ORIGINAL RESEARCH

Using Large-Scale Linkage Data to Evaluate the Effectiveness of a National Educational Program on Antithrombotic Prescribing and Associated Stroke Prevention in Primary Care

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***Background*—**The National Prescribing Service (NPS) MedicineWise Stroke Prevention Program, which was implemented nationally in 2009–2010 in Australia, sought to improve antithrombotic prescribing in stroke prevention using dedicated interventions that target general practitioners. This study evaluated the impact of the NPS MedicineWise Stroke Prevention Program on antithrombotic prescribing and primary stroke hospitalizations.

***Method and Results*—**This population-based time series study used administrative health data linked to 45 and Up Study participants with a high risk of cardiovascular disease (CVD) to assess the possible impact of the NPS MedicineWise program on first-time aspirin prescriptions and primary stroke-related hospitalizations. Time series analysis showed that the NPS MedicineWise program was significantly associated with increased first-time prescribing of aspirin (P=0.03) and decreased hospitalizations for primary ischemic stroke (P=0.03) in the at-risk study population (n=90 023). First-time aspirin prescription was correlated with a reduction in the rate of hospitalization for primary stroke (P=0.02). Following intervention, the number of first-time aspirin prescriptions increased by 19.8% (95% confidence interval, 1.6–38.0), while the number of first-time stroke hospitalizations decreased by 17.3% (95% confidence interval, 1.8–30.0).

***Conclusions*—**Consistent with NPS MedicineWise program messages for the high-risk CVD population, the NPS MedicineWise Stroke Prevention Program (2009) was associated with increased initiation of aspirin and a reduced rate of hospitalization for primary stroke. The findings suggest that the provision of evidence-based multifaceted large-scale educational programs in primary care can be effective in changing prescriber behavior and positively impacting patient health outcomes. **(*J Am Heart Assoc*. 2016;5:e003729 doi: 10.1161/JAHA.116.003729)**

Key Words: antithrombotic • health outcomes • prevention • primary care • stroke

Stroke is the leading cause of disability among adults in Australia. It results in a significant burden on the health system and society.[1,2] Prevention is the key to reducing this burden. Aspirin provides effective ischemic stroke prevention in select patients in both primary and secondary prevention.[3–6] The US Preventive Services Task Force[4] recommends aspirin as the only antithrombotic with sufficient evidence for use in primary prevention in high-risk populations without atrial fibrillation (AF). Despite the availability of clinical guidelines on aspirin use in primary and secondary cardiovascular disease (CVD) prevention, evidence suggests that aspirin use remains suboptimal.[4,7,8] Interviews conducted by National Prescribing Service (NPS) MedicineWise have revealed different attitudes among general practitioners (GPs), primary care physicians, toward the use of aspirin in the primary prevention of CVD and suggest a need to improve prescribing practice. Other studies have found significant gaps between the best available evidence on aspirin use in primary CVD prevention and clinical practice, including insufficient risk assessment and underprescribing of antithrombotic therapy in the primary prevention of stroke.[9,10] These evidences indicate the need for an intervention

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Accompanying Tables S1 and S2 are available at http://jaha.ahajournals.org/content/5/10/e003729/DC1/embed/inline-supplementary-material-1.pdf

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program focusing on aspirin prescription in primary stroke prevention. Practitioner's knowledge, attitude, and behavior are barriers to the adoption of clinical guidelines. To close evidence practice gaps and improve patient outcomes, many intervention programs have been attempted to engage practitioners in behavior change, and the difficulty in achieving substantial impacts have been underlined in their reports.[11–13]

NPS MedicineWise is funded by the Australian government to design, develop, implement, and evaluate national programs to improve the quality use of medicines. It targets areas where medication use may be associated with suboptimal health outcomes or increased costs.[14] In 2009–2010, NPS MedicineWise implemented the multifaceted nationwide Stroke Prevention Program in Australia. The primary care prescribing intervention program combined educational outreach activities, clinical audit, and individualized feedback on prescribing patterns. An emphasis was placed on evidence-based patient risk assessment. The intervention was designed and delivered at national and local levels using evidence-based strategies.[14,15] The aim was to improve antithrombotic prescribing in primary care[16] and improve health outcomes through closure of an identified evidence practice gap.

