

The Clinical Importance of extending the Community Pharmacy Anticoagulation Management Service

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Executive summary

Improving anticoagulant management in New Zealand is an issue of patient safety and requires urgent attention. The existing supervision provides suboptimal care below recommended international standards which puts patients lives at risk and increases the incidence of complications. Several reports including meta-analyses have shown that improving anticoagulant control improves clinical outcomes. This recently led NICE in the UK to recommend patient self-monitoring of warfarin¹ as the best method of supervision as this group of patients achieved the highest level of anticoagulant control. In New Zealand the recently introduced Community Pharmacy Anticoagulation Management Service (CPAMS) has achieved a level of anticoagulant control similar to that achieved by patients who self-test. A recent review of the first two years of the service shows that this high level of control has been maintained. The existing CPAMS provides anticoagulant supervision for 12% of patients on warfarin in New Zealand. We propose to increase this to at least 50% of patients. This will save 300 lives and prevent 150 strokes and 330 hospital admissions for major bleeding each year, with an estimated saving of \$16 million.

Present status of warfarin management

- Approximately 38,000 people take warfarin in New Zealand. The drug requires close supervision with regular monitoring.
- Warfarin is a high risk medication with more hospital admissions related to complications than any other medication.
- The existing process of warfarin management is below recommended International Standards with poor anticoagulant control (the average time in range below 60%), poor record keeping, lack of audit, no national reporting and poor recall processes for non-attenders.
- Poor warfarin management puts patients' lives at risk and increases hospital admissions related to complications, this includes a higher rate of strokes which have long-term consequences.

Benefits of expanding the Community Pharmacy Anticoagulation Management Service

- Improved anticoagulant control with time in range at 75%.
- Improved compliance with regular INR monitoring with approximately 80% of patients attending for testing on time and 89% within 3 days of the expected test date.
- Less fragmentation by the incorporation of sampling, testing and dose adjustment into one consultation involving a single health professional.
- Improved accessibility and convenience for patients.
- Increased job satisfaction for pharmacists.
- Reduced burden on general practice

Process for expansion

- Increase number of pharmacies offering the service to 300 over 2 years

¹ <https://www.nice.org.uk/guidance/dg14/chapter/5-outcomes>

- Increase the number of patients managed at each pharmacy to a maximum of 80 unless otherwise agreed by the DHB, with an average of 66 per pharmacy.
- Expand training with additional online resources to train additional staff in accredited pharmacies
- Expand online resources for re-accreditation of trained pharmacists

Introduction

In this proposal we recommend expanding the Community Pharmacy Anticoagulant management Service (CPAMS) to provide anticoagulant supervision for the majority of patients on warfarin in New Zealand. The main driver for this expansion is to improve patient safety. There is strong clinical evidence that improving anticoagulant control reduces the incidence of stroke and major bleeding and saves lives. Increasing the CPAMS programme to provide warfarin management for 50% of patients on warfarin will have a significant health benefit by saving 300 lives, preventing 150 strokes and 330 hospital admissions related to warfarin complications which will save an estimated \$16 million dollars per year.

Warfarin is recognised as the most dangerous prescription medication with more hospital admissions related to warfarin complications than any other drug. Despite this, warfarin treatment is poorly monitored in New Zealand. Information about the total number of patients on warfarin or the incidence of complications and adverse events is not readily available and there is no standardised process for managing treatment. Most patients are managed by their own general practitioner. Many GPs are knowledgeable and experienced but often have poor systems for supervising treatment and make dosing decisions without access to all previous results or information about concomitant medication. Most do not use any form of dosing algorithm and there is no standard method of record keeping or recall to ensure patients have regular testing. There is no regular audit of practice and no National reporting. Improvements are urgently needed. Small audits of practice have been carried out which show that the GP model achieves suboptimal anticoagulant control below the international recognised standard.

One way to significantly improve control is to expand the CPAMS programme. This service is well established and provides anticoagulant management for approximately 12% of warfarin patients at present. This has shown a consistently high level of warfarin control significantly better than previously achieved by other methods of warfarin supervision. The infrastructure is in place to enable expansion. This includes a national data storage system with links to primary care patient management systems and TestSafe, a training programme for pharmacists with an accreditation process, a quality assurance programme, regular audit with monthly reporting to the Ministry of Health.

