A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack

P M Rothwell, M F Giles, E Flossmann, C E Lovelock, J N E Redgrave, C P Warlow, Z Mehta

Abstract

Background **Effective early management of patients with transient ischaemic attacks (TIA) is undermined by an inability to predict who is at highest early risk of stroke.**

Methods **We derived a score for 7-day risk of stroke in a population-based cohort of patients (n=209) with a probable or definite TIA (Oxfordshire Community Stroke Project; OCSP), and validated the score in a similar population-based cohort (Oxford Vascular Study; OXVASC, n=190). We assessed likely clinical usefulness to front-line health services by using the score to stratify all patients with suspected TIA referred to OXVASC (n=378, outcome: 7-day risk of stroke) and to a hospital-based weekly TIA clinic (n=210; outcome: risk of stroke before appointment).**

Results **A six-point score derived in the OCSP (age [⩾60 years=1], blood pressure [systolic >140 mm Hg and/or diastolic ⩾90 mm Hg=1], clinical features [unilateral weakness=2, speech disturbance without weakness=1, other=0], and duration of symptoms in min [⩾60=2, 10–59=1, <10=0]; ABCD) was highly predictive of 7-day risk of stroke in OXVASC patients with probable or definite TIA ($p<0·0001$), in the OXVASC population-based cohort of all referrals with suspected TIA ($p<0·0001$), and in the hospital-based weekly TIA clinic-referred cohort ($p=0·006$). In the OXVASC suspected TIA cohort, 19 of 20 (95%) strokes occurred in 101 (27%) patients with a score of 5 or greater: 7-day risk was 0·4% (95% CI 0–1·1) in 274 (73%) patients with a score less than 5, 12·1% (4·2–20·0) in 66 (18%) with a score of 5, and 31·4% (16·0–46·8) in 35 (9%) with a score of 6. In the hospital-referred clinic cohort, 14 (7·5%) patients had a stroke before their scheduled appointment, all with a score of 4 or greater.**

Conclusions **Risk of stroke during the 7 days after TIA seems to be highly predictable. Although further validations and refinements are needed, the ABCD score can be used in routine clinical practice to identify high-risk individuals who need emergency investigation and treatment.**

Lancet 2005; 366: 29–36

Published online June 21, 2005
DOI:10.1016/S0140-6736(05)66702-5

Stroke Prevention Research Unit, Department of Clinical Neurology, University of Oxford, Radcliffe Infirmary, Oxford, OX2 6HE, UK (Prof P M Rothwell FRCP, M F Giles MRCP, E Flossmann MRCP, C E Lovelock FRACP, J N E Redgrave MRCP, Z Mehta DPhil); **and Department of Clinical Neurosciences, University of Edinburgh, Western General Hospital, Edinburgh, UK** (Prof C P Warlow FRCP)

Correspondence to:
Prof Peter M Rothwell
peter.rothwell@clneuro.ox.ac.uk

Introduction

Ischaemic strokes are frequently preceded by a transient ischaemic attack (TIA).[1] However, because of methodological problems in early studies of prognosis, the immediate risk of stroke after a TIA was underestimated for many years.[2,3] Hospital-based and population-based cohort studies have reported 7-day risks of stroke of up to 10%.[4-8] However, there is substantial international variation in how patients with suspected TIA are managed in the acute phase, with some health-care systems providing immediate emergency inpatient care and others providing non-emergency outpatient clinic assessment,[9,10] and there is little consensus about which strategy is most cost-effective.[11,12] North American and UK guidelines simply state that all patients in whom a diagnosis of TIA is suspected should be assessed and investigated within 7 days,[13,14] although this aim is frequently not achieved in practice. However, the key question is not, in fact, whether emergency inpatient care or non-emergency outpatient care is most appropriate. Rather, it is: for which patients is emergency assessment needed, and which patients can be appropriately managed in a non-emergency outpatient setting? Only about 50% of patients referred for specialist assessment with suspected TIA have the diagnosis confirmed, and so even if the 7-day stroke risk after a TIA is as high as 10%, 95% of referrals will not have a stroke in that period.

Validated models are available for long-term risk of stroke after TIA or minor stroke,[15-17] and there are some unvalidated reports of predictors of stroke at 3 months or 1 year after a TIA,[4,7,8] but the practical clinical requirement is for prediction of stroke during the first few days after the event, for which there are currently no published models. We therefore aimed to derive and validate a simple risk score to predict stroke during the first 7 days after a TIA with three potential uses in mind: to allow primary-care doctors and other front-line physicians to identify which of the patients in whom they suspect a diagnosis of TIA should be referred-on for assessment as an emergency; to allow secondary-care physicians to determine which patients with probable or definite TIA need emergency investigation and treatment; and to allow public education about the need for medical attention after a TIA to focus on the specific symptoms and characteristics that identify high-risk individuals.

Methods

Derivation of a simple risk score

We derived the score in the population-based cohort of TIA patients in the Oxfordshire Community Stroke Project (OCSP). The methods of the OCSP have been reported elsewhere.[18,19] Briefly, a population of about 105 000 registered with 50 family doctors in ten practices in Oxfordshire, UK, was studied. All patients

with a possible diagnosis of TIA during the study period (1981–86) were reported to a study neurologist and assessed as soon as possible after the event. The characteristics of the event and vascular risk factors were recorded in cases of first-ever probable or definite TIA (about 50% of referrals) defined by the standard definition.[20] Patients with a probable or definite TIA were followed-up by a research nurse at 1 month initially and re-assessed by the study neurologist if a stroke was suspected.

