Pharmaceutical Society of New Zealand

Interim Report - literature review on the impact of medicines therapy assessment

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Introduction

1. Pharmacists can play a role in improving the medication adherence of patients and the ensuring optimised prescribing.

2. There is a continuum of possible intervention – from brief conversations around patient understanding of their medication regime, to thorough review of medications resulting in recommendations to GPs and prescription changes.

3. The focus of this analysis is on Medicines Therapy Assessments (MTA), which in the New Zealand Framework for Pharmacist Services (2007) is defined as a:

> *[...] clinical review of all current therapy where the Service Provider has access to full clinical notes and the interaction and intervention involves either or both Service User and prescribers e.g. participation in a multi-disciplinary team.*

4. MTA therefore goes further than educating the patient on medication use, and will, where appropriate, involve the pharmacist making recommendations to the prescriber to resolve any medication-related problems identified.

5. Of particular interest for this literature review is the evidence of MTA outcomes. However, as terminology and definitions around medication reviews differ internationally, it is not always possible to ascertain whether the intervention being assessed would conform to the above definition of MTA. This review includes examples of studies on wider pharmacist interventions (such as less comprehensive reviews, focussed on patient education of medication use), and where possible, identifies those studies that use a consistent definition of MTA.

6. This review found that there is a growing body of literature describing process outputs and perceptions of pharmacist interventions, but far fewer studies reporting hard clinical and/or economic outcomes and results. This reflects that, in general, there has been some movement away from requiring justification for the intervention, to finding ways to improve implementation. Even where there are hard outcomes, due to differences in interventions, the broader context in which the studies occur, and methodologies used, it is generally not possible to compare or extrapolate the results.

7. A number of authors comments on the need for the evidence base for medication reviews to grow, but many also admit that due to the difficulties mentioned above, this would not be an easy task.

Literature review

International studies

Burden of medication errors

8. There have been a number of international studies into the burden of medication errors, and a number of literature reviews which seek to consolidate these studies – albeit that differences in definitions and methodologies make comparisons difficult.

9. A 2009 literature review (Easton et al. 2009) provided a picture of the prevalence of medication errors, e.g.:

   - In Europe and North America, adverse drug events (ADEs) in the community are common, with up to 3.1% of deaths, 17.5% of general hospital admissions, and 30.7% of admissions in the elderly population associated with such events. ADEs were also found to be associated with up to 38% of re-admissions to hospital and 33.2% of emergency department attendances.
   - The situation is similar in Australia with hospital admissions associated with ADEs ranging from 5.6% of admissions in the general population to 30.4% of admissions in the elderly, and paediatric emergency department attendances reported to be associated with ADEs 3.3% of the time.
   - One United States study found a high rate of adverse drug reactions (ADRs) among people aged 65 or older in aged-care facilities (65%) and another reported that 12.5% of people discharged from hospital had experienced an ADE in the last year. ADRs are a special case of ADEs. Where ADRs describes harm associated with the use of medications at a normal dosage during normal use only ADEs also include harm from wrong dosage and wrong use.

10. Easton et al. (2009) also noted that most studies did not investigate the preventability of the identified ADEs. Where established, the percentage of preventable ADEs ranged from 23% of those identified in a general practice setting to 73% of those in patients who attended hospital emergency departments.

11. The origins and circumstances of adverse drug events can be difficult to establish, and hence so can the preventability of such events. Australia's consumer health forum has found that poor communication was one of the most reported contributing factor to ADEs. This poor communication happened mainly between patients and health professionals, between health professionals themselves at the transfer of care, and between general practitioners and pharmacists (CHF 2011), which was in line with a previous study by Witherington et al. (2008). Another study (O'Neil and Poirer 1998) also mentions cognitive slips, errors and deficiencies and organizational or work-related factors such as inadequate staffing levels and workplace systems, particularly in the pharmacy environment.

12. The literature consistently identifies the at-risk categories as being older people, those taking multiple medications and those taking high-risk medications.

