Management decisions on unruptured intracranial aneurysms before and after implementation of the PHASES score

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Management decisions on unruptured intracranial aneurysms before and after implementation of the PHASES score

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ABSTRACT

Background: In management decisions on saccular unruptured intracranial aneurysms (UIAs) the risk of rupture is an important factor. The PHASES score, introduced in 2014, provides absolute 5-year risks of rupture based on six easily retrievable patient and aneurysm characteristics. We assessed whether management decisions on UIAs changed after implementation of the PHASES score.
Patient and methods: We included all patients with UIAs who were referred to two Dutch tertiary referral centers for aneurysm care in the Netherlands (University Medical Center Utrecht (UMCU) and Leiden University Medical Center (LUMC)) between 2011 and 2017. Analyses were done on an aneurysm level. We calculated the overall proportion of UIAs with a decision to treat before and after PHASES implementation and studied the influence of age and center on post-implementation management changes.
Results: We included 623 patients with 803 UIAs. The proportion of UIAs with a decision to treat was 123/360 (34.2%) before and 117/443 (26.4%) after PHASES implementation (absolute risk difference: −7.8%; 95% CI: −14.1 to −1.4). The decision to treat was made at a higher median PHASES score after implementation (7 points (IQR 5;10) pre- versus 8 points (IQR 5;10) post-implementation; $p = 0.14$). The reduced proportion with a treatment decision after implementation was most pronounced in patients <50 years (−22.3%; 95% CI: −39.2 to −3.4) and was restricted to treatment decisions made at the UMCU (−10.6%; 95% CI: −18.5 to −2.5).
Discussion and conclusions: Management of UIAs changed following implementation of the PHASES score, but the impact of PHASES implementation on treatment decisions differed across age subgroups and centers.

1. Introduction

In management decisions on saccular unruptured intracranial aneurysms (UIAs), the risk of rupture and risk of treatment complications have to be carefully balanced, in the context of other individual aspects such as life expectancy and level of patient anxiety [1,2]. To improve prediction of rupture risk, the PHASES score was developed [3]. The PHASES score is based on a pooled analysis using data from six prospective cohort studies, with individual patient data of 8382 patients and 10,272 UIAs. The resulting score predicts absolute 5-year risks of rupture based on six easily retrievable patient and aneurysm characteristics: hypertension, age, history of subarachnoid hemorrhage (SAH) due to aneurysm rupture, and size and site of the aneurysm. Each characteristic corresponds to a number of points, which are added to calculate the total score. PHASES scores range between 0 and 22 points, with associated absolute 5-year rupture risks from 0.4% to 17.8% [3]. Since its publication in 2014, the PHASES score is frequently used as a prediction tool to support clinical decision making on UIAs. We aimed to evaluate the effect of the clinical implementation of the PHASES score on the management of UIAs in two Dutch tertiary referral hospitals. Based on experiences from clinical practice we hypothesized that the decision to treat is made less often after implementation of the PHASES score.

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2. Material and methods

2.1. Study population

Approval for this study was obtained from the Institutional Research Ethics Board of the University Medical Center Utrecht (UMCU), the Netherlands. Local approval was obtained from the Leiden University Medical Center (LUMC). We collected data at the UMCU and LUMC. We included patients ≥18 years of age with at least one untreated saccular UIA, who presented between January 1st, 2011 and April 1st, 2017 at the outpatient aneurysm clinic. Only UIA patients for whom a management decision was made at the outpatient clinic in a non-acute setting were included. Exclusion criteria were: (1) extradural aneurysm location; (2) non-saccular shape (i.e., fusiform or dissecting); (3) complete thrombosis of an aneurysm; (4) aneurysms related to an arteriovenous malformation; (5) a maximum size of ≤1.5 mm; (6) referral from another UIA treatment center for second or third opinion (i.e., because of complex UIA anatomy or advanced treatments). We divided aneurysms into pre- and post-implementation groups based on time of presentation. As both centers participated in the development of the PHASES score, this may have influenced the management of UIAs in the phase between analysis of the data and publication of the results (January 2014). Moreover, the PHASES score was not consistently used in the decision to treat or observe UIAs in the first six months after publication. Therefore, we took a three month period before the official publication (January 2014) and a six month period after publication as transitional phase [3]. UIA patients who were discussed in the multidisciplinary meeting during the transitional period (1st October 2013 – 30th June 2014) were excluded from our analyses. The pre-implementation group consisted of aneurysms that were discussed in the multidisciplinary meeting before implementation of the PHASES score (before October 1st, 2013); the post-implementation group consisted of aneurysms discussed after implementation (after June 30th, 2014).