This proposal is in line with the MOH Health Targets. The improved control will lead to less emergency department visits which will contribute to the improved patients flow and shorten ED stays. It is also targeting improvements in cardiovascular disease management.

Proposal

To expand the Community Pharmacy Anticoagulant Management Service (CPAMS) to provide anticoagulant management for 20,000 patients on warfarin in New Zealand. This will save lives by reducing the bleeding complications of warfarin and reducing the incidence of stroke, which will result in longer term financial savings.

Background

Anticoagulant Treatment

There are approximately 38,000 people taking the blood thinning drug warfarin in New Zealand. It is life saving for many patients by preventing stroke and serious blood clots, but it is potentially dangerous if not well managed. Warfarin has a narrow treatment range where too much can cause life-threatening bleeding and not enough can increase the risk of thrombosis that can lead to major disability or even death. Patients on warfarin require regular blood tests to maintain safe control.

Warfarin is the most widely used oral anticoagulant in New Zealand. It is used for the management of acute venous thrombosis and pulmonary embolus and to prevent blood clots associated with mechanical heart valves^{2,3}. However the use of warfarin has increased dramatically over the last fifteen years since it was confirmed that warfarin can significantly reduce the risk of stroke in patients with an irregular heart rate due to atrial fibrillation⁴. The incidence of atrial fibrillation is 4.7% in people over 65 years of age rising to 10% in men over 75yrs. The result is that an increasing number of elderly patients are now on long-term warfarin. Atrial fibrillation is now the most common reason for warfarin treatment.

The new anticoagulant, dabigatran became available in New Zealand in 2011. This can be given as an alternative to Warfarin for patients with atrial fibrillation. It was expected that this would have a major impact on the number of patients on Warfarin but a recent review of prescribing data from the National Pharmacy dispensing database has shown that the number of patient on warfarin has only fallen 13% and has remained constant at around 39,000 patients (appendix A).

The use of dabigatran has shown a steady rise to approximately 16,000 patients over 3 years. These results imply that patients established on warfarin are remaining on long-term treatment rather than changing to dabigatran and the majority of patients on dabigatran are newly diagnosed cases or patients who were unsuitable for warfarin. The National Pharmacy dispensing database also showed that 30% of patients stop dabigatran within 4 months of treatment, a proportion of these cases will switch to warfarin. There is no alternative to Warfarin for the management of patients with heart valves (approximately 15% of warfarin patients). Therefore it is likely that a significant proportion of patients on anticoagulants will remain on warfarin for the foreseeable future. It is difficult to estimated precise figures but a review of recent prescribing shows that approximately 600 people start warfarin and 800 people stop warfarin each month. Therefore it is reasonable to estimate that approx 20,000 patients will still be taking warfarin in 5 years.

² Clagett, G.P. et al, Chest. 1998 Nov;114(5 Suppl):531S-560S

³ Cairns, J.A., et al, Chest. 2001 Jan;119(1 Suppl):228S-252S

⁴ Albers, G.W et al., Chest. 2001 Jan;119(1 Suppl):194S-206S

Problems with poor warfarin management

Warfarin is one of the commonest causes of death related to prescription drugs. The FDA's Adverse Event Reporting System indicated that warfarin is among the top 10 drugs with the largest number of serious adverse event reports submitted during the 1990 and 2000 decades. From US death certificates, anticoagulants ranked first in 2003 and 2004 in the number of total mentions of deaths for drugs causing "adverse effects in therapeutic use." Complications account for a high number of hospital admissions. A study in the US reported in 2011 estimated that approximately 100,000 hospital admissions were due to adverse drug reactions and that 33% were due to bleeding associated with warfarin.⁵ Approximately 10% of patients on warfarin will experience at least one bleed each year. The majority are minor but a review of observational studies⁶, showed the average annual rates of fatal, major, and minor bleeding were 0.8, 4.9, and 15%, respectively. In another review⁷, bleeding rates ranged from 0 to 4.8% for fatal bleeding and from 2.4 to 8.1% for major bleeding. More recent studies show a slightly lower rate but major bleeds are still in the order of 2.5%, with life-threatening bleeds at 1.7% and intracranial bleeding at more than 0.5%.

Why is good warfarin control important?

