Pharmacist Medicine Management Review Services

A Case for

Medicine Use Review (MUR)

Medicine Therapy Assessment (MTA)

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EXECUTIVE SUMMARY

Medication is a central part of any health system, but medicines will not have their most beneficial effect for patients unless they are optimally prescribed and patients taken them as prescribed. . Less than optimal prescribing and failures in adherence to the prescribed medication regimen have been found to cause a substantial amount of illness in the population and treating such illness absorbs considerable health system resources. Services which improve the appropriate use of medication have the potential to benefit patients directly, by improving their health status, and indirectly, by freeing up health system resources for more productive uses. New Zealand research has found that 13% of all hospital admissions are related to adverse medical events, and that approximately 1.5% of all hospital admissions are related to drug therapy problems originating in the community.

This business case addresses aspects of a proposal from the Pharmaceutical Society of New Zealand for Medicines Use Review (MUR: intended to improve patient adherence to medication regimes), and Medicines Therapy Assessment (MTA: intended to improve prescribing of complex combinations of medicines). Using a sample of six kinds of medication which are particularly likely to have specific adherence and interaction problems a patient population of 516,238 people in New Zealand was identified of which 291,000 people were receiving 5 or more medications in total. Of the total population analysed, 133,070 people had at least one hospital admission and on average a little more than 2 admissions each, generating 277,250 admissions in one year . Within this population, the people more likely to be receiving a large number of medications, and therefore most likely to have difficulty with adherence or drug interactions, were Maori, Pacific Island people and the most deprived.

The new pharmacy services framework provides DHBs with an opportunity to address this significant problem of poor management of medication. Cost and workforce constraints suggest that any new services should be tightly targeted to maxims the potential to benefit at a patients and a system level. An approach to targeting the services is suggested in the business case, which identified almost 40,000 people taking 14 or more medications who generated 72,038 hospital discharges in one year and 386,049 bed days: an average length of stay of 5.4 days in each hospital episode. This sub-population was identified by working back from an estimate of the number of people who could be managed under Medicines Use Review nationally in the first full year of the programme. The analysis finds that providing the intervention to 39,487 people on the six signal medications who are each receiving more than 14 different medications in total could potentially reduce hospital admissions by 1,081 (1.5%), with an estimated 5,791 hospital bed days being freed up for alternative use. Benefits which have not been quantified in this analysis include potential reductions in average drug cost, and improved quality of life for patients. At $125 per review, this intervention gives a cost of $4,568 per admission avoided. This is a conservative estimate of benefit, in that it considers only a sample of medications, and only measures hospital admissions as a benefit. It is expected that DHBs will modify their targeting based on local population needs , in this context it is worth noting that the analysis indicates a direct association between numbers of medications and likelihood of hospitalisation. Each additional medication is associated with a 5% increase in the risk of hospitalisation . This is an association useful for targeting not a cause and effect relationship.

Given that prescribing is a core primary care activity, and that primary care infrastructure will be necessary to provide the information to target the population for these services, MUR and MTA should be closely aligned with existing services which are intended for similar high need populations such as Care

Plus, Chronic Disease Management and Services to Improve Access. The move to integrate pharmacy professionals into the primary care team is consistent with the direction of the Primary Health Care Strategy, and represents an opportunity to develop PHOs into broader multi-health professional organisations.

Contents

BACKGROUND

Current pharmacist services have developed over time based largely on the supply function of pharmacy. A new service framework has been developed focusing on opportunities for pharmacist to add further value in the primary health care sector. These new services fall into two broad categories ; health information and medicine review. This document focuses on the implementation of medicine review.

In October 2006 the Pharmaceutical Society of New Zealand presented a paper to the Minister of Health outlining the new pharmacy service framework with the five levels of services developed by a Working Group on behalf of DHBNZ. This framework and its development is described in a later section. The purpose of the paper was to discuss the implementation of the framework and propose a model which was consistent with the Primary Health Care Strategy and the role of PHOs.

The discussion identified that the service framework has no specific funding attached and adoption by the DHBs would be dependent on their acceptance that the services have a clinical and financial benefit.

It was agreed that a business case needed to be developed to:

- Consider approaches to implementing the service.
- Estimate the benefit of implementing the service in terms of cost consequences.
- Propose approaches to monitoring and evaluating the service.

The business case was not intended to be a formal cost benefit analysis in terms of cost utility, quality of life etc, as this would be a substantial and specialised task.

As part of developing the business case it became apparent that the issue of identifying the population who will benefit most from the services is intimately related to the problem of targeting the service. For pragmatic reasons the business case narrowed its scope to focus on the implementation of the Medication Use Review and Adherence Support Service which is likely to be the most widely used service in the initial implementation. Realistically, the number of medication reviews which can be delivered is likely to be much less than the maximum number of patients who could benefit. Therefore criteria will be needed for identifying those who will receive the greatest benefit. These criteria will enable DHBs to estimate the number of Medication Use Reviews that will deliver the greatest benefit for their populations. The same criteria will also provide a basis for evaluating the effectiveness of the implementation.

A literature review was undertaken to identify areas where the evidence of benefit is the strongest . This review indicated that the most quantifiable benefit was reduction in hospitalisation and that certain medications and combinations of medications were most likely to lead to a higher risk of hospitalisation. The approach taken in the analysis is to identify a number of medications which are likely to cause side effects and interactions (which we will call ‘signal medications’), and to examine the total medication and hospitalisations of patient populations receiving these signal medications. Criteria are then applied to progressively narrow down the number of patients at greater risk of poor health outcomes and/or hospitalisations to whom a medication review service can be applied.

SERVICE FRAMEWORK DEVELOPMENT

The new service framework was developed after a review of services currently funded by DHBs, work done by pharmacy organisations and services from other countries.

The results of the review were considered by a reference group which included representatives from:

- Consumers.
- PHOs
- DHBs (both funder and provider arms)
- Pacific People.
- Maori
- Community Pharmacy
- General practice

This group identified a number of value added pharmacy services beyond those which are already being provided:

- Enhanced access to medication (both delivery and extended prescribing)
- Enhanced access to information for the patient (costs, adverse reactions, “Yellow cards” or patient medication information summaries, and advice).
- Enhanced access to information for the prescriber (medication history, admission liaison, cost-effectiveness, adherence feedback)
- Enhanced integration with other providers, with other professional cultures, consistent messages, and aligned incentives
- Enhanced medication management reviews, active medication management, chronic disease partnerships, mobile services, improved admission/discharge interface, and targeted health education.

The final framework consists of two types of service: information services and medication review services.

SERVICES

There are five individual services in the framework that fall into two categories :

Information Services

- *Health Education:* Education provided directly to patients.
- *Medicines and Clinical Information Support:* Information for practitioners (this will include the pharmacist facilitator role currently provided by many PHOs).

Medicines Review Services

- *Medicines Use Review and Adherence Support:* A four part review which assesses the patient's use, understanding and adherence to their medication regimen. This service has been aligned with the NZ Pharmacy Council competency standards and titles.
- *Medicines Therapy Assessment:* A comprehensive clinical review of an individual patient's medication as part of a multidisciplinary team.
- *Comprehensive Medicines Management:* Case based active management of prescribing changes and (in the future) collaborative prescribing

These new service areas aim to achieve the best outcomes from medication, to encourage multidisciplinary working, and to foster primary-secondary integration. The services will be prime tools for ensuring that individual patients and the New Zealand taxpayer receive value from pharmaceutical expenditure.

The Pharmacy Council is in the process of developing standards for *Medicine Therapy Assessment* and *Comprehensive Medicines Management* services. These standards will incorporated into the framework, which will be updated when they are reviewed. It is expected that the standards will be reviewed every two years, as the services evolve.

The services proposed in the new framework are not replacements for the clinical obligations which are currently part of the process of dispensing pharmaceuticals. These are additional and advanced clinical services which provide a much more comprehensive and ongoing clinical pharmacy service.

IMPLEMENTING THE SERVICE

Medication Use Reviews are existing service components in other countries such as Australia, the UK and the US. They are delivered in a variety of ways and locations utilizing different configurations of pharmacist and prescriber input. It is clear that both the prescriber and the pharmacist need to be involved and need to support the delivery of the service. Several overseas approaches, such as the Australian model, explicitly incorporate general practice and pharmacist involvement in the service delivery.

In the context of health service delivery MUR are still a very new service and there is limited literature to support their effectiveness. This is partly because some of the positive impact will only appear over the long term and will therefore be hard to measure, and partly because the actual nature of the service being delivered tends to vary substantially so comparison becomes difficult. In a later section we discuss evaluation criteria that can be used to assess the effectiveness of the implementation of this service in New Zealand and also identify some health outcomes. In this section we make some recommendations for DHBs to consider on the elements of the service model implementation that we believe will increase the likelihood of success.

WORKING WITH CONSTRAINTS

Potential constraints to uptake that DHBs will have to contend with include;

- Pharmacy workforce capacity
- Cost of service delivery
- General practice engagement and support

The service model adopted to support the implementation of the service framework needs to address these constraints, work within the context of the current workforce configurations and move the sector forward . This presents an opportunity to promote enhanced collaboration between pharmacists and general practice which would have a flow on impact on other key areas such as over-all medication use and chronic condition management .

LINKAGES WITH EXISTING SERVICES

As identified from international experience and historical local experience a constructive relationship between the pharmacist and the prescriber is an important component of a successful medicines review service. It is intended that pharmacists will provide these new services in a way that is consistent with the direction of the Primary Health Care Strategy. PHOs are the main vehicle by which the Primary Health Care Strategy is being delivered, the PHO role is to manage the continuity of service for their population by making sure that either they or other providers deliver services to their enrolled population in a coherent, cohesive way that reduces the risks of either gaps in service delivery or inefficient duplication of

effort. By connecting closely with PHOs in the implementation of these services the opportunity for collaborative engagement between the prescriber and the pharmacist can be facilitated.

This alignment with PHOs, delivered either by incorporating the services into the PHO Agreement or by other means determined locally, provides an explicit process for linking the new pharmacist services to:

- An enrolled population thus facilitating
    - demographic targeting
    - patient tracking
    - continuity of care
    - access to information
    - collection of data for evaluation and on-going targeting refinement
- Existing PHO funded services thus providing additional support for targeting and access to funding streams to support the prescriber aspect of the intervention e.g.
    - CarePlus
    - Chronic Care Management
- Existing PHO services that provide additional opportunities to provide specific support for the patients or to reduce specifically identified barriers to access i.e.
    - Services to Improve Access Programmes
    - Primary Mental health services
    - Services targeted at supporting Maori or Pacific people
    - Community workers and other types of community based support services.

Linking the new services to PHOs also increases the role of community governance and provides direct access to mechanisms for community engagement processes. Alignment with PHOs would provide direct conduits for the delivery of information services to prescribers, and will ensure access to the enrolled population, diagnostic and prescribing information necessary to provide services to individual patients.

COMPETENCIES AND PROFESSIONAL SUPPORT

The Pharmacy Council of New Zealand has launched a Medicines Management Competence Framework and Competence Standards for Medicine Use Review. Competence Standards for Medicine Therapy Assessment are under development. These standards are supported by a training programme currently being provided by the New Zealand College of Pharmacists. At a local level we expect to see pharmacist delivering the service being able to access support and advice as required.