2.2. Data collection

At the UMCU, a prospectively built UIA database was used to select UIA patients who met our inclusion criteria. At the LUMC, UIA patients who visited the LUMC outpatient clinic for aneurysm care between January 1st, 2011 until April 1st, 2017 were checked for eligibility. We collected the following patient- and aneurysm characteristics from electronic patient files: age at presentation, nationality, medical history of hypertension or subarachnoid hemorrhage, number and configuration of aneurysms, aneurysm site, and maximum aneurysm size. We considered patients to have hypertension if it was reported in their medical history, if they used antihypertensive drugs without another indication, or had a systolic blood pressure > 140 mmHg or a diastolic blood pressure > 90 mmHg on more than one occasion at the outpatient clinic. For partially thrombosed aneurysms the maximum size was defined as the maximum size of the complete aneurysm (including the thrombus), instead of the maximum size of the lumen. If the maximum aneurysm size was not available in the electronic patient files, we measured the aneurysms using in-house software.

For advice on aneurysm management a multidisciplinary meeting with neurologists, neurosurgeons and interventional radiologists is regularly held at both the UMCU and the LUMC. Subsequently, UIA patients are counselled about their aneurysm at the outpatient aneurysm clinic, after which a management decision is made. We used the final management decisions as made at the outpatient clinic for our analyses.

2.3. Statistical analysis

We conducted analyses on aneurysm level. For each UIA, we added the number of points for every PHASES indicator (population, hypertension, age, size of aneurysm, site of aneurysm and history of SAH due to aneurysm rupture; see Appendix) to calculate the total PHASES score [3]. Aneurysms for which no PHASES score could be calculated because of missing data were excluded from the analyses ($n = 4$). To compare the pre- and post-implementation cohorts at baseline, we used the Fisher's exact test for dichotomous variables, the χ^2 test for nominal or ordinal variables and the Mann-Whitney U test to compare medians. For our primary analysis, we calculated the proportion of UIAs for which a decision to treat was made in the pre- and post-implementation cohorts and the absolute pre- versus post-implementation difference with corresponding 95% confidence intervals (CI). Next, we calculated the median PHASES scores and interquartile ranges (IQR) of the pre-implementation and post-implementation groups, as well as the median PHASES scores of the groups with and without a decision to treat. Given the clinical importance of age on UIA management decisions, we conducted additional analyses for age despite its presence in the PHASES score. We performed a subgroup analysis according to three age groups (<50 years; 50–69 years; ≥70 years), whereby we assessed the interaction of age with the relation between PHASES implementation and treatment decision. Finally, we repeated all analyses for the UMCU and LUMC UIA cohorts separately.

3. Results

3.1. Baseline characteristics

We included 623 patients with 803 UIAs: 402 patients with 513 UIAs from the UMCU, and 221 patients with 290 aneurysms from the LUMC (Fig. 1).

Baseline characteristics in the pre- and post-implementation groups did not differ, except for age (Table 1). The median age of patients was 61 years before and 64 years after implementation.

3.2. Before and after PHASES implementation

The proportion of UIAs for which a decision to treat was made was 123/360 (34.2%; 95% CI: 29.5–39.2) before and 117/443 (26.4%; 95% CI: 22.5–30.7) after implementation of the PHASES score, resulting in an absolute difference of −7.8% (95% CI: −14.1 to −1.4). The distribution of PHASES scores for patients with a decision to treat before and after implementation is shown in Fig. 2. For the group with a decision to treat, the median PHASES score increased from 7 (IQR 5;9) to 8 (IQR 5;10) points ($p = 0.14$) after implementation of the PHASES score (Table 1; Fig. 2). Results for the subgroup analysis according to age are provided in Table 2. We observed a trend for a stronger reduction in the decision to treat in younger patients (absolute risk reduction <50 years: −22.3% (95% CI: −39.2 to −3.4); 50–69 years: −6.1% (95% CI: −14.6–2.5) and ≥ 70 years: 1.0% (95% CI: −8.4–9.2), $p_{interaction} = 0.10$).