This study was undertaken to assess the impact of the NPS MedicineWise Stroke Prevention Program on antithrombotic prescribing and prevention of primary stroke hospitalizations across Australia. Although NPS MedicineWise regularly evaluates program impact on prescriber behavior,[17] this is the first time patient outcomes have been evaluated using data linkage between large-scale routinely collected data sets and data from the 45 and Up Study,[18] which is the largest ongoing healthy aging study in Australia. This study evaluates the impact of the Stroke Prevention Program on list of key program outcomes to provide evidence for the effectiveness of this feasible and widely applicable intervention. A positive finding would provide evidence for wider use of this intervention to improve prescribing, address evidence-based practice gaps, and aid in the prevention of stroke in primary care settings.

Methods

The study was a retrospective cohort study using time series analysis based on self-reported survey data linked with routinely collected unit record administrative health data within the study period of July 2004 to October 2011.

NPS MedicineWise Stroke Prevention Program

The program was an intervention to prevent stroke through improved antithrombotic prescribing by GPs. In line with US Preventive Task Force recommendations,[4] one of the key program messages was that aspirin is indicated in primary prevention when cardiovascular risk is high and is the antithrombotic of choice in primary stroke prevention.

An overview of NPS MedicineWise intervention programs is provided elsewhere.[15] The stroke prevention program was multifaceted, commencing in January 2009 with the distribution of *NPS News*. This was followed by a direct mail out to 19 800 GPs and other medical specialists of individualized reports with feedback on their antithrombotic prescribing patterns, together with provision of program materials incorporating the key messages. During this period, a clinical audit was made available to GPs wishing to examine their own practice in detail. During the next 12 months, educational visits were provided to Divisions of General Practice[19] across Australia. The educational visits used academic detailing techniques and facilitated peer group discussions delivered by a workforce of specifically trained health professional facilitators. Half of the facilitators were pharmacists and the remainder were doctors, nurses, and other health professionals, employed by the Divisions of General Practice.[19] Academic detailing entailed a one-on-one peer-to-peer interaction of ≈30 minutes at the GP's place of practice. The detailing applied behavior change principles[15] to provide education and information in an objective, service-based approach that directly related topic material to the clinician's clinical practice. Case studies were used to facilitate problem-based learning for individuals and groups. Opinion leaders were used to deliver and endorse key messages when possible. This intervention was offered to all registered GPs (19 800) in Australia. Nationally, over 8500 GPs participated in at least one active intervention of academic detailing, interactive workshop, group discussion, clinical audit process, or case study review. In New South Wales (NSW), the state under study, there were 2688 participating GPs.

Data Sources and Linkage

The study used both self-reported and routinely collected administrative data linked at the person level from the 45 and Up Study.[18] These data have been used extensively for health services and pharmacoepidemiological studies.[20,21]

The Sax Institute's 45 and Up Study is drawn from the population of the state of NSW, Australia. A total of 267 153 participants joined the study by completing a baseline questionnaire (between January 2006 and December 2009) and giving signed consent for follow-up and linkage of their information to routine health databases. Information regarding the recruitment of the cohort is described elsewhere.[15] The data sources linked and utilized in this study included: (1) the 45 and Up Study baseline questionnaire data; (2) Medicare Benefits Schedule (MBS) claims subsidized by Australian government (2004–2011); (3) Pharmaceutical Benefits Scheme (PBS) subsidized claims (2006–2011); (4)

NSW Admitted Patient Data Collection (APDC) (2000–2011); and (5) NSW Emergency Department Data Collection (EDDC) (2006–2011). The MBS contained data on utilization of medical services, PBS contains prescribing data on subsidized prescriptions, the APDC is a census of all NSW hospital admissions using *International Classification of Diseases, 10th Revision, Australian Modification* (*ICD-10-AM*) coding, and the EDDC data set records emergency department presentation details in NSW.

The linkage of MBS and PBS data was conducted by the Commonwealth Department of Human Services (DHS), and remaining data sets by the NSW Centre for Health Record Linkage.[22]

Institutional ethics committee approval was obtained from the University of New South Wales Human Research Ethics Committee and the NSW Population and Health Services Research Ethics Committee.