ACCESS TO THE SERVICE

Analysis has identified a large number of people who could potentially benefit from a Medicines Review service. But realistically service delivery will be constrained by a combination of workforce capacity and cost. It therefore becomes important to ensure that service is delivered to those people for whom there is likely to be the greatest benefit. The specific targeting required to ensure the greatest value is gained from the service investment dictates that referral processes and criteria need to be well defined. The analysis conducted as part of this business case has provided an approach to demographic targeting criteria which will facilitate this process. Alignment with PHOs ensures access to the patient population information necessary to direct services to those who will receive the greatest benefit. Explicitly involving the general practice in the referral decision making process ensures early engagement with the prescriber, tight targeting and patient access to additional support services. This also opens up the possibility of PHOs employing/contracting pharmacists to deliver these services as part of a broader primary health care team.

The analysis undertaken in this business case also identifies key populations that will experience the greatest benefit and are also likely to offer the greatest economic gain to the DHB. Included in these populations are patients in residential care facilities. Anecdotal reports identify admissions from residential care as a specific issue for secondary care institutions. Evidence also supports that poor medication management in this population increases a number of risks including the risk of falls leading to fractured neck of femur. This would support ensuring that the residential care population are included in the populations to which the services are delivered. Other populations likely to benefit include Maori and Pacific people on multiple medications - specific mechanisms need to be utilised to identify and target these people who are at high risk of poor outcomes.

RISK MANAGEMENT

Financial and Targeting Risk

The workforce capacity to deliver is estimated to grow from 10400 units in the pilot year to 150,000 to 200,000 by Year Three of implementation, (ie from $1.5 million to $18 to $27 million) The initial analysis identified more than 500,000 people on complex and potentially risky medication regimens. This highlights the need to carefully target the service to the highest priority patients.

This is best achieved by aligning the service closely with the PHOs which have the patient population information necessary to direct services to those who will receive the greatest benefit. This alignment could also allow the devolution of service and financial risk management and oversight to the PHO management infrastructure. This reduces the need for DHB staff to directly oversee the service and ensures that the organisation monitoring that the service is being delivered to the target population is also the organisation with the access to the information to assess the effectiveness of the targeting .

Clinical Risk

During the process of any medication review, pharmacists may identify potential prescribing issues that need to be addressed. They have an obligation to bring these issues to the attention of the prescriber through a referral type process. The prescriber needs to take account of this advice and make an active decision about any actions that need to be taken . In the follow-up consultations the pharmacist will have an opportunity to actively follow-up these issues and assure himself/herself that they have received active consideration. If appropriate the pharmacist will ensure that the patient's current stock of medication matches their changed prescribing regimen at the follow-up appointments. This process will require good communication between prescriber and pharmacist.

At this point in the development of these services the prescribing decision and accountability remains with the prescriber, the pharmacist's accountability is to ensure that the prescriber has access to all relevant information.

It cannot be over-emphasised that any proposed changes to medication need to be carefully implemented and the consequences monitored. In this complex population this can be an intensive process and although the service contemplates subsequent visits with pharmacist, additional visits to the general practice are also likely to be required. This again highlights again the need to align with PHO services such as CarePlus, Chronic Care management or acute demand management .

Engaging PHOs and general practitioners in the process provides further opportunities to address the significant risks created by multiple disconnected prescribers which have been identified by BPAC and reported in this document .

Strategically, this service may actually provide a mechanism which can be used to encourage PHOs to further develop multi-professional governance arrangements (in cases where they have hitherto been slow to progress in this direction). Since the service is targeted and patient specific, even small PHOs will be able to manage it.

RESEARCH EVIDENCE

Medicine use review is a relatively recent innovation internationally. Therefore there is limited research upon its implementation and cost effectiveness, and there are problems with interpreting some research findings, particularly if the intention is to apply them to a New Zealand context which may be different from the original environment. But such findings as there are may still have a bearing upon New Zealand services, so long as interpretation is careful and measured. This review does not seek to provide a comprehensive last word on issues to do with drug related morbidity and medicines use review, but aims to identify the main themes in international and New Zealand research literature. Medline was the principal source for identifying abstracts, although some government reports and similar publications were identified by the PSNZ.

BURDEN OF DRUG RELATED MORBIDITY: INTERNATIONAL STUDIES

Adverse drug reactions have been found to be common events in a number of settings. Several US authors have reviewed research in the field, leading to specific estimates of the burden of the problem. Lazarou found that adverse drug reactions (ADRs) which were serious enough to cause hospitalisation, permanent disability or death had an incidence of 6.7% of hospitalised patients, and that ADRs were from the fourth to sixth leading cause of death in the US (Lazarou, Pomeranz et al. 1998). Ernst used decision analysis techniques to estimate that the total burden of ADRs in the US was US$177 billion, of which nearly 70% was accounted for by hospital costs (Ernst and Grizzle 2001).

In a comprehensive review of studies White produced a somewhat lower estimate of the US burden of ADRs, at $130 billion, but provided specific estimates of the consequences of ADRs in different clinical categories (White, Arakelian et al. 1999). Therapeutic groups considerd in this paper which are particularly relevant to primary care management include analgesic agents, antibacterial agents, anticoagulants, cardiovascular drugs, psychotropic drugs (in particular antidepressants), and respiratory agents. US commentators have called for the establishment of an office of drug safety in order to deal with these issues (Moore, Psaty et al. 1998).

While not considering the absolute burden of disease, a recent US study has considered the impact of patient adherence to medication regimes, and found that adherence to statin or beta blocker therapy had a highly statistically significant association with subsequent mortality, although this effect was not observed for some other classes of drugs (Rasmussen, Chong et al. 2007). This direct association of adherence to outcome complements the frequent finding, summarised in a review by DiMatteo, that adherence to prescribed medication is often poor, and that the non adherence rate in the US is 24.8% (DiMatteo 2004). Simpson, in a review, found that good adherence was also associated with improved mortality outcomes, even when adherence is to placebo medication (Simpson, Eurich et al. 2006). This research therefore concludes that there is a ‘healthy adherer’ effect, in which adherence is associated with a wide range of healthier behaviours.

The US research consistently shows that the burden of adverse drug events is large on a population basis, and that hospitalisation cost is a substantial component of the cost arising from such events. While the US health system is unique in a number of important respects, and US evidence alone would not

necessarily translate to a New Zealand context, research in a number of other countries has found similar results. German researchers have estimated that 5.8% of hospital admissions are directly related to ADRs, and that approximately 30% of ADRs were preventable (Goettler, Schneeweiss et al. 1997).

A more specific study finding from Sweden shows similar overall levels of adverse reaction. Backstrom showed that, considering patients who had been admitted to hospital for haemorrhage and thrombotic diagnoses, 7.9% were probably a consequence of ADRs, of which only 14% had actually been identified as such (Backstrom, Mjorndal et al. 2004). This extreme level of under reporting of ADRs is qualitatively consistent with reports from the US and elsewhere.

A recent UK study found that 6.5% of hospital admissions had some component of ADR, with the drug problem leading directly to admission in 80% of those cases (Pirmohamed, James et al. 2004). The estimated annual costs of such admissions in the UK were estimated at £466 million. The agents found to be most commonly implicated in such hospitalisation events were aspirin, diuretics, warfarin and non steroidal anti-inflammatory drugs. However ACE inhibitors, antidepressants, beta blockers and digoxin also had an effect. The incidence of fatal ADRs in this study (0.15%) was estimated to cause approximately 5700 patient deaths per annum in the UK, and was similar to the US finding reported in Lazarou. The authors of this study proposed that reviewing prescriptions, computerised prescribing and the involvement of pharmacists in assessing prescribing behaviour could substantially reduce the burden of ADRs.

A different UK study has also found that 6.5% of hospital admissions are drug related, with prescribing and patient adherence to medication regimes the two most common factors (Howard, Avery et al. 2003). The drug groups most commonly implicated included NSAIDs, antiplatelets, antiepileptics, hypoglycaemics, diuretics, inhaled corticosteroids, cardiac glycosides, and beta-blockers. A very recent systematic review by the same group found that more than half of ADR related hospital admissions were associated with antiplatelet drugs, diuretics, NSAIDS and anticoagulants (Howard, Avery et al. 2007).

Finally, an Australian review of 14 previous studies found that 2.4-3.6% of all hospital admissions were related to drug problems in some degree, with a higher proportion for elderly patients(Roughead, Gilbert et al. 1998). The drug groups typically involved had much in common with the UK and US studies, including cytotoxics, cardiovascular agents, antihypertensives, anticoagulants and non-steroidal anti-inflammatory drugs.

Overall, international research on the frequency and nature of drug related adverse reactions shows a reasonably consistent picture. The burden of disease is substantial in terms of the direct cost of health services required to treat such illness, and a number of commonly prescribed drugs, including cardiovascular drugs, NSAIDS and possibly antidepressants are frequently implicated in such problems. Both medical prescribing and patient adherence to medication regimes are likely to be factors in this considerable burden of illness.

INTERVENTIONS TO REDUCE ADVERSE DRUG EVENTS

The aim of reducing ADRs has resulted in a variety of attempts to use the expertise of pharmacists in order to improve prescribing and adherence. Medicine Use Review (MUR) is an approach that has been developed in a number of settings, although Zermansky has pointed out that the precise definition of MUR, the nature of the intervention and the outcomes examined often make the evaluation of pharmacist interventions difficult to interpret (Zermansky and Freemantle 2007). At a wider level, evaluation of this type of programme can be beset by the commonly observed difficulties of measuring the effects of a complex intervention in a real health service setting (Campbell, Fitzpatrick et al. 2000; Campbell, Murray et al. 2007).

While there has been little evaluation of pharmacist services (of this type) in the US, two studies provide relevant information. Yuan found that targeting high risk patients with additional pharmacist services would decrease mortality and reduce hospitalisation rates by as much as 60% (Yuan, Hay et al. 2003). This was an intensive and highly targeted intervention, in which two intervention programmes were compared to a control group of normal care. Another US study, using previously published data for a novel cost effectiveness analysis, found that providing additional pharmacy care would be highly cost effective at a level of US$2100 per life year, well within usual thresholds for choosing cost effective health interventions (Etemad and Hay 2003). This finding is clearly subject to limitations, as the authors acknowledge, but if the result is correct within an order of magnitude it still indicates a worthwhile health intervention. This is one of the few studies which attempts to estimate benefits in terms of anything other than direct health service resources.

Medicines Use Review has been established in the UK as part of pilot medicines management programmes since 2002, and were rolled out more widely in 2005 (Department of Health 2005). While these services have not been in existence long enough for widespread evaluation, some research is emerging which considers the effectiveness of these schemes in a UK setting.

A well designed randomised controlled trial of pharmacist involvement in reviewing medication was conducted in Scotland in 2001 (Krska, Cromarty et al. 2001). The population was patients over 65, with four or more medications and two or more chronic diseases. The results showed that pharmacists were effective in identifying prescribing issues in the patient population, and in reducing identified problems at followup. The study was too small to measure outcomes with statistical significance, but found a reduction in emergency hospital admissions in the intervention group although this did not meet conventional levels of statistical significance. Direct drug costs neither increased nor decreased for the intervention group.

