Community Pharmacy Anticoagulant Management Service

CPAMS at 10 years.

CPAMS has been provided in New Zealand for 10 years

- Currently over 6000 patients are using the service
- Over 10,000 patients have been treated over the last 5 years.
- Over 160 pharmacies provide the service.

Anticoagulant control

Control is measured by assessing the time within the therapeutic range (TTR). A TTR greater than 60% is regarded as "good" control.

- The TTR for the whole CPAMS population was 73%
- Control has remained stable over the last 5 years.
- Approximately 80% of patients achieve good control (TTR>60%).

The risk of bleeding is associated with a high INR result.

- Only 2% of INR results were greater than 4.5
- Only 0.02% of INR results were greater than 8.0

Conclusion

CPAMS provides an efficient safe anticoagulant monitoring service giving a consistent high level of anticoagulant control.

There is scope to expand the service which could become the standard of care for warfarin management in New Zealand.

A review of the CPAMS anticoagulant management over the last 5 years

Dr Paul Harper, Haematologist

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Introduction

The Community Pharmacy anticoagulant service (CPAMS) enables pharmacists to manage patients on the anticoagulant drug, warfarin using near patient testing and decision support software. Patients on warfarin require regular blood tests (INR) to ensure that treatment is safe. Warfarin control is assessed by measuring the proportion of time the INR measurement is within the therapeutic range (time in therapeutic range: TTR). International guidelines recommend that patients on warfarin should have a TTR of greater than 60% to achieve adequate safe control.

A 6-month pilot study to examine the efficacy of this service was carried out from December 2010 in 15 pharmacies. 693 patients were recruited. The mean TTR for the 671 patients whose results were evaluated was 78.6%, rising to 79.4% and 80.2% for patients who had been in the CPAMS for 16 weeks or 26 weeks respectively. All pharmacy sites achieved a mean TTR in excess of 70% (range 71.4% to 84.1%) well above the recommended target of 60%.

Subsequently the Ministry of Health funded the service which has now expanded to over 160 pharmacies and more than 6000 patients. The aim of this review was to see if the initial high-quality anticoagulant control achieved in the pilot study has been maintained in standard clinical practice. We have reviewed data from the last 5 years to assess control.

Methods

Data have been collected from the INR Online (decision support software) database for all tests from pharmacy patients from 1st January 2015 to 31st January 2020. This information included the patient's unique ID, the Pharmacy the patient attended, the reason the patient was taking warfarin, the date of the test and the INR result. The time in the therapeutic range (TTR) was calculated as previously described. For the TTR calculations, patients were excluded if they had less than 4 INR results.

The time in range was reviewed in two ways, for individual patients and for the whole population.

Individual patients – we calculated the total number of days on treatment for each patient and determined the number of days above, within or below the therapeutic range (target INR $\pm$ 0.5).

Total population – we added together all the results from individual patients to determine the total number of days on treatment and the total numbers of day above, within and below the therapeutic range.

Patient numbers – Data on the number of patients tested each month can be calculated directly from the INR Online database. The number of patients registered on the service is more complex as not all patients undergo testing each month. This is estimated from the average over a 3-month period. Therefore, in our results we have plotted the number of patients tested each month and. in the text, given an estimate of the total number registered.

Results

Patient numbers

In Jan 2015 approximately 4000 patients were registered on CPAMS and 3577 patients were tested that month. The numbers differ, as the testing interval for some patients is up to 6 weeks and therefore not all patients are tested each month, whereas other patients have more than one test a month. The number of patients tested each month has increased steadily to over 6200, with over 6600 registered patients on the service.

The number of INR tests performed each month has increased in parallel from 6100 INR tests in Jan 2015 to over 10,000 tests by January 2020.

