Disparities in Antihypertensive Prescribing After Stroke
Linked Data From the Australian Stroke Clinical Registry

Lachlan L. Dalli, B Biomed Sci (Hons); Joosup Kim, PhD; Amanda G. Thrift, PhD; Nadine E. Andrew, PhD; Natasha A. Lannin, PhD; Craig S. Anderson, PhD; Rohan Grimley, MBBS; Judith M. Katzenellenbogen, PhD; James Boyd, PhD; Richard I. Lindley, MD; Michael Pollack, MBBS; Martin Jude, MBBS; Ramesh Durairaj, MBBS; Darshan Shah, MBBS; Dominique A. Cadilhac, PhD; Monique F. Kilkenny, PhD; on behalf of the Stroke123 Investigators and the AuSCR Consortium

Background and Purpose—Despite evidence to support the prescription of antihypertensive medications before hospital discharge to promote medication adherence and prevent recurrent events, many patients with stroke miss out on these medications at discharge. We aimed to examine patient, clinical, and system-level differences in the prescription of antihypertensive medications at hospital discharge after stroke.

Methods—Adults with acute ischemic stroke or intracerebral hemorrhage alive at discharge were included (years 2009–2013) from 39 hospitals participating in the Australian Stroke Clinical Registry. Patient comorbidities were identified using the *International Statistical Classification of Diseases and Related Health Problems* (*Tenth Edition, Australian Modification*) codes from the hospital admissions and emergency presentation data. The outcome variable and other system factors were derived from the Australian Stroke Clinical Registry dataset. Multivariable, multilevel logistic regression was used to examine factors associated with the prescription of antihypertensive medications at hospital discharge.

Results—Of the 10315 patients included, 79.0% (intracerebral hemorrhage, 74.1%; acute ischemic stroke, 79.8%) were prescribed antihypertensive medications at discharge. Prescription varied between hospital sites, with 6 sites >2 SDs below the national average for provision of antihypertensives at discharge. Prescription was also independently associated with patient and clinical factors including history of hypertension, diabetes mellitus, management in an acute stroke unit, and discharge to rehabilitation. In patients with acute ischemic stroke, females (odds ratio, 0.85; 95% CI, 0.76–0.94), those who had greater stroke severity (odds ratio, 0.81; 95% CI 0.72–0.92), or dementia (odds ratio, 0.65; 95% CI, 0.52–0.81) were less likely to be prescribed.

Conclusions—Prescription of antihypertensive medications poststroke varies between hospitals and according to patient factors including age, sex, stroke severity, and comorbidity profile. Implementation of targeted quality improvement initiatives at local hospitals may help to reduce the variation in prescription observed. **(*Stroke*. 2019;50:3592-3599. DOI: 10.1161/STROKEAHA.119.026823.)**

Key Words: blood pressure ■ comorbidity ■ hypertension ■ medication adherence ■ risk factor

Survivors of stroke have a 43% cumulative risk of a recurrent stroke over 10 years,[1] highlighting the importance of managing risk factors after hospital discharge. Lowering elevated blood pressure (BP), the most prevalent risk factor for stroke,[2] is critical for preventing future serious cardiovascular events poststroke. There is also evidence to indicate that BP-lowering poststroke is effective in reducing absolute cardiovascular disease risk in both normotensive and hypertensive patients.[3,4] Before 2017, it was also recommended in the Australian Clinical Guidelines that all patients with stroke or

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From the Stroke and Ageing Research Group, Department of Medicine, School of Clinical Sciences at Monash Health (L.L.D., J.M.K., A.G.T., R.G., D.A.C., M.F.K.) and Peninsula Clinical School, Central Clinical School (N.E.A.), Monash University, Clayton, VIC, Australia; Stroke Division, The Florey Institute of Neuroscience and Mental Health, Heidelberg, VIC, Australia (J.M.K., D.A.C., M.F.K.); Department of Neuroscience, Central Clinical School, Monash University, Melbourn, VIC, Australia (N.A.L.); Royal Prince Alfred Hospital, Camperdown, NSW, Australia (C.S.A.); The George Institute for Global Health at Peking University Health Science Center, China (C.S.A.); The George Institute for Global Health, Sydney, NSW, Australia (C.S.A.); Sunshine Coast Clinical School, University of Queensland, Birtinya, QLD, Australia (R.G.); School of Population and Global Health (J.M.K.) and Telethon Kids Institute (J.M.K.), The University of Western Australia, Perth, Australia; School of Psychology and Public Health, La Trobe University, Bundoora, VIC, Australia (J.B.); The University of Sydney, NSW, Australia (R.I.L.); Hunter Stroke Service, Hunter New England Health, NSW, Australia (M.P.); The University of Newcastle, NSW, Australia (M.P.); Wagga Wagga Hospital, NSW, Australia (M.J.); Cairns Base Hospital, QLD, Australia (R.D.); and Princess Alexandra Hospital, Brisbane, QLD, Australia (D.S.).