Study Population

Patients at high risk for CVD were the main population target for the program and the focus of this study. The high-risk population was identified using both self-report and administrative health data sets. A clinical steering committee, including a cardiologist and a neurologist, determined the inclusion and exclusion criteria outlined in Table 1. MBS item codes for medical services and PBS item codes for prescriptions that were deemed pathognomonic of a diagnosis of ischemic heart disease (IHD) are listed in Table S1. CVD risk assessment based on 45 and Up Study self-report data is summarized in Table S2, with reference to the Australian cardiovascular risk charts found in the Guidelines for the Management of Absolute Cardiovascular Disease Risk.[23]

The study focused on aspirin use and first-time stroke prevention. Participants with a history of ischemic stroke (hospital diagnosis or self-report) at population entry point were excluded from the study population. Participants with atrial fibrillation (hospital diagnosis or pathognomonic PBS records) were also excluded as anticoagulant medication rather than aspirin is mostly required in this population.[6,7]

The study population was conceptualized and implemented as a dynamic population[24,25] rather than as a cohort. In a dynamic population study, participants enter the study population at the date when they first met the inclusion criteria and exit the population on the date of an outcome event (if first-time events are being enumerated), at the date of death, or at the end of the study. Both entry and exit dates are variable with respect to calendar time.

Outcome Measures

The study evaluated the impact of the NPS Stroke Prevention Program message that aspirin is the antithrombotic of choice in primary stroke prevention in patients with high cardiovascular risk. For the analysis, the population was "at risk for aspirin prescription." The measurable rate of aspirin initiation was used to assess program impact on prescribing in the study population.

We used changes in the rate of first-time aspirin prescriptions as a proxy for changes in aspirin-prescribing behavior in

Table 1. Derivation of the High-Risk CVD Population

Inclusion Criteria	Data Source	Note
Heart disease and/or prior CVD events	APDC*	A hospital separation with a primary or secondary reason for admission, of IHD or TIA, or any mention of a procedure that was deemed to be pathognomonic of IHD*
	MBS	MBS item codes that were deemed pathognomonic of a diagnosis of IHD,* including transluminal coronary angioplasty, percutaneous transluminal rotational atherectomy, coronary artery bypass, open coronary endarterectomy, reconstruction of occluded coronary artery graft, and myocardial infarct study, are listed in Table S1
	PBS	PBS item codes for a prescription that were deemed pathognomonic of IHD,* including glyceryl trinitrate, isosorbide dinitrate, isosorbide mononitrate, nicorandil, perhexiline, and maleate, are listed in Table S1
	45 and Up Study	Self-reported diagnosis or treatment for heart attack/angina; operation for heart disease and/or TIA
Were judged to be at high risk for a CVD event based on CVD risk assessment	45 and Up Study	Individuals were determined to be at high risk for CVD (Table S2) based on their age, sex, status of diabetes, smoking, hypertension, and high cholesterol, from 45 and Up baseline survey data, with reference to the Australian cardiovascular risk charts found in the Guidelines for the Management of Absolute Cardiovascular Disease Risk[23†]

APDC indicates NSW Admitted Patient Data Collection; CVD, cardiovascular disease; IHD, ischemic heart disease; MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme; TIA, transient ischemic attack.

*The clinical steering group reviewed and approved the *International Classification of Diseases, 10th Revision*, MBS, and PBS item codes that were deemed pathognomonic of disease.

†Because of the absence of a measure of blood pressure and ratio of total cholesterol and high-density lipoprotein cholesterol, the CVD risk calculator could not be applied directly for the CVD risk assessment.

primary care. A washout period of 6 months from the start of the PBS data was applied to rule out those with prior prescriptions.

Aspirin cost is below the co-payment threshold for the general population but is recorded when it is prescribed to concessional card holders who receive government subsidy of medication prescriptions including aspirin. The subsidized claims are fully captured in PBS data (the best-available national prescription data) and this data was used to determine aspirin prescribing, which has been a common practice when using Australian PBS data for pharmocoepidemiological studies.[26,27]

We calculated the monthly rate of first-time aspirin prescriptions based on the number of first-time aspirin PBS records (the numerator) divided by the number of participants at risk for aspirin prescription (the denominator) per month. Participants with first-time PBS records for aspirin were removed from the at-risk population on the day following the date of the PBS record since they were no longer at risk for a first-time prescription for aspirin.

