<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Implementation of secondary stroke prevention protocol for ischaemic stroke patients in primary care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author(s)</strong></td>
<td>Choi, YK; Han, JH; Li, R; Kung, K; Lam, A</td>
</tr>
<tr>
<td><strong>Citation</strong></td>
<td>Hong Kong Medical Journal, 2015, v. 21, p. 136-142</td>
</tr>
<tr>
<td><strong>Issued Date</strong></td>
<td>2015</td>
</tr>
<tr>
<td><strong>URL</strong></td>
<td><a href="http://hdl.handle.net/10722/217136">http://hdl.handle.net/10722/217136</a></td>
</tr>
<tr>
<td><strong>Rights</strong></td>
<td>This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.</td>
</tr>
</tbody>
</table>
ABSTRACT

Objective: To investigate the effectiveness of a secondary stroke prevention protocol in the general out-patient clinic.

Design: Cohort study with pre- and post-intervention comparisons.

Setting: Two general out-patient clinics in Hong Kong.

Patients: Ischaemic stroke patients who had long-term follow-up in two clinics were recruited. The patients of one clinic received the intervention (intervention group) and the patients of the second clinic did not receive the intervention (control group). The recruitment period lasted for 6 months from 1 September 2008 to 28 February 2009. The pre-intervention phase data collection started within this 6-month period. The protocol implementation started at the intervention clinic on 1 April 2009. The post-intervention phase data collection started 9 months after the protocol implementation, and ran for 6 months from 1 January 2010 to 30 June 2010.

Main outcome measures: Clinical data before and after the intervention, including blood pressure, glycated haemoglobin level, low-density lipoprotein level and prescription pattern, were compared between the two groups to see whether there was enhancement of secondary stroke management.

Results: A total of 328 patients were recruited into the intervention group and 249 into the control group; data of 256 and 210 patients from these groups were analysed, respectively. After intervention, there were significant reductions in mean (± standard deviation) systolic blood pressure (135.2 ± 17.5 mm Hg to 127.7 ± 12.2 mm Hg), glycated haemoglobin level (7.2 ± 1.0% to 6.5 ± 0.8%), and low-density lipoprotein level (3.4 ± 0.8 mmol/L to 2.8 ± 1.3 mmol/L) in the intervention group (all P<0.01). There were no significant reductions in mean systolic blood pressure, glycated haemoglobin level, or low-density lipoprotein level in the control group. There was a significant increase in statin use (P<0.01) in both clinics.

Conclusion: Through implementation of a clinic protocol, the standard of care of secondary stroke prevention for ischaemic stroke patients could be improved in a general out-patient clinic.
significantly higher in patients with stroke recurrence than in those without.\(^{4,5}\) Prevention of recurrent stroke offers great potential for reducing the burden of this disease.

Over 80% of all strokes are ischaemic stroke. There are effective strategies for secondary prevention of ischaemic stroke, which are summarised as follows:\(^5\):

1. Modification of lifestyle risk factors (smoking, alcohol consumption, obesity, physical inactivity).
3. Antiplatelet therapy for non-cardioembolic ischaemic stroke.
4. Anticoagulation for cardioembolic stroke.
5. Intervention for symptomatic carotid stenosis.

As stroke patients need lifelong monitoring and control of risk factors, family physicians play the most important role in providing secondary stroke prevention care. However, despite the availability of evidence-based guidelines, studies show that adherence to these preventive strategies by physicians is poor.\(^{7-11}\) Local Hong Kong data about secondary stroke prevention in primary care are largely lacking. This study aimed to review the clinical effectiveness of a secondary stroke prevention programme in a general out-patient clinic (GOPC).

Methods
This was a cohort study of pre- and post-intervention comparison between patients receiving or not receiving the intervention to ascertain the effect of a secondary stroke prevention programme on clinical outcomes.