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Correspondence to Monique Kilkenny, PhD, Translational Public Health and Evaluation Division, Stroke and Ageing Research, Department of Medicine, School of Clinical Sciences at Monash Health, Level 3, Hudson Institute Bldg, 27-31 Wright St, Clayton, VIC 3168. Email monique.kilkenny@monash.edu

transient ischemic attack (TIA) have long-term BP-lowering therapy either initiated or intensified, unless contraindicated by symptomatic hypotension.[5] Similar guidelines currently exist for patients with acute ischemic stroke (AIS) and intracerebral hemorrhage (ICH) in Australia and overseas, albeit with minor differences in eligibility and application.[6,7] There is also evidence to indicate these medications should be prescribed before discharge from hospital to enhance long-term adherence to medications[8] and improve patient outcomes.[9]

In Australia between 2009 and 2013, some one-quarter to one-third of patients with stroke or TIA were discharged from acute care without an antihypertensive medication.[10,11] Characterizing the factors that contribute to the prescription of antihypertensive medications is important for identifying opportunities to improve stroke care. Currently, there are limited published studies of patient, clinical, and health system-level factors associated with the prescription of antihypertensive medications after stroke and none specifically in patients with ICH.[10,12] We aimed to examine patient, clinical, and system-level differences in the prescription of antihypertensive medications at the time of hospital discharge, separately for patients with AIS and ICH.

Methods

Study Design and Datasets

This observational cohort study comprised patient-level data from 39 hospitals in Victoria, Queensland, New South Wales, and Western Australia participating in the Australian Stroke Clinical Registry (AuSCR). The AuSCR is a national clinical registry designed to routinely monitor processes of care during hospital admission for patients with a clinical diagnosis of acute stroke/TIA and their health outcomes between 90 and 180 days after discharge.[13] Each year from 2009 to 2013, between 1% and 6% of registrants opted out from the AuSCR.[11] As part of the Stroke123 project,[14] AuSCR cases from 2009 to 2013 were linked with statewide hospital admission and emergency department presentation data. In total, there were 15 482 cases matched with >99% concordance based on age and sex.[14] Of the total linked cohort, we included adult patients with ICH or AIS who were alive at the time of discharge. We also excluded patients with missing information on age and sex and those admitted to palliative care within 30 days poststroke as preventative medications are typically withheld.[15] The data that support the findings of this study are available from the corresponding author on reasonable request.

Outcome Variable

The outcome was documented evidence of being prescribed an antihypertensive medication at discharge after stroke. Evidence of prescription was determined from review of medical records, including patient drug charts and discharge medication lists. As defined in the AuSCR data dictionary (available from www.auscr.com.au), patients who continued with previously prescribed antihypertensive medications or were prescribed these medications for the first time during their admission were recorded as having been prescribed, irrespective of discharge destination. In AuSCR data quality audits conducted 2014 to 2015, only 2.7% of cases had discrepancies for the provision of antihypertensive medications at discharge (unpublished data from the AuSCR). For the main analyses, we assumed that patients with missing data on prescription (12% of cases) were not prescribed antihypertensive medications.

Factors Investigated

Patient factors, such as age and sex, and other determinants of stroke outcomes, such as stroke severity and history of previous stroke, were obtained from the AuSCR. Stroke severity was based on a patient's ability to walk on stroke admission, a parameter that has been validated as a reliable prognostic indicator of stroke severity.[16] Patient comorbidities, such as hypertension and atrial fibrillation, were derived from hospital admission and emergency department data, using *International Statistical Classification of Diseases and Related Health Problems, Tenth Edition, Australian Modification* definitions. For this process, a look-back period of 5 years, before and including the index event, was used to identify patient comorbidities.[17] The Charlson Comorbidity Index (CCI) was used to categorize comorbidity based on the presence of a determined subset of conditions contributing between 1 and 6 points to an overall weighted score that is predictive of 5-year risk of mortality.[18,19] Similar to previous investigations in patients with stroke, the CCI was calculated excluding the comorbidities cerebrovascular events and hemiplegia due to their increased prevalence in patients with stroke.[19]

Clinical factors obtained from the AuSCR included length of stay in hospital, management in a stroke unit, and discharge destination (home, aged care, rehabilitation, and further acute hospital care). Using information supplied from individual hospitals, sites were further classified based on system-level factors, such as rurality, number of beds, and teaching status (academic or nonacademic).

To account for sociodemographic and geographic differences in stroke risk, we considered the impact of hospital location (metropolitan or rural), country of birth, Indigenous status, and socioeconomic position. Socioeconomic position was determined using the Index of Relative Socio-Economic Advantage and Disadvantage,[20] produced by the Australian Bureau of Statistics. The Index of Relative Socio-Economic Advantage and Disadvantage is derived from data collected in the Australian Census of Population and Housing and is used widely to classify geographic areas of Australia based on socioeconomic conditions, such as level of education, income, and housing costs. Using postcodes recorded in the AuSCR, registrants were divided into 5 strata of Index of Relative Socio-Economic Advantage and Disadvantage, with greater Index of Relative Socio-Economic Advantage and Disadvantage quintiles indicating lesser relative socioeconomic disadvantage.

Statistical Analyses

Using AuSCR data for quality of care indicators, for example, use of IV-tPA (intravenous tissue-type plasminogen activator), missing or unknown values were recorded as negative for the main analyses (proportion missing ranged from 1% to 12%). Descriptive statistics were used to compare patient characteristics, between patients with and without an antihypertensive prescription at discharge. Differences between the 2 groups were assessed using $\chi 2$ tests for categorical variables and Mann-Whitney *U* tests for nonparametric continuous variables. Funnel plots were constructed to illustrate hospital-level differences in prescription, based on the number of cases submitted per site. Hospitals with provision of antihypertensive medications >2 SDs below the national average were defined as poor performers.

