bjh research paper

# Predictors of anticoagulation quality in 15 834 patients performing patient self-management of oral anticoagulation with vitamin K antagonists in real-life practice: a survey of the International Self-Monitoring Association of Orally Anticoagulated Patients

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Received 27 April 2016; accepted for publication 17 June 2016

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## Summary

Although patient self-management (PSM) of oral anticoagulation with vitamin K antagonists is recommended for patients requiring long-term anticoagulation, important aspects are still unclear. Using data from a large international survey ($n$ = 15 834; median age 72 years; 30·1% female), we studied predictors of poor anticoagulation control (percentage of International Normalized Ratio values within therapeutic range below 75%) and developed a simple prediction model. The following variables were identified as risk factors for poor anticoagulation control and included in the final model: higher intensity of therapeutic range (odds ratio [OR] on every level 1·9; 95% confidence interval [CI] 1·8–2·0), long intervals between measurements (>14 d; 1·5; 95% CI 1·3–1·7), female sex (OR 1·3; 95% CI 1·2–1·4), and management other than PSM (OR 1·4; 95% CI 1·2–1·6). At a threshold of 0·2 (at least one variable present), the model predicted poor anticoagulation control with a sensitivity of 85·3% (95% CI: 84·0, 86·4) and a specificity of 28·5% (27·6, 29·5). The area under the receiver operated characteristic curve was 0·65. Using the proposed prediction model, physicians will be able to identify patients with a low chance of performing well, considering additional training, regular follow-up, or adjustment of therapeutic ranges.

**Keywords:** vitamin K antagonists/inhibitors, self care, International Normalized Ratio, anticoagulant administration/dosage, drug monitoring.

Broad implementation of patient self-management (PSM) in patients requiring anticoagulation with Vitamin K antagonists (VKA) is still hampered by unsolved issues. PSM is regarded as an important concept to meet the needs of patients with chronic disorders such as diabetes, hypertension or chronic obstructive pulmonary disease (Bodenheimer *et al*, 2002; Effing *et al*, 2007; Uhlig *et al*, 2013). It is not only effective in terms of clinical outcomes but reduces health care costs in patients with arthritis, asthma and other conditions (Bodenheimer *et al*, 2002). There are several reasons why PSM should be implemented in the long-term treatment with VKA (Christensen *et al*, 2016). First, a large number of patients worldwide are treated with anticoagulants and the numbers are expected to increase [1% of the population was estimated for the UK by Pirmohamed (2006)]. Furthermore, many researchers expect that VKA will continue to play a major role, not only in patients with mechanical heart valves (Kirley *et al*, 2012) (Furie, 2013; Lip *et al*, 2015; Potpara *et al*, 2015). Second, the appropriate VKA dosage is highly variable among individuals and treatment must be closely monitored with the International Normalized Ratio (INR) (Juurlink, 2007; Ageno *et al*, 2012). Accurate and easy to handle point-of-care (POCT) devices are available (Christensen & Larsen, 2012; Nagler *et al*, 2013). Third, the efficacy and safety of VKA treatment depends largely on the quality of anticoagulation, which is represented by the time spent

  doi: 10.1111/bjh.14273

within the therapeutic range (TIR) (White *et al*, 2007). Moreover, the quality of anticoagulation is considerably influenced by the treatment setting, with higher TIR achieved in anticoagulation clinics or PSM schemes (van Walraven *et al*, 2006). However, the overall quality of anticoagulation with VKA is still variable (Dlott *et al*, 2014) and only a minority of patients are trained for PSM (Ferguson *et al*, 2016).