It is difficult to consistently maintain stable treatment for patients on warfarin due to many factors that influence anticoagulant control. Warfarin treatment is monitored using a simple blood test called the International Normalised Ratio or INR; a person not taking warfarin should have an INR of 1.0. For most conditions requiring anticoagulants the aim is to maintain the INR between 2.0 and 3.0, but changes in diet, medication, exercise and lifestyle can influence control, giving results outside this range and increasing the risk of complications. Bleeding is the most serious complication with the risk directly related to the INR value. There is a consistent increase in major bleeding (including intracranial bleeding⁸) when the INR exceeds 4.0^{9,10,11} and is up to five fold higher when the INR exceeds 7.0^{12,13}. An audit from Kings College Hospital in the UK showed that the commonest reason for a high INR and bleeding was due to an interaction with concomitant medication¹⁴. Pharmacists are obviously in a position to monitor and review potential drug interactions when managing warfarin patients.

⁵ Emergency Hospitalizations for Adverse Drug Events in Older Americans. Daniel S. Budnitz, M.D., M.P.H., Maribeth C. Lovegrove, M.P.H., Nadine Shehab, Pharm.D., M.P.H., and Chesley L. Richards, M.D., M.P.H.

N Engl J Med 2011; 365:2002

⁶ Landefeld CS, Beyth RJ. Anticoagulant-related bleeding-clinical epidemiology, prediction, and prevention. Am J Med 1993; 95: 315-28.

⁷ Levine MN, Hirsh J, Landefeld CS, Raskob G. Haemorrhagic complications of anticoagulant treatment. Chest 1992; 102: 352s-63s.

⁸ Hylek, E.M. and D.E. Singer. Ann Int Med. 1994 Jun 1;120(11):897-902

⁹ van der Meer, F.J et al, Arch Int Med. 1993 Jul 12;153(13):1557-62

¹⁰ Anonymous. NEJM. 1995 Jul 6;333(1):5-10

¹¹ Fihn, S.D. et al, Ann Int Med. 1993 Apr 1;118(7):511-20

¹² Palareti, G. et al., Lancet. 1996 Aug 17;348(9025):423-8

¹³ Palareti G, Leali N, Coccheri S, Poggi M, Manotti C, D'Angelo A, et al. Bleeding complications of oral anticoagulant treatment: an inception-cohort, prospective collaborative study (ISCOAT). Lancet 1996;348:423-8.

¹⁴http://www.medicinesresources.nhs.uk/upload/documents/Communities/SPS_E_SE_England/53_Causes_and_Mx_of_over_A_C_NPSA_18_AC_Kings_Jun2006.pdf

The efficacy and safety of warfarin also depends on the proportion of time treatment is within the therapeutic range. Two large clinical trials^{15,16} showed that patients on warfarin with good control (INR within range 75% of the time) had an annual mortality of 1.69% and major bleeding events of 1.58%, whereas the poorly controlled patients (INR within the therapeutic range <60% of the time) had an annual mortality of 4.2% and major bleeding of 3.85%. Outside clinical trials anticoagulant control is generally worse than this with only about 50% of measurements within range. International guidelines recommend that the INR should be within the therapeutic range for at least 60% of the time¹⁷. The CPAMS programme consistently achieves a time in range of 75%.

Existing warfarin management

In New Zealand there are 4 models of warfarin management

1. Supervision by General Practitioners: The majority of patients are managed in this way (approx 28,000 patients).
2. Laboratory based anticoagulant service: This is provided in the Central North Island through MedLab Central (Midcentral DHB, Whanganui DHB and Wairapa DHB). The service is well established and an audit a few years ago showed a good level of control. However the service has no recall system, no method for monitoring adverse events and no regular audit process to assess control (approximately 5000 patients). There are no other hospital or laboratory based services in New Zealand. Wellington Hospital had a clinic which has now referred patients back to the community
3. Patient self-management. Approximately 200-300 patients manage their own warfarin using a home testing device. In a recent online survey of these patients approximately 50% manage their own dosing and the others consult with their own doctor for advice when necessary. A study comparing self-testing with laboratory management showed that these patients can achieve a TTR of >80%.
4. Community Pharmacy Anticoagulant Service (approximately 4500 patients).

Problems with general practitioner based warfarin management

The vast majority of patients are managed by their own GP. This has been a long standing practice and provides reasonable care but the process could be improved. There is no standardized process for this service. Doctors rarely use a standardised dosing algorithm to adjust the Warfarin dose and often have poor processes to record results or to assess their control and have no recall system for patients who fail to attend for testing. Clinical audit results show that patients managed in this way have suboptimal control compared with International standards. The details of 5 audits in New Zealand are listed in Table 1.