Because of the small size of the cohort and limited statistical power (18 strokes within 7 days in 209 patients), we limited the likelihood of chance associations by only studying factors that had already been reported to be significant independent predictors of stroke in at least one of the two previous reports of risk factors for stroke at 3 months after a TIA.[4,7] The five potential risk factors were age,[4] clinical features (motor weakness and speech disturbance),[4] duration of symptoms,[4] diabetes,[4] and hypertension.[7] As far as possible, variables were defined and categorised in the same way as had been predictive in these previous studies. Age was dichotomised at 60 years.[4] Clinical features were categorised as motor weakness (focal, usually unilateral, weakness of one or more of face, arm, hand or leg) versus speech disturbance (defined, as previously,[4] as either dysarthria or dysphasia or both) without weakness versus all other symptoms. Limb weakness required a clear description of loss of power as opposed to more vague terms, such as "clumsiness" or "heaviness", in the absence of definite weakness. Duration of symptoms was categorised as less than 10 min, 10–59 min, and 60 min or longer. In patients with more than one TIA in the past month, the duration of the longest event was used. Diabetes was defined as requiring either oral mediation or insulin. Hypertension was coded as a history of hypertension in previous studies,[4,7,8] but was included as two separate variables in our study: a previous diagnosis requiring treatment with medication; and elevated blood pressure on first recording after the TIA (cut-off points of 140 mm Hg systolic and 90 mm Hg diastolic were used as previously).[4]

The 7-day risk of stroke was determined in relation to each variable by univariate Cox regression and significance was assessed with the log rank test. The definition of stroke used in this and subsequent analyses was any stroke (by WHO criteria) occurring after full resolution of the initial TIA. We did not have statistical power to do multivariate modelling in the OCSP cohort or to determine the exact size of risk ratios reliably. We therefore simply included in the score any variable that was a univariate predictor of the 7-day risk of stroke with a significance of $p \leq 0 \cdot 1$, with each bivariate risk factor allocated integer values of 0 and 1, and each trivariate factor allocated values of 0,1, and 2, the overall predictive score being the sum.

Validation of the risk score

The risk score was tested first in a dataset of patients ascertained in the first 2 years (April 1, 2002 to March 31, 2004) of the Oxford Vascular Study (OXVASC) with a diagnosis of probable or definite TIA made by the study neurologist using the same definition as in the OCSP.[20] OXVASC is a population-based study of all incident or recurrent TIA and stroke in a population of 90 542 patients, registered with 63 family physicians, in the same practices as the previous OCSP.[3,21] Methods have been described in detail elsewhere,[21,22] and direct assessment has suggested near-complete case-ascertainment.[22] All patients were assessed by a study neurologist who recorded the characteristics of the events and risk factors, and all patients underwent brain imaging. Initial follow-up was by face-to-face interview with a study nurse at 1 month, with re-assessment by the study neurologist if a stroke was suspected. OXVASC has local research ethics committee approval.

The observed 7-day risk of stroke in the OXVASC cohort was stratified according to the risk score. Significance of the predictive value of the score was assessed with a log rank test. Sensitivities and specificities of prediction were determined at each cut-off of the score and the receiver operating characteristic (ROC) curve was plotted. In a secondary analysis to determine the relative risk of stroke during the 7 days after a probable or definite TIA more precisely for each risk factor, the univariate predictive values were also determined in the OXVASC cohort and in pooled data from OXVASC and OCSP. The risk factors included in the score were then entered into a Cox regression model (stratified by study) derived from the pooled data. The predictive power of the other risk factors that had been collected in both studies was also then determined by adding them individually to the final model using the pooled data: any of the predefined risk factors not included in the score, sex, coronary heart disease (angina or myocardial infarction), peripheral vascular disease, atrial fibrillation (previously diagnosed or on assessment), and current smoking.

We further tested the clinical usefulness of the OCSP-derived score to front-line clinicians by validation in two cohorts of all referrals with suspected TIA. One of these cohorts comprised all referrals to OXVASC by primary care or other sources with a preliminary diagnosis of suspected TIA. This was not a further validation of the score because the population included all OXVASC patients with probable or definite TIA used in the above validation, but it provided additional useful data by inclusion of all patients in whom the study neurologist diagnosed only possible TIA, made an alternative diagnosis, or could not explain the symptoms. Follow-up was the same as for the OXVASC TIAs. The 7-day stroke risk was stratified by the risk score. The other cohort comprised all patients referred to a weekly hospital-based TIA clinic run by PMR covering the non-

	Probable or definite TIA		All referrals of suspected TIA	
	OCSP, derivation (n=209)	OXVASC, validation (n=190)	OXVASC, validation (n=378)	Hospital clinic, validation (n=210)
Age (mean [SD])	69·9 (12·2)	73·7 (12·5)	69·5 (15·0)	64·7 (13·7)
Systolic BP (mean [SD])	172·4 (34·1)	153·0 (28·7)*	148·9 (27·2)†	150·5 (26·4)‡
Diastolic BP (mean [SD])	89·5 (16·4)	82·7 (14·8)*	81·8 (13·9)†	83·5 (13·1)‡
Hypertension	79 (38%)	101 (53%)§	172 (46%)¶	103 (52%)‖
Clinical features				
Unilateral weakness	112 (54%)‡	94 (50%)§	118 (31%)¶	79 (38%)
Speech disturbance without weakness	26 (13%)‡	42 (22%)§	73 (19%)¶	45 (21%)
Other	68 (33%)‡	53 (28%)§	186 (49%)¶	86 (41%)
Duration of symptoms				
⩾60 minutes	75 (37%)‖	96 (51%)§	194 (52%)¶	106 (51%)
10–59 minutes	62 (30%)‖	63 (33%)§	114 (30%)¶	61 (29%)
<10 minutes	68 (33%)‖	30 (16%)§	69 (18%)¶	43 (21%)
Diabetes	9 (4%)	20 (11%)§	35 (9%)¶	21 (10%)**
Male sex	112 (54%)	79 (42%)	167 (44%)	102 (49%)
Angina or myocardial infarction	50 (24%)	42 (22%)§	57 (15%)¶	29 (15%)‖
Peripheral vascular disease	36 (17%)	13 (7%)§	19 (5%)¶	7 (4%)‖
Previously diagnosed atrial fibrillation	30 (14%)	31 (16%)§	46 (12%)¶	13 (7%)‖
Current smoker	61 (29%)	25 (13%)§	54 (14%)¶	45 (23%)‖