PSM training enables patients to self-care with regard to long-term anticoagulation treatment in terms of INR measurements and VKA dosing adjustments. In contrast, patient self-testing (PST) only enables patients to determine INR values, with dose-adjustments being made by medical professionals. Both treatment schemes are summarised under the term 'self-monitoring'. A number of PSM programmes have been developed and a large number of patients were trained, predominantly in Europe (Cromheecke *et al*, 2000; Kortke *et al*, 2001; Sunderji *et al*, 2004; Fitzmaurice *et al*, 2005a; Menendez-Jandula *et al*, 2005; Christensen *et al*, 2006; Siebenhofer *et al*, 2008; Jennings *et al*, 2014; Nagler *et al*, 2014). Efficacy and safety in comparison to standard care was established in a number of randomized clinical trials, and data were pooled in several meta-analyses (Garcia-Alamino *et al*, 2010; Bloomfield *et al*, 2011; Heneghan *et al*, 2012; Sharma *et al*, 2015). According to these data, PSM relevantly reduced thromboembolic events as well as mortality compared with routine management. In addition, two large-scale observational studies investigating long-term effects of PSM in clinical practice reported low numbers of bleeding events, thromboembolism and deaths (Nagler *et al*, 2014; Nilsson *et al*, 2014). In addition, life expectancy was estimated to be comparable to the standard population in patients with mechanical heart valve (Mokhles *et al*, 2011). Moreover, PSM was shown to be cost-effective compared to standard care (Gerkens *et al*, 2012; Sharma *et al*, 2015; Ferguson *et al*, 2016) and a number of scientific societies recommended PSM for eligible patients requiring long-term anticoagulation treatment (Ansell *et al*, 2005; Ageno *et al*, 2012; Witt, 2012; Jennings *et al*, 2014). However, the uptake of PSM is slow (Ferguson *et al*, 2016) and several reports suggest that the most important question is still open: Which patient is most likely to benefit from PSM (Kyrle & Eichinger, 2012; Li Wan Po, 2012)?

To contribute to the discussion, we analysed the data of a large cohort of patients performing PSM in real-life practice aiming to identify predictors of poor anticoagulation control and to develop a simple prediction model for clinical practice.

## Methods

### *Patients and questionnaire*

A questionnaire was distributed among all adult German-speaking members of the International Self-Monitoring Association of Oral Anticoagulated Patients (ISMAAP, http://www.ismaap.org/; $n = 45\,000$) by regular mail. ISMAAP comprises patient organizations from many European countries, including Switzerland (*INRswiss*), Germany (*Arbeitskreis Gerinnungs- und Herzklappen-Patienten*), and Austria (*INR-Austria*). In all three countries, patients were requested to register with the national patient organization during PSM training to maintain contact for information. Questionnaires were distributed in April 2013. Patients were asked to provide a number of patient characteristics, treatment details, thromboembolic and bleeding events since training, and report the last 26 INR measurements. Anonymized, handwritten questionnaires were returned by regular mail. Data were transferred to a database by one person and checked by a second one. In addition, intense consistency checks were conducted to ensure quality of the data.

### *PSM training*

Patients were trained according to applicable guidelines and recommendations (Fitzmaurice *et al*, 2005b; Christensen *et al*, 2006; Fritschi *et al*, 2007). In brief, theoretical aspects regarding mechanisms of action, pharmacology, measurement of prothrombin time, interactions with drugs and nutrition, and effects of concomitant diseases were taught in an intensive one- to two-day course led by specialized physicians and anticoagulation nurses. In addition, patients learned how to measure INR values with the use of the POCT coagulometer, and practiced interpretation and documentation. Finally, the use of dosing algorithms and dose adjustments were trained. Patients were advised to measure the INR value once a week and adjust the dosages according to the cumulative dosage of the previous week. More frequent determinations were recommended in special situations, such as bleeds or very high INR values only ($\geq$5). In the following training phase of several weeks or months, patients conducted PSM under supervision. Knowledge and skills were tested again in a final consultation. However, not all patients adjusted VKA dosing by themselves, but were assisted by general practitioners or relatives.