¹⁵ Olsson SB; Lancet. 2003 Nov 22;362(9397):1691-8.

¹⁶ Akins PT et al, Stroke. 2007 Mar;38(3):874-80. .

¹⁷ Guidelines on oral anticoagulation: J Clin Path. 1990 Mar;43(3):177-83

Table 1

Audits of anticoagulant services.	Time in Therapeutic range
Audit of community-based anticoagulant monitoring <i>Internal Medicine Journal 2004;34:-639-641 Young et al</i>	58.3%
Pukekohe Family Health Centre Audit 2008	55.9%
East Health Trust PHO Vol 14 No 4 May 2008	59.4%
Wellington Anticoagulation Clinic Audit 2001	54.8%
Mangere Family Doctors Nov 2008	46.9%

A GP based service also requires patients to attend a laboratory for a venous blood sample and the process to contact the patient is often cumbersome.

Problems with blood tests

Warfarin is monitored using a blood test. This is usually collected as a venous sample at a laboratory. Many patients have damaged veins as a result of regular blood tests and find sampling uncomfortable. Also attendance at laboratory bleeding rooms is time consuming and disruptive and can lead to poor compliance which compounds the risk of complications, increasing costs.

Poor patient contact

Processes for communicating the blood results and clinical advice to the patients are inconsistent. There is a delay of several hours between collecting the blood sample and the doctor receiving the result, as the sample has to be sent to the laboratory for processing. When the result is available to the doctor the result is then phoned to the patient. In some cases the patient has to take the lead and contact the GP themselves to get the results and advice. There is often no record to confirm the patient contact and difficulties with patients contact can delay dose changes.

Community Pharmacy Anticoagulant Management Service (CPAMS)

CPAMS was introduced to try to address some of the problems with the existing system. A pilot was carried out in 25 pharmacies in 2010 and achieved a high level of control with a TTR >75% which was significantly higher than achieved by GP services. The pilot was expanded over the next 3 years and is now available in 130 pharmacies providing management for over 4000 patients. A recent review of the service from January 2012 to December 2014 shows that the level of control has remained consistently around a TTR of 75% (Appendix B).

Outline of the service

Anticoagulant management is provided through community pharmacies.

The process is simple

- Patients attend at their convenience.
- The trained pharmacists briefly interview the patients asking about adverse events since their last test and records these on the computer system.
- The pharmacist carries out the INR test using a fingerprick blood sample.
- The INR is measured on a near patient testing device and the results are available within a few seconds.
- The results are automatically transferred to a decision support software program which provides immediate treatment advice.
- The patient receives a printed dosing calendar to take away and is advised when to come for the next test.
- The patient receives an e-mail reminder when the next test is due.

The service uses an internet based computer programme which allows all results to be stored centrally on a secure server. Results for the whole service can be analysed centrally. Results are automatically sent to TestSafe and the GP patient management systems.

Advantages of the Community Pharmacy Anticoagulant Service

- Improved anticoagulant control (GP services achieve TTR 55%, CPAMS achieves TTR 75%)
- Improved INR testing adherence. 89% of patients have their INR test within 3 days of their appointment.
- Rapid process; immediate results and immediate advice.
- Detailed record keeping
 - The computer system records all INR tests and dosing
 - Records adverse events, including bleeding episodes, new medication and hospital admissions.
 - Provides an audit trail of all transactions.
- Comprehensive audit