13. There have been studies undertaken on trends in ADR-related hospitalizations, with many concluding that they seem to be rising in prevalence. For example, a study undertaken in The Netherlands found that ADR-related hospital admissions in older persons have shown a rapidly increasing trend in The Netherlands over the last three decades with a temporization since 1997. Although an encouraging flattening in the increasing trend of ADR-related admissions was found around 1997, the incidence is still rising, which warrants sustained attention to this problem. (Hartholt et al. 2010)

14. Many studies also note that that diagnostic coding (either the inconsistency thereof or improvement thereof) may impact on these results. Wu et al. (2010) found that between 1999 and 2008 0.9% of total hospital admissions in England were ADR-associated. The study concluded that the number of ADR admissions increased at a greater rate than the increase in total hospital admissions (but some of this may be due to improved diagnostic coding). In-hospital mortality due to ADR admissions also increased during this period

Interventions to reduce adverse drug events

15. Since the mid-2000s there has been the formalization of medication review by pharmacists in a number of countries. There have been increased efforts to evaluate these services, but it remains the view of some that 'there is a lack of robust research evidence consistently demonstrating any cost or clinical effectiveness compared with traditional care.' (Blenkinsopp et al. 2011).

16. Where clinical outcomes are reported, the medication review service is typically focused on particular medical conditions. These studies also differ significantly in terms of patient population, the nature of the intervention and outcome measures, so it isn't possible to extrapolate the results in any meaningful way.

17. There is notably more literature on process outputs, such as improvements in adherence, polypharmacy, and levels of identified drug interactions.

18. There is also an increasing body of literature focussed on service delivery (including business model, patient uptake, barriers to provision and performance of pharmacists), including those factors that impact on whether or not the benefits of medication review are realised, for example:

    - Quality of recommendations and how they are delivered;
    - Working relationships between the clinician and pharmacist; and
    - Systems and processes.

United States

19. Medicine use review services were formalised in the United States in 2003-2004 when the federal government introduced a requirement that pharmacies providing subsidized drugs establish medication therapy management (MTM) programs for eligible beneficiaries. The broad definition for MTM agreed by a group of national pharmacy organizations in 2004 was:

    'Medication therapy management is a distinct service or group of services that optimize therapeutic outcomes for individual patients. Medication therapy management services are independent of, but can occur in conjunction with, the provision of a medication product.

20. MTM encompasses a broad range of professional activities and responsibilities within the licensed pharmacist's, or other qualified healthcare provider's, scope of practice.

21. In 2008 the American Pharmacists Association and the National Association of Chain Drug Stores Foundation set out a framework for MTM which includes 5 core elements:

    1) Medication therapy review (MTR)

    2) Personal medication record (PMR)

    3) Medication-related action plan (MAP)

    4) Intervention and/or referral

    5) Documentation and follow-up

22. The sequence and delivery of these core elements will vary depending on the service provider and the individual patient's needs, but will often involve the pharmacist consulting or working with the prescriber.

23. There has been limited research into the effectiveness of MTM as a whole. This is partially due to the wide variety of MTM services offered.

24. One notably large study into MTM is that undertaken by de Oliveira et al. (2010), where the authors retrospectively analyzed the electronic therapeutic records of 9,068 patients (in one health system with 48 primary care clinics) who received MTM services during the 10-year period between September 1998 to September 2008. Of the 38,631 drug therapy problems identified and addressed by MTM pharmacists, the most frequent were a need for additional drug therapy (28.1%) and subtherapeutic dosage (26.1%). In the clinical status assessment of the 12,851 medical conditions in 4,849 patients who were not at goal when they enrolled in the program, 55% improved, 23% were unchanged and 22% worsened during the course of MTM services. Pharmacist-estimated cost savings to the health system over the 10-year period were $2,913,850 ($86 per encounter) and the total cost of MTM was $2,258,302 ($67 per encounter), for an estimated ROI of $1.29 per $1 in MTM administrative costs. In the patient satisfaction survey, 95.3% of respondents agreed or strongly agreed that their overall health and wellbeing had improved because of MTM.

25. While this review found no attempts to evaluate MTM as a whole, there have been a number of studies into individual programmes with the aim of understanding the clinical and economic outcomes of MTM. These typically involve a small number of patients who receive an MTM intervention (normally <300), plus the same size control group. Normally the age of the patients is 65+ and they are on multiple medications (e.g. >4). The MTM usually also focuses on certain types of conditions (such as diabetes, cardiovascular).