Among other researchers in the UK, Zermansky and Freemantle have conducted two studies of pharmacist intervention to improve prescribing for the elderly. A randomised controlled trial of pharmacist consultations with patients aged 65 or over found that those patients who had been reviewed had more frequent corrections to their prescribing by GPs, and had a slower rate of increase in prescribing costs during the year of followup (largely as a consequence of having medications stopped) (Zermansky, Petty et al. 2001). The second study from these authors specifically considered patients in care homes. It again found that pharmacists made changes to patient medication, and that there was a statistically significant decrease in falls among patients who had been reviewed. There was a decrease in

hospitalisation among reviewed patients, but this did not attain statistical significance (Zermansky, Alldred et al. 2006).

There has been one major study of medication review in the UK which produced negative results. The HOMER trial of medication review in a home setting found that the service actually produced higher levels of hospitalisation and mortality than the control group(Holland, Lenaghan et al. 2005). This study was widely criticised on methodological grounds when it was first published, and has subsequently been critiqued by Zermansky, who argues that it chooses a population with little to gain from the intervention, uses a weak form of medicine review and avoided measuring the outcomes where benefits was most likely (Zermansky and Freemantle 2007). The anomalous and deeply counterintuitive finding of this study mean that it should probably be disregarded.

A number of studies have considered interventions to improve adherence to medication, and several reviews of the literature have been published in recent years. Krueger concluded that, of several types of possible intervention, pharmacist review (termed 'comprehensive interventions') was effective in increasing adherence to medication, but that some followup component was necessary, while interventions should aim to target the underlying reasons for non adherence (Krueger, Felkey et al. 2003). McDonald found that the literature on adherence was not consistent enough to warrant meta-analysis, but noted that interventions which were successful seemed to be complex, with dimensions of more convenient care, information, counseling, reminders, self-monitoring, reinforcement, family therapy, and other forms of additional supervision or attention (McDonald, Garg et al. 2002). Finally, a very recent review has found that a number of interventions can improve adherence (including those that reduce dosing demands, and those that involve monitoring and feedback), but that the impact upon outcomes is difficult to measure (Kripalani, Yao et al. 2007).

Medication review services have been provided in aged care homes by Australian pharmacists since 1997. An evaluation of this service in 1999 did not report upon health outcomes, but provided survey data on the views of the service among care home nurses, GPs and the pharmacists themselves (Quality of Medication Care Group 1999). The evaluation found high levels of acceptance of the service among GPs and nurses, and recommended that additional education for pharmacists providing the service would continue to improve the quality of care.

Overall, the research on pharmacist interventions tends to find positive results. There is evidence that where pharmacists take part in medication review process measures of care often improve, including adherence, polypharmacy and levels of identified drug interactions. In light of this generally positive finding it is perhaps disappointing that few studies are able to relate these services directly to health outcomes. In the wider context of research on complex interventions, thought, this is less surprising than it might appear. Measuring direct effects upon outcome from a complex health service is a notoriously difficult exercise, and doing so within a randomised controlled trial design is doubly so. As alluded to above, randomised controlled trials often find relatively weak treatment effects as a consequence of the limited size and heterogeneous patient populations typically found in real treatment settings. The wider message of the body of research viewed here is that on process measures pharmacist review can certainly make improvements in patient care, and that on the balance of probability improvements can probably be made in patient health outcomes.

HOSPITALISATIONS IN NZ

Applying the findings of the international literature to a New Zealand setting is possible largely as a result of research carried in the past five years into medical error and hospital admissions. The overall finding of the research group was that 13.1% of all hospital admissions were associated with some sort of adverse medical event, of which about one fifth occurred outside hospital (Davis, Lay-Yee et al. 2002). There was an extremely strong age gradient in the admission rates, with older people more severely affected. The impact upon hospital resources was found to be considerable, with an adverse events adding an average of 9 days to patient stay in hospital. Internationally, this is one of a handful of studies which directly quantifies the impact of non hospital care upon hospital admissions. Overall, about half of the adverse events found in this study were considered to have been preventable, although the out of hospital events were specifically excluded from this analysis (Davis, Lay-Yee et al. 2003).

A more detailed analysis of results from this study found that of drug related adverse events, a much higher proportion (40.1%) originated from outside the hospital, and that cardiovascular drugs were by far the most common area in which an event took place. ACE inhibitors, diuretics and warfarin were all found to be important causes of adverse events. A high level of preventability was identified in the events measured, and the authors called for new approaches to drug prescribing and monitoring (Briant, Ali et al. 2004).

The results from this study showed that approximately 13% of all hospital admissions are related to adverse events, that one fifth of these were drug related, and that in turn 40% of these originate outside the hospital. This implies that something in the region of 1.5% of all hospital admissions are caused by drug related events which originate in the community. This can be considered to be the scope for gain in hospital admission which could be aimed for by improving the quality of prescribing in primary care. NZHIS reports a figure of 828,195 public hospital discharges in 2002/03. If a pharmacist intervention were to reduce admissions by as little as 0.7%, half the total scope for improvement, this would represent a freeing up of approximately 5,800 admissions for other resources. With an average of 7.5 days required by patients as a consequence of drug related adverse event, this would represent over 43,000 bed days per annum nationally. The magnitude of hospital admissions is such that a relatively small, marginal intervention can make a large difference in terms of absolute resources.

POPULATION RECEIVING RISK MEDICATIONS

The approach taken here is to identify a number of medications which are likely to cause side effects and interactions (which we will call 'signal medications'), and to examine the total medication of patient populations receiving these signal medications. Criteria can be applied progressively to narrow down the number of patients at greater risk, to whom a medication review service can be applied.

Demographic data (age, sex ethnicity and deprivation) has been requested for the full group of patients, but to date has only been received for patient who have had hospitalisations, analysed in the next section. More detailed demographics of patients receiving the signal medications will be provided as the data become available.

DATA EXTRACTION

The signal medications chosen for initial analysis were Proton Pump Inhibitors (PPIs), Antidepressants, Digoxin, Warfarin, and New Antiepileptic Drugs (NADs). Nonsteroidal anti-inflammatories (NSAIDS) were also examined, where NSAIDS are taken for a period of 6 months or more.

The rationale for choosing these medications is:

- Warfarin: a drug for which dose is critical, but which interacts with very many other medications which may change the strength of its effect.
- Digoxin: A drug for which dose is critical, which has a number of interactions, and which can cause serious consequences for the patient if not managed carefully.
- Antidepressants: several classes of antidepressants have important interactions with other medications. Patients with comorbid conditions may often require antidepressant treatment in the context of a complex medication regime.
- PPIs: Gastrointestinal side effects are a common consequence of many medications. PPIs are frequently used to treat the side effects of other medication, and may therefore be a signal that a patient is taking too many medicines, or that the doses are not optimal.
- Antiepileptic drugs: these medicines have a number of key interactions. Poor patient adherence to these drugs may lead to a high rate of hospitalisation.
- NSAIDS: where used chronically (for more than six months), these drugs carry high risks of side effects and hospitalisation. Classically, these drugs are likely to produce gastrointestinal problems which may subsequently be treated with a PPI.

Data were extracted on all dispensed medications taken by individual patients, who were taking at least one of the signal medications, in a six month period from 1 February 2006 to 31 July 2006. This period was chosen because it does not include the seasonal peaks and troughs of December and January, and does not include the period of peak prescribing for colds and influenza, which would be likely to increase the medicine count with drugs for acute medications.

Since the coverage of the National Health Index number on prescriptions is incomplete (estimated at 90%), some medications will be missed from this analysis. These results will therefore somewhat underestimate the true size of the population taking many medicines. A counterbalancing effect is that those patients who are taking many chronic medications are likely to be those with NHI numbers which are well used in the health system, and will probably have a greater than 90% coverage. Overall, this analysis is likely to provide a conservative estimate of the number of people who receive many medications.

Pharmac supplied data, under a confidentiality agreement, which identified the number and type of medication taken by individual patients. Individual patient NHI numbers were encrypted, and cannot be identified by the analysts. More details on the demographics and health utilisation of this patient population will be extracted in due course with the assistance of NZHIS.

The NSAID data extract was more complex. This identified a sample of patients where it was possible to estimate how many days of treatment had been prescribed. This extract is particularly dependent upon consistent use of the NHI at pharmacy dispensing in order to aggregate the number of prescriptions and identify the total amount of NSAID prescribed over a six month period. Patients taking this class of drugs were commonly found to be at risk of hospitalisation in several of the studies found in the research literature.

RESULTS

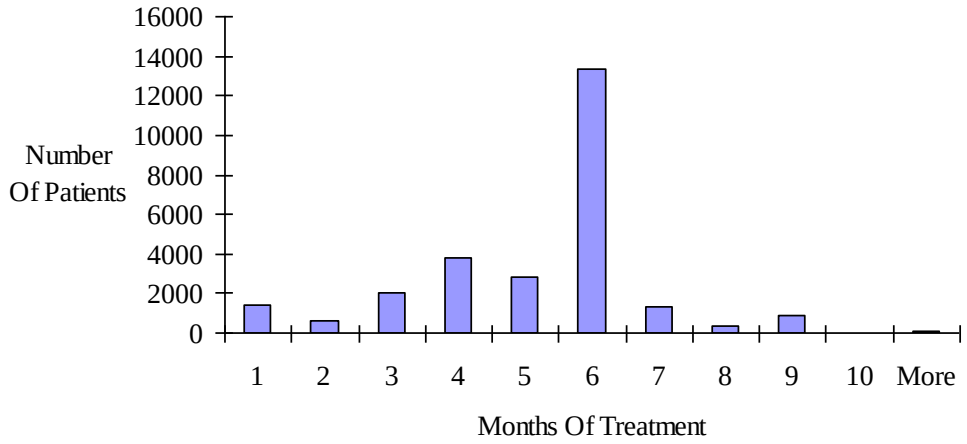
The numbers of patients taking each of the signal medications, and how many of these patients are taking high levels of medication, are shown in Table One. The result for all signal medications combined is not a straight sum of the individual drugs, since the patient groups overlap markedly between some of the drugs.

Table One: Patients Taking Signal Medications

Medication	***Patients***	***5+ Medications***	**10+ Medications**
Antidepressants	225,182	120,951 (54%)	52,457 (23%)
PPIs	280,250	178,961 (64%)	81,689(29%)
Digoxin	23,011	21,345 (93%)	12,625 (55%)
Warfarin	40,555	32,570 (80%)	16,394 (40%)
New Antiepileptic Drugs	61,912	39,310 (63%)	19,367 (31%)
NSAIDS 6+ months	20,795	15,990 (77%)	7,141 (34%)
All signal medications combined	516,238	290,846 (56%)	119,064 (23%)

Many patients were taking more than one of the signal medications. There are at least 519,434 patients in New Zealand who take one or more of these signal medications.