Ischemic stroke was identified in primary and secondary diagnosis fields of the APDC data, taking into account interhospital transfers to prevent overcounting. We calculated the monthly rate of first-time hospitalization due to stroke based on the number of first stroke hospitalizations (the numerator) over the number of participants in the study population at risk for stroke who had not previously experienced stroke (the denominator). Once a hospitalization for stroke occurred, participants were excluded from the denominator for the remainder of the study period.

Statistical Analysis

Statistical analyses were based on the aggregated monthly rate of outcome measures. As the age structure of the at-risk population (denominator) at each month is different, we applied the direct age standardization method[28] to the monthly rate of outcome measures to adjust for differences in the age structure of the study population over time. The age structure of population at the first month of the study period was used as the standard population age structure. The evaluation of the effect of the NPS MedicineWise Stroke Prevention Program on hospitalization for stroke contained three steps.

We applied a time series intervention model[29] to examine the association between the timing of the intervention and the rate of first-time prescriptions for aspirin and to determine whether there was a change in the prescription rate, or trend of prescription rate, following the intervention. The model incorporated an intervention term (PropCumGP) to represent the monthly cumulative number of GPs who had actively participated in the stroke prevention program as a proportion of all GPs in NSW at the time. An interaction term between time (underlying trend) and the cumulative count of GPs participating (Trend×PropCumGP) was adopted when it improved the model fit as determined by residual analysis. The time series intervention model is a special case of the autoregressive integrated moving average (ARIMA) approach.[30] PROC ARIMA[31] was used to fit the general linear regression model assuming the underlying trend is linear, in conjunction with an autoregressive moving average (ARMA) model for the error process incorporating seasonality and autocorrelation. By examining serial autocorrelation in residual series using autocorrelation function (ACF) and partial autocorrelation function (PACF), a seasonal ARMA model SARMA(1,0)X$(0,1)_{12}$ was fitted to the residual series.

Similarly, we used a time series model to evaluate the association between the stroke prevention program and the hospitalization rate for primary stroke. As the monthly stroke hospitalization data are event count time series in nature, and no serial dependence in the time series counts was detected based on ACF and PACF, Poisson regression with interrupted time series analysis was used to estimate the monotonic change of stroke hospitalization in the postintervention period. The PROC GENMOD procedure was used for model fitting.

Time series regression was used to examine the correlation between the two time series, with hospitalization for stroke as the response series and initiation of aspirin as the input series. Lagging of the input series was applied reflecting the time delay from aspirin initiation to stroke prevention. A 2-month lag period was found to achieve the best model fit based on Akaike information criterion.

All the analyses were undertaken in SAS 9.2.[31] A two-sided P value of ≤ 0.05 was considered statistically significant.

Results

Overall, 90 023 participants from the 45 and Up Study were identified as having IHD, or transient ischemic attack, or were at high risk for CVD, without a history of ischemic stroke at the study entry point. The average age of the high-risk CVD population at study entry was 65 years, with 64% being male. Sixty-three percent were concession card holders.

A total of 2457 hospitalizations due to ischemic stroke were observed in the evaluable population during the study period, of which 1659 episodes were first-time strokes.

Trends in Prescribing

The age-standardized monthly rate (cases per 100 000 person months) of first-time prescriptions for aspirin is shown in Figure 1, along with the cumulative counts of GP active participation (scale on the right). GP participation started in January 2009 and gradually reached more than 2500 GPs in NSW (34%) over the following 12 months.

