

Effect of an intake aid with reminder function on timing **adherence to direct oral anticoagulants** in stroke patients – a randomised cross-over trial

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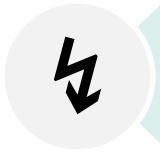
Background & Aim



Stroke patients with atrial fibrillation are at high risk of recurrence ¹



Direct oral anticoagulants (DOAC) are effective in secondary stroke prevention ¹



Low adherence to DOAC has been associated with worse outcomes ²



Stroke population might be prone to non-adherence due to cognitive impairments ³

**→ To investigate the effect of an intake reminder on adherence
in DOAC-treated stroke patients**

Methods

Study design: randomised, cross-over study

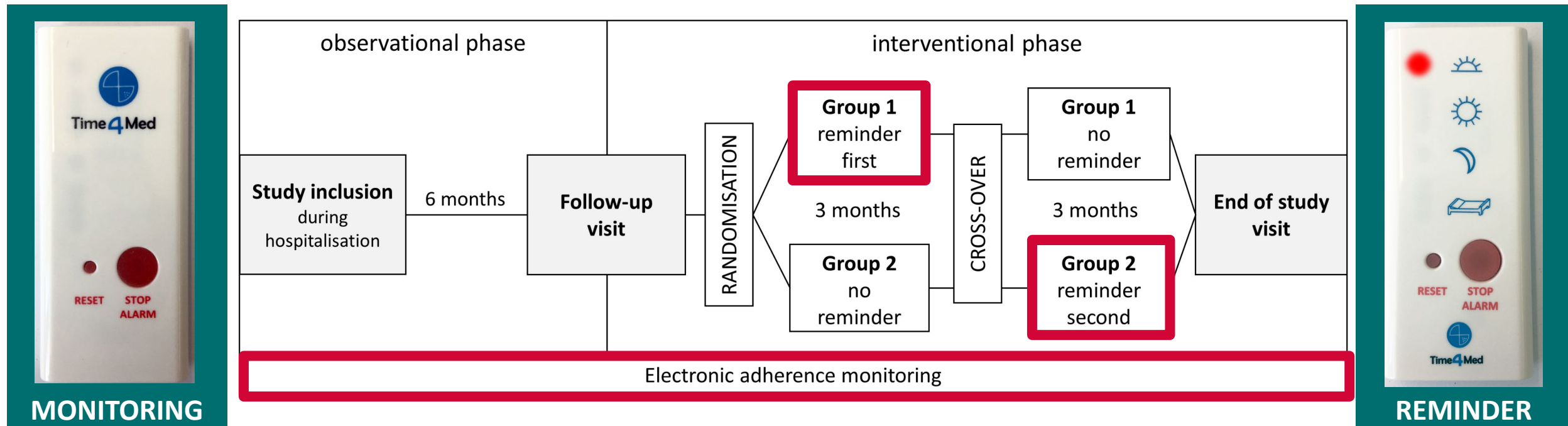
Outcomes: adherence to DOAC

Inclusion criteria: atrial fibrillation, hospitalised for ischaemic stroke, DOAC

- > patients achieving 100%-timing adherence
- > patients achieving 100%-taking adherence
- > overall timing adherence
- > overall taking adherence

Intervention: intake reminder

clinical events



Results

Participants N = 130 recruited
N = 84 analysed

Group 1 reminder first	
N = 42	
Mean age	76 years
Women	41%
DOAC once-daily	30%
Median NIHSS	1.0