GRAPH ONE: DURATION OF NSAID TREATMENT



Appendix One includes graphs of the distribution of these patients on the number of medications they receive. Patients taking warfarin show a peak of medication use at around 7-9 distinct drug per patient. Patients taking antidepressants and PPIs show a more steady decline, but still with a fat tailed distribution with many patients taking 10 or more medications.

In addition to the five signal medications, the NSAID data provides an estimate of the number of NSAID patients taking the drugs for a long period of time. The graph below shows the distribution of time for which NSAID patients were identified as taking the drugs. Of 26,692 patients in the sample, 15,964(60%) took the drugs for the full 6 months. A small number of patients appear to be taking NSAIDS for more than six months, probably as a consequence of having treatments changed before one set of medication is completed (for example, a patient might return to the GP to seek more pain relief and receive a prescription for a new, stronger dose after trying the earlier dose and finding it ineffective). In any case, the data indicate that a high proportion of NSAID patients are taking the drugs for prolonged periods of time, and are therefore at risk of adverse events.

DEMOGRAPHIC CHARACTERISTICS

The population tree graphs in Appendix Two show the age and sex distribution of patients taking each of the signal medications. Overall women tend to appear slightly more often in this population than men, except for those taking antidepressants which are strongly dominated by women, and those taking warfarin, where men are slightly more common. There is clearly a strong age gradient in those taking digoxin, which women increasingly dominating at higher ages, probably as a consequence of better female survival at advanced age.

Table Two below shows the proportion of patients in ethnic groups on each of the signal medications. There are a notably lower proportion of Maori and Pacific Island people in the PPI, NSAID and Antidepressant groups, possibly indicating unmet need in these populations.

Table Two: Signal Medications By Ethnic Group

	Warfarin	Digoxin	PPI	Antiepileptic	NSAID	Antidepressant
Asian	1%	1%	4%	2%	2%	2%
European	77%	77%	75%	75%	79%	79%
Maori	11%	11%	5%	10%	6%	6%
Other	4%	4%	7%	5%	8%	7%
Pacific Island	3%	3%	3%	3%	1%	1%
Unknown	3%	3%	5%	4%	5%	5%

There are also deprivation gradients in these patient populations. Graph Two shows the deprivation profile for patients taking each of the signal medications. Not withstanding the differences in age, sex and ethnicity of patients taking the different medications, the deprivation profile is virtually identical, showing a distinct overall gradient towards the more deprived, with a sharp fall in decile ten, once again possibly indicating poorer access to the medications in the first place for those patients who are most deprived.

Poisson regressions on the total number of medications indicate the relative effect of the various demographic characteristics of patients upon polypharmacy in their treatment. Appendix Three gives detailed tables of results, but in summary, there is a strong relationship between increasing age and receiving larger numbers of medications, as might be expected. But the results show consistently for the signal medications that there is also a strong positive correlation between greater deprivation and polypharmacy, and that Maori and Pacific Island patients often have more medications than European patients. This finding is particularly interesting in light of the result that Maori and Pacific people are less likely than Europeans to receive some of the signal medications. The regression indicates that, once Maori and Pacific people receive these agents, they are more likely to be on a large number of medications. This implies that access to care may be poorer for these populations, but that once access is achieved quality of care may also be lower.

DISCUSSION

Overall, the population of patients receiving multiple medications is large. The precise distribution varies somewhat between the signal medications which have been chosen for this analysis, but in all cases there are a considerable number of individuals who are receiving many medications at once. In absolute terms the number of patients who might benefit from reviews of complex medication regimes is very large, and is almost certain to be greater than the number of reviews which can realistically be funded in a single year.

It is clear that polypharmacy is more common among population with greater deprivation, and among Maori and Pacific Island people, even where age is taken into account. This is a complex finding which could be interpreted in a number of ways, and which must be considered within the wider context of targeting primary health care services to populations with the greatest need. But this result does carry the implication that these demographic groups have a greater need for a service which will address the clinical risks which come with polypharmacy, and which will help patients to realise the greatest possible benefit from primary care services.

These results demonstrate that there is considerable scope for benefit from medication reviews, and imply that some form of targeting will be necessary in order to identify those patients who would be most likely to benefit from such a service.

HOSPITALISATION

Data on hospitalisation events were extracted by NZHIS for the one year period 1 July 2005 to 30 June 2006. Of the population taking the signal medications, 133,070 had had a discharge from a public hospital in the year for which data were extracted, accounting for a total of 277,250 hospital episodes.

The first analysis constructed a poisson regression model of hospitalisation, using a similar specification as the model for multiple medications, with the addition that total number of medications were now included as variable in the regression. The results are summarised in the table below.
Coefficients which are not significant at the conventional 5% level are shaded in grey.

Table Three: Predictors Of Hospitalisation

	Warfarin	Digoxin	PPI	Antiepileptic	NSAID	Antidepressant
Female (reference)	1.000	1.000	1.000	1.000	1.000	1.000
Male	1.015	1.105	1.223	1.144	1.173	1.232
Age	0.982	1.040	0.984	1.001	0.971	0.984
Age Squared	1.000	1.000	1.000	1.000	1.000	1.000
European (reference)	1.000	1.000	1.000	1.000	1.000	1.000
Asian	1.000	0.830	0.799	0.649	0.696	0.865
Maori	1.447	1.481	1.882	1.450	1.180	1.552
Other	0.496	0.446	0.417	0.373	0.378	0.375
Pacific Island	0.992	1.280	1.239	1.066	1.130	1.255
Unknown	0.647	0.524	0.372	0.387	0.400	0.378
NZDep01	1.016	1.009	1.027	1.022	1.023	1.030
Total Medications	1.046	1.039	1.057	1.046	1.050	1.056

This table shows some interesting changes from the results for number of medications. The direction of effect for sex is reversed, with men likely to receive more hospitalisations, but less likely than women to receive more medications. Maori generally tend to be admitted to hospital more often than Europeans, as is frequently the case for Pacific Island people, although several of the results for Pacific Islanders are not statistically significant. This is probably as a result of smaller numbers of people in this part of the data set.

In general, one additional medication is associated with about 5% more hospitalisation, and this result is consistent across all of the signal medication groups. It must be cautioned that this is an increase for the population on average, and that interpreting the association too narrowly for individual patients may not be valid. It must also be borne in mind that this result is association rather than causation – it is likely that sicker patients receive both more medicines and more hospitalisation, and it has not been possible to control for severity of illness in this analysis (in future analyses it may be possible to use techniques such as instrumental variables to take such effects into account).

However, it is clear that measures of the total number of medications are likely to be a good way to define a population which will use hospital services, and that this is the case for all of the signal medication considered here.

NZHIS provided diagnosis codes with the hospital discharge data. Table Four summarises the most common areas of diagnosis among patients for each signal medication. The high proportion of admissions in the "Factors influencing health status" category is driven by a small number of patients on regular

dialysis treatment, and a number of patients receiving chemotherapy. The admissions in the circulatory system category are dominated by myocardial infarction and angina related conditions. Congestive heart failure, pneumonia and COPD are also common causes of admission.

Table Four: Reasons For Hospital Admission

Description	Warfarin	Digoxin	PPI	Antiepileptic	NSAID	Antidepressant
Certain conditions originating in the perinatal period	0%	0%	0%	0%	0%	0%
Certain infectious and parasitic diseases	1%	1%	2%	2%	1%	1%
Congenital malformations, deformations and chromosomal abnormalities	0%	0%	0%	0%	0%	0%
Diseases of the blood and blood-forming organs and immune disorders	3%	4%	4%	3%	3%	3%
Diseases of the circulatory system	32%	29%	15%	8%	10%	10%
Diseases of the digestive system	6%	7%	12%	8%	9%	9%
Diseases of the genitourinary system	3%	3%	4%	3%	5%	5%
Diseases of the musculoskeletal system and connective tissue	4%	4%	6%	5%	17%	6%
Diseases of the nervous system	2%	2%	2%	9%	4%	3%
Diseases of the respiratory system	6%	10%	6%	6%	5%	6%
Diseases of the skin and subcutaneous tissue	2%	2%	2%	2%	3%	2%
Ear nose and throat	2%	3%	2%	2%	3%	2%
Endocrine, nutritional and metabolic diseases	2%	3%	2%	2%	2%	2%
Factors influencing health status and contact with health services	15%	13%	15%	14%	9%	14%
Injury, poisoning and certain other consequences of external causes	6%	6%	7%	10%	8%	10%
Mental and behavioural disorders	1%	1%	2%	9%	2%	6%
Neoplasms	5%	5%	8%	6%	8%	5%
Pregnancy, childbirth and the puerperium	1%	0%	1%	2%	0%	5%
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	8%	8%	11%	12%	9%	10%

TARGET POPULATIONS

The specific approach to targeting a population for this service is likely to vary from area to area. Some District Health Boards may find different patterns of polypharmacy and admissions in local data which would indicate more locally suitable approaches to service implementation. Here we give an example of an approach which might be followed to identify target population, access criteria and the potential benefit of the service.

Signal Medications

We identified six signal medications. These have a specific rationale, but other candidates for inclusion, in light of the research literature, could be diuretics, beta blockers, corticosteroids and antiplatelet drugs.

Hospitalisations

The table below shows the number of discharges in one year for patients on each of the signal medications, and calculates the number of discharges per 1000 patients. NSAID patients have been excluded here, since the data provide only a sample of NSAID patients, and not the absolute number on this class of drugs. In fact, this group of patients also has the lowest discharge rate per capita.

Table Five: Total Numbers Of Hospital Discharges

Medication	Discharges	Patients	Discharge Rate/1000
Warfarin	40485	40,555	998
Digoxin	23526	23,011	1022
PPI	175663	280,250	627
Antiepileptic	45518	61,912	735
NSAID	7902	20,795	380
Antidepressant	108984	225,182	484

RESOURCE AVAILABLE

In the case of a specific DHB area, a decision will have to be made about how much resource can be devoted to this service, and the capacity of local pharmacies to deliver the service will have to be taken into account. For the purpose of this example the national projections of how much service can be provided by the pharmaceutical workforce will be used, and it will be assumed that all of this service capacity will be funded. The PSNZ advises that MUR and MTA can be introduced in a stepped fashion, and predicts that training uptake will allow the volumes of service shown in Table Six.

For the purposes of the exercise we will assume that MUR costs $125 per person to deliver.