### *Predictor and outcome variables*

The percentage of INR values within target range (TIR) was defined as the primary outcome. We did not use the time within therapeutic range (%TIR) (Rosendaal *et al*, 1993), because dates of INR measurements were not provided. The following variables were used as potential predictors: age (at the time of investigation), sex, country, employment status, duration of PSM, indication of anticoagulation, intensity of anticoagulation, interval of measurements, weekly dosage and type of monitoring (PSM *versus* PST). Duration of PSM was calculated by *date of investigation – date of training*. TIR was calculated by dividing the numbers of INR values within target range by all reported INR values. Values were excluded

in case of bridging manoeuvres. Target ranges were transformed into a range of 1·0 if it was narrower. In addition, target ranges were categorised in reasonable intervals for the investigation of intensity of anticoagulation as a predictor variable.

### *Statistical analysis*

Continuous variables were presented as median and interquartile range (IQR), categorical variables as numbers and percentages. Univariate logistic regression was used to calculate associations between various predictors and poor anticoagulation control, odds ratios (OR) were reported. Poor anticoagulation control was defined as TIR below 75%, and the chi-squared test was applied. We selected a cut-off at or below the average TIR in PSM patients (Nagler *et al*, 2014; Nilsson *et al*, 2014). A prediction model was fitted using multivariate logistic regression analysis. Predictors were included in a stepwise fashion according to clinical considerations and previous data. The predictive value of different models was compared using the corresponding areas under the receiver operating characteristic (ROC) curve (chi-squared test). Sensitivity and specificity of the prediction model was calculated at a threshold of 0·2. In a sensitivity analysis, we repeated the analysis with an outcome variable of TIR below 70% and 80% respectively. Observations with missing values were excluded; a sensitivity analysis was conducted after multiple imputation. Analyses were performed using the Stata 13.1 statistics software package. (Stata Statistical Software: Release 13. StataCorp LP, College Station, TX).

### *Ethical considerations*

The study protocol was assessed by the local ethical committee (Zurich, Switzerland) and considered not to be a subject of a formal review because participation was voluntary and the data were obtained completely anonymously. Consent was given by completing the questionnaire. The investigation was carried out in accordance with the declaration of Helsinki.

## Results

### *Patient characteristics*

Out of 45 000 questionnaires distributed, 15 834 returned (35·2%). The majority of questionnaires were returned from Germany (94·0%), followed by Austria (4·4%) and Switzerland (1·6%). Median age was 72 years (IQR 65–77 years) and 30·1% were female. The distribution among age categories is given in Fig I. Indications for anticoagulation