Due to the large number of variables available to analyze, forward and backward stepwise multivariable, multilevel logistic regression was performed, with level defined as hospital. All variables from the univariable model with $P<0.2$ were eligible for inclusion in the final models and were excluded if they were either collinear or were no longer significant ($P>0.05$) following the addition of factors with greater statistical significance. All models were adjusted for age, sex, and stroke severity. Bonferroni adjustments were used in the final multivariable models to adjust for multiple sampling.[21]

Sensitivity analyses were undertaken to determine the influence of discharge destination, hypertension status, and missing data on the final models. Interaction analyses were also undertaken to test whether associations in the final model were altered by age, CCI score, or stroke severity. Goodness of fit was assessed using the Bayesian information criterion, Akaike information criterion, and the area under the receiver operating characteristic curve (C statistic). A standard 2-tailed significance level of $P<0.05$ was used, and standard techniques were implemented to check for collinearity. Data were analyzed using StataSE 15.0 (StataCorp, TX), and results

were reported as odds ratios with 95% CIs. As part of the *Stroke123* project,[14] approvals were received from all relevant data custodians to access and link these data. Ethics approvals were also received from Monash University (CF13/1303 – 2013000641), and other ethics committees to undertake this study.[14,22] The AuSCR holds ethics approval for collection of data using an opt-out model of consent with a waiver of consent for those who die in the hospital.

Results

Of the 15 468 adults available from the linked and merged datasets, 5153 were deemed ineligible for inclusion (Figure I in the online-only Data Supplement). The final cohort comprised 10 315 patients (45.2% female; 1.3% Indigenous; 74.9% aged ≥65 years) with ICH (n=1498) or AIS (n=8817). In total, 7164 patients were discharged from acute care with an antihypertensive prescription (overall 79.0%; AIS, 79.8%; ICH, 74.1%). Of those prescribed, 44.7% were female, and 77.4% were aged ≥65 years. The proportion of patients prescribed antihypertensive medications also varied considerably between the 39 hospitals contributing data (Figure 1). There were 6 hospital sites where the provision of antihypertensive medications was >2 SDs below the national average for AuSCR hospitals (Table I in the online-only Data Supplement).

In both types of stroke, the prescription of antihypertensive medications was less common in patients aged ≤65 years of age than in older patients (Table 1). Compared with patients with less severe stroke (ie, could walk on admission), prescription was less common in patients with severe stroke. Not surprisingly, the prescription of antihypertensive medications was more common in patients with cardiovascular comorbidities (eg, atrial fibrillation, dyslipidemia, or diabetes mellitus) than in those without these conditions.

Following Bonferroni adjustments, the factors independently associated with the prescription of antihypertensive medications in patients with ICH and AIS included age, treatment in a stroke unit, discharge to rehabilitation, history of hypertension, and diabetes mellitus (Table 2). Whereas in AIS, male sex, less severe stroke, absence of dementia, and lesser CCI scores were also independently associated with prescription.

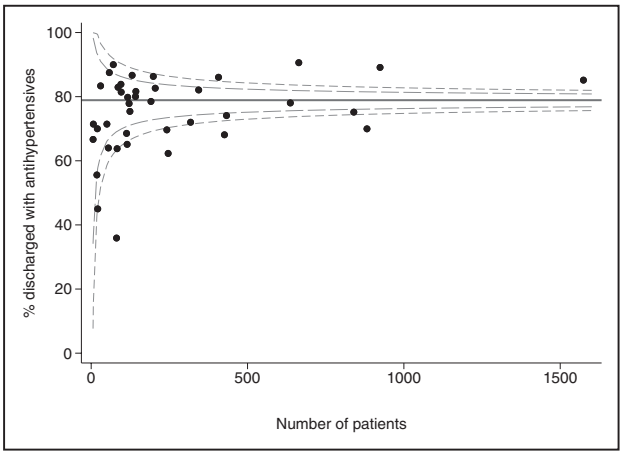

Figure 1. Funnel plot displaying differences in antihypertensive prescription rates between hospitals. Funnel plot displaying proportion of patients discharged with antihypertensive medications (*y* axis) vs the number of patients treated (*x* axis). Dotted lines indicate 1–2 SDs either side of the mean (solid gray line).

Sensitivity Results

There was an interaction between age and CCI score on the probability of prescription (Figure 2; $P<0.001$), indicating that patients aged ≤65 years with a CCI score of ≤5 were less likely to be prescribed antihypertensive medications than older patients with the same CCI score. Interactions were also observed between severity of stroke and history of dementia in patients with AIS ($P=0.005$). The multivariable models did not differ substantially when analyses were restricted to cases with complete prescription data (Table II in the online-only Data Supplement). However, when analyses were restricted to cases with a documented history of hypertension, we were unable to detect an association between prescription and age, sex, and atrial fibrillation (Table III in the online-only Data Supplement). When the results were stratified by discharge destination, the associations between sex, CCI score, stroke severity, and prescription, were only apparent among the group of patients discharged home (Table IV in the online-only Data Supplement).