Table Six: National Capacity For MUR and MTA Services

	Pilot Year	Year 1	Year 3	Year 5
Number of MURs per week per pharmacy	2	2	5	10
Number of pharmacies	900	900	875	850
Number of pharmacy/cists doing MURs	100	390	514	515
% of Pharmacies doing MURs	11.11%	43.33%	58.74%	60.59%
TOTAL MURs	10,400	40,560	133,640	267,800
Number of MTAs per week per pharmacy			2	5
Number of pharmacies			875	850
Number of pharmacy/cists doing MTAs			514	515
% of Pharmacies doing MTAs			58.74%	60.59%
TOTAL MTAs			53,456	133,900

CRITERIA FOR MULTIPLE MEDICATIONS

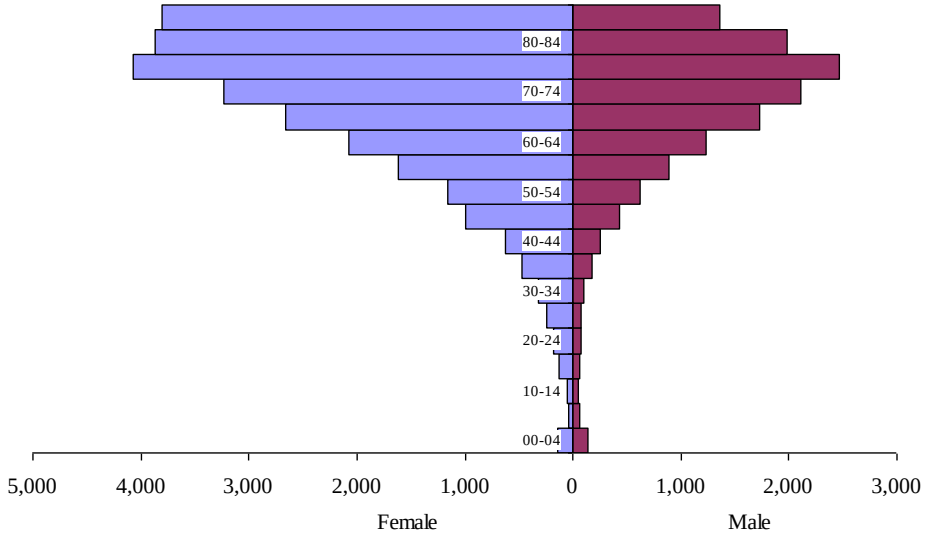
If the first full year of service assesses the care of 40,560 patients, this implies a cost of just of $6 million nationally to provide the service. Table Seven shows that setting a cut-off of more than 14 medications to access the service makes 39,487 people potentially eligible for MUR. This number is likely to be a slight underestimate, since imperfections in NHI linkage will not have identified all drugs for all individual patients.

Table Seven: Cumulative Number Of Patients On Multiple Medications

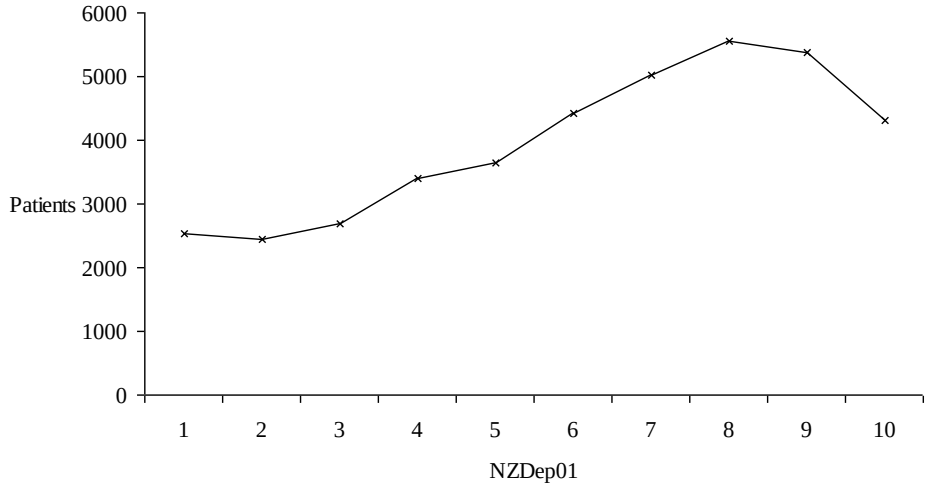
Total Medications	Cumulative Patients
20+	11861
19	15163
18	19281
17	24661
16	31248
15	39487
14	50041
13	62793
12	78068
11	96711
10	119064
9	145181
8	175022
7	209128
6	247690
5	290846
4	339525
3	393542
2	453641
1	516238

The demographic profile of this population tends to be older, female, and deprived. Graphs Two and Three show the age, sex and deprivation profiles of this population. There is a somewhat higher proportion of Europeans in this sub population than in the overall population for signal medications, (81% vs 75%), which probably reflects the predominance of older women on high numbers of medications.

Graph Two: Age And Sex Of People On >14 Medications



Graph Three: Deprivation Profile Of People On >14 Medications



COSTS AND BENEFITS

The hospital admission data shows that the 39,487 people receiving more than 14 medications collectively accounted for 72,038 hospital discharges in one year and 386,049 bed days: an average length of stay of 5.4 days in each hospital episode. Given the high level of hospital discharges in this population, we assume that enhanced pharmaceutical services could reduce admissions in the target population by 1.5% - a small proportion of the avoidable admissions in the population overall. In this case, the total number of admissions avoided would be 1081, corresponding to an expected 5,791 hospital bed days, which would become available for other purposes.

At a price of $120 per person per intervention, this implies a cost of $4,385 per hospital episode avoided in the population. Thus by implementing this service the DHB gains an immediate benefit in the same year by avoiding hospital admissions of 5.5 days on average. These benefits include increased bed availability for elective service delivery, avoidance of post-discharge costs and consequences in this high risk population, such as additional home support. A further effect which will reduce with lower hospitalisation, given the elderly profile of this population, is the increased risk of a hospital admission leading to a rest home admission.

In the medium term better medication management is likely to reduce the rate of further hospitalisations for this population, since their medical conditions will be better managed and the positive benefits of medications will be more fully realised.

This analysis considers only the benefit associated with avoided hospitalisations, since this is a resource which is readily quantifiable, and is an area in which both international and New Zealand research indicate the scope for improvement. But as well the as the benefits to both individual patients and to health services from avoiding unnecessary hospitalisations, there are a wide range of benefits which have not been explicitly considered here. This include increased benefits from adherence to medication, which will ensure that the assumed cost effectiveness of medical therapy is fully realised. Some of the international research which describes the magnitude of poor adherence has been referred to earlier in this document, but there is as yet little quantitative work which has been done on this issue in New Zealand. There is room for analysis of levels of adherence in New Zealand and this would not be a difficult to achieve, given the high quality of patient level data which is increasingly available in the New Zealand health system.

As well as the resource benefits to the system, no attempt has been made in this analysis to consider the benefit to the patient, in terms of improved effectiveness of medication and therefore improved quality of life. This would require complex forms of cost utility analysis, and it is likely that specific data would have to be collected prospectively from patients to establish preferences for different health states relevant to the question. Such an exercise is clearly beyond the scope of this analysis, but may constitute an interesting piece of applied research for investigators in the future. Quantifying the costs of poor medication management in formal cost utility terms would be internationally novel health economic research.

SERVICE EVALUATION

Research on medicines use review services is only emerging, and a clear framework for monitoring such services does not exist. But as with any new service funders will require assurance that the service is providing benefit, and doing so at a level that warrants the resources being placed in it. This section notes considerations which should be taken into account when setting up services and collecting information as the service proceeds.

PROCESS MEASURES

In setting up the service in a given area, process issues should be monitored. These will include:

- Completion of education and training for pharmacists seeking to provide the service.
- Links to local primary health care governance arrangements, and relationships between pharmacists and other professional groups in managing the service.
- Links to providers such as residential homes who are involved in identifying target groups of patients, and how such relationships are developed.
- How the process of referral works, and how effective it is from the point of view of patient, primary care provider and pharmacist.
- Patient satisfaction with the service.
- Any concomitant changes in the way that participating pharmacists manage the rest of their practice.

Process measures such as these are, by their nature, qualitative and are appropriately measured using questionnaires and interviews. Areas where the service is implemented earlier may be able to offer advice and expertise on these issues to other regions where there is later establishment.

As well as these qualitative measures, quantitative process measures which should be monitored include the total number of reviews conducted on a population basis, and how the uptake of these works out across patient demographic groups. These findings could be compared to uptake of other services, such as Care Plus and Services to Improve Access, since some uptake issues may exist in common across these activities.

OUTCOMES

Outcomes are always more difficult to measure, but there are at least two directly measurable outcomes which can be monitored for this service. These include hospitalisation subsequent to receiving the service and the number of medications received by the patient. In light of some of the measures published in research on utilisation review, it would also be appropriate to measure the average cost of pharmaceuticals for patients who have received the service.

These measures will need careful interpretation. The easiest measure is probably hospitalisation, since this service has been developed with the aim of targeting it to those at greatest risk of hospitalisation. Patients who have been reviewed could have hospitalisation data extracted from NZHIS for one year

before and after the review date. It may also be possible to match patients who have been reviewed to randomly chosen control patients with similar age/sex/ethnicity/deprivation characteristics in order to have a contemporaneous comparison against which to measure hospitalisation rates.

Similarly, the number of medications taken by patients may be measured in the year before and after review, and against randomly chosen comparison patients if desired. It should be noted that the raw number of medications taken by patients may sometimes appropriately increase after a review, as well as going down, so this indicator should be interpreted with care.

The average cost of medications easily can be measured from routine primary care data. Again, this indicator can go both up and down for individual patients, but in light of the research literature it could be expected to reduce slightly on average. This is because it captures cost reductions as a result of decreasing dose, as well as the sheer number of medications.

Finally, direct measures of adherence can also be calculated from standard prescribing data. Research literature often considers the proportion of days covered by dispensed prescriptions for an individual patients which, while not a perfect measure, is straightforward to calculate from prescribing databases. Trends in this measure for patients who have received the service (or not) would cast light upon the impact which reviews have upon patient adherence to medication.

As well as these outcomes, which can be measured from routine health system data sources without additional data collection costs, a formal evaluation might choose to repeat medication reviews upon a randomly chosen number of patients after one year. This would provide a check that the original medication issue has not arisen again, and flag any new medication issues that have arisen. This measure could provide an important check on the longer term effectiveness of utilisation reviews, and would be able to feed back into quality improvement processes for the service.

DISCUSSION

Internationally, recent years have seen emerging interest in medication review services of various kinds. Both the UK and Australia have implemented such services, while Health Maintenance Organisations such as Kaiser Permanente have experimented with medication review services in the US. New Zealand's current approach to exploring these services is thus consistent with international trends.

There is evidence from several countries that in some circumstances medication review services can reduce hospitalisation, reduce direct drug costs and improve patient wellbeing. These findings exist within the context of the substantial research results which indicate the magnitude of avoidable hospitalisations, and particularly avoidable hospitalisations which arise as a consequence of problems with medication in the community. New Zealand research produce results which are in line with international findings in this area.

So both service trends and research support the introduction of medication utilisation review services. Analysis of New Zealand prescribing data suggests that those patient populations who receive the greatest polypharmacy are the elderly, Maori, Pacific Islanders, and the deprived. It is well known that these populations are at risk of poor health outcomes in the health system, but this finding adds the result that they may also be receiving a lower quality of therapeutic care. Medicines use review therefore has some potential to address an inequality in care for those populations most in need of effective medication.

Given the target population for these interventions, medical utilisation review must be considered within the context of a range of services which are intended to improve access and quality of care for populations with the greatest need for health services. Care Plus, Chronic Disease Management, Services to Improve Access are now widely implemented in primary care, and have begun to produce information at the service level for identifying and targeting care to those with the highest levels of need. This is essentially the same approach which will be required to deliver medication review to high need patients and to ensure that the greatest possible benefit is achieved from the service, for both patients and health service organisations.