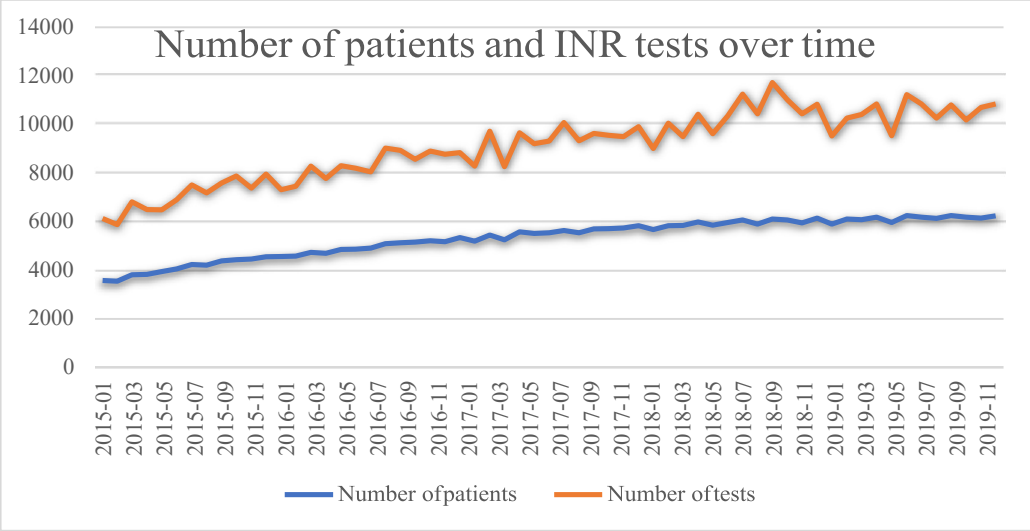

Figure 1. Total number of patients tested each month on CPAMS and the total number of tests performed each month.

Diagnostic groups

10,230 patients had at least 1 INR test performed during the study period. Approximately 60% were on warfarin for stroke prevention in atrial fibrillation.

Table 1 – Number of CPAMS patients in each diagnostic group

Diagnosis	Number of patients
Atrial fibrillation	6010
Mechanical heart valve	1499
Deep vein thrombosis	1028
Pulmonary embolus	764
Other	521
Tissue heart valve	178
TIA	96
Mural thrombus	76
Post myocardial infarction	58
Grand Total	10230

Time in therapeutic range

Time in range for whole population

A total of 10,075 patients had at least 4 INR tests and were included in the analysis. The time on treatment (in days), the time within, above and below the therapeutic range (target INR ± 0.5) was calculated for each patient. The sum of all results was calculated to determine the time within, above and below the range for the total population.

A total of 560,359 tests were performed over the 5 year period giving a total time on treatment of 10.8million days. The INR result was within the therapeutic range 7.9million days; 73% of the time.