26. The vast majority of such studies reviewed here found that the outcomes of the MTM were positive, in terms of both clinical and economic outcomes. Due to the differences in the nature of the MTM services and the methodology used for

evaluation, it is not possible to aggregate any of the studies to quantify the average benefits.

27. For example:

- (Isetts et al. 2008). Patients receiving face-to-face MTM services provided by pharmacists in collaboration with prescribers experienced improved clinical outcomes and lower total health expenditures. Clinical outcomes of MTM services have chronic care improvement and value-based purchasing implications, and economic outcomes support inclusion of MTM services in health plan design. The reduction in total annual health expenditures exceeded the cost of providing MTM services by more than 12 to 1. Sample size of 285 intervention patients.
- (Moczygemba et al. 2012). Study into the impact of telephone medication therapy management (TMTM) on medication- and health- related problems (MHRPs), medication adherence and total drug costs in Texas in 2007. 60 patients received TMTM (and there was a control group of 60). Age, medications, et cetera were similar, but not sex (51% intervention group vs. 28% in control group). The study showed that TMTM resulted in a reduction in MHRPs. Unadjusted cost comparisons showed cost savings in the intervention group.
- (Pinto et al. 2012). Aimed to measure the impact of an employer-sponsored, pharmacist-provided medication therapy management program on clinical outcomes and social and process measures for patients with diabetes with or without associated co-morbid conditions. Patients with diabetes experienced improvements in multiple clinical, social, and process measures.
- (Planas et al. 2009). Randomized controlled trial of 52 patients with diabetes and hypertension over 9 months. MTM was effective in improving blood pressure control among managed care enrolees with diabetes and hypertension.

28. Other studies have evaluated the outputs of MTM, such as the number of medication therapy problems identified, percentage of pharmacist recommendations implemented, and drug costs.

29. Where patients are surveyed as part of the study, questions are often included which aim to further understand their perceptions of the service and its implications, such as whether the MTM has led to improved convenience in taking medications, lower costs and reduction of the use of prescription drugs. Patients' satisfaction with the programs was notably positive (Shimp et al. 2012 and Dale et al. 2007), but results regarding costs and drug use decrease were mixed, with more positive results than negative. (Shimp et al. 2012, Michaels et al. 2010, Winston et al. 2009 and Dale et al. 2007)

30. Whilst there is generally a recognition that the evidence-base of outcomes from MTM should be improved, there is a significant body of literature that shows a movement away from measuring benefits to a focus on implementation issues (such as service delivery and cost models, encouraging patient buy-in). So the issue is one of designing a commercially viable MTM service which maximises the expected benefits.

31. Examples of literature focussing on implementation issues include:

- Ried (2012) who found that 'there is evidence and persuasive research that demonstrates its quality and effectiveness outcomes. However, the development of economic models for compensation and reimbursement for MTM have not kept pace because of external resistance and the lack of a comprehensive macro-level strategy'.
- (Schommer et al. 2012) Who propose that MTM providers have been developing capacity for providing MTM services and view MTM as part of their responsibility and a way to help meet patient care needs. But conclude that widely accepted business models for these services have not been established.
- Lounsbery et al. (2009) show that the most important barriers to implementing MTM services in the outpatient setting identified by pharmacist survey respondents were related to interprofessional relationships, documentation, and compensation. Despite the resources available to pharmacists, barriers continue to hinder the expansion of MTM and direct patient care services. Studies into the barriers of providing MTM e.g.

United Kingdom

32. Medication reviews have become widespread across the UK since 2005. Medication reviews undertaken by pharmacists in the National Health Service tend to fall within the following categories (Blenkinsopp et al. 2012):

    a) **Medicines Use Review (MUR)**, conducted by community pharmacists in England and Wales, where they help to assess any problems patients have with their medicines, to help educate patient's and make recommendations to prescribers;
    b) **Chronic medication service**, conducted by community pharmacists in Scotland, which is similar to an MUR, but has a 'slightly more holistic remit than the MUR service, delivering a full pharmaceutical care assessment, plan and implementation. It also includes the use of serial prescriptions to allow repeat prescribing of long term medication and communication and data storage is all electronic, with transfer of information between GP and pharmacist';
    c) **Comprehensive medication review**, conducted by hospital pharmacists, often as part of medicines reconciliation when a patient is admitted to hospital;
    d) **Clinical medication review**, conducted by GP practice-based pharmacists and community pharmacists, is a more structured, critical examination of patient's medicines than an MUR. The objective is to reach an agreement with the patient about the continued appropriateness and effectiveness of the treatment, optimizing the impact of medicines, minimizing the number of medication related problems and reducing waste.