Data are number (%) unless otherwise indicated. *n=188. †n=375. ‡n=206. §n=189. ¶n=377. ‖n=205. **n=208.

Table 1: **Characteristics of patients included in the OCSP cohort used to derive the risk score and the three other cohorts used to validate the score**

OXVASC population of Oxfordshire during the same period—ie, a second independent validation of the OCSP-derived score. To ensure inclusion of all follow-up strokes, all patients who were referred but did not attend the clinic appointment were traced and clinical details obtained from the patient and the referring physician. The risk of stroke before the scheduled clinic appointment was stratified by the risk score.

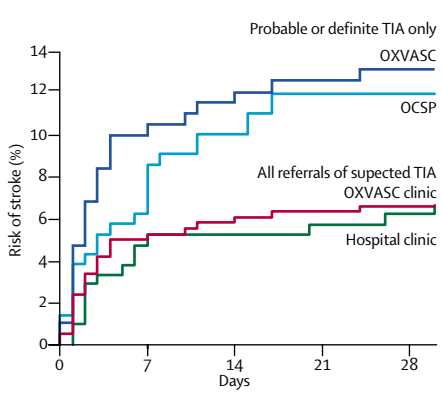
Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Table 1 shows the baseline characteristics of the OCSP and OXVASC cohorts of patients with probable or definite TIA. Data were missing on duration of TIA in four patients in OCSP, three of whom also had missing data on clinical features, leaving 205 of 209 (98%) patients with complete data (table 1). Complete data were available for 188 of 190 (99%) OXVASC patients. The OXVASC cohort was older than the OCSP cohort (p=0·002), had a higher proportion of women (p=0·02), higher rates of previously diagnosed hypertension (p=0·002) and diabetes (p=0·02), and lower systolic and diastolic blood pressures (both p<0·0001). These differences, which have been reported previously and which are similar for incident strokes,[21] are due to changes in population demographics and premorbid screening and treatment of risk factors between the periods during which the two studies were done.[21] However, there was also a tendency for the recorded duration of TIA to be greater in OXVASC than in OCSP (p=0·001). Figure 1 shows the early risk of stroke in the OCSP and OXVASC cohorts. The 7-day risks were 8·6% (4·8–12·4) and 10·5% (6·2–14·9), respectively (p=0·51 for difference).

Table 2 shows the associations between the six pre-defined potential risk factors and 7-day risk of stroke in the OCSP derivation cohort. Age 60 years or older, clinical features, duration of symptoms, and raised blood pressure at presentation were predictive of stroke at the significance level of p⩽0·1, but diabetes and a



Numbers at risk

Probable or definite TIA only					
OXVASC	209	190	187	183	183
OCSP	190	170	167	165	164
All referrals of supected TIA					
OXVASC clinic	378	358	355	353	352
Hospital clinic	210	199	199	198	197

Figure 1: **Risk of stroke from time of presenting TIA in the two cohorts with probable or definite TIA and the two cohorts of all referrals with a preliminary diagnosis of suspected TIA**