Discussion

This was a large and comprehensive investigation of patient, clinical, and system-level factors associated with the prescription of antihypertensive medications in patients with stroke, and the first to be performed in patients with ICH. We found that patients with preexisting hypertension were ≈3- to 4-fold more likely to be discharged with antihypertensive medications than patients without a hypertension diagnosis. However, the prescription of antihypertensive medications varied considerably between hospitals and among patients with certain factors. This is concerning since variations in clinical care are associated with worse patient outcomes and inefficient utilization of healthcare resources.[9]

In multivariable analyses, we found women with AIS were 15% less likely to be prescribed antihypertensive medications than men. This finding is of considerable concern since the incidence of stroke is greater in women and is declining at a slower rate than men.[23] Furthermore, the mechanism of stroke in women is more commonly due to high BP,[23] highlighting the need for long-term and more comprehensive treatment of hypertension in this group. In previous studies within Australia, sex differences were not found,[10,24] potentially as the analyses of these studies were not stratified by type of stroke. Early screening and treatment of cardiovascular risk factors is needed to reduce the burden of stroke in women.

Patients with greater CCI scores (and a greater risk of 5-year mortality) were less likely to be prescribed antihypertensive medications than those with lesser CCI scores. This may indicate a prescription bias in patients with poorer prognosis, potentially attributable to perceived futility of secondary prevention medication.[15] Alternatively, patients with severe CCI scores may be taking multiple medications to manage other chronic conditions and diseases. Therefore, antihypertensive medications may have been withheld to minimize the burden of polypharmacy and potential drug side effects. As outlined in the 2018 European Practice Guidelines for Management of Hypertension,[7] the benefits of BP-lowering in patients at risk of major cardiovascular events extends to all individuals, not

Table 1. Characteristics of Patients With and Without an Antihypertensive Prescription at Discharge, Stratified by Type of Stroke

	Acute Ischemic Stroke			Intracerebral Hemorrhage		
	Not prescribed (N=2561)	Prescribed (N=6256)		Not prescribed (N=590)	Prescribed (N=908)	
	n (%)	n (%)	*P* Value	n (%)	n (%)	*P* Value
Female	1167 (45.6)	2782 (44.5)	0.35	292 (49.5)	422 (46.5)	0.25
Age group, y						
<65	899 (35.1)	1418 (22.7)	<0.001	219 (37.1)	204 (22.5)	<0.001
65–74	529 (20.7)	1550 (24.8)	<0.001	119 (20.2)	228 (25.0)	<0.001
75–84	629 (24.6)	2040 (32.6)	<0.001	155 (26.3)	317 (35.0)	<0.001
85+	504 (19.7)	1248 (20.0)	<0.001	97 (16.4)	159 (17.5)	<0.001
Born in Australia	1646 (64.2)	4023 (64.3)	0.92	367 (62.2)	544 (59.9)	0.38
Indigenous	29 (1.2)	87 (1.4)	0.35	10 (1.7)	8 (0.9)	0.16
Socioeconomic position*						
Most disadvantaged	462 (18.0)	997 (16.0)	<0.001	125 (21.2)	171 (18.8)	0.29
Second most disadvantaged	389 (15.2)	1161 (18.6)	<0.001	97 (16.4)	136 (15.0)	0.29
Third most disadvantaged	432 (16.9)	1049 (16.8)	<0.001	82 (13.9)	158 (17.4)	0.29
Fourth most disadvantaged	442 (17.3)	1266 (20.2)	<0.001	104 (17.6)	175 (19.3)	0.29
Least disadvantaged	836 (32.6)	1783 (28.5)		182 (30.9)	268 (29.5)	
Previous stroke†	465 (18.2)	1250 (20.0)	0.05	97 (16.4)	151 (16.6)	0.92
In-hospital stroke‡	127 (5.0)	310 (5.0)	0.99	29 (4.9)	34 (3.7)	0.27
Unable to walk on admission†	1272 (56.8)	3498 (60.2)	0.004	342 (67.5)	620 (73.4)	0.02
Treated in a rural hospital	538 (21.0)	1029 (16.5)	<0.001	117 (19.8)	137 (15.1)	0.017
Treated in a teaching hospital	965 (37.7)	3332 (53.3)	<0.001	209 (35.4)	474 (52.2)	<0.001
Treated in a large hospital (>300 beds)	2131 (83.2)	5108 (81.7)	0.08	490 (83.1)	768 (84.6)	0.43
Stroke unit care	2068 (80.8)	5431 (86.8)	<0.001	337 (57.1)	714 (78.6)	<0.001
Transferred from another hospital‡	366 (14.5)	689 (11.1)	<0.001	158 (27.5)	217 (24.1)	0.15
Received IV- tPA‡	248 (9.7)	707 (11.3)	0.027	…	…	…
Discharge destination‡						
Home	1207 (47.3)	2666 (42.8)	<0.001	184 (31.2)	245 (27.1)	0.08
Aged care	194 (7.6)	372 (6.0)	0.005	53 (9.0)	75 (8.3)	0.63
Rehabilitation	639 (25.0)	2393 (38.5)	<0.001	136 (23.1)	412 (45.5)	<0.001
Other acute hospital	430 (16.8)	750 (12.0)	<0.001	197 (33.4)	161 (17.7)	<0.001
Median LOS (Q1, Q3)‡	6 (3, 11)	6 (3, 11)	0.35	6 (2, 14)	7 (4, 15)	<0.001
Comorbidities						
Hypertension	1414 (55.2)	5042 (80.6)	<0.001	372 (63.1)	808 (89.0)	<0.001
Dyslipidemia	362 (14.1)	1165 (18.6)	<0.001	40 (6.8)	130 (14.2)	<0.001
Atrial fibrillation	732 (28.6)	2219 (35.5)	<0.001	114 (19.3)	232 (25.6)	0.005
Diabetes mellitus	376 (14.7)	1391 (22.2)	<0.001	64 (10.9)	180 (19.8)	<0.001
Angina	353 (13.8)	1237 (19.8)	<0.001	62 (10.5)	133 (14.7)	0.02
Smoking	613 (23.9)	1352 (21.6)	0.017	122 (20.7)	140 (15.4)	0.009
Obesity	102 (4.0)	340 (5.4)	0.005	10 (1.7)	42 (4.5)	0.003
Carotid stenosis	150 (5.9)	431 (6.9)	0.08	11 (1.9)	20 (2.2)	0.65
Congestive heart failure	273 (10.7)	867 (13.9)	<0.001	46 (7.8)	94 (10.4)	0.10
Myocardial infarction	240 (9.4)	860 (13.8)	<0.001	43 (7.3)	81 (8.9)	0.26