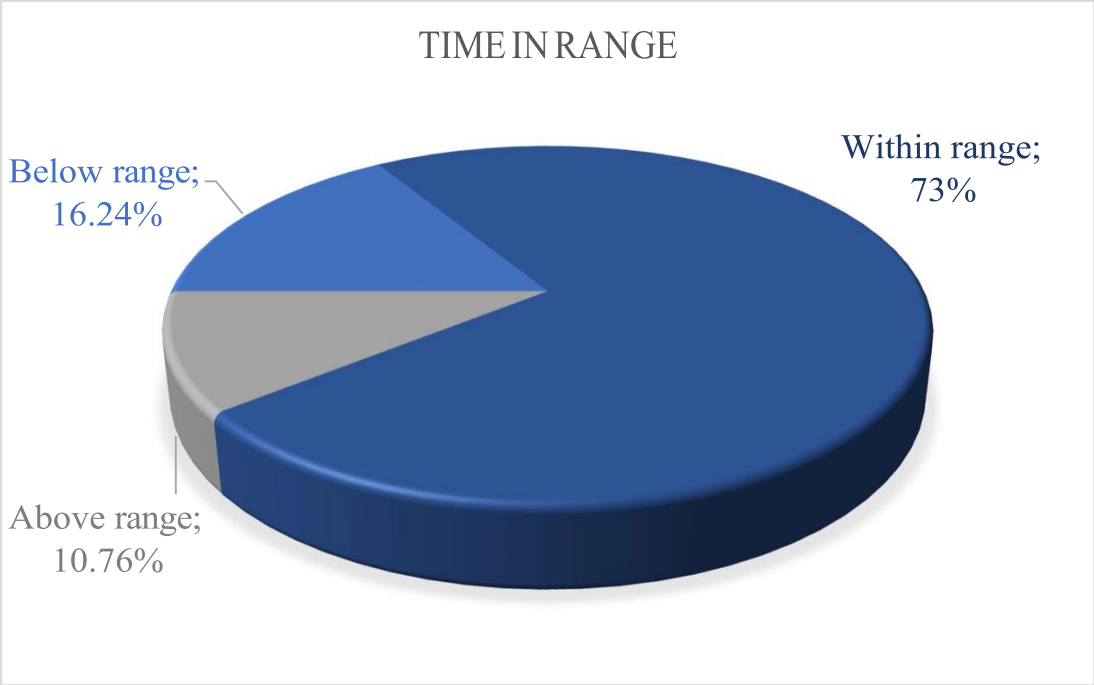

Figure 2. Time within, above and below the therapeutic range for whole population. Data based on 560,359 tests. Time on treatment 10,774,798 days.

Time in range for diagnostic groups

Results were analysed based on the underlying diagnosis and further separated into groups based on the target INR; either "All" patients or those with a target INR at the recommended value for their condition.

The majority of groups have a time in range over 70%.

The results show that patients with a higher target INR, in particular the mechanical heart valve patients, have a lower proportion of time in range with a higher percentage of time below the therapeutic range.

Table 2. Time in range for each diagnostic group. All patients in each group and separate analysis of diagnostic group managed with recommended target INR.

Diagnosis	Number of tests	Target INR	Days on treatment	% time above range	% time in range	% time below range
Atrial fibrillation	323048	All	6338802	10.34	74.54	15.12
	296247	2.5	5877180	10.20	75.00	14.80
DVT	49625	All	980860	10.47	73.94	15.59
	43500	2.5	876748	10.33	74.53	15.13
PE	39042	All	759664	10.98	73.75	15.27
	32622	2.5	650691	10.87	74.43	14.71
TIA	5675	All	112278	10.36	76.28	13.36
	4772	2.5	96374	9.81	76.24	13.95
Mural	2951	All	53836	11.45	70.78	17.77
	2455	2.5	45866	10.34	73.73	15.93
Other	27070	All	521720	11.25	71.77	16.98
Post MI	2688	All	55267	12.64	73.48	13.88
Tissue valves	9546	All	168602	10.81	70.20	18.99
	4829	2.5	89764	10.89	74.35	14.77
	4113	3	66545	11.48	64.09	24.42
Mechanical Valves	101114	All	1784796	12.10	67.10	20.80
	23597	2.5	496394	11.30	74.44	14.25
	63572	3	1055789	12.39	63.09	24.52
	3240	3.25	45409	13.14	59.96	26.90
	1754	4	21052	14.80	59.14	26.07

Time in range related to the therapeutic target INR

The results show a relationship between the target INR for each patient and time in range. As the target INR increases the time in range decreases and the time below range increases.

Table 3. Time in range related to target INR.

Target INR	Number of tests	Days on treatment	% time above range	% time in range	% time below range
All	560359	10774798	10.76	73.00	16.24
1.75	1136	26538	19.73	76.41	3.86
2.25	16684	341065	12.57	80.29	7.13
2.5	430139	8574126	10.39	74.76	14.85
2.75	12768	228893	10.39	70.26	19.35
3	90852	1494035	12.09	62.85	25.06
4	8780	110139	14.41	55.94	29.65

Time in extended INR range

Previous studies have suggested that the INR does not need adjusting if it is within the range 1.8 to 3.2 (for patients with a target INR of 2.5) and that treatment is safe within this range. We analysed our data and these shows that the INR is within the extended range 88.4% of the time.