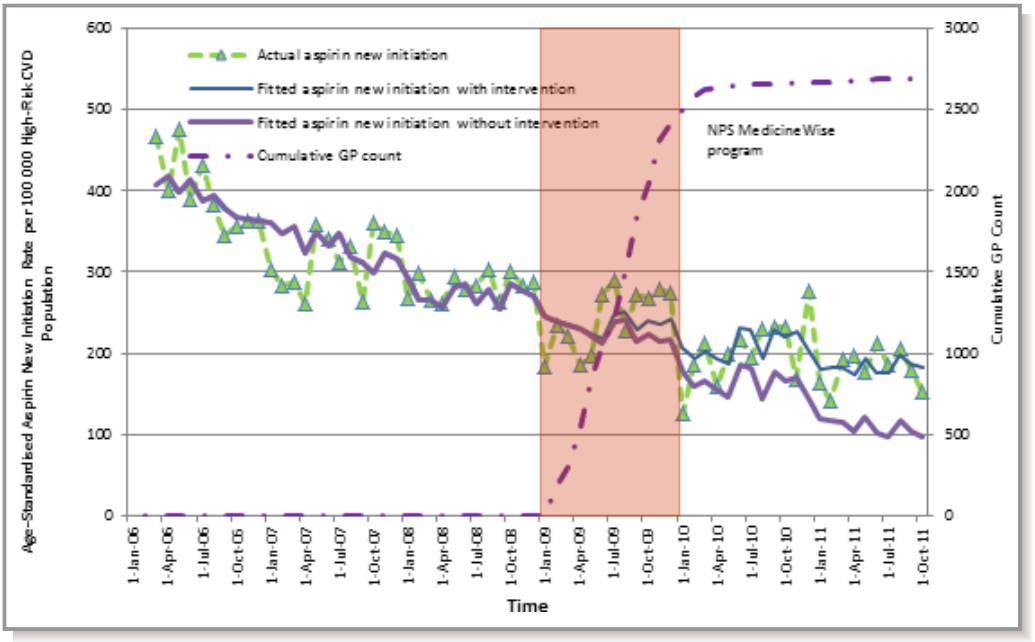

Figure 1. Age-standardized rate of first-time prescriptions for aspirin and model-based predictions with and without intervention (per 100 000 high-risk cardiovascular disease [CVD] population). GP indicates general practitioner; NPS, National Prescribing Service.

The model-based monthly rates estimate of new-initiation aspirin with and without intervention are also presented in Figure 1. There are 33 monthly time points prior to intervention and 32 time points after the program within the analysis period of January 2006 to October 2011. The fitted model provides a predicted comparison of how the model-fitted aspirin initiation would be expected to continue with and without the NPS MedicineWise Stroke Prevention Program.

Findings summarized in Table 2 demonstrated a significant association between the NPS MedicineWise program and an increased rate of first-time aspirin prescriptions (intervention coefficient=2.59; P=0.03), with a decreasing baseline trend (trend coefficient=−4.73; P<0.0001). The impact of the intervention can be calculated for each month postintervention by subtracting the intervention model terms without the intervention from the actual data. The number of first-time aspirin prescriptions increased by 19.8% (95% confidence interval, 1.6–38.0) over the postintervention study period (33 months). Compared with before intervention, the average aspirin initiation increased by 502 cases per 100 000 person years after the intervention in the high-risk CVD population.

Trend in First-Time Hospitalization for Stroke

Figure 2 displays the age-standardized monthly rate (cases per 100 000 person months) of first-time hospitalization for ischemic stroke. There are 54 monthly time points prior to intervention and 32 time points after intervention within the analysis period of July 2004 to October 2011. Also displayed are the modeled predictions with and without the intervention to provide a comparison based on how the model-fitted hospitalization rate would be expected to continue with and without the NPS MedicineWise Stroke Prevention Program.

Table 2. Parameter Estimates From Time Series Models

	Parameter Estimate	Standard Error	*P* Value
Time series intervention model			
Monthly rate aspirin initiation			
Baseline trend	−4.727	0.683	<0.0001
Interaction term of PropCumGP×Trend change postintervention	2.594*	1.218	0.03
Monthly rate stroke hospitalization			
Baseline trend	0.010	0.002	<0.0001
Interaction term of PropCumGP×Trend change postintervention	−0.096*	0.004	0.03
Time series regression model			
Monthly rate stroke hospitalization			
Aspirin initiation (2-month lag)	−0.013	0.006	0.02

*The intervention effect was calculated based on the intervention term estimates with the proportion of general practitioner (GP) participation and time trend at each month since program start. The average effect over the postintervention study period (33 months) was then obtained. On average, the number of first-time aspirin prescriptions increased by 19.8% (95% confidence interval, 1.6–38.0), and the first-time hospitalization for stroke decreased by 17.3% (95% confidence interval, 1.8–30.0), when compared with the expected underlying trend without intervention.