3.3. PHASES implementation per center

The baseline characteristics of the UIAs per center are given in Table 3. Patients counselled at the UMCU more often had a history of hypertension (UMCU: 259/402 (64%) versus LUMC: 124/221 (56%)), whereas a history of SAH was more common among LUMC patients (UMCU: 37/402 (9%) versus LUMC: 42/221 (19%)). At the UMCU, UIAs were larger (median size 6.0 versus 4.0 mm) and median PHASES scores were higher (5 versus 4 points) than at the LUMC.

The median PHASES score in the group of UIAs for which a decision to treat was made was higher at the UMCU (8 points; IQR 5;10) than at the LUMC (6 points; IQR 3.5;8) ($p = 0.003$) (Table 3).

At the UMCU, the proportion of UIAs for which a decision to treat was made was 85/231 (36.8%; 95% CI: 30.8–43.2) before implementation of the PHASES score and 74/282 (26.2%; 95% CI: 21.5–31.7) after implementation, resulting in an absolute difference of −10.6% (95% CI: −18.5 to −2.5). For the group with a decision to treat, the median PHASES score increased from 7 (IQR 5;10) to 8 (IQR 6;11) points

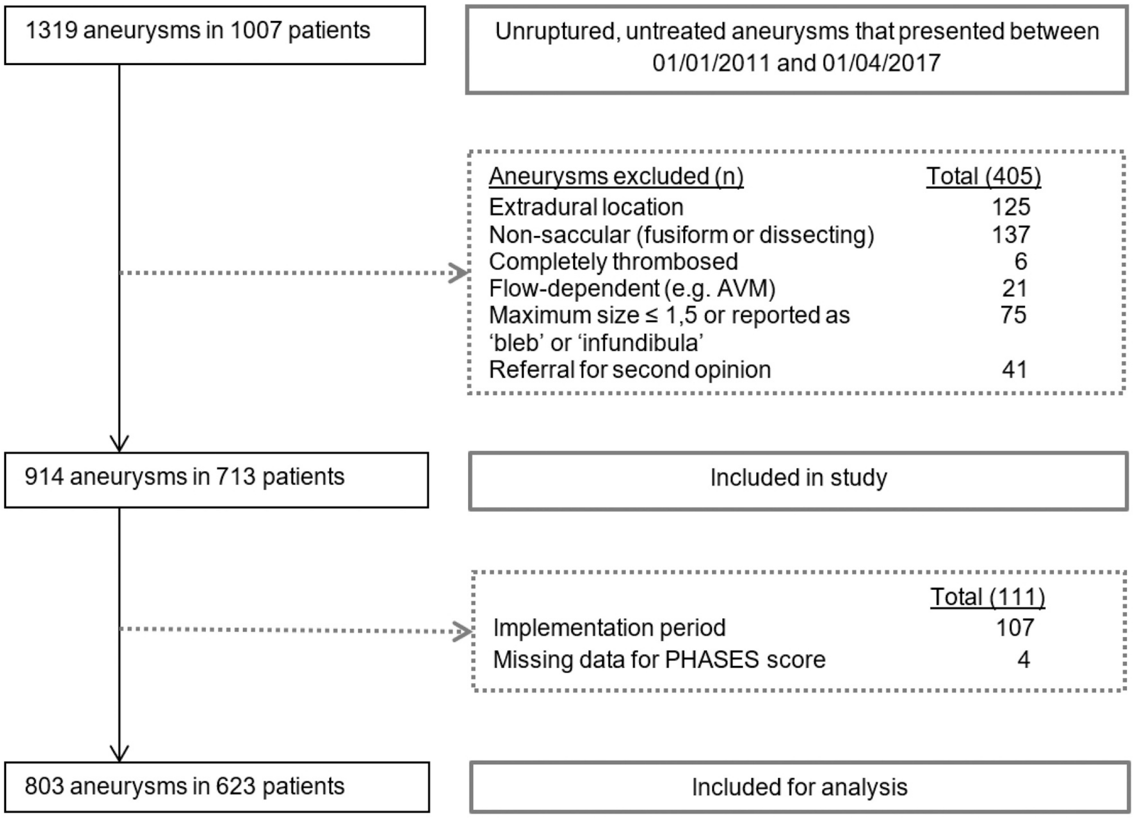

Fig. 1. Flowchart of included UIAs.

Table 1
Baseline characteristics of included aneurysms before and after implementation.

