School of Pharmacy

The Impact of Cost Containment Reforms to the Pharmaceutical Benefits Scheme (PBS) on Prescribing Volumes and Expenditure in Australia: 1992 - 2011

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This thesis is presented for the Degree of

Master of Philosophy

of

Curtin University

October 2014

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgement has been made. This thesis contains no material which has been accepted for the award of any other degree or diploma in any university

24th October 2014

To my wonderful parents, Mr Lee Fok Kim and Mdm Teh Siew Li,

loving wife, Sandy Ong,

sons and daughter, Daemian, Daerius and Daena

for supporting me all the way

Acknowledgments

First and foremost, I would like to express my sincere appreciation and heartfelt thanks to my supervisor, Dr Delia Hendrie, for her guidance during my research and study at Curtin University, Perth. Her perpetual energy and enthusiasm in research had greatly motivated me in bringing out the best in myself. In addition, she was always accessible and eager to help students with their research. Hence, research life for the past two years was smooth and rewarding for me.

Besides my supervisor, I would like to thank my co-supervisors, Emeritus Professor Bruce Sunderland and Associate Professor Rachael Moorin. Their constructive contributions, invaluable advice and critical comments have helped me immensely in every way.

In addition, my deepest gratitude goes to my family members for their continuous encouragement, support and unflagging love they have given me whilst working on this dissertation. Last but not least, I wish to thank my lovely wife, Dr. Sandy Ong. Her patience and love have sustained me when I thought I could not carry on. Thank you.

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Glossary/Acronyms

ACE inhibitors	Angiotensin Converting Enzyme Inhibitor
DDDs	Defined Daily Doses
GDP	Gross Domestic Product
H2RAs	Histamine-2 Receptor Antagonist
HMG-CoA reductase	3-hydroxy-3-methyl-glutaryl-CoA reductase
Level	The estimated differences in absolute value between pre-intervention and post-intervention immediately following an intervention
OECD	Organisation for Economic Co-operation and Development
PBAC	Pharmaceutical Benefits Advisory Committee
PBPA	Pharmaceutical Benefits Pricing Authority
PBS	Pharmaceutical Benefits Scheme
Trend	The estimated differences in growth rate or slope over a segment

Abstract

Over the last two decades, the rise of government expenditure on pharmaceutical across many countries and in Australia has led governments and policy makers in these countries to implement cost containment measures. In Australia, cost containment reforms such as the requirement of economic evaluation (1993), re-supply limits (1994), a brand substitution policy (1994), co-payment increases (1997 and 2005), a therapeutic group premium policy (1998), the safety net 20 days rule (2006), the creation of F1 and F2 formularies (2007), premium-free dispensing (2008) and price cuts (2008 onwards) have been implemented between 1992 and 2011.

The objective of this study was to investigate the impact of cost containment reforms to the PBS on prescribing volumes and expenditure. Monthly government expenditure (benefit) and prescription volume (service) data was retrieved from Medicare Australia's PBS Statistics database and segmented linear regression models were used to analyse the time series data starting from 1 January 1992 to 31 March 2012. In each segment, two parameters, the level and trend were used to estimate the impact of the intervention. The level parameter estimates the differences in absolute value between pre-intervention and post-intervention immediately following the intervention while the trend parameter estimates the differences in growth rate or slope over the segment. The data were classified into three categories, Category 1 (all ATC main drug groups), Category 2 (all HMG-CoA reductase inhibitor drug groups) and Category 3 (all Atorvastatin drug groups). The Category 1 analysis provided a general perspective of the PBS cost containment reforms while the statins group was selected for analysis in Category 2 because this group is most widely dispensed and incurs the highest total expenditure in the PBS. In the Category 3 analysis, Atorvastatin was selected for further analysis because Atorvastatin was the most prescribed drugs and incurred the highest

expenditure in PBS for the year ending June 2012. Seven cost containment policies mainly the requirement of economic evaluation, re-supply limits, co-payment increases, the therapeutic group premium policy, the safety net 20 days rule and price cuts were investigated. In addition to these policies, four new listing dates of statins (Pravastatin, Fluvastatin, Atorvastatin, and Rosuvastatin) in the Pharmaceutical Benefits Scheme were included as breakpoints, applicable only to Category 2 and 3 analyses. Nine dependent variables, Total Service (General + Concessional), Total Benefits (General + Concessional), Total Service (General), Total Benefit (General), Total Service (Concessional), Total Benefits (Concessional), Total Service per thousand of the population (Total Service/1000), Total Benefits per thousand of the population (Total Benefits/1000) and the Defined Daily Doses (DDDs) per thousand of the population per day (DDDs/1000/day) were included in the analysis. The concessional beneficiary category consists of low-income earners and unemployed people who are on social security payments while the general beneficiary category includes all Australian insured by Medicare excluding those in the concessional beneficiary category.

In the Category 1 analysis, seven cost containment policies were analysed and all except the re-supply limits policy were found to have significant impact on at least one of the outcome variables. For the category 2 analysis, six cost containment policies (re-supply limits, two co-payment increases, the therapeutic group premium policy, the safety net 20 days rule and price cuts) and four new listing dates of statins were analysed and were found to have significant impact on at least one of the outcome variables except the listing of Pravastatin. For the category 3 analysis, three cost containment policies (co-payment increase, the safety net 20 days rule and price cuts) and the new listing date of Rosuvastatin were analysed and all interventions were found to have significant impact on at least one of the outcome variables. The two increases in patient's co-payment implemented in January 1997 and January 2005 resulted in

an immediate drop in the level of services and benefits but the interventions effects were reversed in the following months post intervention where the trend continued to increase. The safety net 20 days rule was the only measure that displayed outcomes that matched with the expected impact, where reductions in both the level and trend for all beneficiaries were observed. For the therapeutic group premium policy, the category 1 analysis showed a deceasing direction for both level and trend of services and benefits after the policy implementation while in the category 2 analysis, no significant changes were observed in the trend in benefits. The implementation of the price cuts resulted in an increase in the levels of services and benefits across all categories. However, in the following months the trends of services and benefits returned to the pre-intervention trend.

Generally, the study found that not all cost containment measures were effective in containing costs. Among those measures, the safety net 20 days rule was found to be the most effective in reducing drugs utilisation and expenditure with the overall trend in services and benefits reduced after its implementation in addition to initial decrease in level. The therapeutic group premium policy was effective in containing utilisation and cost but its effectiveness may be limited to only a short time of period.

The main limitation of the study was the PBS data not capturing PBS prescriptions priced below the general co-payment level prior to April 2012, so results relating to number of services may not reflect the actual effect of the interventions. This limitation does not extend to analyses of the level and trend of PBS benefits paid as the focus of the study was the impact of cost containment measures on government spending on pharmaceuticals.

This study has considered the impact of cost containment policies on prescription volumes and expenditure. Future research should examine the

impact of these policies on other areas such as adherence with medications, health outcomes and health-related quality.

Chapter 1.0 Introduction

Globally, the rise of government expenditure on pharmaceuticals in most developed countries over the last two decades poses a major public health problem (Almarsdóttir et al., 2005). Rising pharmaceutical expenditure places a financial burden on the healthcare system and if left unchecked may result in a healthcare funding crisis. Due to high healthcare costs, patients' accessibility to and affordability of medical care may be restricted and threaten coverage for healthcare. In Australia, similar trends are developing in the healthcare system in relation to the Pharmaceutical Benefits Scheme (PBS) with health and pharmaceutical expenditures having more than doubled over the ten year period from 2001/02 (Department of Health and Ageing, 2012).

The issue of rising pharmaceutical expenditure has received considerable critical attention by governments and policy makers. Various cost containment measures have been implemented to contain expenditure by influencing the demand and supply for pharmaceuticals (Busse et al., 2005). To date there has been little agreement on the impact and effectiveness of these cost containment measures. Due to the variety of cost containment measures, and coupled with cross-country differences in healthcare systems and populations, a conclusive assessment of the impact of individual measures has not been made. Most studies of the impact of cost containment policies have only focussed on a single type of measure and have been limited to measures such as the introduction of a reference pricing system and patient cost sharing. In addition, systematic reviews of cost containment measures have been restricted to a narrow range of measures, usually a single type of measure (Weir et al., 2012). No previous systematic reviews have reviewed different cost containment measures in the same study, thus making comparison between measures problematic. For Australia, the number of studies is even more limited despite numerous cost

containment measures having been introduced by the Australian Commonwealth government.

The aim of this dissertation is to investigate the impact of cost containment reforms to the PBS on prescribing volumes and expenditure. Data for this study was retrieved from Medicare Australia's PBS Statistics database that provides monthly government expenditure (benefit) and prescription volume (service) data. Analysis of the time series data in this study is by the application of segmented linear regression models. Two parameters, the level and trend were used to estimate the impact of the intervention in each segment.

This dissertation comprises six chapters, including this introductory chapter. Chapter Two provides an overview of the global pharmaceutical industry and the types of healthcare system as well as the different categories of cost containment measures.

The third chapter focuses on the Australian healthcare system and the PBS. An overview of past healthcare and PBS expenditure trends and the key drivers to the growth in PBS expenditure are discussed. Cost containment reforms and measures implemented by the Australian Commonwealth government between 1992 and 2011 are also discussed.

The fourth chapter comprises a systematic review of the pharmaceutical cost containment measures implemented in different jurisdictions. Chapter Five then presents the methods and results of the analysis examining the impact of cost containment reforms to the PBS. The analysis was undertaken for three categories: category 1 (all ATC main drug groups), category 2 (all HMG-CoA reductase inhibitor drug groups) and category 3 (all Atorvastatin drug groups). Seven cost containment measures were investigated for the category 1 analysis while the category 2 analysis evaluated six cost containment measures and four new statins listings and the category 3 analysis evaluated three cost containment measures and one new statins listing.

The final chapter concludes the dissertation by interpreting the overall research findings, including from the systematic review and the statistical analysis. These findings and their significance are discussed in the wider context of similar research findings about the impact of cost containment policies both in Australia and internationally.

Chapter 2.0 Pharmaceutical Industry and Its Stakeholders: A Global Perspective

2.1 Introduction

This chapter begins with an overview of the pharmaceutical industry and its stakeholders from a global perspective. Globally, the pharmaceutical industry is a sizeable industry and is regarded by many countries as a vital industry in their economy. Types of pharmaceutical products are described in the following section. As the majority of the pharmaceutical expenditure is borne by the government, this chapter will then examine the level of government's pharmaceutical expenditure in several OECD countries. Next, types of healthcare systems are described, and the scope of cost containment measures discussed in the following section was restricted to those implemented in national or tax-based health care systems and social health insurance systems. Only cost containment measures implemented to control the increase in public healthcare spending were included. Cost containment measures were categorised into measures that influence the demand for pharmaceuticals and those that influence the supply for pharmaceuticals.

2.2 Overview of the Global Pharmaceutical Industry

The global pharmaceutical market is a multibillion dollar industry and ranked as one of the most profitable industries in the United States (Gottlieb, 2002). In 2011, global pharmaceutical spending was at US$956 billion, an increase of nearly US$351 billion from the US$605 billion recorded in 2005 (IMS Institute for Healthcare Informatics, 2011a). This figure is expected to escalate to nearly US$1.2 trillion by 2016 with an annual global growth of US$30 billion in 2012 and likely up to US$70 billion in 2016. Geographically, in 2011 the traditional markets of North America, Europe and Japan dominated the global

share of pharmaceutical spending with 36%, 24% and 12% respectively. These markets are expected to shrink in their market share of pharmaceutical spending with an annual growth of 1 to 4% through 2016. On the other hand, the future growth in the pharmaceutical industry will depend much on the emerging markets such as China, Brazil, India and Russia where domestic healthcare consumption is growing rapidly. China and Russia are expected to register a strong growth in pharmaceutical spending, doubling the amount spent on pharmaceutical by 2016. According to IMS Health, the China market alone is expected to reach US$161 billion, Brazil US$47 billion and Russia US$27 billion by 2016 (IMS Institute for Healthcare Informatics, 2012a).

There are more than 2000 pharmaceutical and biotech companies worldwide with the majority of these companies based in the United States. In 2011, the top 20 pharmaceutical companies by sales earned approximately US$520 billion, representing 60% of global pharmaceutical sales (IMS Institute for Healthcare Informatics, 2011b). These companies generally hold numerous blockbuster drugs that generate big profits. At the top of the list is Pfizer's Lipitor (atorvastatin calcium) used treating dyslipidemia and for cardiovascular disease prevention, which recorded sales of US$12.5 billion in 2011, followed by Bristol-Myers Squibb and Sanofi-Aventis's Plavix (clopidogrel), an antiplatelet agent with sales of US$9.3 billion, and GlaxoSmithKline's Seretide (fluticasone/salmeterol) used in the management of asthma and chronic obstructive pulmonary disease (COPD) with US$8.7 billion of sales (IMS Institute for Healthcare Informatics, 2012b).

Both the developed and developing countries view the pharmaceutical industry as a vital component to their economic sustainability and growth. The pharmaceutical industry contributes significantly to employment, trade and research and development (R&D). In 2010, around 650,000 people in the United States and 663,500 people in Europe were involved directly in the

pharmaceutical industry while in China 1,604,800 people were employed in the pharmaceutical industry (International Federation of Pharmaceutical Manufacturers and Associations, 2012). In pharmaceutical trade, Europe remains the world's top exporter of pharmaceuticals. Europe exported nearly US$360 billion worth of pharmaceuticals in 2010 while the United States exported US$39.4 billion (International Federation of Pharmaceutical Manufacturers and Associations, 2011). The revenues from pharmaceutical sales are reinvested into pharmaceutical R&D activities. In 2007, the United States lead in R&D investments reaching US$47 billion, followed by US$10.4 billion in Japan and US$3.9 billion in France. The continuous investment in R&D results in major breakthrough in the fight against disease and provides a steady stream of new drugs. In 2012 alone, the United States Food and Drug Administration (FDA) approved 35 new drugs, with the majority of the drugs to be used for cancer treatments (U.S. Food And Drug Administration, 2012b). Although the new cutting edge drugs are better in treating diseases, these newer drugs are usually more expensive than their predecessor with some even double or triple in prices.

2.3 Generic versus Brand Name Pharmaceutical Products

Pharmaceuticals can be divided into two broad categories: generic drugs and brand name drugs. The United States FDA defines a generic drug as *"a drug product that is comparable to brand/reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use"* (U.S. Food And Drug Administration, 2012a). Generic drug are generally drugs that are marketed after the patent and exclusive protection of a brand name drug ends and typically cost 30 to 80 percent less than the brand name drug (IMAP, 2001). A brand name drug is a drug marketed under a proprietary, trademark-protected name. The company that holds the patent for the drug has the exclusive right to produce and sell the drug (U.S. Food And Drug Administration, 2012a).

The global generic drugs market was worth US$242.0 billion in 2009, representing a market share of 25% of total pharmaceutical spending and is projected to reach US$400.0 to US$430.0 billion by 2014 with a larger market share of 35% of total pharmaceutical spending (IMS Institute for Healthcare Informatics, 2012a). The growth in the generic market was due to the large numbers of drugs that went off patent since the beginning of 2010. This phenomenon of large patent expirations is referred to as the "patent cliff." In 2011, two blockbuster drugs Plavix's Lipitor (atorvastatin calcium) and Eli Lilly's Zyprexa (olanzapine) went off patent protection (IMS Institute for Healthcare Informatics, 2011a). Jointly, these two drugs eroded US$18.2 billion from the companies' annual sales. In 2012, more blockbuster drugs were taken off their patent protection such as Bristol-Myers Squibb and Sanofi-Aventis's Plavix (clopidogrel), AstraZeneca's Seroquel (quetiapine), and Merck's Singulair (montelukast) with combined annual sales of US$23 billion. Between 2012 and 2016, at least nine blockbuster drugs are scheduled to lose their patent protection, costing pharmaceutical companies US$62.6 billion in annual sales (IMS Institute for Healthcare Informatics, 2012b).

2.4 Pharmaceutical Expenditure in Public Healthcare

Pharmaceuticals are regarded as one of the main focus points in delivering excellent healthcare, with public pharmaceutical expenditures constituting a significant and increasing share of national Gross Domestic Product (GDP). In 2011, OECD countries spent between 0.1 and 1.9% of the national GDP subsidising pharmaceuticals (Figure 2.1) (Organisation for Economic Co-operation and Development, 2013). Pharmaceuticals include prescription medicines and over-the-counter medicines (OTC medicines) while in some countries, other medical non-durables such as bandages, elasticized stockings, incontinence articles, condoms and other mechanical contraceptive devices were included. Ten countries consisting of Greece, Slovak Republic,

Japan, Hungary, France, Ireland, Germany, Spain, Belgium and Portugal recorded pharmaceutical expenditure of more than 1% of their national GDP. Public pharmaceutical spending in Greece was the highest among OECD countries at 1.92% of its national GDP (Organisation for Economic Co-operation and Development, 2013).

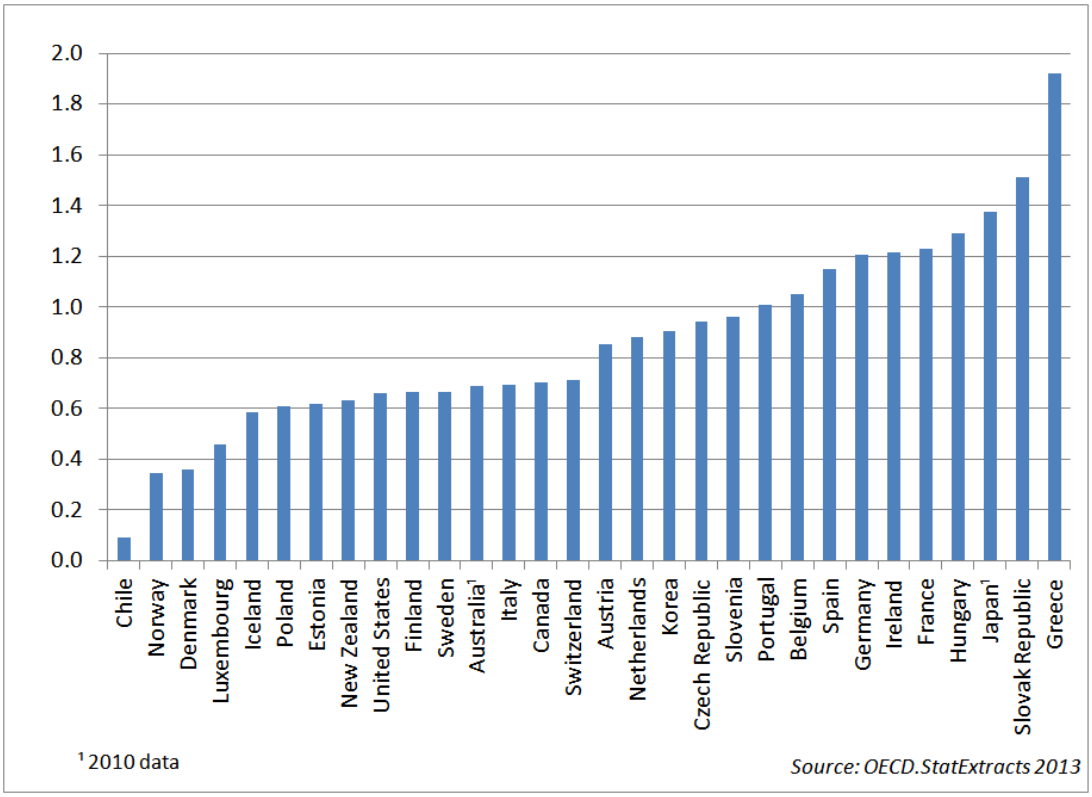


Figure 2.1 Public expenditure on pharmaceuticals as a percentage of gross domestic product (GDP) in selected OECD countries, 2011

Over the last decade, government expenditure on pharmaceuticals in OECD counties increased by an average of 76.2% (Table 2.1). The most notable increase was in Ireland where pharmaceutical expenditure increased by 211.9% from US$741 million to US$2,313 million in 2011; followed by the United States where government pharmaceutical expenditure increased by 200% from US$33,008 million in 2001 to US$98,994 million in 2011. Others European Union

(EU) countries such as Greece and Netherlands recorded an increase of 150.6% and 126.1% respectively. In the Asian region, Korea has the highest increase in pharmaceutical spending with a 151.7% increase from US$5,352 million in 2001 to US$13,472 million in 2011 (Organisation for Economic Co-operation and Development, 2013).

The continuous increase in public pharmaceutical expenditures places financial constraints on overall public healthcare expenditure. A larger portion of the public healthcare budget must be allocated for pharmaceutical purchases, therefore reducing the budget allocation for other essential public healthcare services. In 2011, pharmaceutical expenditure accounted for between 2.88% and 32.3% of healthcare budgets (Figure 2.2). Greece has the highest percentage of pharmaceutical expenditure among the 30 OECD countries with 32.3% followed by the Slovak Republic (27.0%), Hungary (26.1%), Korea (22.8%), and Ireland (21.0%) (Organisation for Economic Co-operation and Development, 2013).

Table 2.1 Public expenditure on pharmaceutical, 2001 and 2011

Country	Amount (Million US$)		Growth rate (%)
	2001	2011	
Ireland	741	2,312	211.9
United States	33,008	98,994	199.9
Korea	5,352	13,472	151.7
Greece	2,239	5,611	150.6
Netherlands	2,778	6,282	126.1
Canada	4,979	9,809	97.0
Slovak Republic	1,006	1,968	95.6
Estonia	93	182	95.4
Poland	2,787	4,955	77.8
Finland	759	1,345	77.1
Japan	33,916	59001[1]	74.0
Switzerland	1,666	2,893	73.7
Australia	3,806	6476[1]	70.1
Spain	10,382	17,049	64.2
Germany	24,179	38,908	60.9
Hungary	1,726	2,761	59.9
Austria	1,948	3,033	55.7
France	19,144	28,391	48.3
Luxembourg	146	211	45.2
Sweden	1,946	2,612	34.2
Norway	786	1,042	32.6
Portugal	2,097	2,727	30.0
Czech Republic	2,003	2,587	29.1
Denmark	654	823	25.7
Iceland	65	68	4.6
Italy	15,362	13,785	-10.3
Belgium	N/A	4,483	N/A
Chile	N/A	337	N/A
New Zealand	N/A	861	N/A
Slovenia	N/A	540	N/A
Average growth rate			76.2

[1] 2010 data

Source: OECD StatExtracts 2013

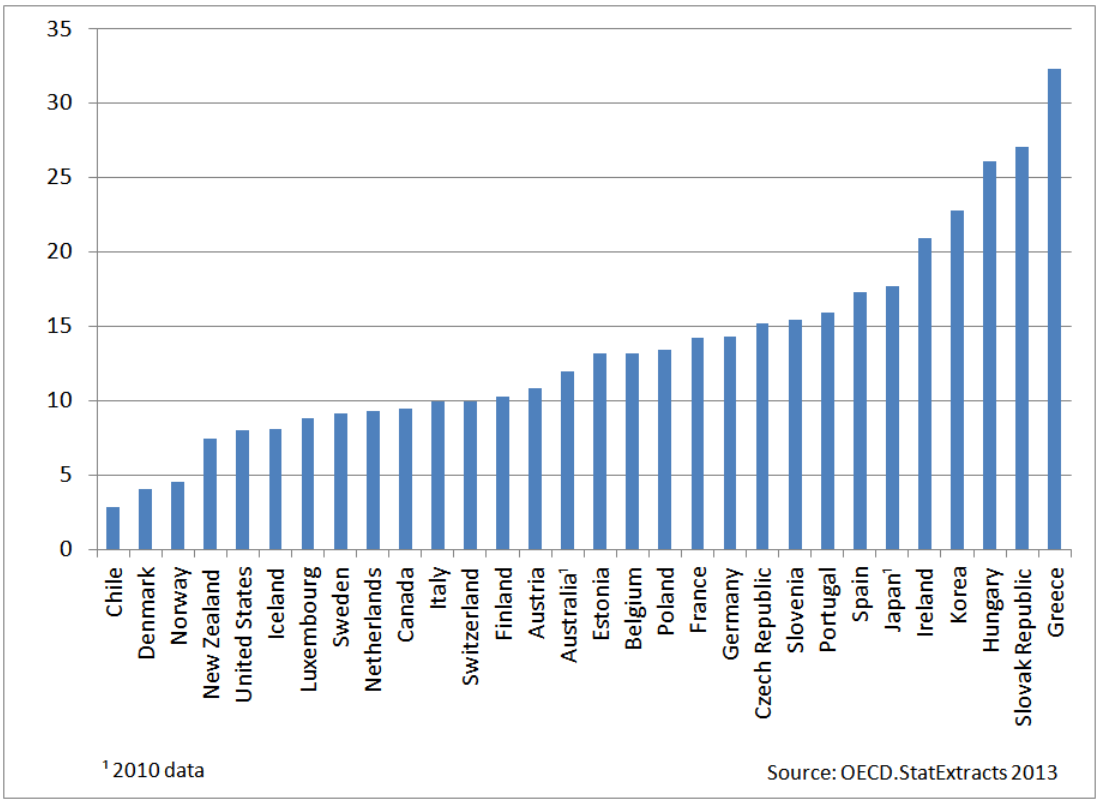


Figure 2.2 Public expenditure on pharmaceutical as a percentage of health expenditure in selected OECD countries, 2011

2.5 The Healthcare System

Since 1963, there has been much research done on the classification of healthcare systems (Freeman et al., 2010). However, the most commonly accepted classification of a healthcare system is by the Organisation for Economic Co-operation and Development (1987) where three main models were proposed; the national health service, a social health insurance system, and a private health insurance system. The national health service, also known as the Beveridge model, provides universal coverage and derives its funding mainly from taxation (direct and indirect). Examples of countries with a national health service are the United Kingdom, Italy, Spain, Sweden, Canada and Australia. The social health insurance system or Bismarck model is a quasi-universal coverage system with compulsory health insurance usually financed jointly by employers

and employees and funding channelled through non-profit insurance funds. Countries such as France, Germany, Switzerland, Belgium and Japan have social health insurance systems (Böhm et al., 2013; Wallace, 2013).

The third model, the private health insurance system is solely funded by the private sectors (Lameire et al., 1999). This system is widely use in the United States where the majority of the population is covered by private health insurance with other insurance coverage provided by the government. Government health insurance including Medicare, Medicaid, the State Children's Health Insurance Program (CHIP), and the Veteran's Administration (VA) is limited to special groups of the population such as those aged 65 years old and over (Medicare), the low-income and disabled (Medicaid), children without insurance (CHIP) and the military's veterans (VA) (Stone, 2000). Private health insurance is purchased either by the employer or by individuals from a private company. The main disadvantage of the private health insurance system is in its failure to provide universal healthcare coverage to its population (Garson, 2000). In 2011, it is estimated that 15.7% of the population were without any insurance coverage (DeNavas-Walt et al., 2012). In examining the impact of cost containment measures on pharmaceutical expenditures and prescribing volumes, the scope of this study will be limited to countries that have a national health service and a social health insurance system. The rationale for limiting the scope to these types of health systems is to focus on cost containment measures implemented by governments aiming to curb public expenditures. Therefore, cost containment measures introduced by health insurance organisations operating in a private health insurance system will be excluded.

2.6 Cost Containment Measures

The global economic uncertainties and the European financial crisis in recent years have made pharmaceutical expenditures a central part of policy to control the increase in public healthcare spending. Governments around the world, particularly in Europe, have introduced austerity measures to contain pharmaceutical expenditures. Pharmaceutical expenditures are often singled out as a target of cost containment in healthcare by policy makers due to the relative ease of measuring pharmaceutical costs compared to measuring other healthcare costs (Towse, 2003).

For the past two decades, numerous cost containment measures have been introduced with only a few of these policies succeeding in containing pharmaceutical expenditures in the long run. Most of the policies introduced were not supported by evidence in regards to their effectiveness in containing cost (Maynard et al., 2003). However, more recently, an increase in experimental and quasi-experimental research on pharmaceutical cost containments policies has provided a better evidence-base to help policy makers make decisions.

Implementation of pharmaceutical policy is extremely difficult due to the fact that the sector involves multiple stakeholders: insurers (in most cases governments and their agencies), pharmaceutical manufacturers, prescribers and pharmacies, and residents with a role as patients and taxpayers (Ess et al., 2003). Each of the stakeholder groups may have some common objectives such as having safe, effective and quality pharmaceuticals. However, in the area of policies to contain pharmaceutical costs, each stakeholder has different objectives. Insurers act to contain pharmaceutical expenditures by, for example, reducing the price and putting constraints on the demand for pharmaceuticals. Pharmaceutical manufacturers view this as a threat to their profit margin while patients see this as restricting their access to pharmaceuticals especially new pharmaceuticals that are more expensive.

Cost containment policies are put in place to either influence the supply or the demand of pharmaceuticals. Atella (2000) concluded that cost containment policies can only be sustainable in the long term by manipulating both the supply and demand side of the market. Failure to influence both will result in short term success and escalating cost in the long run. A cost containment model, adapted from Busse et al (2005), categorises cost containment policies into three different regulatory measures according to their point of intervention: price control, volume control and spending control (Figure 2.3). Price control works by limiting the amount reimbursed or requires patients to pay a portion of the cost of pharmaceuticals. Volume control either limits the range of selections available for reimbursement or the quantities of pharmaceuticals dispensed at one time, while spending control works by capping the total pharmaceutical expenditure.

2.6.1 Influencing the demand for pharmaceuticals

In contrast to many others products, the demand for pharmaceuticals is unique being influenced by prescribers, pharmacists and insurers in addition to the patients themselves. Demand can either be initiated by the patients or the prescribers. The patient's demand for pharmaceuticals is derived directly from the demand for health, seeking for the relief from or prevention of illness. Patients are usually not involved in the drug selection process but bear the financial commitments with payment ranging from full, partial, to zero payment of the price of the drug. The insurer makes the payment for the balance of the price. The prescriber, on the other hand, acts as an agent for the patient in choosing the best drugs for the patient's medical conditions. Prescribers are the decision makers in the drug selection process but are not involved in financial consequences of their decisions (Kanavos, 2003).

In principle, cost containment measures influence the demand for pharmaceuticals at the point of utilisation. Measures implemented in various countries are as follows.

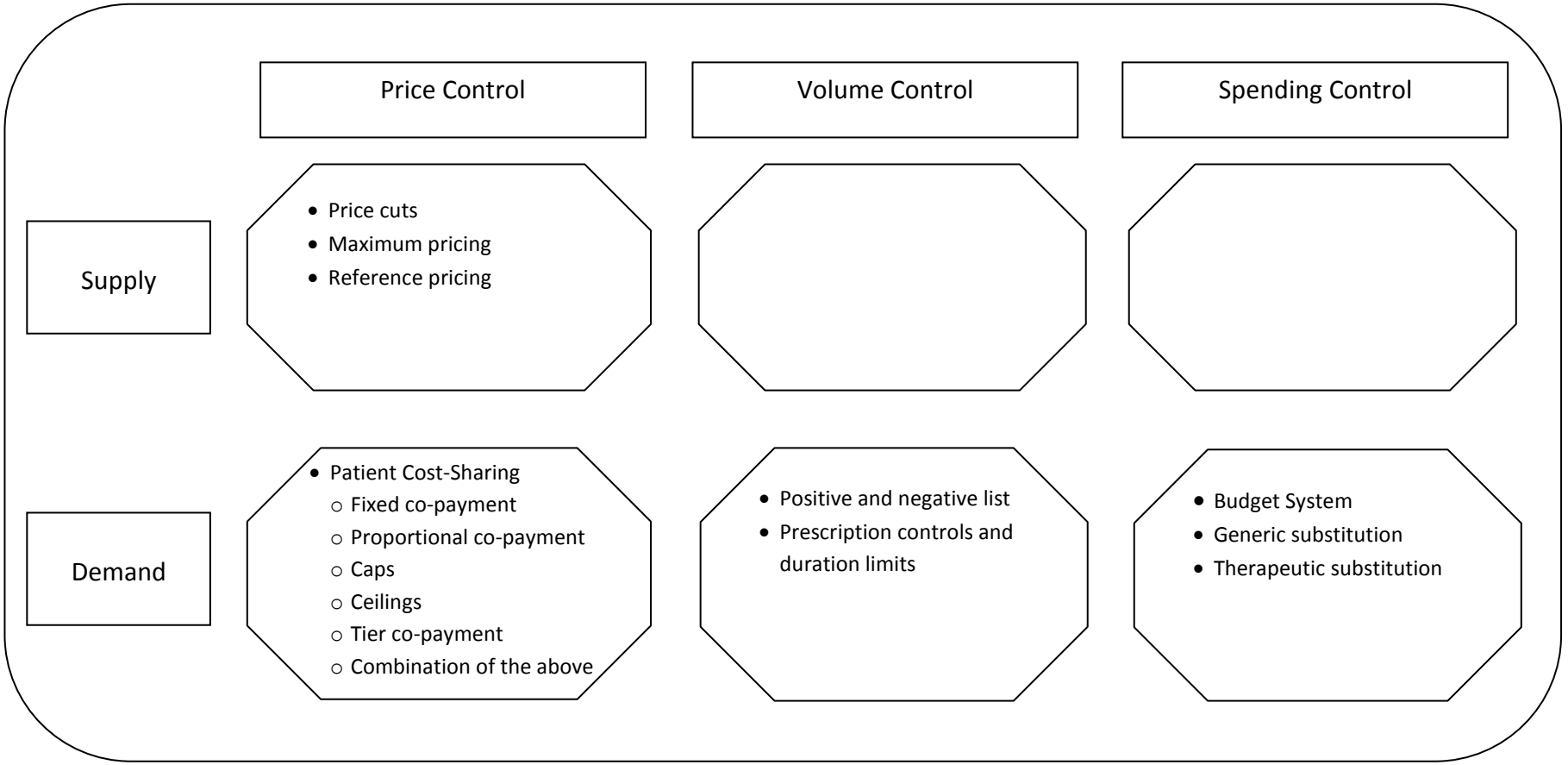


Figure 2.3 Types of cost containment measures

2.6.1.1 Patient cost-sharing

Patient cost-sharing is by far the most popular demand-related measure implemented by policy makers. It reduces the insurer's pharmaceutical expenditure by shifting the financial burden from the insurer to the patients and making patients more cost-conscious by shifting to cheaper drugs (Gross et al., 1994). It also prevents unnecessary demand by creating financial disincentives for patients to use pharmaceuticals (Doran et al., 2011). Studies show that patients with higher cost-sharing tend to use less drugs and cheaper drugs compare to those with lower cost-sharing (Joyce et al., 2002). Patient cost-sharing measures are described in different terms and definitions with regards to the numbers and types of drugs covered, types of patient groups covered and the size of the patient's financial share. The different types of cost-sharing implemented by policy makers are fixed co-payments, proportional co-payment/coinsurance, caps, ceilings and tier co-payments (Austvoll-Dahlgren et al., 2008).

2.6.1.1.1 Fixed Co-payment

A fixed co-payment is defined as a fixed amount of payment paid by the patient per drug or prescription. The purpose of a fixed co-payment is to reduce drugs utilisation and overall drug expenditures. Co-payments for every prescription are the same amount regardless of whether a brand or generic drug. Thus, patients have no incentives to choose less expensive drugs (Gross et al., 1994). A fixed co-payment policy is practised in countries such as United Kingdom and Australia. In the United Kingdom, a fixed co-payment is applied in all National Health System (NHS) prescription items. This payment of £7.85 (from April 2013) per prescription was required regardless of the underlying cost of the drugs supplied (Government Digital Service, 2013). In Australia, a maximum co-payment of A$36.10 (from January 2013) per prescription was required to be paid by patients in the general category for most Pharmaceutical Benefits Scheme (PBS) medicines

while patients in the concessional category paid A$5.90 per prescription. In the event of medicines costing below the co-payment amount, patients will only be charged for the medicines cost (Department of Health and Ageing, 2013).

2.6.1.1.2 Proportional co-payment/coinsurance

Proportional co-payment also known as coinsurance is defined as an amount paid by the patient based on the percentage of the drug or prescription cost. In contrast to fixed co-payment, proportional co-payment gives patients incentives to choose less expensive drugs and reduce drugs utilisation and overall drug expenditures. For example, since January 2004, patients in Germany paid 10% of the prescription cost but this was limited to a maximum payment of €10.0 (Herr et al., 2011).

2.6.1.1.3 Caps

A cap imposes a limit on either the volume or the amount of prescriptions purchased by the patient at no cost or minimal payment. If the cap is reached, the patient is required to pay all additional pharmacy costs out of pocket. The purpose of caps is to encourage patients and prescribers to use fewer medications and prioritise their drugs usage (Austvoll-Dahlgren et al., 2008). In the United States, with the Medicare Part D benefit, patients were required to pay a deductible of US$325.0 (for the year 2013) and an additional 25% of the drugs cost up to an Initial Coverage Limit of US$2,970 (for the year 2013). Once the Initial Coverage Limit was reached, patients were required to pay full payment of the cost of drugs (Q1Group LLC, 2013).

2.6.1.1.4 Ceilings

A ceiling, also known as a deductible or safety net, is defined as a co-payment or contribution by patients to the cost of the drugs up to a certain threshold or ceiling in a defined period of time. Once the ceiling is reached,

the safety net applies and patient's co-payments are reduced or exempted. The ceiling policy benefits high users of medicines such as patients with chronic disease or those using multiple drugs (Brown et al., 2006). For the year 2011, patients in Sweden were entitled to full reimbursement for any expenditure above an annual ceiling of DKK2,200 (€244) while chronically ill patients in Denmark were given full reimbursement for drug purchases above the annual ceiling of DKK3,555 (€477) (Anell et al., 2012; Olejaz et al., 2012). In Australia, the safety net thresholds beginning January 2013 were at A$354.00 and A$1,390.60 for the concessional beneficiary category and the general beneficiary category respectively. Once the safety net was reached, the general category patient paid A$5.90 per prescription while the concessional category patient got the medicine for free (Department of Health and Ageing, 2013).

2.6.1.1.5 Tier co-payment

A tier co-payment is a co-payment structure where patients pay a different co-payment for drugs, depending on the tier of the drugs. Generic drugs usually comprise the lowest tier, with the lowest co-payment required while brand drugs are usually in the second tier where it a higher patient's co-payment is required. In the case of a multi-tier structure, the second tier is usually for preferred brands, the third tier for branded drugs and the fourth tier is typically for drugs that require prescription by a specialist. The higher the drugs in the tier hierarchy, the higher the patient's co-payment required. The purpose of tier co-payments is to encourage patients to use generic or cheaper drugs by choosing a lower tiered drug. Tier co-payment policy also gives insurers the bargaining power to negotiate with manufacturers for a price rebate in exchange for a preferred tier by the manufacturers (Goldman, 2007).

2.6.1.2 Positive and negative list

A positive and negative list is basically a formulary that defines the drugs eligible for reimbursement. A positive list formulary includes drugs that are eligible for reimbursement while a negative formulary list includes drugs that are not reimbursed with the full cost of the drug has to be borne by patients (Ess et al., 2003). The lists are revised regularly to include new drugs and to exclude drugs with low therapeutic value. The aims of the listing are to reduce overall pharmaceutical expenditures and drugs overutilization. However, the need to individualise a patient's treatment may lead to the selection of second best alternative drugs due to the limited choice available to the patient (Dewa et al., 2003). This creates a "balloon effect", whereby restraining expenditures in one part of the health sector (in this case, pharmaceutical expenditure) will inflate expenditures in another part (for example, hospitalisation cost) and lead to increases in the overall healthcare expenditures (Julio López et al., 2000). For example, in 1998, Greece introduced a positive list to curb the growth of pharmaceutical expenditures but it was found to be ineffective in controlling pharmaceutical expenditure growth (Yfantopoulos, 2008). In Spain, the introduction of a negative list in September 1998 not only failed to reduce the total pharmaceutical expenditure but resulted in higher pharmaceutical expenditure. Patients shifted from using medicines in the negative list to medicines in the positive list which contained more expensive drugs (Darbà, 2003).

2.6.1.3 Prescription controls and duration limits

Prescription controls policy imposes certain conditions that must be fulfilled prior to the reimbursement of a drug. The conditions attached are usually to a specific drug or a group of drugs that are likely to be misused or a drug that is costly (Rietveld et al., 2003). In the province of British Columbia, Canada, physicians are required to obtain prior authorisation from the health insurer before prescribing

cyclooxenase-2 inhibitor drugs while in Ontario, Canada, physicians are required to justify the prescribing of cyclooxenase-2 inhibitor drugs by filing in a special prescription form (Marshall et al., 2007). For the duration limits measures, the quantity of drugs allowed to be reimbursed over a period are restricted by the insurer. It can be imposed during the prescribing or the dispensing of the drug where the maximum total quantity allowed is limited. Besides restricting the quantities, it can also be applied to a minimum resupply period that allows a repeat prescription to be resupplied. Usually called resupply limits, the policy will not reimburse prescriptions that are resupplied before the imposed period and will attract a full payment from patients who will not be reimbursed by insurers. The aims of resupply limit are to reduce drugs stockpiling by patients and allow drugs to be distributed evenly throughout the year (Donnelly et al., 2000). In Australia, a resupply limit policy was introduced in November 1994 to increase the minimum resupply period for drugs that had five or more repeats from three days to twenty days.

2.6.1.4 Generic Substitution

Generic substitution refers to switching between a branded drug and its therapeutically equivalent generic version (Committee on Drugs, 1987). Pharmacists are allowed to substitute with equivalent generics of the prescribed product as long as certain criteria are met such as having the same active ingredient, dosage form, dose, and route of administration (Holmes et al., 2011). The aim of generic substitution is to lower the overall pharmaceutical expenditure by increasing the dispensing of less expensive generic medicines. Generic substitution also increases the price competition between pharmaceutical manufacturers, thus reducing the price in the long term (Timonen et al., 2009). In 1994, Australia introduced a generic substitution policy, which made it possible for pharmacists to substitute for the prescribed drug brand at the time of dispensing (Chong et al., 2011). Pharmacists are usually given financial incentives to encourage patients to switch to generics. In

France, a fixed sum of €0.53 per prescription has been paid to pharmacists when a generic substitution takes place (Catherine et al., 2010).

2.6.1.5 Therapeutic substitution

Therapeutic substitution also known as therapeutic interchange is a policy where pharmacists are permitted to switch the prescribed drug with a chemically different drug but within the same therapeutic category (Holmes et al., 2011). An example is the substitution of the anti-depressant drug Escitalopram with Citalopram, both belonging to the selective serotonin reuptake inhibitor (SSRI) class but chemically different drugs.