	Derivation cohort (OCSP)			Validation cohort (OXVASC)			OCSP and OXVASC pooled		
	Events/patients	HR (95% CI)	p	Events/patients	HR (95% CI)	p	HR (95% CI)	p	P(Het)
Pre-defined risk factors (present *vs* absent)									
Age ⩾60 years	17/167 *vs* 1/42	4·48 (0·60–33·68)	0·10	18/165 *vs* 2/25	1·36 (0·32–5·86)	0·68	2·37 (0·73–7·73)	0·14	0·35
SBP >140 or DBP ⩾90 mm Hg	18/178 *vs* 0/31	..	0·068	18/121 *vs* 2/67	5·29 (1·23–22·79)	0·012	7·02 (1·67–29·43)	0·0018	1·00
Hypertension	9/79 *vs* 9/130	1·73 (0·69–4·37)	0·23	11/101 *vs* 9/88	1·05 (0·44–2·54)	0·91	1·34 (0·70–2·55)	0·37	0·45
Clinical features									
Unilateral weakness	14/112	4·39 (1·00–19·31)	0·029	16/94	..	0·0014	9·24 (2·21–38·65)	0·0001	0·99
Speech disturbance without weakness	2/26	2·61 (·37–18·55)		4/42	..		5·28 (1·06–26·23)		
Other	2/68	1		0/53	..		1		
Duration of symptoms									
⩾60 min	9/75	4·29 (0·93–19·86)	0·051	18/96	..	0·0005	8·18 (1·93–34·72)	0·0001	0·20
10–59 min	6/62	3·48 (0·70–17·27)		2/63	..		3·24 (0·68–15·34)		
<10 min	2/68	1		0/30	..		1		
Diabetes	1/9 *vs* 17/200	1·34 (0·18–10·05)	0·78	4/20 *vs* 16/169	2·22 (0·74–6·66)	0·14	1·94 (0·75–5·03)	0·16	0·66
Other risk factors (present *vs* absent)									
Male	8/112 *vs* 10/97	0·67 (0·27–1·71)	0·40	13/79 *vs* 7/111	2·70 (1·08–6·76)	0·026	1·39 (0·73–2·65)	0·31	0·037
MI or angina	1/50 *vs* 17/159	0·18 (0·02–1·37)	0·061	3/42 *vs* 17/147	0·60 (0·18–2·04)	0·40	0·38 (0·14–1·08)	0·056	0·33
PVD	1/36 *vs* 17/173	0·27 (0·04–2·03)	0·17	2/13 *vs* 18/176	1·51 (0·35–6·49)	0·58	0·62 (0·19–2·03)	0·42	0·18
Atrial fibrillation	3/30 *vs* 15/179	1·24 (0·36–4·27)	0·74	3/31 *vs* 17/158	0·89 (0·26–3·05)	0·86	1·04 (0·43–2·49)	0·93	0·73
Current smoker	4/61 *vs* 14/148	0·68 (0·22–2·07)	0·49	4/25 *vs* 16/164	1·65 (0·55–4·94)	0·36	1·01 (0·46–2·24)	0·98	0·27

All analyses are univariate. HR=hazard ratio from univariate Cox regression. P(Het)=signficance of the difference in risk association between the two cohorts. SBP=systolic blood pressure. DBP=diastolic blood pressure. MI=myocardial infarction. PVD=peripheral vascular disease.

***Table 2*: 7-day risk of stroke after presenting TIA in relation to potential risk factors**

previous diagnosis of hypertension were not. The resulting risk score was therefore: age 60 years or older=1, raised blood pressure (systolic >140 mm Hg and/or diastolic ⩾90 mm Hg)=1, clinical features (unilateral weakness=2, speech disturbance without weakness=1, other=0), and duration of symptoms in min (⩾60=2, 10–59=1, <10=0). The score was termed ABCD (age, blood pressure, clinical features, duration).

Table 3 shows the 7-day risk of stroke stratified by the OCSP-derived ABCD score in the OXVASC cohort of patients with probable or definite TIA. The score was highly predictive of stroke at 7 days ($p<0·0001$). There was only one stroke in patients with a score of less than 5, whereas the 7-day risk was 35·5% in those with a score of 6. The area under the ROC curve (figure 2) was 0·85 (0·78–0·91).

Table 2 also shows the 7-day stroke risk associated with each risk factor in the OXVASC TIA cohort separately and pooled with the OCSP cohort (399 patients with probable or definite TIA and 38 strokes at 7 days). The predictive values of the six original potential components of the risk score were consistent between the studies, with no significant heterogeneity. Of the four components that were predictive of stroke in the OCSP, all apart from age were significantly predictive in OXVASC. No other risk factor was significantly associated with risk of stroke in the pooled data, and only diabetes became significant when added to a logistic regression model containing the four components of the ABCD score (table 4). Notably, the patient with the lowest ABCD score (4) in the OXVASC cohort who had a stroke within 7 days had diabetes.

The clinical usefulness of the model to front-line clinicians was assessed in the population-based

	Patients (%)	Strokes (%)	% risk (95% CI)
ABCD score			
⩽1	2 (1%)	0	0
2	28 (15%)	0	0
3	32 (17%)	0	0
4	46 (24%)	1 (5%)	2·2 (0–6·4)
5	49 (26%)	8 (40%)	16·3 (6·0–26·7)
6	31 (16%)	11 (55%)	35·5 (18·6–52·3)
Total	188 (100%)	20 (100%)	10·5 (6·2–14·9)

***Table 3*: 7-day risk of stroke stratified according to ABCD score at first assessment in the OXVASC validation cohort of patients with probable or definite TIA**

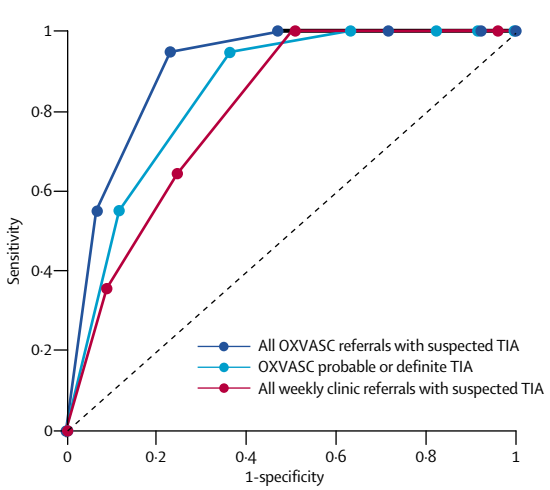


***Figure 2*: ROC curves for predictive value of ABCD score in the three validation cohorts**

	HR (95% CI)	P
Age ⩾60 years	2·57 (0·75–8·81)	0·133
SBP>140 or DBP ⩾90 mm Hg	9·67 (2·23–41·94)	0·002
Clinical features		
Unilateral weakness	6·61 (1·53–28·50)	0·016
Speech disturbance without weakness	2·59 (0·50–13·56)	
Other	1·0	
Duration of symptoms		
⩾60 minutes	6·17 (1·43–26·62)	0·019
10–59 minutes	3·08 (0·64–14·77)	
<10 minutes	1·0	
Diabetes	4·39 (1·36–14·22)	0·014

SBP=systolic blood pressure. DBP=diastolic blood pressure.