Given that medication review can be targeted to populations which will achieve the greatest benefit from the service, there is clear scope for benefits both in terms of resources to the health system, and in quality of life for individual patients. This analysis has made a conservative estimate of the benefits which could be achieved by implementing the service, considering only a sample of specific signal medications, and measuring only the number of potentially avoided hospitalisations which could be achieved in a relatively small target population. But even with this conservative approach to estimating the consequences of implementing the service, the balance of probability is that gains will be realised for both patients and health boards. The potential to free up hospital resources for other purposes carries substantial benefits, both for the patients whose admissions are avoided, and for the patients whose elective procedures are consequently delivered.

Medical utilisation review therefore has the potential to realise gains for a wide range of players, while developing new services in a way consistent with the principles adopted in the primary health care strategy. By building upon the infrastructure of primary care, and by improving the effectiveness of the

medications which are prescribed and managed in primary care, the interdisciplinary work of prescribers and pharmacists will generate the best results for patients.

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APPENDIX ONE: DISTRIBUTION OF PATIENTS TAKING MULTIPLE MEDICATIONS

Figure One: Distribution Of Medications For Patients Taking Antidepressants

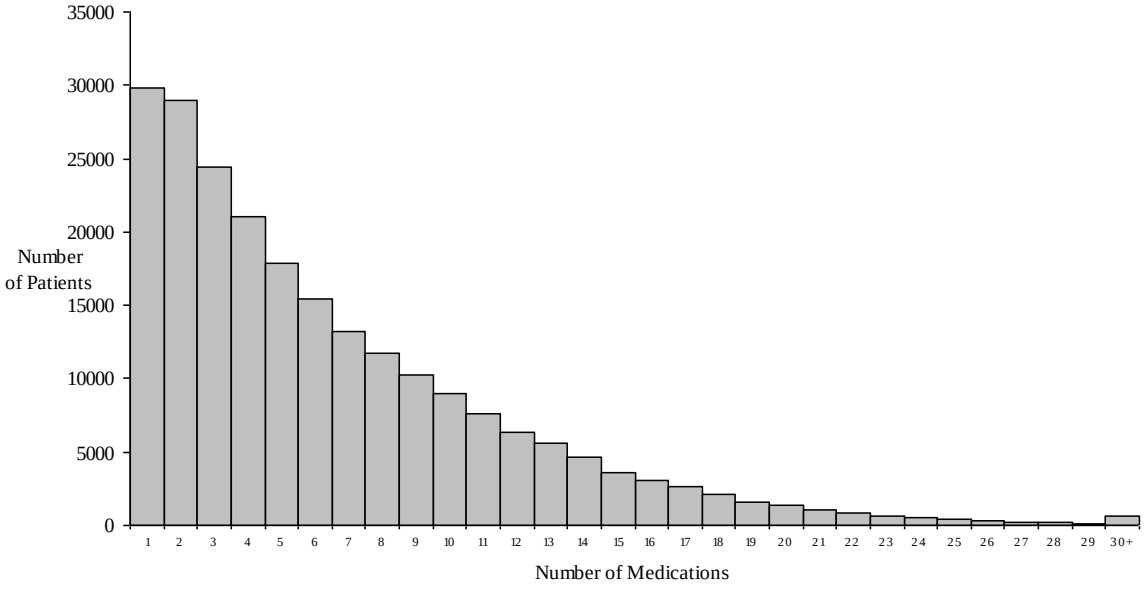


Figure Two: Distribution Of Medications For Patients Taking Digoxin

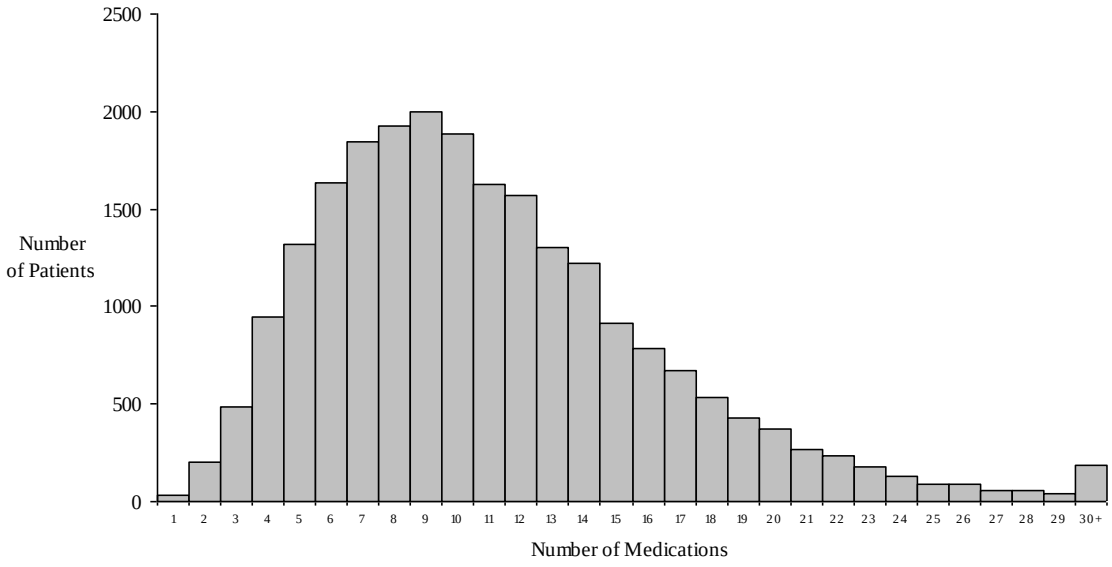


Figure Three: Distribution Of Medications For Patients Taking PPIs

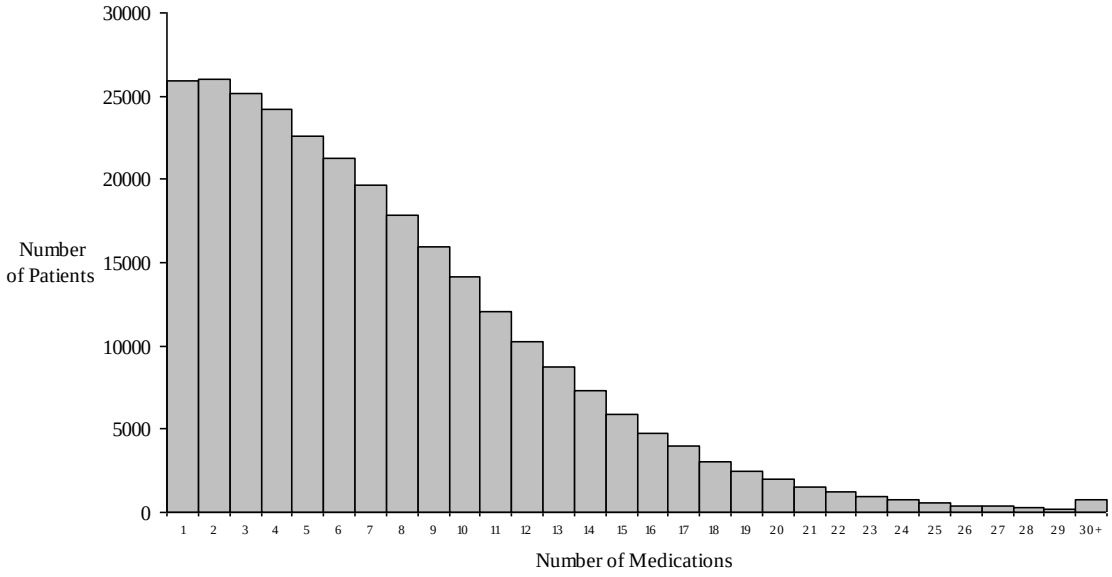


Figure Four: Distribution Of Medications For Patients Taking Warfarin

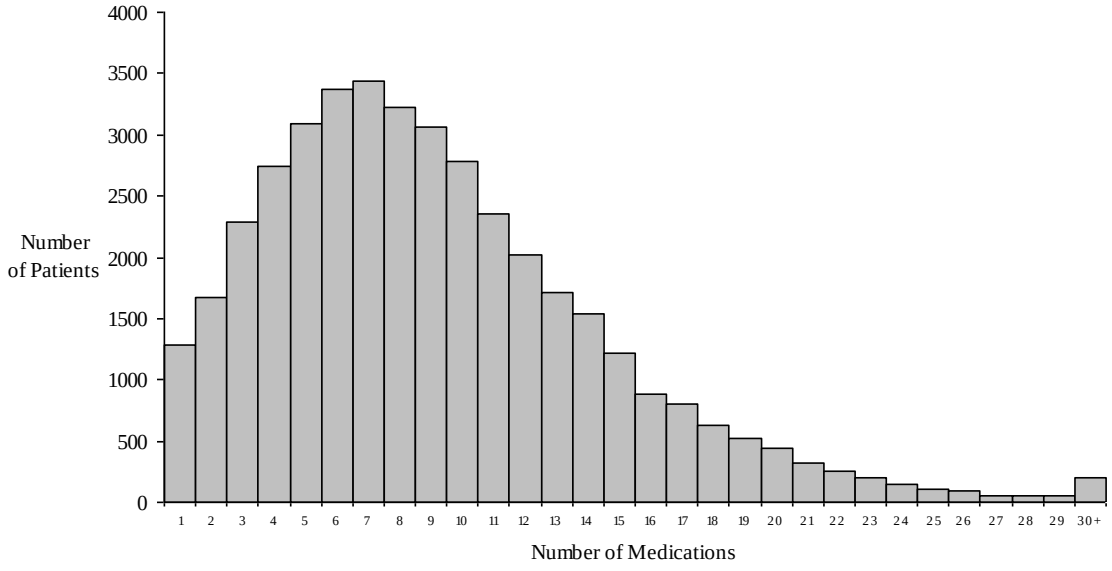


Figure Five: Distribution Of Medications For Patients Taking New Antiepileptics

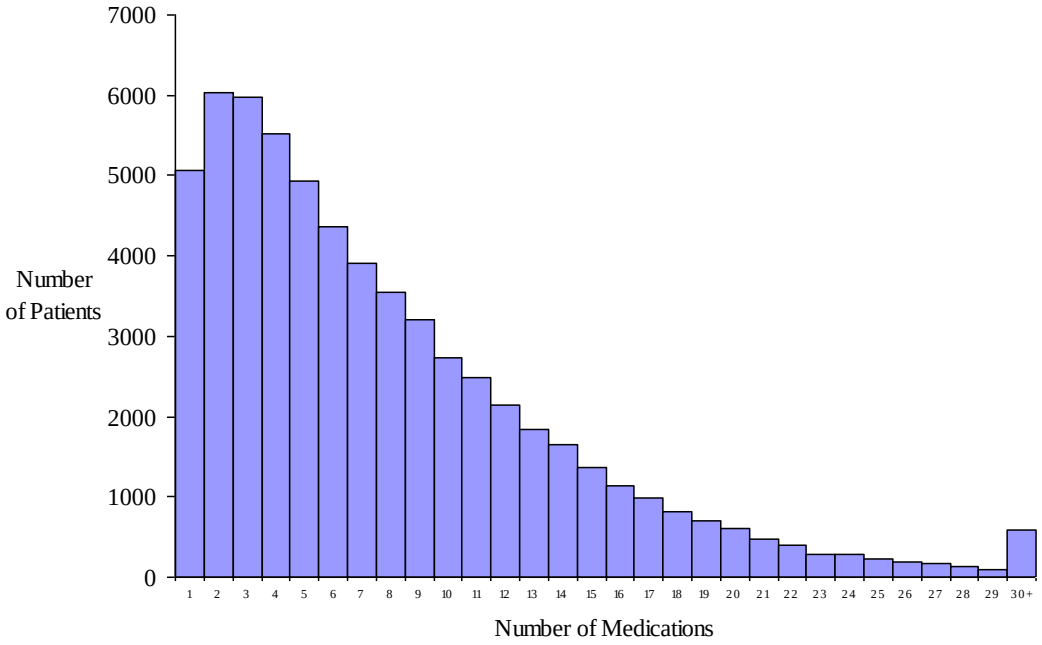
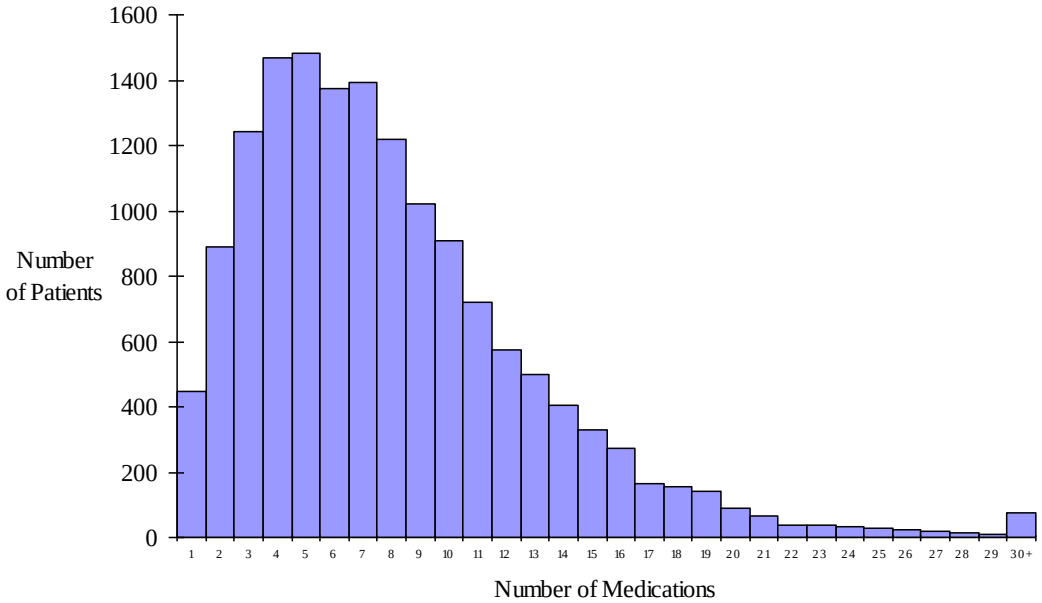
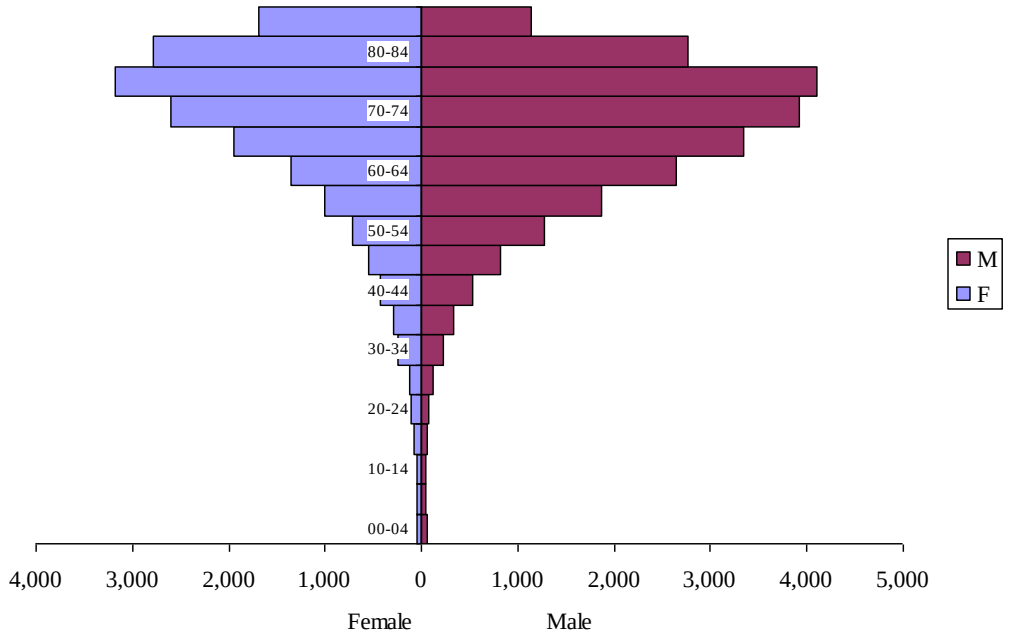


Figure Six: Distribution Of Medications For Patients Taking NSAIDS For 6+ Months

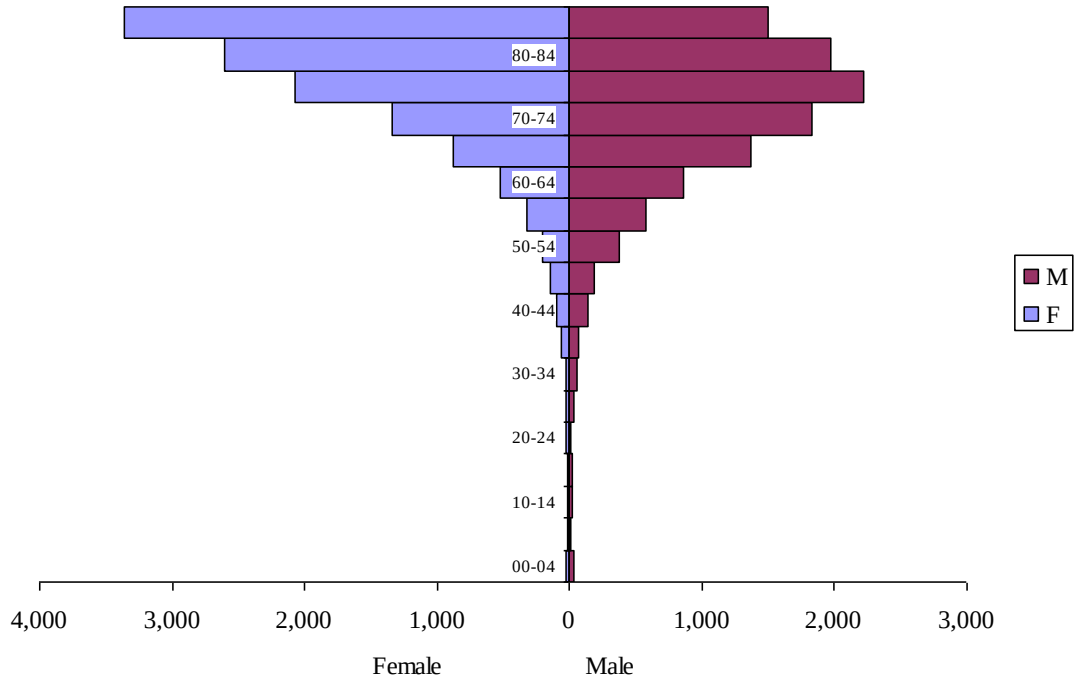


APPENDIX TWO: AGE AND SEX DISTRIBUTIONS

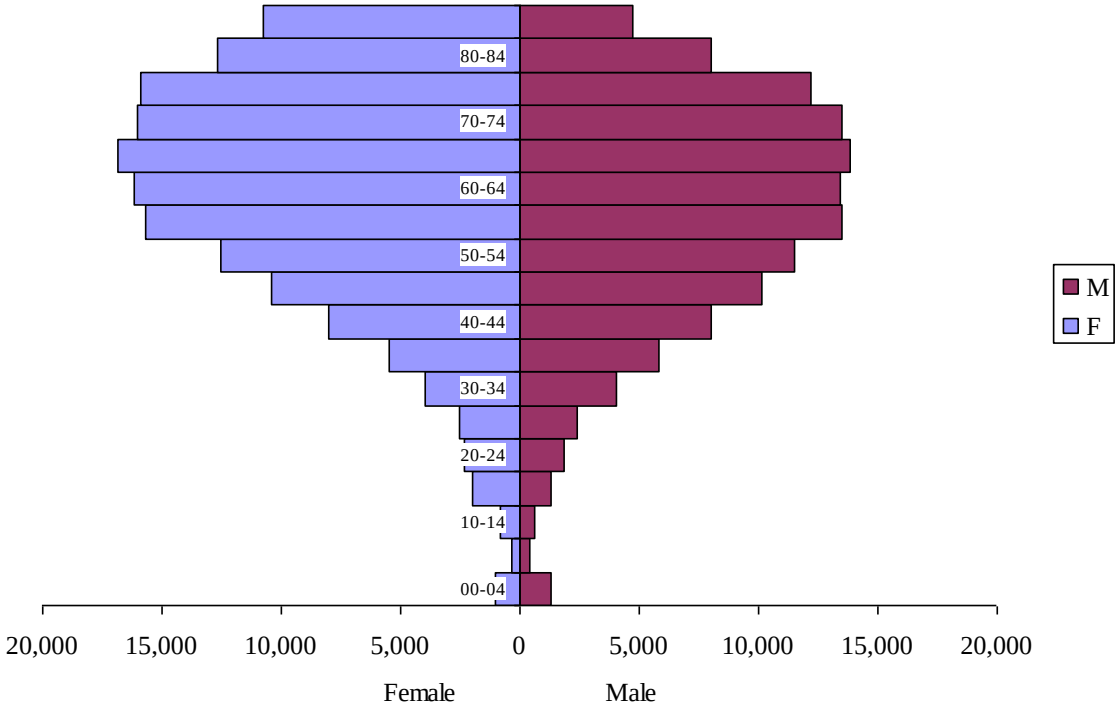
Graph One: Age And Sex of Warfarin Patients