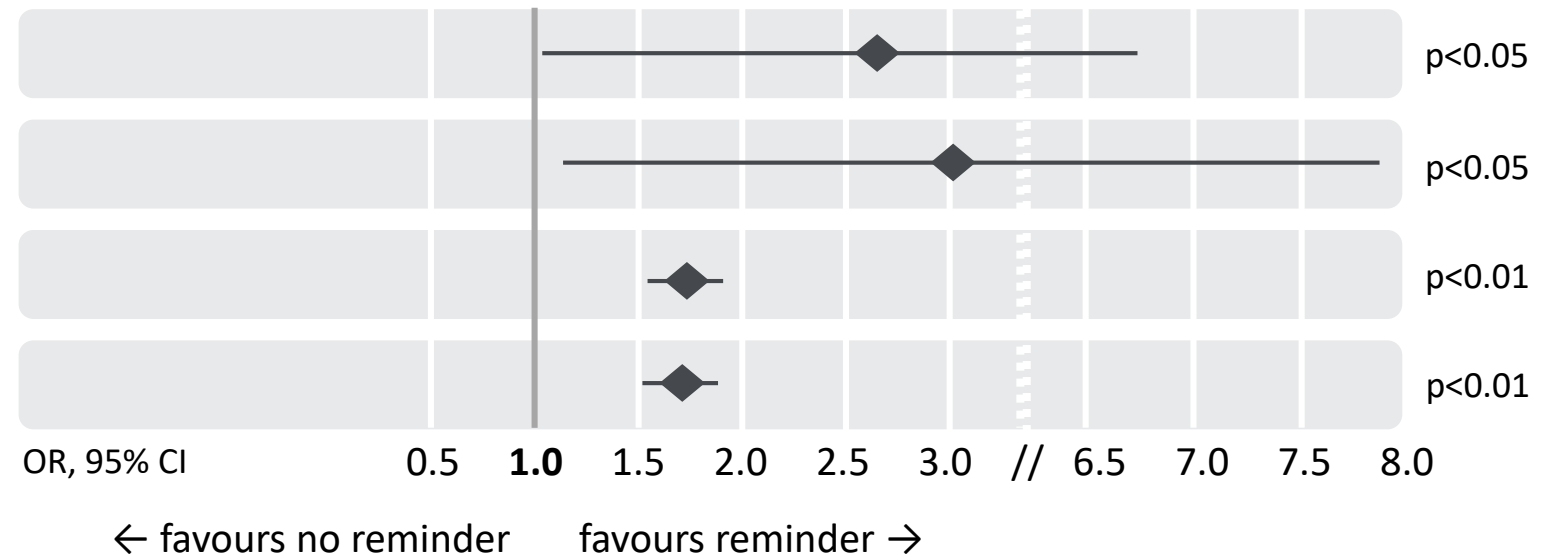
Group 2 reminder second	
N = 42	
Mean age	77 years
Women	38%
DOAC once-daily	24%
Median NIHSS	1.0

Patient characteristics

Adherence outcomes

100%-timing was achieved by 10 patients with reminder and by 0 patients without

100%-taking was achieved by 10 patients with reminder and by 2 patients without



Results

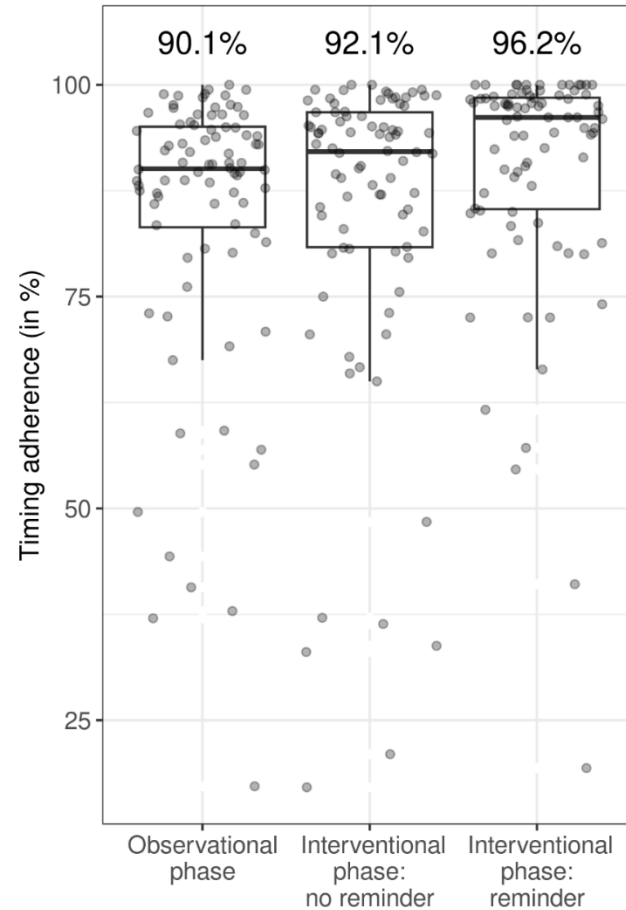


Figure Boxplot of the median overall timing and taking adherence of 84 participants per study phase

Clinical events

- 9 patients (11%) suffered ischaemic events (= recurrent ischaemic strokes, transient ischaemic attacks, or myocardial infarctions)

Conclusion

- Intake reminders increased adherence to DOAC in stroke patients
- Reminders should be offered in patients with recent stroke to improve adherence to DOAC and to potentially reduce recurrent events



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Thank you for your attention!