Table 4: **Multivariate Cox regression analysis of predictors of 7-day risk of stroke in patients with probable or definite TIA derived from the pooled data (stratified by study) from OCSP and OXVASC**

OXVASC and hospital-based weekly TIA clinic cohorts of all patients referred with a potential diagnosis of TIA. Table 1 shows the baseline clinical characteristics of these two cohorts and figure 2 shows the risk of stroke from the time of the presenting TIA. The 7-day risks of stroke were 5·3% (3·0–7·5) and 5·2% (2·2–8·3) respectively.

In the OXVASC population-based cohort of all 377 referrals, 19 (95%) of the 20 strokes that occurred within 7-days of the presenting TIA occurred in the 101 (27%) patients with a risk score of 5 or greater (table 5). The 7-day risks were 0·4% (0–1·1) in 274 (73%) patients with a score of less than 5, 12·1% (4·2–20·0) in 66 (18%) patients with a score of 5, and 31·4% (16·0–46·8) in 35 (9%) patients with a score of 6. The corresponding area under the ROC curve (figure 2) was 0·91 (0·86–0·95). Table 5 also shows that the score was still highly predictive ($p<0·0001$) when the five 7-day strokes that occurred before the patient sought medical attention after the initial TIA were excluded.

As a potential aid to focusing public education about the need to seek urgent medical attention after a TIA, we assessed the predictive value of various combinations of clinical features and the other components of the risk score (excluding blood pressure, which will usually be unknown to the patient at the time that he or she has a TIA-like episode) in the OXVASC cohort of all patients presenting to medical attention with a suspected TIA. Table 6 shows the proportion of patients and strokes that would be captured by each possible scenario. For example, all of the strokes in the first 7 days occurred in the 51% of patients who had focal weakness or speech disturbance. If the event also lasted 60 min or longer, the subset was reduced to 30% of the cohort, but still included 90% of the strokes that occurred within 7 days.

Of 210 consecutive referrals to the non-OXVASC hospital-referred TIA clinic with suspected TIA, 206 (98%) had complete data on the ABCD score variables, including all patients who had a stroke before the clinic appointment. The median (IQR) time from referral to clinic and the appointment was 9 (4–16) days, with 42% seen within 7 days of referral. 14 (7·5%) patients had a stroke before their scheduled clinic appointment, of which 11 occurred after the patient had sought medical attention. Of these 11 patients, two had a minor stroke not requiring immediate hospital admission and were able to attend the clinic appointment, but nine patients were unable to attend because they had been admitted to hospital following a major stroke that occurred before their scheduled appointment. Table 5 shows that the ABCD score predicted stroke before the clinic appointment ($p=0·007$), with no events in patients with a score of less than 4, and figure 2 shows that the associated area under the ROC curve was 0·80 (0·72–0·89). Again, the score was still predictive

	Risk of stroke within 7 days			Excludes strokes prior to seeking medical attention	
	Patients (%)	Events (%)	% risk (95% CI)	Events (%)	% risk (95% CI)
OXVASC					
⩽1	28 (7%)	0	0	0	0
2	74 (20%)	0	0	0	0
3	82 (22%)	0	0	0	0
4	90 (24%)	1 (5%)	1·1 (0–3·3)	0	0
5	66 (18%)	8 (40%)	12·1 (4·2–20·0)	5 (33%)	7·6 (1·2–14·0)
6	35 (9%)	11 (55%)	31·4 (16·0–46·8)	10 (67%)	28·6 (13·6–43·5)
Total	375 (100%)	20 (100%)	5·3 (3·0–7·5)	15 (100%)	4·0 (2·0–6·0)
Weekly clinic					
⩽1	18 (9%)	0	0	0	0
2	36 (18%)	0	0	0	0
3	40 (20%)	0	0	0	0
4	55 (26%)	5 (36%)	9·1 (1·5–16·7)	3 (27%)	5·6 (0–11·7)
5	34 (16%)	4 (29%)	11·8 (0·9–22·6)	3 (27%)	8·9 (0–18·6)
6	23 (11%)	5 (36%)	23·8 (5·6 – 42·0)	5 (45%)	21·7 (4·9–38·6)
Total	206 (100%)	14 (100%)	6·7 (3·3–10·0)	11 (100%)	5·2 (2·2–8·3)

Table 5: **7-day risk of stroke stratified according to ABCD score at first assessment in all referrals with suspected TIA to OXVASC and risk of stroke before scheduled clinic appointment in all referrals with suspected TIA to the non-OXVASC hospital-referred weekly TIA clinic**