(*Continued*)

Table 1. Continued

	Acute Ischemic Stroke			Intracerebral Hemorrhage		
	Not prescribed (N=2561)	Prescribed (N=6256)		Not prescribed (N=590)	Prescribed (N=908)	
	n (%)	n (%)	*P* Value	n (%)	n (%)	*P* Value
Peripheral vascular disease	99 (3.9)	304 (4.9)	0.043	25 (4.2)	29 (3.2)	0.29
Dementia	191 (7.5)	373 (6.0)	0.009	62 (10.5)	63 (6.9)	0.015
Hemiplegia	1542 (60.2)	3824 (61.1)	0.42	300 (50.9)	517 (56.9)	0.021
Cancer	270 (10.5)	643 (10.3)	0.71	77 (13.1)	92 (10.1)	0.08
Liver disease	20 (0.8)	51 (0.8)	0.87	8 (1.4)	11 (1.2)	0.81
Renal disease	268 (10.5)	825 (13.2)	0.001	40 (6.8)	103 (11.3)	0.003
CCI score						
0	1380 (53.9)	2891 (46.2)	<0.001	320 (54.2)	463 (51.0)	0.27
1	440 (17.2)	1144 (18.3)	<0.001	105 (17.8)	154 (17.0)	0.27
2	263 (10.3)	800 (12.8)	<0.001	59 (10.0)	119 (13.1)	0.27
≥3	478 (18.7)	1421 (22.7)	<0.001	106 (18.0)	172 (18.9)	0.27

Q1 denotes 25th percentile, and Q3 denotes 75th percentile. CCI indicates Charlson Comorbidity Index Score; IV-tPA, intravenous tissue-type plasminogen activator; and LOS, length of stay.

*Measured by Index of Relative Socioeconomic Advantage and Disadvantage.

†5%–10% missing.

‡1%–5% missing.

just those who are fit and independent. Because patients with stroke are already at high risk of subsequent major cardiovascular events, perceptions of futility should be balanced by consideration of the benefits of antihypertensive medications in mitigating serious cardiovascular events.[3,4]

Young patients (aged ≤65 years) with a CCI score of ≤5 were less likely to be prescribed antihypertensive medications than older patients with comparable comorbidity profiles. Variation in care based on age may indicate suboptimal prescription among younger patients with less severe comorbidity profile. Similar inequities for younger patients with stroke have been observed for other processes of care in the AuSCR, such as management in a stroke unit and use of swallow screen assessments.[25] This is especially problematic considering the incidence of stroke is increasing among young adults,[26] coinciding with an increase in many cardiovascular risk factors, including hypertension.[27] As atypical mechanisms of stroke are also more common in younger patients, treatment with antihypertensive medications may not always be justified.[26] Other potential reasons for age-related differences in the prescription of secondary prevention medications for stroke may reflect patient preferences influenced by a patient's knowledge and beliefs surrounding medication use.[28] Development of resources and interventions which target both clinician and patient factors may help to reduce the observed variation in care and improve patient outcomes for this at-risk group.

It is unclear whether fears of further cognitive decline in patients with dementia may contribute to the reduced prescription of antihypertensive medications in those with AIS and dementia than in those without dementia.[29] The fact that there is little evidence on the effects of antihypertensive medications in patients with stroke and cognitive dysfunction may partly explain this finding.[29] Although there is evidence to indicate that BP lowering is effective at reducing incident dementia risk,[30] further studies are needed to provide reliable data on the efficacy of antihypertensive medications in patients with stroke and preexisting dementia. In sensitivity analyses, the association between dementia and reduced prescription was only apparent in patients with severe stroke and in those discharged to aged care. Therefore, it is likely that patients with dementia were not prescribed due to greater cumulative functional impairment resulting from the combination of preexisting dementia and more severe stroke than patients without dementia.