Patient characteristics

	Group A	Group B	p	SMD
N	42	42		
Age, years (mean (SD))	75.9 (8.5)	77.0 (9.8)	0.569	0.125
Female (%)	17 (40.5)	16 (38.1)	1.000	0.049
Comorbidities (%)				
Hypertension	36 (85.7)	37 (88.1)	1.000	0.071
Diabetes	5 (11.9)	12 (28.6)	0.103	0.424
Dyslipidemia	29 (69.0)	36 (85.7)	0.118	0.407
DOAC agent (%)			0.898	0.169
Dabigatran	10 (23.8)	9 (21.4)		
Apixaban	20 (47.6)	23 (54.8)		
Rivaroxaban	7 (16.7)	5 (11.9)		
Edoxaban	5 (11.9)	5 (11.9)		
DOAC regimen, once-daily (%)	12 (30.0)	10 (23.8)	0.702	0.140
Days of hospitalization (median [IQR])	7.5 [5.0-10.8]	5.0 [3.2-8.0]	0.042	0.500
Stroke hemisphere (%)			0.383	0.389
left	16 (38.1)	14 (33.3)		
right	11 (26.2)	16 (38.1)		
both	10 (23.8)	5 (11.9)		
none	5 (11.9)	7 (16.6)		
Fazekas score (%)			0.903	0.104
1	18 (48.6)	20 (52.6)		
2	14 (37.8)	14 (36.8)		
3	5 (13.5)	4 (10.5)		
MoCA score (mean (SD))	23.9 (4.8)	24.5	0.543	0.133
mRS (median [IQR])	2.0 [1.0-2.0]	2.0 [1.0-2.0]	0.892	0.067
NIHSS (median [IQR])	1.0 [0.0-2.0]	1.0 [0.0-2.0]	0.245	0.145
Daily pill burden (median [IQR])	7.5 [5.0-9.8]	7.0 [5.0-9.8]	0.743	0.074
Prior pillbox use (%)	16 (38.1)	18 (42.8)	0.824	0.097

Abbreviations

DOAC: direct oral anticoagulant,
IQR: interquartile range,
MoCA: Montreal Cognitive Assessment
mRS: modified Rankin Scale,
NIHSS: National Institutes of Health
Stroke Scale,
SD: standard deviation,
SMD: standardized mean difference

