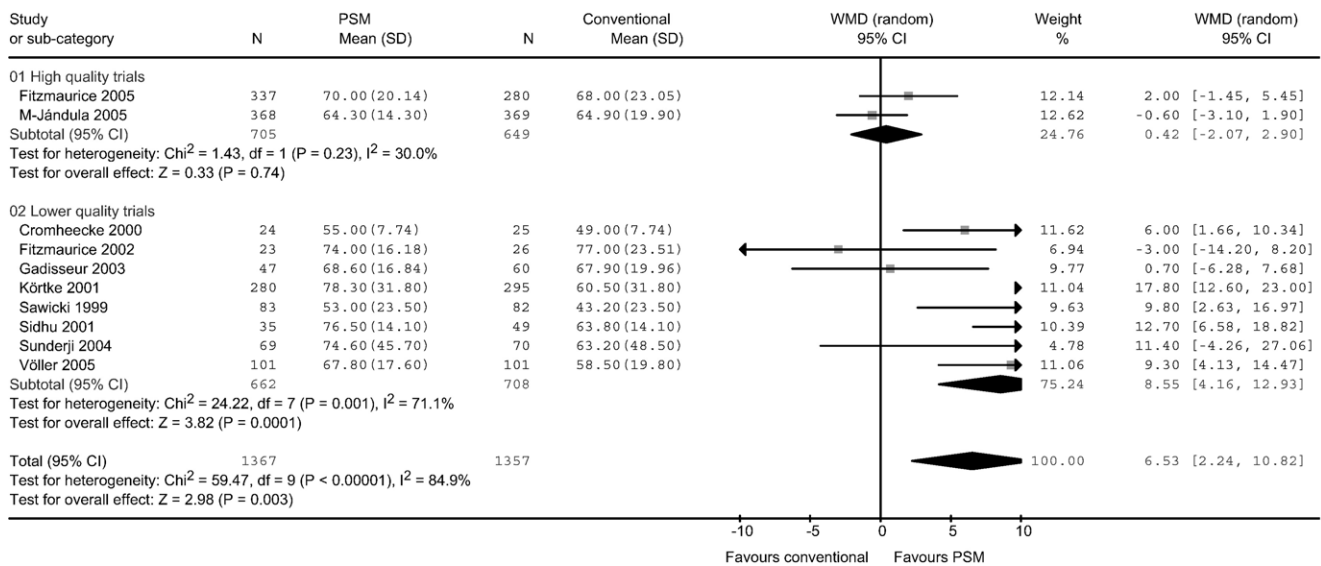
Study or sub-category	N	PSM Mean (SD)	N	Conventional Mean (SD)	WMD (random) 95% CI	Weight %	WMD (random) 95% CI
01 High quality trials							
Fitzmaurice 2005	337	70.00(20.14)	280	68.00(23.05)		12.14	2.00 [-1.45, 5.45]
M-Jándula 2005	368	64.30(14.30)	369	64.90(19.90)		12.62	-0.60 [-3.10, 1.90]
Subtotal (95% CI)	705		649			24.76	0.42 [-2.07, 2.90]
Test for heterogeneity: Chi² = 1.43, df = 1 (P = 0.23), I² = 30.0%							
Test for overall effect: Z = 0.33 (P = 0.74)							
02 Lower quality trials							
Cromheecke 2000	24	55.00(7.74)	25	49.00(7.74)		11.62	6.00 [1.66, 10.34]
Fitzmaurice 2002	23	74.00(16.18)	26	77.00(23.51)		6.94	-3.00 [-14.20, 8.20]
Gadisseur 2003	47	68.60(16.84)	60	67.90(19.96)		9.77	0.70 [-6.28, 7.68]
Körtke 2001	280	78.30(31.80)	295	60.50(31.80)		11.04	17.80 [12.60, 23.00]
Sawicki 1999	83	53.00(23.50)	82	43.20(23.50)		9.63	9.80 [2.63, 16.97]
Sidhu 2001	35	76.50(14.10)	49	63.80(14.10)		10.39	12.70 [6.58, 18.82]
Sunderji 2004	69	74.60(45.70)	70	63.20(48.50)		4.78	11.40 [-4.26, 27.06]
Völler 2005	101	67.80(17.60)	101	58.50(19.80)		11.06	9.30 [4.13, 14.47]
Subtotal (95% CI)	662		708			75.24	8.55 [4.16, 12.93]
Test for heterogeneity: Chi² = 24.22, df = 7 (P = 0.001), I² = 71.1%							
Test for overall effect: Z = 3.82 (P = 0.0001)							
Total (95% CI)	1367		1357			100.00	6.53 [2.24, 10.82]
Test for heterogeneity: Chi² = 59.47, df = 9 (P < 0.00001), I² = 84.9%							
Test for overall effect: Z = 2.98 (P = 0.003)							

-10   -5   0   5   10
Favours conventional   Favours PSM

Fig. 5. Time within therapeutic INR target range (in percent) of self-management of oral anticoagulant therapy compared to conventional treatment. Abbreviations: CI: confidence interval, PSM: patient self-management, SD: standard deviation, WMD: weighted mean difference (in percent). Subtotals designate the subgroup analysis of trials of high quality and lower quality. A random effect model is applied. I^2 quantifies the percentage of variation between study results that is not due to sampling error.

studies, we found that RR was 0.41 (95% CI 0.31–0.54, $p < 0.00001$).