Clinic setting
The Lek Yuen GOPC was selected as the intervention site where the secondary stroke prevention programme was implemented. Another clinic, the Ma On Shan GOPC, was selected as the control site, where usual care was provided. Both clinics are large public primary care clinics under the management of the Department of Family Medicine of the New Territories East Cluster of the Hospital Authority. Both clinics are accredited Family Medicine Training Centres with similar service throughput annually, covering a population of around 600,000 and providing approximately 30,000 attendances monthly.

Most of the stroke patients in the clinics are referred from the public hospitals. The patients usually have a history of minor stroke with good functional recovery and are clinically stable.

Clinic protocol development and implementation
A protocol of secondary stroke prevention (Box) was developed with reference to evidence-based guidelines (mainly according to the American Heart Association and American Stroke Association stroke guidelines).\(^{12-14}\)

**Box.** Clinic protocol and treatment goals of secondary stroke prevention for ischaemic stroke patients

1. Record smoking and alcohol status, with appropriate management
2. Record amount of exercise (>30-minute moderate activity), give advice
3. Record BMI: aim for BMI <23 kg/m\(^2\), with management for obesity
4. Check blood pressure at each visit
   - aim for <140/90 mm Hg for patients without diabetes
   - aim for <130/80 mm Hg for patients with diabetes
   - be aware of symptomatic hypotension
   - less tight control in the presence of carotid stenosis
5. Annual blood test for fasting blood glucose and lipids
6. Patients with diabetes: aim for normoglycaemia, \(\text{HbA}_1c\) <7%
7. Cholesterol: aim for LDL <1.9 mmol/L
   - recheck lipids and liver function test after initiation of a statin
8. Antithrombotic for patients with ischaemic stroke unless contra-indicated, options:
   - aspirin
   - aspirin + extended-release dipyridamole
   - clopidogrel
9. Warfarin for patients with atrial fibrillation unless contra-indicated

Abbreviations: BMI = body mass index; HbA\(_1c\) = glycated haemoglobin; LDL = low-density lipoprotein
Study design
The target population of the study was all the ischaemic stroke patients with long-term follow-up in the two clinics. The recruitment period lasted for 6 months from 1 September 2008 to 28 February 2009. As the usual follow-up interval of long-term patients is about 3 to 4 months, the 6-month recruitment period included all stroke patients who have regular follow-up. The pre-intervention phase data collection started within this 6-month period. The protocol implementation started at the intervention clinic on 1 April 2009. The post-intervention phase data collection started 9 months after the protocol implementation, that is, for 6 months from 1 January 2010 to 30 June 2010.

Sampling
The clinical data were collected by reviewing the medical records of all patients assigned with the International Classification of Primary Care coding of K90 (stroke/cerebrovascular accident) or K91 (cerebrovascular disease). Only those patients diagnosed with ischaemic stroke and who had at least two consecutive follow-up visits within the recruitment period were included. Patients who had a history of haemorrhagic stroke were excluded. In order to exclude patients with sporadic follow-up, only those patients with two consecutive follow-up visits in the post-intervention phase were regarded as eligible for data collection. Those patients without two consecutive follow-up visits in the post-intervention phase were classified as dropouts.

Protocol implementation
One month before initiation of the protocol, two 1-hour training sessions were arranged for medical officers and nurses in the intervention clinic. During the training sessions, the treatment goals for secondary ischaemic stroke prevention and the relevant clinical evidence were presented. The workflow and applicability of the protocol were also discussed. Medical officers were required to have good documentation of all the lifestyle and cardiovascular risk factors of the ischaemic stroke patients and provide care according to the protocol. Nurses were trained to be familiar with the treatment goals and provide patient education and lifestyle modification interventions in line with the doctors’ referrals. Allied health services such as a dietitian, smoking cessation clinic, diabetes complication screening programme, and patient empowerment programmes for diabetic and hypertensive patients were available in both the intervention and control clinics. Doctors in the intervention clinic were encouraged to refer appropriate patients to these services. There was no additional consultation time allocated to these patients. In order to monitor progress, the electronic consultation notes were reviewed monthly for each patient to assess compliance with the protocol. If suboptimal care was noted, an electronic reminder with appropriate management advice was issued to the patient’s electronic medical record. The consulting doctor would then be able to provide the appropriate management at the next follow-up. Throughout the protocol implementation period, interim clinic meetings were held quarterly to present the data for protocol compliance with the medical and nursing staff of the intervention clinic.