2.6.1.6 Budget System

A budget system for pharmaceutical expenditures allocates a certain amount of budget to prescribers for a certain time period, usually a year. Only certain countries have implemented this system including, the United Kingdom, Germany and Taiwan. In United Kingdom, the budget system was known as General Practitioner (GP) fundholding. The GP fundholding was introduced in 1991 and abolished in 1999. Annually, GP fundholders were given a certain budget to cover the cost of prescriptions for patients on their list. The amount of the budget was based on spending in the previous year but negotiable with health authority in order to obtain a higher budget (Delnoij et al., 2000; Harris et al., 1996).

2.6.2 Influencing the supply for pharmaceuticals

2.6.2.1 Price Cut

With price cut measures, policy makers cut the manufacturer's selling price of pharmaceuticals either across the therapeutic group or individually. Price cuts are usually applied to products that are off-patent and its generic equivalent is submitted for listing. The purpose of price cuts is to reduce the total pharmaceutical expenditure but it does not necessarily reduce the volume of prescriptions. In

recent years, France and Ireland have imposed price cuts on pharmaceuticals. In 2006, France imposed a 15% price cut on nearly 238 products and made an annual saving of €70 to 100 million (Catherine et al., 2010). Ireland carried out a series of price cuts in phases between 2007 and 2010. In phase 1, a 20% price cut was introduced in March 2007 while phase 2 saw a further 15% price cut in January 2009. The third phase was introduced in February 2010 where the prices of off-patent products were cut by 40% (Usher et al., 2012). In Australia, a price cut for pharmaceuticals was implemented as part of the creation of two separate formularies. Formulary 1 (F1) and Formulary 2 (F2) were created in August 2007 with all medicines listed on F2 subjected to either a drop of 2% per year for three years or a one-off price reduction of 25% on 1 August 2008 (Centre for Strategic Economic Studies, 2009).

2.6.2.2 Maximum pricing

A maximum pricing mechanism works by setting a maximum price for pharmaceuticals whether universally for all pharmaceuticals covered by the insurer or for a specific group of pharmaceuticals. The setting of a maximum price by policy makers varies between countries, taking into consideration several factors such as prescribing and utilisation patterns, budget size, and the role and importance of pharmaceutical industries in the economy (Mossialos et al., 2004).

2.6.2.3 Reference pricing

Reference pricing was first introduced in Germany in 1989, and refers to where drugs that have certain equivalence criteria are grouped together and a reference price is set for the group based on the lowest price quoted by manufacturers. The reference price is the price that insurers agree to reimburse for the drug and patients will pay the difference if the drug cost is higher than the reference price. If patients buy a drug that is lower or equal to the reference price, then the drug is reimbursed up to the reference price. The criteria for grouping the drugs depend on the level of equivalence, either chemically, pharmacologically or

therapeutically (Galizzi et al., 2011). Chemically equivalent grouping is where identical products with the same active ingredients are grouped together and are considered therapeutically interchangeable. This is used in some countries, for example, Sweden, Denmark and Norway. Pharmacologically equivalent grouping consists of drugs that are chemically slightly different but pharmacologically related drugs. This approach is used in British Columbia and Australia. In therapeutic equivalence grouping, drugs that are used to treat a particular condition (e.g. hypercholesterolemia) are clustered together. Germany, the Netherlands and New Zealand use this method of classification (López-Casasnovas et al., 2000). Over the years, the reference pricing term had expanded to include term such as reference drug pricing, reference based pricing, maximum allowable costs, best available prices and minimum pricing (Aaserud et al., 2006). Reference pricing acts to encourage patients to switch to cheaper drugs, thus reducing the demand for expensive drugs. The reduction in demand leads to a reduction of price by manufacturers to gain market share, creating an efficient mechanism for reducing drug prices (Galizzi et al., 2011).

2.7 Conclusion

As discussed above, there are a variety of cost containment measures available for policy makers to select from in order to contain pharmaceutical volumes and expenditures. However, each country implementing those cost containment policies has a unique and different set of characteristics in term of its demographic, social, and political features, the structure of its health care system and its economic position, therefore producing uncertainty in the effectiveness of implementing any of these cost containment measures. It is essential for policy makers in each country to select and customise cost containment measures that suit the need of their country in order to achieve its objective in containing the pharmaceutical expenditure. This choice should be made after consideration of the evidence base of effective studies conducted in that country or similar countries,

and relative to the specific characteristics of that country which might impact on effectiveness of local implementation of measures.

Chapter 3.0 Australia's Healthcare System and the Pharmaceutical Benefits Scheme

3.1 Introduction

The previous chapter presented a brief global perspective of the pharmaceutical industry, the different types of healthcare system and different cost containment measures that countries can implement. This chapter focuses more narrowly on the Australian context. First, Australia's healthcare system and the PBS are discussed. Australia's healthcare system is based on a national health service model, similar to the United Kingdom, with public funding covering primary health care, ambulatory services and inpatient care in public hospitals, and PBS subsidised medicines. The next two sections in this chapter examine the trend in volume of scripts and expenditure for the PBS from 1991 to 2011 and key drivers to the growth of spending on the PBS respectively. Following this, reforms to the PBS including cost containment measures implemented by the Australian Commonwealth government between 1991 and 2011 are outlined. The final two sections discuss the prevalence of hypercholesterolemia and hyperlipidaemia in Australia and the usage of HMG-CoA reductase inhibitors in the PBS. The examination of HMG-CoA reductase inhibitors, also known as statins, is important as statins were the most widely dispensed PBS medicine and incurred the highest total expenditure. Furthermore, pharmaceutical expenditure for cardiovascular disease has been projected to increase from A$2.8 billion in 2003 to A$5.2 billion in 2033, exceeding projected increases in other diseases expenditure such as respiratory disease and endocrine, nutritional and metabolic disorders (Goss, 2008). This discussion provides background to the statistical analysis in Chapter 5.0, in which statins are the class of drugs selected for the category 2 analysis.

3.2 Healthcare System

The Australian healthcare system is modelled on the United Kingdom's national health service model with the goal of providing universal healthcare coverage to all Australian citizens. Initially, Medibank, a national health insurance scheme was introduced in July 1975 by the Labour government under Prime Minister Whitlam to provide universal healthcare coverage. Medibank was administered by the Health Insurance Commission and funded entirely from taxation. Medibank reimbursed 85% of the schedule fee paid by patients for medical services and also provided universal and free access to hospital care through state run public hospitals. However, when the Liberal-National Coalition under Prime Minister Fraser (1975 – 1982) came into power, significant changes were made to the Medibank's universal coverage features. On October 1976, individuals were allowed to opt out of Medibank and purchase private health insurance. Those who chose to remain in Medibank were required to pay a levy of 2.5% of taxable income, which resulted in a large portion of the population being uninsured for hospital care (Behan, 2012; Healy et al., 2006; Scotton et al., 1993). Medibank Private, a private health insurance arm of Medibank, was created in the same year to increase competition in the private health insurance industry (Medibank Private Limited, 2014). In April 1981, the Medibank scheme was terminated and access to free hospital and medical care was limited to pensioners and the poor. When the Labour party returned to power in 1983 under Prime Minister Hawke, the original Medibank scheme was reintroduced with a new name, Medicare. Since 1984, Medicare has undergone numerous changes and levy increases but the main features of providing universal health coverage to all Australians remain largely intact (Duckett, 2011). The basic Medicare Levy was calculated at 1.5% of taxable income, with low income earners with income below the thresholds exempted from paying the Medicare levy. However, starting from 1 July 2014, the Medicare levy rate was increased to 2.0% of taxable income to help fund the National Disability Insurance Scheme ("Medicare Levy Amendment (DisabilityCare Australia) Bill," 2013). An additional levy of between 1.0% and 1.5%

is applied to individuals with high annual incomes (above A$88,000 for singles and A$176,000 for families, 2013-14) who do not have adequate levels of private hospital health insurance cover (Australian Taxation Office, 2014). The levies and a subsidy from the Commonwealth government provide the basic funding for Medicare. Medicare rebates up to 100% of the scheduled fee incurred for any consultation with a general practitioner or 85% of the fee for an out-of-hospital specialist visit. Patients are required to pay the 15% balance for specialist visits as co-payment plus any additional charges. To protect individuals and families that require frequent medical attentions, a Medicare Safety Net arrangement was created. Once the Medicare Safety Net threshold (A$430.90 for 2014) is reached, Medicare fully reimburses the schedule fee for out-of-hospital services (Biggs, 2003; Department of Human Services, 2013a). Besides providing direct payments to primary health care services, Medicare also provides funding to public hospitals where patients receive free access to hospital care (Boxall et al., 2013; Palmer et al., 2000; Willis et al., 2012).

Along with Medicare, private health insurance scheme plays an important role in the Australian healthcare system. One of the largest private health insurance funds is the government-owned Medibank. Private health insurance is available to cover private hospital costs, ambulance costs and the cost of ancillary health services such as dental, chiropractic, podiatry and physiotherapy. Total expenditure on healthcare (health goods and services incurred by governments, private health insurers and individuals) is on the rise. In 2010/11, total expenditure on healthcare was A$130,266 million, up from A$28,738 million in 1991/92. Health expenditure in the 10-year period from 2001/02 to 2010/11 grew at a rate of 8.4% per year, above the rate of growth of 7.3% in the previous 10-year period from 1991/92 to 2000/01 (Table 3.1) (Australian Institute of Health and Welfare, 2011).

Table 3.1 Total health expenditure (current prices[^]) and annual growth rates, 1990/91 to 2010/11

Year	Health expenditure (A$ million)	Annual growth rate (%)
1991/92	30,505	6.1
1992/93	32,450	6.4
1993/94	34,323	5.8
1994/95	36,473	6.3
1995/96	39,047	7.1
1996/97	42,116	7.9
1997/98	44,802	6.4
1998/99	48,428	8.1
1999/00	52,570	8.6
2000/01	58,269	10.8
2001/02	63,099	8.3
2002/03	68,798	9.0
2003/04	73,509	6.8
2004/05	81,061	10.3
2005/06	86,685	6.9
2006/07	94,938	9.5
2007/08	103,563	9.1
2008/09	113,445	9.5
2009/10	121,355	7.0
2010/11	130,266	7.3
Average annual growth rates		
1991/92 to 2000/01		7.3
2001/02 to 2010/11		8.4
1991/92 to 2010/11		7.9

Source: Australian Institute of Health and Welfare

[^] Current prices are the prices for each year in the value of the currency for that particular year

The ratio of total health expenditure to gross domestic product has grown steadily from 7.2% in 1991/92 to 9.7% in 2009/10 and remained constant in 2010/11 (Table 3.2).

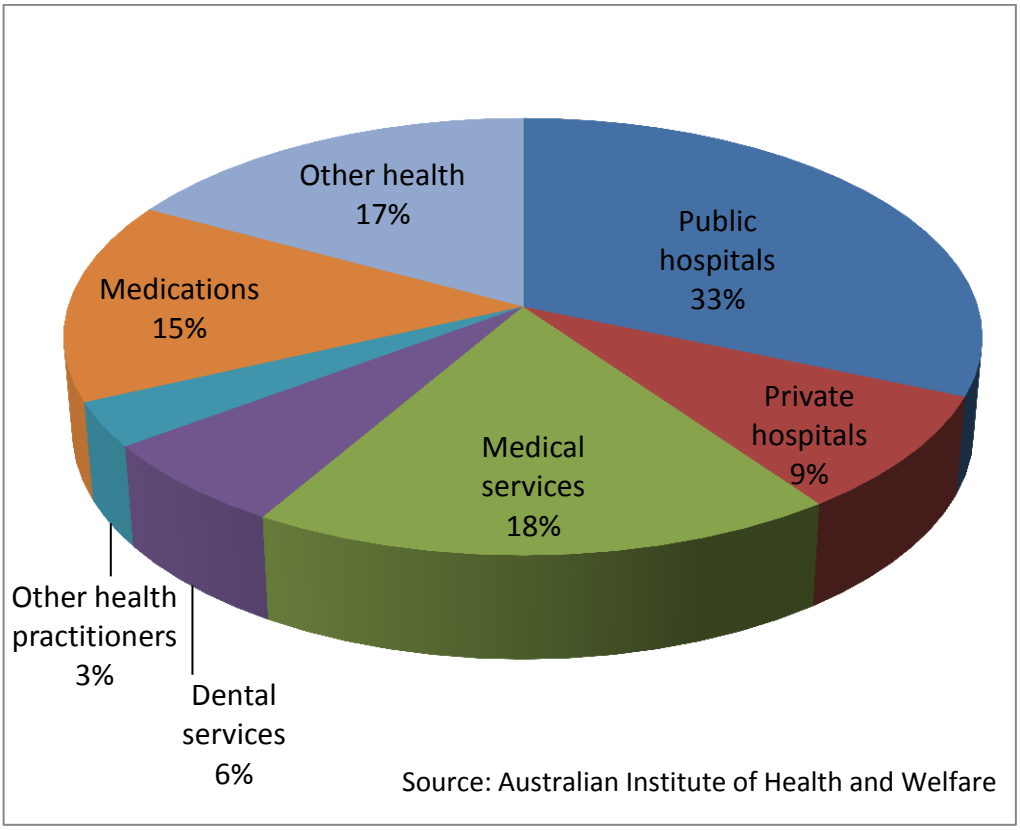
Table 3.2 Total health expenditure (current prices) and Gross Domestic Product (GDP) and annual health expenditure to GDP ratios, 1991/92 to 2010/11

Year	Health expenditure (A$ million)	GDP (A$ million)	Ratio of health expenditure to GDP (%)
1991/92	30,505	420,969	7.2
1992/93	32,450	436,448	7.4
1993/94	34,323	458,863	7.5
1994/95	36,473	486,411	7.5
1995/96	39,047	514,902	7.6
1996/97	42,116	546,198	7.7
1997/98	44,802	575,549	7.8
1998/99	48,428	607,153	8.0
1999/00	52,570	640,694	8.2
2000/01	58,269	688,573	8.5
2001/02	63,099	732,647	8.6
2002/03	68,798	783,616	8.8
2003/04	73,509	832,895	8.8
2004/05	81,061	894,496	9.1
2005/06	86,685	965,113	9.0
2006/07	94,938	1,041,294	9.1
2007/08	103,563	1,137,253	9.1
2008/09	113,445	1,240,595	9.1
2009/10	121,355	1,249,307	9.7
2010/11	130,266	1,345,692	9.7
Average ratios			
1991/92 to 2000/01			7.7
2001/02 to 2010/11			9.1
1991/92 to 2010/11			8.4

Source:
Australian Institute of Health and Welfare
and International Monetary Fund

A large share of the healthcare expenditure is spent on in the public hospital sector (33%) with the next biggest shares of expenditure for medical services (18%) and pharmaceuticals (15%), including those reimbursed by the PBS or paid out-of-pocket by patients (Figure 3.1) (Australian Institute of Health and Welfare, 2011).

Figure 3.1 Proportion of total recurrent expenditure by area of expenditure, 2010/11



The majority of the health expenditure in Australia was funded by the government, the Commonwealth and the states and territories combined. Over the period of 10 years, from 2001/02 to 2010/11, government funding for healthcare has been relatively stable, averaging 70% of total healthcare expenditure (Biggs, 2013). Out-of-pocket payment, private health insurance and other non–government funding sources accounted for the balance of 30% of total healthcare expenditure (Table 3.3). As healthcare expenditure continues to rise, the level of government funding has also increased from approximately A$42 million in 2001/05 to A$90 million in 2010/11 (Australian Institute of Health and Welfare, 2011).

Table 3.3 Total funding for health expenditure by source of funds (current prices) and proportion of total funding, 2001/02 to 2010/11

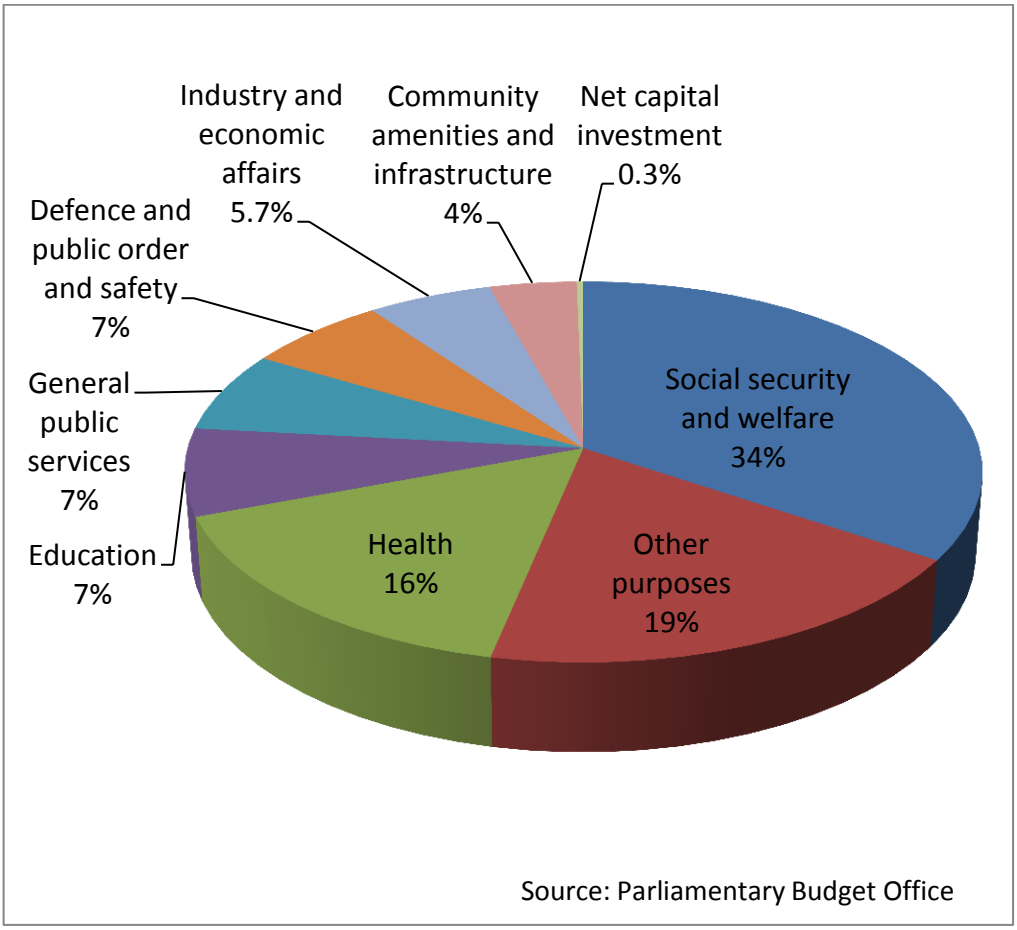
Year	Government (including State and territory governments)		Non-government		
	Health expenditure (A$ million)	Proportion (%)	Health expenditure (A$ million)	Proportion (%)	Total
2001/02	42,413	67.2	20,686	32.8	63,099
2002/03	46,785	68.0	22,013	32.0	68,798
2003/04	49,382	67.2	24,127	32.8	73,509
2004/05	54,918	67.7	26,143	32.3	81,061
2005/06	58,981	68.0	27,704	32.0	86,685
2006/07	64,358	67.8	30,581	32.2	94,938
2007/08	71,152	68.7	32,411	31.3	103,563
2008/09	78,563	69.3	34,882	30.7	113,445
2009/10	84,789	69.9	36,566	30.1	121,355
2010/11	90,064	69.1	40,202	30.9	130,266
Average		**68.3**		**31.7**	

Source: Australian Institute of Health and Welfare

In the 2012/13 Australian Commonwealth government budget, healthcare expenditure accounted for 16% of total spending at A$61 billion. Healthcare

spending was the third largest spending item after the social security and welfare component (34%) and the other purposes component (mainly general revenue assistance to the States and Territories) (19%) (Figure 3.2) (Parliamentary Budget Office, 2013).

Figure 3.2 Composition of government spending by functions, 2012/13



Source: Parliamentary Budget Office

3.3 Pharmaceutical Benefits Scheme

The PBS, a key component of Australia's health system, was created under the Pharmaceutical Benefits Act in 1949 and commenced on 4 September 1950 with 139 medications (Sloan, 1995). It is part of the National Medicines Policy (NMP), with the role of the PBS to provide timely, reliable and affordable access to necessary medicines for Australians. In addition to the objective of dealing with equity of access to medicines, other objectives of the NMP are to ensure medicines meet appropriate standards of quality, safety and efficacy, to promote the quality use of medicines, and to maintain a responsible and viable medicines industry (Department of Health, 2016).

At the present time, the PBS is managed by the Department of Health and Ageing and administered by Medicare Australia. Initially, all drugs were provided free of charge to all residents. In order to provide some control on PBS volumes and expenditure, in 1960, two beneficiary categories were created with patients either in the Pensioner beneficiary category or in the General beneficiary category. A patient co-payment of A$0.50 was introduced for General beneficiary category patients. In 1983, a Concessional beneficiary category was created. The concessional beneficiary category consists of low-income earners and unemployed people who are on social security payments. A co-payment for concessionary beneficiary patients was introduced in 1990 (Biggs, 2002). Three beneficiary categories existed until December 1991 when the pensioner beneficiary category was removed. The co-payment for both concessional beneficiary category patients and general beneficiary patients is increased each year in line with the Consumer Price Index (CPI) and currently stands at A$6.00 (2014) for concessional beneficiary category patients and A$36.90 (2014) for general beneficiary category patients (Department of Health, 2013a).

In order to lessen the financial burden for those patients and their families who require a lot of PBS-listed drugs, a protective mechanism known as the safety

net arrangements was created. Once the annual total cost of drugs exceeds the threshold specified as the Safety Net level, the patient's co-payment is reduced or no payment is required. As of January 2014, the safety net thresholds were A$360.00 and A$1,421.20 for concessional beneficiary category and general beneficiary category respectively (Department of Health and Ageing, 2013). Once the threshold is exceeded, general beneficiary category patients pay for their drugs at the concessional beneficiary category rate while concessional beneficiary category patients get prescriptions free for the rest of the calendar year.

3.3.1 The listing of medicines and medicinal preparations

The listing of medicines and medicinal preparations on the PBS are under the purview of the Pharmaceutical Benefits Advisory Committee (PBAC). The PBAC recommends medicines and its preparations to the Minister for Health for funding under the PBS if the new medicine is more effective or less toxic than the existing medicines, is needed to treat or prevent important diseases or conditions not covered by existing medicines or is as effective and safe as existing medicines listed for the same indications (Department of Health, 2014b). The PBS list is regularly reviewed by the PBAC and medicines may be removed from the list if a more effective and less toxic medicine is available; or if the medicine is no longer cost-effective, is found to be toxic, or the potential for it to be abused outweighs its therapeutic value.

On the other hand, the prices for medicines listed on the PBS are governed by the Pharmaceutical Benefits Pricing Authority (PBPA). The PBPA reviews the prices of medicines listed on the PBS and recommends prices for new items that are to be listed (Pharmaceutical Benefits Pricing Authority, 2010).

3.4 Trends in PBS Volume and Expenditure

Since its inception, PBS expenditure has been rising steadily in line with the ageing and growth of the population, expansion of the number of drugs listed particularly new and relatively expensive medicines, and increases in the incidence of chronic diseases (National Commission of Audit, 2014). About 80 per cent of prescriptions dispensed in Australia are subsidised under the PBS (Medicare Australia, 2010). In 1991-1992, the Australian Commonwealth Government paid a total of A$1.22 billion for PBS-subsidised medicines. This expenditure increased to A$8.73 billion in 2010-2011, a growth of approximately seven times in a period of 20 years (Figure 3.3) (Department of Health and Ageing, 2012)

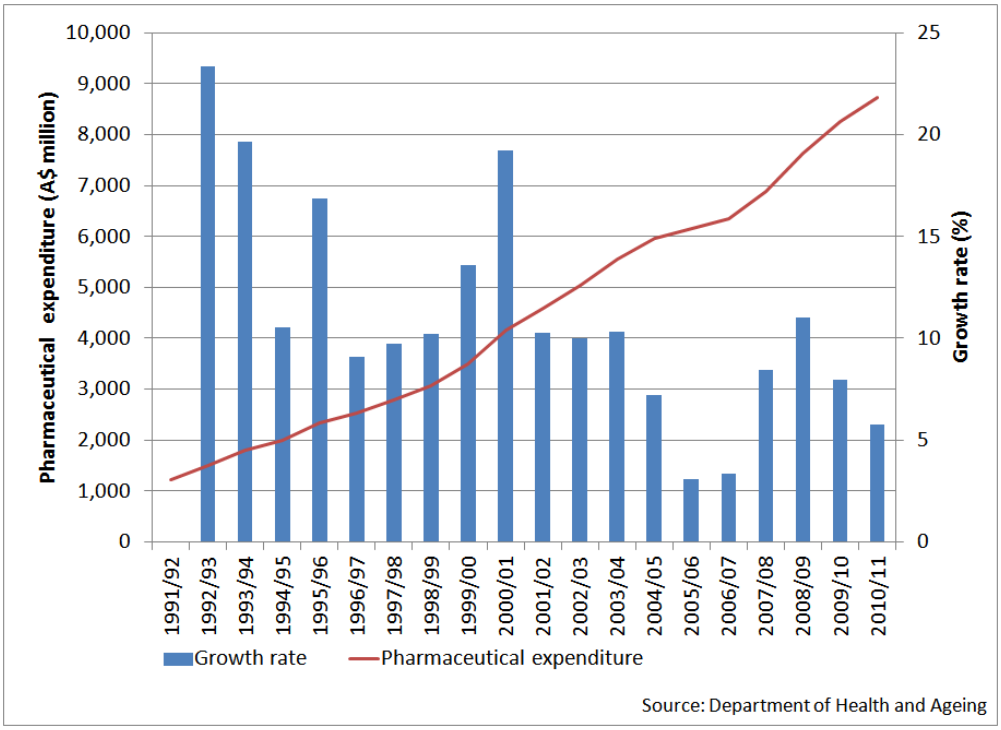


Figure 3.3 Total PBS expenditure by Australian government, current prices, and annual growth rates, 1991/92 to 2010/11

Since 1991, PBS expenditure has grown at an average rate of 10% annually. Although the growth rate in recent years had slowed compared with the early 1990s, average PBS expenditure continued to grow at a rate of 7.7% from 2001/02

to 2010/11. This remains above the corresponding growth rate of GDP, which grew at an annual rate of 6.5% over the period (International Monetary Fund, 2013).

On average, between 1991/92 and 2010/11, the ratio of PBS expenditure to health health expenditure was 9.5% (

Table 3.4). Its share of health expenditure grew steadily from 6.0% in 1991/92 to 11.3% in 2003/04 before declining and stabilising at 9.7% in the past few years.

Table 3.4 Total PBS and health expenditure by Australian government (current prices) and annual pharmaceutical expenditure to health expenditure ratios, 1991/92 to 2010/11

Year	Government expenditure (including State and territory governments)		
	PBS (incl. Section 100) (A$ million)	Health (A$ million)	Ratio of PBS to health (%)
1991/92	1,220	20,210	6.0
1992/93	1,505	21,327	7.1
1993/94	1,801	22,506	8.0
1994/95	1,991	23,911	8.3
1995/96	2,327	25,884	9.0
1996/97	2,538	27,711	9.2
1997/98	2,785	30,184	9.2
1998/99	3,070	32,460	9.5
1999/00	3,488	36,380	9.6
2000/01	4,158	39,465	10.5
2001/02	4,584	42,413	10.8
2002/03	5,043	46,785	10.8
2003/04	5,562	49,382	11.3
2004/05	5,964	54,918	10.9
2005/06	6,148	58,981	10.4
2006/07	6,352	64,358	9.9
2007/08	6,888	71,152	9.7
2008/09	7,645	78,563	9.7
2009/10	8,252	84,847	9.7
2010/11	8,727	90,064	9.7
Average ratios			
1991/92 to 2000/01			8.6
2001/02 to 2010/11			10.3
1991/92 to 2010/11			9.5

Source: Australian Institute of Health and Welfare and Department of Health and Ageing

In terms of prescriptions, both the prescriptions count and average prescriptions per person has increased over the period. Although the increase in prescriptions count has not matched the growth in PBS expenditure, the number of prescriptions recorded by PBS doubled between 1991/92 and 2010/11 (Table 3.5). In 2010/11, PBS recorded an average of 8.4 prescriptions per person, up from an average of 5.4 prescriptions per person in 1991/92.

Table 3.5 Total PBS prescriptions count and average prescriptions per person, 1991/92 to 2010/11

Year	PBS prescriptions count	Average prescriptions per person
1991/92	94,120,154	5.4
1992/93	106,181,617	6.0
1993/94	115,042,043	6.4
1994/95	118,720,677	6.6
1995/96	124,888,282	6.8
1996/97	124,099,563	6.7
1997/98	125,111,809	6.7
1998/99	128,921,219	6.8
1999/00	138,081,923	7.2
2000/01	148,050,778	7.6
2001/02	154,978,239	7.9
2002/03	158,956,686	8.0
2003/04	165,862,101	8.2
2004/05	170,279,502	8.3
2005/06	168,322,615	8.1
2006/07	168,535,519	8.0
2007/08	171,296,023	8.0
2008/09	181,836,127	8.3
2009/10	183,911,537	8.3
2010/11	188,142,255	8.4
Average prescriptions per person		
1991/92 to 2000/01		6.6
2001/02 to 2010/11		8.2
1991/92 to 2010/11		7.4

Source: Department of Health and Ageing and Australian Bureau of Statistics

On a per capita basis, the average PBS expenditure per person has been increasing over the 20-year study period. In 2010/11, the average PBS expenditure per person was at A$390.9, an increase of A$321.2 from 1991/92 (Figure 3.4).

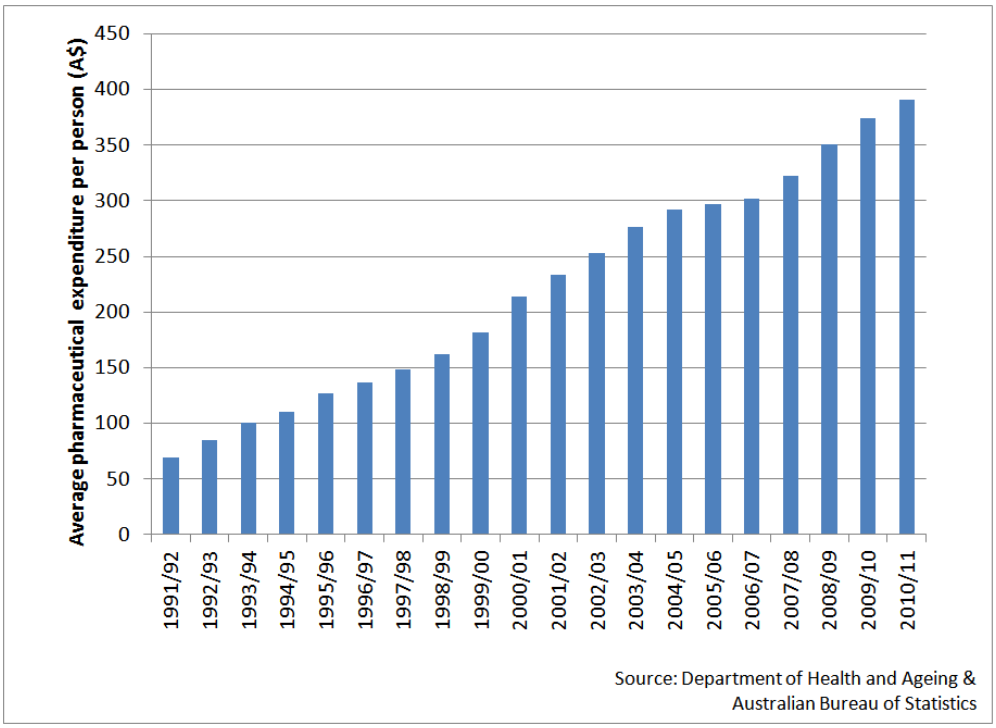


Figure 3.4 Average PBS expenditure per person, current prices, 1991/92 to 2010/11

In comparison to other countries, growth in spending on pharmaceuticals by the Australian Government increased by 51.5% from 2003 to 2009. This put Australia slightly above the average of the 26 countries reporting to the OECD. In that time period, countries with larger GDPs than Australia such as Japan, Germany, Spain and Italy recorded smaller percentage growth in pharmaceutical spending (Figure 3.5) (International Monetary Fund, 2013).

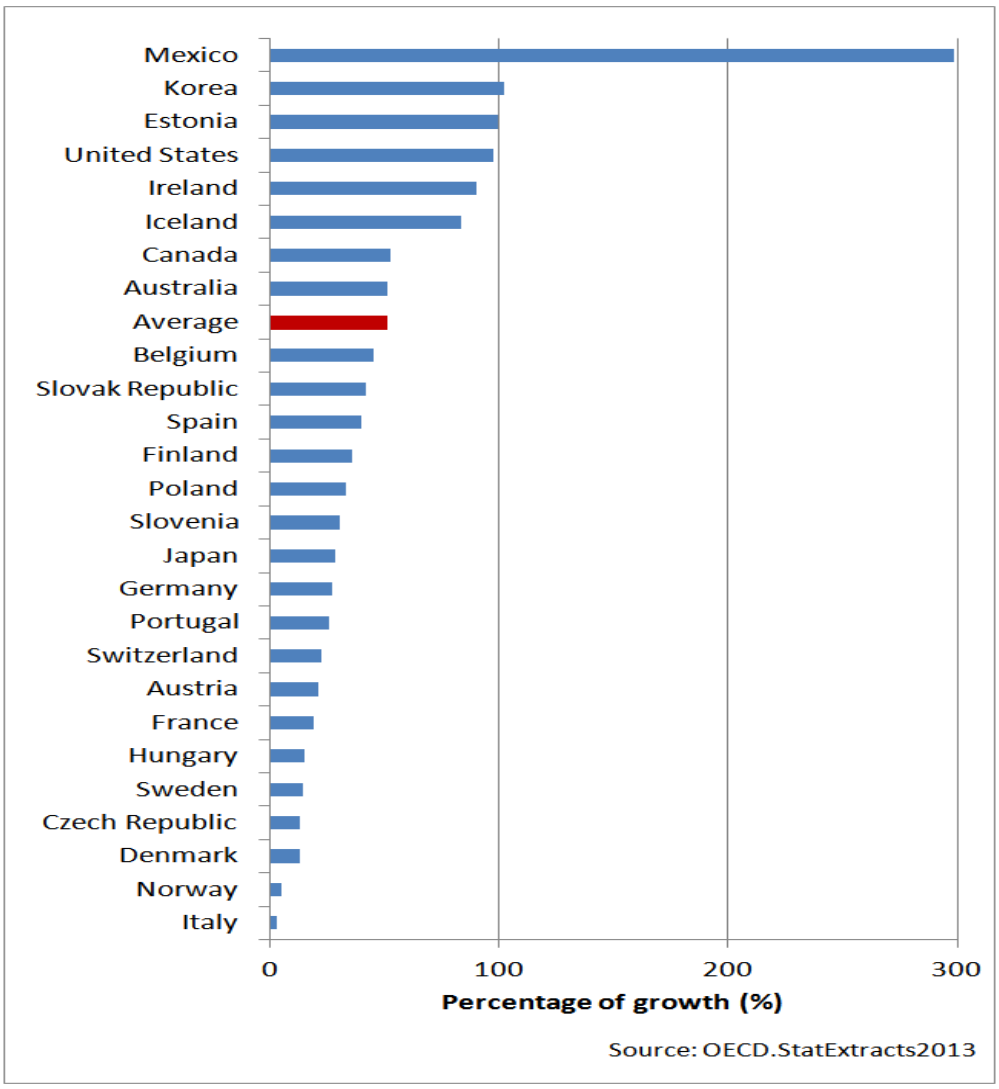


Figure 3.5 Percentage of growth in government's pharmaceutical expenditure in selected OECD countries, 2003 to 2009

3.5 Key Driver to PBS growth

The growth in PBS volume and expenditure in the last two decades has been of concern to the Australian government. Several reports on the PBS have been presented to Parliament for debate and key drivers of PBS growth have been identified (Biggs, 2002; Rickard, 2002). Factors contributing to the growth include ageing population, increases in concessional cardholders, new listing of drugs, and disease prevalence.

3.5.1 Ageing population

Higher living standards and better healthcare provided in Australia has resulted in an increase in life expectancies, thus increasing the proportion of the aged population. Over the past two decades, the proportion of the Australian population aged 50 years and over increased by 9%, representing 33% of the total population (Figure 3.6) (Australian Bureau of Statistics, 2013). Aged people are more susceptible to chronic disease and utilize more drugs for treatment. Although they accounted for nearly a third of the population, patients in the age category of 55 and above were responsible for nearly 70% of total PBS expenditure (Department of Health and Ageing et al., 2013).

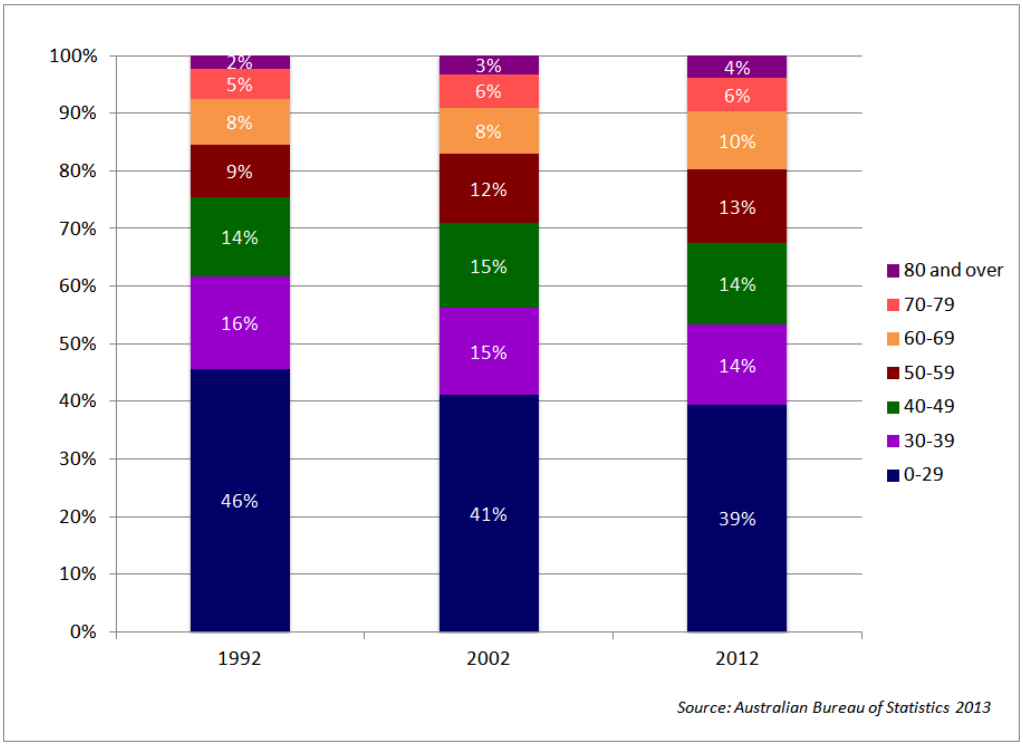


Figure 3.6 Australian population by age groups - 1992, 2002, 2012

3.5.2 Increases in concessional cardholders

Concessional cardholders are entitled to purchase drugs listed on the PBS at a discounted rate. Concessional patients pay a minimal amount of A$6.00 (in 2014) and no payment is required if the safety net threshold is reached. Therefore, the Australian government bears a big percentage of the cost of drugs purchased by concessional patients. There are four types of concessional cards issued by the Australian government: Health Care Cards, (Low Income) Health Care Cards, Pensioner Concession Cards and Commonwealth Seniors Health Cards. The Health Care Card is for people receiving social security allowances while the (Low Income) Health Care Card is for people with an income below a certain level. The largest group of the four, the Pensioner Concession Card, is available to pensioners and certain elderly receiving income-support payments, while the Commonwealth Seniors Health Card is available to people who have reached the qualifying age of pension age and are not receiving an income support payment (The Department of Families Housing Community Services and Indigenous Affairs, 2012). Figure 3.7 shows the number of concessional card holders and the annual growth of concessional card holders in the time period from 2000/01 to 2011/12. The numbers of concessional card holders were relatively constant, approximately five million card holders between 2000/01 and 2007/08. However, in 2008/09, there was a 6% increase in the number of card holders and the number of concessional card holder has continued to grow. One of the main reasons for this increase was the global financial crisis in mid-2008 that resulted in higher unemployment allowance recipients (Department of Human Services, 2010; The Department of Families Housing Community Services and Indigenous Affairs, 2009).

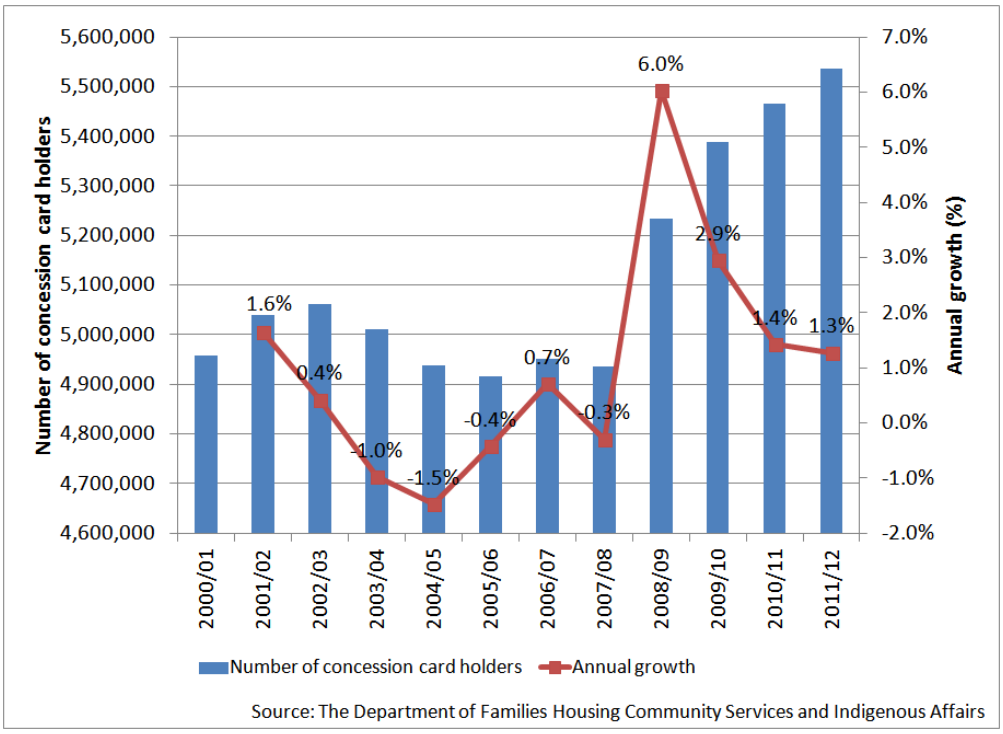


Figure 3.7 Total number of concessional card holders and annual growth rates, 2000/01 to 2011/12

3.5.3 New listing of drugs on the PBS

The listing of newer and effective but often more expensive drugs on the PBS has also contributed to the growth of PBS expenditure. From 1991 to 2012, a total of 535 new drugs were listed on the PBS, bringing the overall number of drugs listed from 536 in 1991 to 781 in 2012 (Figure 3.8) (Sweeny, 2013). Each new drug approved to be listed contributes to PBS expenditure an average of A$9.9 million annually (Sweeny, 2007b). For example, Atorvastatin, an HMG-CoA reductase inhibitor was the most prescribed and highest total expenditure drug in PBS for the year 2012. From its listing in February 1998 till December 2012, Atorvastatin has added A$6.43 billion to the PBS expenditure. On average, Atorvastatin cost the Australian government A$ 429 million per year (Medicare Australia, 2013).