33. As with the US, there is good evidence that medication review improves process outcomes, such as reducing numbers of medications, and implementation of recommendations. In a study on elderly patients living in care homes in Leeds Zermansky et al (2006) found that general practitioners do not review most care home patients' medication. A clinical medication review by a pharmacist is usually accepted, leading to substantial change in patients' medication regimens without change in drug costs.

34. However there remains a paucity of evidence on clinical and economic outcomes.

35. One literature review concluded that 'studies evaluating directed MUR services, focusing on a particular disease were most likely to report clinical outcomes' (Hinchcliffe, 2011)

36. Some clinical outcomes reported for targeted or individual programs, with mixed results.

- (Phelan and Foster et al 2008) 106 patients with knee pain, from thirteen general medical practices, received a structured medicines review from a pharmacist in the general practice setting. The control group received only an information leaflet and a telephone call. The study identified substantial opportunities to improve pharmacological treatment for knee pain, and to reduce side effects from analgesic medicines.
- A study done by Community Pharmacy Medicines Management Project Evaluation Team (2007) targeted patients with coronary heart disease. The study involved 1493 patients (980 intervention and 513 control). The 12-month intervention comprised an initial consultation with a community pharmacist to review appropriateness of therapy, compliance, lifestyle, social and support issues. Control patients received standard care. No significant differences between intervention and control groups were shown at follow-up for any of the primary outcome measures such as numbers on aspirin or lifestyle measures, but the pharmacist-led service was more expensive than standard care. However, significant improvements were found in the satisfaction score for patients' most recent pharmacy visit for prescription medicines among the intervention group, compared with control group

37. Robust health economic studies of medication reviews remain rare, but when 'harder' outcome measures have been included, such as hospitalizations or mortality in elderly patients, available evidence indicates that whilst interventions could improve knowledge and adherence they did not reduce mortality or hospital admissions with one study showing an increase in hospital admissions. (Blenkinsopp et al. 2012).

38. 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 hospitalization and mortality than the control group (Holland et al. 2005). This study was heavily criticized on methodological grounds when it was first published, and has subsequently been critiqued by Zermansky and Freemantle (2007) that a population was chosen with little to gain from the intervention, a weak from of medicine review was used, and outcome measures were chosen that avoided measuring the outcomes where benefits were most likely to be found.

39. However, in a 2009 review of cost-effectiveness of medication reviews, Zermansky concluded that 'there were no reports of studies in which the cost of the intervention was greater than the benefit, and several reported a cost saving when measuring drug cost change only' (Zermansky et al. 2009)

40. Other examples include:

- Desborough (2012) conducted a 'before and after' economic evaluation of a pharmacist-led medication review service given to 117 patients. The study found the costs of providing the review were offset by the reduction in emergency hospital admissions and savings in medication cost. No significant change in health-related quality of life was observed.
- Lenaghan and Holland (2007) assessed whether home-based medication review by a pharmacist for at-risk older patients (136) in one general practice reduced hospital admissions. At six months there was no difference in hospital admissions and no difference in care home admissions or deaths were detected between groups, the intervention did, however, appear to reduce prescribing. This is in line with other evidence and suggests that this form of intervention may not have a clear health gain, but may lead to modest savings in terms of reduced prescribing.

41. In recent years there has been a number of studies dedicated to the uptake of MURs in the UK, the nature and performance of MUR services, the perceptions of those involved (pharmacists, GPs and patients) and/or implementation issues.

42. Barriers identified on the supply side include lack of time, inadequate support staff and negative GP views of the service, and negative effects of the organizational set up. Bradley et al. (2008) found the greatest barrier to MUR implementation to be a lack of support from GPs, a lack of communication about MURs between community pharmacists and GPs. The findings suggest that the organisational setting of the pharmacy is an important factor influencing the uptake of MURs. There is also a need for greater communication and collaboration with GPs regarding the MUR service. Latif et al. (2011) found that MURs did little to increase patients' knowledge and rarely affected medicine use, although some felt reassured about their medicines. Pragmatic constraints of workload and pharmacy organisation undermined pharmacists' capacity to implement the MUR service effectively. They found pharmacists taking a 'tick-box approach' to medication reviews in the UK, which means that any benefits from educating patients are not realised.