It is well known that management in a stroke unit, compared with a general ward, is associated with improved adherence to recommended processes of care for stroke and patient outcomes.[31] Our finding that patients who were treated in a stroke unit were more likely to be prescribed antihypertensive medications at discharge, compared with patients treated in an alternative ward, is important confirmation of the improved quality of care in stroke units. Furthermore, the prescription of antihypertensive medication at discharge is reported to have additive benefits on survival, independent of treatment in a stroke unit. In an earlier study by Cadilhac et al,[32] patients who were managed in a stroke unit and discharged with antihypertensive medications were at a 30% lesser risk of 180-day mortality than patients treated in a stroke unit only. Therefore, there is potential to improve both the prescription of antihypertensive medications, and patient survival, by increasing the utilization of stroke units.

Implementation of standardized discharge processes, computerized clinical decision tools, and quality improvement activities may help to reduce the variation in prescription observed.[33]

Table 2. Multivariable Model of Factors Associated With the Prescription of Antihypertensive Medications at Discharge After Stroke

	Acute Ischemic Stroke (n=8012)		Intracerebral Hemorrhage (n=1348)	
	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Patient factors				
Age (per year increase)	1.01 (1.01–1.02)	<0.001*	1.02 (1.01–1.03)	0.001*
Female	0.85 (0.76–0.94)	0.003*	0.89 (0.69–1.16)	0.39
Unable to walk at admission	0.81 (0.72–0.92)	0.001*	0.81 (0.61–1.09)	0.16
Comorbidities				
Hypertension	3.44 (3.05–3.88)	<0.001*	4.38 (3.18–6.03)	<0.001*
Diabetes mellitus	1.60 (1.35–1.88)	<0.001*	1.95 (1.31–2.91)	0.001*
Dementia	0.65 (0.52–0.81)	<0.001*	†	†
Atrial fibrillation	1.17 (1.03–1.33)	0.012	†	†
Myocardial infarction	1.26 (1.04–1.51)	0.016	†	†
Increased CCI (per 1-point increase)	0.95 (0.92–0.98)	0.001*	0.92 (0.86–0.98)	0.011
Clinical factors				
Stroke unit care	1.59 (1.35–1.86)	<0.001*	1.89 (1.35–2.64)	<0.001*
Discharged to rehabilitation	1.40 (1.24–1.58)	<0.001*	2.29 (1.73–3.04)	<0.001*
C statistic (95% CI)	0.69 (0.68–0.71)		0.69 (0.68–0.70)	

CCI indicates Charlson Comorbidity Index.
*Factors that were significantly associated with outcome following Bonferroni adjustment.
†Variables not included in the final multivariable model.

All hospitals that participate in the AuSCR have access to live summary reports of their performance that include benchmarks to peer hospitals. In a recent prospective study, additional direct support was provided to hospitals to interpret the local results using AuSCR data and plan quality improvement interventions to target areas of underperformance in clinical care.[34] Participation in this quality improvement program led to improvements in various clinical processes of care for stroke, including the prescription of antihypertensive medications at discharge. Expansion of these targeted quality improvement initiatives are underway in participating AuSCR hospitals to enhance the delivery of feedback to local sites, drive improvements in stroke care, and to ultimately improve patient outcomes.

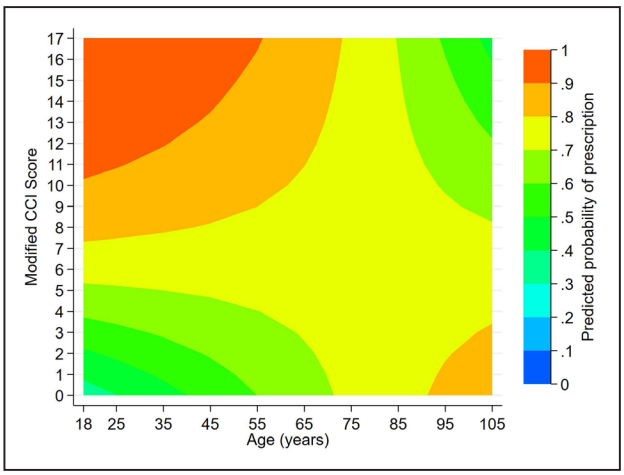

Figure 2. Predicted probability of being prescribed antihypertensive medications after stroke. Contour graph displaying predicted probability (*z* axis) of being prescribed antihypertensive medications at discharge following stroke vs increasing age (*x* axis) and modified Charlson Comorbidity Index (CCI; *y* axis); *P* value for interaction: <0.001.

A strength of our study was the comprehensive cross-jurisdictional linkage of hospital administrative data from 4 Australian states. This enabled analysis of all comorbidities related to admissions and emergency department presentations in the 5 years before and including the index event. Although this is the optimal look-back period for identifying comorbidities in administrative data,[17] some comorbidities may have been missed if not coded in the data. As the majority of hospitals participating in the AuSCR have stroke units, we may have biased our sample to better-performing hospitals. However, acute audit data from 124 hospitals across all states and territories of Australia provides evidence that a similar proportion of patients with stroke (77%) were discharged with antihypertensive medications in 2013.[35] Therefore, the findings from the present study may be applicable to other hospitals within Australia. However, as this study was observational, caution must be taken when generalizing findings to broader contexts as there may be unmeasured sources of confounding that were not adjusted for in our analyses. Although 12% of our sample had missing data for our primary outcome, there was minimal change to our multivariable models when restricted to cases with complete outcome data or a documented history of hypertension.