	OXVASC suspected TIA referrals		
	Patients (%)	Strokes (%)	% risk (95% CI)
Focal weakness or speech disturbance			
No	186 (49%)	0	0
Yes	191 (51%)	20 (100%)	10·5 (6·1–14·8)
Focal weakness or speech disturbance and			
Duration of symptoms <10 min	25 (7%)	0	0
Duration of symptoms ≥10 min	166 (44%)	20 (100%)	12·1 (7·1–17·0)
Duration of symptoms <60 min	78 (21%)	2 (10%)	2·6 (0–6·1)
Duration of symptoms ≥60 min	113 (30%)	18 (90%)	15·9 (9·2–22·7)
Age<60 years	42 (11%)	2 (10%)	4·8 (0–11·2)
Age ≥60 years	149 (40%)	18 (90%)	12·1 (6·8–17·3)
Focal weakness or speech disturbance and duration ≥10 min and			
Age <60 years	37 (10%)	2 (10%)	5·4 (0–12·7)
Age ≥60 years	129 (34%)	18 (90%)	14·0 (8·0–19·9)
Focal weakness or speech disturbance and duration ≥60 min and			
Age <60 years	24 (6%)	2 (10%)	8·3 (0–19·4)
Age ≥60 years	89 (24%)	16 (80%)	18·0 (10·0–26·0)
Focal weakness			
No	259 (69%)	4 (20%)	1·5 (0–3·0)
Yes	118 (31%)	16 (80%)	13·6 (7·4–19·7)
Focal weakness and			
Duration of symptoms <10 min	9 (2%)	0	0
Duration of symptoms ≥10 min	109 (29%)	16 (80%)	14·7 (8·0–21·3)
Duration of symptoms <60 min	40 (11%)	1 (5%)	2·5 (0–7·3)
Duration of symptoms ≥60 min	78 (21%)	15 (75%)	19·2 (10·5–28·0)
Age <60 years	28 (7%)	2 (10%)	7·1 (0–16·7)
Age ≥60 years	90 (24%)	14 (70%)	15·6 (8·1–23·0)
Focal weakness and duration ≥10 min and			
Age <60 years	26 (7%)	2 (10%)	7·7 (0–17·9)
Age ≥60 years	83 (22%)	14 (70%)	16·9 (8·8–24·9)
Focal weakness and duration ≥60 min and			
Age <60 years	18 (5%)	2 (10%)	11·1 (0–25·6)
Age ≥60 years	60 (16%)	13 (65%)	21·7 (11·2–32·1)

Table 6: **Numbers of patients, numbers of strokes, and 7-day risks of stroke in all patients referred to OXVASC with suspected TIA stratified by clinical characteristics of presenting event, duration of event, and age**

(p=0·01) when the three strokes that occurred before the patient sought medical attention after the initial TIA were excluded.

Discussion

We have derived and validated a simple score to predict stroke in the 7 days after a TIA, based on age, blood pressure, clinical features, and duration of symptoms. We used data from three rigorous clinical studies. OXVASC and OCSP are two of only a very few prospective, truly population-based studies of TIA with high levels of ascertainment and detailed assessment by neurologists. The hospital-referred clinic series was also valuable in that, unlike other such studies, all referrals were traced and assessed irrespective of whether they attended the clinic—the majority of early strokes occurred before the scheduled appointment and prevented attendance. Finally, the OXVASC cohort of all patients presenting with what was thought by the primary care or other front-line physician to be a potential TIA was essential in determining the usefulness of the risk score from this important perspective.

The consistency of prediction of the component risk factors in the ABCD score in OCSP and OXVASC, and the fact that each risk factor had been reported to predict the 3-month or 1-year risk of stroke after a TIA,[4,7] indicate that the score is likely to have good external validity. This degree of reliability, although unusual,[23] is consistent with the reliability of prediction of stroke in other clinical settings.[15-17,24] Moreover, the multivariate model derived from the unrestricted group of risk factors in the pooled data from OCSP and OXVASC was similar to the 90-day risk model developed by Johnston and co-workers.[4] However, our finding of no early strokes in any of the validation cohorts in patients with an ABCD score of 4 or less should not be taken as a generalisable observation. Such patients will have a finite risk of early stroke, albeit relatively low.

The prognostic value of age and raised blood pressure were not unexpected. Nearly 90% of strokes in the general population occur in patients aged 60 years or older,[21] and an exponential relation exists between usual blood pressure and stroke risk.[25] That raised blood pressure at presentation was more predictive of early stroke than a history of treated hypertension possibly reflects a greater relevance of current blood pressure to immediate risk of stroke. The predictive value of particular clinical symptoms is more difficult to explain. Monocular TIAs have a good prognosis in the subacute and chronic phase,[15-17] but exclusion of these cases from our cohorts did not significantly reduce the predictive value of focal weakness and speech disturbance (unpublished data). TIA is a subjective diagnosis based usually only on clinical history and with no objective test, and although in each of our cohorts of probable or definite TIA we applied standard diagnostic criteria stringently, excluding 50% of referrals, it is possible, as suggested previously,[4] that focal weakness and speech disturbance simply identify patients who are most likely to have actually had transient cerebral ischaemia. Indeed, although focal weakness and speech disturbance were no less predictive in our patients with TIA of 60 min duration or longer (unpublished data), in whom diagnostic certainty is usually greater, preliminary findings of a study relating the nature of the clinical symptoms to the appearance of an appropriate acute ischaemic lesion on magnetic resonance diffusion-weighted imaging (DWI) do show that speech disturbance and weakness are most commonly associated with definite ischaemia (unpublished data). Why weakness appears to be associated with a higher risk of stroke than speech disturbance is unclear. The predictive value of duration of TIA is more intuitive; prolonged episodes probably reflect the severity of the pathological process or cerebral susceptibility to ischaemia, due to poor collateral circulation or other factors. Duration of TIA is also correlated with the likelihood of seeing an acute ischaemic lesion on DWI.[26] Indeed, it is possible that the

association between an acute lesion on DWI and an increased early risk of stroke after a TIA[26] would be much reduced after adjustment for clinical features and duration of TIA.