	Pre-implementation	Post-implementation
Patient characteristics	$n = 282$	$n = 341$
Female (%)	191 (68)	229 (67)
Median age (years) [range]	61 [20–90]	64 [21–96]
Hypertension (%)	164 (58)	219 (64)
History of SAH* (%)	35 (12)	44 (13)
Aneurysm characteristics	$n = 360$	$n = 443$
Aneurysm size (%)		
Median size (mm) [range]	5.5 [1.6–45.0]	5.0 [1.6–45.0]
<7.0 mm	220 (61)	288 (65)
7.0–9.9 mm	72 (20)	86 (19)
10.0–19.9 mm	53 (15)	57 (13)
≥20.0 mm	15 (4)	12 (3)
Aneurysm site (%)		
ICA	63 (18)	88 (20)
MCA	146 (41)	159 (36)
ACA/PCOM/posterior	151 (42)	196 (44)
Median PHASES score [Q1;Q3]	5 [3;7]	5 [3;7]
Treatment cohort**	7 [5;9]	8 [5;10]
Observation cohort	4 [3;6]	4 [2;6]

Median scores are presented with first and third quartile values [Q1;Q3]. *History of SAH: history of subarachnoid hemorrhage due to rupture from another aneurysm. ** Treatment cohort includes the UIAs for which a decision to treat was made. Observation cohort includes the UIAs for which a decision to observe was made.
ICA: internal carotid artery; MCA: middle cerebral artery; ACA: anterior cerebral arteries (anterior cerebral artery, anterior communicating artery, pericallosal artery); PCOM: posterior communicating artery; posterior circulation: vertebral artery, basilar artery, cerebellar arteries, posterior cerebral artery [3].

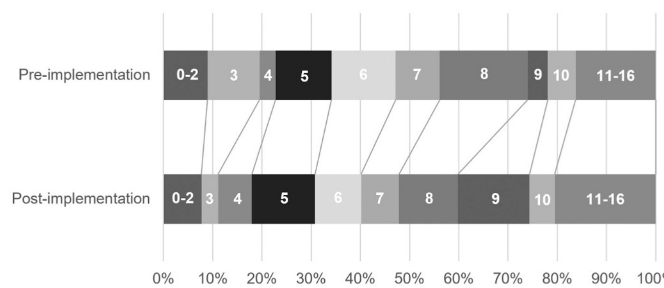

Fig. 2. Distribution of PHASES scores pre- and post-implementation in the UIA group with a decision to treat.

(p = 0.04) after implementation of the PHASES score (Fig. 3). We observed a trend for a stronger reduction in the decision to treat in younger patients ($p_{interaction} = 0.06$; Table 2).

At the LUMC, the proportion of UIAs for which a decision to treat was made was 38/129 (29.5%; 95% CI: 22.3–37.8) before implementation of the PHASES score and 43/161 (26.7%; 95% CI: 20.5–34.0) after implementation, resulting in an absolute difference of −2.8% (95% CI: −13.2–7.5). In the group with a decision to treat, the median PHASES score remained 6 (IQR 4;8) before and after implementation (Fig. 3). We found no differences in management decisions across age subgroups ($p_{interaction} = 0.95$; Table 2).

4. Discussion

Our study shows that the proportion of UIAs for which a decision to treat was made decreased after implementation of the PHASES score. However, the impact of PHASES implementation on treatment decisions was dependent on age subgroup and differed between centers.

Table 2
Relationship between the decision to treat and implementation of the PHASES score by age subgroup for the total group and for both centers separately.

	Pre-implementation (n) (%)	Post-implementation (n) (%)	Absolute difference in % (95% CI)
Total			
Overall	123/360 (34.2)	117/443 (26.4)	−7.8 (−14.1 to −1.4)
Age < 50 years	25/48 (52.1)	17/57 (29.8)	−22.3 (−39.2 to −3.4)
Age 50–69 years	89/226 (39.4)	85/255 (33.3)	−6.1 (−14.6–2.5)
Age ≥ 70 years	9/86 (10.5)	15/131 (11.5)	1.0 (−8.4–9.2)
UMCU			
Overall	85/231 (36.8)	74/282 (26.2)	−10.6 (−18.5 to −2.5)
Age < 50 years	18/34 (52.9)	13/39 (33.3)	−19.6 (−39.7–3.0)
Age 50–69 years	61/138 (44.2)	51/157 (32.5)	−11.7 (−22.5 to −0.6)
Age ≥ 70 years	6/59 (10.2)	10/86 (11.6)	1.5 (−10.1–11.5)
LUMC			
Overall	38/129 (29.5)	43/161 (26.7)	−2.8 (−13.2–7.5)
Age < 50 years	7/14 (50.0)	4/18 (22.2)	−27.8 (−54.5–4.9)
Age 50–69 years	28/88 (31.8)	34/98 (34.7)	2.9 (−10.6–16.1)
Age ≥ 70 years	3/27 (11.1)	5/45 (11.1)	0 (−18.1–14.4)

Absolute differences in the proportion of aneurysms for which a decision to treat was made before and after implementation of the PHASES score.