It is also important to note that the clinical guidelines in effect during the study period (2009–2013) stipulated that all patients with stroke and TIA were eligible for antihypertensive medications unless contraindicated by symptomatic hypotension.[5] As information on contraindications and stroke cause

were not collected in the AuSCR during our study period, we could not exclude patients who were not prescribed due to valid reasons. We also did not have information on whether antihypertensive medications were commenced in-hospital or in the community-setting following discharge. Linkages of our sample to the Australian Pharmaceutical Benefits Scheme database are underway to determine the utilization of these medications after hospital discharge for acute stroke/TIA.

Conclusions

Variation was observed in the prescription of antihypertensive medications at discharge according to various patient-level factors. In particular, we found young patients with stroke and women were less likely to receive antihypertensive medications, suggesting further refinement of guidelines and resources are necessary to bridge these disparities in access to evidence-based care. Future interventions should target hospitals with poor prescription as a first step in reducing the variation in access to antihypertensive medications at discharge.

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Disclosures

Prof Cadilhac is the current Data Custodian for Australian Stroke Clinical Registry (AuSCR). Professors Thrift, Lannin, Anderson, Cadilhac, and Dr Grimley are members of the AuSCR Steering or Management Committees. Prof Thrift is a member of the Board of the Stroke Foundation. Dr Grimley is the clinical lead for the Queensland Statewide Stroke Clinical Network and member of the Stroke Foundation Clinical Council. Prof Cadilhac reports receiving restricted grants from Boehringer Ingelheim, Ipsen, Medtronic, and Shire outside the submitted work. Prof Anderson reports receiving restricted grants from Boehringer Ingelheim, Allergan Australia, Ipsen and Takeda outside the submitted work. Dr Grimley reports receiving restricted grants from Boehringer Ingelheim outside the submitted work. Dr Shah reports receiving grants from Boehringer Ingelheim, Medtronic, and Bayer outside the submitted work. The other authors report no conflicts.

References

1. Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-year risk of first recurrent stroke and disability after first-ever stroke in the Perth Community Stroke Study. *Stroke*. 2004;35:731–735. doi: 10.1161/01.STR.0000116183.50167.D9
2. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, et al; INTERSTROKE investigators. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet*. 2016;388:761–775. doi: 10.1016/S0140-6736(16)30506-2
3. Arima H, Chalmers J, Woodward M, Anderson C, Rodgers A, Davis S, et al; PROGRESS Collaborative Group. Lower target blood pressures are safe and effective for the prevention of recurrent stroke: the PROGRESS trial. *J Hypertens*. 2006;24:1201–1208. doi: 10.1097/01.hjh.0000226212.34055.86
4. National Vascular Disease Prevention Alliance. Guidelines for the management of absolute cardiovascular disease risk. 2012. Available at: www.informme.org.au/Guidelines. Accessed June 1, 2019.
5. Stroke Foundation. Clinical guidelines for stroke management 2010. Melbourne, Australia. Available at: www.informme.org.au/Guidelines. Accessed June 1, 2019.
6. Hemphill JC 3rd, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46:2032–2060. doi: 10.1161/STR.0000000000000069
7. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al; ESC Scientific Document Group. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J*. 2018;39:3021–3104. doi: 10.1093/eurheartj/ehy339
8. Thrift AG, Kim J, Douzmanian V, Gall SL, Arabshahi S, Loh M, et al. Discharge is a critical time to influence 10-year use of secondary prevention therapies for stroke. *Stroke*. 2014;45:539–544. doi: 10.1161/STROKEAHA.113.003368
9. Andrew NE, Kim J, Thrift AG, Kilkenny MF, Lannin NA, Anderson CS, et al; Australian Stroke Clinical Registry Consortium. Prescription of antihypertensive medication at discharge influences survival following stroke. *Neurology*. 2018;90:e745–e753. doi: 10.1212/WNL.0000000000005023
10. Eissa A, Krass I, Bajorek BV. Use of medications for secondary prevention in stroke patients at hospital discharge in Australia. *Int J Clin Pharm*. 2014;36:384–393. doi: 10.1007/s11096-013-9908-3
11. Cadilhac DA, Lannin NA, Anderson CS, Andrew NE, Kim J, Kilkenny M, et al. The Australian Stroke Clinical Registry Annual Report 2013. Available at: www.auscr.com.au/auscr/annual-reports/. Accessed March 29, 2018.
12. Ovbiagele B, Hills NK, Saver JL, Johnston SC. Antihypertensive medications prescribed at discharge after an acute ischemic cerebrovascular event. *Stroke*. 2005;36:1944–1947. doi: 10.1161/01.STR.0000177522.80092.b7
13. Cadilhac DA, Lannin NA, Anderson CS, Levi CR, Faux S, Price C, et al. Protocol and pilot data for establishing the Australian stroke clinical registry. *Int J Stroke*. 2010;5:217–226. doi: 10.1111/j.1747-4949.2010.00430.x
14. Kilkenny MF, Kim J, Andrew NE, Sundararajan V, Thrift AG, Katzenellenbogen JM, et al. Maximising data value and avoiding data waste: a validation study in stroke research. *Med J Aust*. 2019;210:27–31. doi: 10.5694/mja2.12029
15. Lavan AH, Gallagher P, Parsons C, O'Mahony D. STOPPFrail (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy): consensus validation. *Age Ageing*. 2017;46:600–607. doi: 10.1093/ageing/afx005
16. Counsell C, Dennis M, McDowall M, Warlow C. Predicting outcome after acute and subacute stroke: development and validation of new prognostic models. *Stroke*. 2002;33:1041–1047. doi: 10.1161/hs0402.105909
17. Preen DB, Holman CD, Spilsbury K, Semmens JB, Brameld KJ. Length of comorbidity lookback period affected regression model performance of administrative health data. *J Clin Epidemiol*. 2006;59:940–946. doi: 10.1016/j.jclinepi.2005.12.013
18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383. doi: 10.1016/0021-9681(87)90171-8
19. Schmidt M, Jacobsen JB, Johnsen SP, Bøtker HE, Sørensen HT. Eighteen-year trends in stroke mortality and the prognostic influence of comorbidity. *Neurology*. 2014;82:340–350. doi: 10.1212/WNL.0000000000000062
20. Australian Bureau of Statistics. Socio-Economic Indexes For Areas: Robustness, Diversity Within Larger Areas and the New Geography