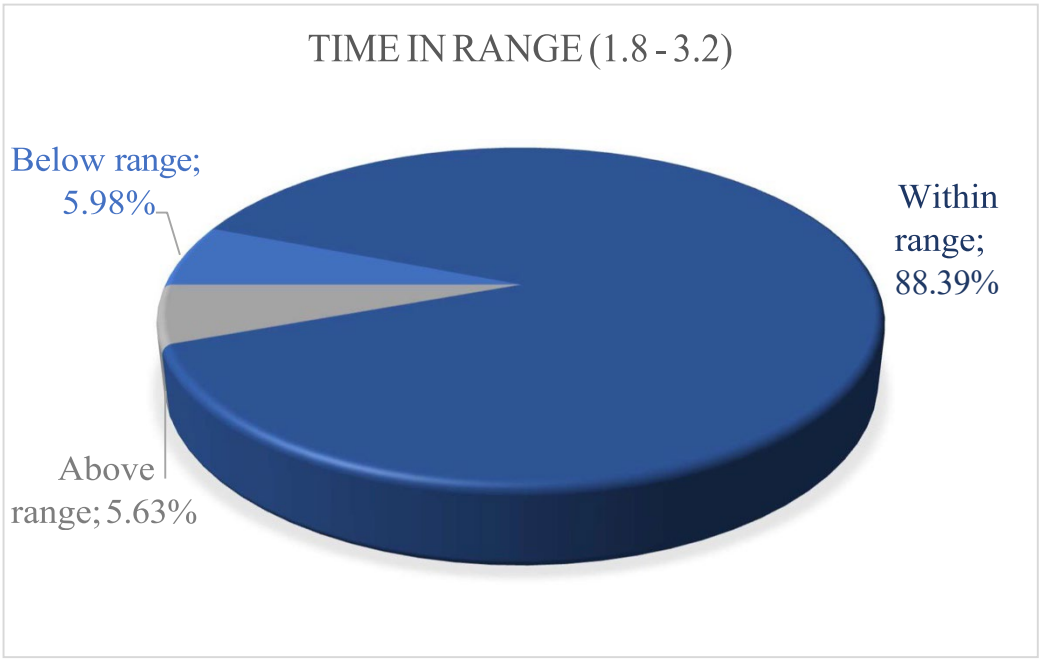

Figure 3. Time in INR range 1.8 – 3.2 for patients with a target INR of 2.5. Data based on 430,139 tests. On treatment for 8,574,126 days.

Time in range for individual patients

The time above, within and below the therapeutic range was calculated for each patient. The number of patients with a TTR >60%, >70%, >80% and >90% was calculated. The analysis was performed for all patients and for those on treatment for at least 6 months.

Table 4. Proportion of patients with time above a specified time in range (all patients)

Percentage time in range	Number of patients	% of patients
>60%	8003	79.4
>70%	5998	59.5
>80%	3020	30.0
>90%	733	7.3

These results show that 79.4% of patients have INR results in range more than 60% of the time and this increased to 83.2% when limited to patients who had been on treatment for at least 6 months.

Atrial fibrillation (Target INR 2.0 to 3.0)

In patients on warfarin for atrial fibrillation, 82.8% had the INR within the therapeutic range more than 60% of the time, and 86.4% in those patients who had been on treatment for more than 6 months

Total 5915 patients, 5249 on treatment for more than 6 months.

Table 5. Proportion of patients on warfarin for atrial fibrillation with time above a specified time in range.

Percentage time in range	All patients. % of patients	Patients on treatment more than 6 mths. % of patients
>60%	82.8	86.4
>70%	63.5	66.3
>80%	32.3	32.9
>90%	7.3	6.1

Distribution of time in range for patients on warfarin for atrial fibrillation

We calculated the time in range for each patient and plotted them in order on the graph below. This shows the distribution of results with over 83% with TTR above 60%.