43. (Laaksonen et al. 2010) undertook a performance assessment based on a sample of 244 referrals written by 20 community pharmacists. The referrals written by the community pharmacists were compared with those written by a clinical pharmacist. The community pharmacists beneficially identified most drug related problems and suggested many solutions.

44. The Primary Care Pharmacy Association and National Pharmacy Association undertook an evaluation of MUR services at four sites in the UK in 2008-2009 and made a number of recommendations for improving the way in which MUR services are delivered – in relation to organisational arrangements, systems and processes, and the skills and training of pharmacists.

Australia

45. The Australian Government introduced 'home medication reviews' (HMR) in 2001. In this model, patients who may benefit from a review are identified by a GP or community pharmacist, who then collaboratively develop a Medication Management Plan for the patient. The pharmacist will normally visit the patient in their own home (or in a care home). The 'Residential Medication Management Review' (RMMR) is a

similar service, introduced in 1997, for permanent residents of a residential aged care facility.

46. An evaluation of the HMR programme was undertaken in 2005 by Urbis Keys Young for the Pharmacy Guild of Australia. The report concluded that the Australian Government should continue to fund the pharmacy component of the Home Medicines Review Program, but made a number of recommendations relating to running of the program. The report noted the lack of clear clinical evidence supporting the effectiveness of the HMR model (based on a literature review), and advised that this be remedied – but also acknowledged that building up this evidence is likely to be a relatively complex and costly process given the nature of the intervention and that the impacts may take a long time to become clear. The report noted some of the perceived benefits of HMR as viewed by various stakeholders:

> "Stakeholder organisations, pharmacists and consumers who were consulted in the course of this evaluation generally saw the HMR program as addressing genuine and ongoing community needs, and as delivering benefits for consumer health and wellbeing. Consumers with HMR experience have generally been pleased and well satisfied with the services provided. While pharmacists expressed reservations about the adequacy of HMR remuneration, many regarded participation in the program as a stimulating and satisfying way of using their professional skills and of strengthening their customer and community relationships".

47. In 2007 the Australian Government Department of Health and Aging engaged Campbell Research & Consulting to undertake qualitative research into the HMR Program. This research aimed to identify gaps in access to the Program and the reasons for these, and to determine what drives participation in the Program. The RMMR program was evaluated in 2010 by Campbell Research, but this also did not measure health and economic outcomes.

48. Several recent studies have been identified which aim to quantify the benefits of medication reviews in specific settings. For example:

- (Castelino et al. 2010). The analysis of a sample of 270 HMR cases in New South Wales found that the medication reviews improved the appropriateness of prescribing (as demonstrated by the change in the Medication Appropriateness Index score) and hence, have the potential to improve patient outcomes.
- (Roughead et al. 2009 and 2011) – two cohort studies in Australian veterans which showed that HMR reduced hospitalisations associated with heart failure or warfarin.

49. A recent survey of consumer perceptions to HMR (White et al. 2011) found that 'the major benefits reported were acquisition of medicine information, reassurance, feeling valued and cared for, and willingness to advocate medication changes to the general practitioner. Perceived barriers were concerns regarding upsetting the general practitioner, pride and independence, confidence issues with an unknown pharmacist, privacy and safety concerns regarding the home visit, and lack of information about the program. Participants agreed that the potential benefits of the service outweighed its potential barriers.'

50. In the most recent Australian study Stafford (2012) set out to evaluate HMRs: an observational cohort study was conducted across all states in Australia. Pharmacists accredited to perform HMRs submitted a random sample of HMRs that they had undertaken in 2008. DRPs are frequently identified and reported in HMRs. However, the economic and clinical benefits of addressing most of them are minor in the 12 months following the HMR. On average, each HMR was estimated to result in a saving to the health system of $85.79, which was insufficient to offset the cost of the HMR ($323.80). Quality of life was estimated to improve minimally (0.001 QALYs per patient, $P<0.001$), and the cost per QALY gained (incremental cost-effectiveness ratio) was $177 566.