In the control clinic, no specific protocol was applied. Medication prescription and adjustment was based solely on the physicians’ discretion. The drug formulary was the same in both clinics. Statins were introduced to both clinic formularies in July 2009. There were no training sessions for doctors and nursing staff in the control clinic, and no electronic reminders or interim meetings for progress monitoring.

Data collection
Baseline characteristics on sex, age, chronic illness status, chronic drug use, laboratory results, and blood pressure (BP) values were extracted from the Clinical Data Analysis and Reporting System. The latest laboratory results and BP values within the data collection period were taken as the study data. Individual case records were also reviewed for the following lifestyle parameters: smoking status, alcohol consumption, body mass index (BMI), and exercise and diet history.

Statistical analysis
All statistical analysis was performed using the Statistical Package for the Social Sciences (Windows version 20.0; SPSS Inc, Chicago [IL], US). Continuous variables were expressed as mean and standard deviation. Baseline comparisons were made with the Student’s t test or the Chi squared test as appropriate. The mean BP glycated haemoglobin (HbA1c) level, and low-density lipoprotein (LDL) level before and after intervention were compared by paired-samples t test in both the intervention and control clinics.

Results
In the intervention clinic, 328 patients were recruited to the intervention group and 72 dropped out. In the control clinic, 249 were recruited to the control group and 39 dropped out. The reasons for dropping out are shown in Table 1. More patients in the intervention group than in the control group dropped out due to restroke (9 vs 2, respectively) and death (22 vs 11, respectively), but these were not statistically significant due to the small number of
patients. In both the intervention and control groups, most of the patients who died had no medication changes during the intervention period (Table 1).

A total of 256 patients in the intervention group and 210 in the control group were recruited for data analysis. At baseline, there were no significant differences in the demographic and cardiovascular risk factor profiles between the two groups, except that patients in the intervention group had a higher mean LDL level and a lower mean diastolic BP (Table 2).

After the intervention period, significant improvements in systolic BP, HbA1c and LDL levels were observed in the intervention group (Table 3). There were significant improvements in all lifestyle modification parameters (alcohol and smoking status, obtaining exercise and diet history, and BMI measurement) in the intervention group (P<0.01), and the control group had improvements in smoking status (P<0.01) and BMI measurement (P<0.05) (Table 3).

There was no significant increase in the number of antihypertensive drugs prescribed in either group (Table 4). Approximately 96% of patients were taking an antiplatelet after the intervention period in both clinics (Table 4) and the antiplatelet was always aspirin. The proportion of patients prescribed statins increased significantly in both groups since the introduction of simvastatin to the GOPC formulary in 2009. However, the overall proportion of statin use was still below 50%. Statins were less frequently prescribed to patients older than 80 years (Table 5).

Statins were stopped for 1.6% of patients in the intervention group and 4.3% in the control group (Table 4). Statins were discontinued because of dyspepsia for all patients in the intervention group. The reasons for stopping statins for the control group were dyspepsia, myalgia, mild liver function derangement, hypotension, hypoglycaemia, and drug-induced hepatitis. Only two patients in the control group required emergency admission for hypoglycaemia during the intervention period. There was no restroke in the intervention group.
and four restrokes in the control group during the intervention period.

**Discussion**

This study showed that the implementation of a secondary stroke prevention programme in GOPCs could improve control of cardiovascular risk factors, including BP, HbA1c, and LDL levels among ischaemic stroke patients. We observed an improvement of BP control in the intervention group, although there was no significant increase in the number of antihypertensives used. However, since simvastatin was introduced into the GOPC drug formulary in 2009, the use of statins increased in both the control and intervention clinics, although the effect of LDL reduction was only observed in the intervention group. This result implies that the improvement in outcome for this group is due to more than just the effects of medications. Lifestyle modifications may provide additional benefits.