The multivariate modelling on the pooled data from OCSP and OXVASC suggests that prediction might be improved by more precise weighting of each variable (table 4), and by addition of new variables, particularly diabetes. Prediction might also be improved by considering age, symptom duration, and blood pressure as continuous variables, by further subdividing the clinical features, and by exploration of interactions between the factors in the score. Further research is needed, but will require pooled analysis of data from several studies to have a sufficient number of early strokes to allow more detailed modelling.

Our findings will be useful at several key stages in the management of TIA. First, they might focus public education. Public awareness of the symptoms of TIA and the need to seek medical attention urgently is poor.[27,28] One recent nationwide telephone survey of adults in the USA showed that only 8·6% of the population could correctly identify any symptoms of a TIA.[28] However, public education has been difficult thus far because of the wide variation and the sometimes non-specific nature of the clinical manifestations of TIA. Yet, our data show that most early strokes occur after TIAs with specific and clearly definable characteristics (table 6). These descriptions of "high-risk mini-strokes" should allow public education to be simple and effectively focused.

Second, the ABCD score will allow front-line health services, such as primary care or emergency department physicians, or telephone advice centres, to rapidly and reliably assess risk, and hence the urgency required in referral for specialist assessment, in patients with symptoms suggestive of a TIA. Third, the score will allow specialist physicians to triage referrals. The consequences of reliable risk assessment will depend on local practice. Health-care systems that provide emergency inpatient care for all patients might consider rapid-access outpatient clinics for those with low ABCD scores. In countries, such as the UK, where patients with TIA are seen in weekly outpatient clinics, often after a delay of 2 weeks or more, the risks of stroke seen in those with high ABCD scores should lead to immediate changes in policy. Such patients will need to be assessed, investigated, and treated as an emergency, a point perhaps best made by the high rates of stroke before scheduled clinic appointment seen in our study of a weekly clinic.

Several treatments are likely to be effective in preventing stroke in the acute phase after a TIA, including aspirin,[29] possibly in combination with clopidogrel,[30-32] anticoagulation in patients with atrial fibrillation,[33] and possibly statins.[34] Carotid disease is the most common underlying cause in patients who have an early recurrent stroke,[35] and endarterectomy for 50–99% symptomatic carotid stenosis is safe and highly effective in neurologically stable patients within 1–2 weeks after a TIA.[36,37] Further research is needed to assess the risks and benefits of blood pressure lowering acutely after TIA, and of the prophylactic use of neuroprotective agents, such that patients are pre-treated before any stroke occurs, thereby mimicking the animal models of stroke in which many agents are highly effective.[38]

The early risk of stroke of about 30% in TIA patients with an ABCD score of 6 necessitates not only emergency investigation and treatment but also admission to hospital during the acute phase. Even if acute prevention is ineffective, admission would probably still be cost-effective given the potential for immediate thrombolysis for any subsequent stroke. The benefits of thrombolysis given within 1 h of stroke onset are substantial,[39] and treatment within minutes should be even more effective. Emergency admission to hospital of patients with an ABCD score of 6 should be possible in most healthcare systems given their relatively small number: 9% of all referrals to OXVASC, or 16 patients per 100 000 population per year.

In conclusion, the risk of stroke during the 7 days after a TIA appears to be highly predictable. Further validations of the ABCD score are required, and it is likely to be refined in larger studies. Further research is also required to determine predictive value in different aetiological subtypes of TIA. In the meantime, however, the current score can be used in routine clinical practice to identify high-risk individuals who require emergency investigation and treatment.

Contributors

P M Rothwell is the principal investigator of the OXVASC study and the hospital-referred TIA cohort, designed the current study, planned the analysis, and wrote the paper. M F Giles was responsible for assessment of patients in OXVASC and for collation of data. E Flossmann, C E Lovelock, and J Redgrave also contributed to the recruitment, assessment and collection of data on the OXVASC cohorts. C P Warlow was the principal investigator on the Oxfordshire Community Stroke Project and commented on a draft of this paper. Z Mehta is the OXVASC statistician and was responsible for analysis of data.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

The study was funded by the UK Stroke Association, the BUPA Foundation, and the UK Medical Research Council. We thank all our colleagues who collaborated on the Oxfordshire Community Stroke Project and the Oxford Vascular Study.

References

1 Rothwell PM, Warlow CP. Timing of transient ischaemic attacks preceding ischaemic stroke. *Neurology* 2005; **64:** 817–20.

2 Coull A, Rothwell PM. Under-estimation of the early risk of recurrence after first stroke by the use of restricted definitions. *Stroke* 2004; **35:** 1925-29.

3 Rothwell PM. Incidence, risk factors and prognosis of stroke and transient ischaemic attack: the need for high-quality large-scale epidemiological studies. *Cerebrovascular Disease* 2003; **16** (suppl 3): 2–10.

4 Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. *JAMA* 2000; **284:** 2901–06.

5 Lovett J, Dennis M, Sandercock PAG, Bamford J, Warlow CP, Rothwell PM. The very early risk of stroke following a TIA. *Stroke* 2003; **34:** e138–e40

6 Coull A, Lovett JK, Rothwell PM, on behalf of the Oxford Vascular Study. Early risk of stroke after a TIA or minor stroke in a population-based incidence study. *BMJ* 2004; **328:** 326–28.

7 Hill MD, Yiannakoulias N, Jeerakathil T, Tu JV, Svenson LW, Schopflocher DP. The high risk of stroke immediately after transient ischemic attack. A population-based study. *Neurology* 2004; **62:** 2015–20

8 Lisabeth LD, Ireland JK, Risser JMH, et al. Stroke risk after transient ischaemic attack in a population-based setting. *Stroke* 2004; **35:** 1842–46.

