APPENDIX 4: CHARACTERISTICS OF INCLUDED PRIMARY STUDIES

Study Year Country	Study Design Sample Size	Patient Population	Intervention	Comparator	Outcomes
Specialized Anticoagulation Clinics vs. Usual Care					
Aziz et al.[15] 2011 USA	Cohort study (2,397 patients)	Mean age: NR Indication: NR Warfarin only	Nurse-managed anticoagulation service with physician oversight. No POC testing (n = 131)	Usual physician care (n = 2,266)	ER visit: Nurse AMS: 2 patients (1.5%) UC: 247 patients (10.9%) Hospitalization: Nurse AMS: 3 patients (2.3%) UC: 289 patients (12.8%) P-values reported for cost data only
Garton and Crosby[16] 2011 USA	Retrospective medical record review (64 patients)	Mean age: 74 Indication: 81% AF Warfarin only	Pharmacist-managed anticoagulation clinic with POC testing (n = 64)	Usual physician care before clinic referral (n = 64)	Percentage of INR values in range: Pharmacist AMS: 81.1% UC: 71.1% P < 0.0001 Estimated variance in therapeutic INR rates Pharmacist AMS: 185.2 UC: 365.7 P = 0.004
Hall et al.[17] 2011 USA	Retrospective cohort (350 patients)	Mean age: AMS 63.7 UC 65.1 Indication: AMS 68.6% AF UC 60.0% AF Warfarin only	Pharmacist-managed anticoagulation clinic with laboratory INR measurement (n = 175)	Usual physician care (n = 175)	TTR (Rosendaal method): Pharmacist AMS: 73.7% UC: 61.3% P < 0.0001 Adverse events (anticoagulation-related, details not provided): Pharmacist AMS: 14 events in 9 patients (5.1%) UC: 41 events in 27 patients (15.4%) P < 0.0001 ER visits: Pharmacist AMS: 58 UC: 134

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Study Year Country	Study Design Sample Size	Patient Population	Intervention	Comparator	Outcomes
					P < 0.00001 Hospitalizations: Pharmacist AMS: 3 UC: 14 P < 0.00001
Rudd and Dier[18] 2010 USA	Retrospective medical record review (996 patients)	Mean age: 72 to 75 (across study groups) Indication: 50% to 56% AF (across study groups) Warfarin only	Pharmacist-managed AMS with POC or laboratory testing (n = 489), or nurse-managed AMS (lab testing only) (n = 307)	Primary care provider with laboratory INR testing (n = 200)	TTR (Rosendaal method) Pharmacist AMS: 83.6% Nurse AMS: 71.8% Primary care: 57.4%, P < 0.05 between all models Hospitalization rate (per 100 patient-years) Pharmacist AMS: 5.4 Nurse AMS: 12.3 Primary care: 13.9, P < 0.05 between pharmacist AMS and other models ER visit rate (per 100 patient-years) Pharmacist AMS: 1.2 Nurse AMS: 5.6 Primary care: 5.6, P < 0.05 between pharmacist AMS and other models
Garwood et al.[19] 2008 USA	Retrospective before-after study (40 patients)	Mean age: 61.7 Indication: 35% AF Warfarin only	Pharmacist-managed anticoagulation clinic	Transition to physician-managed care after INR stabilization	% of INRs in range: Pharmacist: 76% Physician: 48%, P < 0.0001 INRs in range for each patient (median %) Pharmacist: 75% Physician: 36.5%, P < 0.0001 Cases requiring additional medical care (e.g., hospitalization, emergency room visit) Pharmacist: 2 (2 bleeding related) Physician: 13 (12 bleeding related), P =