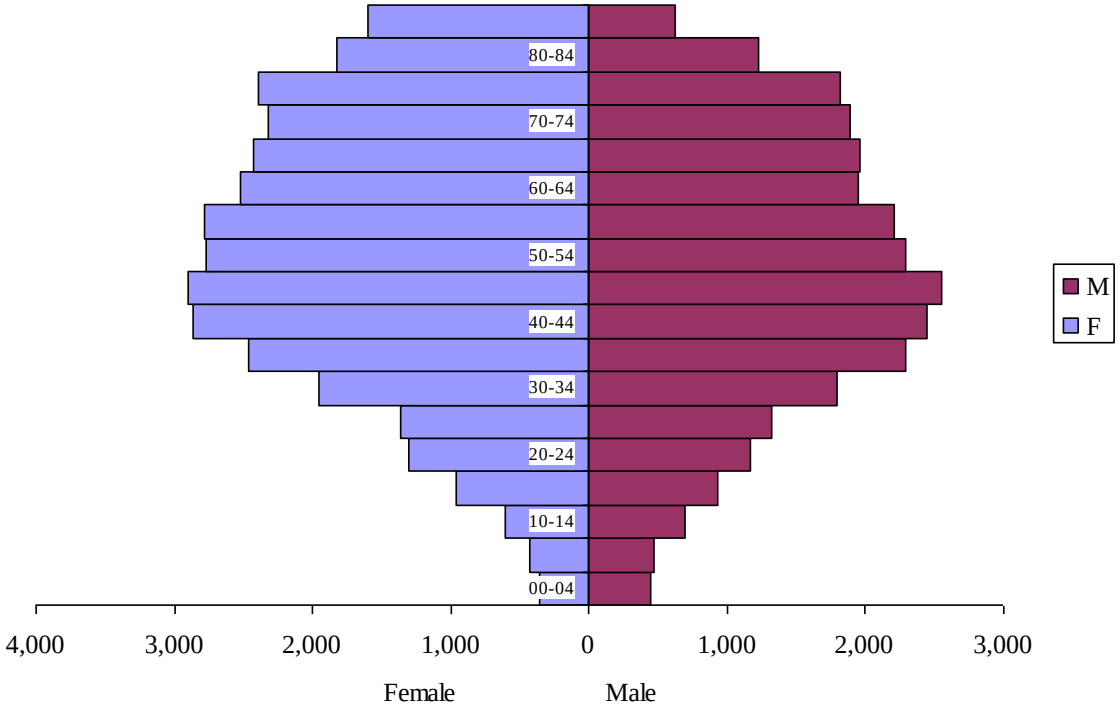
Graph Two: Age And Sex of Digoxin Patients



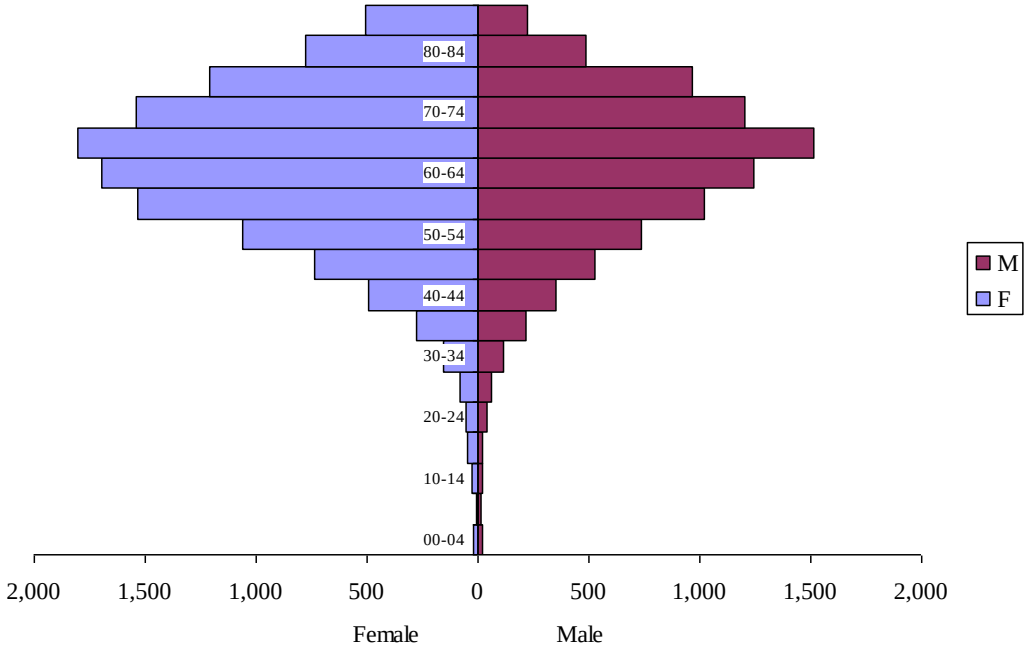
Graph Three: Age And Sex of PPI Patients



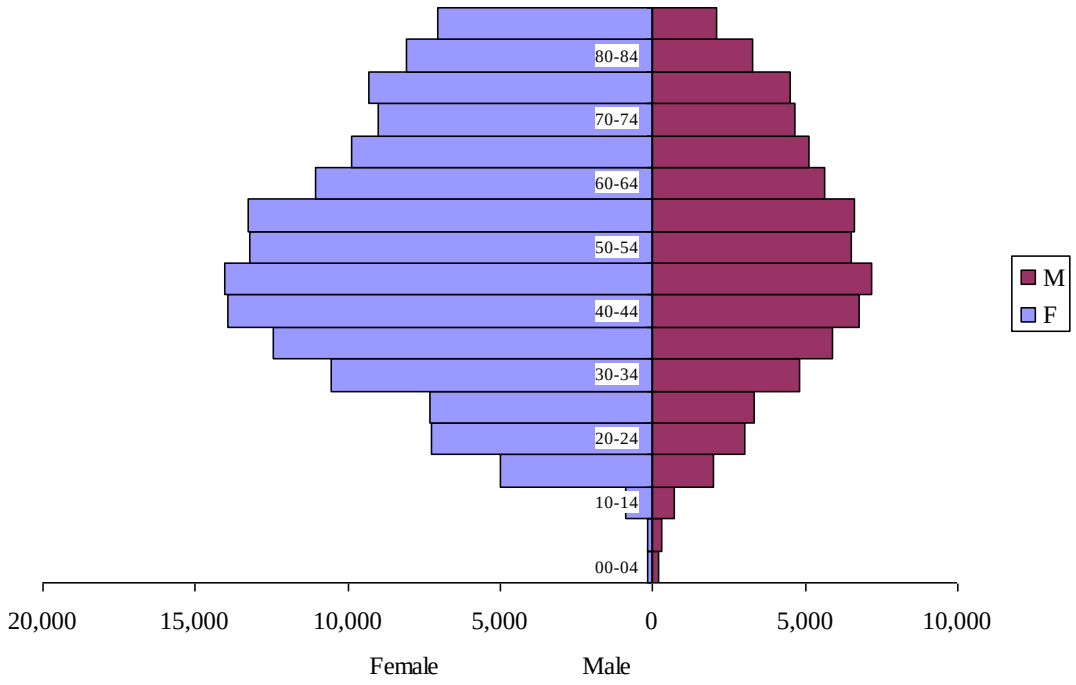
Graph Four: Age and Sex of Antiepileptic Patients



Graph Five: Age And Sex Of NSAID Patients



Graph Six: Age and Sex of Antidepressant Patients



APPENDIX THREE: NUMBER OF MEDICATIONS

MODEL SPECIFICATION

This analysis was conducted as a poisson regression upon the number of medications received by a patient. The regression was conducted with the *glm* command in R, using a quasipoisson function which provides an explicit estimate of overdispersion.

The data were originally supplied with five year age bands. Age was initially fitted as a categorical variable, which showed that there were extreme and discontinuous values for the small numbers of patients who were very young. For simplicity in the output, and to avoid the anomalous values for children, age was then modeled as a quadratic relationship, using the mid point of each age band as the age estimate for individual patients.

A version of the model was specified with interaction terms between ethnicity and deprivation, but these were not significant, and were dropped from the model.

Deprivation was modeled as both a categorical and continuous variable. The categorical fit showed a linear relationship across the 10 deprivation categories, and so deprivation was thereafter specified as a linear continuous variable, providing more concise output.

Sex and ethnicity were modeled as categorical variables, with Female and European chosen as the references respectively.

RESULTS

Warfarin

	Count Ratio	95% CI	
Female (reference)	1.000		
Male	0.867	0.857	0.878
Age	1.020	1.016	1.023
Age Squared	1.000	1.000	1.000
European (reference)	1.000		
Asian	1.074	1.020	1.131
Maori	1.152	1.129	1.175
Other	0.861	0.832	0.890
Pacific Island	1.154	1.113	1.196
Unknown	0.840	0.809	0.871
NZDep01	1.013	1.011	1.015

NB: The results are shown as a count ratio. This is interpreted as the difference in the number of medications for the group in question. For example, in this table Males tend to have 13.3 percent fewer medications than women. Maori and Pacific Island people both have 15% more medications on average than European people, and every increase of one year in age means an increase of 2% in the number of

medications. Because none of the 95% confidence intervals crosses the value of 1.000, all results in this table are statistically significant at conventional levels.

Digoxin

	Count Ratio	95% CI	
Female (reference)	1.000		
Male	0.929	0.916	0.942
Age	1.000	0.996	1.005
Age Squared	1.000	1.000	1.000
European (reference)	1.000		
Asian	0.990	0.926	1.057
Maori	1.011	0.987	1.035
Other	0.850	0.818	0.883
Pacific Island	0.983	0.942	1.025
Unknown	0.837	0.802	0.874
NZDep01	1.007	1.004	1.010

NB: Results which are *not* significant at the 5% level are shaded.

PPI

	Count Ratio	95% CI	
Female (reference)	1.000		
Male	0.865	0.860	0.870
Age	1.016	1.015	1.017
Age Squared	1.000	1.000	1.000
European (reference)	1.000		
Asian	1.128	1.113	1.142
Maori	1.248	1.234	1.262
Other	0.798	0.789	0.807
Pacific Island	1.228	1.208	1.247
Unknown	0.771	0.761	0.781
NZDep01	1.023	1.022	1.024

Antiepileptics

	Count Ratio	95% CI	
Female (reference)	1.000		
Male	0.871	0.860	0.881
Age	1.023	1.021	1.025
Age Squared	1.000	1.000	1.000
European (reference)	1.000		
Asian	1.091	1.046	1.138
Maori	1.050	1.027	1.074
Other	0.779	0.756	0.803
Pacific Island	1.016	0.973	1.059
Unknown	0.791	0.764	0.819
NZDep01	1.013	1.010	1.015

NSAIDS

	Count Ratio	95% CI	
Female (reference)	1.000		
Male	0.857	0.842	0.872
Age	0.988	0.984	0.993
Age Squared	1.000	1.000	1.000
European (reference)	1.000		
Asian	1.174	1.098	1.253
Maori	1.111	1.069	1.154
Other	0.808	0.779	0.837
Pacific Island	1.059	0.983	1.139
Unknown	0.804	0.770	0.839
NZDep01	1.011	1.007	1.014

Antidepressants

	Count Ratio	95% CI	
Female (reference)	1.000		
Male	0.945	0.938	0.951
Age	1.021	1.020	1.022
Age Squared	1.000	1.000	1.000
European (reference)	1.000		
Asian	1.224	1.199	1.248
Maori	1.222	1.205	1.238
Other	0.811	0.800	0.822
Pacific Island	1.279	1.246	1.313
Unknown	0.789	0.776	0.802
NZDep01	1.023	1.022	1.025