Table 3
Baseline characteristics of included aneurysms per center.

	Total group	UMCU	LUMC
Patient characteristics	$n = 623$	$n = 402$	$n = 221$
Female (%)	420 (67)	274 (68)	146 (66)
Median age (years) [range]	63 [20–96]	63 [21–96]	62 [20–90]
Hypertension (%)	383 (62)	259 (64)	124 (56)
History of SAH* (%)	79 (13)	37 (9)	42 (19)
Aneurysm characteristics	$n = 803$	$n = 513$	$n = 290$
Aneurysm size (%)			
Median size (mm) [range]	5.0 [1.6–45.0]	6.0 [1.6–45.0]	4.0 [1.7–24.0]
<7.0 mm	508 (63)	288 (56)	220 (76)
7.0–9.9 mm	158 (20)	123 (24)	35 (12)
10.0–19.9 mm	110 (14)	80 (16)	30 (10)
≥20.0 mm	27 (3)	22 (4)	5 (2)
Aneurysm site (%)			
ICA	151 (19)	91 (18)	60 (21)
MCA	305 (38)	193 (38)	112 (39)
ACA/PCOM/posterior	347 (43)	229 (45)	118 (41)
Median PHASES score [Q1; Q3]	5 [3;7]	5 [3;8]	4 [2;6]
Treatment cohort**	7 [5;9]	8 [5;10]	6 [3.5;8]
Observation cohort	4 [2;6]	4 [3;6]	4 [2;5]

Median scores are presented with first and third quartile values [Q1;Q3]. *History of SAH: history of subarachnoid hemorrhage due to rupture from another aneurysm. **Treatment cohort includes the UIAs for which a decision to treat was made. Observation cohort includes the UIAs for which a decision to observe was made.
ICA: internal carotid artery; MCA: middle cerebral artery; ACA: anterior cerebral arteries (anterior cerebral artery, anterior communicating artery, pericallosal artery); PCOM: posterior communicating artery; posterior circulation: vertebral artery, basilar artery, cerebellar arteries, posterior cerebral artery [3].

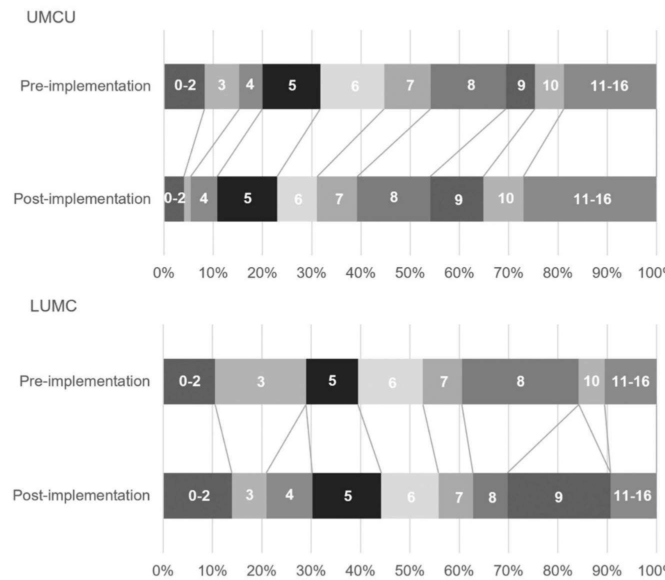

Fig. 3. Distribution of PHASES scores pre- and post-implementation in the UIA group with a decision to treat for both centers. At the LUMC no UIA had a mean PHASES score of 4 or 9 prior to implementation and no UIA had a mean PHASES score of 10 after implementation.

To our best knowledge, this is the first study to evaluate changes in management decisions in UIA patients following implementation of the PHASES score. One previous study retrospectively calculated PHASES scores in different UIA subgroups, but did not assess its influence on management decisions [4].