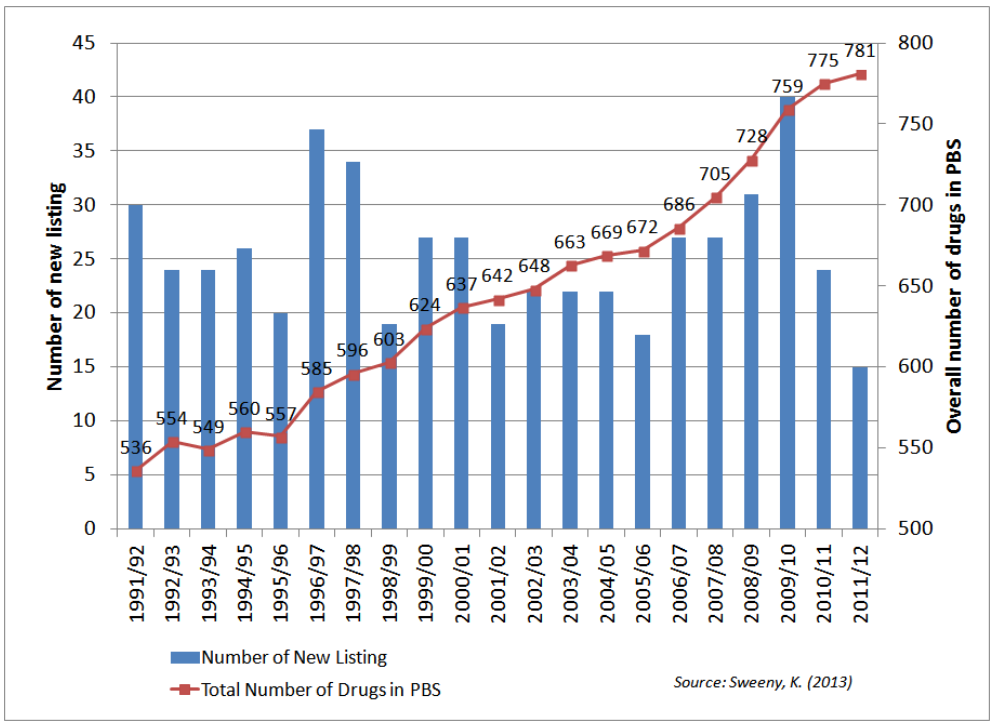


Figure 3.8 Total number of new drugs listed and the overall number of drugs in the PBS, 1991/92 to 2011/12

3.5.4 Disease prevalence

The 2007-2008 the National Health Survey (2009) showed a high prevalence of chronic diseases among Australians. The prevalence of diseases such as cancer was 2%, up from 1.6% in 2001 while diabetes prevalence increased to 4% from 2.9% in 2001. The prevalence of long-term mental or behavioural conditions increased to 11% from below 10% in 2001 and the prevalence of arthritis increased by 1% to 15% (Australian Bureau of Statistics, 2009). In a recent health report by the Australian Bureau of Statistics (2014), nearly 3.3 million persons or 14.8% of the population in Australia suffered from arthritis. The second highest condition reported was mental and behavioural conditions, with 3.0 million persons or 13.6% of the population followed by asthma with 2.4 million persons or 10.2% of the population. Other long-term conditions suffered by Australians include heart disease, diabetes, osteoporosis, cancer and kidney disease (Table 3.6).

The increase in the number of persons with chronic diseases such as neoplasms, diabetes mellitus, hypertensive disease, asthma and hypercholesterolemia is likely to increase the government's pharmaceuticals expenditure due to its subsidising drugs to those patients on a long term basis. In 2004–05, a total of A$21.1 billion representing 40% of health expenditure was spent on treating five disease groups: cardiovascular diseases (A$5.9 billion), mental disorders (A$4.1 billion), musculoskeletal diseases (A$4.0 billion), neoplasms (A$3.8 billion) and respiratory diseases (A$3.3 billion) (Australian Institute of Health and Welfare, 2010).

Table 3.6 Proportion and number of persons with long-term conditions, 2011/12

Long-term conditions	Proportion of persons (%)	Number of persons (n, million)
Arthritis	14.8	3.3
Mental and behavioural conditions	13.6	3.0
Asthma	10.2	2.3
Heart disease	5.0*	1.1
Diabetes	4.6*	1.0
Osteoporosis	3.3	0.7
Cancer	1.5	0.3
Kidney disease	0.9*	0.2

Source: Australian Bureau of Statistics

* population aged 2 years and over

3.6 PBS Reforms and Cost Containment Measures

The continuous increase in pharmaceutical expenditure has the potential to jeopardise the sustainability of the PBS and the relevance of the National Medicines Policy. One of the four objectives of the National Medicines Policy is to provide timely access to medicines that Australians need, at a cost individuals and the community can afford (Department of Health and Ageing, 2000). High prices of medicines have been found to keep patients away from filling their prescriptions at pharmacies. One survey found that 20% of patients did not completely fill their prescription while 10% of patients reduced the dose of prescribed medicines, citing high medicines cost as the reason (Doran et al., 2004). In a more recent study, the Steering Committee for the Review of Government Service Provision in 2014 reported that 8.5 per cent of respondents delayed or did not purchase prescribed medicines due to cost in the 12 month period between 2012 and 2013 (Steering Committee for the Review of Government Service Provision, 2014). Failing to adhere to medication increases medical costs in term of the hospitalisation rate and also contributes to loss of quality of life years (Sokol et al 2005; Harvey 2005).

In the last two decades, the escalation of PBS spending has forced the Commonwealth Government to implement several cost containment measures (Figure 3.9) (Rickard, 2002). These include:-

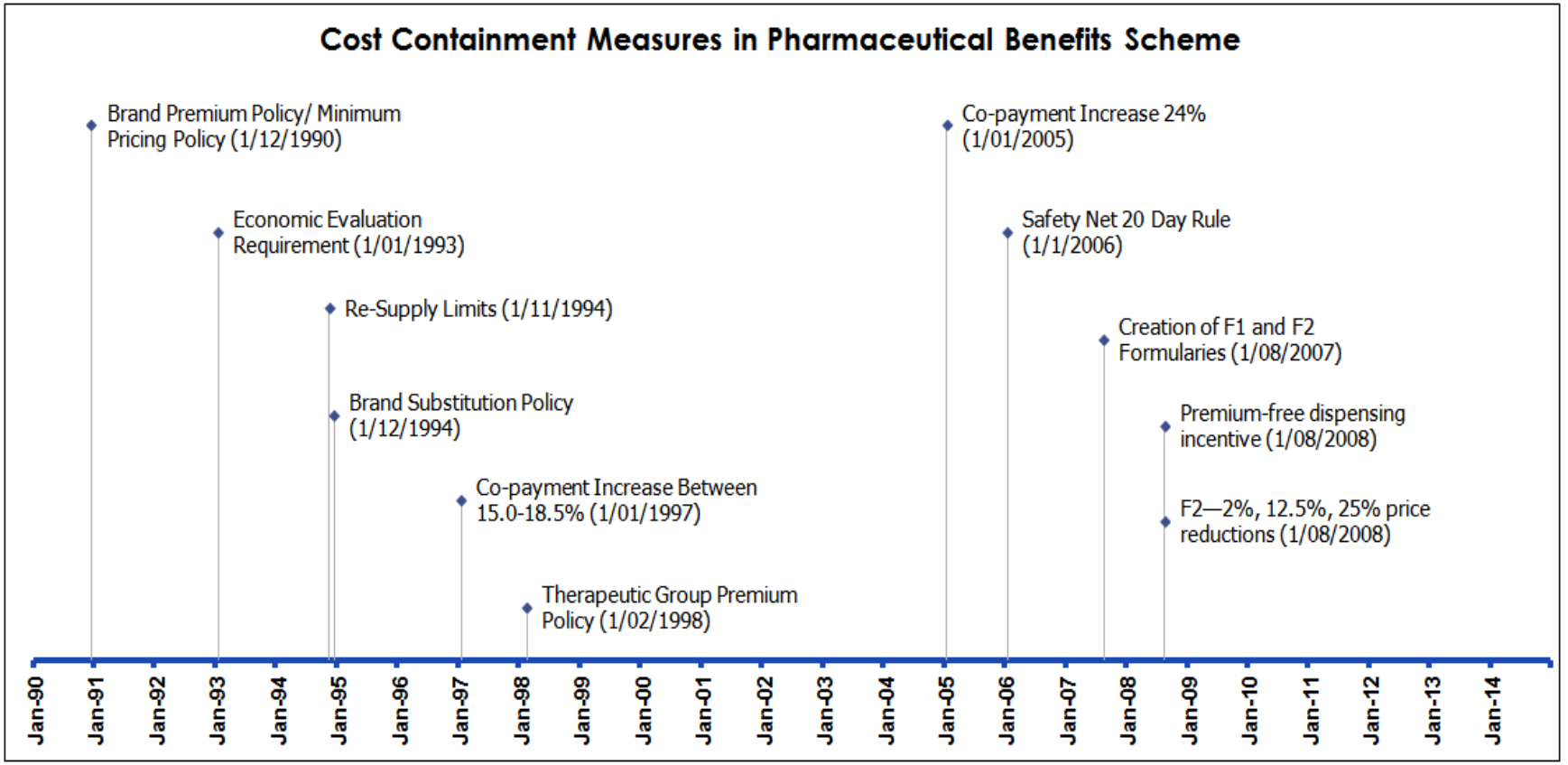


Figure 3.9 Cost containment measures in Pharmaceutical Benefits Scheme, 1991 to 2012

3.6.1 Brand Premium Policy

On 1 December 1990, the Brand Premium Policy was introduced to increase price competition among pharmaceutical manufacturers and promote the development of the generic pharmaceutical industry. Under this policy, where there is more than one brand of a particular drug available, the Australian Government subsidises a drug to the level of the lowest priced brand. If a patient is prescribed a brand drug that is priced above the price charged by the lowest priced brand, a brand premium, which is the price difference between the lowest price brand and the brand prescribed, has to be paid by the patient. This extra amount does not count towards their PBS safety net threshold (Department of Health, 2013b; Sweeny, 2007a).

3.6.2 Economic Evaluation requirement

Since January 1993, economic evaluation has been required by the Commonwealth Government in support of applications for listing of new medicines under the PBS. The Economics Sub Committee (ESC) secretariat evaluates the economic evaluation submission and ensures new drugs or new indications are cost-effective so as to encourage efficient use of resources. The types of economic evaluation needed depend on whether the proposed drug is therapeutically superior or non-inferior (equivalent) to the main comparator. If the proposed drug is non-inferior (equivalent) to the main comparator, cost-minimisation analysis is sufficiently adequate for submission. However, if the proposed drug is therapeutically superior to the main comparator, four types of economic evaluation may be required depending on the outcome of the clinical evidence: cost-utility analysis, cost-effectiveness analysis, cost-benefit analysis or cost-consequences analysis (Pharmaceutical Benefits Pricing Authority, 2009).

3.6.3 Re-Supply Limits and Safety Net 20 day rule

In November 1994, a minimum re-supply period for a range of pharmaceuticals was increased from three to twenty days. Once a medicine has been supplied to a patient, it may not be supplied to that patient again on the same day or within the next 20 days. This was introduced to prevent patients from taking advantage of the safety net to get multiple prescriptions towards the end of the year (Donnelly et al., 2000). However, in January 2006, the Safety Net 20 day rule was introduced to improve the effectiveness of the re-supply limit policy. For certain PBS medicines, if repeated within 20 days, the patient co-payment amount does not count towards the calculation of the safety net threshold. If the patient has exceeded the threshold of the safety net level, the patient's co-payment will be charged at the standard amount and not the reduced safety net co-payments (Department of Health and Ageing, 2005). Besides preventing patients from abusing the safety net benefits, this measure was introduced to encourage good practice for safe use of drugs. Savings from this measure to the government were estimated at around A$70 million over four years from 2006 to 2009 ("National Health Amendment," 2005).

3.6.4 Brand Substitution Policy

Introduced in 1994, brand substitution enabled pharmacists to substitute the prescribed drug brand with a generic at the time of dispensing, unless otherwise indicated on the prescription (McManus et al., 2001). Prescribers were concerned that this policy might potentially cause confusion to patients as different products are dispended each time their prescriptions are filled by pharmacists. However, Kalisch et al. (2007a, 2007b) found that the majority of patients were supplied the same product on each dispensing and pharmacists rarely supplied different products on repeats of the same prescription. In a later study, Ortiz et al. (2010) concluded that the potential for patient confusion due to brand substitution is relatively small.

3.6.5 Co-payment increase and safety net threshold increase

In the span of 20 years, from 1991 to 2011, patient co-payments have increased on two occasions, January 1997 and January 2005, over and above the annual increment adjustment to the Consumer Price Index (CPI). In January 1997, patient co-payments were increased by 15.0% for the general beneficiary category and 18.5% for the concessional beneficiary category. General beneficiary category patients had to pay A$20.0 instead of A$17.40 before the increase and concessional beneficiary category patients had to pay A$3.20 instead of A$2.70. In January 2005, patient co-payments were increased by 24.0% across the two beneficiary categories with general beneficiary patients having to pay A$28.60 while concessional beneficiary patients paying A$4.60. Along with the increase in co-payments, the safety net threshold was also increased on both occasions. In January 1997, the safety net threshold for the general beneficiary category was A$612.60 while the safety net threshold for the concessional beneficiary patients was A$166.40. In January 2005, the safety net thresholds for the general beneficiary and the concessional beneficiary category were A$874.90 and A$239.20 respectively (Sweeny, 2007a). Effective from January 2015, the the safety net threshold for the general beneficiary category was increased from A$1,421.20 to A$1,453.90 while the safety net threshold for the concessional beneficiary patients was increased from $360.00 to $366.00 (Department of Health, 2015).

3.6.6 Therapeutic Group Premium Policy

On 1 February 1998, the Therapeutic Group Premium Policy was introduced to promote greater competition between manufacturers of drugs. Medicines are grouped together under the same sub-groups if they are similar in terms of safety, efficacy and health outcomes. The Australian Government subsidises drugs within a defined therapeutic sub-group to the level of the lowest priced drug in the

subgroup. The difference between the lowest price drug and the drug prescribed is paid by the patient (Senate Community Affairs References Committee, 2010). Four therapeutic groups were formed when this policy was introduced. These groups were the ACE inhibitors, the calcium channel blockers, the HMG CoA Reductase inhibitors and the H2RAs (Sayer et al., 2000). However, as of May 2014, there are only three drugs (telmisartan, olmesartan medoxomil and eprosartan) in the PBS that attract a therapeutic group premium ranging from A$2.50 to A$3.50 (Department of Health, 2014c).

3.6.7 Creation of F1 and F2 formularies

In 2007, the PBS formulary was split into two separate formularies, Formulary 1 (F1) and Formulary 2 (F2), with different pricing strategies for each (de Boer, 2009). Formulary 1 comprises single brand medicines which are not changeable at the patient level with multiple brand medicines. Formulary 2 comprises multiple brand medicines and any single brand medicines which are interchangeable with multiple brand medicines at the patient level. The reform was implemented to take advantage of the fact that patents on a number of PBS medicines would expire in the next few years. Medicines listed on F1 will be moved to F2 when new competition brands that are bioequivalent to an existing brand of an F1 drug are listed on the PBS and subject to statutory price reductions. Medicines listed on F2 were temporarily split into two sub-formularies, F2T and F2A. Formulary F2T comprises medicines that were significantly discounted by some manufacturers or suppliers to pharmacists and were subject to a 25% mandatory price reduction on 1 August 2008. Medicines listed on F2A were believed not to be subject to significant price discounts by manufacturers or suppliers to pharmacists and were subject to staged price reductions of 2% per year for three years commencing on 1 August 2008. On January 2011, F2T and F2A were merged into a single formulary – F2. Medicines listed on F2 have moved to a system of price disclosure where suppliers listing a new brand on or after 1 January 2011 must

disclose the actual market price paid by the pharmacist as a condition of listing. Price disclosure ensures that the price that the Government pays reflects more closely the actual price at which the medicine is being sold (Department of Health and Ageing, 2007; Searles et al., 2007) (IMS Health Service Centre, 2009).

3.6.8 Premium-free dispensing incentive

A premium-free dispensing incentive was introduced in August 2008 as part of a pharmacy compensation package to encourage pharmacies to dispense premium free PBS listed medicine that costs the patient no more than the standard patient co-payment. Under-co-payment medicines and private scripts are not entitled to this incentive. In the first year of implementation, a payment of A$1.50 was paid for each substitutable medicine dispensed. This incentive is indexed annually and as at July 2013, the payment is at A$1.65. This incentive was introduced to encourage greater use of generic medicine and increase awareness of the safety, health and economic benefits of generic medicines (Department of Human Services, 2013c). In the first 12 months after its implementation, from 1 August 2008 to 31 July 2009, over 75 million prescriptions were eligible for the incentive (Attorney-General's Department, 2010).

3.6.9 Formulary 2 – 12.5%, 2% and 25% price reductions

In accordance with the creation of two formularies, all medicines listed on F2 were subject to 12.5%, 2% or 25% price reductions. As discussed earlier, medicines on F2T were subject to a mandatory 25% cut in the price to pharmacist while medicines on F2A were subject to a staged price reductions of 2% per year for three years starting on 1 August 2008. However, when a patent for an original medicine expires and a bioequivalent brand of medicine is listed, that medicine will be subject to a mandatory 12.5% price reduction. The 12.5% price reduction is different from the 2% and 25% price reduction where the former is due to the

listing of bioequivalent brand while latter is the results of formulary allocation (Centre for Strategic Economic Studies, 2009).

3.7 Hypercholesterolemia and Hyperlipidaemia Prevalence in Australia

High blood cholesterol is one of the major cardiovascular disease risk factors along with others risk factor such as smoking, obesity, hypertension and diabetes (National Heart Foundation of Australia, 2013). A total cholesterol level of more than 5.5mmol/L in blood sample is considered as high risk in developing cardiovascular disease. In the 2007/2008 National Health Survey, it was estimated that 5.7% of the Australian population had a high level of blood cholesterol (Australian Bureau of Statistics, 2009). In 2011/2012, the proportion of population with high blood cholesterol increased by 323,000 person, representing 6.8% of the population (Australian Bureau of Statistics, 2012). In a study done by Harrison et al. (2013), the prevalence of hyperlipidaemia in the population was estimated at 12.3% where patients suffer high plasma lipid and raised serum cholesterol. High blood cholesterol has been identified as the fifth leading causes of disease burden after tobacco smoking, high blood pressure, high body mass and physical inactivity (Australian Institute of Health and Welfare, 2012). In 2010, high total cholesterol was responsible for 145,307 disability-adjusted life years (DALYs) and 9,644 deaths per year. Diseases associated with high blood cholesterol such as ischemic heart disease, stroke and peripheral vascular disease are the leading causes of death among Australians. In 2010, Ischemic heart disease caused the greatest disease burden in Australia with 31,364 deaths and 386,435 DALYs followed by stroke with 14,126 deaths and 152,430 DALYs (Global Burden of Disease Study 2010, 2013).

High blood cholesterol is a modifiable risk for cardiovascular disease and reducing the blood cholesterol concentration by 10% can lower the risk of ischemic heart disease by 20 to 50% for men aged between 40 and 80 years old (Law et al.,

1994). Therefore, lipid modifying drugs play an important role in reducing mortality from ischemic heart disease. Several groups of lipid modifying drugs are available in the market. They are the HMG-CoA reductase inhibitors, the fibrates, bile-acid binding resins, nicotinates, omega-3 triglycerides, and ezetimibe (Martindale: The Complete Drug Reference, 2010). The HMG-CoA reductase inhibitors are known as statins and are the most commonly used drug in hypercholesterolemia treatment. Statins work by inhibiting the enzyme HMG-CoA reductase, a rate-limiting enzyme in cholesterol biosynthesis, and therefore stimulate the low-density-lipoprotein (LDL) receptors in the liver. This results in an increase of LDL clearance from the circulation and decreases the total blood cholesterol level (Brown et al., 1986; Goldstein et al., 2009). As of 2013, seven drugs in the statins group are available in pharmaceutical form, the Atorvastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, and Simvastatin.

3.8 HMG-CoA Reductase Inhibitors in the Pharmaceutical Benefits Scheme

Out of the seven statins available globally, only five statins are listed on the PBS in Australia. The five statins are Atorvastatin, Fluvastatin, Pravastatin, Rosuvastatin, and Simvastatin (Department of Health, 2013c). Simvastatin was listed on January 1992, followed by Pravastatin on June 1993, Fluvastatin on February 1996, Atorvastatin on February 1998, and lastly Rosuvastatin on December 2006. From January 1992 to December 2012, the total prescriptions count and the total expenditure for the statins group were 245 million prescriptions and A$12.7 billion respectively. Atorvastatin accounted for the highest prescriptions count and expenditure with nearly 109 million prescriptions and a total expenditure of A$6.1 billion since its inception (Medicare Australia, 2013).

In the 2012 annual Pharmaceutical Benefits Scheme report by the Department of Health and Ageing (2012), the lipid modifying agents group recorded

the highest total prescriptions count and total expenditure. For the year ending June 2012, the lipid modifying agents group was prescribed 25.7 million times costing the government around A$1.33 billion. Overall, the lipid modifying agents group accounted for 13.2% of the total number of prescriptions and 17.7% of the total expenditure of PBS (Table 3.7 and Table 3.8). At the individual drug level, Atorvastatin and Rosuvastatin were the two most used drugs and incurred the highest expenditure. The prescriptions count for Atorvastatin and Rosuvastatin were 10.5 million and 6.7 million prescriptions respectively while the total cost to the government was A$593 million and A$359 million respectively (Table 3.9 and Table 3.10).

Table 3.7 Drug groups by highest government cost, year end June 2012

No.	Drug groups	Government expenditure, A$
1	Lipid modifying agents	1,330,892,919
2	Immunosuppressants	468,457,064
3	Antineoplastic agents	466,321,598
4	Ophthalmologicals	445,132,860
5	Agents acting on the renin-angiotensin system	441,168,333
6	Psycholeptics	437,857,081
7	Drugs for obstructive airway diseases	429,318,387
8	Drugs used in diabetes	419,103,510
9	Drugs for acid related disorders	403,813,882
10	Psychoanaleptics	401,671,311

Source: Department of Health and Ageing

Table 3.8 Drug groups by highest volume, year end June 2012

No.	Drug groups	Number of prescriptions
1	Lipid modifying agents	25,656,690
2	Agents acting on the renin-angiotensin system	22,206,196
3	Drugs for acid related disorders	15,241,461
4	Psychoanaleptics	14,740,041
5	Analgesics	14,337,661
6	Antibacterials for systemic use	12,862,665
7	Drugs for obstructive airway diseases	10,338,196
8	Psycholeptics	7,854,957
9	Drugs used in diabetes	7,469,348
10	Ophthalmologicals	7,323,596

Source: Department of Health and Ageing

Table 3.9 Drug by highest government cost, year end June 2012

No.	Drug	Government expenditure, A$
1	Atorvastatin[1]	593,307,859
2	Rosuvastatin[1]	359,207,846
3	Ranibizumab[2]	307,816,693
4	Adalimumab[3]	198,802,937
5	Fluticasone Propionate + Salmeterol Xinafoate[4]	169,267,494
6	Esomeprazole Magnesium Trihydrate[5]	168,095,363
7	Olanzapine[6]	159,545,861
8	Clopidogrel[7]	133,172,362
9	Etanercept[3]	127,752,968
10	Tiotropium Bromide Monohydrate[4]	117,857,405

[1]Lipid modifying agents, [2]Ophthalmologicals, [3]Immunosuppressants, [4]Drugs for obstructive airway diseases, [5]Drugs for acid related disorders, [6]Psycholeptics, [7]Antithrombotic agents.

Source: Department of Health and Ageing

Table 3.10 Drug by highest volume, year end June 2012

No.	Drug	Number of prescriptions
1	Atorvastatin[1]	10,507,613
2	Rosuvastatin[1]	6,729,477
3	Esomeprazole Magnesium Trihydrate[2]	5,677,991
4	Paracetamol[3]	4,834,008
5	Perindopril[4]	3,690,650
6	Simvastatin[1]	3,638,727
7	Pantoprazole Sodium Sesquihydrate[5]	3,500,393
8	Metformin Hydrochloride[6]	3,298,661
9	Fluticasone Propionate + Salmeterol Xinafoate[7]	3,007,412
10	Irbesartan[4]	2,884,818

[1]Lipid modifying agents, [2]Drugs for acid related disorders, [3]Analgesics, [4]Agents acting on the renin-angiotensin system, [5]Drugs for acid related disorders, [6]Drugs used in diabetes, [7]Drugs for obstructive airway diseases.

Source: Department of Health and Ageing

Under the Pharmaceutical Benefits Scheme's prescribing guidelines, statins should only be given to patients in very high risk categories. Those patients can have one of a number of conditions with any cholesterol level (Table 3.11). If the patient does not fall into any of the very high risk categories, statins can only be commenced when the lipid levels satisfied the certain conditions (Table 3.12) (Department of Health, 2013d).

Table 3.11 Conditions of patients in the very high risk categories

Conditions
• coronary heart disease which has become symptomatic • cerebrovascular disease which has become symptomatic • peripheral vascular disease which has become symptomatic • diabetes mellitus with microalbuminuria (defined as urinary albumin excretion rate of >20mcg/min or urinary albumin to creatinine ratio of > 2.5 for males, > 3.5 for females) • diabetes mellitus in Aboriginal or Torres Strait Islander patients • diabetes mellitus in patients aged 60 years or more • family history of coronary heart disease which has become symptomatic before the age of 55 years in two or more first degree relatives • family history of coronary heart disease which has become symptomatic before the age of 45 years in one or more first degree relatives

Source: Department of Health

Table 3.12 Lipid levels for patients not in the very high risk categories

Patient Category	Lipid Levels for PBS Subsidy
• Patients with diabetes mellitus not otherwise included	total cholesterol > 5.5 mmol/L
• Aboriginal or Torres Strait Islander patients • Patients with hypertension	total cholesterol > 6.5 mmol/L or total cholesterol > 5.5 mmol/L and HDL cholesterol < 1 mmol/L
• Patients with HDL cholesterol < 1 mmol/L	total cholesterol > 6.5 mmol/L
• Patients with familial hypercholesterolaemia identified by: o DNA mutation; or o tendon xanthomas in the patient or their first or second degree relative	If aged 18 years or less at treatment initiation: LDL cholesterol > 4 mmol/L
• Patients with: o family history of coronary heart disease which has become symptomatic before the age of 60 years in one or more first degree relatives; or o family history of coronary heart disease which has become	If aged more than 18 years at treatment initiation: LDL cholesterol > 5 mmol/L or total cholesterol > 6.5 mmol/L

symptomatic before the age of 50 years in one or more second degree relatives	or total cholesterol > 5.5 mmol/L and HDL cholesterol < 1 mmol/L

• Patients not eligible under the above:
  ○ men aged 35 to 75 years
  ○ post-menopausal women aged up to 75 years
	total cholesterol > 7.5 mmol/L
	or
	triglyceride > 4 mmol/L

• Patients not otherwise included	total cholesterol > 9 mmol/L or triglyceride > 8 mmol/L

Source: Department of Health

3.9 Conclusion

Over the period of 20-years, from 1991/1992 to 2010/2011, PBS expenditure and prescriptions grew from A$1,220 million to A$8,727 million and 94 million prescriptions to 188 million prescriptions respectively. A significant contributor to this growth was the increase in the proportion of the aged population and the number of concessional card holders, both groups utilising more drugs and claiming the higher level of subsidies. Other factors that contributed to the growth of PBS expenditure and prescriptions count were the new listing of drugs and the increase in the total number of persons with chronic diseases. Chronic diseases such as neoplasms, diabetes mellitus, hypertensive disease, asthma and hypercholesterolemia tend to increase government expenditure on pharmaceuticals, particularly as more new drugs are listed on the PBS and patients take those medicines on a long term basis. Several cost containment policies have been implemented by the Commonwealth government to slow down the growth of PBS expenditure and volume of prescriptions. These measures include the brand premium policy, the requirement for economic evaluation as a condition for listing on the PBS, the re-supply limits and safety net 20 day rule, brand substitution policy, co-payment increases, the therapeutic group premium policy, the creation of the F1 and F2 formularies, the premium-free dispensing incentive and the 12.5%, 2% and 25% price reductions for drugs in Formulary 2.

Chapter 4.0 Systematic Review of Cost Containment Measures

4.1 Introduction

Globally, numerous pharmaceutical policy reforms to contain cost have been implemented with some countries reportedly succeeded in containing cost while others have failed (Carone et al., 2012). Numerous studies have investigated the impact of various pharmaceutical policy reforms on prescribing patterns and pharmaceutical expenditure. However, these studies have focused on either an individual reform or a limited range of reforms rather than evaluating the reforms collectively over time. In this chapter, the results of a systematic review of a comprehensive range of pharmaceutical cost containment policies are presented. As the review addresses a wide range of interventions, it adopts what is termed a 'lumping' perspective. A 'lumped' review has the advantage over a 'split' review, which addresses a narrow range of interventions, of being more useful for policy makers in informing decisions about which interventions to implement (Grimshaw et al., 2003). Previous reviews of pharmaceutical cost containment policies have adopted a 'split' perspective, involving only a specific cost containment policy or a combination of several policies (Weir et al., 2012). Examples of 'split' reviews include (1) Austvoll-Dahlgren et al. (2008) and Qingyue et al. (2011) on patient cost-sharing, (2) Aaserud et al. (2006), Galizzi et al. (2011) and Morgan et al. (2009) on reference pricing, (3) Green et al. (2010) and Puig-Junoy et al. (2007) on restrictions on reimbursement, (4) Goldman (2007) on a combination of the above, and (5) Eddama et al. (2008) on economic evaluation. The findings of the systematic review presented in this chapter will contribute to the existing literature by providing guidance to policymakers, practitioners and researchers about the effectiveness of cost containment policies and alternative policy options available.

4.2 Objectives

The objectives of this systematic review are (1) to identify the types of pharmaceutical cost containment policies that have been implemented, (2) to synthesise and compare methodologically the reported impacts of pharmaceutical cost containment policies on drug utilisation, drug costs and public pharmaceutical expenditure.

4.3 Criteria for Inclusion of Studies

4.3.1 Types of studies

The following types of studies were included in the review: randomised controlled trials (RCTs), non-randomised controlled trials (CCTs), repeated measures (RM) studies, interrupted time series (ITS) analyses, and before-after (BA) studies. The inclusion of these types of studies was based on the Cochrane Effective Practice and Organisation of Care Group (EPOC) guidelines (Cochrane Effective Practice and Organisation of Care Group, 2013). For BA studies, the inclusion of studies specified in the Cochrane EPOC guidelines are limited to controlled BA studies. However, due to the limited number of controlled BA studies, the inclusion criteria were expanded to include uncontrolled BA studies. Descriptive, editorial, review studies, and studies without statistical analysis were excluded.

4.3.2 Inclusion criteria

Only studies evaluating the impact of cost containment policies implemented in health systems with a tax-based national health service or a social health insurance system were included. Studies of the impact of cost containment policies implemented by private health insurance schemes were excluded. Included studies were also limited to those evaluating policies that were implemented regionally and nationally. Studies evaluating policies implemented in local health care facilities were excluded.

4.3.3 Types of cost containment interventions

Pharmaceutical cost containment policies that are intended to control either the volume or the expenditure of drugs or both were included. These policies have been discussed in an earlier chapter and were grouped into two categories, namely policies influencing either the supply or the demand of pharmaceuticals. Table 4.1 summarises policies included in this review, showing how they were grouped. The term policy in this review refers to a health related public policy that consists of rules or regulations made by legislators that are intended to influence the actions, behaviours or decisions of others (Harrington et al., 2008; Longest, 2009).

Table 4.1 Types of pharmaceutical cost containment policies

1. **Policies influencing the supply for pharmaceuticals**
   a. Price cuts
   b. Maximum pricing
   c. Reference pricing

2. **Policies influencing the demand for pharmaceuticals**
   a. Patient cost sharing
      i. Fixed co-payment
      ii. Proportional co-payment
      iii. Caps
      iv. Ceilings
      v. Tiered co-payment
      vi. Combination of the above
   b. Positive and negative lists
   c. Prescription controls and duration limits
   d. Budget System
   e. Generic substitution
   f. Therapeutic substitution

4.3.4 Types of outcome measures

Studies accepted in this review had to measure the impact of cost containment policies on at least one of the following outcomes:

i. Drug volume including the number of prescribed drugs, the number of dispensed drugs or the actual usage of drugs
ii. Drug expenditure including total drug expenditure, the cost of drugs or the price of drugs

4.4 Methods

4.4.1 Searched databases and websites

An electronic search for English-language journal articles was conducted in three major databases MEDLINE (Ovid), EMBASE (Ovid) and EconLit. Additional search was also conducted in the internet through Google Scholar. Articles were restricted to publication date from 1 January 1991 to 31 December 2012. Additionally, hand-searches of core journals and reference tracking of reviewed articles were carried out.

4.4.2 Search strategy

The search was based on a combination of keywords covering four themes: Pharmaceuticals and Insurances, Cost Containment Measures, Health Care Policies, and Outcome Measures. Search terms used in the Pharmaceuticals and Insurances theme included terms such as *'Pharmaceutical'* or *'Insurance, Pharmaceutical Services'* or *'Insurance, Health, Reimbursement'* while search terms in the Health Care Policies theme included *'Public Policy'* or *'Health Policy'* or *'Policy'*. In the Cost Containment Measures theme, search terms included '*Cost Control'* or *'Cost Savings'* or *'Cost Sharing'* or *'Prescription Fees'* or *'Fees, Pharmaceutical'* or

'Formularies' or *'Reference Pricing'* or *'Copayment'* or *'Drug Substitution'*. The fourth primary theme of Outcome Measures included terms such as *'Drug Costs'* or *'Health Expenditures'* or *'Prescriptions'* or *'Drug Utilization'*.

4.4.3 Review method

Every relevant study identified from the search was independently appraised by two reviewers (KS Lee and D Hendrie). The reviewers assessed the search results and the abstracts and reference lists of reviewed articles before the full text of shortlisted articles were retrieved.

4.4.4 Data extraction

Relevant data from each study was independently extracted by two reviewers (KS Lee and D Hendrie) using a modified version of the data abstraction form developed by the Scottish Intercollegiate Guidelines (SIGN) (Scottish Intercollegiate Guidelines Network, 2008) (Table A1). Qualitative and quantitative data that were extracted included study design, study population, geographic setting, data source, types of drugs, types of interventions, study period, outcome measures, size of the intervention effect, study funding, study limitation and quality criteria.

4.4.5 Evidence grading of included studies

The evidence level of each article was graded according to the SIGN grading system (Table 4.2) (Scottish Intercollegiate Guidelines Network, 2008). However, due to the nature of pharmaceutical cost containment policies, the design of studies evaluating their effectiveness were rarely randomised controlled trials (RCTs) or non-randomised controlled trials (CCTs). Most of the study designs were repeated measures (RM) studies, interrupted time series (ITS) analyses and before-after (BA) studies. These study designs constitute an evidence level 3 for non-analytic studies.

Table 4.2 Levels of evidence

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1 -	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 -	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Source: Scottish Intercollegiate Guidelines (SIGN)

4.5 Results

The searches in MEDLINE (Ovid) generated 283 articles and in EMBASE (Ovid) generated 1,576 articles. The search in the third database, EconLit produced 41 articles. The search results were combined and duplicates were removed, yielding a total of 1,705 articles. The titles and abstracts of articles were identified and screened, and 286 articles were selected for full article review. From these articles, 265 articles were excluded with 111 articles being descriptive, editorials or reviews, 103 articles not evaluating a pharmaceutical cost containment measure, 21 articles evaluating policies implemented in the context of a private health insurance system, five articles evaluating policies conducted in a local or institutional setting, the evaluation in nine articles having no relevant outcomes, 15 articles were excluded due to study design and one article could not be found. An additional 18 articles were identified through reference list searches, bringing the total number of articles included in the final review to 39 (Figure 4.1). Studies that were excluded from this review are listed in Appendix (Table A2)

4.5.1 Characteristics of the included studies

4.5.1.1 Study design

Of the 39 articles included in the review, the design of 32 of the studies were interrupted time series analyses while seven were before-after studies.

4.5.1.2 Study site

Studies included in the review were carried out in 15 different countries. The majority of studies investigated cost containment policies in Canada (19) where studies were carried out in the provinces of British Columbia (9), Quebec (4), Nova Scotia (3), Ontario (1), Manitoba (1) and one study across British Columbia, Quebec and Ontario. Other studies were conducted in Australia (4), Austria (1), Belgium (1), Denmark (1), Finland (1), France (1),

Iceland (1), Ireland (1), South Korea (1), Spain (1), Sweden (2) and Taiwan (5) (Table 4.3).

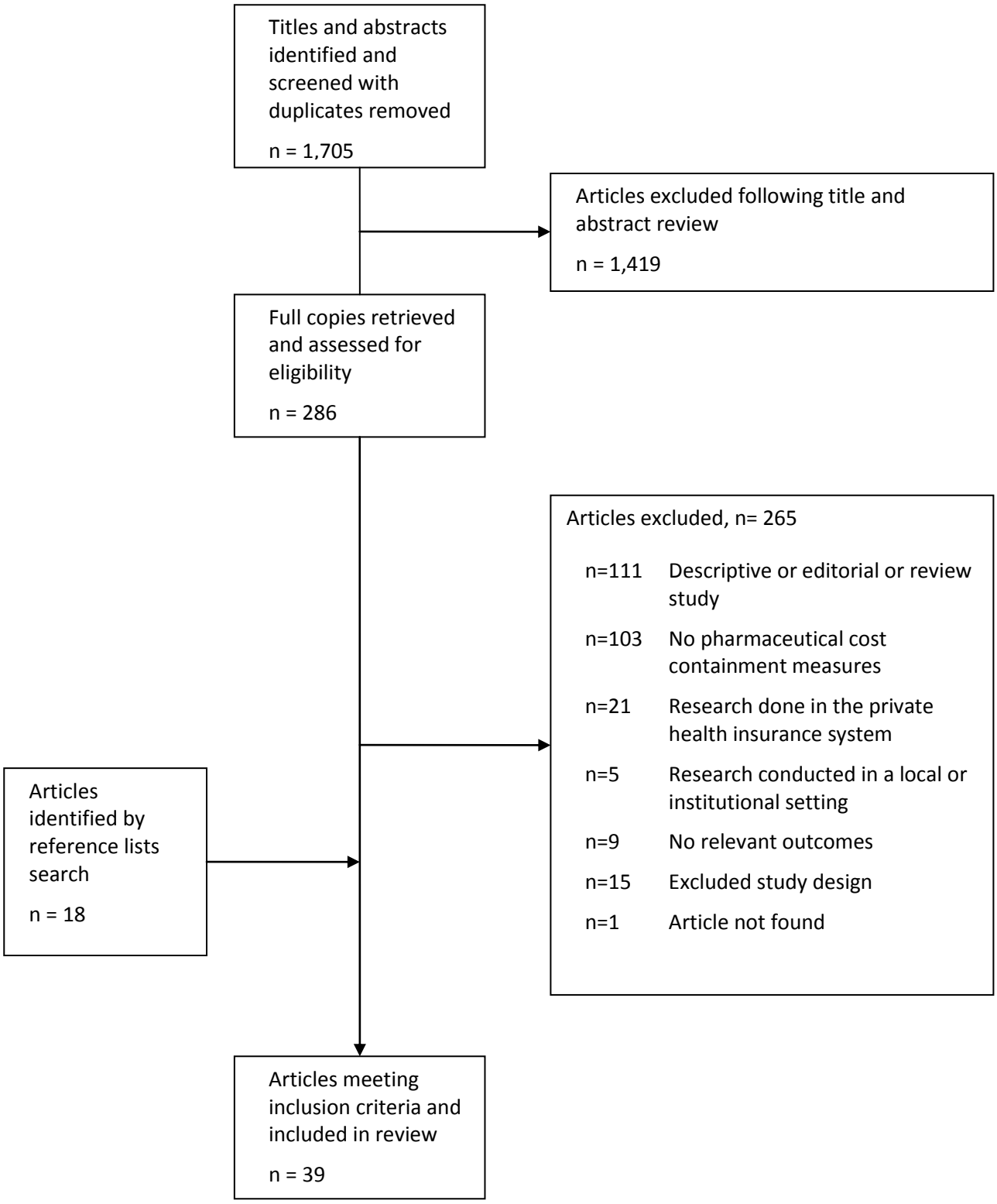


Figure 4.1 Flow chart of study selection process

4.5.1.3 Study time

Of the 39 studies, the majority (37) were carried out over a period of two to 10 years (Table 4.3). The longest time period of 12 years was used in the studies by Moreno-Torres et al. (2011) in Spain and Huang et al. (2012) in Taiwan. Both studies required a longer study period due to the multiple interventions investigated. Moreno-Torres et al. (2011) investigated 16 cost containment measures while Huang et al. (2012) studied seven price adjustments under reference pricing. In contrast, the studies by Liu et al. (2003, 2004) were carried out over 20 months and involved only one intervention.

4.5.1.4 Study interventions

Most of the policies investigated were intended to influence the demand for pharmaceuticals. Seventeen[θ] of the studies investigated patient cost sharing polices, which included fixed co-payments (2), proportional co-payments (1), ceilings (2) and a combination of cost sharing policies (12). Four studies analysed either positive or negative list policies, while 10 studies investigated prescription controls and duration limits. Budget policy and generic substitution were investigated in one study each. Policies influencing the supply of pharmaceuticals consisted mainly of a reference pricing policy (9) and price cut measures (3). A breakdown of the interventions studied is shown in Table 4.4.

[θ] The total studies in this section do not match the total studies included in the review as some of the studies investigated more than one policy.