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Study Year Country	Study Design Sample Size	Patient Population	Intervention	Comparator	Outcomes
					0.0412 Perceived quality of care (based on patient satisfaction survey) was higher for pharmacist-managed care
Comparison of Clinic Models					
Fitzmaurice[20] 2006 UK	RCT (224 patients)	Mean age: NR Indication: NR Warfarin only	Nurse-led POC testing and computer-based decision support in primary practice (n = 122)	"Traditional" hospital-based anticoagulation management (n = 102)	TTR (Rosendaal method) Nurse-led: 69%, 95% CI 66% to 73% Hospital: 57%, 95% CI 50% to 63% No significant difference in serious adverse events (3 versus 3, P = NR), including death (1 versus 0, P = NR) between the two groups
Rudd and Dier[18] 2010 USA	See above				
Edgeworth and Coles[21] 2010 UK	Retrospective before-after study (46 patients)	Mean age: 69.7 (at recruitment) Indication: 65.2% AF Warfarin only	Nurse-led POC-testing and computer-based decision support in primary practice	Phlebotomy and secondary care (hospital) anticoagulation service	TTR (method not described) Nurse-led primary care: 72.1% Secondary (hospital) care: 76.4% Mean difference: 4.3 (5.6% reduction), 95% CI –2.7% to +13.9%
Patient Self-testing or Self-management vs. Clinic Care					
Christensen et al.[22] 2011 Denmark	RCT (123 patients)	Mean age: 62 to 66 (across study groups) Indication: 51 to 67% AF (across study groups)	PST once or twice weekly, with hospital clinic adjusted dosing (INR and dose adjustments reported using online system) (n = 83)	Hospital-clinic management with laboratory INR measurements every 4 weeks (n = 40)	TTR (Rosendaal method) PST (1x): 79.7%, 95% CI 79.0% to 80.3% PST (2x): 80.2%, 95% CI 79.4% to 80.9% Clinic: 72.7%, 95% CI 71.9% to 73.4% One hospitalization reported across all groups

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Study Year Country	Study Design Sample Size	Patient Population	Intervention	Comparator	Outcomes
McCahon et al.[23] 2011 UK	Survey of RCT participants (SMART trial) (363 responders)	Mean age: NR Indication: NR Warfarin only	PSM with self INR testing every 2 weeks (n = 202)	Hospital or practice-based anticoagulation clinic care (n = 161)	Quality of life: self-efficacy improvement favours PSM: 1.67 versus 0.43, P = 0.01 Social network strain increased with routine care after adjusting for age: 1.36 (clinic) versus 0.34 (PSM), P = 0.02 No significant difference in daily hassle, psychological distress, treatment satisfaction, or anxiety
Gardiner et al.[24] 2009 UK	Prospective cohort study (318 patients enrolled)	Median age (PST): 58 Median age (UC): 68 Indication (PST): 38% AF Indication (UC): 56% AF	PST every 2 weeks with computer dosing performed by specialist nurse (n = 67 in final analysis)	Routine care at a hospital-based anticoagulation clinic (n = 88 in final analysis)	TTR (Rosendaal method): PST: 71%, 95% CI 64.1% to 75.3% Clinic: 60%, 95% CI 55.0% to 63.2% Major bleed (defined as requiring hospitalization or transfusion): PST: 1.7 per 100 patient-years Clinic: 5.4 per 100 patient-years Minor bleed: PST: 8.4 per 100 patient-years Clinic: 16.2 per 100 patient-years Thrombosis: PST: 3.4 per 100 patient-years Clinic: 1.4 per 100 patient-years
O'Shea et al.[25] 2008 USA	Prospective before-after study (58 patients)	Median age: 54.1 (range 27 to 82) Indication: 31% AF Warfarin only	Internet-supervised PSM with self INR testing every 1 or 2 weeks	Routine care at the Duke Anticoagulation Clinic	TTR (Rosendaal method) PST: 74.4% Clinic: 63.0% Mean difference 11.4% 95% CI, 5.5% to 17.3% No bleeding or thrombosis reported during the study period