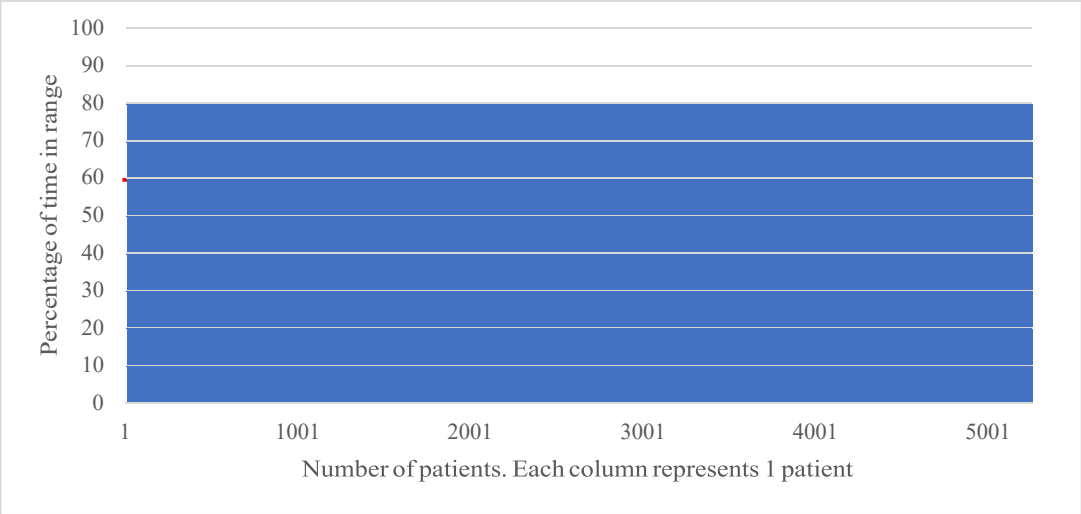

Figure 4. Distribution of TTR for all patients on warfarin for atrial fibrillation on treatment for more than 6 months.

Control over time

The main question from this study was to see if the high level of anticoagulant control achieved in the pilot study was maintained over time as the service expanded. We calculated the time in range for each year based on all INR results performed in that year. The days on treatment for each year ranged from 1.6 million in 2015 to 2.4 million in 2019. The time in range remained constant at approximately 73% for all 5 years studied.

Table 6. Time in therapeutic range for all patients for each year during the study period.

Year	Number of patients	Days on treatment	% time below range	% time in range	% time above range
2015	5539	1651037	17.2	72.6	10.3
2016	6281	1976579	16.4	73.2	10.4
2017	6892	2208865	16.1	73.4	10.4
2018	7294	2362889	15.6	72.5	11.9
2019	7616	2413569	15.8	73.8	10.5

High INR results

Another assessment of control is to measure the proportion of high INR results.

The graph below shows the distribution of INR results for all patients collected during the 5 year study period

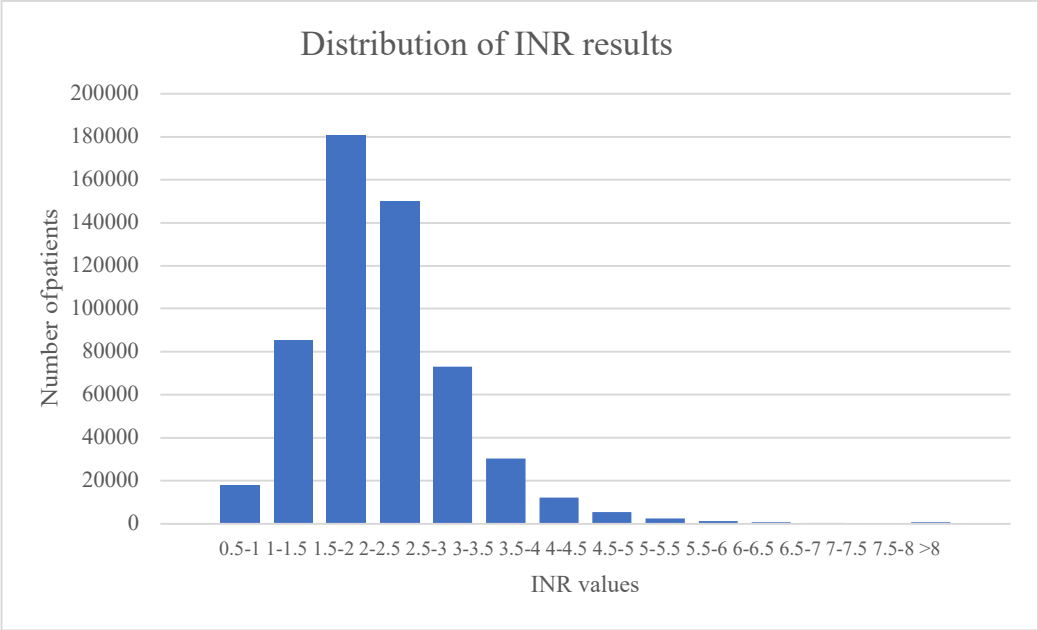

Figure 5. Distribution of INR results over 5 years

Table 7 . Percentage of INR results above a specific INR value

INR value	Percentage
>4.5	2%
>6.0	0.4%
>8.0	0.02%

In patients on warfarin the risk of bleeding is related to the INR. The bleeding risk is low when the INR is below 4.5 but rises as the INR increases. In our series only 2% of INR results were above 4.5 and only 0.02% above 8.0 (the highest value recorded on the CoaguChek device used in CPAMS).