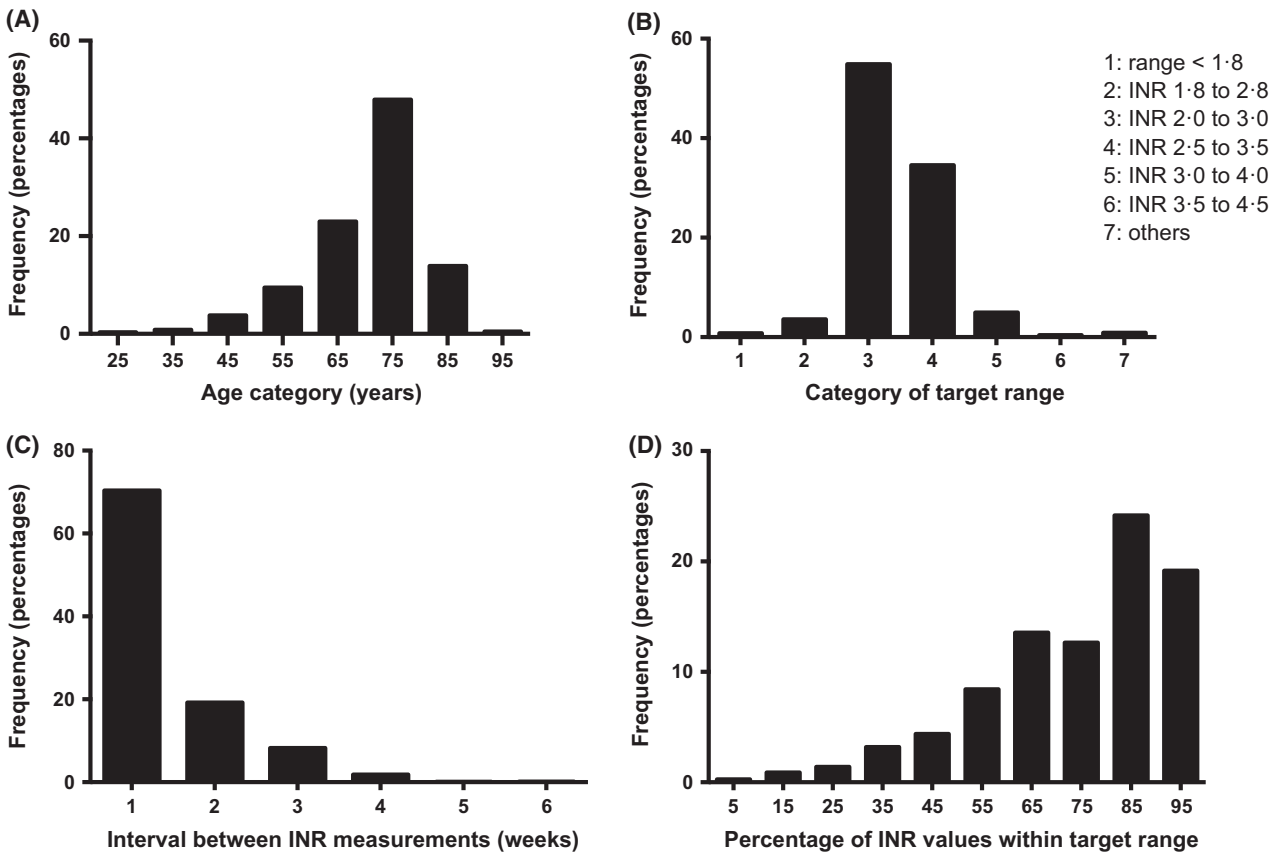


**Fig 1.** Characteristics of patients performing patient self-management in real-life clinical practice. (A) Age categories, (B) Target ranges, (C) Interval between INR measurements, (D) Percentages of INR values within target range. INR, International Normalized Range.

included: mechanical heart valve ($n$ = 7350; 46·5%), atrial fibrillation (AF; $n$ = 5418; 34·3%), venous thromboembolism ($n$ = 2589; 16·4%) and others ($n$ = 450; 2·8%; 0·2% missing values). Phenprocoumon was used almost exclusively. The majority of patients conducted self-management (85·7%) and the others self-testing (13·0%). Median TIR was 88·5% (IQR 76·9, 96·2), mean 83·8% (SD 15·2). Detailed patient characteristics are given in Table I, see also Fig 1.

### *Predictors of anticoagulation quality*

Associations between predictor variables and poor anticoagulation control (TIR below 75%) are shown in Table II (univariate analysis). Categorized intensity of therapeutic range was associated with poor anticoagulation control. Compared to a therapeutic range of INR 2·0–3·0, the probability increased for a range of 2·5–3·5 by OR 2·3 (95% confidence interval [CI] 2·1, 2·5; $P < 0·001$), for a range of 3·0–4·0 by OR 3·9 (95% CI 3·3, 4·6; $P < 0·001$), and for a range of 3·5–4·5 by OR 7·9; 95% CI 4·5, 13·8; $P < 0·001$). The risk was also higher in patients with a lower target range below 1·8 (OR 1·4; 95% CI 0·8, 2·4) but this was not statistically significant ($P = 0·263$; $n$ = 122 patients only).