Although the BP and HbA1c level in the intervention group were comparable with recent recommendations (BP <140/90 mm Hg for patients without diabetes; BP <130/80 mm Hg and HbA1c level of <7% for patients with diabetes), the mean LDL levels remained well above the recommended target of 1.9 mmol/L. Only about half of the patients were taking statins. There is a suggestion that doctors may not prescribe or maximise statin therapy because treatment may be considered futile, especially among older people whose life expectancy is limited.15 This trend was observed in both the control and intervention sites in this study (Table 4). The percentage of patients taking statins was relatively low in this study as some doctors may have

---

**TABLE 3. Changes in clinical parameters and lifestyle modifications before and after the intervention**

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Intervention group (n=256)*</th>
<th>Control group (n=210)*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td>Post-intervention</td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>135.2 ± 17.5</td>
<td>127.7 ± 12.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>70.4 ± 9.7</td>
<td>68.1 ± 9.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.2 ± 1.0</td>
<td>6.5 ± 0.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>3.4 ± 0.8</td>
<td>2.8 ± 1.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>-</td>
<td>24.0 ± 3.6</td>
<td>-</td>
</tr>
</tbody>
</table>

**Alcohol consumption**

| Unknown | 179 (69.9) | 16 (6.3) | <0.01 | 165 (78.6) | 160 (76.2) | 0.85 |
| Non-drinker | 62 (24.2) | 225 (87.9) | 35 (16.7) | 40 (19.0) | |
| Current drinker | 3 (1.2) | 0 | 2 (1.0) | 1 (0.5) | |
| Ex-drinker | 12 (4.7) | 15 (5.9) | 8 (3.8) | 9 (4.3) | |

**Smoking status**

| Unknown | 111 (43.4) | 1 (0.4) | <0.01 | 59 (28.1) | 19 (9.0) | <0.01 |
| Non-smoker | 84 (32.8) | 187 (73.0) | 83 (39.5) | 117 (55.7) | |
| Current smoker | 25 (9.8) | 20 (7.8) | 19 (9.0) | 17 (8.1) | |
| Ex-smoker | 36 (14.1) | 48 (18.8) | 49 (23.3) | 57 (27.1) | |

**Diet**

| Diet history obtained | 52 (20.3) | 238 (93.0) | <0.01 | 91 (43.3) | 68 (32.4) | 0.02 |
| No diet history | 204 (79.7) | 18 (7.0) | 119 (56.7) | 142 (67.6) | |

**Exercise**

| Exercise history obtained | 62 (24.2) | 237 (92.6) | <0.01 | 54 (25.7) | 64 (30.5) | 0.62 |
| No exercise history | 194 (75.8) | 19 (7.4) | 156 (74.3) | 166 (79.0) | |

**BMI**

| BMI measured | 11 (4.3) | 203 (79.3) | <0.01 | 0 | 40 (19.0) | <0.01 |
| No BMI measured | 245 (95.7) | 53 (20.7) | 210 (100) | 170 (81.0) | |

Abbreviations: BMI = body mass index; BP = blood pressure; HbA1c = glycated haemoglobin; LDL = low-density lipoprotein

* Data are shown as mean ± standard deviation, or No. (%)
† The last values were recorded for patients who had more than one measurement during the intervention phase
‡ Pre-intervention BMI record rate too low for comparison
TABLE 5. Statin usage stratified according to age-group

<table>
<thead>
<tr>
<th>Age-group (years)</th>
<th>Intervention group (n=256)</th>
<th>Control group (n=210)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤80</td>
<td>13/29 (44.8)</td>
<td>12/37 (32.4)</td>
<td>0.32</td>
</tr>
<tr>
<td>61-70</td>
<td>36/70 (51.4)</td>
<td>24/46 (52.2)</td>
<td>1</td>
</tr>
<tr>
<td>71-80</td>
<td>42/97 (43.3)</td>
<td>28/81 (34.6)</td>
<td>0.28</td>
</tr>
<tr>
<td>≥81</td>
<td>16/60 (26.7)</td>
<td>12/46 (26.1)</td>
<td>1</td>
</tr>
</tbody>
</table>

* Significant difference between pre- and post-intervention data in both groups, P<0.01

Concerns about the possible side-effects. However, no severe adverse effects of statins were noted in the intervention group despite the more aggressive treatment approach.