New Zealand evidence

The burden of adverse drug reactions in New Zealand

51. Research carried out into medical error and hospital admissions found 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 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 event adding an average of 9 days to patient stay in hospital. Overall, about half of the adverse events found in this study were considered to be preventable, although the out-of-hospital events were specifically excluded from this analysis (Davis et al. 2003).

52. 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 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 originated outside the hospital. This implies that something in the region of 1.5% of all hospital admissions are caused by drug related events originating in the community.

53. More recently, Counties Manukau, Capital & Coast and Canterbury DHBs have worked together to measure the extent of adverse drug events in their regions. The investigation found that 29% of the hospital admissions reviewed were due to adverse drug events. 94.5% of the adverse drug events identified were in the lower severity scales with temporary harm, with most of the balance consisting of patients who needed intervention to sustain life, or they suffered permanent harm, or it was considered that adverse drug events (ADEs) contributed to their death. No attempt was made to determine preventability of harm. The most commonly implicated drugs were morphine and other opioids, anticoagulants, antibiotics, non-steroidal anti-inflammatory drugs and diuretics. Patients who suffered an ADE were more likely to be female, older with more complex medical illnesses, and have a longer length of stay.(Seddon et al. 2013)

54. In 2009 a study was undertaken into adverse drug events in a Dunedin paediatric setting. This study focused on in-hospital events, so the results on the extent of adverse drug events are not particularly useful in considering pharmacist-led medication reviews (Kunac et al. 2009). However, the conclusion that ADEs represent a large cost imposition upon the healthcare sector is relevant regardless of where the ADE occurs.

Medication reviews

55. Pharmacists in New Zealand have been working collaboratively with GPs for some time, but as seen internationally, there has been a gradual formalisation of the process and efforts to roll these services out more widely. The 2007 National Pharmacist Services Framework (DHBNZ, 2007) included three levels of medication review:

    a) **Medicines Use Review and Adherence Support**: Structured and systematic, consultation-based review of all current therapy where there is not necessarily access to clinical information and the interaction and intervention is largely at the Service User level. Services are usually not single episode or ad-hoc, but most often involve regular interaction between the Service Provider and the Service User in an effort to optimise the outcomes from medicines, improve Service User understanding of their medicines and/or minimise the generation of pharmaceutical waste. The Service Provider must have full access to the Service User's medicines profile.
    b) **Medicines Therapy Assessment Services**: Clinical review of all current therapy where the Service Provider has access to full clinical notes and the interaction and intervention involves either or both Service User and prescribers e.g. participation in a multi-disciplinary team.
    c) **Comprehensive Medicines Management Services:** as for Medicines Therapy Assessment, but Comprehensive Medicines Management operates at a higher level of autonomy, hence there are different liability issues in the clinical decision making role where specialised Pharmacists provide a case-based management service to improve therapeutic effectiveness and health outcomes for Service Users. The service involves a clinical review of all current and potential therapy and active management of changes.

56. Subsequently, there has been some research seeking to evaluate one or more of these types of medication review. However, as is the case internationally, there is a paucity of evidence on clinical and economic outcomes from pharmacist interventions in New Zealand.

57. There have been several studies undertaken in recent years to understand, for example, uptake of MUR in New Zealand, barriers to provision, and GPs and pharmacists perceptions of medication reviews. (Lee et al. 2009) (Hatah et al. 2012).

58. One such study (based on an Auckland MUR pilot) identified qualitative benefits in terms of a stronger relationship between community pharmacists and their patients, and increased knowledge and confidence regarding medicine and health-related issues, but did not attempt to measure longer-term health gains (and recognised that

further investigation is needed in this regard) (Sheridan et al. 2011). The article noted the wide range of challenges identified in relation to the delivery of MURs by pharmacists, including a lack of confidence and a lack of time in undertaking MURs, difficulty in recruiting patients, inadequate remuneration for the service and associated paperwork being complex and time-consuming to complete.