In addition, an interval between measurements of more than 14 d was associated with poor anticoagulation control (OR 1·5; 95% CI 1·3, 1·7; $P < 0·001$). Female sex was also associated with poor anticoagulation control (OR 1·3; 95% CI 1·2, 1·4; $P < 0·001$), as well as management other than PSM (i.e., patient self-testing; OR 1·4; 95% CI 1·2, 1·6). Furthermore, a high weekly dosage (more than 30 mg phenprocoumon) was associated with lower anticoagulation control (OR 1·6; 95% CI 1·2, 2·1; $P = 0·002$). A higher risk of poor anticoagulation control was also observed for certain indications (venous thromboembolism, mechanical heart valve), but these effects disappeared after adjusting for intensity of target range (data not shown). No associations were observed for age, duration of anticoagulation and employment status. A sensitivity analysis was performed to study associations between predictors and poor anticoagulation control in all patients and in patients with atrial fibrillation only (Table SI). Even though there were only a few patients in some categories, resulting in a considerable imprecision of the estimates, the extent and direction of the associations were comparable to all patients. To further explore the cause of the gender difference, we analysed menopausal women (≥45 years) and pre-menopausal women (<45 years) separately, without any difference (OR 1·3; 95% CI 1·2, 1·4 and OR 1·2; 95% CI 0·8, 2·0 respectively).

### *Prediction model*

The following variables were included stepwise: intensity of target range, interval of measurements, type of management, sex and weekly dosage (Table III). The final model for predicting poor anticoagulation control included intensity of target range, interval of measurements, type of management and sex, with an area under the ROC curve of 0·65 (95% CI 0·64, 0·66; see Fig 2). At a threshold of 0·2, sensitivity was 85·3% (95% CI: 84·0, 86·4) and specificity 28·5% (95% CI: 27·6, 29·5). Several sensitivity analyses were conducted: (i) using

**Table I.** Characteristics of patients performing PSM in real-life practice.

| | Values *n*; % | Missing observations *n*; % |
|---|---|---|
| Patient characteristics | | |
| Participants | 15 834; 100% | |
| Age, years – median | 72 (IQR: 65, 77) | 233; 1·5% |
| Sex | | |
| Male | 11 071; 69·9% | 0 |
| Female | 4763; 30·1% | |
| Residence | | |
| Germany | 14 881; 94·0% | 0 |
| Austria | 699; 4·4% | |
| Switzerland | 254; 1·6% | |
| Indication for anticoagulation | | |
| Mechanical heart valve | 7350; 46·5% | 27; 0·2% |
| Atrial fibrillation | 5418; 34·3% | |
| Venous thromboembolism | 2589; 16·4% | |
| Others | 450; 2·8% | |
| Observation period, years – median (IQR) | 10 (IQR: 6, 14) | |
| Employment status | | |
| Retired | 13 645; 86·2% | 46; 0·3% |
| Working | 2143; 13·5% | |
| Treatment characteristics | | |
| Percentage of INR values in therapeutic range (TIR) | | |
| median | 88·5 (IQR: 76·9, 96·2) | 1318; 8·3% |
| mean | 83·8 (SD: 15·2) | |
| TIR below 75% | 3305; 20·9% | |
| Intensity of therapeutic range | | |
| Lower INR limit < 1·8 | 122; 0·8% | 310; 2·0% |
| 1·8–2·8* | 560; 3·5% | |
| 2·0–3·0 | 8599; 54·3% | |
| 2·5–3·5 | 5410, 34·1% | |
| 3·0–4·0 | 771; 4·9% | |
| 3·5–4·5 | 62; 0·4% | |
| Interval between measurements | | |
| 7–14 d | 13 921; 87·9% | 291; 1·9% |
| Less frequently | 1622; 10·2% | |
| Type of management | | |
| PSM | 13 563; 85·7% | 211; 1·3% |
| PST or other support | 2060; 13·0% | |
| Weekly dosage | | |
| Up to 30 mg phenprocoumon | 15 271; 96·4% | 313; 2·0% |
| More than 30 mg phenprocoumon | 250; 1·6% | |

INR, International Normalized Range; IQR, interquartile range; PSM, patient self-management; PST, patient self-testing.
*Low INR target ranges are recommended by some experts (Koertke *et al*, 2007, 2015).