- Enables detailed reports to be generated each month listing
 - Time in range for all patients at each Pharmacy
 - Time in range for the full service
 - Incidence of adverse events
 - Number of tests at each site
 - Average test interval
 - Adherence to testing
- Recall system
 - A list of which patients are due for a testing is generated each day.
 - Overdue patients remain highlighted until testing complete.
 - Provides automatic e-mail reminders to the patient.
- Automated Warfarin dosing
 - The decision support software uses a validated dosing algorithm which has been shown to provide a high level of anticoagulant control¹⁸.
- Appropriate trained personnel
 - The service can only be provided by trained pharmacists who have completed accredited training.
 - Staff undergo reaccreditation every 3 years.
- Appropriately supported
 - If the results are outside set parameters the pharmacist consults the GP practice immediately.
 - Software support available during working hours through a help-line and e-mail contact.
 - Support for the near patient testing device by the manufacturer with regular site visits.
 - Medical support by the clinical lead (Dr P Harper , Haematologist) as required.
- Increased job satisfaction for pharmacists.
 - A survey of the pilot study showed that Pharmacists derived satisfaction from the expansion of their role to involve the management of warfarin. Many of them felt that their clinical skills and knowledge were being underutilised and they welcomed the challenge of developing a new model of care that made better use of these.
 - Pharmacists enjoyed the opportunity to develop a closer relationship with their patients.
- Reduced burden on general practice
 - A survey of the pilot study showed that the majority of GPs and practice nurses who responded thought that the CPAMS had saved time for them and for other members of staff at their practices. It was difficult for them to quantify how much time was saved because the workload related to warfarin management varied from week to week and often involved multiple members of staff at a practice.

¹⁸ Harper P; Harper J; Hill C, An audit of anticoagulant management to assess anticoagulant control using decision support software. *BMJ Open* 4 (9), pp e005864 2014.

- Some GPs were pleased to have the responsibility for day-to-day management taken on by the pharmacist.
- It was thought by some participants that the CPAMS was of particular benefit in rural areas where GP shortages meant that there were very heavy workloads for practice staff.

The benefit of improved anticoagulant control

The recent clinical trials of the new anticoagulants have provided a large amount of data about warfarin patients as warfarin treatment was the control arm in these studies. From these and prior studies it is possible to compare well controlled warfarin patients with those with poorer control. A meta-analysis of 47 studies showed that a 6.9% improvement in TTR reduced major haemorrhage by 1 per 100 patients-years and an improvement of an 11.9% improvement in TTR resulted in one less thromboembolic event per 100 patient years. Two more recent studies have shown that the incidence of both thrombosis and bleeding is between 2 to 3 fold lower in patients with a TTR of >75% than is those with a TTR <60% (table 2). There is also a significant reduction in the death rate from all causes in well controlled patients. Data from the SPORTIF study showed that the mortality rate in patients with poor control (TTR <60%) was 4.2% compared with 1.7% in patients with a TTR >75%, and in the RELY study (Comparison of dabigatran versus warfarin) vascular deaths (Stroke, systemic embolism, pulmonary embolism, myocardial infarction, and cardiovascular death) were reported at 6.2% when the TTR was <57% and only 3.0% when the TTR was >72%.¹⁹

Table 2: Event rate (%/yr) in patients with atrial fibrillation

Group by TTR	Thromboembolic events Including ischaemic stroke and MI	Major bleeding	Combination.
White, et al. INR 2 to 3 ²¹			
Entire group, n = 3,587	2.46	2.46	4.92
Top 3 rd >75%	1.69	1.58	3.27
Mid 3 rd 60 – 75%	2.23	1.96	4.19
Bottom 3 rd < 60%	3.48 (RR 2.1)	3.85 (RR 2.4)	7.33 (RR 2.2)
Veeger, et al. – INR 2.5 to 3.5 ²⁰			
Entire group n = 2,614	1.7	1.6	3.3
Top 3/4 th (mean 51%)	1.3	1.3	2.6

¹⁹ Wallentin et al. *Lancet* 2010; 376: 975–83

²⁰ Veeger NJGM, et al. *J Thromb Haemost* 2006; 4:1625-1627

Bottom 1/4 th < 30%	4.1 (RR 2.7)	4.1 (RR 3.2)	8.2 (RR 3.2)
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From this data it is possible to calculate the reduction in the incidence of stroke, major bleeding and death that would be achieved if warfarin control is improved.

INR Control and difference in Event Rates (per 1,000 patients per year)

Event (%/yr)	Top 1/3 vs bottom 1/3 (>75% vs < 60% TTR) Total n=3587 ²¹	Top 1/2 vs bottom 1/4 (>67% vs < 53% TTR) Total n=6,022 ²²
Stroke* + SEE	10	9
Heart attack	8	Not reported
Maj Bleed	22	20
Death	25	50
Total/Composite	65	66
NNT ^{##}	15.4	15.2

^{##}Number needed to treat per year is the number of patients managed with good INR control to prevent one major event compared to standard INR control. Comp = Stroke, systemic embolism, MI, PE, death, major bleeding.