Flow diagram

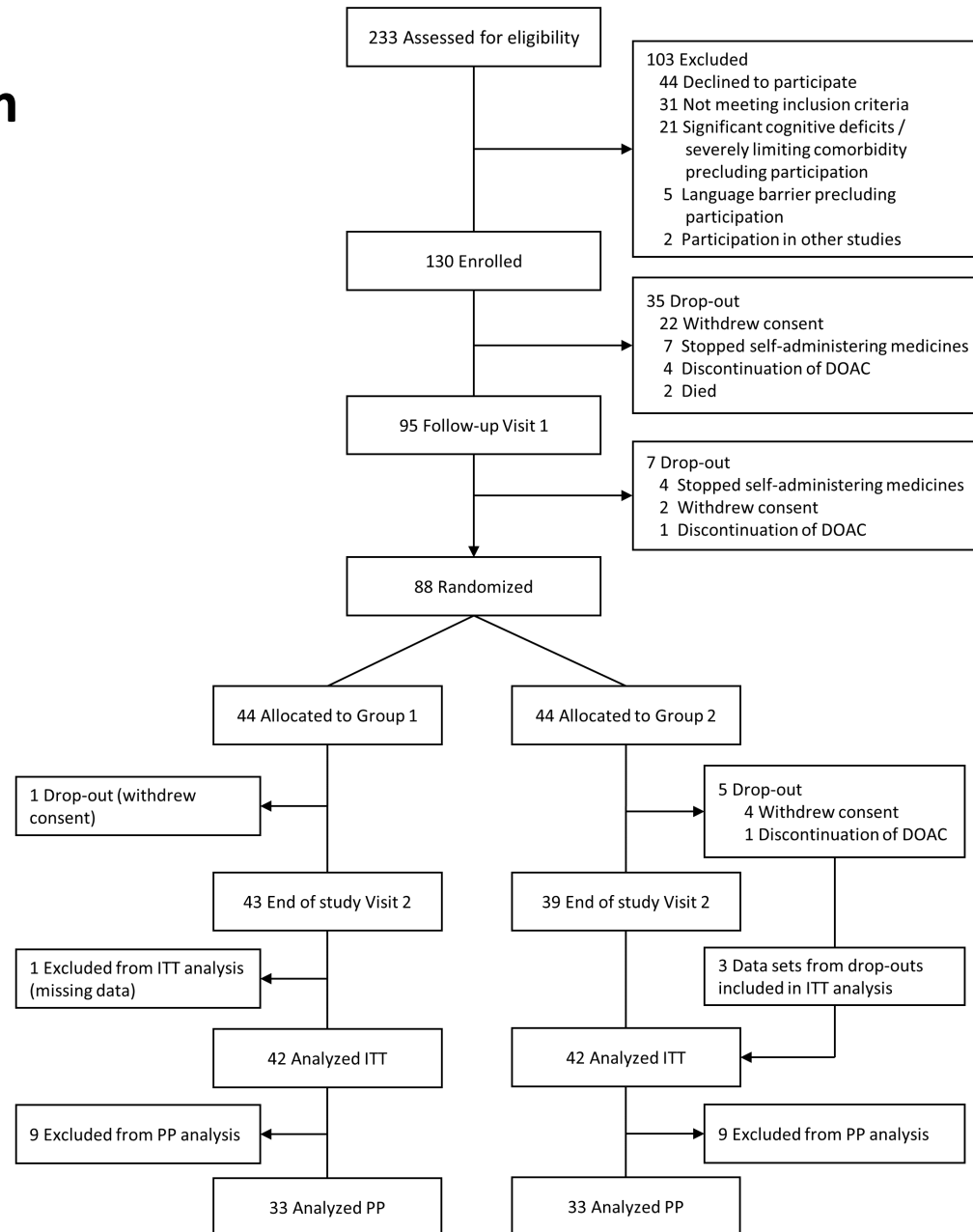


Figure Flow diagram of study participants. DOAC: direct oral anticoagulant, ITT: intention-to-treat, PP: per-protocol

Intake aid with reminder function



Adherence outcomes

Number of patients who reached different cut-offs of *timing adherence* and *taking adherence* with and without the use of the reminder.

Patients, (%)	always	without reminder	with reminder	never
100%-timing	2 (2.4)	0 (0)	10 (11.9)	72 (85.7)
90%-timing	43 (51.2)	5 (5.9)	15 (17.9)	21 (25.0)
80%-timing	64 (76.2)	3 (3.6)	10 (11.9)	7 (8.3)
100%-taking	4 (4.8)	2 (2.4)	10 (11.9)	68 (80.9)
90%-taking	47 (55.9)	5 (5.9)	17 (20.2)	15 (17.9)
80%-taking	65 (77.4)	3 (3.6)	10 (11.9)	6 (7.1)

Sensitivity analyses

Effect of the reminder on patient ratio with *90%-timing adherence*

		OR	95% CI	p value
Time-trend effect	first 3 months interventional phase vs second 3 months interventional phase	0.66	[0.27-1.62]	0.366
Carry-over effect	interventional phase with reminder vs interventional phase without reminder	0.92	[0.05-17.1]	0.950
Per-protocol analysis	in patients who used the reminder as intended (N = 66)	2.53	[0.86-7.41]	0.091

Sub-group analysis

Effect of the reminder on patient ratio with *90%-timing adherence* in four predefined subgroups.