Table 4.3 Characteristics of the included studies

Paper	Type of study	Population studied	Duration of study	Country	SIGN
(Donnelly et al., 2000)	ITS	NA	9 years 6 months	Australia	3
(Hynd et al., 2008)	ITS	All Australian residents; both concessional and general beneficiaries	7 years 9 months	Australia	3
(Hynd et al., 2009)	ITS	All Western Australian residents; both concessional and general beneficiaries	7 years	Australia	3
(McManus et al., 1996)	ITS	All Australian residents covered by the Pharmaceutical Benefits Scheme	7 years 9 months	Australia	3
(Winkelmayer et al., 2010)	ITS	Patients with at least one claim for any medication used for treating diabetes: any sulfonylurea, biguanide, α-glucosidase inhibitor, thiazolidinedione, repaglinid, or insulin	2 years	Austria	3
(van Driel et al., 2008)	ITS	NA	9 years	Belgium	3

(Dormuth et al., 2006)	ITS	British Columbia residents aged >65 years who used inhaled steroids, β-agonists, or anticholinergics between 31 December 1996 and 1 July 2004	7 years 6 months	British Columbia, Canada	3
(Dormuth et al., 2009)	ITS	British Columbia residents aged >65 years, not federally insured for drug benefits who were dispensed inhaled steroids, β-agonists or anticholinergics on or after January 1996	8 years 2 months	British Columbia, Canada	3
(Grootendorst et al., 2001)	ITS	Senior citizens >65 years and taking anti-anginal drugs (calcium channel blockers (CCBs), nitrates, or beta-blockers)	4 years 2 months	British Columbia, Canada	3
(Hazlet et al., 2002)	BA	Senior citizens >65 years who received two or more separate prescriptions for an antisecretory drug in the period before implementation of the policy	5 years	British Columbia, Canada	3
(Marshall et al., 2002)	BA	Senior citizens >65 years and taking Histamine-2 receptor antagonist (H2RAs) or proton pump inhibitors (PPIs)	6 years 5 months	British Columbia, Canada	3
(Schneeweiss et al., 2002)	ITS	Senior citizens >65 years and taking at least one ACE inhibitor during the period from Oct. 1, 1995, to Mar. 31, 1996	3 years 4 months	British Columbia, Canada	3

(Schneeweiss et al., 2003)	ITS	Senior citizens >65 years and taking Dihydropyridine CCBs between December 1995 and March 1996	3 years 6 months	British Columbia, Canada	3
(Schneeweiss et al., 2004)	ITS	Patients covered by Pharmacare aged >18 years who had filled at least one prescription for a nebulised respiratory drug in the preceding 12 months (3 March 1998 to 28 February 1999)	2 years	British Columbia, Canada	3
(Schneeweiss et al., 2006)	ITS	Senior citizens >65 years using one of the restricted PPIs during a 6-month identification period (Jan 15, 2003, to July 14, 2003)	2 years 6 months	British Columbia, Canada	3
(Kozyrskyj et al., 2001)	BA	6612 school-aged children with mild to moderate asthma and 1420 school-aged children with severe asthma aged between 5 and 15 years old	3 years	Manitoba, Canada	3

(Campbell et al., 2003)	ITS	Nova Scotia residents aged >65 years, not federally, provincially, or privately insured for drug benefits who received at least one drug for any of these products (topical corticosteroid, antibiotic, antifungal, or combination product) between April 1, 1999, and March 31, 2001	2 years	Nova Scotia, Canada	3
(Kephart et al., 2005)	ITS	Senior citizens >65 years, not covered by any other provincial, federal, or private drug insurance program who received at least one prescription for inhaled respiratory drugs during the reference year	3 years 11 months	Nova Scotia, Canada	3
(MacCara et al., 2001)	BA	Senior beneficiaries >65 years and with at least one drug claim for an oral antimicrobial between December 1, 1994, and December 31, 1997	3 years 1 month	Nova Scotia, Canada	3
(Marshall et al., 2006)	ITS	Senior beneficiaries >65 year	3 years 9 months	Ontario, Canada	3
(Blais et al., 2001)	ITS	Individuals aged > 65 years with at least one prescription of one or more of the study medications dispensed between 1 August 1992 – 31 August 1997	6 years 1 month	Quebec, Canada	3

(Blais et al., 2003)	ITS	Individuals aged < 64 years and receiving social assistance (welfare group) with at least one prescription of one or more of the study medications dispensed between 1 August 1991 – 30 June 1997	6 years	Quebec, Canada	3
(Pilote et al., 2002)	ITS	Quebec residents aged >65 years who were admitted to acute care hospitals in Quebec between Jan. 1, 1994, and Dec. 31, 1998, with a discharge diagnosis of acute myocardial infarction	5 years	Quebec, Canada	3
(Tamblyn et al., 2001)	ITS	Quebec residents who were recipients of welfare-funded medications or elderly persons who filled at least 1 prescription for a drug in the year before the policy and who were not exempted from the cost-sharing policy	4 years 1 month	Quebec, Canada	3
(Marshall et al., 2007)	ITS	Senior beneficiaries >65 years with high rates of analgesic use	5 years 9 months	Québec, Ontario and British Columbia, Canada	3
(Bjerrum et al., 2001)	BA	Residents of Funen, Denmark	5 years	Denmark	3

(Martikainen et al., 2007)	ITS	All permanent residents covered by the National Health Insurance Scheme	5 years	Finland	3
(Pichetti et al., 2011)	ITS	NA	11 years 6 months	France	3
(Almarsdottir et al., 2000)	ITS	All patients covered under the Icelandic State Social Security Institute	5 years 8 months	Iceland	3
(Usher et al., 2012)	ITS	Patients covered under the General Medical Services (GMS) Scheme and Drugs Payment (DP) Scheme	5 years 10 months	Ireland	3
(Lee et al., 2012)	ITS	Patients covered under the Health Insurance Review and Assessment Service (HIRA)	5 years 6 months	South Korea	3
(Moreno-Torres et al., 2011)	ITS	Spanish population covered by the National Health System (NHS) excluding civil servants	12 years	Spain	3
(Andersson et al., 2007)	ITS	NA	5 years	Sweden	3
(Ong et al., 2003)	ITS	NA	9 years 6 months	Sweden	3
(Hsiao et al., 2010)	ITS	NA	4 years	Taiwan	3

(Huang et al., 2012)	ITS	147,157 patients who either received angiotension-converting enzyme inhibitors (ACEIs) (between January 1997 - December 2008) or angiotensin receptor blockers (ARBs) (between February 1998 - December 2008	12 years	Taiwan	3
(Lee et al., 2006)	ITS	NA	8 years	Taiwan	3
(Liu et al., 2003)	BA	Patients aged 65 years or older from 21 selected hospitals in Taipei	1 year 8 months	Taipei, Taiwan	3
(Liu et al., 2004)	BA	Patients aged 65 years or older from 21 selected hospitals in Taipei	1 year 8 months	Taipei, Taiwan	3

NA - Not available, ITS - Interrupted time series, BA - Before- after

Table 4.4 Interventions studied and the countries involved

Policy addressed and reference	Countries												
Total	AUS	AUT	BEL	CAN	DEN	FIN	FRA	ISL	IRL	KOR	ESP	SWE	TPE
Influencing the demand for pharmaceuticals													
1. Patient Cost-Sharing													
• Fixed co-payment	1[1]					1[2]							
• Proportional co-payment										1[3]			
• Caps													
• Ceilings				1[4]				1[5]					
• Tier co-payment													
• Combination of the above	2[6]			6[7]								1[8]	3[9]
2. Positive and negative list				2[10]			1[11]				1[12]		
3. Prescription controls and duration limits	1[13]	1[14]	1[15]	6[16]	1[17]								
4. Budget System													1[18]
5. Generic substitution												1[19]	
6. Therapeutic substitution													

[1] (McManus et al., 1996)
[2] (Martikainen et al., 2007)
[3] (Lee et al., 2012)
[4] (Kozyrskyj et al., 2001)
[5] (Almarsdottir et al., 2000)
[6] (Hynd et al., 2008, 2009)
[7] (Blais et al., 2001; Blais et al., 2003; Dormuth et al., 2006; Dormuth et al., 2009; Pilote et al., 2002; Tamblyn et al., 2001)
[8] (Ong et al., 2003)
[9] (Lee et al., 2006; Liu et al., 2003, 2004)
[10] (Campbell et al., 2003; Schneeweiss et al., 2006)
[11] (Pichetti et al., 2011)
[12] (Moreno-Torres et al., 2011)
[13] (Donnelly et al., 2000)
[14] (Winkelmayer et al., 2010)
[15] (van Driel et al., 2008)
[16] (Kephart et al., 2005; MacCara et al., 2001; Marshall et al., 2006; Marshall et al., 2007; Marshall et al., 2002; Schneeweiss et al., 2004)
[17] (Bjerrum et al., 2001)
[18] (Lee et al., 2006)
[19] (Andersson et al., 2007)

Policy addressed and reference	Countries												
Total	AUS	AUT	BEL	CAN	DEN	FIN	FRA	ISL	IRL	KOR	ESP	SWE	TPE
Influencing the supply for pharmaceuticals													
1. Price cuts									1[20]	1[21]	1[22]		
2. Maximum pricing													
3. Reference pricing				5[23]							1[24]		3[25]

AUS – Australia; AUT – Austria; BEL – Belgium; CAN – Canada; DEN – Denmark; FIN – Finland; FRA – France; GER – Germany; HUN – Hungary; ISL – Iceland; IRL – Ireland; KOR – South Korea; ESP – Spain; SWE – Sweden; TPE - Taiwan

[20] (Usher et al., 2012)
[21] (Lee et al., 2012)
[22] (Moreno-Torres et al., 2011)
[23] (Grootendorst et al., 2001; Hazlet et al., 2002; Marshall et al., 2002; Schneeweiss et al., 2002; Schneeweiss et al., 2003)
[24] (Moreno-Torres et al., 2011)
[25] (Hsiao et al., 2010; Huang et al., 2012; Lee et al., 2006)

4.5.2 Characteristics of outcomes

The majority of the studies reviewed evaluated the cost containment measures in terms of their impact on drug volumes followed by their impact on drug costs and total expenditure. Prescription counts or prescription rates were adopted as the outcome measure in 17 studies with one study (Bjerrum et al., 2001) evaluating prescription counts using annual prevalence, which is defined as the proportion of the population who had collected at least one prescription during a year. Prescription duration was used as an outcome by Liu et al. in their two studies evaluating the impact of coinsurance and ceilings (Liu et al., 2003, 2004). In studies that adopted drug cost as an outcome measure, 11 studies adopted the cost per patient or cost per prescription as an outcome while only one study (Lee et al., 2012) adopted the cost per unit as an outcome. The outcome measure used less often was the cost per day, with Liu et al. (2004) the only study to have used it. Total drug expenditure was used as an outcome measure across all types of cost containment measures either independently or in combination with other outcome measures.

4.5.3 Effects of interventions

Detailed results for the included studies are provided in Table 4.5.

4.5.3.1 Patient cost sharing

Two studies by McManus et al. (1996) in Australia and Martikainen et al. (2007) in Finland investigated the impact of changes in fixed co-payments. The changes investigated by these studies were contrary to each other, with McManus et al. analysing an increase in co-payment for general beneficiaries and the introduction of co-payments for repatriation beneficiaries while Martikainen et al. investigated the impact of a decrease in co-payments. McManus's study found that an increase in the co-payment led to a statistically significant decrease in the level of prescription counts

for essential medicines and for discretionary medicines for both general and repatriation beneficiaries. However, no changes in trend for either type of beneficiary were demonstrated following the policy implementation. On the other hand, Martikainen et al. found a decrease in co-payment resulted in a statistically significant increase in the level and trend in defined daily doses (DDDs) for both antiglaucoma drugs, Dorzolamide and Latanoprost.

Lee et al. (2012) investigated the conversion of the co-payment system in South Korea from a fixed co-payment of 1500 South Korean won (KRW) per prescription to a 30% proportional co-payment. They found no significant changes to the utilisation level and trend for all prescriptions except for a reduction in antihyperlipidemics. In terms of drug cost, no significant changes to the cost per unit dispensed and cost per patient were demonstrated with the exception of a reduction in the trend reduction per month per patient.

Changes in deductible were investigated by two studies, Kozyrskyj et al. (2001) in Manitoba, Canada and Almarsdottir et al. (2000) in Iceland. In April 1996, Manitoba's drug benefit program, Pharmacare, changed the patient's annual deductible from a fixed payment of C$237 per family plus a 40% co-payment on prescription costs over C$237 to an income-based deductible of 2% of income for families with annual income of C$15,000 or less and 3% of income for families with higher incomes. These changes resulted in a reduction in the number of inhaled corticosteroid doses dispensed to children aged 5 to 15 years old with asthma, with relatively similar reductions found for children with stable or mild to moderate asthma and those with stable, severe asthma. In contrast to the Kozyrskyj et al. study, Almarsdottir et al. (2000) found no significant changes in total drug expenditure following the increase in patient's deductibles.

Twelve studies investigated changes in patient cost sharing which used a combination of different types of cost sharing. In Australia, Hynd et al. (2008, 2009) examined the impact of an increase in patient fixed co-payment and safety net and the impacts varied according to the categories of medicines considered. The majority of medicine categories such as statins, proton-pump inhibitors and a combination of asthma medicines showed a reduction in utilisation level or trend but medicine categories such as hypnotics, anxiolytics and anti-gout showed no significant changes or even increases in the case of atypical antipsychotics. Four of the six studies carried out in Canada were based in Quebec province (Blais et al., 2001; Blais et al., 2003; Pilote et al., 2002; Tamblyn et al., 2001). Those studies investigated the introduction of 25% coinsurance and annual ceilings in August 1996 followed by the introduction of an annual deductible with coinsurance and an annual ceiling based on income in January 1997. Blais et al. (2001) and Pilote et al. (2002) found no significant changes to the drug utilisation trend in elderly patients (aged more than 65 years) following the changes in patient cost sharing. However, in a later study by Blais et al. (2003) with individuals aged less than 65 years and receiving social assistance or classified as welfare recipients, a 37% trend reduction in the number of inhaled corticosteroid prescriptions dispensed was reported. No significant changes were observed in this study for two other drug groups, the neuroleptics and the anticonvulsants. In a study using two categories of the population as subjects, the elderly and welfare groups, Tamblyn et al. (2001) found a significant reduction in both categories but the intervention impacted the welfare group more that the elderly group. The overall daily drug utilisation trend for elderly persons was reduced by 9.14% while the welfare recipients reduced their usage by 15.94%. Higher rate of serious adverse events and emergency department visits were reported to be associated with the reduction in drug utilisation.

In the province of British Columbia, two studies by Dormuth et al. (2006; 2009) investigated the introduction in January 2002 of patient fixed co-payment of C$10 per-dispensing for those with household incomes below $50,000 and C$25 for those with incomes above $50,000. This plan was changed to a 25% coinsurance plus family deductible equal to 0%, 1% or 2% of family income with an out-of-pocket ceiling equal to 1.25%, 2%, or 3% of income in May the following year. With DDD/10,000 patients/month as an outcome, Dormuth et al. (2006) found a reduction in the utilisation trend following both interventions while Dormuth et al. (2009) reported a similar finding in total drug expenditure, albeit a different outcome measure. Both studies found the combination of coinsurance with deductible and ceiling to be more effective in reducing utilisation and expenditure that the fixed co-payment.

In Sweden, Ong et al. (2003) investigated two cost sharing changes in July 1995 and January 1997. The first change was the increase of fixed co-payment from 125 Swedish Krona (SEK) to 160 SEK for an initial prescription and coinsurance of 60 SEK for additional drugs from 25 SEK previously, while the second change was the increase of fixed co-payment to 400 SEK followed by a coinsurance up to a ceiling of 1300 SEK. This study found that the first cost sharing changes permanently increased the antidepressants and sedatives DDDs dispensed to men while the second cost sharing changes permanently reduced the antidepressants DDDs dispensed to women.

In two other studies that investigated the impact of introducing coinsurance and a ceiling in Taiwan, Liu et al. (2003; 2004) found significant reduction in the average prescription duration and the average drug cost per prescription. However, Lee et al. (2006) reported no significant changes in the total drug expenditure.

4.5.3.2 Positive and negative list

Four studies (Campbell et al., 2003; Moreno-Torres et al., 2011; Pichetti et al., 2011; Schneeweiss et al., 2006) were included in the review under the positive and negative list measure. Two Canadian studies (Campbell et al., 2003; Schneeweiss et al., 2006) investigated the removal of reimbursement eligibility of drugs that were previously available for reimbursement. Schneeweiss et al. studied the removal of reimbursement eligibility of three non-preferred PPIs, namely Omeprazole, Pantoprazole and Lansoprazole. Only one preferred PPI, Rabeprazole, was covered by PharmaCare, the province-funded drug benefits plan. The rationale of this regulation was to increase the negotiating power of PharmaCare and reduce the cost of PPIs. Following the implementation of this intervention in July 2003, the level of daily doses per 10,000 residents of non-preferred PPIs was significantly reduced while usage of preferred PPIs increased. However, the overall impact of this intervention did not result in any significant changes to the level and trend on all PPIs. In Campbell's study, the removal of 10 topical combination corticosteroid products from reimbursement eligibility did not result in any changes in the cost per patient of the topical combination corticosteroid products but instead increased the overall cost of all topical products mainly due to the increase in the cost per patient of potent topical corticosteroids.

In a more recent study by Pichetti et al. (2011) in France, the removal of 128 types of mucolytics and expectorants from the list of reimbursable drugs decreased the trend of prescription rate for mucolytics and expectorants but increased the rate for bronchodilator, antitussive and antibacterial prescriptions. The study also found significant saving in drug expenditure due to the removal of mucolytics and expectorants. In a similar study design by Moreno-Torres et al. (2011) in Spain, the exclusion of 984

products from public financing beginning September 1998 reduced the number of prescriptions per capita while increasing the price per prescription. The saving from the reduction in utilisation was not able to adequately compensate for the increase in cost, and therefore resulted in no significant saving in total drug expenditure.

4.5.3.3 Prescription controls and duration limits

Ten studies (Bjerrum et al., 2001; Donnelly et al., 2000; Kephart et al., 2005; MacCara et al., 2001; Marshall et al., 2006; Marshall et al., 2007; Marshall et al., 2002; Schneeweiss et al., 2004; van Driel et al., 2008; Winkelmayer et al., 2010) were identifies that examined prescription controls and duration limit measures.

The only study (Donnelly et al., 2000) on duration limits was carried out in Australia. The minimum prescription re-supply period was increased from three days to 20 days. In the first month following the changes in the re-supply period, the number of prescriptions dispensed was significantly reduced but no significant impact was observed in the second month. Therefore the impact of increasing the re-supply period had a temporary effect in reducing the drug utilisation but not in the longer period.

Two studies (van Driel et al., 2008; Winkelmayer et al., 2010) reported the impact of relaxing the restrictions of preferred drugs to switch patients from the non-preferred drugs in order to reduce drug expenditures. In Belgium, van Driel et al. (2008) studied the impact of moving the status of preferred (cheaper) H2AH and PPIs drugs from 'restricted' to 'open benefits'. In March 2001, Cimetidine and Ranitidine were shifted from 'restricted' to 'open benefit' where no authorizations were required while in March 2003, Omeprazole (20 mg) and Rabeprazole (small packages) were shifted to 'open benefit'. Liberation of Cimetidine and Ranitidine reimbursement in 2001 increased the volume and expenditure of overall

H2AH without any significant impact on the volume or expenditure of PPIs. However, following the 2003 intervention, the utilisation and expenditure of PPIs were increased while the H2AH drug group were reduced. Van Driel et al. concluded that lifting of reimbursement restrictions to make preferred acid suppressant drugs more favourable to prescribers did not result in significant changes in utilization or cost saving. In Austria, Winkelmayer et al. (2010) studied the expansion of indications for preferred statins and found no significant changes in the level and trend of drug utilisation for overall statins. However, their study reported a statistically significant increase in the trend of preferred statins while the trend of non-preferred statins decreased.

Six Canadian studies (Kephart et al., 2005; MacCara et al., 2001; Marshall et al., 2006; Marshall et al., 2007; Marshall et al., 2002; Schneeweiss et al., 2004) provided estimates of the impact of implementing reimbursement restrictions. Schneeweiss's study found significant savings in the overall drug cost per patient following the removal of reimbursement eligibility of nebulised bronchodilators, steroids and cromoglycates. Although the increase in drug cost per patient for inhaler drugs and decrease in drug cost per patient for nebuliser drugs were initially not statistically significant, the study result was later corrected for non-compliance in sensitivity analysis and resulted in a significant decrease in overall drug cost per patient.

In a cross-country study by Marshall et al. (2007), three provinces with three different reimbursement policies on Cox-2 inhibitors were investigated. No restrictions on Cox-2 inhibitors reimbursement was present in Québec while the reimbursement policy in Ontario was based on a policy of 'Limited Use' when certain clinical criteria were met and the most restricted policy of all the provinces was in British Columbia where the

prescribing physician was required to request for a Special Authority before reimbursement was approved. Marshall et al. (2007) found that NSAIDs utilisation, measured by DDDs per 100 senior beneficiaries per month, was higher in Québec and Ontario, provinces with relax reimbursement restrictions; while no significant changes in utilisation were observed in British Columbia, where restrictions were more strict.

Other Canadian studies estimated a reduction in drug utilisation (Kephart et al., 2005; MacCara et al., 2001) and total drug expenditure (Marshall et al., 2002). Kephart et al. (2005) found significant trend reduction in the wet nebulisation therapy utilisation rate after the implementation of reimbursement restrictions for wet nebulisation therapy. However, the utilisation trend of other respiratory drugs such as oral corticosteroids, inhaled short-acting β-agonists and inhaled anticholinergics were higher after the implementation. MacCara's study found a significant reduction in the number of prescription for fluoroquinolones as well as in the total antimicrobial usage after the implementation of reimbursement restrictions for fluoroquinolones in January 1997. The study also found that the average cost per patient for fluoroquinolones increased by 8.7% while the average cost per patient for overall antimicrobial decreased by 21.9%. In Marshall (2002) study, the implementation of reimbursement restrictions for PPIs resulted in the reduction of total drug expenditure. However, Marshall et al. (2006) found no significant changes in the total number of prescriptions and total expenditure after the implementation of reimbursement restrictions for ciprofloxacin and ofloxacin.

In a study (Bjerrum et al., 2001) that examined the relaxation of the reimbursement restrictions of lipid lowering drugs in order to improve the prevention of cardiovascular heart disease, Bjerrum et al. found a significant increase in the annual prevalence of lipid lowering drugs use in the

population. The proportion of the population who had collected at least one prescription for lipid lowering drugs during a year had increased by 0.4% after the intervention. The lipid lowering drugs utilisation of in patients with diabetes mellitus and patients with cardiovascular heart disease increased by 2.3% and 8.1% respectively.

4.5.3.4 Budget system

A single study was reviewed that evaluated the budget system measure. Lee et al. (2006) investigated the introduction of a global budget for clinics and hospitals as one of the interventions in their study. Global budgets for clinics were initiated in July 2001 while budgets for hospitals were implemented a year later in July 2002. Lee's study found no significant changes to the monthly pharmaceutical expenditure trend after implementation of the July 2001 intervention while the expenditure trend after July 2002 resulted in a significant increase in monthly expenditure.

4.5.3.5 Generic substitution

As with budget system measures, only a single study was included in the review about generic substitution. Andersson et al. (2007) studied the introduction of mandatory generic substitution in Sweden on October 2002. Pharmacists were obligated to provide patients with the cheapest available generic drug in the Medical Products Agency's list unless substitution was restricted. After the implementation of this measure, the total cost per 1000 inhabitants per working day of all prescribed pharmaceuticals was reduced by 51.4% and pharmaceuticals on regular prescriptions was reduced by 43.0%.

4.5.3.6 Price cuts

The search identified three studies on pharmaceutical price cuts. Price reduction for off-patent drugs was investigated by Usher et al. (2012)

in Ireland and Lee et al. (2012) in South Korea. In Usher's study, three occasion of price cuts over the study period resulted in a significant reduction in the level and trend of expenditure for off-patent drugs but no significant changes were observed for patent and generic drugs. The study by Lee et al. yielded similar results with no significant changes in the level and trend of drug utilisation and drug cost. Instead, the monthly per person trend of antihyperlipidemics utilisation was significantly increased following the price cuts. In a third study, Moreno-Torres et al. (2011) found only one measure out of four price reduction measures in Spain was effective in reducing the total expenditure per capita. The first price cut measure in November 1999 increased the number of prescriptions per capita but decreased the price per prescription, reducing the total expenditure per capita. Another measure found to reduce the drug cost was the March 2005 price cut while the others price cuts showed no significant changes.

4.5.3.7 Reference pricing

Nine studies (Grootendorst et al., 2001; Hazlet et al., 2002; Hsiao et al., 2010; Huang et al., 2012; Lee et al., 2006; Marshall et al., 2002; Moreno-Torres et al., 2011; Schneeweiss et al., 2002; Schneeweiss et al., 2003) provided trend estimates post implementation of reference pricing. Out of five Canadian studies (Grootendorst et al., 2001; Hazlet et al., 2002; Marshall et al., 2002; Schneeweiss et al., 2002; Schneeweiss et al., 2003), two studies (Grootendorst et al., 2001; Marshall et al., 2002) reported a significant reduction in drug expenditure while two studies by Schneeweiss et al. (2002; 2003) reported significant decreases in drug cost per patient. In the 2002 study by Schneeweiss et al., the monthly doses per 10,000 senior citizens of ACEIs were found to be unaffected by the implementation of ACEIs reference pricing while the 2003 study found reduction in overall dihydropyridine CCB utilisation after the implementation of CCB reference

pricing. Grootendorst's study estimated a saving of C$4.2 million annually following the implementation of reference based pricing of nitrates while Marshall's study estimated a saving of C$1.8 million per year post introduction of reference based pricing of H2AH. Hazlet's study did not find any significant changes to the utilisation trend of antisecretory drugs following the introduction of reference based pricing for H2AH.

Three studies in Taiwan (Hsiao et al., 2010; Huang et al., 2012; Lee et al., 2006) investigated a series of reference pricing measures implemented between November 1996 and September 2007. Hsiao et al. (2010) found no significant trend changes in the cost of NSAIDs per ambulatory visit and NSAIDs DDDs per ambulatory visit post introduction of two reference pricing measures on April 2001 and March 2003. However, Huang's study found reduction in drug expenditure for reference pricing measures introduced on November 2004 while in Lee's study, the reductions were observed on April 2001, January 2002 and March 2003. There were no significant differences in outcomes following the implementation of other reference pricing measures.

Moreno-Torres et al. (2011) in Spain studied five reference pricing measures implemented on December 2000 to December 2003, May 2002, May 2003, January 2004 and August 2004. Only the August 2004 reference pricing measure was found to decrease the trend of price per prescription and the total expenditure per capita. Surprisingly, the May 2003 reference pricing was found to increase the trend of prescriptions volume per capita.

Table 4.5 Summary of findings

Intervention	Patient Cost-Sharing				
Variables	Study				
	McManus et al (1996)	Martikainen et al. (2007)	Lee et al. (2012)	Kozyrskyj et al. (2001)	Almarsdottir et al. (2000)
Country	Australia	Finland	South Korea	Canada	Iceland
Intervention studied	Increase in patient's fixed co-payments (general beneficiary) and introduction of patient's fixed co-payment (repatriation beneficiary)	Decrease in patient's co-payment	Change from fixed co-payment to proportional co-payment	Change from fixed annual deductible to income based deductible	Increase in deductible
Characteristics					
Population studied	All Australian residents covered by the Pharmaceutical Benefits Scheme	All permanent residents covered by the National Health Insurance Scheme	Patients covered under the Health Insurance Review and Assessment Service (HIRA)	Children aged 5 to 15 years old with asthma	All patients covered under the Icelandic State Social Security Institute
Drug classes studied	Twelve groups of essential medicines and nine groups of discretionary medicines[1]	Dorzolamide, latanoprost	All prescriptions, antihypertensives, antihyperlipidemics	Inhaled corticosteroid (beclomethasone, budesonide, fluticasone, flunisolide, triamcinolone)	All prescriptions

[1] The essential medicines group includes antiasthmatic inhalants, antiepileptics, antithrombotic agents, antiparkinson drugs, antihypertensives, antiglaucoma preparations and miotics, beta-blocking agents, cardiac glycosides, plain corticosteroids for systemic use, diuretics, drugs used in diabetes and thyroid preparations. The discretionary medicines group include antacids, antihistamines for systemic use, nonsteroid anti-inflammatory products, antiobesity preparations, cough and cold preparations, hypnotics/sedatives, other analgesics and antipyretics, throat preparations, vitamins

Outcomes					
Drug volume					
Prescription counts/rates	[-][2] Level (essential and discretionary medicines) [Not significant] Trend (essential and discretionary medicines)	N.T	[Not significant] Level and trend (All prescriptions, Antihypertensives) [-] Level and trend (Antihyperlipidemics)	N.T	N.T
Doses/ defined daily dose	N.T[3]	[+][4] Level and trend	N.T	[-] Year before v. 2nd year after intervention (int.)	N.T
Prescription duration	N.T	N.T	N.T	N.T	N.T
Drug cost					
Cost per unit	N.T	N.T	[Not significant] Level and trend (All prescriptions)	N.T	N.T
Cost per patient/ prescription	N.T	N.T	[Not significant] Level (All prescriptions) [-] Trend (All prescriptions)	N.T	N.T
Cost per day	N.T	N.T	N.T	N.T	N.T
Total drug expenditure	N.T	N.T	N.T	N.T	[Not significant]

[2] [-] - Decrease
[3] N.T - Not tested
[4] [+] - Increase

Table 4.5 Summary of findings / continued

Intervention	**Patient Cost-Sharing**					
Variables	Study					
	Hynd et al. (2008)	Hynd et al. (2009)	Blais et al. (2001)	Blais et al. (2003)	Dormuth et al. (2006)	Dormuth et al. (2009)
Country	Australia	Australia	Canada	Canada	Canada	Canada
Intervention studied	Increase in patient's fixed co-payments and safety net (ceiling)	Increase in patient's fixed co-payments and safety net (ceiling)	Introduction of coinsurance and annual ceiling Introduction of annual deductible and coinsurance and annual ceiling (based on income), prorated quarterly	Introduction of coinsurance and annual ceiling Introduction of annual deductible and coinsurance and annual ceiling (based on income), prorated quarterly	Int. 1: Introduction of fixed co-payment Int. 2: Change to coinsurance and family deductible (based on family income) and ceiling (based on income)	Int. 1: Introduction of fixed co-payment Int. 2: Change to coinsurance and family deductible (based on family income) and ceiling (based on income)
Characteristics						
Population studied	All Australian residents; both concessional and general beneficiaries	All Western Australian residents; both concessional and general beneficiaries	Individuals aged > 65 years with at least one prescription of one or more of the study medications dispensed	Individuals aged < 64 years and receiving social assistance (welfare group) with at least one prescription of one or more of the study medications dispensed	British Columbia residents aged >65 years who used inhaled steroids, β-agonists, or anticholinergics	British Columbia residents aged >65 years, not federally insured for drug benefits who used inhaled steroids, β-agonists, or anticholinergics
Drug classes studied	17 categories of medicine[5]	Atypical antipsychotics, comb. of asthma med., statins, proton-pump inhibitors	Nitrates, antihypertensive, anticoagulants and benzodiazepines	Inhaled corticosteroids, neuroleptics and anticonvulsants	Inhaled steroids, inhaled β-agonists and inhaled anticholinergics	Inhaled steroids, inhaled β-agonists and inhaled anticholinergics

[5] Anti-epileptics, anti-gout, anti-Parkinson's, anxiolytics, atypical antipsychotics, β-blockers, combination (comb.) of asthma medicines (med.), eye-drops, glaucoma treatments, hypnotics, insulin, muscle relaxants, non-aspirin antiplatelets, osteoporosis treatments, proton-pump inhibitors (PPIs), statins, thyroxine.

Outcomes						
Drug volume						
Prescription counts/rates	[-] Level and/or trend for 12[6] out of 17 categories (concessional beneficiary)	[-] Level (statins, PPIs) [-] Trend (comb. of asthma med., PPIs) [+] Trend (atypical antipsychotics)	[Not significant] Trend	[-] Trend (Inhaled corticosteroids)	N.T	N.T
Doses/ defined daily dose	N.T	[-] Level (statins, PPIs) [-] Trend (atypical antipsychotics, comb. of asthma med., PPIs)	N.T	N.T	[-] Trend (Both intervention) [-] Trend (Int. 2 v. Int. 1)	N.T
Prescription duration	N.T	N.T	N.T	N.T	N.T	N.T

[6] Anti-epileptics, anti-Parkinson's, comb. asthma med., eye-drops, glaucoma treatments, insulin, muscle relaxants, non-aspirin antiplatelets, osteoporosis treatments, PPIs, statins, thyroxine.

Drug cost						
Cost per unit	N.T	N.T	N.T	N.T	N.T	N.T
Cost per patient/ prescription	N.T	N.T	N.T	N.T	N.T	N.T
Cost per day	N.T	N.T	N.T	N.T	N.T	N.T
Total drug expenditure	N.T	N.T	N.T	N.T	N.T	[-] Trend (Int. 1) [-] Trend (Int. 2 v. Int. 1)

Table 4.5 Summary of findings / continued

Intervention	**Patient Cost-Sharing**					
Variables		Study				
	Pilote et al. (2002)	Tamblyn et al. (2001)	Ong et al. (2003)	Lee et al. (2006)	Liu et al. (2003)	Liu et al. (2004)
Country	Canada	Canada	Sweden	Taiwan	Taiwan	Taiwan
Intervention studied	Introduction of coinsurance and annual ceiling Introduction of annual deductible and coinsurance and annual ceiling (based on income), prorated quarterly Change the annual ceiling to monthly prorated	Introduction of coinsurance and fixed annual ceiling (for welfare recipient) or based on income (for others)	Int. 1 – Increase in fixed co-payment and coinsurance Int. 2 - – Increase fixed co-payment and introduction of ceiling with coinsurance	Introduction of coinsurance and ceiling	Introduction of coinsurance and ceiling	Introduction of coinsurance and ceiling
Characteristics						
Population studied	Quebec residents aged >65 years who were admitted to acute care hospitals	Quebec residents who were (i) recipients of welfare-funded medications or (ii) elderly person	NA[7]	NA	Patients aged 65 or older from 21 selected hospitals in Taipei	Patients aged 65 or older from 21 selected hospitals in Taipei
Drug classes studied	β-blockers, ACEIs, lipid-lowering agents, ASA[8]	21 essential drugs and 4 less essential drugs	Antidepressants, anxiolytics and sedatives	All drugs prescribed by physicians but excludes drugs prescribed by dentists and Chinese medical doctors	NA	NA

[7] NA – Not available
[8] ACEIs - angiotension-converting enzyme inhibitors, ASA - acetylsalicylic acid

Outcomes						
Drug volume						
Prescription counts/rates	[Not significant] Trend[9]	[-] Trend (elderly persons) [-] Trend (welfare persons)	N.T	N.T	N.T	N.T
Doses/ defined daily dose	N.T	N.T	[+] Men Step[10] (Int.1 - antidepressants, sedatives [-] Women Step (Int.2 - antidepressants)	N.T	N.T	N.T
Prescription duration	N.T	N.T	N.T	N.T	[-]	[-]
Drug cost						
Cost per unit	N.T	N.T	N.T	N.T	N.T	N.T
Cost per patient/ prescription	N.T	N.T	N.T	N.T	[-]	[-]
Cost per day	N.T	N.T	N.T	N.T	N.T	[Not significant]
Total drug expenditure	N.T	N.T	N.T	N.T	N.T	N.T

[9] Proportion of patients receiving prescriptions for any of these medications within 30 days after discharge

[10] Step - changes in which the error terms move above or below the 99% (2-tailed test) CI of their expected levels and remain, on average, outside the CI for the remainder of the test period

Table 4.5 Summary of findings / continued

Intervention	**Positive and negative list**			
Variables	Study			
	Campbell et al. (2003)	Schneeweiss et al. (2006)	Pichetti et al. (2011)	Moreno-Torres et al (2011)
Country	Canada	Canada	France	Spain
Intervention studied	Reduced from 12 to only 2 topical combination corticosteroid products available for reimbursement	Removed the reimbursement eligibility of Omeprazole, pantoprazole and lansoprazole	Removed the reimbursement eligibility of 128 mucolytics and expectorants	Removed the reimbursement eligibility of 984 products
Characteristics				
Population studied	Nova Scotia residents aged >65 years	Senior citizens >65 years using one of the restricted PPIs	NA	Spanish population covered by the NHS (National Health System) excluding civil servants
Drug classes studied	Varieties of topical products[11]	Non-preferred PPIs (omeprazole, pantoprazole, lansoprazole) and preferred PPIs (rabeprazole)	Mucolytics and expectorants, bronchodilators, antitussives, antibacterials	All prescription pharmaceuticals covered under NHS

[11] single-entity topical corticosteroids, topical corticosteroid combination products, other combination products, single-entity topical antibiotics, single-entity topical antifungal products

Outcomes				
Drug volume				
Prescription counts/rates	N.T	N.T	[-] Trend (mucolytics and expectorants) [+] Trend (Bronchodilators, antitussives, antibacterials)	[-] Trend
Doses/ defined daily dose	N.T	[-] Level (non-preferred PPIs) [Not significant] Level and trend (total PPIs)	N.T	N.T
Prescription duration	N.T	N.T	N.T	N.T
Drug cost				
Cost per unit	N.T	N.T	N.T	N.T
Cost per patient/ prescription	[+] Trend (all topical products, potent topical corticosteroids) [Not significant] Trend (Topical combination corticosteroid products)	N.T	N.T	[+] Trend
Cost per day	N.T	N.T	N.T	N.T
Total drug expenditure	N.T	N.T	[-] (overall saving)	[Not significant] Trend

Table 4.5 Summary of findings / continued

Intervention	**Prescription controls and duration limits**				
Variables	Study				
	Donnelly et al. (2000)	Winkelmayer et al. (2010)	van Driel et al. (2008)	Kephart et al. (2005)	MacCara et al. (2001)
Country	Australia	Austria	Belgium	Canada	Canada
Intervention studied	Increase in the minimum re-supply period from three days to 20 days	Expansion of the indications for preferred statin	Moved preferred (cheaper) drugs from 'restricted' to 'open benefit':- Int. 1 – H2AH (cimetidine and ranitidine) Int. 2 - PPIs (omeprazole, 20 mg and rabeprazole)	Implemented reimbursement restrictions for wet nebulization therapy	Implemented reimbursement restrictions for Fluoroquinolones
Characteristics					
Population studied	NA	Patients with at least one claim for any medication used for treating diabetes	NA	Senior citizens >65 years, not covered by any other provincial, federal, or private drug insurance program who received at least one prescription for inhaled respiratory drugs during the reference year	Senior beneficiaries >65 years and with at least one drug claim for an oral antimicrobial
Drug classes studied	All drugs covered under the PBS	Preferred statins and nonpreferred statins[12]	PPIs, H2AH[13]	Wet nebulization, oral corticosteroids, inhaled long-acting β-agonists, inhaled short-acting β-agonists, inhaled corticosteroids, inhaled anticholinergics	Penicillins, fluoroquinolones, cephalosporins, sulfonamides and trimethoprim, macrolides and lincosamides, tetracyclines, nitrofurantoin

[12] Preferred statins - Simvastatin 20 and 40 mg, Lovastatin, Pravastatin, Fluvastatin, Atorvastatin 10mg; Nonpreferred statins - Atorvastatin > 10 mg, All strengths of rosuvastatin

[13] H2AH - H2-antihistamines

Outcomes					
Drug volume					
Prescription counts/rates	[-] Level (1st month post intervention) [Not significant] (2nd month post intervention)	[Not significant] Level and Trend (Overall statins) [+] Trend (preferred statins) [-] Trend (nonpreferred statins)	N.T	[-] Trend (wet nebulization therapy) [+] Trend (oral corticosteroids, inhaled short-acting β-agonists, inhaled anticholinergics)	[-] All antimicrobial
Doses/ defined daily dose	N.T	N.T	[Not significant] Level and trend (PPIs - Int. 1) [+] Level and trend (H2AH - Int. 1, PPIs - Int. 2) [-] Level and trend (H2AH - Int. 2)	N.T	N.T
Prescription duration	N.T	N.T	N.T	N.T	N.T

Drug cost					
Cost per unit	N.T	N.T	N.T	N.T	N.T
Cost per patient/ prescription	N.T	[-] Level	N.T	N.T	[-] Average cost
Cost per day	N.T	N.T	N.T	N.T	N.T
Total drug expenditure	N.T	N.T	[Not significant] Level and trend (PPIs - Int. 1) Trend (PPIs – Int. 2) [+] Level and trend (H2AH - Int. 1) Level (PPIs - Int. 2) [-] Level and trend (H2AH - Int. 2)	N.T	N.T

Table 4.5 Summary of findings / continued

Intervention	Prescription controls and duration limits				
Variables	Study				
	Marshall et al. (2006)	Marshall et al. (2007)	Marshall et al. (2002)	Schneeweiss et al. (2004)	Bjerrum et al. (2001)
Country	Canada	Canada	Canada	Canada	Denmark
Intervention studied	Implemented reimbursement restrictions for ciprofloxacin and ofloxacin	Three different reimbursement policies on coxib; without restrictions (Québec), Limited Use (Ontario), prior authorization (British Columbia)	Implemented reimbursement restrictions for PPIs	Removed the reimbursement eligibility of nebulised bronchodilators, steroids and cromoglycate	Relaxed the reimbursement restrictions for LLDs[14]
Characteristics					
Population studied	Senior beneficiaries >65 years	Senior beneficiaries >65 years with high rates of analgesic use	Senior citizens >65 years and taking Histamine-2 receptor antagonist (H2RAs) or PPIs	patients aged >18 years	Residents of Funen, Denmark
Drug classes studied	β-Lactam, macrolide, fluroquinolone, cephalosporin, tetracycline, clindamycin, fosfomycin	NSAIDs (coxibs plus nsNSAIDs)[15]	H2AH, PPIs	nebulised bronchodilators, steroids, cromoglycate	LLDs

[14] LLDs - lipid lowering drugs
[15] NSAIDs - Non-steroidal anti-inflammatory drugs; nsNSAIDs – Non-selective non-steroidal anti-inflammatory drugs

Outcomes					
Drug volume					
Prescription counts/rates	[Not significant] Trend	N.T	N.T	N.T	[+] annual prevalence of LLD use[16]
Doses/ defined daily dose	N.T	[+] Trend (Québec and Ontario) [Not significant] Trend (British Columbia)	N.T	N.T	N.T
Prescription duration	N.T	N.T	N.T	N.T	N.T
Drug cost					
Cost per unit	N.T	N.T	N.T	N.T	N.T
Cost per patient/ prescription	N.T	N.T	N.T	[+] inhaler drugs [-] nebuliser drugs, overall cost	N.T
Cost per day	N.T	N.T	N.T	N.T	N.T
Total drug expenditure	[Not significant] Trend	N.T	[-] Trend	N.T	N.T