**Table II.** Predictors of poor anticoagulation control (univariate analysis).

| Variable | Odds ratio* | 95% Confidence interval | Probability ($X^2$-test) |
|---|---|---|---|
| Intensity of therapeutic range | | | |
| Lower INR limit < 1·8 | 1·4 | 0·8, 2·4 | $P = 0·263$ |
| 1·8–2·8 | 1·1 | 0·8, 1·4 | $P = 0·593$ |
| 2·0–3·0 | 1·0 | | |
| 2·5–3·5 | 2·3 | 2·1, 2·5 | $P < 0·001$ |
| 3·0–4·0 | 3·9 | 3·3, 4·6 | $P < 0·001$ |
| 3·5–4·5 | 7·9 | 4·5, 13·8 | $P < 0·001$ |
| Interval between measurements | | | |
| 7–14 d | 1·0 | | |
| Less frequently | 1·5 | 1·3, 1·7 | $P < 0·001$ |
| Sex | | | |
| Male | 1·0 | | |
| Female | 1·3 | 1·2, 1·4 | $P < 0·001$ |
| Type of management | | | |
| PSM | 1·0 | | |
| PST or other support | 1·4 | 1·2, 1·6 | $P < 0·001$ |
| Indication of anticoagulation | | | |
| Atrial fibrillation | 1·0 | | |
| Venous thromboembolism | 1·2 | 1·0, 1·3 | $P = 0·013$ |
| Mechanical heart valve | 1·5 | 1·4, 1·7 | $P < 0·001$ |
| Others | 1·1 | 0·8, 1·4 | $P = 0·552$ |
| Weekly dosage | | | |
| Up to 30 mg phenprocoumon | 1·0 | | |
| More than 30 mg phenprocoumon | 1·6 | 1·2, 2·1 | $P = 0·002$ |
| Duration of PSM (continuous variable) | 1·0 | 1·0, 1·0 | |
| Age (continuous variable) | 1·0 | 1·0, 1·0 | |
| Retired | 1·0 | 0·9, 1·2 | |

INR, International Normalized Range; PSM, patient self-management; PST, patient self-testing; TIR, percentage of INR values in therapeutic range.

*Odds ratio of achieving a TIR lower than 75%.

different outcome variables (TIR < 70%, and TIR < 80%), (ii) analysing patients with lower TIR only (below 88%), (iii) analysing patients with atrial fibrillation only, and (iv) after multiple imputation of missing values. All resulted in the same collection of predictors (data not shown).

## Discussion

By studying the present, large cohort of patients conducting PSM in clinical practice, we identified several predictors for poor anticoagulation control: therapeutic ranges above an INR of 2·0–3·0, intervals between measurements of more than 14 d, management other than PSM, and female sex. A fitted, simple prediction model comprising these factors was able to identify patients fairly accurately.

This is the first large cohort study developing a prediction model for anticoagulation quality in PSM patients. However, a number of predictors have been studied before, most often in different target populations (Oake *et al*, 2008; Rose *et al*, 2008, 2010; Apostolakis *et al*, 2013; Lip *et al*, 2014; Nilsson *et al*, 2014; Ward *et al*, 2015), and our results are essentially in agreement with these results. In particular, a prediction model was developed in a large cohort of standard VKA care patients with AF, recruited from a randomized controlled trial (the SAME-$TT_2R_2$ Score (Apostolakis *et al*, 2013)), and confirmed in a different cohort (Lip *et al*, 2014). Female sex, younger age, ethnic minority status, smoking, more than two comorbidities and amiodarone treatment were associated with a lower anticoagulation quality, whereas treatment with $\beta$-blocker or verapamil was associated with a higher control. Female sex was also identified as a predictor in different PSM cohorts (Nilsson *et al*, 2014; Ward *et al*, 2015) and general VKA populations as well (Rose *et al*, 2010). An association between intensity of target range and quality of anticoagulation was observed in several studies focusing on a general VKA population (Oake *et al*, 2008; Rose *et al*, 2008). In addition, the interval between measurements correlated with measures of anticoagulation quality in a number of studies focused on a broad range of populations (White *et al*, 1989; Ansell *et al*, 1995; Horstkotte *et al*, 1998; Sawicki, 1999; DeSantis *et al*, 2014; Matchar *et al*, 2015). Moreover, other authors suggested that PSM patients are probably more likely to achieve better TIR than patients performing self-testing (PST) (Ward *et al*, 2015).