		OR	95% CI	p value
DOAC type	once-daily (N=22) vs twice daily (N=60)	3.02	[0.30-30.8]	0.350
Stroke location	right (N=27) vs left (N=30) hemisphere	0.72	[0.06-9.05]	0.800
Fazekas score	2 (N=28) vs 1 (N=38)	7.08	[0.72-69.8]	0.094
	3 (N=9) vs 1 (N=38)	2.50	[0.12-50.6]	0.551
MoCA score	values between 0-30 (N=84)	1.04	[0.85-1.27]	0.680

Abbreviations: DOAC: direct oral anticoagulant, MoCA: Montreal Cognitive Assessment

Patient satisfaction with the reminder

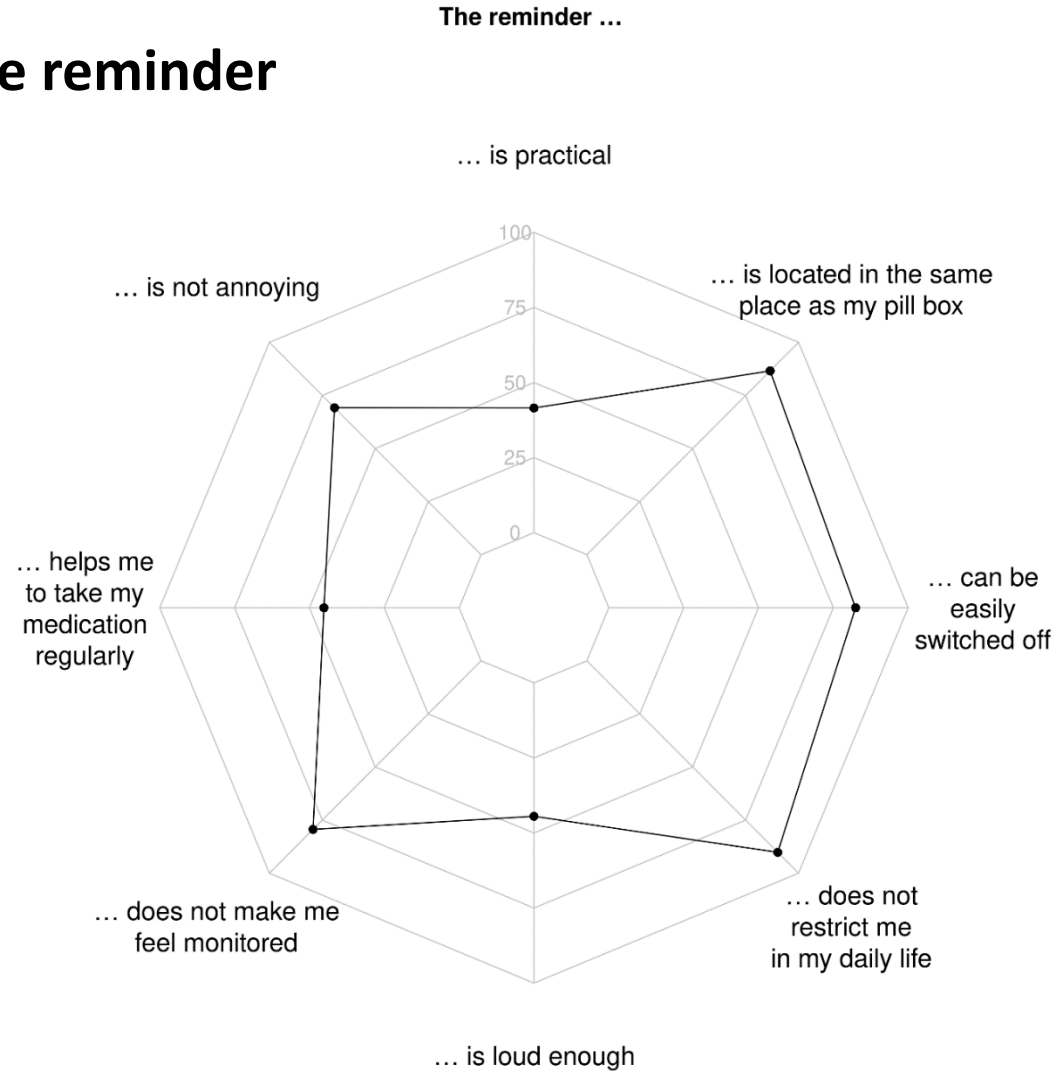


Figure Answers to eight items regarding the satisfaction with the reminder from 84 patients. A value near the centre (0%) indicates poor agreement with the statement.