[16] annual prevalence - proportion of the population who had collected at least one prescription for LLDs during a year

Table 4.5 Summary of findings / continued

Intervention	**Budget system**		**Generic substitution**
Variables	Study		Study
	Lee et al. (2006)		Andersson et al. (2007)
Country	Taiwan		Sweden
Intervention studied	Global budget for clinics and hospitals		Generic substitution
Characteristics			
Population studied	NA		NA
Drug classes studied	All drugs prescribed by physicians but excluded drugs prescribed by dentists and Chinese medical doctors		All prescribed pharmaceuticals and pharmaceuticals on regular prescriptions
Outcomes			
Drug volume			
Prescription counts/rates	N.T		N.T
Doses/ defined daily dose	N.T		N.T
Prescription duration	N.T		N.T
Drug cost			
Cost per unit	N.T		N.T
Cost per patient/ prescription	N.T		N.T
Cost per day	N.T		N.T
Total drug expenditure	[+] Trend (hospitals)	[Not significant] Trend (clinics)	[-] Trend (All prescribed and regular pharmaceuticals)

Table 4.5 Summary of findings / continued

Intervention	**Price cuts**		
Variables	Study		
	Usher et al. (2012)	Lee et al. (2012)	Moreno-Torres et al. (2011)
Country	Ireland	South Korea	Spain
Intervention studied	Int. 1 – 20% price reduction for off patents Int. 2 – 15% price reduction for off patents Int. 3 – 40% price reduction in off patents	20% price cut after patient expiry	Four reduction of ex-factory prices – Nov 1999, Jul 2001, Mac 2005, Mac 2006
Characteristics			
Population studied	Patients covered under the General Medical Services (GMS) Scheme and Drugs Payment (DP) Scheme	Patients covered under the Health Insurance Review and Assessment Service (HIRA)	Spanish population covered by the NHS (National Health System) excluding civil servants
Drug classes studied	All prescription pharmaceuticals covered under General Medical Services (GMS) Scheme and Drugs Payment (DP) Scheme	All prescriptions, antihypertensives, antihyperlipidemics	All prescription pharmaceuticals covered under the NHS

Outcomes			
Drug volume			
Prescription counts/rates	N.T	[Not significant] Level and Trend (all prescriptions) [+] Trend (antihyperlipidemics)	[+] Trend (Nov 1999) [Not significant] (others)
Doses/ defined daily dose	N.T	N.T	N.T
Prescription duration		N.T	N.T
Drug cost			
Cost per unit	N.T	[Not significant] Level and Trend (all prescriptions)	N.T
Cost per patient/ prescription	N.T	[Not significant] Level and Trend (all prescriptions)	[-] Trend (Nov 1999 and Mac 2005) [Not significant] (others)
Cost per day	N.T	N.T	N.T
Total drug expenditure	[-] Level and Trend (off-patent) (Int. 1, 2 and 3) [Not significant] Level and Trend (patent and generic) (Int. 1, 2 and 3)	N.T	[-] Trend (Nov 1999) [Not significant] (others)

Table 4.5 Summary of findings / continued

Intervention	**Reference pricing**				
Variables	Study				
	Grootendorst et al. (2001)	Hazlet et al. (2002)	Marshall et al. (2002)	Schneeweiss et al. (2002)	Schneeweiss et al. (2003)
Country	Canada	Canada	Canada	Canada	Canada
Intervention studied	Reference-based pricing of nitrates	Reference-based pricing of H2AH	Reference-based pricing of H2AH	Reference-based pricing for ACEIs	Reference-based pricing for dihydropyridine calcium channel blockers
Characteristics					
Population studied	Senior citizens >65 years and taking anti-anginal drugs (CCBs, nitrates, or β-blockers)	Senior citizens >65 years who received two or more separate prescriptions for an antisecretory drug in the period before implementation of the policy	Senior citizens >65 years and taking Histamine-2 receptor antagonist (H2RAs) or PPIs	Senior citizens >65 years and taking at least one ACE inhibitor	Senior citizens >65 years and taking Dihydropyridine calcium channel blockers (CCB)
Drug classes studied	Nitrates, CCBs, β-blockers[17]	H2AH, PPIs, sucralfate, and several others	H2AH, PPIs	No-cost ACEIs (Cost covered) and cost-shared ACEIs (Patients pay the balance)[18]	Dihydropyridine calcium channel blockers[19]

[17] Nitrates - Isosorbide Mononitrate, Isosorbide Dinitrate(ISDN), Nitroglycerin; CCBs - Calcium channel blockers
[18] No-cost ACEIs – Captopril, Quinapril, Ramipril; Cost-shared ACEIs – Benazepril, Cilazapril, Enalapril, Fosinopril, Lisinopril
[19] Dihydropyridine calcium channel blockers – Felodipine, Nifedipine, Amlodipine, Nicardipine, Verapamil, Diltiazem

Outcomes					
Drug volume					
Prescription counts/rates	N.T	[Not significant] Trend	N.T	N.T	N.T
Doses/ defined daily dose	N.T	N.T	N.T	[Not significant] Trend (Overall ACEIs)	[-] Trend (Overall dihydropyridine calcium channel blockers)
Prescription duration	N.T	N.T	N.T	N.T	N.T
Drug cost					
Cost per unit	N.T	N.T	N.T	N.T	N.T
Cost per patient/ prescription	N.T	N.T	N.T	[-] Trend	[-] Trend
Cost per day	N.T	N.T	N.T	N.T	N.T
Total drug expenditure	[-] Trend	N.T	[-] Trend	N.T	N.T

Table 4.5 Summary of findings / continued

Intervention	**Reference pricing**			
Variables	Study			
	Moreno-Torres et al. (2011)	Hsiao et al. (2010)	Huang et al. (2012)	Lee et al. (2006)
Country	Spain	Taiwan	Taiwan	Taiwan
Intervention studied	Five reference pricing systems - Dec 2000 - Dec 2003, May 2002, May 2003, Jan 2004, Aug 2004	Two reference pricing systems - Apr 2001, Mac 2003	Seven reference pricing systems – Apr 2000, Apr 2001, Mac 2003, Nov 2004, Sept 2005, Nov 2006, Sept 2007	Six reference pricing systems – Nov 1996, Dec 1997, Apr 2000, Apr 2001, Jan 2002, Mac 2003
Characteristics				
Population studied	Spain population covered by the NHS (National Health System) excluding civil servants	NA	Patients who either received ACEIs or ARBs	NA
Drug classes studied	All prescription pharmaceuticals covered under NHS	NSAIDs and cyclooxygennse-2 (COX-2) inhibitors	ACEIs and ARBs (angiotensin receptor blockers)	All drugs prescribed by physicians but excludes drugs prescribed by dentists and Chinese medical doctors

Outcomes				
Drug volume				
Prescription counts/rates	[+] Trend (May 2003) [Not significant] (others)	N.T	N.T	N.T
Doses/ defined daily dose	N.T	[Not significant] Trend	[-] Level (Apr 2000 - overall renin-angiotensin) [Not significant] Level and Trend (others - overall renin-angiotensin)	N.T
Prescription duration	N.T	N.T	N.T	N.T

Drug cost				
Cost per unit	N.T	N.T	N.T	N.T
Cost per patient/ prescription	[-] Trend (Jan 2004) [Not significant] (others)	[Not significant] Trend	N.T	N.T
Cost per day	N.T	N.T	N.T	N.T
Total drug expenditure	[-] Trend (Jan 2004) [Not significant] (others)	N.T	[-] Level (Nov 2006 - overall renin-angiotensin) [-] Trend (Nov 2004 - overall renin-angiotensin) [Not significant] Level and Trend (others - overall renin-angiotensin)	[-] Trend (Apr 2001, Jan 2002, Mac 2003) [Not significant] (others)

4.6 Discussion

Of the cost containment measures included in this study, three measures, namely patient cost sharing, prescription controls and duration limits and reference pricing had been evaluated most often. Various types of patient cost sharing have been implemented across different countries. Seven of thirteen countries had introduced cost sharing or implemented changes to cost sharing. Many countries had used a combination of different types of cost sharing, for instance proportional co-payment with a ceiling or fixed co-payment with a ceiling. For prescription controls and duration limits, most of the studies involved implementing reimbursement criteria to switch patient usage to preferred cheaper drugs. Only a single study had evaluated the impact of imposing duration limits.

Geographically, nearly half of the studies were carried out in Canada and these studies had evaluated measures such as changes in cost sharing, removal of certain drugs reimbursement eligibility, implementation of reimbursement criteria and reference pricing. Only four studies had been conducted in Australia (Donnelly et al., 2000; Hynd et al., 2008, 2009; McManus et al., 1996), and these studies investigated the introduction of an increase in fixed co-payments as well as the increase in the re-supply period.

All studies in the review fell into Level 3 (non-analytic studies) of the SIGN grading system. Due to the nature of public policy investigations that are difficult to carry out in a laboratory mode with a control, interrupted time series analyses and before-after studies were the preferred study designs in all of the studies. Although studies without controls were accepted and included in this review, three before-after studies (Hazlet et al., 2002; Kozyrskyj et al., 2001; Liu et al., 2004) and four interrupted time series studies (Kephart et al., 2005; Marshall et al., 2007; Schneeweiss et al., 2004; Schneeweiss et al., 2003) included a control group in their study design.

Most of the studies covered a sufficient time period. Generally, for interrupted time series studies, a minimum of 12 points are required between interventions in order to detect any significant changes in trends. However, four studies (Huang et al., 2012; Lee et al., 2012; Lee et al., 2006; Moreno-Torres et al., 2011) suffered serious limitations due to insufficient time points between interventions.

4.6.1 Patient cost sharing

Generally, the introduction of patient's cost sharing or increasing patient's share of cost sharing decreased drug cost but did not necessarily reduce drug volume. Without an influence on drug utilisation, overall savings in total drug expenditure might not have been achieved. A reduction in drug cost was found in all studies that used cost as an outcome measure but, in studies with drug volume as an outcome measure, several studies found no significant changes to drug utilisation or total drug expenditure. The intention of implementing cost sharing is to reduce patient demand by creating financial disincentives for patients to use pharmaceuticals (Doran et al., 2011). However, the results of this review suggest this was not the case. The implementation of cost sharing encouraged patients to switch to cheaper drugs that required lower payment without changes in their utilisation pattern. This behaviour was more noticeable in healthcare systems that implemented proportional co-payments. The change from fixed to proportional co-payment on August 2007 in South Korea resulted in the reduction in drug cost without any significant changes in drug utilisation (Lee et al., 2012). For better control of drug volume and cost, the combination of proportional or coinsurance with a ceiling appeared to be a better option for cost containment. With proportional co-payment, the amount the patient pays to fill a prescription is based on the percentage of the drug or prescription cost. Therefore, proportional co-payment is a better

representation of patient burden of co-payment in cost sharing as compared to fixed co-payment. Several studies in Canada (Blais et al., 2003; Dormuth et al., 2006; Tamblyn et al., 2001) and Taiwan (Liu et al., 2003, 2004) suggested better cost containment with such a combination. However, the optimal level of patient share in cost sharing is hard to determine. If the level is set too high, patients risk being exposed to adverse effects due to their discontinuing their medications or switching to cheaper medicines that are not the best choice for treatment.

Contrary to the three systematic reviews studies available on patient cost sharing measures, Austvoll-Dahlgren et al. (2008), Qingyue et al. (2011) and Goldman et al. (2007) concluded that the implementation of patient's cost sharing reduced both the drug usage and drug expenditures. These studies also found limited evidence of adverse effects on health following the implementation of cost sharing.

4.6.2 Positive and negative lists

The removal of drugs reimbursement eligibility reduced the volume of the delisted drugs but did not result in an overall saving in drug expenditure. In most cases, the volume and cost of others drugs in similar therapeutic group that were still available for reimbursement increased as a result of patients switching to the subsidised drugs in the positive list which contained more expensive drugs (Moreno-Torres et al., 2011; Pichetti et al., 2011; Schneeweiss et al., 2006). Moreno-Torres et al. (2011) concluded that the effectiveness of negative lists as a cost containment measure for reducing pharmaceutical expenditure was limited.

4.6.3 Prescription controls and duration limits

The duration limits imposed in Australia by limiting the re-supply period from three days to 20 days was not effective in containing drug

utilisation. Reduction in utilisation was observed in the first month post implementation but no significant changes were observed in the following months. However, due to the limited studies available, comparison of results from the Donnelly et al. (2000) study with others cannot be done.

For the prescription control measure, six studies were carried out in Canada. The results from these Canadian studies demonstrated a reduction in drug cost but did not necessarily reduce the total drug expenditure. Marshall et al. (2002) found a significant reduction in total drug expenditure whereas the Marshall et al. (2006) study was unable to demonstrate any saving from the prescription controls measure. In term of drug utilisation, the utilisation of non-preferred drugs (subjected to stricter reimbursement criteria) was decreased while the utilisation of preferred drugs (subjected to less reimbursement criteria or not subjected to any reimbursement criteria) increased. Other studies (Kephart et al., 2005; Marshall et al., 2007) did not include total drug expenditure as one of the outcomes in their studies, thus the cost saving impact of prescription control measures on overall drug expenditure in these studies was inconclusive. Patients tended to switch from non-preferred drugs to preferred drugs and even increased utilisation of other drugs, thus eliminating the potential saving from the reduction in non-preferred drugs utilisation.

In studies that investigated the relaxation of the reimbursement criteria by either expanding the indication for preferred drugs or placing the preferred drugs under 'open benefits', no significant changes in trend were observed. Despite Bjerrum et al. (2001) reporting a significant increase in the annual prevalence use of lipid lowering drugs post intervention, they concluded that the increase in prescribing of lipid lowering drugs had been observed in the years before the interventions.

Therefore, the impact of prescription controls and duration limits were limited to a decrease in drug cost without significant changes in drug utilisation and total expenditure.

However, the findings of the study by Bjerrum et al. (2001) do not support the results of other systematic review studies. Green et al. (2010) concluded that the impact of prescription control measures varies by different drug classes. Drug utilisation and expenditure were found to decrease in gastric-acid suppressant and non-steroidal anti-inflammatory drug classes while no significant impact on drug expenditure was found for antipsychotic drugs. In another study, Puig-Junoy et al. (2007) concluded that the implementation of prescription control measures resulted in a saving in drug expenditure by reducing drug utilisation and drug cost.

4.6.4 Budget system

With only one study covering the implementation of a budget system, no conclusions can be drawn in this cost containment measure. Furthermore, the study in Taiwan did not provide encouraging results with total drug expenditure for hospitals increasing post budget implementation (Lee et al., 2006). Lee et al. recommended that incentives for keeping expenditure within budget should be directly tailored to individual physicians to be able to achieve cost savings.

4.6.5 Generic substitution

Similarly to the implementation of a budget system, only a single study was included in the review that evaluated generic substitution as a cost containment policy. Andersson et al. (2007) concluded that the generic substitution policy shifted the drug expenditure trend from an increase into a decrease. However, patients remain as one of the main obstacles in generic substitution. Patients tend to refuse substitution if the saving from substitution was low, thus drug utilisation behaviour appears to be influenced by price differences between brand and generic products (Andersson et al., 2005).

4.6.6 Price cuts

Price cut measures resulted in a reduction in total drug expenditure by reducing the cost of drugs particularly drugs that were subjected to price cuts with no significant changes to drug utilisation. However, price cut measures were not found to be consistently effective. Of the four price cut measures implemented in Spain between 1999 and 2006, the November 1999 price cut was effective in reducing drug cost and total expenditure (Moreno-Torres et al., 2011). In the Lee et al. (2012) study, price cuts after patent expiry resulted in an increase of antihyperlipidemics utilisation. This was mainly attributed to patients seeking treatment that persisted before the price cuts and consuming more expensive drugs that were previously unaffordable, thus causing the increase in drug utilisation.

4.6.7 Reference pricing

In general, the reference pricing implemented in Canada for various types of drugs resulted in significantly lower drug cost and total drug expenditure. However, no significant reduction in drug utilisation trends was observed except in one study (Schneeweiss et al., 2003). Although Schneeweiss's study demonstrated a reduction in the doses of dihydropyridine calcium channel blockers, the use of antihypertensive did not decline. This result is consistent with the aim of reference pricing, which is to encourage patients to switch to cheaper drugs, thus reducing the demand for expensive drugs, rather than to reduce demand.

The results of studies evaluating reference pricing in other countries including Spain (Moreno-Torres et al., 2011) and Taiwan (Hsiao et al., 2010; Huang et al., 2012; Lee et al., 2006) demonstrated an inconclusive impact of reference pricing. Of the five reference pricing policies implemented in Spain, only the January 2004 one was effective in reducing total expenditure. In Taiwan, 10 reference pricing policies were implemented between November 1996 and September 2007. Only four of these policies (April 2001, January 2002, March 2003 and November 2004) were found to be effective in reducing overall drug expenditure. These findings support the view of Giuliani et al. (1998) that reference pricing policies are only partially effective in containing cost. Giuliani et al. suggested two main weaknesses of reference pricing. Firstly, reference pricing cannot be applied to branded drugs for the fear of negatively affecting pharmaceutical innovation. Secondly, the criteria for grouping drugs may not be categorised appropriately and some of the drugs may not be perfectly 'interchangeable'.

Findings in this study concur with systematic review studies on reference pricing policy. Galizzi et al. (2011) concluded that reference pricing policies were associated with a reduction in expenditure but this was

generally limited to the first year of implementation. Aaserud et al. (2006) found similar findings but with a shorter duration of impact, estimated to last for six months only. Another systematic review by Morgan et al. (2009) found a reduction in overall drug utilisation as well as a reduction in total drug expenditure. In addition, all systematic review studies found no significant link between the implementation of reference pricing policies and adverse health impacts.

4.7 Conclusion

Due to differences in the types and intensity of cost containment measures that have been implemented in different countries, together with cross-country differences in health systems and populations, it is difficult to make direct comparisons across studies. However, this systematic review, which covers all cost containment measures in a single review, provides policy makers with an important public health tool that presents the current evidence base about the impact of the various cost containment on pharmaceuticals volumes and expenditure.

The results of this review suggest that price cuts and reference pricing measures have been effective in reducing total drug expenditure mainly by reducing drugs cost. However, limited changes in drug volume were observed for both measures. Three cost containment measures, namely cost sharing, positive and negative lists and prescription controls and duration limits, were found to have reduced drug volume or drug cost but their impact on total drug expenditure was inconclusive. Due to the limited number of studies evaluating the impact of budget systems and generic substitution measures, the impact of these measures cannot be ascertained until more comprehensive evidences becomes available.

The current systematic review was limited by the types of study designs included, with all studies being interrupted time series analyses or before-after studies. Randomized controlled trials provide better insights into the impact of

interventions but are difficult to conduct in health and many other areas of public policy.

A possible area of future research in this field would be to apply the Economic, Clinical, and Humanistic Outcomes (ECHO) methodology in evaluation of cost containment measures (Kozma et al., 1993). This methodology includes clinical and humanistic outcomes included as outcome measures in addition to economic outcomes. Pharmaceutical cost containment measures have uncertain effects and may cause harm such as a decline in quality of life or increase in hospitalisation rate. By applying the ECHO model in future research, a more holistic approach in evaluating the impact of cost containment measures can be achieved.

Chapter 5.0 Methods and Statistical Analysis

5.1 Introduction

This chapter presents the results of the statistical analysis examining the impact of cost containment reforms to the Pharmaceutical Benefits Scheme on prescribing volumes and expenditure. The results are arranged according to three drugs classifications, which are referred to as Category 1 (all ATC main drug groups), Category 2 (all HMG-CoA reductase inhibitor drug groups) and Category 3 (all Atorvastatin drug groups). The first section of Chapter 5 provides an overview of the data source and the time-series properties of the analysis. It describes the Medicare database of government expenditure (benefit) and volume (service) for PBS medicines. The next section elaborates on the statistical analysis. This section discusses the classification of drugs, types of interventions investigated, outcome variables analysed, data organisation and layout and how the analysis was conducted. Finally, the last part of this chapter describes the results of the analysis.

5.2 Data Source and Time-Series Properties

The PBS statistics are publicly available on Medicare Australia's website (https://www.medicareaustralia.gov.au/statistics/pbs_item.shtml). The database provides time-series data of the monthly government's expenditure (benefit) or volume (service) of PBS medicines that has been processed by Medicare Australia. Monthly, quarterly, or financial year reports can be retrieved for either individual medicines or groups of medicines based on the Anatomical Therapeutic Chemical (ATC) code (Table 5.1) and arranged according to the patient category (general beneficiary category and concessional beneficiary category) or by the state.

Table 5.1 Anatomical Therapeutic Chemical Classification System

ATC Main Group	
A	Alimentary tract and metabolism
B	Blood and blood forming organs
C	Cardiovascular system
D	Dermatologicals
G	Genito urinary system and sex hormones
H	Systemic hormonal preparations, excluding sex hormones and insulins
J	Antiinfectives for systemic use
L	Antineoplastic and immunomodulating agents
M	Musculo-skeletal system
N	Nervous system
P	Antiparasitic products, insecticides and repellents
R	Respiratory system
S	Sensory organs
V	Various

Source: Department of Health and Ageing

In this study, the data retrieved from the Medicare database were limited to the Pharmaceutical Benefits Scheme (PBS) with the Repatriation Pharmaceutical Benefits Scheme (RPBS) data being excluded. The RPBS, governed by the Department of Veterans' Affairs is a special scheme created for military veterans, war widows or widowers and their dependants (Department of Veterans' Affairs, 2014). Beneficiaries under the RPBS pay the same co-payment amount and have the equivalent Safety Net threshold as concessional beneficiaries under the PBS (Department of Health and Ageing, 2013). Over the years, the expenditure and volume by RPBS have been relatively small, representing around 4.5% of the total benefits paid and 5.9% of the total services processed by the PBS in 2012-13

(Department of Human Services, 2013b). Due to the uniqueness of the RPBS, which is restricted to a small portion of the population and a small percentage of the overall expenditure and volume, the RPBS was not included as part of this study.

The monthly time-series data does not necessarily represent the actual month the medicine was supplied to patients by the pharmacy but rather the month the service was processed by Medicare Australia (Medicare Australia, 2013). This may result in significant fluctuations in the trend data, which may therefore not consistently be a true reflection of actual dispensing activity. In June 2012, the numbers of PBS prescriptions were 75% higher than the corresponding month in the previous year and 30% higher relative to any other month before it. A study has shown that Medicare slowed down the average processing time for the nine months prior to April 2012 but sped up the processing in May and June before the end of the financial year in June 2012 (Medicines Partnership of Australia, 2012). This artificially inflates the June 2012 data thus giving an incorrect representation of the true scenario. Therefore, those periods were excluded from this study and only the time periods from 1 January 1992 to 31 March 2012 were included in this study.

5.3 Statistical Analysis

5.3.1 Regression model

Aggregate monthly time series data provides data to conduct a 'natural experiment' to study the impact of cost containment policies implemented over the years. Time series is simply defined as a sequence of observations, measured at uniformly spaced intervals over a period of time (Brockwell, 1987; Kirchgässner et al., 2012). The design of this research is an interrupted time-series study, a quasi-experimental approach using quantitative data. An interrupted time-series design is the strongest, quasi-experimental approach for evaluating longitudinal effects of interventions (Lagarde, 2012; Wagner et al., 2002).

To evaluate the impact of PBS policy changes on prescription expenditure (benefit) and volumes (service), segmented linear regression models were used to analyse the time series data starting from 1 January 1992 to 31 March 2012. The identified cost containment measures provide the specific point in the series and are a practical choice for interrupted time-series studies (Matowe et al., 2003). The segmented regression interrupted time series analysis is preferred over the auto-regressive integrated moving average (ARIMA) analysis as segmented regression is statistically better in examining group trends compared to ARIMA which is best used for examining individual subjects (Martin et al., 2013). Segmented regression analysis was also adopted because of its ability to control for non-stationarity, auto-correlation and seasonality characteristics in the time series data (Lagarde, 2012; Wagner et al., 2002). Non-stationarity is the systematic trend (either upward or downward) of the time series that consistently changes over time (e.g. population increase) while seasonality refers to the repetitive cycles which are predictable in one year or less due to seasonal effects. Auto-correlation occurs when a value at one point is being correlated in part to the previous value (Brockwell, 1987; Kitagawa, 2010).

In each segment, two parameters, the level and trend are used to estimate the impact of the intervention. The level parameter estimates the differences in absolute value between pre-intervention and post-intervention immediately following the intervention. The trend parameter estimates the differences in growth rate or slope over the segment (Ansari et al., 2003; Gillings et al., 1981; Institute of Medicine, 2007). Figure 5.1 presents a hypothetical example to illustrate the level and trend parameters before and after an intervention using segmented regression analysis.

In the biomedical field, segmented linear regression models have been used in several studies to estimate the impact of health policies and educational interventions. Hynd et al. (2008, 2009) used segmented regression analysis and the

Australian Medicare data to determine the impact of co-payment changes for selected drug groups while Andersson et al. (2006) used this approach to evaluate the impact of several pharmaceutical sector policies including the introduction of reference pricing, a new pharmaceutical benefits scheme and co-payment changes on cost, volume and cost per volume trends in Sweden. In Ireland, Usher et al. (2012) studied the impact of price cuts and margin reduction on the Community Drugs Schemes expenditure using this segmented regression analysis.

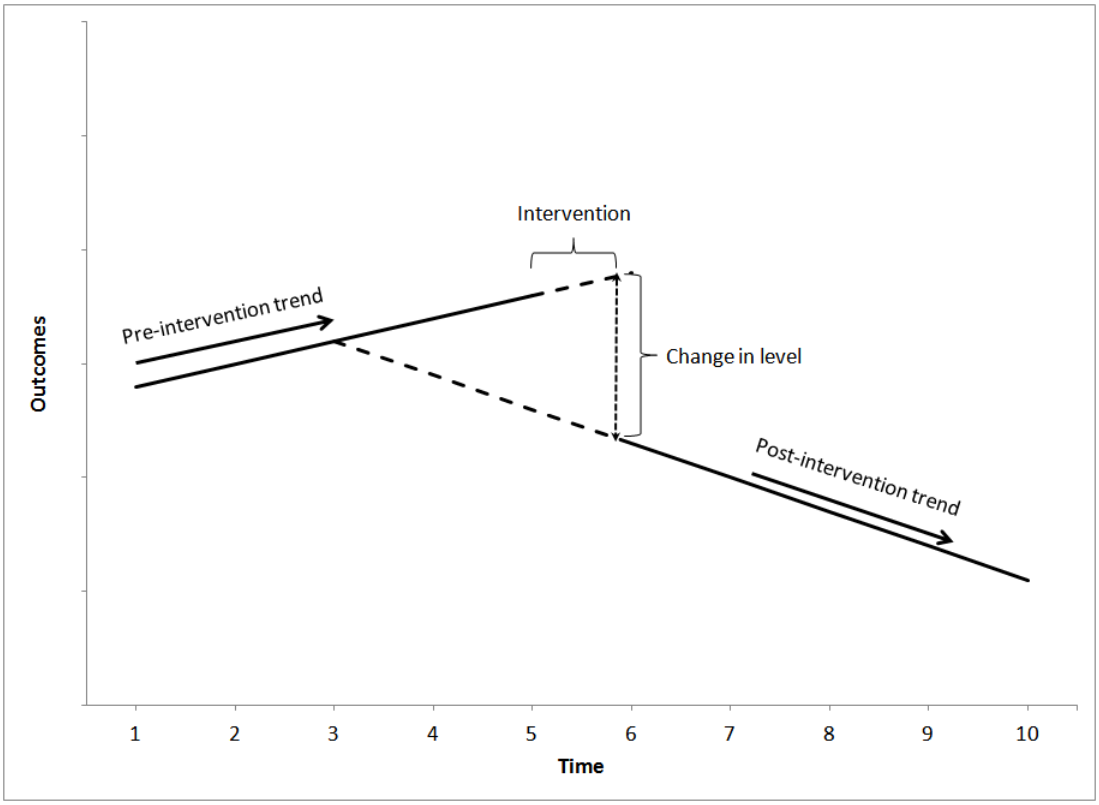


Figure 5.1 Hypothetical example illustrating the general elements of a segmented time series regression analysis before and after an intervention

5.3.2 Drugs classification

The Medicare data were classified into three categories. Category 1 consisted of all ATC main drug groups listed in the PBS schedule (Table 5.1). It included both the general beneficiary and concession beneficiary patient's data. In Category 2, all five statins (Simvastatin, Pravastatin, Fluvastatin, Atorvastatin, and Rosuvastatin)

that were available on the PBS under the HMG-CoA reductase inhibitors group were chosen. For Category 3, Atorvastatin of all strengths were included. In the Category 1 analysis, the inclusion of all drug groups listed in the PBS schedule provides a general perspective of the PBS cost containment reforms. In the Category 2 analysis, the statins group was selected because this group is most widely dispensed and incurs the highest total expenditure in the PBS. Atorvastatin was singled out for further analysis due to the fact that Atorvastatin was the most prescribed drugs and incurred the highest expenditure in PBS for the year ending June 2012 (Department of Health and Ageing, 2012).

5.3.3 Interventions investigated

Seven cost containment policies that are considered as major policies were investigated. These interventions were expected to have an impact on prescription expenditures and volumes of the PBS. In addition to these policies, four new listing dates of statins (Pravastatin, Fluvastatin, Atorvastatin, and Rosuvastatin) in the PBS were included as breakpoints, applicable to Category 2 and 3 analyses (Table 5.2). The listing of Simvastatin on 1st January 1992 was excluded as one of the breakpoints since it was the first month of the study period as well as the first available statins data. The listing of new statins are not cost containment policies but were expected to impact on both the prescription expenditure and volume in Category 2 and 3 analyses. New statins give prescribers more alternatives in treating hyperlipidaemia especially patients who previously did not tolerate older generation statins. Prescribers may also switch from older generation statins (e.g. Atorvastatin) to newer generation statins (e.g. Rosuvastatin) which are more effective in reaching the recommended lipid target (Binbrek et al., 2006; Jones et al., 2003; Shepherd et al., 2003; Strandberg et al., 2004). However, newer statins are more expensive relative to the older ones, thus possibly increasing PBS expenditure.

For a better understanding of the analysis and to facilitate the discussion in the later part, the expected impact of each policy on the level and trend of both expenditure and volume are summarised in Table 5.3. The level and trend parameters can either indicate increases, decreases or no changes. The two co-payment increases (Intervention C and E) would be expected to decrease the level and trend of PBS expenditure and volume across the three categories. Co-payment increases would be expected to reduce patients' demand by making them more cost-conscious in selecting drugs and reduce unnecessary drugs use. The re-supply limits (Intervention B) and Safety Net 20 day rule (Intervention F) would also be expected to decrease the level and trend of PBS expenditure and volume. Both policies would be expected to reduce drug stockpiling by patients, thus reducing the total cost subsidised by the government. The policy requiring an economic evaluation (Intervention A) might have the effect of delaying the listing of new and more expensive drugs on the PBS. Due to the long period to get listing approval (Australian National Audit Office, 1997), the immediate effect of this policy on expenditure levels and volume levels would not be expected to be significant. However, PBS expenditure and volumes might be expected to trend downwards as more cost-effective drugs are listed.

For the Therapeutic Group Premium policy (Intervention D), the level and trend of PBS expenditure would be expected to decrease due to the drugs grouping, where government subsidise the lowest price drug in that group. The level of service and its trend would be likely to remain unchanged as the number of drugs listed on the PBS will remain the same. With the introduction of the F2 Formulary and the 2%, 12.5% or 25% price reductions, the level and trend of PBS expenditure and volumes would be expected to decrease. The amount of drugs subsidised by the government will be reduced in addition to the decreased in the number of subsidised drugs, where drugs that cost below co-payment level were not captured by PBS database.

For the listing of new statins (Intervention H – K), there are likely to be no changes to the volume for Category 1 and Category 2 due to drug switching. However, drug switching may decrease the expenditure and volume of Atorvastatin (Category 3) when Rosuvastatin (Intervention K) is listed. The listings of new, more expensive statins would be expected to increase the level and trend of expenditure for Category 1 and Category 2.

Table 5.2 Interventions investigated and included as breakpoints

Intervention		Date
Cost Containment Policy		
A	Economic Evaluation Requirement	1/01/1993
B	Re-Supply Limits	1/11/1994
C	Co-payment Increase Between 15.0-18.5%	1/01/1997
D	Therapeutic Group Premium Policy	1/02/1998
E	Co-payment Increase 24%	1/01/2005
F	Safety Net 20 Day Rule	1/01/2006
G	F2—2%, 12.5%, 25% price reductions	1/08/2008
New Listing of Statins		
H	Pravastatin Listed	1/06/1993
I	Fluvastatin Listed	1/02/1996
J	Atorvastatin Listed	1/02/1998
K	Rosuvastatin Listed	1/12/2006

Table 5.3 Expected impact of the interventions

Intervention		Category 1 (All PBS Medicines)				Category 2 (All Statins)				Category 3 (All Atorvastatin)			
		Service		Benefits		Service		Benefits		Service		Benefits	
		Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend
Cost Containment Policy													
A	Economic Evaluation Requirement	<->	↓	<->	↓	<->	↓	<->	↓	N.A	N.A	N.A	N.A
B	Re-Supply Limits	↓	↓	↓	↓	↓	↓	↓	↓	N.A	N.A	N.A	N.A
C	Co-payment Increase Between 15.0-18.5%	↓	↓	↓	↓	↓	↓	↓	↓	N.A	N.A	N.A	N.A
D	Therapeutic Group Premium Policy	<->	<->	↓	↓	<->	<->	↓	↓	N.A	N.A	N.A	N.A
E	Co-payment Increase 24%	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
F	Safety Net 20 Day Rule	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
G	F2—2%, 12.5%, 25% price reductions	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓

New Listing of Statins													
H	Pravastatin Listed	<->	<->	↑	↑	<->	<->	↑	↑	N.A	N.A	N.A	N.A
I	Fluvastatin Listed	<->	<->	↑	↑	<->	<->	↑	↑	N.A	N.A	N.A	N.A
J	Atorvastatin Listed	<->	<->	↑	↑	<->	<->	↑	↑	N.A	N.A	N.A	N.A
K	Rosuvastatin Listed	<->	<->	↑	↑	<->	<->	↑	↑	↓	↓	↓	↓

N.A – Not applicable

5.3.4 Outcome variables analysed

Nine dependent variables, Total Service (General + Concessional), Total Benefits (General + Concessional), Total Service (General), Total Benefit (General), Total Service (Concessional), Total Benefits (Concessional), Total Service per thousand of the population (Total Service/1000), Total Benefits per thousand of the population (Total Benefits/1000) and the Defined Daily Doses (DDDs) per thousand of the population per day (DDDs/1000/day) were included in the analysis. In order to determine the effect of an intervention on general beneficiary patients and concessional beneficiary patients, the service and benefit data were analysed as a combination of both categories and also as individual categories. To calculate the rate of services and benefits, the monthly estimated population was used as a denominator. The monthly population data were obtained by linear extrapolation from the quarterly estimated resident population produced by the Australian Bureau of Statistics (Australian Bureau of Statistics, 2013). The DDDs/1000/day variable is an international unit to represent the level of drug utilization in the studied population (World Health Organization et al., 2003). The World Health Organization defines DDD as 'the assumed average maintenance dose per day for a drug used for its main indication in adults' (WHO Collaborating Centre for Drug Statistics Methodology, 2009). For this study, the DDDs/1000/day variable was only applicable to Category 2 and Category 3 data, namely the HMG-CoA reductase inhibitors drugs group. Monthly DDDs/1000/day variable were calculated using Equation 1 by taking into account the number of scripts in that particular month. Details of each drug used to calculate the DDDs/1000/day are given in Table 5.4.

Equation 1.0 Calculation of DDD/1000 population/day

$$\text{DDD/1000 population/day} = \frac{\text{Number of benefits per month X Strength (mg) X Packaging size X 1000}}{\text{DDD (mg) X Population X days in that particular month}}$$

Table 5.4 HMG-CoA reductase inhibitors drugs with the strength available, packaging size and DDDs

Drug	Strength available (mg)	Packaging size (n)	DDD (mg)
Pravastatin	10, 20, 40, 80	30	30
Fluvastatin	20, 40, 80	28	60
Atorvastatin	10, 20, 40, 80	30	20
Rosuvastatin	5, 10, 20, 40	30	10

Source: Department of Health and World Health Organisation, 2014

5.3.5 Data organization for analysis

Using data of total services (general + concessional) as an example, Table 5.5 illustrates how the data were organised for analysis. The months before the implementation of an intervention are indicated by 0 and months after the intervention are indicated by 1. The month and month after the implementation of an intervention are given sequential integer variables.

Table 5.5 Structure of data for analysis of the impact of two policy changes on the total service (General + Concessional)

Time	Total Service (Gen. + Conc.)	Observation	Intervention A[1]	Time after Intervention A	Intervention B[2]	Time after Intervention B
01-01-1992	9616464	1	0	0	0	0
01-02-1992	6291465	2	0	0	0	0
01-03-1992	6806613	3	0	0	0	0
⋮	⋮	⋮	⋮	⋮	⋮	⋮
01-10-1992	8912714	10	0	0	0	0
01-11-1992	8870800	11	0	0	0	0
01-12-1992	10991649	12	0	0	0	0
01-01-1993	10472069	13	1	1	0	0
01-02-1993	6862123	14	1	2	0	0
01-03-1993	7853524	15	1	3	0	0
⋮	⋮	⋮	⋮	⋮	⋮	⋮
01-08-1994	10535352	32	1	20	0	0
01-09-1994	10122927	33	1	21	0	0
01-10-1994	9960653	34	1	22	0	0
01-11-1994	10261066	35	1	23	1	1
01-12-1994	10648698	36	1	24	1	2
01-01-1995	10690134	37	1	25	1	3
⋮	⋮	⋮	⋮	⋮	⋮	⋮
⋮	⋮	⋮	⋮	⋮	⋮	⋮

[1] Intervention A introduced on 1st January 1993
[2] Intervention B introduced on 1st November 1994

5.3.6 Analysis

The time series data were initially plotted graphically and visual inspections performed to detect breakpoints, abnormal patterns and seasonality. Breakpoints are intervention points that divide the time series into segments. Next, using the STATA/MP version 10 statistical package, segmented linear regression was applied to the time series data to determine statistically the significance of the level and trend. To control for auto-correlation in the data series, Newey-West estimators were used to estimate the coefficients (Newey et al., 1986; StataCorp, 2013). In addition, a lag of 12 months was applied to adjust for seasonal noise (Sims, 1974). Visually, the data were found to spike in December every year before falling in the first month of the year, thus having lags 12. Donnelly et al. (2000) demonstrated that due to the arrangement of the PBS, patients tend to increase drugs usage toward the end of the year to take advantage of the safety net by accumulating drugs for the following year consumption, thus creating an annual seasonal noise.

In order to obtain a parsimonious model, forward stepwise eliminations were applied in the analysis. Variables parameters at breakpoints that produced both insignificant coefficients (level and trend) were eliminated. P-values of 0.05 and higher were considered insignificant. However, if either one of the parameters was significant, the variables at that breakpoint were included in the analysis. The stepwise eliminations were done systematically in chronological order.

Generally, time series with 50 to 100 observations is preferred in order to produce a reliable estimate (Helfenstein, 1986). However, the available literature shows no consensus on the numbers of observations needed. Wagner et al. (2002) recommended a minimum of 12 observations before and 12 observations after the intervention for the nature of the pattern to be established. Systematic review on reference pricing by Aaserud et al. (2006) accepted interrupted time series studies with a at least 12 observations before and after the intervention into their review. This recommendation concurred with Marshall et al. (2002) by using 12 data points before and after intervention in their study. On the other hand, the EPOC Cochrane

Group defines time series with at least 3 observations before and 3 observations after the intervention, as qualifying as interrupted time series studies, not accounting for seasonal variation. However, if seasonality is observed in the model, a minimum of 10 pre- and 10 post-data points are required (Cochrane Effective Practice and Organisation of Care Group, 2013; Ramsay et al., 2003). Several studies used less than 10 observations before the intervention in their analysis model, Soumerai et al (1992) applied 6 observations before and 8 after the intervention while Mol et al. (2005) used between 10 and 18 observations. In this study, a minimum of 12 observations before and 12 observations after the intervention was adopted. Several interventions were omitted from the analysis due to the proximity of those interventions with each other. For the Category 1 analysis, in cases where the interventions were implemented 12 months apart or less, the earlier policy was prioritised and included in the analysis while the latter policy was removed from the analysis. As a result, the brand substitution policy introduced in December 1994 was dropped from the analysis due to the proximity to the introduction of the re-supply limits policy introduced a month earlier in November.

For the Category 2 and 3 analyses, the data available contained primarily the expenditure and volume of statins prescriptions. Therefore, key incidents such as the listing of new statins were expected to significantly impact the prescription expenditure and volume and were given priority over the cost containment measures if both interventions occurred less than 12 months apart. For instance, the economic evaluation requirement policy was introduced in January 1993 and Pravastatin was listed in the PBS six months later on June 1993. The listing of Pravastatin was taken as a breakpoint in the analysis whereas the economic evaluation requirement policy was dropped from the analysis. In summary, Category 1 statistical analysis was performed by including breakpoints from intervention A to G while Category 2 and 3 statistical analyses included breakpoints from intervention B to K (Figure 5.2).