These data show that improving anticoagulant control has a large clinical benefit with a number needed to treat of only 15. The CPAMS service achieves a TTR in the order of 75% whereas existing warfarin management at best achieves a TTR of 60%. So these figures are representative of the level of improvement that could be achieved by expanding CPAMS for a larger number of patients.

Cost-benefit analysis

We are proposing to increase the number of patients managed by the CPAMS programme from the present 4,500 to 20,000. This will prevent 150 strokes per year and 330 major bleeding episodes and save up to 300 lives. The cost-benefit analysis compares the cost of providing the service against the savings from reduced thromboembolic events, bleeding episodes and lives saved.

This is not a fully comprehensive cost-benefit analysis. It is based on the prior analysis presented in the CPAMS report present by Shaw et al²³ using the Economic Model of Oral Anticoagulation Therapy (OAT)

²¹ White HD, et al. Arch Intern Med. 2007; 167:239-245

²² Connolly SJ, et al. N Engl J Med 2009; 361:1139-1151. and Wallentin, L. www.theheart.org/article/1046957.do

²³ Shaw J, Harrison J, Harrison J 2011 Community Pharmacist-led Anticoagulation Management Service Final Report, <http://www.centrautas.co.nz/LinkClick.aspx?fileticket=B9rFT2EvcF8%3D&tabid=278&mid=1312>

developed by Oblisque Consulting. This tool is based on a published decision analysis and Markov model²⁴ that compares the costs of anticoagulation management with the costs of thromboembolic events and bleeding. It has been updated to include data from more recent studies on warfarin management.

The cost of providing the service

Cost of CPAMS service: The charge for providing this service through pharmacies is now established at a fixed cost. New pharmacies receive an establishment fee of \$1,600. Pharmacies are reimbursed \$540 per patient per year which is the total cost to the DHB. The pharmacists purchase consumables, quality assurance materials and access to the decision support software from this reimbursement. The cost is less than was estimated in the model proposed in the CPAMS report²¹ (the estimate was over \$900 per patient per year).

Cost of existing GP based service: Comparative data on staff costs incurred under the standard model of care (including GP time, nurse time and professional fees) were derived from a published study of warfarin management in general practice in New Zealand²⁵. The cost of laboratory testing was based on a published report from one DHB²⁶. Costs of laboratory consumables and the cost of laboratory quality control programmes were assumed to be overheads included in the laboratory test fee and were not added to the model for the standard care arm. No costs for blood collection at the general practice were included. No costs for quality assurance of practice management (practice audits) were included. From the model presented by Shaw et al it was assumed that testing would be at a rate of 2.0 per month, however data from the last 2 years show that the rate of testing in pharmacies is 1.7 per month. Therefore for comparison we have assumed the same rate of testing for the standard model of care, which results in a total cost of \$1106 per patient per year.

The cost of thromboembolic events and haemorrhagic events

The cost of a stroke

The cost of a stroke is difficult to calculate as the ongoing cost of rehabilitation and the intangible costs due to loss of earnings are hard to assess. Warfarin prevents ischaemic stroke. This type of stroke has a lower mortality rate than haemorrhagic stroke (Mortality rate at 30 days 7.6% ischaemic stroke versus 37% of haemorrhagic strokes) but causes more severe disability; 50% of patients with a stroke before age 65yrs will not return to work. Various estimates of the cost of stroke have been reported the immediate direct costs for the first 90 days of treatment are in the order of US\$15,000 with 10% of patients costing up to US\$35,000 and ongoing rehabilitation costs in the order of US\$17,000 per year²⁷. In the previous report

²⁴ Connock M, Stevens C, Fry-Smith A, Jowett S, Fitzmaurice D, Moore D, et al. Clinical effectiveness and cost-effectiveness of different models of managing long-term oral anticoagulation therapy: a systematic review and economic modelling. Health Technology Assessment (Winchester, England). 2007 Oct;11(38):iii-iv, ix-66.

²⁵ Geevasinga N, Turner N, Mackie D. Therapeutic monitoring of warfarin - an audit of monitoring protocols and outcomes. New Zealand Family Physician. 2004;31(5):307-9.

²⁶ Canterbury Clinical Network. Canterbury Laboratory Service Report. Christchurch [September 2011]; Available from: www.ccnweb.org.nz/activities/labsconsultation.aspx.