The implementation of secondary stroke prevention protocol has raised doctors’ awareness of lifestyle modification for patients with ischaemic stroke. This was reflected by the significant increase in the use of lifestyle modifications in the intervention group. We encouraged doctors to provide appropriate advice on lifestyle modification when lifestyle risk factors were identified during the consultation. However, due to heavy patient loads in the GOPC, no additional time can be allocated for medical consultations. During clinic meetings, our staff expressed difficulty in providing quality lifestyle education due to limited consultation time. The lack of additional resources for lifestyle education was a main shortcoming of this programme.

Certain subgroups of ischaemic stroke patients are not well represented by this study, for example, those with atrial fibrillation. Atrial fibrillation is one of the major risk factors for recurrent stroke.16 However, as warfarin was not available in the drug formulary of the GOPCs during the study period, most patients with atrial fibrillation were not referred to these clinics. Only a few patients with atrial fibrillation were identified in our study and all of them had a contra-indication for warfarin. At the time of writing, warfarin has become available in the GOPCs and several novel anticoagulants have been introduced as self-finance items. The use of anticoagulants in GOPCs is an important aspect of secondary stroke prevention that warrants further investigation.

Implementation of evidence-based guidelines into routine clinical practice is complicated.17,18 Physicians usually have concerns about the applicability of new trial data to individual patients, and it takes time for them to change their practice. Apart from considering the best available evidence, we also need to take into account the practical barriers in the clinical practice setting. The heavy workload in the clinic, shortage of consultation time, and limited scope of the drug formulary may impose difficulty in introducing an evidence-based protocol to local GOPCs.

From the experience of this study, a dedicated training session for clinic staff is necessary before the implementation of any new protocol. Additional review sessions are needed to audit clinicians’ compliance with the protocol. Review of the GOPC drug formulary, for example, to include...
greater choices of statins and antiplatelets, may be helpful to improve the care of stroke patients. Lifestyle modification is an important aspect for secondary stroke prevention, but time constraints in busy GOPCs are always an issue. A designated nurse clinician for patient education and annual risk factor monitoring should be introduced. For better utilisation of resources, it is beneficial to recruit community partners from allied health services to provide a structured secondary stroke prevention programme for patient empowerment and engagement.

In our study, approximately 5% to 6% of patients were lost to other GOPCs and medical clinics (Table 1). This may introduce some bias. In addition, differences between the two clinics such as proportions of health care workers, doctors' qualifications, and differences in the socio-economic groups of the patients are possible confounders that might introduce bias. The intervention group had a higher rate of dropouts due to death and restroke although this was not statistically significant. As most of these patients had no change in medications during the intervention period (Table 1), the higher death and restroke rates were unlikely to be related to any adverse effects from the implementation of the protocol. However, we do not have data on the rates of stroke recurrence, adverse events, and mortality over a longer period, which are the most important outcomes for effective secondary stroke prevention. Furthermore, we may need to take into account the Hawthorne effect when looking at the effectiveness of the protocol implementation, in that physicians perform better simply because they are aware that they are in a study rather than because of the nature of the protocol.19,20 This is an unavoidable bias in clinical research.

Conclusion

This study demonstrates that through implementation of a standardised treatment protocol, the standard of care of secondary stroke prevention for ischaemic stroke patients could be improved in local GOPCs. However, due to the relatively small sample size in this study, this preliminary result should be interpreted with caution and further studies involving more primary care clinics are required to test its clinical value.

References