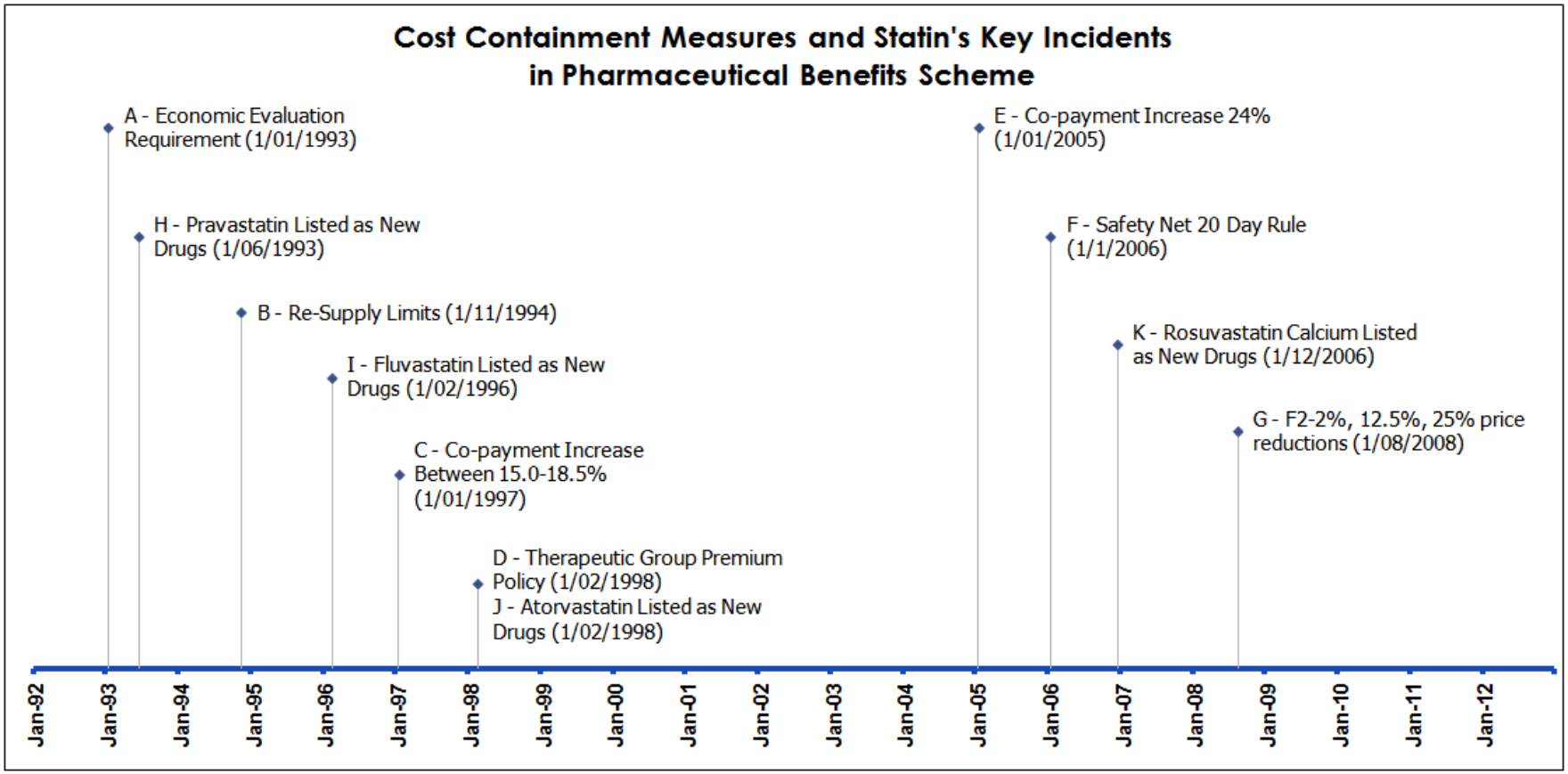


Figure 5.2 Cost containment measures and statin's key incidents in the Pharmaceutical Benefits Scheme, January 1992 to March 2012

5.3.7 Interpretation of results

Results of the analysis must be interpreted taken into consideration limitations in the PBS data, in particular that for the duration of the study the PBS database did not include non-subsidised medicines falling below the co-payment level. This will not have impacted on the Category 3 analysis as the price of Atorvastatin was above the co-payment level throughout the duration of the study. The price of Rosuvastatin was also above the co-payment level throughout the period. However, the price of lower strengths of Simvastatin, Pravastatin and Fluvastatin did fall below the co-payment level for general beneficiaries progressively from 2006 onwards, with higher strengths (40mg plus for Simvastatin and Pravastatin and 80mg plus for Fluvastatin) remaining above the co-payment level throughout the period. In the Category 1 analysis, which included all ATC main drug groups, new drugs priced above the co-payment level will have been added to the PBS while the price of others will have fallen below the co-payment level during the period. This latter analysis sought to capture broad trends overall.

5.4 Results

5.4.1 Category 1 – all ATC main drug groups

Out of seven interventions (A – G) analysed, all interventions were found to have significant impact on at least one of the outcome variables except intervention B, the re-supply limits policy. Changes in level and trend of services and benefits for the concessional beneficiary, the general beneficiary, all beneficiaries and per 1000 population are shown in Table 5.6 to Table 5.11. The results are presented graphically in Appendices (Figure A3 to Figure A10).

The introduction of intervention A (economic evaluation requirement policy) was found to have no effect on all levels and trends of PBS services and benefits except services for concessional beneficiaries. The intervention resulted in an immediate drop of 599,500 prescriptions [95% CI 119,600; 1,079,000] (*p=0.015*) and a trend reduction of 106,870 prescriptions in each month [95% CI 50,750; 162,990] (*p<0.001*).

Following the implementation of intervention C (co-payment increase between 15.0-18.5%), there were immediate drops in the level of services and benefits but the impact was temporary with the trend of services and benefits increasing in the following months post intervention. The level of service and benefits for all beneficiaries were reduced by 1,708,776 prescriptions [95% CI 1,064,560; 2,352,990] (*p<0.001*) and A$37,300,000 [95% CI 21,400,000; 53,300,000] (*p<0.001*) respectively, with the average reduction rate per 1000 population of 93.90 prescriptions [95% CI 58.37; 129.42] (*p<0.001*) and A$2,086 [95% CI 1,202.81; 2,971.13] (*p<0.001*). Post intervention, the estimated trend for all beneficiaries added an additional 128,314 prescriptions [95% CI 69,640; 186,990] (*p<0.001*) and A$3,643,142 [95% CI 1,820,000; 5,460,000] (*p<0.001*) each month to the PBS, averaging 6.93 prescriptions per 1000 population [95% CI 3.76; 10.11] (*p<0.001*) and A$191.63 per 1000 population [95% CI 94.04; 289.21] (*p<0.001*).

All estimated level and trend of services and benefits post intervention D (Therapeutic Group Premium policy) were decreased except the service trend in the general beneficiary, where no statistically significant impact was found. Significant decreases were found in the level for all beneficiaries, with the number of services decreasing by 1,273,978 prescriptions [95% CI 768,870; 1,779,090] (*p<0.001*) and the total benefits decreasing by A$42,700,000 [95% CI 28,700,000; 56,800,000] (*p<0.001*) while the trend in the service reduced by 117,206 prescriptions each month [95% CI 58,350; 176,070] (*p<0.001*) and total benefits reduced by A$2,327,346 each month [95% CI 541,200; 4,110,000] (*p=0.011*). The bulk of the decreases were attributed to concessional beneficiaries with the levels of service decreased by 866,796 prescriptions [95% CI 490,590; 1,243,010] (*p<0.001*) and total benefits decreased by A$31,600,000 [95% CI 22,800,000; 40,300,000] (*p<0.001*). The concessional beneficiary trends were estimated to decrease by 83,161 prescriptions [95% CI 33,070; 133,250] (*p=0.001*) and A$1,518,304 each month [95% CI 427,000; 2,610,000] (*p=0.007*).

The implementation of a second co-payment increment in intervention E (co-payment increase by 24%) resulted in a slightly different impacts compared to intervention C. There were immediate drops in the number of services and total benefits across all outcome variables, with changes in level similar to the first co-payment increment. However, for concessional beneficiaries, the monthly estimated trend of service and benefits increased by 66,319 prescriptions [95% CI 23,460; 109,180] (*p=0.003*) and A$2,485,974 [95% CI 369,500; 4,600,000] (*p=0.022*) respectively while for general beneficiaries, the trend of service decreased by 20,193 prescription [95% CI 14,930; 25,460] (*p<0.001*) and no significant effect was found on the trend of benefits.

The impact of intervention F (Safety Net 20 day rule) was largely on the services and benefits for concessional beneficiaries. The intervention resulted in an immediate reduction of 774,746 prescriptions [95% CI 332,750; 1,216,740] (*p=0.001*) and A$35,300,000 [95% CI 20,700,000; 49,800,000] (*p<0.001*) while the monthly trend reduction were estimated at 84,010 prescriptions [95% CI 37,190; 130,840] (*p<0.001*) and A$3,360,000 [95% CI 1,170,000; 5,550,000] (*p=0.003*). For general beneficiaries, there were no significant effect on the services and benefits except an increase in the level of total benefits by A$12,400,000 [95% CI 3,800,000; 21,000,000] (*p=0.005*) immediately after the intervention being implemented.

The increase in services post intervention G (2%, 12.5% or 25% price reductions in F2) was limited to the level only while the trend remained unchanged. The level of service for all beneficiaries was increased by 1,034,020 prescriptions [95% CI 435,830; 1,632,210] (*p=0.001*) with the majority of the increase attributed to concessional beneficiaries with 786,730 prescriptions [95% CI 280,970; 1,292,490] (*p=0.002*) while the general beneficiary service increased by 232,378 prescriptions [95% CI 42,620; 422,130] (*p=0.017*). There were also increases in the estimated level of benefits for all beneficiaries by A$47,300,000 [95% CI 17,800,000; 76,700,000] (*p=0.002*), for general beneficiaries by A$12,600,000 [95% CI

5,400,000; 19,700,000] (*p=0.001*) and for concessional beneficiaries by A$34,700,000 [95% CI 11,500,000; 57,900,000] (*p=0.003*). However, there were no significant changes in the trend of both services and benefits save for the total benefits of general beneficiaries with a decrease of A$361,689 [95% CI 16,000; 707,300] (*p=0.040*).

Table 5.6 Estimated number of services and benefits before and after intervention A

Intervention			A				
			Economic Evaluation *1/01/1993*				
All ATC main drug groups	**Term**		**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	6,944.88	217.68	9,557.09	-174.81	-792.28
		95% CI	6,023.44 to 7,866.32	90.26 to 345.11	-	-299.02 to -50.61	-1,699.15 to 114.59
		P>t	0.000	0.001	-	0.006	0.087
	Benefits (A$, million)	Coef.	92.40	1.86	-	NS	NS
		95% CI	87.00 to 97.80	1.706 to 2.01	-	-	-
		P>t	0.000	0.000	-	-	-
General	**Service (n, '000)**	Coef.	1,261.52	7.28	-	NS	NS
		95% CI	1,038.49 to 1,484.56	1.83 to 12.74	-	-	-
		P>t	0.000	0.009	-	-	-
	Benefits (A$, million)	Coef.	20.50	0.3560	-	NS	NS
		95% CI	17.80 to 23.20	0.2884, 0.4235	-	-	-
		P>t	0.000	0.000	-	-	-
Concessional	**Service (n, '000)**	Coef.	6,164.94	145.90	7,915.68	-106.87	-599.50
		95% CI	5,734.77 to 6,595.11	87.95 to 203.84	-	-162.99 to -50.75	-1,079.40 to -119.60
		P>t	0.000	0.000	-	0.000	0.015
	Benefits (A$, million)	Coef.	71.90	1.50	-	NS	NS
		95% CI	68.90 to 74.90	1.40 to 1.60	-	-	-
		P>t	0.000	0.000	-	-	-
Per 1000 Population	**Service (n)**	Coef.	399.57	11.99	543.50	-10.15	-43.46
		95% CI	346.81 to 452.33	4.70 to 19.28	-	-17.24 to -3.06	-95.84 to 8.93
		P>t	0.000	0.001	-	0.005	0.104
	Benefits (A$)	Coef.	5,379.90	95.87	-	NS	NS
		95% CI	5,052.86 to 5,706.94	87.02 to 104.73	-	-	-
		P>t	0.000	0.000	-	-	-

NS – Non Significant

Table 5.7 Estimated number of services and benefits before and after intervention C

Intervention			C				
			Co-payment increase *1/01/1997*				
All ATC main drug groups	**Term**		**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	8,764.82	42.87	10,822.63	128.31	-1,708.78
		95% CI	-	-	-	69.64 to 186.99	-2,352.99 to -1,064.56
		P>t	-	-	-	0.000	0.000
	Benefits (A$, million)	Coef.	92.40	1.86	203.67	3.64	-37.30
		95% CI	87.00 to 97.80	1.706 to 2.01	-	1.82 to 5.46	-53.30 to -21.40
		P>t	0.000	0.000	-	0.000	0.000
General	**Service (n, '000)**	Coef.	1,261.52	7.28	1,698.43	40.23	-531.30
		95% CI	1,038.49 to 1,484.56	1.83 to 12.74	-	5.79 to 74.68	-880.24 to -182.37
		P>t	0.000	0.009	-	0.022	0.003
	Benefits (A$, million)	Coef.	20.50	0.3560	41.86	1.11	-10.70
		95% CI	17.80 to 23.20	0.2884, 0.4235	-	0.3087 to 1.92	-17.80 to -3.71
		P>t	0.000	0.000	-	0.007	0.003
Concessional	**Service (n, '000)**	Coef.	7,316.18	39.03	9,189.35	84.65	-1,242.63
		95% CI	-	-	-	36.83 to 132.46	-1,737.09 to -748.18
		P>t	-	-	-	0.001	0.000
	Benefits (A$, million)	Coef.	71.90	1.50	162.01	2.53	-26.60
		95% CI	68.90 to 74.90	1.40 to 1.60	-	1.42 to 3.64	-36.60 to -16.60
		P>t	0.000	0.000	-	0.000	0.000
Per 1000 Population	**Service (n)**	Coef.	500.05	1.85	588.70	6.93	-93.90
		95% CI	-	-	-	3.76 to 10.11	-129.42 to -58.37
		P>t	-	-	-	0.000	0.000
	Benefits (A$)	Coef.	5,379.90	95.87	11,132.12	191.63	-2,086.97
		95% CI	5,052.86 to 5,706.94	87.02 to 104.73	-	94.04 to 289.21	-2,971.13 to -1,202.81
		P>t	0.000	0.000	-	0.000	0.000

Table 5.8 Estimated number of services and benefits before and after intervention D

Intervention			D				
			TGP *1/02/1998*				
All ATC main drug groups	**Term**		**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	9,113.85	171.19	11,339.26	-117.21	-1,273.98
		95% CI	-	-	-	-176.07 to -58.35	-1,779.09 to -768.87
		P>t	-	-	-	0.000	0.000
	Benefits (A$, million)	Coef.	166.57	5.50	238.08	-2.33	-42.70
		95% CI	-	-	-	-4.11 to -0.5412	-56.80 to -28.70
		P>t	-	-	-	0.011	0.000
General	**Service (n, '000)**	Coef.	1,167.13	47.52	1,784.83	-34.05	-407.18
		95% CI	-	-	-	-68.76 to 0.670	-651.08 to -163.28
		P>t	-	-	-	0.055	0.001
	Benefits (A$, million)	Coef.	31.16	1.47	50.25	-0.8090	-11.20
		95% CI	-	-	-	-1.61 to -0.0097	-17.00 to -5.28
		P>t	-	-	-	0.047	0.000
Concessional	**Service (n, '000)**	Coef.	7,946.72	123.67	9,554.43	-83.16	-866.80
		95% CI	-	-	-	-133.25 to -33.07	-1,243.01 to -490.59
		P>t	-	-	-	0.001	0.000
	Benefits (A$, million)	Coef.	135.41	4.03	187.83	-1.52	-31.60
		95% CI	-	-	-	-2.61 to -0.4270	-40.30 to -22.80
		P>t	-	-	-	0.007	0.000
Per 1000 Population	**Service (n)**	Coef.	494.80	8.78	609	-6.64	-65.24
		95% CI	-	-	-	-9.83 to -3.46	-93.29 to -37.20
		P>t	-	-	-	0.000	0.000
	Benefits (A$)	Coef.	9,045.15	287.50	12,782.61	-141.31	-2,100.07
		95% CI	-	-	-	-237.11 to -45.51	-2,898.91 to -1,301.22
		P>t	-	-	-	0.004	0.000

Table 5.9 Estimated number of services and benefits before and after intervention E

Intervention			E				
			Co-payment increase *1/01/2005*				
All ATC main drug groups	**Term**		**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	10,065.28	53.98	14,545.55	85.43	-1,494.06
		95% CI	-	-	-	3.89 to 166.98	-2,253.77 to -734.35
		P>t	-	-	-	0.040	0.000
	Benefits (A$, million)	Coef.	195.38	3.17	458.79	3.29	-59.00
		95% CI	-	-	-	-0.3619 to 6.94	-89.30 to -28.70
		P>t	-	-	-	0.077	0.000
General	**Service (n, '000)**	Coef.	1,377.65	13.47	2,495.72	-20.19	-207.71
		95% CI	-	-	-	-25.46 to -14.93	-394.20 to -21.21
		P>t	-	-	-	0.000	0.029
	Benefits (A$, million)	Coef.	39.05	0.6600	93.81	0.8027	-15.50
		95% CI	-	-	-	-0.7928 to 2.40	-27.30 to -3.71
		P>t	-	-	-	0.323	0.010
Concessional	**Service (n, '000)**	Coef.	8,687.63	40.51	12,049.84	66.32	-1,047.12
		95% CI	-	-	-	23.46 to 109.18	-1,528.25 to -565.99
		P>t	-	-	-	0.003	0.000
	Benefits (A$, million)	Coef.	156.23	2.51	364.88	2.49	-43.50
		95% CI	-	-	-	0.3695 to 4.60	-62.50 to -24.50
		P>t	-	-	-	0.022	0.000
Per 1000 Population	**Service (n)**	Coef.	543.68	2.14	721	3.90	-76.41
		95% CI	-	-	-	-0.0969 to 7.89	-114.94 to -37.88
		P>t	-	-	-	0.056	0.000
	Benefits (A$)	Coef.	10,682.54	146.19	22,816	144.92	-3,072.33
		95% CI	-	-	-	-33.20 to 323.03	-4,615.96 to -1,528.70
		P>t	-	-	-	0.110	0.000

Table 5.10 Estimated number of services and benefits before and after intervention F

Intervention			F				
			Safety Net 20 days *1/01/2006*				
All ATC main drug groups	**Term**		**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	13,051.49	139.41	14,724.45	-123.89	-1,004.31
		95% CI	-	-	-	-206.18 to -41.61	-1,698.94 to -309.68
		P>t	-	-	-	0.003	0.005
	Benefits (A$, million)	Coef.	399.79	6.46	477.33	-4.04	-47.60
		95% CI	-	-	-	-7.81 to -0.2713	-70.00, -25.30
		P>t	-	-	-	0.036	0.000
General	**Service (n, '000)**	Coef.	2,288.01	-6.72	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	Benefits (A$, million)	Coef.	78.31	1.46	95.86	-0.6848	-12.40
		95% CI	-	-	-	-2.35 to 0.9769	-21.00 to -3.80
		P>t	-	-	-	0.418	0.005
Concessional	**Service (n, '000)**	Coef.	11,002.72	106.83	12,284.65	-84.01	-774.75
		95% CI	-	-	-	-130.84 to -37.19	-1,216.74 to -332.75
		P>t	-	-	-	0.000	0.001
	Benefits (A$, million)	Coef.	321.38	5.00	381.38	-3.36	-35.30
		95% CI	-	-	-	-5.55 to -1.17	-49.80 to -20.70
		P>t	-	-	-	0.003	0.000
Per 1000 Population	**Service (n)**	Coef.	644.48	6.03	717	-6.17	-48.77
		95% CI	-	-	-	-10.20 to -2.13	-82.84 to -14.70
		P>t	-	-	-	0.003	0.005
	Benefits (A$)	Coef.	19,743.57	291.10	23,237	-205.32	-2,289.18
		95% CI	-	-	-	-389.48 to -21.16	-3,391.62 to -1,186.75
		P>t	-	-	-	0.029	0.000

Table 5.11 Estimated number of services and benefits before and after intervention G

Intervention			G				
			F2 price cut *1/08/2008*				
All ATC main drug groups	**Term**		**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	13,720.14	15.52	14,201.23	-14.46	1,034.02
		95% CI	-	-	-	-55.68 to 26.76	435.83 to 1,632.21
		P>t	-	-	-	0.490	0.001
	Benefits (A$, million)	Coef.	429.73	2.42	504.74	-0.9307	47.30
		95% CI	-	-	-	-2.44, 0.5768	17.80 to 76.70
		P>t	-	-	-	0.225	0.002
General	**Service (n, '000)**	Coef.	2,288.01	-6.72	1,998.95	3.89	232.38
		95% CI	-	-	-	-1.64 to 9.43	42.62 to 422.13
		P>t	-	-	-	0.167	0.017
	Benefits (A$, million)	Coef.	83.46	0.7776	107.56	-0.3617	12.60
		95% CI	-	-	-	-0.7073 to -0.0160	5.40 to 19.70
		P>t	-	-	-	0.040	0.001
Concessional	**Service (n, '000)**	Coef.	11,509.90	22.82	12,217.19	-18.93	786.73
		95% CI	-	-	-	-55.11 to 17.26	280.97 to 1,292.49
		P>t	-	-	-	0.304	0.002
	Benefits (A$, million)	Coef.	346.08	1.64	396.98	-0.5690	34.70
		95% CI	-	-	-	-1.77 to 0.6352	11.50 to 57.90
		P>t	-	-	-	0.353	0.003
Per 1000 Population	**Service (n)**	Coef.	668.12	-0.13	664	-0.58	44.38
		95% CI	-	-	-	-2.50 to 1.35	16.71 to 72.06
		P>t	-	-	-	0.555	0.002
	Benefits (A$)	Coef.	20,947.62	85.79	23,607	-47.02	2,073.38
		95% CI	-	-	-	-116.88 to 22.83	747.57 to 3,399.20
		P>t	-	-	-	0.186	0.002

5.4.2 Category 2 – all HMG-CoA reductase inhibitor drug groups

For the category 2 analysis, nine[45] interventions (intervention B – G and H – K) were analysed and one intervention, the listing of Pravastatin (intervention H) was found to have no statistically significant effect on the level and trend of services and benefits across any of the outcome variables. Changes in the level and trend of services and benefits for concessional beneficiaries, general beneficiaries, all beneficiaries, the rate per 1000 population and DDDs/1000/day are shown in Table 5.12 to Table 5.19. These results are presented graphically in Appendix (Figure A11 to Figure A19).

The implementation of intervention B (Re-supply limits) did not statistically change the level of services and benefits for all variables. However, the intervention resulted in an increase in trend for all variables with an additional 659,000 prescriptions per month [95% CI 4,330; 8,840] (*p<0.001*) and A$270,000 per month [95% CI 97,700; 442,300] (*p=0.002*) added to the all beneficiaries trends. The increments in services and benefits trends were largely attributed to concessional beneficiaries with an increase of 4,030 prescriptions per month [95% CI 2,730; 5,340] (*p<0.001*) and A$171,900 per month [95% CI 76,800; 266,900] (*p<0.001*) while the general beneficiary services and benefits were increased by 2,550 prescriptions per month [95% CI 1,610; 3,500] (*p<0.001*) and A$98,100 per month [95% CI 20,400; 175,800] (*p=0.014*) respectively. The trend of DDD per 1000 population was estimated to have increased by 0.1695 per day [95% CI 0.1142; 0.2248] (*p<0.001*).

[45] Both intervention D (Therapeutic Group Premium policy) and J (Atorvastatin listing) were implemented in the same date, 1st February 1998 and were counted as one intervention.

Following the implementation of intervention C (co-payment increase between 15.0–18.5%), there was an immediate drop in the levels of services and benefits across every outcome variable. The number of services dropped by 66,990 prescriptions [95% CI 48,500; 85,480] (*p<0.001*) for all beneficiaries, 45,260 prescriptions [95% CI 32,820; 57,690] (*p<0.001*) for concessional beneficiaries and 21,730 prescriptions [95% CI 15,370; 28,100] (*p<0.001*) for general beneficiaries while the levels of benefits dropped by A$3,810,000 [95% CI 2,590,000; 5,020,000] (*p<0.001*) for all beneficiaries, A$2,450,000 [95% CI 1,750,000; 3,140,000] (*p<0.001*) for the concessional beneficiary benefits and A$ 958,700 [95% CI 581,600; 1,340,000] (*p<0.001*) for general beneficiaries. The effects of the intervention in decreasing the levels of both services and benefits were momentary. There were no statistically significant changes estimated for the trends of services and benefits in any of the outcome variables apart from a reduction in benefits of A$39,300 per month [95% CI 17,400; 61,200] (*p<0.001*) for general beneficiaries and an increase of 0.0923 DDD per 1,000 population [95% CI 0.0175; 0.1671] (*p=0.016*).

The second co-payment increases (intervention E), implemented in January 2005 reduced the level of both services and benefits for all outcome variables with the exception of general beneficiary's services and DDDs/1000/day. The level of services for all beneficiaries was decreased by 82,050 prescriptions [95% CI 33,920; 130,170] (*p=0.001*), which was primarily attributable to the decrease of 72,410 prescriptions [95% CI 38,030; 106,800] (*p<0.001*) for concessional beneficiaries. The levels of benefits was also estimated to have decreased by A$6,670,000 [95% CI 2,940,000; 10,400,000] (*p=0.001*) for all beneficiaries with decreases of A$1,260,000 [95% CI 252,700; 2,280,000] (*p=0.015*) and A$4,540,000 [95% CI 2,400,000; 6,680,000] (*p<0.001*) respectively for general and concessional beneficiaries. The effect of this intervention on trends was similar to the previous co-payment increment intervention (intervention C). The trend in benefits for general beneficiaries was reduced by A$113,500 per month [95% CI 87,200; 139,700] (*p<0.001*) while the trend of DDDs/1000/day went in the opposite

direction, increasing by 0.3279 DDDs [95% CI 0.0729; 0.5829] (*p=0.012*). There were no statistically significant changes estimated for other outcome variables.

The concurrent impact of intervention D (Therapeutic Group Premium policy) and intervention J (Atorvastatin Listed) had mixed results. No statistically significant changes were identified in the level or trend of benefits for general beneficiaries and benefits per 1,000 population. However, the trend of services was estimated to have decreased by 3,900 prescriptions per month [95% CI 1,830; 5,980] (*p<0.001*) for all beneficiaries and 0.2629 prescriptions per month for per 1,000 population [95% CI 0.1498; 0.3761] (*p<0.001*). The level of benefits for all beneficiaries decreased by A$1,830,000 [95% CI 90,400; 3,580,000] (*p=0.039*) following the implementation of these interventions, attributable primarily to the decrease of A$1,290,000 [95% CI 146,400; 2,430,000] (*p=0.027*) for concessional beneficiaries. For the DDDs/1000/day variable, the level was decreased by 1.60 DDDs per 1,000 population [95% CI 0.4397; 2.75] (*p=0.007*) while the trend increased by 0.3102 DDDs per 1,000 population [95% CI 0.2303; 0.3900] (*p<0.001*).

On January 2006, intervention F (Safety Net 20 day rule) was implemented and was found to have no statistically significant effect on the general beneficiary's services or benefits. For concessional beneficiaries, the level and trend in services were estimated to have decreased by 42,510 prescriptions [95% CI 14,520; 70,490] (*p=0.003*) and 5,660 prescriptions per month [95% CI 2,440; 8,880] (*p=0.001*) respectively. Over all, the level of services for all beneficiaries was reduced by 52,450 prescriptions [95% CI 12,640; 92,290] (*p=0.01*) with the trend of services reduced by 6,750 prescriptions per month [95% CI 1,930; 11,570] (*p=0.006*). However, while the intervention resulted in a decrease in the level of benefits of A$4,770,000 [95% CI 1,370,000; 8,170,000] (*p=0.006*), no statistically significant change was found in the corresponding for concessional beneficiaries. The average rate of change for benefits per 1000 population demonstrated an opposite response by decreasing the trend by A$25.86 per month [95% CI 4.17; 47.56]

(*p=0.02*) without any statistically significant changes to the level. Statistically, there was no significant change to the level of DDDs/1000/day but the trend was decreased by 0.4482 DDDs [95% CI 0.1826; 0.7138] (*p=0.001*).

Following the implementation of intervention G (2%, 12.5% or 25% price reductions in F2), the levels of services and benefit for all beneficiaries increased by 92,720 prescriptions [95% CI 11,400; 1,740,300] (*p=0.026*) and A$5,700,000 [95% CI 1,090,000; 10,300,000] (*p=0.016*). On closer examination, all levels of services and benefits were higher post intervention except for the services of general beneficiary where no statistically significant changes were identified. The increase in the level of services were temporary with the trend of services for all beneficiaries reducing by 5,810 prescriptions per month [95% CI 920; 10,710] (*p=0.02*) except for concessional beneficiary where no statistically significant changes were identified. The trends of benefits for all variables were also found to be statistically not significant. The level of DDDs/1000/day increased by 7.12 DDDs [95% CI 1.16; 13.09] (*p=0.019*) while the trend decreased by 0.5026 DDDs per month [95% CI 0.1375; 0.8677] (*p=0.007*).

In February 2006, Fluvastatin was listed on the Pharmaceutical Benefits Scheme and resulted in an immediate decrease in the levels of services, benefits and DDDs across all variables. On the other hand, the trends of these variables were increased except for the non-significant changes in benefits for general beneficiaries. The levels of services and benefits for all beneficiaries were reduced by 55,690 prescriptions [95% CI 38,400; 72,980] (*p<0.001*) and A$2,900,000 [95% CI 1,710,000; 4,080,000] (*p<0.001*) while the trends were increased by 4,980 prescriptions per month [95% CI 2,480; 7,480] (*p<0.001*) and A$270,900 per month [95% CI 79,100; 462,700] (*p=0.006*) respectively. For DDDs/1000/day, the level was decreased by 1.24 DDDs [95% CI 0.8541; 1.63] (*p<0.001*) while the trend increased by 0.1303 [95% CI 0.0648; 0.1959] (*p<0.001*).

The latest listing of the HMG-CoA reductase inhibitor drug group, Rosuvastatin, on December 2006 resulted in no statistically significant changes in the levels and trends in any of outcome variables except for a decrease in the trend by A$544,200 per month [95% CI 69,400; 1,020,000] (*p=0.025*) for concessional beneficiaries.

Table 5.12 Estimated number of services, benefits and DDDs/1000/day before and after intervention B

Intervention			B				
			Re-supply limit *1/11/1994*				
All HMG-CoA reductase inhibitor drug groups		Term	Intercept	Pre-intervention		Changes	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	Service (n, '000)	Coef.	128.79	1.72	187.23	6.59	-10.91
		95% CI	122.19 to 135.37	1.37 to 2.07	-	4.33 to 8.84	-30.91 to 9.08
		P>t	0.000	0.000	-	0.000	0.283
	Benefits (A$, million)	Coef.	5.75	0.0894	8.79	0.2700	-1.08
		95% CI	5.42 to 6.09	0.0704 to 0.1083	-	0.0977 to 0.4423	-2.67 to 0.5210
		P>t	0.000	0.000	-	0.002	0.186
General	Service (n, '000)	Coef.	55.95	0.2379	64.04	2.55	-3.65
		95% CI	53.11 to 58.80	0.0795 to 0.3964	-	1.61 to 3.50	-12.66 to 5.35
		P>t	0.000	0.003	-	0.000	0.425
	Benefits (A$, million)	Coef.	2.21	0.0116	2.60	0.0981	-0.4135
		95% CI	2.01 to 2.40	0.0004 to 0.0229	-	0.0204 to 0.1758	-1.21 to 0.3819
		P>t	0.000	0.043	-	0.014	0.307
Concessional	Service (n, '000)	Coef.	72.82	1.48	123.19	4.03	-7.26
		95% CI	68.70 to 76.94	1.27 to 1.69	-	2.73 to 5.34	-18.30 to 3.78
		P>t	0.000	0.000	-	0.000	0.196
	Benefits (A$, million)	Coef.	3.54	0.0777	6.19	0.1719	-0.6624
		95% CI	3.34 to 3.75	0.0670 to 0.0884	-	0.0768 to 0.2669	-1.48 to 0.1543
		P>t	0.000	0.000	-	0.000	0.111
Per 1000 Population	Service (n)	Coef.	7.42	0.0895	10.46	0.3544	-0.5896
		95% CI	7.05 to 7.79	0.0698 to 0.1091	-	0.2316 to 0.4773	-1.69 to 0.5124
		P>t	0.000	0.000	-	0.000	0.293
	Benefits (A$)	Coef.	331.47	4.70	491.22	14.48	-59.18
		95% CI	312.43 to 350.51	3.63 to 5.77	-	5.06 to 23.90	-147.16 to 28.80
		P>t	0.000	0.000	-	0.003	0.186
	DDD	Coef.	3.15	0.0413	4.55	0.1695	-0.2633
		95% CI	3.01 to 3.30	0.0332 to 0.0492	-	0.1142 to 0.2248	-0.7627 to 0.2362
		P>t	0.000	0.000	-	0.000	0.300

Table 5.13 Estimated number of services, benefits and DDDs/1000/day before and after intervention I

Intervention			I				
			Fluvastatin listed *1/02/1996*				
All HMG-CoA reductase inhibitor drug groups		**Term**	**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	176.32	8.30	300.89	4.98	-55.69
		95% CI	-	-	-	2.48 to 7.48	-72.98 to -38.40
		P>t	-	-	-	0.000	0.000
	Benefits (A$, million)	Coef.	7.71	0.3593	13.10	0.2709	-2.90
		95% CI	-	-	-	0.07909 to 0.4627	-4.08 to -1.71
		P>t	-	-	-	0.006	0.000
General	**Service (n, '000)**	Coef.	60.39	2.79	102.24	1.57	-21.18
		95% CI	-	-	-	0.6023 to 2.53	-29.07 to -13.29
		P>t	-	-	-	0.002	0.000
	Benefits (A$, million)	Coef.	2.19	0.1098	3.84	0.0733	-1.21
		95% CI	-	-	-	-0.0117 to 0.1584	-1.76 to -0.6589
		P>t	-	-	-	0.091	0.000
Concessional	**Service (n, '000)**	Coef.	115.92	5.51	198.64	3.41	-34.51
		95% CI	-	-	-	1.85 to 4.98	-44.06 to -24.96
		P>t	-	-	-	0.000	0.000
	Benefits (A$, million)	Coef.	5.52	0.2496	9.27	0.1976	-1.69
		95% CI	-	-	-	0.0898 to 0.3053	-2.33 to -1.05
		P>t	-	-	-	0.000	0.000
Per 1000 Population	**Service (n)**	Coef.	9.87	0.4439	16.53	0.2629	-3.05
		95% CI	-	-	-	0.1270 to 0.3988	-4.00 to -2.11
		P>t	-	-	-	0.000	0.000
	Benefits (A$)	Coef.	432.04	19.18	719.75	14.43	-158.60
		95% CI	-	-	-	3.99 to 24.87	-223.46 to -93.74
		P>t	-	-	-	0.007	0.000
	DDD	Coef.	4.29	0.2107	7.45	0.1303	-1.24
		95% CI	-	-	-	0.0648 to 0.1959	-1.63 to -0.8541
		P>t	-	-	-	0.000	0.000

Table 5.14 Estimated number of services, benefits and DDDs/1000/day before and after intervention C

Intervention			C				
			Co-payment increase *1/01/1997*				
All HMG-CoA reductase inhibitor drug groups		**Term**	**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	245.20	13.28	391.29	0.3542	-66.99
		95% CI	-	-	-	-1.86 to 2.57	-85.48 to -48.50
		P>t	-	-	-	0.753	0.000
	Benefits (A$, million)	Coef.	10.21	0.6303	17.14	0.0875	-3.81
		95% CI	-	-	-	-0.0694 to 0.2444	-5.02 to -2.59
		P>t	-	-	-	0.273	0.000
General	**Service (n, '000)**	Coef.	81.06	4.36	128.97	-0.0153	-21.73
		95% CI	-	-	-	-0.7891 to 0.7585	-28.10 to -15.37
		P>t	-	-	-	0.969	0.000
	Benefits (A$, million)	Coef.	2.63	0.1831	4.64	-0.0393	-0.9587
		95% CI	-	-	-	-0.0612 to -0.0174	-1.34 to -0.5816
		P>t	-	-	-	0.000	0.000
Concessional	**Service (n, '000)**	Coef.	164.13	8.93	262.32	0.3695	-45.26
		95% CI	-	-	-	-1.11 to 1.85	-57.69 to -32.82
		P>t	-	-	-	0.623	0.000
	Benefits (A$, million)	Coef.	7.58	0.4472	12.50	0.0575	-2.45
		95% CI	-	-	-	-0.0282 to 0.1432	-3.14 to -1.75
		P>t	-	-	-	0.188	0.000
Per 1000 Population	**Service (n)**	Coef.	13.48	0.7068	21.25	0.0103	-3.63
		95% CI	-	-	-	-0.1095 to 0.1300	-4.63 to -2.63
		P>t	-	-	-	0.866	0.000
	Benefits (A$)	Coef.	561.15	33.61	930.89	-1.89	-175.22
		95% CI	-	-	-	-5.57 to 1.78	-229.28 to -121.16
		P>t	-	-	-	0.312	0.000
	DDD	Coef.	6.21	0.3410	9.96	0.0923	-1.75
		95% CI	-	-	-	0.0175 to 0.1671	-2.30 to -1.19
		P>t	-	-	-	0.016	0.000

Table 5.15 Estimated number of services, benefits and DDDs/1000/day before and after intervention D and J

Intervention			D & J TGP and Atorvastatin listed *1/02/1998*				
All HMG-CoA reductase inhibitor drug groups		**Term**	**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	324.30	13.64	501.56	-3.90	-5.19
		95% CI	-	-	-	-5.98 to -1.83	-43.28 to 32.89
		P>t	-	-	-	0.000	0.788
	Benefits (A$, million)	Coef.	13.33	0.7178	22.66	-0.0491	-1.83
		95% CI	-	-	-	-0.1901 to 0.0920	-3.58 to -0.0904
		P>t	-	-	-	0.494	0.039
General	**Service (n, '000)**	Coef.	107.24	4.34	163.65	-1.86	-2.10
		95% CI	-	-	-	-2.54 to -1.19	-10.60 to 6.40
		P>t	-	-	-	0.000	0.627
	Benefits (A$, million)	Coef.	3.68	0.1438	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
Concessional	**Service (n, '000)**	Coef.	217.06	9.30	337.90	-2.01	-4.24
		95% CI	-	-	-	-3.46 to -0.56	-34.92 to 26.44
		P>t	-	-	-	0.007	0.786
	Benefits (A$, million)	Coef.	10.05	0.5047	16.61	0.0194	-1.29
		95% CI	-	-	-	-0.0585 to 0.0973	-2.43 to -0.1464
		P>t	-	-	-	0.624	0.027
Per 1000 Population	**Service (n)**	Coef.	17.62	0.7170	26.94	-0.2629	0.2969
		95% CI	-	-	-	-0.3761 to -0.1498	-2.04 to 2.64
		P>t	-	-	-	0.000	0.803
	Benefits (A$)	Coef.	755.67	31.72	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	DDD	Coef.	8.22	0.4333	13.85	0.3102	-1.60
		95% CI	-	-	-	0.2303 to 0.3900	-2.75 to -0.4397
		P>t	-	-	-	0.000	0.007

Table 5.16 Estimated number of services, benefits and DDDs/1000/day before and after intervention E

Intervention			E				
			Co-payment increase *1/01/2005*				
All HMG-CoA reductase inhibitor drug groups		**Term**	**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	496.37	9.73	1304.17	4.17	-82.05
		95% CI	-	-	-	-0.34 to 8.67	-130.17 to -33.92
		P>t	-	-	-	0.070	0.001
	Benefits (A$, million)	Coef.	20.83	0.67	76.33	-0.0297	-6.67
		95% CI	-	-	-	-0.4751 to 0.4157	-10.40 to -2.94
		P>t	-	-	-	0.896	0.001
General	**Service (n, '000)**	Coef.	161.55	2.48	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	Benefits (A$, million)	Coef.	3.68	0.1438	17.48	-0.1135	-1.26
		95% CI	-	-	-	-0.1397 to -0.0872	-2.28 to -0.2527
		P>t	-	-	-	0.000	0.015
Concessional	**Service (n, '000)**	Coef.	333.67	7.28	938.04	2.76	-72.41
		95% CI	-	-	-	-0.2145 to 5.73	-106.80 to -38.03
		P>t	-	-	-	0.069	0.000
	Benefits (A$, million)	Coef.	15.33	0.5241	58.83	-0.0583	-4.54
		95% CI	-	-	-	-0.2848 to 0.1682	-6.68 to -2.40
		P>t	-	-	-	0.613	0.000
Per 1000 Population	**Service (n)**	Coef.	27.24	0.4541	64.93	0.1530	-4.59
		95% CI	-	-	-	-0.0689 to 0.3749	-7.14 to -2.03
		P>t	-	-	-	0.176	0.000
	Benefits (A$)	Coef.	755.67	31.72	3800.85	-4.62	-360.88
		95% CI	-	-	-	-26.24 to 16.99	-545.47 to -176.29
		P>t	-	-	-	0.674	0.000
	DDD	Coef.	12.25	0.7434	73.96	0.3279	-0.8222
		95% CI	-	-	-	0.0729 to 0.5829	-3.31 to 1.66
		P>t	-	-	-	0.012	0.515

Table 5.17 Estimated number of services, benefits and DDDs/1000/day before and after intervention F

Intervention			F				
			Safety Net 20 days *1/01/2006*				
All HMG-CoA reductase inhibitor drug groups		**Term**	**Intercept**	**Pre-intervention**		**Changes**	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	1222.12	13.90	1388.92	-6.75	-52.45
		95% CI	-	-	-	-11.57 to -1.93	-92.29 to -12.64
		P>t	-	-	-	0.006	0.010
	Benefits (A$, million)	Coef.	69.67	0.6390	77.34	-0.5132	-2.96
		95% CI	-	-	-	-0.9568 to -0.0696	-6.99 to 1.07
		P>t	-	-	-	0.024	0.149
General	**Service (n, '000)**	Coef.	161.55	2.48	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	Benefits (A$, million)	Coef.	16.22	0.0303	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
Concessional	**Service (n, '000)**	Coef.	865.63	10.04	986.09	-5.66	-42.51
		95% CI	-	-	-	-8.88 to -2.44	-70.49 to -14.52
		P>t	-	-	-	0.001	0.003
	Benefits (A$, million)	Coef.	54.29	0.4658	59.88	0.0450	-4.77
		95% CI	-	-	-	-0.4681 to 0.5582	-8.17 to -1.37
		P>t	-	-	-	0.863	0.006
Per 1000 Population	**Service (n)**	Coef.	60.34	0.6071	67.63	-0.3571	-2.48
		95% CI	-	-	-	-0.5950 to -0.1191	-4.47 to -0.4915
		P>t	-	-	-	0.003	0.015
	Benefits (A$)	Coef.	3439.97	27.10	3765.16	-25.86	-143.04
		95% CI	-	-	-	-47.56 to -4.17	-340.05 to 53.98
		P>t	-	-	-	0.020	0.154
	DDD	Coef.	73.14	1.07	85.99	-0.4482	-1.46
		95% CI	-	-	-	-0.7138 to -0.1826	-4.18 to 1.27
		P>t	-	-	-	0.001	0.294

NS – Non Significant

Table 5.18 Estimated number of services, benefits and DDDs/1000/day before and after intervention K

Intervention			K				
			Rosuvastatin listed 1/12/2006				
All HMG-CoA reductase inhibitor drug groups		Term	Intercept	Pre-intervention		Changes	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	Service (n, '000)	Coef.	1336.46	7.15	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	Benefits (A$, million)	Coef.	74.38	0.1258	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
General	Service (n, '000)	Coef.	161.55	2.48	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	Benefits (A$, million)	Coef.	16.22	0.0303	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
Concessional	Service (n, '000)	Coef.	943.59	4.38	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	Benefits (A$, million)	Coef.	55.11	0.5108	60.73	-0.5442	-0.3802
		95% CI	-	-	-	-1.02 to -0.0694	-2.63 to 1.87
		P>t	-	-	-	0.025	0.739
Per 1000 Population	Service (n)	Coef.	65.15	0.2500	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	Benefits (A$)	Coef.	3622.12	1.23	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	DDD	Coef.	84.54	0.6231	-	NS	NS
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-

NS – Non Significant

Table 5.19 Estimated number of services, benefits and DDDs/1000/day before and after intervention G

Intervention			G				
			F2 price cut *1/08/2008*				
All HMG-CoA reductase inhibitor drug groups		Term	Intercept	Pre-intervention		Changes	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	**Service (n, '000)**	Coef.	1336.46	7.15	1558.21	-5.81	92.72
		95% CI	-	-	-	-10.71 to -0.92	11.40 to 174.03
		P>t	-	-	-	0.020	0.026
	Benefits (A$, million)	Coef.	74.38	0.1258	78.27	0.0027	5.70
		95% CI	-	-	-	-0.2788 to 0.2843	1.09 to 10.30
		P>t	-	-	-	0.985	0.016
General	**Service (n, '000)**	Coef.	161.55	2.48	473.77	-2.15	22.39
		95% CI	-	-	-	-3.27 to -1.04	-0.43 to 45.21
		P>t	-	-	-	0.000	0.054
	Benefits (A$, million)	Coef.	16.22	0.0303	17.52	-0.0291	1.81
		95% CI	-	-	-	-0.0777 to 0.0195	0.8111 to 2.81
		P>t	-	-	-	0.240	0.000
Concessional	**Service (n, '000)**	Coef.	943.59	4.38	1079.40	-3.37	75.36
		95% CI	-	-	-	-6.90 to 0.17	13.88 to 136.85
		P>t	-	-	-	0.062	0.017
	Benefits (A$, million)	Coef.	55.11	-0.0333	59.68	0.1606	4.96
		95% CI	-	-	-	-0.0431 to 0.3642	0.5474 to 9.38
		P>t	-	-	-	0.122	0.028
Per 1000 Population	**Service (n)**	Coef.	65.15	0.2500	72.90	-0.2718	3.8617
		95% CI	-	-	-	-0.4968 to -0.0468	0.2807 to 7.44
		P>t	-	-	-	0.018	0.035
	Benefits (A$)	Coef.	3622.12	1.23	3660.37	0.3415	245.08
		95% CI	-	-	-	-12.69 to 13.37	40.11 to 450.04
		P>t	-	-	-	0.959	0.019
	DDD	Coef.	84.54	0.6231	103.85	-0.5026	7.12
		95% CI	-	-	-	-0.8677 to -0.1375	1.16 to 13.09
		P>t	-	-	-	0.007	0.019

5.4.3 Category 3 – all Atorvastatin drug groups

For the category 3 analysis, four interventions (intervention E-G and K) were analysed and the result are shown in Table 5.20 to Table 5.23. These results are presented graphically in Appendix (Figure A20 to Figure A28). Following the implementation of intervention E (co-payment increase of 24%), the levels of services and benefits across all variables was estimated to decrease except for the general beneficiary and DDDs/1000/day variables. For all beneficiaries, the level of services was reduced by 33,900 prescriptions [95% CI 6,710; 61,090] (*p=0.015*) while the level of benefits was reduced by A$2,940,000 [95% CI 616,300; 5,270,000] (*p=0.014*). These reductions were primarily due to concessional beneficiaries, where the number of services was reduced by 28,430 prescriptions [95% CI 11,720; 45,140] (*p=0.001*) and the benefits paid was reduced by A$ 1,820,000 [95% CI 567,000; 3,070,000] (*p=0.005*). However, the decrease in levels was followed by an increase in the trends of services and benefits across all outcome variables except for benefits for general beneficiaries. The trends of services and benefits for all beneficiaries increased by 4,660 prescriptions per month [95% CI 2,340,000; 6,990,000] (*p<0.001*) and A$470,900 per month [95% CI 164,400; 777,300] (*p=0.003*). Services and benefits for concessional beneficiaries increased by 3,030 prescriptions per month [95% CI 1,610; 4,440] (*p<0.001*) and A$320,000 per month [95% CI 186,400; 453,600] (*p<0.001*) respectively.