Pharmacy Numbers

164 Pharmacies have treated patients over the last 5 years. The number of patients currently (December 2019) on treatment at each pharmacy range from 6 to 115 (Figure 6). There is a steady turnover of patients starting and stopping warfarin over time, therefore the total number of patients seen by each pharmacy over the 5 year period is higher (Figure 7).

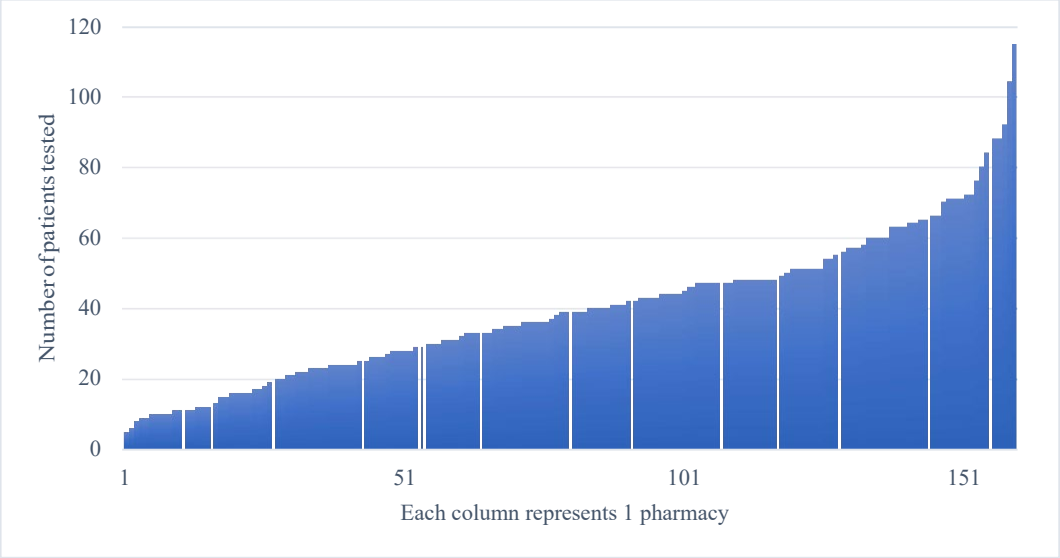

Figure 6. The number of patients undergoing INR testing at each pharmacy in December 2019

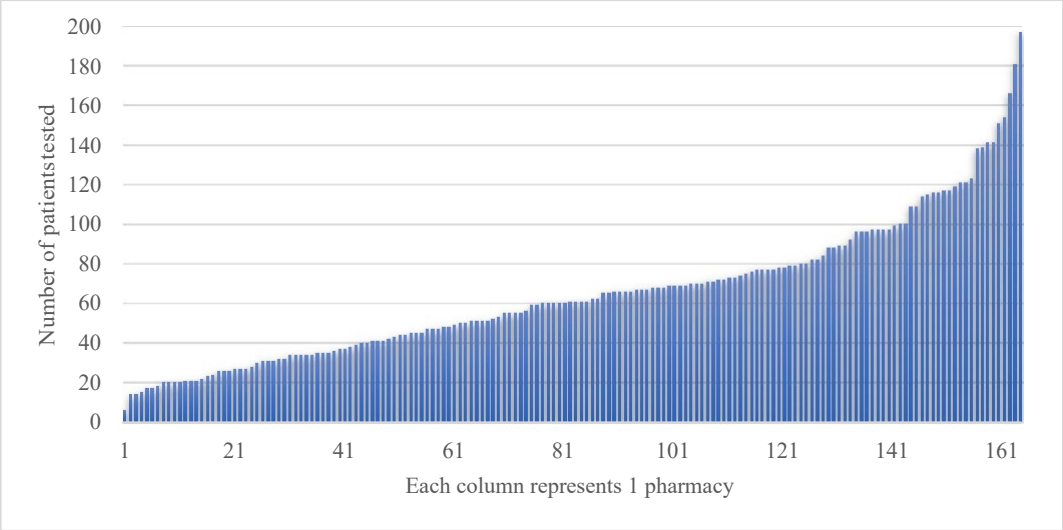

Figure 7. The total number of patents managed at each pharmacy over the 5 year study period.