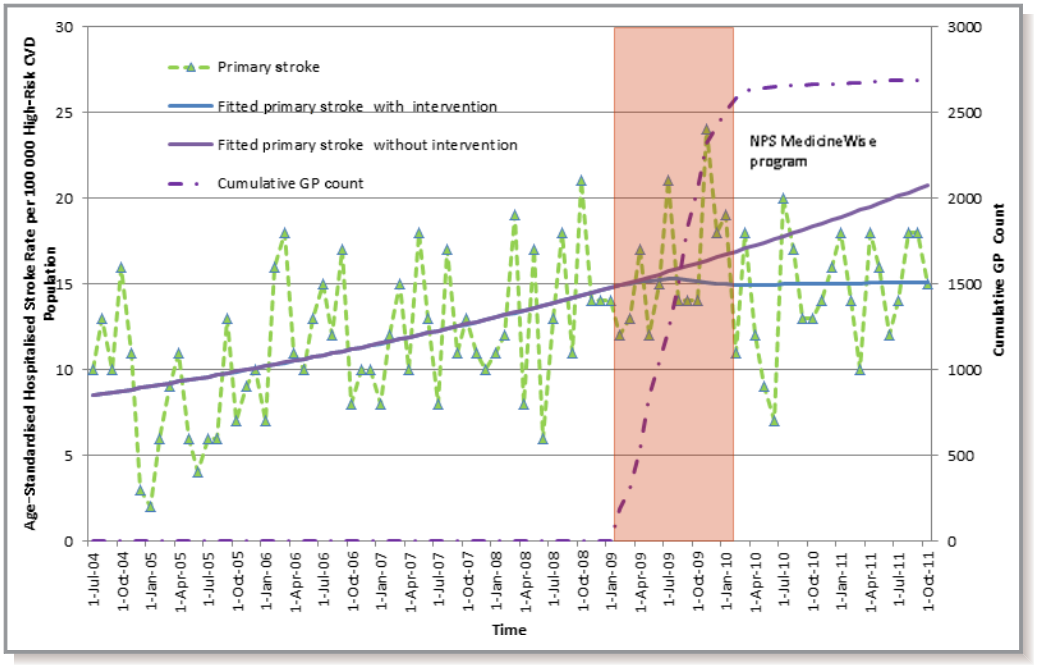

Figure 2. Age-standardized rate of first-time hospitalization for stroke per 100 000 high-risk cardiovascular disease (CVD) population, including model-based predictions with and without intervention. GP indicates general practitioner; NPS, National Prescribing Service.

Analysis (Table 2 and Figure 2) confirmed that there was a significant decrease in the rate of first-time hospitalization due to stroke associated with the introduction of the NPS MedicineWise program in the high-risk CVD population (intervention coefficient=−0.01, P=0.03), with an increasing baseline trend (trend coefficient=0.1; P<0.0001). The number of first-time hospitalizations due to stroke decreased by 17.3% (95% confidence interval, 1.8–30.0) in the postintervention period. Compared with rates before the intervention, the average stroke hospitalization rate decreased by 31 cases per 100 000 person years after the intervention in the high-risk CVD population.

Correlation Between Prescribing and Hospitalization

The time series regression analysis (Table 2) on the correlation between first-time prescription for aspirin and first-time hospitalization for stroke revealed that the rate of aspirin initiation (2-month lag) was significantly associated with a decreased rate of hospitalization for stroke (correlation coefficient=−0.013, P=0.02).

Discussion

The NPS MedicineWise Stroke Prevention Program aimed to reduce stroke occurrence through improved antithrombotic prescribing in primary care. An earlier study demonstrated the program's significant impact on appropriate antithrombotic use.[17] The current study evaluates both the direct (the impact on aspirin prescribing) and indirect (the change in first-time stroke hospitalization rates) effects and the correlation between the two in a population with high cardiovascular risk.

Consistent with the core message and goals of the NPS MedicineWise program, we observed an increase of 19.8% in first-time prescribing of aspirin, with an associated decrease of 17.3% in stroke hospitalization for persons aged 45 years and older at high CVD risk. Additionally, the time series plots indicate that the intervention program had a sustainable effect on changing prescribing behavior and patient outcome. New aspirin initiation had been decreasing in the preintervention years, slightly rose through the intervention period, and was stable postintervention. Similarly, the hospitalization rate of stroke had been increasing in the preintervention years and was seen to decrease during the intervention year and remain stable in the postintervention years.