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Study Year Country	Study Design Sample Size	Patient Population	Intervention	Comparator	Outcomes
McCahon et al.[26] 2007 UK	Retrospective multicentre matched control study (78 patients from SMART trial)	Mean age (PSM): 64 Mean age (control): 66 Indication: 54% AF Warfarin only	PSM with self INR testing every two weeks (n = 38)	Hospital or practice-based anticoagulation clinic care (n = 40)	TTR (Rosendaal method) TTR calculated within and post-SMART trial PSM: trial 75%, post-trial 70%, P = 0.12 Control: trial 64%, post-trial 57%, P = 0.54 No significant difference in change in mean TTR between PSM and control, P = 0.54
Patient Self-testing or Self-management vs. Usual Care					
Harper and Pollock[27] 2011 New Zealand	Prospective before-after study (41 patients)	Mean age: NR Indication: NR Warfarin only	PSM using Internet-based decision support	Laboratory INR tests with dose management by general practitioner or lab staff	TTR (Rosendaal method) Overall PSM 81.3% vs. UC 72.4%, P = 0.16 In patients with poor control (TTR < 60%) prior to PSM PSM 71.1% vs. UC 38.8%, P = 0.01 In patients with good control (TTR > 60%) prior to PSM PSM 82.5% vs. UC 83.0%, P = NS
Salvador et al.[28] 2008 Spain	Prospective cohort study (108 patients)	Mean age (PST): 72.5 Mean age (control): 72.9 Indication (PST): 76% AF Indication (control): 76% AF	PST every 3 weeks with dose adjustment by general practitioner using a decision-support tool (INR and dose adjustments reported using telemedicine system)	Laboratory INR tests with dose management by general practitioner using a decision support tool	TTR (Rosendaal method) PST 65.7% vs. UC 66.4%, P = 0.85 *Mortality*: PST 5.5% vs. UC 5.5%, P = 1.0 *Major bleeding (not defined)*: PST 0% vs. UC 1.8%, P = 1.0 *Minor bleeding*: PST 7.4% vs. UC 3.7%, P = 0.67 *Thrombosis*: PST 1.8% vs. UC 3.7%, P = 1.0 *Hospital admissions*: PST 3 vs. UC 4 Significant improvements in quality of life outcomes were reported with PST

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Study Year Country	Study Design Sample Size	Patient Population	Intervention	Comparator	Outcomes
Computer vs. Manual Dosing					
Poller et al.[29] 2009 Multicentre	RCT 2,631 patients	Mean age: 65.9 Indication: 48% AF	Dawn AC dosing program (n = 1,315)	Manual dosing by clinic medical staff (n = 1,316)	TTR (Rosendaal method) Manual dosing: 63.4% Computer dosing: 66.8% Difference: 3.5%, 95% CI 2.3% to 4.9%, P < 0.001 Total adverse events per 100 patient-years (bleeds, thrombosis, death) Manual dosing: 5.8, 95% CI 4.6 to 7.0 Computer dosing: 5.6, 95% CI 4.6 to 6.9 Total adverse events (AF only) Manual dosing: 5.9 per 100 patient-years Computer dosing: 6.1, P = NS
Poller et al.[30] 2008 Multicentre	RCT 10,421 patients	Mean age: 67.1 Indication: 45% AF	Parma-5 dosing program (n = 5,290)	Manual dosing by clinic medical staff (n = 5,131)	TTR (Rosendaal method) Manual dosing: 65.0% Computer dosing: 65.7% Difference: 0.7%, 95% CI 0.1% to 1.3%, P = 0.021 Total adverse events per 100 patient-years (bleeds, thrombosis, death) Manual dosing: 6.0, 95% CI 5.5 to 6.6 Computer dosing: 5.5, 95% CI 4.9 to 6.0 Incidence rate ratio: 0.89, 95% CI 0.78 to 1.01 Total adverse events (AF only) Manual dosing: 5.1 Computer dosing: 4.6, P = NS

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Study Year Country	Study Design Sample Size	Patient Population	Intervention	Comparator	Outcomes
Poller et al.[31] 2008 Multicentre	RCT 13,052 patients	Mean age: 66.9 Indication: 46% AF	Dawn AC or Parma-5 dosing program (n = 6,605)	Manual dosing by clinic medical staff (n = 6447)	TTR (Rosendaal method) Manual dosing: 64.7% Computer dosing: 65.9% Mean difference: 1.2%, 95% CI 0.7% to 1.8% TTR (AF patients only, Rosendaal method) Manual dosing: 66.2% Computer dosing: 67.6%, P = NR Total adverse events (bleeds, thrombosis, death) Incidence rate ratio (favours computer dosing): 0.90, 95% CI 0.8 to 1.02, P = NS Total adverse events (AF only) Incidence rate ratio (favours computer dosing): 0.93, 95% CI 0.78 to 1.12, P = NS
Onundarson et al.[32] 2008 Iceland	Retrospective cohort study 1,182 patients	Before (1992): Mean age: 64 Indication: 31% AF After (2006): Mean age: 73 Indication 71% AF	Dawn AC dosing program (n = 941)	Manual dosing by clinic cardiologist (n = 241)	TTR (AF patients, Rosendaal method) Manual dosing: 46% Computer dosing: 81%, P = NR

AF = atrial fibrillation; AMS = anticoagulation management service; NR = not reported; NS = not significant; POC = point of care; PSM = patient self-management; PST = patient self-testing; RCT = randomized controlled trial; UC = usual care; vs. = versus.

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