Tests per patient per month

The average number of tests per patient each month was calculated from the total number of tests performed in that month divided by the total number of patents tested during that month (blue line in the graph). This tends to give a higher than expected result as the number of patients tested in any month is lower than the number of registered patients. To correct for this, we took data from the monthly reports provided to the Ministry of Health and used the registered number of cases and calculated the average number of tests per patient in each pharmacy each month and reported the median of these results (orange line on graph). This is a closer estimate of the rate of testing per patient per month for the whole population.

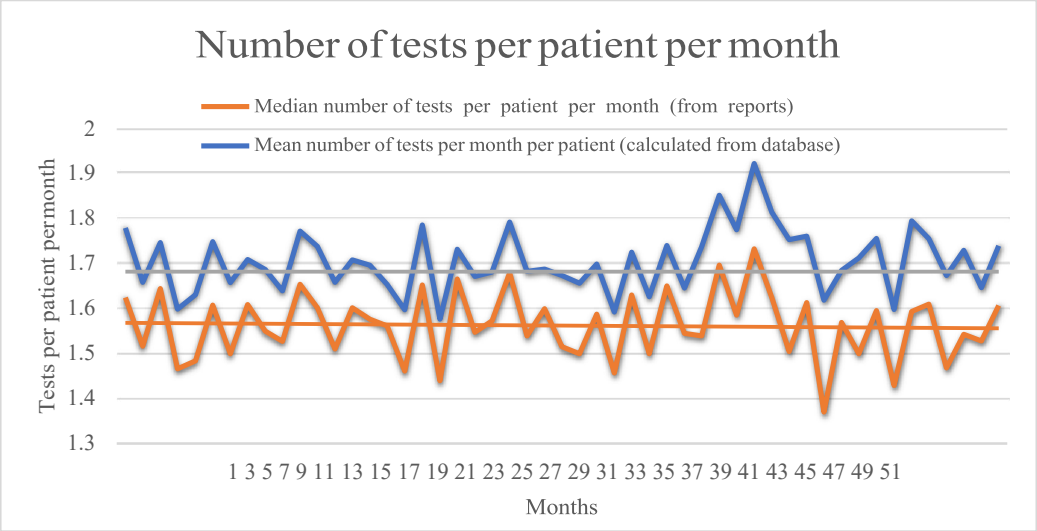

Figure 8. The number of tests per patient per month. The blue line shows the mean based on all results with the trend line showing a value around 1.7.

Discussion

Warfarin Control

The Community Pharmacy Anticoagulant Management Service is now well established in New Zealand available through more than 160 pharmacies. Over 10,000 patients have used the service at some point in the last 5 years with over 6600 currently managed by pharmacists. The number of patients using the service has increased during the study period but has shown only a small rise over the last 3 years.

The results of this review show that patients on warfarin managed through CPAMS achieve good anticoagulant control with the INR results within the therapeutic range 73 % of the time, and that this level of control was consistent over the 5 years of the study period. Control was best in patients who had a target INR of 2.5; largely patients with atrial fibrillation and venous thromboembolic disease (DVY/PE). Whereas patients with a higher target INR of greater than 3.0, had poorer control with the TTR below 70% but in the majority was still above the recommended 60%. The poorer control was largely in patents with mechanical valves where there was a clear correlation between the target INR and the level of control. These patients had a higher proportion of time with the INR below the therapeutic range.

From International guidelines the target INR for atrial fibrillation and VTE is 2.0 – 3.0, however it has been shown previously that patients with an INR between 1.8 and 3.2 have a low risk of thrombosis or bleeding and that the INR does not need to be adjusted when in this range. Our results show that the INR for the population studied was within this range for 88% of the time.