In January 2006, following the introduction of intervention F (Safety Net 20 days), there were significant reductions in the level of services and benefits for across all variables except for general beneficiaries and DDDs/1000/day. Services and benefits for all beneficiaries decreased immediately by 42,200 prescriptions [95% CI 5,880; 78,520] (*p=0.023*) and A$3,410,000 [95% CI 287,600; 6,540,000] (*p=0.033*). On average, the rate of decrease for the level of services was 2.07 prescriptions per 1000 population [95% CI 0.3076; 3.84] (*p=0.022*) while benefits

were reduced by A$166.97 per 1000 population [95% CI 15.22; 318.72] (*p=0.031*). There were no statistically significant changes in the underlying trend of services or benefits.

When Rosuvastatin was listed on December 2006, changes were limited to the trend of services and benefits, and no significant changes were estimated for the level of services and benefits. Trends of services and benefits reduced by 7,820 prescriptions per month [95% CI 2,850; 12,790] (*p=0.002*) and A$516,600 per month [95% CI 53,500; 979,600] (*p=0.029*). The number of prescriptions dispensed to general beneficiaries fell by additional 2,010 prescriptions per month [95% CI 1,340; 2,680] (*p<0.001*) and the equivalent fall for concessional beneficiary services was 5,290 prescriptions per month [95% CI 2,040; 8,530] (*p=0.002*). The cost of prescriptions subsidised for general beneficiaries decreased by A$112,300 per month [95% CI 44,100; 180,600] (*p=0.001*) and for concessional beneficiaries by A$360,700 per month [95% CI 104,800; 616,600] (*p=0.006*).

Immediately after the implementation of intervention G (2%, 12.5% or 25% price reductions in F2), there were immediate increases in the level of all outcome variables. Services to all beneficiaries increased by 58,340 prescriptions [95% CI 16,520; 100,150] (*p=0.007*), with 16,130 prescriptions [95% CI 4,380; 27,890] (*p=0.007*) dispensed to general beneficiaries and 42,210 prescriptions [95% CI 11,880; 72,540] (*p=0.007*) dispensed to concessional beneficiaries. Benefits to all beneficiaries were also significantly increased by A$4,940,000 [95% CI 2,510,000; 7,360,000] (*p<0.001*), with increases for general and concessional beneficiaries of A$1,250,000 [95% CI 477,600; 2,030,000] (*p=0.002*) and A$3,690,000 [95% CI 1,650,000; 5,720,000] (*p<0.001*) respectively. In the months following the implementation of intervention G, the trend of services was reduced significantly but benefits remained unchanged. The number of Atorvastatin prescriptions dispensed to all beneficiaries was 3,880 prescriptions [95% CI 1,140; 6,610]

(*p=0.006*) less, with reduction for general beneficiaries of 1,830 prescriptions per month [95% CI 922; 2,730] (*p<0.001*) and for concessional beneficiaries of 2,050 prescriptions per month [95% CI 215; 3,880] (*p=0.029*). The DDDs/1000/day saw an immediate increase in the level by 4.83 DDDs [95% CI 1.51; 8.14] (*p=0.005*), but 0.3062 DDDs less per month [95% CI 0.0945; 0.5179] (*p=0.005*) following the intervention implementation.

5.5 Strengths and Weaknesses

5.5.1 PBS data

The Medicare database provides accurate data on the volume of prescriptions dispensed and prescription expenditure for the PBS. The PBS data are collected by the Department of Human Services when pharmacists lodge claims for pharmaceutical benefits that are accepted for reimbursement processing. Pharmacists are required to lodge claims once a month to cover pharmaceutical benefits supplied during one month within 30 days from when the benefits were supplied (Department of Health, 2014a). The claims processing are mainly automated and therefore the chance for errors is relatively small. Accurate information on volume, benefits, patient category (general and concessional beneficiaries) and location (state) of dispensing are the strength of the database (Medicare Australia, 2013).

The longitudinal nature of the PBS data enables it to provide retrospective data since January 1992, thus providing a longer time period for statistical analysis. Furthermore, the retrospective nature of the data provides an additional strength to the analysis as the outcomes is not affected by contact with researchers.

Although the PBS data provides insight into the trend of medicine usage and the government's pharmaceutical expenditure, it does not necessarily give a true

representation of overall medicine utilisation. The PBS is a dynamic scheme where the PBS schedule is reviewed every few months with medicines being removed and new medicines being added to the schedule. The utilisation of medicines that have being removed from the schedule are no longer captured by the Medicare database while new listing of medicines adds additional patients that were previously not captured, thus distorting the real utilisation rate. Furthermore, the Australian population and the number of concessional cardholders are constantly changing over time. These scenarios created 'noise' to the data.

There are a number of limitations to the PBS data. Firstly, medicines listed on the PBS and supplied to outpatients that cost less than the co-payment (A$36.90 for general beneficiary patients and A$6.00 for concession beneficiary patients in 2014) do not receive a PBS benefit and are not included in the database. Furthermore, some drugs price may fall between the co-payment value of the general beneficiary patients and the concessional beneficiary patients. For these drugs, the PBS database will include transactions by concessional beneficiary patients but not general beneficiary patients unless the general beneficiary patients have reached the safety net threshold. Therefore, the data for general beneficiary patients may be underreported (Research Economics Support Team, 2011). In addition, prices of some drugs may drop for a variety of reasons such as a price cut after a patent has expired and these drugs would be captured in a previous year but excluded in the following year when drug prices drop below co-payment level.

A second limitation of PBS data is the failure to capture the utilisation of medicines not listed on the Pharmaceutical Benefits Schedule such as private prescriptions, over the counter drugs, in-patient drugs usage in public hospital and new drugs (available to the Australian market but not yet listed on the PBS). Only approximately 75% of all prescriptions dispensed in community pharmacies are subsidized under the PBS (Lofgren, 2009; Sansom, 2004).

The Medicare database is unable to provide the actual month the medicine is dispensed to the patients by the pharmacy. There may be a significant gap between the service date and the claim date, as the latter represents the time the service was processed by Medicare Australia (Medicare Australia, 2013).

A seasonal effect was present in the PBS data due to the safety net arrangement. A high level of prescriptions was being filled towards the end of the year to accumulate medicines for the consumption in the following year (Donnelly et al., 2000). To account for this data seasonality, a lag of 12 months was incorporated into the statistical analysis.

Taking into consideration the above limitations, the findings presented in this study may not reflect the actual effect of the interventions. Medicines supplied through community pharmacy that cost less than the general co-payment may be an underestimate of prescription volumes particularly for the general beneficiaries. In addition, the degree of the changes in level and trend may not necessarily be fully attributed to the interventions but other external factors that have not been taken into consideration.

5.5.2 Statistical analysis

The segmented interrupted time series design used in this study cannot determine a strong cause-effect relationship and hence the changes in utilisation and expenditure patterns cannot be definitively attributed to the interventions studied (Hanbury et al., 2013). Due to the quasi-experimental nature of this study where no control group is available, it is only possible to imply that the interventions studied were associated with statistically valid changes in outcomes. The shortfall of no comparison group in the analysis is partially overcome by taking

the pre intervention period as a comparison group for the post intervention period (Ferrand et al., 2011; Huang et al., 2012).

In addition to the above limitation, one intervention, the brand substitution policy was found to be implemented a month later after the implementation of the re-supply limits policy. Due to the proximity of both interventions, the brand substitution break point was dropped from the analysis while the re-supply limits break point was included. The brand substitution policy allows pharmacists to supply interchangeable brand name medicines with bioequivalent generic medicines without seeking advice from prescribers, unless otherwise indicated on the prescription. The implication of excluding the brand substitution break point is limited as this policy does not influence the selection of medicines by prescribers and the amount of subsidies bear by the PBS.

5.6 Conclusion

Comparing the results of category 1 with category 2 and 3, the interventions analysed in this study resulted in impacts that were either similar throughout all three categories or had different impacts between these categories. Intervention B, the re-supply limits policy was not statistically significant in category 1 but was shown to increase the trend of services and benefits in category 2 and decrease the level of services and benefits, particularly for concessional beneficiaries in category 3. Both co-payment increment policies, interventions C and E, decreased the level of services and benefit across all categories. However, both interventions impacts on the trend of services and benefits were limited to category 1 while no significant impacts on the trend were estimated for category 2. Category 3 analysis was performed only on intervention E and showed similar impacts as for category 1. Intervention D (Therapeutic group premium policy) and J (Atorvastatin listed) were implemented concurrently and resulted in mixed results. The impacts on category 1

were generally in a deceasing direction for both level and trend but the level of benefits and the trend of services were the only variables significantly decreased in category 2. The next policy to be introduced, intervention F (Safety Net 20 days rule), was found to decrease the level and trend of services and benefits in all three categories, limited only to the concessional beneficiary. General beneficiaries were not significantly affected by this policy. For intervention G, the drug price reduction in F2 resulted in various types of impacts. Generally, the levels of both services and benefits were increased in all categories and the trends of benefits were not significantly changed. However, the trends of services were decreased in category 2 and 3 while no changes were estimated in category 1.

The listing of new statins resulted in a mixed responses. Fluvastatin listing was found to have an immediate effect in reducing the number of statin prescriptions and expenditure but the effect was short-lived with an increase of the trend in the months following the listing. In the case of the listing of Atorvastatin, the impact was primarily confined to the number of services with a decrease in trend while the levels and trends of benefits were mainly unchanged. The latest addition to the statins group, Rosuvastatin, did not make a statistically significant difference to the level or trend for the combined statins drug group. However, its listing decreased the trends of services and benefits of the all Atorvastatin drug group.

The following chapter provides further discussion of the results of the statistical analysis of the impact of cost containment reforms to the PBS on prescribing volumes and expenditure policies and compares these results to the evidence found in the systematic review (Chapter 4.0).

Table 5.20 Estimated number of services, benefits and DDDs/1000/day before and after intervention E

Intervention			E				
			Co-payment increase *1/01/2005*				
All Atorvastatin group		Term	Intercept	Pre-intervention		Changes	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	Service (n, '000)	Coef.	216.37	5.77	626.26	4.66	-33.90
		95% CI	191.66 to 241.07	5.23 to 6.31	-	2.34 to 6.99	-61.09 to -6.71
		P>t	0.000	0.000	-	0.000	0.015
	Benefits (A$, million)	Coef.	10.20	0.3556	35.45	0.4709	-2.94
		95% CI	9.26 to 11.10	0.3225 to 0.3887	-	0.1644 to 0.7773	-5.27 to -0.6163
		P>t	0.000	0.000	-	0.003	0.014
General	Service (n, '000)	Coef.	83.80	1.71	205.14	1.06	-2.70
		95% CI	73.96 to 93.65	1.49 to 1.93	-	0.64 to 1.47	-12.87 to 7.46
		P>t	0.000	0.000	-	0.000	0.600
	Benefits (A$, million)	Coef.	-	-	-	-	-
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
Concessional	Service (n, '000)	Coef.	132.56	4.06	421.12	3.03	-28.43
		95% CI	117.59 to 147.53	3.74 to 4.39	-	1.61 to 4.44	-45.14 to -11.72
		P>t	0.000	0.000	-	0.000	0.001
	Benefits (A$, million)	Coef.	6.93	0.2687	26.01	0.3200	-1.82
		95% CI	6.39 to 7.47	0.2492 to 0.2883	-	0.1864 to 0.4536	-3.07 to -0.5670
		P>t	0.000	0.000	-	0.000	0.005
Per 1000 Population	Service (n)	Coef.	11.74	0.2734	31.15	0.2007	-1.89
		95% CI	10.31 to 13.17	0.2434 to 0.3035	-	0.0862 to 0.3152	-3.29 to -0.5015
		P>t	0.000	0.000	-	0.001	0.008
	Benefits (A$)	Coef.	556.68	16.97	1,761.71	21.34	-157.03
		95% CI	512.36 to 601.00	15.43 to 18.51	-	6.43 to 36.24	-271.21 to -42.86
		P>t	0.000	0.000	-	0.005	0.007
	DDD	Coef.	8.09	0.4571	40.54	0.2367	1.30
		95% CI	6.91 to 9.27	0.4163 to 0.4978	-	0.1533 to 0.3201	-0.9942 to 3.59
		P>t	0.000	0.000	-	0.000	0.265

Table 5.21 Estimated number of services, benefits and DDDs/1000/day before and after intervention F

Intervention			F				
			Safety Net 20 days *1/01/2006*				
All Atorvastatin group		Term	Intercept	Pre-intervention		Changes	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	Service (n, '000)	Coef.	592.36	10.44	717.60	-0.3440	-42.20
		95% CI	-	-	-	-5.82 to 5.13	-78.52 to -5.88
		P>t	-	-	-	0.901	0.023
	Benefits (A$, million)	Coef.	32.51	0.8265	42.42	-0.2584	-3.41
		95% CI	-	-	-	-0.8259 to 0.3090	-6.54 to -0.2876
		P>t	-	-	-	0.370	0.033
General	Service (n, '000)	Coef.	-	-	-	-	-
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
	Benefits (A$, million)	Coef.	-	-	-	-	-
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-
Concessional	Service (n, '000)	Coef.	392.69	7.09	477.75	-0.2856	-33.71
		95% CI	-	-	-	-0.3777 to 0.3206	-57.21 to -10.20
		P>t	-	-	-	0.872	0.005
	Benefits (A$, million)	Coef.	24.19	0.5888	31.26	-0.1508	-2.46
		95% CI	-	-	-	-0.4326 to 0.1309	-4.23 to -0.6930
		P>t	-	-	-	0.292	0.007
Per 1000 Population	Service (n)	Coef.	29.25	0.4741	34.94	-0.0285	-2.07
		95% CI	-	-	-	-0.2949 to 0.2379	-3.84 to -0.3076
		P>t	-	-	-	0.833	0.022
	Benefits (A$)	Coef.	1604.68	38.31	2064.40	-13.32	-166.97
		95% CI	-	-	-	-40.91 to 14.26	-318.72 to -15.22
		P>t	-	-	-	0.341	0.031
	DDD	Coef.	-	-	-	-	-
		95% CI	-	-	-	-	-
		P>t	-	-	-	-	-

Table 5.22 Estimated number of services, benefits and DDDs/1000/day before and after intervention K

Intervention			K				
			Rosuvastatin listed 1/12/2006				
All Atorvastatin group		Term	Intercept	Pre-intervention		Changes	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	Service (n, '000)	Coef.	675.40	10.09	786.42	-7.82	-5.16
		95% CI	-	-	-	-12.79 to -2.85	-34.07 to 23.75
		P>t	-	-	-	0.002	0.725
	Benefits (A$, million)	Coef.	39.01	0.5680	45.26	-0.5166	-0.74
		95% CI	-	-	-	-0.9796 to -0.0535	-3.25 to 1.77
		P>t	-	-	-	0.029	0.560
General	Service (n, '000)	Coef.	202.44	2.77	266.03	-2.01	0.7220
		95% CI	-	-	-	-2.68 to -1.34	-8.42 to 9.87
		P>t	-	-	-	0.000	0.876
	Benefits (A$, million)	Coef.	3.24	0.0865	11.37	-0.1123	0.1533
		95% CI	2.99 to 3.49	0.0821 to 0.09099		-0.1806 to -0.0441	-0.7624 to 1.07
		P>t	0.0000	0.0000		0.001	0.741
Concessional	Service (n, '000)	Coef.	444.05	6.80	518.88	-5.29	-4.37
		95% CI	-	-	-	-8.53 to -2.04	-22.72 to 13.97
		P>t	-	-	-	0.002	0.638
	Benefits (A$, million)	Coef.	28.79	0.4380	33.61	-0.3607	-0.6461
		95% CI	-	-	-	-0.6166 to -0.1048	-1.99 to 0.6966
		P>t	-	-	-	0.006	0.343
Per 1000 Population	Service (n)	Coef.	32.87	0.4456	37.77	-0.3914	-0.2323
		95% CI	-	-	-	-0.6319 to -0.1508	-1.63 to 1.17
		P>t	-	-	-	0.002	0.744
	Benefits (A$)	Coef.	1,897.42	24.99	2,172.29	-25.54	-34.82
		95% CI	-	-	-	-47.93 to -3.16	-155.86 to 86.23
		P>t	-	-	-	0.026	0.571
	DDD	Coef.	41.84	0.6938	57.80	-0.5070	0.4655
		95% CI	-	-	-	-0.6413 to -0.3727	-1.39 to 2.32
		P>t	-	-	-	0.000	0.621

Table 5.23 Estimated number of services, benefits and DDDs/1000/day before and after intervention G

Intervention			G				
			F2 price cut *1/08/2008*				
All Atorvastatin group		Term	Intercept	Pre-intervention		Changes	
				Trend	Level	Trend	Level
All Beneficiaries (General + Concessional)	Service (n, '000)	Coef.	781.26	2.27	826.69	-3.88	58.34
		95% CI	-	-	-	-6.61 to -1.14	16.52 to 100.15
		P>t	-	-	-	0.006	0.007
	Benefits (A$, million)	Coef.	44.52	0.0515	45.55	-0.1085	4.94
		95% CI	-	-	-	-0.2931 to 0.0761	2.51 to 7.36
		P>t	-	-	-	0.247	0.000
General	Service (n, '000)	Coef.	266.75	0.7550	281.85	-1.83	16.13
		95% CI	-	-	-	-2.73 to -0.9218	4.38 to 27.89
		P>t	-	-	-	0.000	0.007
	Benefits (A$, million)	Coef.	3.39	-0.0258	11.01	-0.0239	1.25
		95% CI	-	-	-	-0.0938 to 0.0461	0.4776 to 2.03
		P>t	-	-	-	0.501	0.002
Concessional	Service (n, '000)	Coef.	514.51	1.52	544.84	-2.05	42.21
		95% CI	-	-	-	-3.88 to -0.2148	11.88 to 72.54
		P>t	-	-	-	0.029	0.007
	Benefits (A$, million)	Coef.	32.96	0.0772	34.51	-0.0846	3.69
		95% CI	-	-	-	-0.2083 to 0.0391	1.65 to 5.72
		P>t	-	-	-	0.179	0.000
Per 1000 Population	Service (n)	Coef.	37.54	0.0543	38.63	-0.1688	2.49
		95% CI	-	-	-	-0.2946 to -0.0431	0.6500 to 4.33
		P>t	-	-	-	0.009	0.008
	Benefits (A$)	Coef.	2,137.47	-0.5562	2,126.34	-4.46	218.37
		95% CI	-	-	-	-13.08 to 4.16	109.50 to 327.24
		P>t	-	-	-	0.308	0.000
	DDD	Coef.	58.26	0.1867	62.00	-0.3062	4.83
		95% CI	-	-	-	-0.5179 to -0.0945	1.51 to 8.14
		P>t	-	-	-	0.005	0.005

Chapter 6.0 Discussion

6.1 Introduction

The global pharmaceutical industry has been growing rapidly along with the increase in demand for pharmaceuticals. Global pharmaceutical expenditure for 2014 is expected to reach US$1 trillion for the first time and is expected to continue to rise further (IMS Institute for Healthcare Informatics, 2013a). The Increase in demand for pharmaceuticals is mainly attributed to the ageing population, advances in health technology and rising patient expectations. Globally, there were approximately 810 million persons aged 60 years or over in 2012, representing one out of every nine persons. This age group is projected to increase to one out of every five persons by 2050 (Department of Economic and Social Affairs, 2012). Aged people are generally more susceptible to chronic diseases and utilize more drugs for treatment. Over the last decade, the discovery of newer drugs had improved the population's health status but new drugs usually cost more than their predecessors. Drugs such as AstraZeneca's Crestor (rosuvastatin calcium) and Nexium (esomeprazole magnesium), Pfizer's Lipitor (atorvastatin calcium), GlaxoSmithKline's Seretide (fluticasone/salmeterol), AbbVie's Humira (adalimumab) and Bristol-Myers Squibb and Sanofi-Aventis's Plavix (clopidogrel) are labelled 'blockbuster' drugs and have achieved sales of over US$1 billion a year (IMS Institute for Healthcare Informatics, 2012b, 2013b, 2014). A study by de Wolf et al. (2005) found that the introduction of new drugs contributed approximately two per cent of the annual growth of pharmaceutical expenditure in the Netherlands while the growth and ageing of the population increased pharmaceutical expenditure by 1.3 per cent. Other studies have also found that the introduction of new drugs increases pharmaceutical expenditure not only in outpatient setting but in inpatient settings as well (Liu et al., 2012). As medical technologies advances, patients have

higher health care expectations, particularly seeking better quality drugs. Drugs are expected to produce more efficient and effective results, in addition to being safer.

In tandem with the increase in demand for pharmaceuticals, in many countries government expenditure on pharmaceutical has been increasing. Statistics from the OECD showed government expenditure on pharmaceuticals increasing by an average of 76.2% between 2001 and 2011. Countries such as Ireland, United States, Korea, Greece and Netherlands all reported strong growth in expenditure, with expenditure in 2001 doubling by 2011 (Organisation for Economic Co-operation and Development, 2013).

Over the past 20 years, the world had experienced several economic downturns, notably the Asian economic crisis in 1997, the global financial crisis of 2008 and the Euro crisis in 2010-2011. These crises have served as a trigger for governments in affected countries to implement austerity measures to improve their budget positions and keep spending under control, with pharmaceuticals expenditure one of the main areas to be cut. Pharmaceuticals expenditure is more often a target for cost reduction policies compared to spending in other health care sectors due to it being relatively easy to identify and measure (Towse, 2003).

In recent years, the European Union (EU) zone has seen many cost containment measures related to the pharmaceutical sector being implemented. Measures such as price cuts, co-payment changes, reduction of distribution margins and increased of value-added tax (VAT) rates on medicines, all of which can be introduced rather quickly, have often been used as the first option (Vogler et al., 2011). Greece, one of the most severely affected countries by the Euro crisis, introduced a new reference pricing policy with the average prices set based on the three lowest EU prices and reintroduced a positive list with strict pricing criteria for drugs eligible for reimbursement between 2010 and 2012 (Bouvy et al., 2013; Leopold, 2013). In Ireland, reference pricing was implemented in 2013 with drug prices being cut by up to 70 per cent of the original price (Department of Health,

2013e). In 2010, Portugal and Spain introduced mandatory price cuts of both generic and branded drugs. Generic drug prices were reduced by 30 per cent and branded drug prices by 6 per cent in Portugal while price reductions of 25 per cent for generic drugs and 10 to 16 per cent for branded drugs were implemented in Spain (Deloitte, 2013). Cost containment measures were not limited to the EU but Asian-Pacific and other countries followed this trend. For example, pharmaceutical price cuts were implemented in countries such as China (2011), Australia (2008), Philippines (2009 and 2010) and South Korea (2011) (IMS Consulting Group, 2012).

In Australia, several cost containment measures have been implemented including the requirement of economic evaluation (1993), re-supply limits (1994), a brand substitution policy (1994), co-payment increases (1997 and 2005), a therapeutic group premium policy (1998), the safety net 20 days rule (2006), the creation of F1 and F2 formularies (2007), premium-free dispensing (2008) and price cuts (2008 onwards). Although, numerous cost containment measures have been implemented over the past two decades, the Australian government is still concerned about the growth and sustainability of the expenditure on the PBS. Since 1991, PBS expenditure has been growing at an average rate of 10% annually although slower growth rates were observed in the last decade between 2002 and 2011 (Department of Health and Ageing, 2012). Recently, the National Commission of Audit highlighted PBS expenditure as one of the fastest growing areas of government expenditure and this is expected to continue in the medium to longer term. The Commission suggested that co-payments should be increased as well as the safety net and that a predetermined funding envelope should be established to freeze expenditure for seven years. The proposal made was to increase the co-payment for general beneficiaries by A$5.00 and the safety net from A$1,421.20 currently to A$1,613.77. For concessional beneficiaries, the suggested co-payment was A$2.00 as compared to no charges currently when the safety net threshold is reached (National Commission of Audit, 2014).

However, not all cost containment measures have been found to be successful in controlling expenditure on pharmaceuticals. Some countries have succeeded in containing these costs while others have seen expenditure on pharmaceuticals continue to increase. Moreno-Torres et al. (2011) studied 16 cost containment measures in Spain and found that only four measures were effective in containing pharmaceutical expenditure. In Norway, a study by Håkonsen et al. (2009) yielded similar result with certain measures for instance, the international reference pricing successfully in containing pharmaceutical expenditure, while in-market reference pricing along with index pricing and generic substitution showed limited effect. In contrast to Håkonsen et al's study, Lee et al. (2006) investigated six reference pricing measures in Taiwan and found that international reference pricing and in-market reference pricing were not effective in containing pharmaceutical expenditure. Instead, reference pricing based on generic grouping significantly reduced pharmaceutical expenditure. These examples illustrate that not all cost containment measures work well for all countries. Policy makers tend to implement cost containment measures from other countries without considering differences in cultures or healthcare systems. This so-called 'penguin effect' has been mainly caused by a lack of research on the effectiveness of cost containment measures (Guillén et al., 2003). The poor understanding of cost containment measures was pointed out by de Bont et al. (2007) who suggested that policy makers in Netherlands rarely used evidence from healthcare databases in their decision making, especially in regard to cost control measures and quality assurance.

Most policy makers also often overlook the fact that the demand for pharmaceuticals is different from other commodities. For example, the demand for pharmaceuticals is relatively inelastic, which implies measures to change their price and influence patients have little effect on the demand for pharmaceuticals. Also, while patients might be financially responsible for at least a portion of the cost of their purchases of pharmaceuticals, they are usually not the decision makers in determining the choice of medicines and are not aware of the availability and

characteristics of competing medicines. The choice of medicines is determined by the prescribers based on a patient's conditions, with prescribers not financially accountable for the decisions they make (Fisher, 1991; Parvis, 2002; Samuelson et al., 2010).

The implementation of pharmaceutical cost containment measures is an extremely complex process. Insurers (in most cases, governments and their agencies), introduce cost containment measures with the objective to efficiently use the limited resources available and maximize outcomes. This, however, conflicts with the objectives of other stakeholders, especially patients and taxpayers, who generally want to have equality of access to healthcare and medicines (Drummond et al., 2003). Therefore, it is important for policy makers to take into consideration the following factors during the conception and implementation of cost containment measures (Almarsdóttir et al., 2005; Ess et al., 2003; Garrison et al., 2003).

1. Interests of the various stakeholder including insurers, pharmaceutical manufacturers, prescribers and pharmacies, and residents with a role both as patients and taxpayers need to be considered to avoid any one group being unduly disadvantaged. This requires policy makers having to balance the interest of stakeholders, for instance ensuring the profitability of pharmaceutical industry in order to boost the development of new drugs at the same time as containing pharmaceutical expenditure.

2. Measures should be comprehensive and include a broad perspective, rather than being limited only to conventional measures such as utilisation and pricing constraints, and should include measures such as altering patient's and prescriber's behaviour to ensure effective pharmaceutical outcomes in the long run.

3. All measures suggested should be evidence-based and supported with research on their nature and impact.

4. The measures should be proactive rather than reactive. Cost containment should be an ongoing process at all times instead of a 'quick fix' every time a crisis occurs. Very often, the introduction of spontaneous measures lack consultation and input from interest groups and produce knee-jerk reactions that fall short of their aims.

5. The evaluation of cost containment measures should be made through using both quantitative and qualitative research methodology. This broad evaluation is more likely to be able to draw better conclusions on the full impact of measures and avoid situations where, for example, reducing expenditure on one area (pharmaceuticals) may lead to higher expenditure on other areas such as hospital care.

6.2 Cost Containment Measures

This section presents an overview of the statistical analysis of the PBS cost containment reforms and discusses these in the context of the finding of the systematic review presented in Chapter 4.0. To facilitate discussion in this section, a summary of the results obtained from the Chapter 5.0 are presented in Table 6.1 to Table 6.3.

6.2.1 Patient cost-sharing

The two increases in patient co-payment implemented in January 1997 (intervention C) and January 2005 (intervention E) resulted in an immediate drop in the level of services and benefits but the intervention's effects were reversed in the months post intervention where the trend continued to increase. The immediate decrease in the level in January 1997 and 2005 concurred with the expected impact suggested in Chapter 5. Patients tend to accumulate medications once the safety net threshold is achieved to take advantage of low co-payments (general

beneficiaries) and no charges (concessional beneficiaries) for medicines before the new co-payment rates imposed in January the following year. The news of co-payment increases was announced months before its implementation and therefore hoarding of medications by patients in anticipation of co-payment increased may occur. However, once the reserve of their medications was used up, patients gradually returned to their prescriber and pharmacist to refill their medications. In Australia, McManus et al. (1996) studied the increase in the general beneficiary co-payment and found similar results. The numbers of prescriptions dispensed were decreased immediately following the implementation of the intervention but later reverted to the pre intervention trend in the following months.

Comparing between both co-payment increases, intervention E (co-payment increase by 24%) was found to be more effective in containing services and benefits than intervention C (co-payment increase between 15.0 to 18.5%). The rate of services and benefits per 1000 population continued to increase at a higher rate after the implementation of intervention C but no significant changes in trend were observed after the implementation of intervention E. This may be due to the greater magnitude of the patient's co-payment increase in intervention E (25.0%) compared to intervention C (15.0 to 18.5%). Given the relatively low price elasticity of demand for pharmaceuticals (Landsman et al., 2005), the increase in co-payments in intervention C may have been too low to significantly decrease utilisation and expenditure. Some studies have suggested that a 10% increase in price will lead to a decrease in drug use of 1% to 4% (Leibowitz et al., 1985; Smith et al., 1992). However, the price elasticity may vary among difference drugs (Goldman et al., 2004; Johnson et al., 1997).

In this study, both general beneficiaries and concessional beneficiaries reacted to intervention C in a similar way with trends of services and benefits increasing at a higher rate compared to the pre-intervention period. However, the

implementation of intervention E resulted in a difference reaction between general and concessional beneficiaries. The trend of services and benefits for concessional beneficiaries continued to increase at a higher rate while the increase in the trend of services for general beneficiaries was reduced to a slower pace while the trend in benefits remain unchanged. This finding was reinforced in the category 2 and 3 analyses where the increasing trend of services and benefits were either slowed down or remain unchanged for general beneficiaries. It is often assumed that concessional beneficiaries (the elderly and/or the poor) are likely to be most sensitive to cost-sharing changes and negatively impacted by these changes. This assumption was supported by the studies by Hynd et al. (2008, 2009) that found co-payment increases had more profound effects in decreasing the medicine utilisation of concessional beneficiaries compared to general beneficiaries. Studies from Canada (Blais et al., 2001; Blais et al., 2003) had similar findings to the studies by Hynd et al. with individuals receiving welfare and paying a lower co-payment decreasing their usage of inhaled corticosteroids while older individuals (paying a higher co-payment compared to the welfare group) not significantly affected by the co-payment increases. Contrary to these studies, Johnson et al. (1978) found no differences in drugs utilisations after a co-payment increase between low-income and poor patients compared with the rest of the population. A systematic review by Goldman (2007) concluded that an increase in cost-sharing reduced the use of prescription drugs but the impact was not necessarily greater on low-income patients.

Besides changes to services and benefits, an interesting change was found in the category 2 analysis of overall statins DDDs per 1000 population. The trend in services and benefits was unaffected by the implementation of both interventions but the DDDs per 1000 population trends were increased at a higher rate post intervention. This finding suggested that patients taking statins may have resorted to pill spitting to alleviate the increased cost of the co-payment. Many statins are available at increased dosage at a fractional cost of the lower dosage. By splitting

higher doses medicines, patients can save as much as half of the drugs cost (Alexander et al., 2004; Cohen et al., 2000; Stafford et al., 2002). For example, in January 2005, Simvastatin tablets of 5mg and 10mg strength cost A$30.11 and A$39.82 respectively. Both strengths were priced above the co-payment of A$28.60 for general beneficiaries and A$4.60 for concessional beneficiaries. By splitting the 10 mg tablet into half, patients taking 5mg were able to reduce the cost by 50%, paying only A$14.60 (general beneficiaries) and A$4.30 (concessional beneficiaries).

In conclusion, cost-sharing increases were ineffective in reducing drugs utilisation and expenditure. This finding is consistent with the finding from Chapter 4.0 systematic review, where the impact of cost-sharing were limited to reducing drug cost but did not necessarily reduce drug utilisation and drug expenditure. In addition, the implementation of cost-sharing may have changed patient drug consumption behaviour by encouraging pill splitting that might cause unintended effect in health. Most cost-sharing studies reviewed in Chapter 4.0 reported an increase in the use of other healthcare services such as hospital care and nursing home admissions which offset any or some savings from the cost-sharing measures. Therefore, the overall saving to the health care system from cost-sharing policy remains uncertain.

Table 6.1 Estimated impact of cost containment measures for all PBS medicines

Intervention		Category 1 (All PBS Medicines)															
		All Beneficiaries (General + Concessional)				General				Concessional				Per 1000 Population			
		Service		Benefits		Service		Benefits		Service		Benefits		Service		Benefits	
		Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend
A	Economic Evaluation	<->	↓	<->	<->	<->	<->	<->	<->	↓	↓	<->	<->	<->	↓	<->	<->
C	Co-payment Increase Between 15.0-18.5%	↓	↑	↓	↑	↓	↑	↓	↑	↓	↑	↓	↑	↓	↑	↓	↑
D	Therapeutic Group Premium Policy	↓	↓	↓	↓	↓	<->	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
E	Co-payment Increase 24%	↓	↑	↓	<->	↓	↓	↓	<->	↓	↑	↓	↑	↓	<->	↓	<->
F	Safety Net 20 Day Rule	↓	↓	↓	↓	<->	<->	↓	<->	↓	↓	↓	↓	↓	↓	↓	↓
G	F2—2%, 12.5%, 25% price reductions	↑	<->	↑	<->	↑	<->	↑	↓	↑	<->	↑	<->	↑	<->	↑	<->

Table 6.2 Estimated impact of cost containment measures for all statins

Intervention		Category 2 (All Statins)																	
		All Beneficiaries (General + Concessional)				General				Concessional				Per 1000 Population					
		Service		Benefits		Service		Benefits		Service		Benefits		Service		Benefits		DDD	
		Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend
B	Re-Supply Limits	<->	↑	<->	↑	<->	↑	<->	↑	<->	↑	<->	↑	<->	↑	<->	↑	<->	↑
C	Co-payment Increase Between 15.0-18.5%	↓	<->	↓	<->	↓	<->	↓	↓	↓	<->	↓	<->	↓	<->	↓	<->	↓	↑
D	Therapeutic Group Premium Policy	<->	↓	↓	<->	<->	↓	<->	<->	<->	↓	↓	<->	<->	↓	<->	<->	↓	↑
E	Co-payment Increase 24%	↓	<->	↓	<->	<->	<->	↓	↓	↓	<->	↓	<->	↓	<->	↓	<->	<->	↑
F	Safety Net 20 Day Rule	↓	↓	<->	↓	<->	<->	<->	<->	↓	↓	↓	<->	↓	↓	<->	↓	<->	↓
G	F2—2%, 12.5%, 25% price reductions	↑	↓	↑	<->	<->	↓	↑	<->	↑	<->	↑	<->	↑	↓	↑	<->	↑	↓

Table 6.3 Estimated impact of cost containment measures for all Atorvastatin

Intervention		Category 3 (All Atorvastatin)																	
		All Beneficiaries (General + Concessional)				General				Concessional				Per 1000 Population					
		Service		Benefits		Service		Benefits		Service		Benefits		Service		Benefits		DDD	
		Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend
E	Co-payment Increase 24%	↓	↑	↓	↑	<->	↑	<->	<->	↓	↑	↓	↑	↓	↑	↓	↑	<->	↑
F	Safety Net 20 Day Rule	↓	<->	↓	<->	<->	<->	<->	<->	↓	<->	↓	<->	↓	<->	↓	<->	<->	<->
G	F2—2%, 12.5%, 25% price reductions	↑	↓	↑	<->	↑	↓	↑	<->	↑	↓	↑	<->	↑	↓	↑	<->	↑	↓

6.2.2 Re-supply limits and safety net 20 days rule

This study results showed no significant impact of the re-supply limits (intervention B) measure on services and benefits of the all ATC main drug groups. The ineffectiveness of this measure was to be expected as the Australian government had to introduce an additional measure, the safety net 20 days rule in January 2006, to improve the effectiveness of the re-supply limit policy (Department of Health and Ageing, 2005). Increasing the duration of the next allowable resupply and allowing the cost to continue to contribute to the safety net caused the re-supply limits policy to be misused and fail to contain services and benefits. Patients took advantage of the safety net to get multiple prescriptions at a reduced rate once the safety net threshold was reached, particularly towards the end of the year. The abuse of the safety net by patients to hoard medication was pointed out by the Australian Treasurer during the budget speech for 2005-06 (Costello, 2005). The accumulated medicines were for use in the following year when the safety net thresholds were reset at the beginning of the year and higher co-payments were required to purchase medicines. Donnelly et al. (2000) also found no significant changes to the monthly trend in the number of prescriptions dispensed in subsequent months following the implementation of the re-supply limits measure. No comparisons can be made internationally as similar measures have not been introduced.

Generally, the safety net 20 days rule was the only measure that displayed outcomes that matched with the expected impact, where reductions in both the level and trend for all beneficiaries were observed. However, when both beneficiaries were analysed independently, the reductions were only noticeable for the concessional beneficiaries while no significant trend changes were observed for general beneficiaries. This finding suggests that concessional beneficiaries were affected by this policy change and more likely to have taken advantage of the safety net to accumulate medicines. Concessional beneficiaries, mainly comprised pensioners and elderly are likely to be more susceptible to diseases, especially

chronic diseases, which generally lead to greater use of medicines and require longer duration of treatment (Department of Health and Ageing et al., 2013). This may explain the success of the safety net 20 days rule in reducing both the level and trend of services and benefits.