²⁷ Godwin KM, Wasserman J, Ostwald SK. Cost associated with stroke: outpatient rehabilitative services and medication Top Stroke Rehabil. 2011 Oct;18 Suppl 1:676-84..

the cost of stroke was estimated at approximately NZ\$11,000 based on data from the Center for Health Service Research, School of Population Health, University of Auckland. However a more detailed report from a New Zealand study reported in 2012 estimated costs at between NZ\$20,000 to \$25,000 for the first year²⁸. Therefore in our model we have assumed a cost of \$20,000 per stroke.

The cost of major bleeding is also difficult to assess. A study from the US reported the cost of gastrointestinal bleeding at US\$12,000²⁹ but it is likely to be significantly lower in New Zealand. Analysis of discharge codes and DRGs gave an estimated cost of \$8000 per bleed. The cost of an intracranial bleed is less than a thrombotic stroke as the ongoing costs are less. The estimated cost is around \$14,000. These are conservative estimates as the New Zealand Stroke Association quotes the cost of a stroke at \$50,000.

Estimates have been reported assessing the cost of a patient dying but this is highly dependent on the underlying reason for death. The deaths reported related to warfarin in the studies mentioned above are largely cardiovascular deaths. These can range from sudden death to prolonged hospital stay with intensive investigation and intervention. A study from Counties Manukau³⁰ in 2008 estimated the average cost of a patient with cardiovascular disease at \$5,400. The immediate mortality rate from myocardial infarction is in the order of 30%, therefore we have used an average cost of \$3000 for our assessment.

From these figures increasing the CPAMS service to provide warfarin management for half the patients on warfarin in New Zealand will save approximately \$16 million each year.

Savings from changing from standard model to CPAMS

	Cost per patient per year	Changing 15,000 patients to CPAMS service
CPAMS	\$540	
Standard model	\$1100	
Saving	\$560	\$8,400,000

Savings as a result of a lower event rate

Event	Number of events prevented per year/ 1000 patients by improving TTR from 60% to 75%	Cost of each event	Number of cases prevented if the CPAMS programme	Savings

²⁸Te Ao BJ, Brown PM, Feigin VL, Anderson CS Are stroke units cost effective? Evidence from a New Zealand stroke incidence and population-based study. *Int J Stroke*. 2012 Dec;7(8):623-30.

²⁹ Cryer BL, Wilcox CM, Henk HJ, Zlateva G, Chen L, Zarotsky V. The economics of upper gastrointestinal bleeding in a US managed-care setting: a retrospective, claims-based analysis. *J Med Econ*. 2010 Mar;13(1):70-7.

³⁰ http://www.countiesmanukau.health.nz/about_cmdhb/planning/health-status/Public-Health/cost-of-CVD-diabetes-in-2008.pdf

			increased to 20,000 patients	
Stroke	8	\$20,000	160	\$3,200,000
Major bleeding				
Gastrointestinal bleed	12	\$8,000	180	\$1,440,000
Haemorrhagic stroke	10	\$14,000	150	\$2,100,000
Death	20	\$3,000	300	\$ 900,000
Total				\$7,640,000

Proposed process for expansion

The present CPAMS service has placed some limitations on the number of patients that can be managed by each pharmacy. The initial proposal allowed a maximum of 45 patients at any one pharmacy, however some pharmacies have negotiated a higher limit. The feed-back from existing pharmacies is that some could manage up to 80-100 patients. At present there are 130 pharmacies registered to provide the service. This could be expanded to 300 pharmacies over the next 2 years with an average of 66 patients per pharmacy this would provide the service to approximately 20,000 patients.

Conclusion

This proposal primarily focuses on the clinical benefit and patients safety aspects of improving anticoagulant management. The existing service has been in place for many years and it was assumed that this provided safe management, however it is only from recent data that it has become apparent that other models of anticoagulant management can improve control with significant clinical benefit. The CPAMS model has achieved better outcomes than originally expected which makes a compelling argument for expanding the service to all patients on warfarin. This may not be practical immediately but a significant expansion should be considered. The cost benefit analysis lacks some detail but gives a clear indication that the service is cost-effective. Clearly further work would need to be done on the implementation of this model, but the brief assessment of numbers give some indication that it is possible to expand the service to provide management for approximately 20,000 patients.