9 Johnston SC, Smith WS. Practice variability in management of transient ischaemic attacks. *Eur Neurol* 1999; **42:** 105–08.

10 Goldstein LB, Bian J, Bonito AJ, Lux LJ, Matchar DB. New transient ischemic attack and stroke: outpatient management by primary care physicians. *Arch Intern Med* 2000; **160:** 2941–46.

11 Gubitz G, Phillips S, Dwyer V. What is the cost of admitting patients with transient ischaemic attacks to hospital? *Cerebrovasc Dis* 1999; **9:** 210–14.

12 Ovbiagele B, Saver JL, Fredieu A, et al. In-hospital initiation of secondary stroke prevention therapies yield high rates of adherence at follow-up. *Stroke* 2004; **35:** 2879–83.

13 The Intercollegiate Working Party for Stroke. National Clinical Guidelines for Stroke. London: RCPL, 2004.

14 Wolf PA, Clagett GP, Easton JD, et al. Preventing ischemic stroke in patients with prior stroke and transient ischemic attack: a statement for healthcare professionals from the Stroke Council of the American Heart Association. *Stroke* 1999; **30**:1991–94.

15 Hankey GJ, Slattery JM, Warlow CP. Transient ischaemic attacks: Which patients are at high (and low) risk of serious vascular events? *J Neurol Neurosurg Psychiatry* 1992; **55:** 640–52.

16 Kernan WN, Viscoli CM, Brass LM, et al. The Stroke Prognosis Instrument II (SPI II): A clinical prediction instrument for patients with transient ischaemia and non-disabling ischaemic stroke. *Stroke* 2000; **31:** 456–62.

17 Rothwell PM, Mehta Z, Howard SC, Gutnikov SA, Warlow CP. From subgroups to individuals: general principles and the example of carotid endartectomy. *Lancet* 2005; **365:** 256–65.

18 Dennis M, Bamford J, Sandercock P, Warlow C. Prognosis of transient ischemic attacks in the Oxfordshire Community Stroke Project. *Stroke* 1990; **21:** 848–53.

19 Dennis MS, Bamford JM, Sandercock PA, Warlow CP. Incidence of transient ischemic attacks in Oxfordshire, England. *Stroke* 1989; **20:** 333–39.

20 Hatano S. Experience from a multicentre stroke register: a preliminary report. *Bull WHO* 1976; **56:** 541–53.

21 Rothwell PM, Coull A, Giles M, et al. Changes in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire from 1981-2004: the Oxford Vascular Study. *Lancet* 2004; **363:** 1925–33.

22 Coull AJ, Silver L, Bull L, Giles M, Rothwell PM. Direct assessment of completeness of ascertainment in a stroke incidence study. *Stroke* 2004; **35:** 2041–45

23 Altman DG, Royston P. What do we mean by validating a prognostic model? *Statist Med* 2000; **19:** 453–73.

24 Pearce LA, Hart RG, Halpern JL. Assessment of three schemes for stratifying stroke risk in patients with non-valvular atrial fibrillation. *Am J Med* 2000; **109:** 45–51.

25 Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; **360:** 1903–13.

26 Purroy F, Montaner J, Rovira A, Delgado P, Quintana M, Alvarez-Sabin J. Higher risk of further vascular events among transient ischaemic attack patients with diffusion-weighted imaging acute lesions. *Stroke* 2004; **35:** 2313–19.

27 Giles MF, Rothwell PM. Determinants of delay in seeking medical attention after a TIA or minor stroke. *Cerebrovasc Dis* 2004; **17** (suppl 5)**:** 6.

28 Johnston SC, Fayad PB, Gorelick PB, et al. Prevalence and knowledge of transient ischemic attack among US adults. *Neurology* 2003; **60:** 1429–34

29 International Stroke Trial Collaborative Group. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. *Lancet* 1977; **349:** 1569–81.

30 Kennedy J, Eliasziw M, Hill MD, Buchan AM. The Fast Assessment of Stroke and Transient ischemic attack to prevent Early Recurrence (FASTER) trial. *Semin Cerebrovasc Dis Stroke* 2003; **3:** 25–30.

31 Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001; **345:** 494–502.

32 Markus HS, Droste DW, Kaps M, et al. Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using doppler embolic signal detection: the Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial. *Circulation* 2005; **111:** 2233–40.

33 European Atrial Fibrillation Trial Study Group. Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. *Lancet* 1993; **342:** 1255–62.

34 Schwartz GG, Olsson AG, Ezekowitz MD, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes. The MIRACL Study: a randomized controlled trial. *JAMA* 2001; **285:** 1711–18.

35 Lovett JK, Coull A, Rothwell PM, on behalf of the Oxford Vascular Study. Early risk of recurrent stroke by aetiological subtype: implications for stroke prevention. *Neurology* 2004; **62:** 569–74.

36 Bond R, Rerkasem K, Rothwell PM. A systematic review of the risks of carotid endarterectomy in relation to the clinical indication and the timing of surgery. *Stroke* 2003; **34:** 2290–301.

37 Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJM, for the Carotid Endarterectomy Trialists Collaboration. Effect of endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and to the timing of surgery. *Lancet* 2004; **363:** 915–24.

38 Gladstone DJ, Black SE, Hakim AM. Toward wisdom from failure: lessons from neuroprotective stroke trials and new therapeutic directions. *Stroke* 2002; **33:** 2123–36.

39 Hacke W, Donnan G, Fieschi C, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet* 2004; **363:** 768–74.