This is an observational study and therefore causality cannot be confirmed. However, a review of the clinical practice guidelines, the literature, and a discussion with the clinical expert steering committee failed to identify other changes in practice or policy to account for an observed reduction in the rate of first-time stroke hospitalization. It appears that the improved health outcomes captured in this study are attributable to the NPS MedicineWise primary care intervention. The observed reduction in first-time

stroke, with an expected reduction in the high individual, social, and economic burden of fatal and disabling stroke, supports the cost-effectiveness of this type of primary care intervention.

A high-risk CVD population was the target population of the NPS MedicineWise Stroke Prevention Program. Our use of large-scale linked records at the individual level allowed the retrospective derivation of a specific study population with high cardiovascular risk and with no history of stroke. The use of a dynamic population, rather than a conventional fixed cohort, reduced the effect of confounding associated with the length of time since meeting the entry criteria or the natural history of the illness. The advantages of enumerating a clinical population of this type to serve as the domain for the evaluation research is that both internal and external validity were enhanced, increasing confidence that the observed effects can be attributed to the intervention under investigation.[24,25]

Acute stroke care outcomes in Australia have improved in recent years through improved access to stroke units,[32] and there was a concern that reductions in the rate of hospitalization for recurrent stroke could reflect the improved secondary prevention after first-time stroke. To remove this potential confounding effect on stroke rate estimates associated with the NPS MedicineWise intervention, the analysis was restricted to patients with first-time stroke in a stroke-naive population.

Study Limitations

There was a potential limitation in ascertainment of aspirin prescribing. As the study method could not capture the use of over-the-counter aspirin, although measurement of prescribed aspirin is expected to be indicative, the analysis was limited to first-time aspirin prescribing within 63% of the cohort who were concessional card holders. This is an effective proxy that has previously been used to measure prescribing in pharmocoepidemiological studies[27] using Australian PBS data.

A further potential limitation of the study is that individual GP participation in the educational program could not be identified; therefore, a comparable group with no exposure to active intervention was difficult to establish and a measure of the differential contribution of active versus passive participation was not feasible.

Finally, the 45 and Up Study cohort is a sample of the NSW state, which is derived from the general population; however, the modest response rate (18%) means that the cohort may not be directly representative of the general population.[18]

Improving prescribing behavior requires a coherent, integrated approach.[33] Many educational and support strategies have been investigated to close evidence practice gaps and their results have highlighted the difficulty in achieving substantial impacts with such programs.[11–13,33–35] NPS MedicineWise's use of educational outreach and individualized feedback coupled with its access to large numbers of GPs appears effective in improving the quality of prescribing and health outcomes. The results support the further use of this methodology, which may be widely applicable, where primary care interventions are needed to improve both prescribing behavior and health outcomes. The NPS MedicineWise model, a government-funded independent public company operating at "arm's length" with a highly trained health professional workforce for implementation, may have enhanced program credibility and effectiveness and may be adaptable for wider use.

Conclusions

This study demonstrates the effectiveness of a large-scale multifaceted educational intervention to improve prescribing practices for stroke prevention in primary care. The NPS MedicineWise Stroke Prevention Program (2009) was associated with an intended increase in aspirin prescribing and a reduced rate of hospitalization for patients with first-time stroke in a target population with high cardiovascular risk. The findings suggest that the provision of evidence-based multifaceted educational programs in primary care can be effective in changing prescriber behavior and positively impacting patient health outcomes.

Based on health outcome evaluation findings, cost-effectiveness analysis can be further carried out to evaluate the financial impact of the stroke prevention program on the healthcare system and society. Meanwhile, analyses of soon to be available prescriber data may allow identification of prescribers who are more likely to change behavior, permitting more precisely targeted interventions.

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NPS MedicineWise approved this manuscript before submission.