59. Two Auckland DHB MUR pilots were the subject of a 2009 evaluation (Brandt et al. 2009). The first pilot involved six community pharmacists from across the region delivering MUR services. The evaluation found that:

- Patients used fewer medicines at the time of the follow ups compared to the initial MUR
- Largest reductions were in the use of calcium channel blockers, sedatives and analgesics
- Pharmacists believed that patients took their medicines 'as directed' more often at the time of follow ups than the initial MUR
- Patient perception of adherence did not appear to improve over time
- Pharmacists perception of patients' overall knowledge of medicines improved over time
- Patients' self rated quality of life improved over time

60. The second pilot involved the provision of an annual medicines review service to all rest home and hospital residents residing at four sites of a residential care provider. The evaluation focused upon the use of medicines, fall data, hospital admissions data and GPs' opinions of the pilot. The findings in terms of fall data and hospital admissions are largely inconclusive. There appeared to be less falls in the six months after a patient's annual medicines review than before and the study noted that the number of inpatient and outpatient admissions decreased, but went on to say that it is not appropriate or possible to make any causal link with the annual medicines review.

61. In 2010 a randomised controlled trial was undertaken of community pharmacist conducted medication reviews, which found that the reviews in collaboration with general practitioners can have a positive effect on the Medication Appropriateness Index. However, only a third of the pharmacists who agree to participate in the study provided adequate data which raised questions about generalisability (Bryant et al. 2011).

The impact of medicines therapy assessment in New Zealand

62. The evidence presented in the literature review supports predominantly qualitative and some positive but largely non-significant quantitative benefits from Medication Use Reviews and Medication Therapeutic Assessments. As stated previously, these are for relatively small studies with low statistical power and with non-overlapping measures of clinical and economic outcomes.

63. A randomised, controlled trial of the effectiveness of a multidisciplinary service model delivering medication review to patients at risk of medication misadventure in the community found a number of positive reductions in drug use, service use and healthcare costs and severity (Sorensen, 2004).

64. GPs in the study reported a non-significant but positive reduction in number of drugs per patient between the intervention and control group of 0.8, although the cost of medications during the study increased at the same rate in both groups, it was slightly higher on average in the intervention group. The average cost of medical services however, was AUS$275 (NZ$324) lower for the intervention group than the control group. The net cost saving per patient in the intervention group was AUS$54 (NZ$64) when compared to the control group.

65. GPs also reported that the percentage of patients experiencing ADEs fell from 36.9% to 9.3% at trial end for intervention patients while almost no change was reported for the control patients (34.9% at baseline and 34.0% at end). The most common type of ADE reported by patients was of a gastrointestinal nature (12 patients before and nine during the trial).

66. A 2009 New Zealand study (Kunac, 2009) into adverse drug events in a paediatric setting found a total of 67 ADEs occurring at rate of 12.1 per 100 admissions and that 56.7% of the ADEs were preventable. 15 of the ADEs were found to have caused the hospital admission or prolonged the stay. Of the 92 days attributed to the ADEs, 58 were deemed preventable at a total annual cost to the paediatric service of NZ$148,287. While only a subset of the 15 preventable ADEs causing the admission or prolonging it would have occurred outside the hospital setting, it still suggests the potential for some secondary care cost savings from medication reviews of children.

67. A 2009 Australian randomized controlled trial of collaborative medication reviews (Roughead, 2009) showed an adjusted reduction of the rate of hospitalisation for heart failure of 45%. The study population was veterans over the age of 65 years with a median number of between 7 and 8 co-morbidities. The Ministry of Health reported that in 2009/10 there were 6,789 discharges with a primary diagnosis of Heart failure for patients 65 years and over. It is uncertain how the study definition relates to Ministry figures but with mean throughput costs for Heart Failure Diagnostic Related Groups of (MOH, 2006) between $3,370 and $4,916 and interquartile range for length of stay of 4-23, savings could be considerable.

68. A Ministry of Health report on indicators for people with intellectual disability found the average number of pharmaceutical types dispensed in a year increased steadily with age for both people with and without intellectual disability (MOH, 2011). People without intellectual disability aged 55-64 were dispensed more than 6 pharmaceutical types on average and those 65 years and over were dispensed more than 9 pharmaceutical types per year. The higher average number of pharmaceutical types dispensed to the group of patients with an intellectual disability supports the idea that selected groups with high needs have higher polypharmacy and complexity and will likely benefit from medication therapy assessments in New Zealand.