3.7. Time within therapeutic INR target range (in percent)

Including all trials in a fixed effect model the weighted mean difference was 4.36% (95% CI 2.87–5.86, $p < 0.00001$). The heterogeneity test was significant ($I^2 = 84.9\%$). A random effect model was therefore applied and the result was still significant, weighted mean difference = 6.53% (95% CI 2.24–10.82, $p = 0.003$). When restricting the analyses to the high quality studies, the weighted mean difference was 0.42% (95% CI −2.07 to 2.90, $p = 0.74$).

The forest plots for each of the outcomes are shown in Figs. 2–5.

Funnel plots were performed for all outcomes, and substantial asymmetry regarding minor complications and time within therapeutic INR target range was found (plots not shown).

4. Discussion

We found that highly selected patients performing self-management had a reduced risk of death, major complications and spent an increased proportion of time within therapeutic INR target range compared to patients in conventional management. No clear difference in the risk of minor complications was found. There was substantial heterogeneity regarding two of the outcomes (minor complications and time within therapeutic INR target range).

The trials included were all (except two) ranked as lower quality trials and the results and conclusions should be viewed and interpreted taking this drawback into consideration. As described above and as seen in Figs. 2–5, the positive effect of self-management is not so evident in the high quality trials. However, the limited number of studies (two trials) renders us from drawing firm conclusions.

We did not perform further sub-analyses, e.g., to test self-management versus highly specialized anticoagulation clinics and self-management versus routine management/hospital outpatient clinics. This was due to the limited number of trials and a variation between the trials in the exact definition and function of the type of management provided to the conventional managed group, e.g., regarding highly specialized anticoagulation clinic. Quality of life has only been examined in a few trials [7,12,18,19] using non-comparable parameters. Neither did we include measures of cost-effectiveness in the analyses due to possible inaccuracy and inconsistency of the available data [4].

A published systematic review based on four studies has previously concluded that self-management is safe, improves treatment related quality of life and the quality of oral anticoagulant therapy [2]. However, the review only included four studies of which one was not a randomized controlled trial.

A similar conclusion was reached in a recent meta-analysis performed by Odegaard [3]. However, the mixing of observational and randomized studies and the lack of assessment of the methodological quality of the included studies makes it difficult to draw conclusions from this study.

Time within therapeutic INR target range is merely a surrogate endpoint. Despite this it is often used since the required number of patients is low [20]. It is well described that the number of complications increases in parallel with the time patients spend outside the therapeutic INR target range [20,21]. The result is highly dependent on the therapeutic INR target range; a target range of 2.0–4.0 will provide a higher time

within therapeutic INR target range compared to a target range of 2.0–3.0. Substantial differences existed regarding the INR target range among the trials included in our meta-analysis (Table 1), and this makes comparison between the studies difficult. Furthermore, time within therapeutic INR target range is also highly dependent on the frequency of testing [22].

The high heterogeneity and the asymmetry in the funnel plot found when analyzing time within therapeutic INR target range is therefore most likely due to an inappropriate effect measure. This should be taken in considerations when using time within therapeutic INR target range to estimate the quality of treatment.

The incidence of minor complications also exhibited a high heterogeneity and asymmetry in the funnel plot, and it may be due to the difficulties in finding and reporting these complications and a variation between the included studies in a precise definition of these complications.

Most of the studies have included patients with various indications of oral anticoagulant therapy (Table 1), which makes it difficult to extrapolate the results to a specific patient population.

Further, it is possible that the effect of self-management may differ between different groups of patients, i.e., according to the indication for anticoagulation (e.g., atrial fibrillation versus mechanical heart valve) or age. However, it was unfortunately not possible to subdivide the published data regarding these covariates.

In the included trials, the target-and sample population is often not well-described and there is a variation between the trials regarding in- and exclusion criteria's. Furthermore, the information/knowledge of oral anticoagulant therapy given to the patients shows variation; both between trials and whether both randomized groups received the same level of information regarding oral anticoagulant therapy before randomization or if it was only provided to the group randomized to self-management.

However, it should be noted that all of the trials only included a highly selected group of patients, with a presumed high level of compliance and with adequate mental and physical abilities to operate the coagulometer, dosage the coumarin, etc. The fraction of patients, who are capable of self-management in routine clinical settings has been estimated ranging from 16% to 80% [10,23–25].

The potential large heterogeneity of patients and care provided between the trials is displayed when comparing the two high quality trials; the events of death and complications are relatively high in the study by Menendez-Jandula et al. [11] compared to that of Fitzmaurice et al. [15]. However, this could also be partly due to differences in detecting events.

Our study was an efficacy study looking at the overall efficacy and safety of self-management, and thereby investigating if self-management works under ideal study conditions. The results of this meta-analysis can therefore probably not be generalized to routine clinical practice.

The results of this meta-analysis are limited by the lack of complete availability of relevant data. Furthermore, the methodological flaws in the included low-quality trials have to be taken into consideration when interpretations are made of the results.

In conclusion, a majority of the existing trials have various methodological problems. However, self-management of oral anticoagulant therapy appeared at least as good and possible better than conventional treatment in highly selected patients. Further randomized controlled trials of high methodological quality with well-defined clinical end points (death and major complications) are therefore needed in order to more accurately assess the efficacy of self-management of oral anticoagulant therapy.

Acknowledgements

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