Conflict of interest: Paul Harper is a director of INR Online which provides the online software for the service

Appendix A

THE IMPACT OF THE INTRODUCTION OF DABIGATRAN ON ANTICOAGULANT MANAGEMENT IN NEW ZEALAND

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Background: In New Zealand (NZ), dabigatran became available on 1st July 2011. It was expected that it would lead to a reduction in the number of patients taking warfarin but an increase in the total number of patients on anticoagulants for atrial fibrillation (AF).

Aims: To audit warfarin usage and the growth of dabigatran in NZ since July 2011.

Methods: The change in anticoagulant use was evaluated from (1) prescribing data collected from the National Pharmaceutical database (NPD) and (2) using INR data from a cohort of patients on warfarin managed in the Central North Island of NZ (pop. 310,000). Data were collected from 1/4/11 to 30/9/14. Ethics approval was obtained.

Results: Before July 2011, ≈7000 INR tests were performed per month on ≈ 3400 patients in the central region of NZ. During the first 3 months following the introduction of dabigatran the INR test rate dropped to 6300/mth on ≈3000 patients and plateaued at this rate over the next 30mths. The proportion of patients with AF on warfarin fell from 64% to 59% and median age increased from 76.8 to 78.4 yrs over 30mths. Data from the NPD showed ≈21,000 prescriptions/month were issued for warfarin before July 2011 for ≈42,000 patients. This dropped to ≈17,000 prescriptions for ≈38,000 patients within 3 months and has remained constant since. The number of patients starting warfarin in NZ fell from 800 to 650/mth over 3yrs. Since July 2011 the number of patients on dabigatran has grown steadily; within 3 months 8000 patients were taking dabigatran and this has gone up to ≈16,000; ≈ 600 start and ≈300 stop dabigatran each month.

Conclusion: The introduction of dabigatran led to an initial 12% fall in the number of patients taking warfarin. The stable numbers since with an increased median age suggests that established patients remain on warfarin with a small number changing to dabigatran. The majority of dabigatran patients are new to anticoagulants. The total number of patients on anticoagulants in NZ has increased 30% (42,000 to 55,000) mainly for AF.

Appendix B

A NATIONAL ANTICOAGULANT MANAGEMENT SERVICE PROVIDED BY COMMUNITY PHARMACIES IN NEW ZEALAND ACHIEVES A HIGH LEVEL OF ANTICOAGULANT CONTROL WHICH IS SAFE AND CONVENIENT FOR PATIENTS.

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Background: A community pharmacy based anticoagulant management service using point of care (POC) testing (CoaguChek, Roche Diagnostics) and online decision support software (DSS) (INR Online) was introduced in New Zealand in 2011. Pharmacists can provide the service if they have completed a 1 day training course and gained accreditation. The service is supported by funding from the Ministry of Health.

Aims: To assess anticoagulant control (Time in range (TTR)), testing frequency, patient adherence with testing and frequency of adverse events for this service.

Methods: An audit for the period 2012 to 2014 using data collected from the online support software. The test date, INR result, warfarin dose and adverse events were recorded at each visit.

Results: 5065 patients on warfarin had at least 2 INR tests during the audit (1/1/12 to 31/12/14). 126 pharmacies provided the service. Overall TTR was 74.1% (based on 1.8million days on treatment and 106,500 INR tests), with 9.9% above and 15.9% below the range. 75.1% of patients had a TTR > 60% and 17.2% had a TTR >90%. Median test interval was 18.9 days (interquartile range (IQR) 13.6- 24.3) with a median of 1.6 tests/month (IQR 1.25-2.24). Testing adherence was high with 74.6% of INR tests performed on the recommended date and 89.1% within 3 days, only 5.3% of tests were more than 7 days overdue. 3441 bleeding episodes were reported (82% minor, 16%moderate, 2% major); one bleed for every 540 days on warfarin.

Conclusion: Pharmacists in community pharmacies are able to achieve a high level of anticoagulant control using POC testing and DSS. The internet based data collection allows accurate audit of results. Anticoagulant control was good (TTR 74.1%) with 75% of patients with a TTR above the recommended 60%.The incidence of major bleeding was low. Testing adherence was high, in part due to follow-up procedures and patient email reminders. This type of service offers patients easy access to warfarin monitoring with rapid results and immediate treatment advice.