The explanation for the above-mentioned effects remains mainly unclear and it is beyond the focus of the current study to explore the mechanism involved. It appears obvious that frequent INR measurements might improve TIR. It is also conceivable that PSM improves quality because patients gain experience in which situations (e.g. diet, drugs) the INR value might have changed. It is more complex to explain why intensity of target range affects TIR. We speculate that patients with higher target ranges are suffering from different diseases and are taking more drugs, which might influence the anticoagulation quality. Another possible explanation is that INR measurements might be less precise at higher values compared to lower target ranges. Why female sex predicts poor quality of anticoagulation remains unclear. We did not find any arguments for hormonal influences; a sensitivity analysis in menopausal and pre-menopausal women did not identify differences in the association between sex and poor anticoagulation control (OR 1·3 vs. 1·2 respectively). However, the associations were observed in a number of studies targeting very different populations. Future studies might examine the pathophysiology of these effects.

The strength of our study is the large number of patients. This enables precise estimates for the parameters of the prediction model. Moreover, in contrast to other studies, a relatively large proportion of female patients were included. In addition, most patients in our cohort conducted PSM, allowing the application of the prediction model to this specific group of patients. Our study has potential limitations, with a

**Table III.** Prediction model for poor anticoagulation quality*.

| Model | Predictors | Area under ROC curve Area (95% CI) | Probability of the model† | Probability of difference‡ |
|---|---|---|---|---|
| 1 | Intensity of therapeutic range | 0·618 (0·608, 0·628) | $P < 0{\cdot}0001$ | |
| 2 | Intensity of therapeutic range, Interval of measurements | 0·638 (0·627, 0·649) | $P < 0{\cdot}0001$ | $P < 0{\cdot}0001$ |
| 3 | Intensity of therapeutic range, Interval of measurements, Type of management | 0·643 (0·633, 0·655) | $P < 0{\cdot}0001$ | $P = 0{\cdot}0005$ |
| **4§** | **Intensity of therapeutic range, Interval of measurements, Type of management, Sex** | **0·647 (0·636, 0·658)** | **$P < 0{\cdot}0001$** | **$P = 0{\cdot}005$** |
| 5 | Intensity of therapeutic range, Interval of measurements, Type of management, Sex, Weekly dosage | 0·648 (0·637, 0·660) | $P < 0{\cdot}0001$ | $P = 0{\cdot}059$ |

TIR, percentage of INR values in therapeutic range; ROC, receiver operating characteristic; 95% CI, 95% confidence interval.
*TIR below 75%; †likelihood ratio test; ‡chi-squared test; compared to the previous model; §final model, at least one of the mentioned variables must be present (threshold 0·2): sensitivity: 85·3% (95% CI: 84·0, 86·4), specificity: 28·5% (95% CI: 27·6, 29·5). [Correction added on 13 October 2016, after first online publication: "sensitivity" was added].