Our finding that the decrease in proportion of UIAs for which a decision to treat was made after PHASES implementation was most pronounced in younger patients may be explained by a tendency to treat aneurysms in people of working age more aggressively than aneurysms in elderly people [5]. The differences we found between centers may be explained by various factors. First, compared to the LUMC cohort, UIAs were larger and median PHASES scores were higher in the UMCU cohort. This may be the reason why the pre-implementation proportion of UIAs with a decision to treat was higher in the UMCU cohort (36.8%) than in the LUMC cohort (29.5%) and why perhaps no large implementation effect of PHASES was to be expected in the LUMC cohort. Second, we found that aneurysms were treated at lower median PHASES scores in the LUMC than the UMCU (6 vs. 8 points, respectively). Differences in threshold to advise preventive treatment may reflect variation in the weight attributed to the individual factors included in the PHASES score, or may be explained by organizational differences per center. At the UMCU, the outpatient aneurysm clinic is run by neurologists only, whereas at the LUMC it is run by neurologists, neurosurgeons and interventional radiologists.

4.1. *Limitations and strengths*

Our study has some limitations. First, the observational and retrospective design of this study carries a risk of bias. For before-after studies, relevant changes during the time period of the study should be taken into account [6]. Over time, the organization of the aneurysm clinics and the specialists involved remained the same in both centers. However, there has been a noticeable growth in the absolute number of aneurysms treated, especially with the availability of various new advanced endovascular treatment modalities [7,8]. This may have, at least partially, counteracted the decision to refrain from treatment based on the use of the PHASES risk score. Second, this study was not powered to assess the long-term influence of PHASES implementation on aneurysm rupture and treatment complication rates [9,10].

Finally, the interpretation and clinical application of the PHASES score may differ between centers and countries, restricting the generalizability of our findings. As the PHASES score was developed in Utrecht, the UMCU team was prompted to implement its own score consistently in their management decisions.

Our study also has several strengths. First, by collecting data from two Dutch tertiary referral centers for aneurysm care, we were able to set up a large database with detailed individual patient and aneurysm data. This enabled us to perform several prespecified subgroup analyses to better understand the UIA decision-making process and clinical variation in patient selection for preventive UIA treatment between centers. Second, this the first study to assess the clinical impact of implementation of a risk prediction score on intracranial aneurysm management, an important and often neglected first step in evaluating the effect of an evidence-based decision tool.

4.2. Conclusion

In conclusion, we have shown that the implementation of the PHASES risk score influenced treatment decisions made at the UMCU, but not at the LUMC. Clinical variation in the use of the PHASES score, such as the weight given to age and other risk factors, as well as differences in referral populations and the decision-making process, may account for this contrast between centers. Further research is needed to confirm the PHASES implementation effect we found, with the eventual goal to assess the risk score in terms of increased or decreased rates of aneurysm rupture and treatment complications, as well as quality of life changes in UIA patients.

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Informed consent

Informed consent was not sought for the present study because of its retrospective nature.

Ethical approval

Approval for this study was obtained from the Institutional Research Ethics Board of the University Medical Centre Utrecht, Utrecht, the Netherlands [approval number:18-073/C].

CRediT authorship contribution statement

Laurie J. Hollands: Data curation, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **Mervyn D.I. Vergouwen:** Conceptualization, Methodology, Writing - review & editing. **Jacoba P. Greving:** Methodology, Formal analysis, Writing - review & editing, Software. **Marieke J.H. Wermer:** Methodology. **Gabriël J.E. Rinkel:** Methodology, Writing - review & editing. **Annemijn M. Algra:** Conceptualization, Data curation, Methodology, Formal analysis, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

None.

Acknowledgements

None

Appendix A. APPENDIX

PHASES aneurysm risk score. ICA: internal carotid artery; MCA: middle cerebral artery; ACA: anterior cerebral arteries (anterior cerebral artery, anterior communicating artery, pericallosal artery); pcom: posterior communicating artery; posterior circulation: vertebral artery, basilar artery, cerebellar arteries, posterior cerebral artery. SAH: subarachnoid hemorrhage [3].

	Points
Population	
North American, European (other than Finnish)	0
Japanese	3
Finnish	5
Hypertension	
No	0
Yes	1
Age	
<70 years	0
≥ 70 years	1
Size of aneurysm	
<7.0 mm	0
7.0–9.9 mm	3
10.0–19.9 mm	6
≥ 20 mm	10
Earlier SAH from another aneurysm	
No	0
Yes	1
Site of aneurysm	
ICA	0
MCA	2
ACA/pcom/posterior circulation	4

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