The TTR of 73% is based on pooled data from all patients, but an alternative way to assess control is to measure the TTR for each patient. This showed that 79.4% of patients had INR results within the therapeutic range more than 60% of the time. These data include patients who recently started treatment when warfarin control can be unstable. If these cases are excluded and we only evaluate patient who have been on treatment for at least 6 months, the level of control improves to 83.3% with results in the therapeutic range more than 60% of the time. In the subgroup of patients with atrial fibrillation and a target INR of 2.5, an even higher proportion of patients (86%) achieved good control.

Bleeding is the major complication of warfarin treatment and is directly related to the INR. The risk of bleeding is relatively low when the INR is below 4.5 but increases rapidly above this point. Another assessment of warfarin control is to measure the proportion of high INR results. In our series only 2% of INR results were above 4.5, 0.4% above 6.0 and in over half-a-million tests, only 95 (0.02%) were over 8.0.

Pharmacy Management

When CPAMS was introduced there was no definitive advice on the number of patients each pharmacy should manage, but to maintain experience it was suggested that a pharmacy team should manage a minimum of 10 patients regularly. The maximum number was also not fixed but around 70 patients was thought to be the upper limit manageable. Our results show the number of patients currently managed through each pharmacy varies considerably from less than 10 patients to those with over 150. The pharmacists experience is wider than these results show as there is a regular turnover of patients. Our data for the whole 5-year period shows that over 50% of pharmacies have managed over 60 patients during this time.

The frequency of testing was also an unknown when the program began. The need for testing varies considerably between patients, those with stable control can be managed with a test every 4 to 6

weeks whereas unstable patients may require testing every few days. Earlier audit data had suggested that the testing rate averaged out at 1.6 to 1.7 tests per patient per month and it would be reasonable if CPAMS achieved this rate. There were concerns that testing may be more frequent at the outset as pharmacists had less experience than doctors, however our data show that the rate of testing has remained highly consistent over the whole study period at around 1.6 tests per patient per month.

Concerns were also expressed at the start of the service that pharmacists would only be managing stable patients and that complex cases would remain under the care of the GPs. Although we do not have definitive data on this, anecdotal reports from pharmacists confirm that many pharmacies manage all the patient within their region including complex and unstable cases.

Strengths of the study

The main strength of this study is that it is a large complete data set; we have all the results for over 10,000 patients managed over 10 million days. All patients are managed in the same way. All pharmacists undergo the same training have an assessment exam prior to managing patients and use the same decision support software.

Limitations of the study

Measuring the time in therapeutic range is an indirect measurement of warfarin control. The ideal is to measure the frequency of bleeding episodes and thrombotic events to truly measure control, but these data are difficult to collect. There is a definite correlation between the time in range and warfarin complications and a link between the risk of bleeding and high INR results, but they remain surrogates to the actual complications of warfarin.

This study was not designed to examine the efficacy of the decision support software or to assess how frequently the software was over-ridden by the managing pharmacist.

Conclusion

This review confirms that CPAMS provides an efficient service with safe anticoagulant control where the time within the therapeutic range is greater than 70% for the total population and more than 80% of patients would be classified as having "good" anticoagulant control. This level of control was maintained over the 5 years of the study period. In addition, the proportion of high INR results is low. This level of control is higher than seen in many published international studies.

Using a pharmacy bases service is a highly effect way to manage warfarin patients. In many respects, pharmacists are the best people to manage this treatment; they are highly trained and undergo specific training for this service, they have experience of medicines management and understand the potential drug interactions. Another strength is that they perform the test themselves which gives them an opportunity to develop a close relationship with their patients and gauge the patient's compliance and understanding of their treatment. This enables the pharmacist to make appropriate dose adjustment with all the relevant clinical information.

Our data also shows that individual pharmacies can manage more patients than initially proposed with some having over 100 patients in their care.

I believe that CPAMS could be the standard of care for warfarin management in New Zealand. At the end of 2018 approximately 28,000 patients were regularly taking warfarin. This number has probably dropped during the COVID pandemic as doctors were advised to change patients to the new oral

anticoagulants where possible to reduce the need for bloods during the lockdown. Currently CPAMS manages over 6600 patients and this number could easily be increased two or three -fold to deal with over 20,000 patients. This would remove the burden from laboratories and general practitioners and provide a standardised closely supervised service.