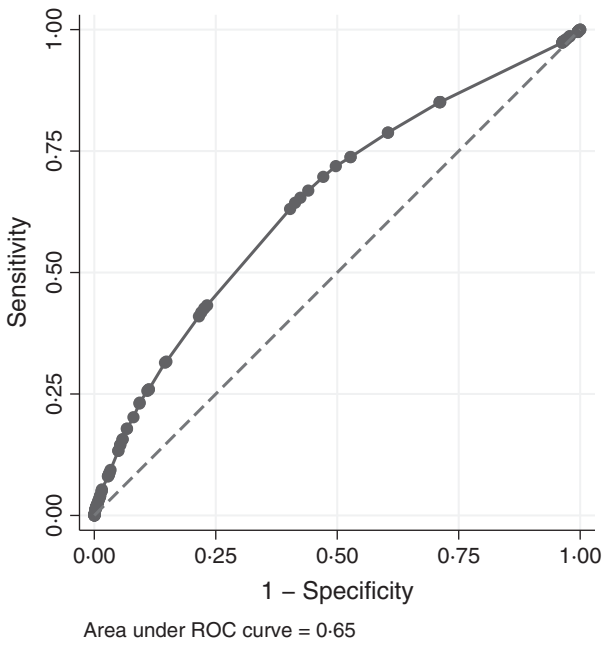


**Fig 2.** Receiver operating characteristics (ROC) of prediction model for poor anticoagulation quality [percentage of INR values in therapeutic range (TIR) below 75%].

possible selection bias being the most important issue. Not all patients successfully completed the training programme and – as with every questionnaire-based study – only some of the patients responded to the questionnaire (35% in this study). It is conceivable that the characteristics of the analysed patients differed systematically from the cohort of all patients who received training. Thus, we cannot fully exclude that this has introduced a selection bias and the extent and direction of this bias remains unclear. Considering the high TIR and the advanced age of the patients, one might suspect that younger patients with a worse TIR were less likely to respond. However, we conducted two sensitivity analyses: the first, in patients with a lower TIR only (below 88%) and, the second, with a higher and lower threshold (70% TIR; 80% TIR) without finding different results. Moreover, age was not identified as a predictor for anticoagulation quality. Furthermore, our results are in line with those of previous investigations in other populations. In addition, one might argue that determination of variables by the use of the questionnaire is subjective and therefore imprecise. To account for this, we decided not to report clinical outcomes. The primary outcome measure TIR were calculated from 26 reported INR values, which were measured objectively. The INR values, as well as most other variables (e.g. sex, target range, indication), are fairly objective measurements with a low risk of reporting bias.

How shall physicians apply the model to clinical practice? The prediction model is considered as positive if one of the following factors is present: (i) target range above an INR of 2·0–3·0, (ii) interval between measurements longer than every 14 d, (iii) management other than PSM, or (iv) female sex. Using the proposed, simple prediction model, physicians will be able to identify patients with a low chance of performing well.

They can consider additional training for patients or organise regular follow-up. In patients with AF or venous thromboembolism, they can also consider switching to new,

direct oral anticoagulants. Intensifying support in this patient group will improve care in PSM patients.

In conclusion, by studying a large cohort of patients with PSM, we were able to identify predictors of poor anticoagulation quality and develop a simple prediction model incorporating a limited number of clinical factors that are easy to access. Using this model, physicians are able to identify patients with a low chance of performing well and consider treatment adjustments.

## Acknowledgements

We thank all patients for participating and all ISMAAP staff for their enthusiastic work on the present project. We thank Raphael Müllner for recording the data of Swiss patients. Roche diagnostics supported distribution of the questionnaire.

## Disclosure of interest

CS is president of the ISMAAP. WAW has received research grants, lecture fees, or consultant fees from Novo Nordisk, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, MEDA Pharma, Pfizer, and Roche Diagnostics. MN has received research grants or lecture fees from Bayer and CSL Behring.

## Author contributions

CS planned and organized the study, designed the questionnaire, collected the data, and reviewed the manuscript. MN and FS developed the analysis plan and reviewed the analysis. MN conducted the statistical analysis, and wrote the manuscript. WAW and AJ reviewed the analysis plan, statistical analysis and the manuscript. All authors approved the final manuscript.

## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Table SI.** Sensitivity analysis: predictors of poor anticoagulation control (univariate analysis) all patients *versus* atrial fibrillation only.

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