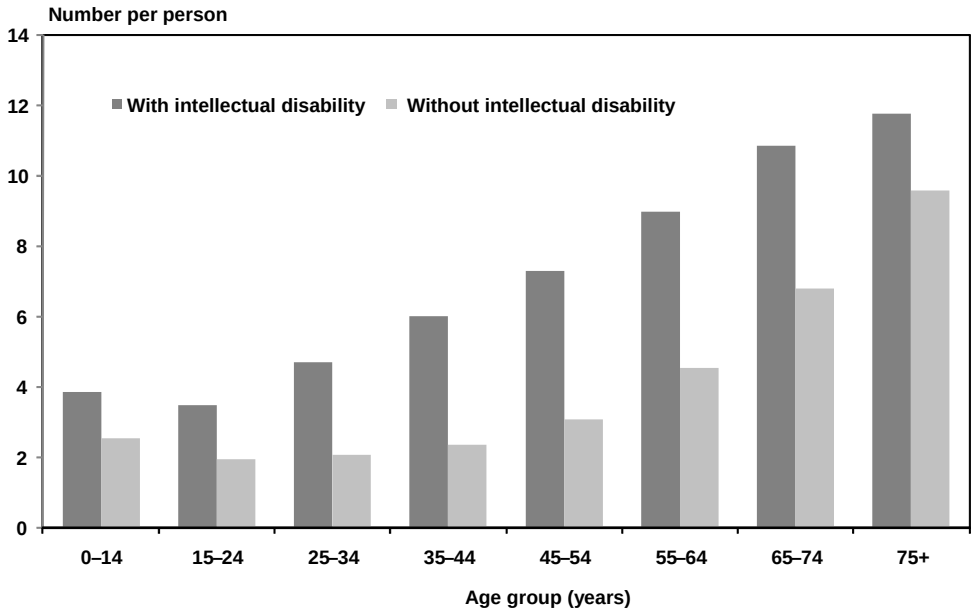

Figure 1 Average number of different pharmaceutical types per person, people with and without intellectual disability, by age, year to 30 June 2008 (Source: MOH, 2011)

69. 'Pharmaceutical types' are distinct chemicals. Community pharmacy dispensed drugs only.

70. A recent DHB collaborative study found 29% of hospital admissions reviewed were due to adverse drug events and patients who suffered an ADE were more likely to be female, older with more complex medical illnesses, and have a longer length of stay (Sedden and Jackson, et al. 2013). Preventability was not determined, but if the paediatric ADE study and much higher rate of ADEs in the general population is anything to go by, the potential for secondary care cost savings should be higher as well especially in older people and those with higher polypharmacy.

71. An earlier study into medical error and hospital admissions found overall 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 event 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).

72. 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).

73. The results from the earlier studies showed that approximately 13% of all hospital admissions are related to adverse events, that one fifth of these were related to an adverse drug event, and that in turn 40% of these originate outside the hospital. The more recent studies showed that between 12%-29% of all hospital admissions relate to an adverse drug event, with as much as 22% being preventable and originating outside the hospital. This implies that somewhere in the region of 1.5% to 6.5% 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. The Ministry of Health reports a figure of 1,035,954 public hospital discharges in 2009/10. If a pharmacist intervention were to reduce admissions by as little as 0.7%, half the minimum total scope for improvement, this would represent a freeing up of approximately 7,250 admissions for other resources. With an average of 8.6 days required by patients as a consequence of drug related adverse event, this would represent over 63,250 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.

74. The table below summarises the impacts found in the various studies reviewed:

Study	Impact found
Sorensen, 2004	Non-significant but positive reduction in number of drugs per patient between the intervention and control group of 0.8 Net cost saving per patient in the intervention group was AUS$54 (NZ$64) when compared to the control group Patients experiencing ADEs fell from 36.9% to 9.3% at trial end for intervention patients
Kunac, 2009	Potential for some secondary care cost savings from medication reviews of children

Study	Impact found
Roughead, 2009	Adjusted reduction of the rate of hospitalisation for heart failure of 45%.
Seddon and Jackson, et al. 2013	29% of hospital admissions reviewed were due to adverse drug events (potential for savings from reduced hospital admission rates)
Davis, Lay-Yee et al. 2002	13.1% of all hospital admissions were associated with some sort of adverse medical event Adverse event adding an average of 9 days to patient stay in hospital About half of the adverse events found in this study were considered to have been preventable

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