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SUPPLEMENTAL MATERIAL

Table S1. Disease mapping with ICD10-AM, ACHI, MBS and PBS codes

Inclusion	Code	CodeSet	Comments
Hospitalisations			
AF in diagnostic field 1 or 2	I48	ICD-10-AM	Atrial fibrillation & flutter
Ischaemic Heart Disease in diagnostic field 1 or 2	I20	ICD-10-AM	Angina pectoris
	I21		AMI
	I22		Subsequent MI
	I23		Complications following MI
	I24		Other acute ischaemic heart diseases
	I25		Chronic ischaemic heart diseases
Procedures pathognomic of IHD in procedure code 1 or 2	35304.xx - 35305.xx 38300-xx, 38303-xx	ACHI (7th ED)	Transluminal coronary angioplasty
	35310.xx, 38306-xx,		Transluminal coronary angioplasty with stenting
	38497-xx, 38503-xx, 38500-xx		Coronary artery bypass graft
	38637-00		Re-operation for reconstruction of occluded coronary artery graft
	38309-00, 38312-xx, 38315-00, 38318-xx		Percutanoeus transluminal rotational atherectomy
	38505-00		Open coronary endarterectomy

	90201-xx		Coronary artery bypass, using other material graft, not elsewhere classified
	90221-00		Direct intracoronary artery injection or infusion of a thrombolytic agent
	61310-00		Avid imaging study for myocardial infarct
TIA (cerebrovascular disease) in diagnostic field 1 or 2	G45	ICD-10-AM	Transient cerebral ischaemic attacks and related syndromes
	I65		Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction
	I66		Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction
Procedures pathognomic of TIA (cerebrovascular disease) in procedure code 1 or 2			
Ischaemic stroke (cerebrovascular disease) in diagnostic field 1 or 2	I63x	ICD-10-AM	Cerebral infarction
	I64		Stroke not specified as haemorrhage or infarction
	34100-00		Exploration of the carotid artery*
	33500-00		Carotid endarterectomy*
	33800-00		Embolectomy or thrombectomy of carotid artery
Other cardiovascular disease in diagnostic field 1 or 2	I65.x	ICD-10-AM	Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction
	I66.x		Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction
	I67.2		Cerebral atherosclerosis

MBS			
Procedures pathognomic of IHD	38300, 38303,		Transluminal coronary angioplasty
	38306,		Transluminal coronary angioplasty with stenting
	38309, 38312, 38315, 38318		Percutaneous transluminal rotational atherectomy of coronary artery
	38496, 38497, 38498, 38500, 38501, 38503, 38504		Coronary artery bypass
	38637		Re-operation for reconstruction of occluded coronary artery graft
	38309, 38312, 38315, 38318		Percutanoeus transluminal rotational atherectomy
	38505		Open coronary endarterectomy
	61310		Myocardial infarct study
Procedures pathognomic of ischaemic stroke	34100		Exploration of the carotid artery
	33500		Carotid endarterectomy*
	33800		EMBOLUS, removal of, from artery of neck
PBS			
Drugs pathognomic of IHD	1459T, 8171C, 8027L, 1515R, 8010N, 8028M, 1516T, 8011P, 8119H, 8026K, 3475X	PBS item number	Glyceryl trinitrate
	2587E, 2588F		Isosorbide dinitrate
	1558B, 8273K		Isosorbide mononitride
	8228C, 8229D		Nicorandil
	1822X		Perhexiline Maleate

Table S2. High risk CVD assessment using 45 and Up Study self-report data

Diabetes	Sex	Age	Smoker*	high BP	high Cholesterol	Flag_HCVD_risk**
Y	F/M	age>=60	Y/N	Y/N	Y/N	1
Y		age (55,59)	N	Y	Y	1
Y		age (55,59)	Y	Y/N	Y	1
Y		age (55,59)	Y	Y	Y/N	1
Y		age (45,54)	N	Y/N	Y/N	0
Y		age (45,54)	Y	Y	Y/N	1
Y		age (45,54)	Y	Y/N	Y	1
N	F	age >=55	Y	Y	Y/N	1
N		age >=55	Y	Y/N	Y	1
N		age (45,54)	Y	Y/N	Y/N	0
N		age >=65	N	Y	Y	1
N	M	age>=65	Y	Y/N	Y/N	1
N		age (55,64)	Y	Y/N	Y/N	1
N		age (55,64)	Y	Y/N	Y/N	1
N		age (45,54)	Y	Y	Y	1
N		age>=55	N	Y	Y/N	1

*smoker: ever smoke or current smoker
** flag of '1' indicates high CVD risk

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