Standard 2012. Available at:www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/1351.0.55.038Mar%202012. Accessed June 28, 2019.
21. Bender R, Lange S. Adjusting for multiple testing–when and how? *J Clin Epidemiol*. 2001;54:343–349. doi: 10.1016/s0895-4356(00)00314-0
22. Andrew NE, Sundararajan V, Thrift AG, Kilkenny MF, Katzenellenbogen J, Flack F, et al. Addressing the challenges of cross-jurisdictional data linkage between a national clinical quality registry and government-held health data. *Aust N Z J Public Health*. 2016;40:436–442. doi: 10.1111/1753-6405.12576
23. Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, et al; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council for High Blood Pressure Research. Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:1545–1588. doi: 10.1161/01.str.0000442009.06663.48
24. Phan HT, Gall SL, Blizzard CL, Lannin NA, Thrift AG, Anderson CS, et al. Sex differences in care and long-term mortality after stroke: Australian stroke clinical registry. *J Womens Health (Larchmt)*. 2019;28:712–720. doi: 10.1089/jwh.2018.7171
25. Lannin NA, Anderson CS, Kim J, Kilkenny M, Bernhardt J, Levi C, et al. Treatment and outcomes of working aged adults with stroke: results from a national prospective registry. *Neuroepidemiology*. 2017;49:113–120. doi: 10.1159/000484141
26. Ekker MS, Boot EM, Singhal AB, Tan KS, Debette S, Tuladhar AM, et al. Epidemiology, aetiology, and management of ischaemic stroke in young adults. *Lancet Neurol*. 2018;17:790–801. doi: 10.1016/S1474-4422(18)30233-3
27. George MG, Tong X, Bowman BA. Prevalence of cardiovascular risk factors and strokes in younger adults. *JAMA Neurol*. 2017;74:695–703. doi: 10.1001/jamaneurol.2017.0020
28. Crayton E, Fahey M, Ashworth M, Besser SJ, Weinman J, Wright AJ. Psychological determinants of medication adherence in stroke survivors: a systematic review of observational studies. *Ann Behav Med*. 2017;51:833–845. doi: 10.1007/s12160-017-9906-0
29. Jongstra S, Harrison JK, Quinn TJ, Richard E. Antihypertensive withdrawal for the prevention of cognitive decline. *Cochrane Database Syst Rev*. 2016;11:CD011971. doi: 10.1002/14651858.CD011971.pub2
30. Sprint Mind Investigators for the SPRINT Research Group, Williamson JD, Pajewski NM, Auchus AP, Bryan RN, Chelune G, et al. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. *JAMA*. 2019;321:553–561
31. Cadilhac DA, Ibrahim J, Pearce DC, Ogden KJ, McNeill J, Davis SM, et al; SCOPES Study Group. Multicenter comparison of processes of care between Stroke Units and conventional care wards in Australia. *Stroke*. 2004;35:1035–1040. doi: 10.1161/01.STR.0000125709.17337.5d
32. Cadilhac DA, Andrew NE, Lannin NA, Middleton S, Levi CR, Dewey HM, et al; Australian Stroke Clinical Registry Consortium. Quality of acute care and long-term quality of life and survival: the Australian stroke clinical registry. *Stroke*. 2017;48:1026–1032. doi: 10.1161/STROKEAHA.116.015714
33. Roshanov PS, Fernandes N, Wilczynski JM, Hemens BJ, You JJ, Handler SM, et al. Features of effective computerised clinical decision support systems: meta-regression of 162 randomised trials. *BMJ*. 2013;346:f657. doi: 10.1136/bmj.f657
34. Cadilhac DA, Grimley R, Kilkenny MF, Andrew NE, Lannin NA, Hill K, et al. Multicenter, prospective, controlled, before-and-after, Quality Improvement Study (Stroke123) of acute stroke care. *Stroke*. 2019;50:1525–1530. doi: 10.1161/STROKEAHA.118.023075
35. Stroke Foundation. National Stroke Audit Acute Services– Clinical Audit Report 2013. Available at: www.informme.org.au/-/media/95C36BDF7A4849E8B0E009BDA647ECDD. Accessed September 13, 2019.