6.2.3 Therapeutic group premium policy

The therapeutic group premium is a type of reference pricing. Introduced in February 1998, the initial implementation involved four therapeutic groups, ACE inhibitors, the calcium channel blockers, the HMG CoA Reductase inhibitors and the H2 receptor antagonists. By grouping those drugs into therapeutic sub-groups, the government subsidises drugs to the level of the lowest priced drug in the subgroup. This measure was expected to reduce the benefits paid by the government, but services were not expected to be significantly affected as the number of drugs listed in the PBS remains unchanged and patients would not have any reasons to reduce drugs usage. The results from the category 1 analysis showed a deceasing direction for both level and trend of services and benefits. The unexpected reduction of services raises a question about the impact of the policy on patient's medication compliance. To mitigate the additional cost, patients may opt to switch to cheaper medicines that do not attract a premium or discontinue the medicines altogether. Patients forced to switch to medicines may be exposed to a higher risk of health detriment due to different drug response to genetic and environmental variability. However, the observed reduction in services may be due to limitation of the data that failed to capture prescriptions costing below the co-payment level. By grouping drugs into sub-groups, some drugs prices may fall below the co-payment levels and have not been captured in the PBS data, thereby artificially reducing the utilization. The implementation of this measure also coincided with the listing of Atorvastatin in the PBS. Therefore, the impact of this intervention cannot be solely attributed to the therapeutic group premium due to other confounding factors.

The impacts of reference pricing have been subjected to considerable debate. Several studies on reference pricing such as Schneeweiss et al. (2002) and Schneeweiss et al. (2003) reported the switching of drugs from medicines requiring a co-payment to medicines that were fully subsidised. Schneeweiss et al. (2003) found reduction in overall utilisation of drugs that were subjected to reference pricing measure as well as reducing drugs cost. In contrast, Hazlet et al. (2002), Huang et al. (2012) and Hsiao et al. (2010) concluded that referencing pricing had no significant effect on drugs utilisation while the study by Moreno-Torres et al. (2011) indicated an increase in the number of prescriptions filled along with a reduction in drugs cost and expenditure.

The findings of this study seem to be consistent with three systematic reviews included in Chapter 4 which found a reduction in expenditure following the implementation of reference pricing. Aaserud et al. (2006) and Morgan et al. (2009) concluded reference pricing induced patients to shift to less expensive drugs and reduced overall drug expenditures. However, Galizzi et al. (2011) and Aaserud et al. (2006) suggested that savings in drug expenditures were more significant and consistent during the first six to 12 months following implementation of reference pricing.

In the category 2 analysis, no significant changes were observed in the trend in benefits. Due to the new listing of Atorvastatin, it is likely that prescribers may have switched their patients to Atorvastatin, offsetting any saving from the implementation of the therapeutic group premium. Before the listing of Atorvastatin on the PBS, much publicity had been given to prescribers demonstrating that Atorvastatin was better in controlling patient's lipid profile compared to other available statins (Dart et al., 1997; Insull et al., 2001; Marais et al., 1997; Wolffenbuttel et al., 1998; Yee et al., 1998). Atorvastatin was widely prescribed when it was made available on the PBS in February 1998. Medicare data showed 150,000 prescriptions were filled in the first month costing A$8 million. A

year later, the number of prescriptions doubled to 310,000 prescriptions costing A$16.7 million. By June 1999, the total cost of Atorvastatin has become the third highest cost for government, behind Omeprazole and Simvastatin (Pharmaceutical Benefits Pricing Authority, 1999).

In summary, the introduction of the therapeutic group premium appears to have led to a reduction in services and benefits. However, an unanswered question remains as to the impact of the policy on the health of patients. By bringing together a therapeutically similar but chemically different drugs in a group and attaching a single reference price to the group, some patients are likely to be treated with a drug that may not perfectly suited to them but were selected because of their lower price.

6.2.4 Price cuts

The results of this study showed an increase in the levels of services and benefits across all categories immediately after the implementation of the price cuts. However, the increases were short lived with the trends of services and benefits returning to the pre-intervention trend in the following months. The initial increase in the level can be interpreted as a temporary 'knee-jerk' reaction to the price cuts that may due to patients seeking treatment that persisted before the price cuts and prescribers prescribing more costly medication that were previously unaffordable (Lee et al., 2012). This phenomenon will offset any long-term saving from price cuts as the increase in utilisation will directly increase costs to government. Therefore, in order for price control mechanisms to be effective, they need to be supplemented with volume controls to constrain overall spending such as the safety net 20 days rule (Maynard et al., 2003).

However, a closer examination of the trend in benefits in different beneficiaries showed a reduction in the trend for general beneficiaries while no significant changes were observed for concessional beneficiaries. This suggests that

general beneficiaries may have switched from more expensive medicines usually priced above the co-payment to cheaper medicines priced below the co-payment. However, concessional beneficiaries were less likely to switch medicines as the co-payment paid by them were minimal and the price differences were unlikely to have any impact on their medicines choices. In a previous study, Lee et al. (2012) reported that price cut measures in Korea did not have any impacts on drugs utilisation or expenditure while Moreno-Torres et al. (2011) found limited success of price cut measures in containing drug cost and pharmaceutical expenditure. However, Usher et al. (2012) study concluded that price cuts were effective in reducing the cost of drugs and overall expenditures. The study, however, did not investigate drug utilisation as one of the outcome variables and therefore the impacts on drug utilisation were unknown.

Of interest was the decrease in trend observed in services of the all statins drugs and Atorvastatin following the implementation of price cuts in the category 2 and category 3 analyses. Compared to the no changes in the trend for benefits in both categories, this finding suggests that the implementation of price cuts encouraged statins switching by patients who used statins that were priced above co-payment, particularly Atorvastatin and Rosuvastatin, with the switching to cheaper statin drugs. During the August 2008 price cuts, only the prices of two statin groups, namely Pravastatin and Simvastatin were cut, with Fluvastatin, Atorvastatin and Rosuvastatin not subjected to price cuts. Pravastatin used to cost between A$25.24 (10mg) and A$79.52 (80mg) while Simvastatin cost between A$23.03 (5mg) and A$76.54 (80mg), depending on the strength of the medicine. After the implementation of the price cuts, Pravastatin prices were reduced to between A$21.23 (10mg) and A$61.28 (80mg) while the price of Simvastatin now was between A$19.49 (5mg) and A$59.04 (80mg) (Department of Health and Ageing, 2008a, 2008b). The patient's co-payment for the year 2008 was A$31.30 for general beneficiaries while concessional beneficiaries paid A$5.00. Statins that were priced below the patient's co-payment now required less payment while co-

payment for statins priced above the co-payment remained unchanged. Patients taking statins priced above the co-payment may have switched to those priced below the co-payment to reduce their cost of medicines.

In conclusion, price cuts were ineffective in containing the volume of and expenditure on pharmaceuticals. The saving to government was offset by the short term increase in utilisation and expenditure. The ineffectiveness of price cuts may also be due to the limited coverage of this measure that only involved medicines listed on F2 which comprises generic medicines.

6.2.5 Economic evaluation requirement

The implementation of the economic evaluation requirement in January 1993 resulted in a reduction in the trend in services while other outcomes remained unchanged. The economic evaluation requirement policy was introduced as part of the requirement for drugs to be listed on the PBS. With the additional requirement, the listing of new and more expensive drugs in the PBS may have been delayed and therefore reduced the trend of services in the long-term (Harris, 1994). No immediate impacts were predicted for this measure as the number of medicines and prices remained unchanged. In addition to the reduction of the trend in services, the trend in benefits was expected to decrease as more cost-effective medicines were listed. However, no changes to benefits were observed in this study. The economic evaluation requirement policy does not focus solely on drugs being listed in the PBS based on cost-minimisation analysis but also allows new drugs to be listed if they are therapeutically superior to the main comparator and of acceptable cost-effectiveness. Thus, drugs approved for listing are not necessarily cheaper than the comparator already listed. The main purpose of requiring an economic evaluation prior to listing was to achieve efficiency or value for money rather than being a cost containment measure. Birkett et al. (2001) concluded that

in countries that required economic evaluation as part of the listing process, the government drug budget has been increasing by 10 percent annually.

6.3 New Listing of HMG-CoA Reductase Inhibitor Drug

This section presents an overview of the statistical analysis of the new listing of HMG-CoA Reductase Inhibitor Drug. To facilitate discussion in this section, a summary of the results obtained from the Chapter 4.0 are presented in Table 6.4 to Table 6.5.

Generally, the listing of new statins (Pravastatin, Fluvastatin, Atorvastatin and Rosuvastatin) on the PBS resulted in non-significant changes in the services and benefits in the category 2 analysis with the exception of Fluvastatin. Listed on February 1996, the number of prescriptions of statins and expenditures were reduced before the effect was reversed with an increase in trend in the months following the listing. The unexpected increase of statins utilisation and expenditure following the listing of Fluvastatin may be attributable to the increase in prescribing by prescribers who were initially reluctant to prescribe statins due to the lack of sufficient evidence in improving the survival rate in patients with high blood cholesterol levels (Gopinath, 1996). As more epidemiological studies became available that showed the benefits of statins in reducing the risk of heart attack in patients with coronary disease who have average cholesterol levels (Sacks et al., 1996; Shepherd et al., 1995), prescribers were more convinced of the effectiveness of statins and thus increased the utilisation of statins.

Collectively as a group, the findings showed that the expenditure on statins was not significantly affected by the new listing of Atorvastatin and Rosuvastatin. However, it was predicted before the analysis that total benefits paid for statins would increase following the listing due to the switching of newer and more expensive statins. As discussed in section 6.2.3, the listing of Atorvastatin coincided with the introduction of the therapeutic group premium policy. The therapeutic

group premium policy was found to decrease the volume of statins dispensed in the months following the policy implementation but no impact was observed in expenditure on statins. This finding can be explained in part by the switching of statins by prescriber and patients. Similarly, the listing of Rosuvastatin resulted in patients switching to the new statin and this observation is consistent with the reduction in the trends of services and benefits that were observed in the category 3 analysis. The switch from Atorvastatin to Rosuvastatin decreased the trend of Atorvastatin but did not change overall utilisation and expenditure on statins. Numerous studies had reported better control of lipid and cholesterol with Rosuvastatin as compared to Atorvastatin and others statins, which encouraged prescribers to switch to Rosuvastatin (Ballantyne et al., 2006; Clearfield et al., 2006; Fonseca et al., 2005; Fox et al., 2007; Schuster et al., 2004; Strandberg et al., 2004)

In summary, the listing of new statins encouraged prescribers and patients to switch to newer and more expensive drug.

Table 6.4 Estimated impact of statins listing for all statins

Intervention		Category 2 (All Statins)																	
		All Beneficiaries (General + Concessional)				General				Concessional				Per 1000 Population					
		Service		Benefits		Service		Benefits		Service		Benefits		Service		Benefits		DDD	
		Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend
I	Fluvastatin Listed	↓	↑	↓	↑	↓	↑	↓	<->	↓	↑	↓	↑	↓	↑	↓	↑	↓	↑
J	Atorvastatin Listed	<->	↓	↓	<->	<->	↓	<->	<->	<->	↓	↓	<->	<->	↓	<->	<->	↓	↑
K	Rosuvastatin Listed	<->	<->	<->	<->	<->	<->	<->	<->	<->	<->	<->	↓	<->	<->	<->	<->	<->	<->

Table 6.5 Estimated impact of statins listing for all Atorvastatin

Intervention		Category 3 (All Atorvastatin)																	
		All Beneficiaries (General + Concessional)				General				Concessional				Per 1000 Population					
		Service		Benefits		Service		Benefits		Service		Benefits		Service		Benefits		DDD	
		Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend	Level	Trend
K	Rosuvastatin Listed	<->	↓	<->	↓	<->	↓	<->	↓	<->	↓	<->	↓	<->	↓	<->	↓	<->	↓

6.4 Limitation and Future Research

There are a number of limitations in this study. Firstly, there were limited numbers of Australian studies investigating the impact of cost containment measures. Only four studies (Donnelly et al., 2000; Hynd et al., 2008, 2009; McManus et al., 1996) were found and therefore a comprehensive comparison with other studies conducted in Australia was not possible. However, comparison with cost containment measures in other countries may not provide conclusive findings due to the differences in health systems and populations.

Secondly, findings in this study were based on the changes in post-intervention levels and trends relative to pre-intervention levels and trends. The magnitude of these changes in services and benefits cannot necessarily be attributed to the cost containment policies as other external factors might have impacted on the results.

It is recommended that further research be undertaken using a more comprehensive database such as the Drug Utilization Sub-Committee (DUSC) database to better reflect the true drugs utilisation. In addition to the PBS prescription counts and expenditures, the DUSC database provides estimated prescription counts of drugs in the non-subsidised categories, mainly prescriptions that were under the co-payment and private prescriptions from the Pharmacy Guild Survey (Edmonds et al., 1993). The Pharmacy Guild of Australia conducts monthly random survey of approximately 300 pharmacies to collect dispensing information. However, it is important to note that the Pharmacy Guild Survey was terminated beginning 1 April 2012 and this responsibility was taken over by the Department of Human Services (Australian Institute of Health and Welfare, 2014).

It would be also interesting to assess the impacts of cost containment measures using different types of drug groups such as the proton pump inhibitors, antipsychotics and nonsteroidal anti-inflammatory drugs (NSAIDs). Patients taking different groups of medication react differently to cost containment measures.

Essential drugs such as lipid modifying agents and antipsychotics might be more resistant to cost containment measures while discretionary drugs such as proton pump inhibitors and NSAIDs might be more sensitive to cost containment measures. By knowing how cost containment measures impact on services and cost for individual drug groups, policy makers will be able to customise cost containment measure to effectively contain volume and expenditure.

Finally, the focus of this study has been on the impact of cost containment policies on prescription volumes and expenditure on pharmaceuticals. The study has not covered the impact of cost containment policies on adherence with medications, health outcomes, health related quality of life or the economic impact. While outside the scope of this study, these are important issues that can be addressed in future research. By considering these impacts also, a more complete understanding will be obtained of the full impact of cost containment measures that have been imposed on the PBS (Kozma et al., 1993).

6.5 Conclusion

This aim of the study was to determine the impact of cost containment policies on prescription volumes and expenditure on pharmaceuticals listed in the PBS. The impact of seven cost containment policies and four new listing dates of statins were investigated. Generally, the study found that not all cost containment measures were effective in containing costs. Among those measures, the safety net 20 days rule was found to be the most effective in reducing drugs utilisation and expenditure with the overall trend in services and benefits reduced after its implementation in addition to initial decrease in level. The therapeutic group premium policy was effective in containing utilisation and cost but its effectiveness may be limited to only a short time of period. Furthermore, during the initial implementation, the therapeutic group premium policy was only imposed on four therapeutic groups, namely the ACE inhibitors, the calcium channel blockers, the

HMG CoA Reductase inhibitors and the H2RAs. Due to the limited number of drugs covered by the therapeutic group premium policy, the impact of this policy on prescription volumes and expenditure may not be long lasting. The number of drugs covered by this policy was apparently reduced to only three drugs (telmisartan, olmesartan medoxomil and eprosartan) in the PBS as of May 2014.

This study has found that different types of cost containment measures impacted differently on different groups of patients. Cost sharing measures such as co-payment increases were found to impact general beneficiaries more than concessional beneficiaries. General beneficiaries were more sensitive to changes in cost as they were subjected to higher co-payment compared to concessional beneficiaries and may be negatively impacted by these changes. On the other hand, the safety net 20 days rule impacted more on concessional beneficiaries compared to general beneficiaries.

This study also found that patient's behaviour in regards to drugs utilisations was influenced by the cost containment measures and listing of new drugs. The cost borne by patients played a major role in shaping patient's behaviour. Patients tended to prefer medicines that required lower payment when co-payments increased or medicines price cuts occurred. However, when a new medicine was listed, patients were more likely to switch to the new drug. For example, in the case of switching from Atorvastatin to Rosuvastatin, switching was more likely to occur as both drugs were priced above the co-payment for general and concessional beneficiaries and attracted the same co-payment.

This study also found that patients, especially the concessional beneficiaries tend to misuse the safety net by hoarding medication particularly towards the end of the year. However, with the implementation of the safety net 20 days rule, following the failure of the re-supply limits measure, the likelihood of patients misusing the safety net were reduced and resulted in saving in pharmaceutical expenditure.

In summary, the findings of this study have a number of important implications for policy makers. The effectiveness of cost containment measures varies among countries due to differences in healthcare system and culture. There is no one measure that fits all countries. Therefore, policy makers must be able to modify cost containment measures to suit one country. Besides containing volume and expenditure, cost containment measures were found to alter the drugs utilisations behaviour of patients such as drugs switching and hoarding. Changes in drug consumption behaviour may result in adverse health and pose additional burden to healthcare system. Therefore, the impact of cost containment policies on patient health must be taken into consideration in addition to their effectiveness to contain volume and cost.

References

Aaserud, M., Dahlgren, A. T., Kosters, J. P., Oxman, A. D., Ramsay, C., & Sturm, H. (2006). Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. *Cochrane Database of Systematic Reviews*(2), CD005979. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16625648

Alexander, G. C., & Tseng, C.-W. (2004). Six strategies to identify and assist patients burdened by out-of-pocket prescription costs. *Cleveland Clinic Journal of Medicine, 71*(5), 433-437. Retrieved from http://www.ccjm.org/content/71/5/433.abstract. doi:10.3949/ccjm.71.5.433

Almarsdottir, A. B., Morgall, J. M., & Grimsson, A. (2000). Cost containment of pharmaceutical use in Iceland: the impact of liberalization and user charges. *Journal of Health Services Research & Policy, 5*(2), 109-113. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10947545

Almarsdóttir, A. B. A. B., & Traulsen, J. M. J. M. (2005). Cost-containment as part of pharmaceutical policy. *Pharmacy world & science : PWS, 27*(3), 144-148. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16096878

Andersson, K., Bergstrom, G., Petzold, M., & Carlsten, A. (2007). Impact of a generic substitution reform on patients' and society's expenditure for pharmaceuticals. *Health Policy, 81*(2-3), 376-384. doi:10.1016/j.healthpol.2006.07.005

Andersson, K., Petzold, M. G., Sonesson, C., Lonnroth, K., & Carlsten, A. (2006). Do policy changes in the pharmaceutical reimbursement schedule affect drug expenditures? Interrupted time series analysis of cost, volume and cost per volume trends in Sweden 1986-2002. *Health Policy, 79*(2-3), 231-243. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16473436

Andersson, K., Sonesson, C., Petzold, M., Carlsten, A., & Lönnroth, K. (2005). What are the obstacles to generic substitution? An assessment of the behaviour of prescribers, patients and pharmacies during the first year of generic substitution in Sweden. *Pharmacoepidemiology and Drug Safety, 14*(5), 341-348. Retrieved from http://dx.doi.org/10.1002/pds.1055. doi:10.1002/pds.1055

Anell, A., Glenngård, A. H., & Merkur, S. (2012). *Sweden: Health system review*. W. World Health Organization.

Ansari, F., Gray, K., Nathwani, D., Phillips, G., Ogston, S., Ramsay, C., et al. (2003). Outcomes of an intervention to improve hospital antibiotic prescribing: interrupted time series with segmented regression analysis. *Journal of Antimicrobial Chemotherapy, 52*(5), 842-848. Retrieved from http://jac.oxfordjournals.org/content/52/5/842.abstract. doi:10.1093/jac/dkg459

Atella, V. (2000). Drug cost containment policies in Italy: are they really effective in the long-run?: The case of minimum reference price. *Health Policy, 50*(3), 197-218. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851099000706. doi:10.1016/s0168-8510(99)00070-6

Attorney-General's Department. (2010). *The Impact of PBS Reform*. Barton: Commonwealth of Australia. Retrieved from

http://www.health.gov.au/internet/main/publishing.nsf/Content/95DCCB478B78DBD9CA2576C500130B0A/$File/Impact%20of%20PBS%20Reform%20Report.pdf
Australian Bureau of Statistics. (2009). *National Health Survey: Summary of Results, 2007-2008 (Reissue)*. Canberra: Commonwealth of Australia. Retrieved from http://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/4364.0Main+Features12007-2008%20(Reissue)?OpenDocument
Australian Bureau of Statistics. (2012). *Australian Health Survey: First Results, 2011–12*. Canberra: Commonwealth of Australia. Retrieved from http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/4364.0.55.0012011-12?OpenDocument
Australian Bureau of Statistics. (2013). *Australian Demographic Statistics, Sep 2012*. Canberra: Commonwealth of Australia. Retrieved from http://www.ausstats.abs.gov.au/Ausstats/subscriber.nsf/0/20927044868802B5CA257B50001A9D5E/$File/31010_sep%202012.pdf
Australian Bureau of Statistics. (2014). *Profiles of Health, Australia, 2011-13*. Canberra: Commonwealth of Australia. Retrieved from http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/4338.0~2011-13~Main%20Features~Profiles%20of%20Health%20homepage~1
Australian Institute of Health and Welfare. (2010). *Health system expenditure on disease and injury in Australia, 2004–05* (Cat. no. HSE 87). Canberra: AIHW. Retrieved from http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=6442457087
Australian Institute of Health and Welfare. (2011). *Health expenditure Australia 2010-11* (Cat. no. HWE 56). Canberra: AIHW. Retrieved from http://www.aihw.gov.au/publication-detail/?id=10737420435&tab=2
Australian Institute of Health and Welfare. (2012). *Australia's health 2012*. Canberra: AIHW. Retrieved from http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737422169
Australian Institute of Health and Welfare. (2014). *Expenditure on mental health services. Mental health services in Australia* Retrieved from https://mhsa.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=12884901983
Australian National Audit Office. (1997). *The Pharmaceutical Benefits Scheme*. Canberra. Retrieved from http://www.anao.gov.au/~/media/Uploads/Documents/1997%2098_audit_report_12.pdf
Australian Taxation Office. (2014). *Private health insurance income thresholds for 2012–13 and 2013–14. Medicare levy* Retrieved from https://www.ato.gov.au/Individuals/Medicare-levy/In-detail/Medicare-levy-surcharge/Changes-to-private-health-insurance-rebate-and-Medicare-levy-surcharge/?page=14
Austvoll-Dahlgren, A., Aaserud, M., Vist, G., Ramsay, C., Oxman, A. D., Sturm, H., et al. (2008). Pharmaceutical policies: effects of cap and co-payment on rational drug use. *Cochrane Database of Systematic Reviews*(1), CD007017. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18254125
Ballantyne, C. M., Bertolami, M., Garcia, H. R. H., Nul, D., Stein, E. A., Theroux, P., et al. (2006). Achieving LDL cholesterol, non-HDL cholesterol, and apolipoprotein B target levels in high-risk patients: Measuring Effective Reductions in Cholesterol Using Rosuvastatin therapY (MERCURY) II. *American heart journal, 151*(5), 975.e971-975.e979. Retrieved from

http://www.sciencedirect.com/science/article/pii/S0002870306000160. doi:http://dx.doi.org/10.1016/j.ahj.2005.12.013

Behan, P. (2012). *Solving the Health Care Problem: How Other Nations Succeeded and Why the United States Has Not*: State University of New York Press.

Biggs, A. (2002). *The Pharmaceutical Benefits Scheme - an Overview.* Retrieved from http://www.aph.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Library/Publications_Archive/archive/pbs

Biggs, A. (2003). *Medicare - Background Brief.* Retrieved from http://www.aph.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Library/Publications_Archive/archive/medicare

Biggs, A. (2013). *Health spending: patients bearing higher costs. Parliamentary Library Blog* Retrieved from http://www.aph.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Library/FlagPost/2013/May/Health_spending_patients_bearing_higher_costs

Binbrek, A. S., Elis, A., Al-Zaibag, M., Eha, J., Keber, I., Cuevas, A. M., et al. (2006). Rosuvastatin versus atorvastatin in achieving lipid goals in patients at high risk for cardiovascular disease in clinical practice: A randomized, open-label, parallel-group, multicenter study (DISCOVERY Alpha study). *Current Therapeutic Research, 67*(1), 21-43. Retrieved from http://www.sciencedirect.com/science/article/pii/S0011393X06000178. doi:http://dx.doi.org/10.1016/j.curtheres.2006.02.005

Birkett, D. J., Mitchell, A. S., & McManus, P. (2001). A Cost-Effectiveness Approach To Drug Subsidy And Pricing In Australia. *Health Affairs, 20*(3), 104-114. Retrieved from http://content.healthaffairs.org/content/20/3/104.abstract. doi:10.1377/hlthaff.20.3.104

Bjerrum, L., Larsen, J., & Kragstrup, J. (2001). Guidelines accompanied by changes in reimbursement rules. Effects on lipid-lowering drug prescribing. *Scandinavian Journal of Primary Health Care, 19*(3), 158-162. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11697556

Blais, L., Boucher, J.-M., Couture, J., Rahme, E., & LeLorier, J. (2001). Impact of a cost-sharing drug insurance plan on drug utilization among older people. *Journal of the American Geriatrics Society, 49*(4), 410-414. Retrieved from http://dx.doi.org/10.1046/j.1532-5415.2001.49084.x. doi:10.1046/j.1532-5415.2001.49084.x

Blais, L., Couture, J., Rahme, E., & LeLorier, J. (2003). Impact of a cost sharing drug insurance plan on drug utilization among individuals receiving social assistance. *Health Policy, 64*(2), 163-172. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851002001586. doi:10.1016/s0168-8510(02)00158-6

Böhm, K., Schmid, A., Götze, R., Landwehr, C., & Rothgang, H. (2013). Five types of OECD healthcare systems: Empirical results of a deductive classification. *Health Policy, 113*(3), 258-269. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851013002285. doi:http://dx.doi.org/10.1016/j.healthpol.2013.09.003

Bouvy, J., & Vogler, S. (2013). *Pricing and Reimbursement Policies: Impacts on Innovation*.

Boxall, A. M., & Gillespie, J. (2013). *Making Medicare: The Politics of Universal Health Care in Australia*: NewSouth Publishing.

Brockwell, P. J. (1987). *Time series : theory and methods*. New York: New York : Springer-Verlag.

Brown, L., Abello, A., & Harding, A. (2006). Pharmaceuticals Benefit Scheme: Effects of the Safety Net. *Agenda, Vol. 13*(No. 3), pp. 211-224. Retrieved from http://www.canberra.edu.au/centres/natsem/publications?sq_content_src=%2BdXJsPWh0dHAlM0ElMkYlMkZ6aWJvLndpbi5jYW5iZXJyYS5lZHUuYXUlMkZuYXRzZW0lMkZpbmRleC5waHAlM0Ztb2RlJTNEcHVibGljYXRpb24lMjZwdWJsaWNhdGlvbiUzRDkyNyZhbGw9MQ%3D%3D

Brown, M., & Goldstein, J. (1986). A receptor-mediated pathway for cholesterol homeostasis. *Science, 232*(4746), 34-47. Retrieved from http://www.sciencemag.org/content/232/4746/34.short. doi:10.1126/science.3513311

Busse, R., Schreyögg, J., & Henke, K.-D. (2005). Regulation of pharmaceutical markets in Germany: improving efficiency and controlling expenditures? *The International Journal of Health Planning and Management, 20*(4), 329-349. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16335081. doi:10.1002/hpm.818

Campbell, C. A., Cooke, C. A., Weerasinghe, S. D., Sketris, I. S., McLean-Veysey, P. R., & Skedgel, C. D. (2003). Topical corticosteroid prescribing patterns following changes in drug benefit status. *The Annals of Pharmacotherapy, 37*(6), 787-793. Retrieved from http://www.theannals.com/content/37/6/787.abstract. doi:10.1345/aph.1C196

Carone, G., Schwierz, C., & Xavier, A. (2012). *Cost-containment policies in public pharmaceutical spending in the EU*. Brussels. Retrieved from http://ec.europa.eu/economy_finance/publications/economic_paper/2012/pdf/ecp_461_en.pdf

Catherine, S., Veronique, A., Brian, G., Eric Van, G., Alan, H., & Jean-Pierre, R. (2010). Ongoing Pharmaceutical Reforms in France. *Applied Health Economics and Health Policy, 8*(1), 7-24. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20038190. doi:10.2165/11313900-000000000-00000

Centre for Strategic Economic Studies. (2009). *The impact of PBS reforms on PBS expenditure and savings*. Melbourne: Victoria University. Retrieved from http://medicinesaustralia.com.au/files/2010/02/The-impact-of-PBS-reforms-on-PBS-expenditure-and-savings.pdf

Chong, C. P., March, G., Clark, A., Gilbert, A., Hassali, M. A., & Bahari, M. B. (2011). A nationwide study on generic medicines substitution practices of Australian community pharmacists and patient acceptance. *Health Policy, 99*(2), 139-148. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851010002265. doi:10.1016/j.healthpol.2010.08.002

Clearfield, M., Amerena, J., Bassand, J.-P., Garcia, H., Miller, S., Sosef, F., et al. (2006). Comparison of the efficacy and safety of rosuvastatin 10 mg and atorvastatin 20 mg in high-risk patients with hypercholesterolemia - Prospective study to evaluate the Use of Low doses of the Statins Atorvastatin and Rosuvastatin (PULSAR). *Trials, 7*(1), 35. Retrieved from http://www.trialsjournal.com/content/7/1/35

Cochrane Effective Practice and Organisation of Care Group. (2013). *EPOC Resources for review authors*. Oslo: Norwegian Knowledge Centre for the Health Services. Retrieved from http://epocoslo.cochrane.org/epoc-specific-resources-review-authors

Cohen, C. I., & Cohen, S. I. (2000). Potential cost savings from pill splitting of newer psychotropic medications. *Psychiatric Services, 51*(4), 527-529. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10737832

Committee on Drugs. (1987). Generic Prescribing, Generic Substitution, and Therapeutic Substitution. *Pediatrics, 79*(5), 835. Retrieved from http://pediatrics.aappublications.org/content/79/5/835.abstract

Costello, P. (2005). *Budget Speech 2005-06. Delivered on 10 May 2005 on the second reading of the appropriation Bill (no. 1) 2005-06.* Retrieved from http://www.budget.gov.au/2005-06/speech/html/speech.htm

Darbà, J. (2003). Pharmaceutical expenditure in Spain: evolution and cost containment measures during 1998-2001. *The European Journal of Health Economics, 4*(3), 151-157. Retrieved from http://www.jstor.org/stable/3570080

Dart, A., Jerums, G., Nicholson, G., d'Emden, M., Hamilton-Craig, I., Tallis, G., et al. (1997). A multicenter, double-blind, one-year study comparing safety and efficacy of atorvastatin versus simvastatin in patients witb hypercholesterolemia. *The American Journal of Cardiology, 80*(1), 39-44. Retrieved from http://www.sciencedirect.com/science/article/pii/S0002914997002804. doi:http://dx.doi.org/10.1016/S0002-9149(97)00280-4

de Boer, R. (2009). PBS reform - a missed opportunity? *Australian Health Review, 33*(2), 176-185. Retrieved from <Go to ISI>://WOS:000274627900002

de Bont, A., Stoevelaar, H., & Bal, R. (2007). Databases as policy instruments. About extending networks as evidence-based policy. *BMC Health Services Research, 7*(1), 200. Retrieved from http://www.biomedcentral.com/1472-6963/7/200

de Wolf, P., Brouwer, W. B. F., & Rutten, F. F. H. (2005). Regulating the Dutch pharmaceutical market: improving efficiency or controlling costs? *International Journal of Health Planning & Management, 20*(4), 351-374. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16335082

Delnoij, D., & Brenner, G. (2000). Importing budget systems from other countries: what can we learn from the German drug budget and the British GP fundholding? *Health Policy, 52*(3), 157-169. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851000000749. doi:http://dx.doi.org/10.1016/S0168-8510(00)00074-9

Deloitte. (2013). *Impact of austerity on European pharmaceutical policy and pricing: Staying competitive in a challenging environment*. Retrieved from http://www.deloitte.com/assets/Dcom-Switzerland/Local%20Assets/Documents/EN/LSHC/ch_en_impact_of_austerity_on_pharma_policy_and_pricing.pdf

DeNavas-Walt, C., Proctor, B. D., & Smith, J. C. (2012). *Income, Poverty, and Health Insurance Coverage in the United States: 2011*. Washington, DC: U. S. G. P. Office. Retrieved from http://www.census.gov/prod/2012pubs/p60-243.pdf

Department of Economic and Social Affairs. (2012). *Population Ageing and Development 2012*. New York. Retrieved from http://www.un.org/esa/population/publications/2012WorldPopAgeingDev_Chart/2012PopAgeingandDev_WallChart.pdf

Department of Health. (2013a). *2014 PBS co-payment and safety net amounts.* Retrieved from http://www.pbs.gov.au/info/news/2014/01/co-payment-safety-net-amounts-update

Department of Health. (2013b). *Brand Premium Policy.* Retrieved from http://www.pbs.gov.au/browse/brand-premium
Department of Health. (2013c). *Browse the PBS. Pharmaceutical Benefits Scheme* Retrieved from http://www.pbs.gov.au/browse/body-system
Department of Health. (2013d). *General Statement for Lipid-Lowering Drugs Prescribed As Pharmaceutical Benefits Pharmaceutical Benefits Scheme* Retrieved from http://www.pbs.gov.au/info/healthpro/explanatory-notes/gs-lipid-lowering-drugs
Department of Health. (2013e). *Reference pricing to see patients and taxpayers benefit from reduced costs Press information* Retrieved from http://www.dohc.ie/press/releases/2013/20131101.html
Department of Health. (2014a). *How Pharmacists Claim Reimbursement: Documents to be Submitted. Pharmaceutical Benefits Scheme* Retrieved from http://www.pbs.gov.au/info/healthpro/explanatory-notes/section1/Section_1_8_Explanatory_Notes
Department of Health. (2014b). *Role of the Pharmaceutical Benefits Advisory Committee.* Retrieved from http://www.pbac.pbs.gov.au/information/role-of-pbac.html#Box1-2
Department of Health. (2014c). *Therapeutic Group Premium Policy.* Retrieved from http://www.pbs.gov.au/browse/group-premium
Department of Health. (2015). *2015 PBS co-payment and safety net amounts. The Pharmaceutical Benefits Scheme* Retrieved from http://www.pbs.gov.au/info/news/2015/01/2015-pbs-co-payment-safety-net-amounts
Department of Health and Ageing. (2000). *National Medicines Policy* Canberra ACT: Commonwealth of Australia Retrieved from http://www.health.gov.au/internet/main/publishing.nsf/Content/nmp-objectives-policy.htm-copy3.
Department of Health and Ageing. (2005, 23 December). *Pharmaceutical Benefits Scheme Safety Net 20 day rule Frequently Asked Questions. PBS Initiatives* Retrieved from http://www.health.gov.au/internet/main/publishing.nsf/Content/pbs-safetynet-20day-faq
Department of Health and Ageing. (2007). *Fact Sheet - Pharmaceutical Benefits Scheme (PBS) Reform*. Canberra.
Department of Health and Ageing. (2012). *Expenditure and prescriptions twelve months to 30 June 2012*. Canberra. Retrieved from http://www.pbs.gov.au/statistics/2011-2012-files/expenditure-and-prescriptions-2011-2012.pdf
Department of Health and Ageing. (2013). *About the PBS. Pharmaceutical Benefits Scheme* Retrieved from http://www.pbs.gov.au/info/about-the-pbs#What_are_the_current_patient_fees_and_charges
Department of Health and Ageing, & Medicines Australia. (2013). *Trends in and drivers of Pharmaceutical Benefits Scheme expenditure*. Department of Health and Ageing. Retrieved from http://www.pbs.gov.au/publication/reports/trends-in-and-drivers-of-pbs-expenditure.pdf
Department of Health and Ageing, D. (2008a). *Schedule of pharmaceutical benefits 31 August 2008*. Barton, ACT: Commonwealth of Australia Retrieved from http://www.pbs.gov.au/publication/schedule/2008/2008-08-01-general-schedule.pdf.

Department of Health and Ageing, D. (2008b). *Schedule of pharmaceutical benefits 31 July 2008*. Barton, ACT: Commonwealth of Australia Retrieved from http://www.pbs.gov.au/publication/schedule/2008/2008-07-01-general-schedule.pdf.

Department of Human Services. (2010). *State concessions and hardship programs 2008–09 and 2009–10*. Melbourne, Victoria. Retrieved from http://www.dhs.vic.gov.au/__data/assets/pdf_file/0009/606807/state-concessions-hardship-programs-2008-09-and-2009-10.pdf

Department of Human Services. (2013a). *2014 Medicare Safety Net thresholds. Medicare Safety Net* Retrieved from http://www.humanservices.gov.au/customer/enablers/medicare/medicare-safety-net/medicare-safety-net-thresholds

Department of Human Services. (2013b). *Annual Report 2012-13*. Manuka, ACT Retrieved from http://www.humanservices.gov.au/corporate/publications-and-resources/annual-report/resources/1213/

Department of Human Services. (2013c, 3 October 2013). *PBS reforms.* Retrieved from http://www.medicareaustralia.gov.au/provider/pbs/pharmacists/reforms.jsp

Department of Veterans' Affairs. (2014). *Repatriation Pharmaceutical Benefits Scheme.* Retrieved from http://www.dva.gov.au/SERVICE_PROVIDERS/DOCTORS/Pages/rpbs.aspx

Dewa, C. S., & Hoch, J. S. (2003). Fixed and flexible formularies as cost-control mechanisms. *Expert Review of Pharmacoeconomics & Outcomes Research, 3*(3), 303-315. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19807378. doi:10.1586/14737167.3.3.303

Donnelly, N., McManus, P., Dudley, J., & Hall, W. (2000). Impact of increasing the re-supply interval on the seasonality of subsidised prescription use in Australia. *Australian and New Zealand Journal of Public Health, 24*(6), 603-606. Retrieved from http://dx.doi.org/10.1111/j.1467-842X.2000.tb00524.x. doi:10.1111/j.1467-842X.2000.tb00524.x

Doran, E., Robertson, J., Rolfe, I., & Henry, D. (2004). Patient co-payments and use of prescription medicines. *Australian and New Zealand Journal of Public Health, 28*(1), 62-67. Retrieved from http://dx.doi.org/10.1111/j.1467-842X.2004.tb00634.x. doi:10.1111/j.1467-842X.2004.tb00634.x

Doran, E., Robertson, J., & Salkeld, G. (2011). Pharmaceutical Benefits Scheme cost sharing, patient cost consciousness and prescription affordability. *Australian Health Review, 35*(1), 37-44. Retrieved from http://search.informit.com.au/documentSummary;dn=780908806579521;res=IELHEA

Dormuth, C. R., Glynn, R. J., Neumann, P., Maclure, M., Brookhart, A. M., & Schneeweiss, S. (2006). Impact of two sequential drug cost-sharing policies on the use of inhaled medications in older patients with chronic obstructive pulmonary disease or asthma. *Clinical Therapeutics, 28*(6), 964-978. Retrieved from http://www.sciencedirect.com/science/article/pii/S0149291806001433. doi:10.1016/j.clinthera.2006.06.007

Dormuth, C. R., Neumann, P., Maclure, M., Glynn, R. J., & Schneeweiss, S. (2009). Effects of prescription coinsurance and income-based deductibles on net health plan spending for older users of inhaled medications. *Medical Care, 47*(5), 508-516.

Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19365295. doi:http://dx.doi.org/10.1097/MLR.0b013e318190d482

Drummond, M., & Jönsson, B. (2003). Moving Beyond the Drug Budget Silo Mentality in Europe. *Value in Health, 6*, S74-S77. Retrieved from http://dx.doi.org/10.1046/j.1524-4733.6.s1.8.x. doi:10.1046/j.1524-4733.6.s1.8.x

Duckett, S. (2011). *The Australian healthcare system*. South Melbourne, Vic.: South Melbourne, Vic. : Oxford University Press.

Eddama, O., & Coast, J. (2008). A systematic review of the use of economic evaluation in local decision-making. *Health Policy, 86*(2–3), 129-141. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851007002825. doi:10.1016/j.healthpol.2007.11.010

Edmonds, D. J., Dumbrell, D. M., Primrose, J. G., McManus, P., Birkett, D. J., & Demirian, V. (1993). Development of an Australian drug utilisation database: a report from the Drug Utilization Subcommittee of the Pharmaceutical Benefits Advisory Committee. *PharmacoEconomics, 3*(6), 427-432. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10184168

Ess, S. M., Schneeweiss, S., & Szucs, T. D. (2003). European Healthcare Policies for Controlling Drug Expenditure. *PharmacoEconomics, 21*(2), 89-103. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12515571

Explanatory Memorandum, National Health Amendment (Budget Measures - Pharmaceutical Benefits Safety Net) Bill, Commonwealth of Australia (2005).

Ferrand, Y., Kelton, C. M. L., Guo, J. J., Levy, M. S., & Yu, Y. (2011). Using time-series intervention analysis to understand U.S. Medicaid expenditures on antidepressant agents. *Research in Social and Administrative Pharmacy, 7*(1), 64-80. Retrieved from http://www.sciencedirect.com/science/article/pii/S1551741110000021. doi:10.1016/j.sapharm.2009.12.002

Fisher, S. H. (1991). The economic wisdom of regulating pharmaceutical "freebies". *Duke law journal*(1), 206-239. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10114416

Fonseca, F. A. H., Ruiz, A., Ernesto, G. C.-M., Silva, J. M., & et al. (2005). The DISCOVERY PENTA study: a DIrect Statin COmparison of LDL-C Value - an Evaluation of Rosuvastatin therapY compared with atorvastatin*. *Current Medical Research and Opinion, 21*(8), 1307-1315. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16083541. doi:10.1185/030079905x56529

Fox, K. M., Gandhi, S. K., Ohsfeldt, R. L., & Davidson, M. H. (2007). Comparison of low-density lipoprotein cholesterol reduction after switching patients on other statins to rosuvastatin or simvastatin in a real-world clinical practice setting. *American Journal of Managed Care, 13*(10 Suppl), S270-275. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=2009765680&site=ehost-live

Freeman, R., & Frisina, L. (2010). Health Care Systems and the Problem of Classification. *Journal of Comparative Policy Analysis: Research and Practice, 12*(1-2), 163-178. Retrieved from http://dx.doi.org/10.1080/13876980903076278. doi:10.1080/13876980903076278

Galizzi, M. M., Ghislandi, S., & Miraldo, M. (2011). Effects of reference pricing in pharmaceutical markets: a review. *PharmacoEconomics, 29*(1), 17-33. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21142276. doi:http://dx.doi.org/10.2165/11537860-000000000-00000

Garrison, L., & Towse, A. (2003). The Drug Budget Silo Mentality in Europe: An Overview. *Value in Health, 6*, S1-S9. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12846921. doi:10.1046/j.1524-4733.6.s1.1.x

Garson, A. (2000). The US Healthcare System 2010: Problems, Principles, and Potential Solutions. *Circulation, 101*(16), 2015-2016. Retrieved from http://circ.ahajournals.org/content/101/16/2015.short. doi:10.1161/01.cir.101.16.2015

Gillings, D., Makuc, D., & Siegel, E. (1981). Analysis of Interrupted Time Series Mortality Trends: An Example to Evaluate Regionalized Perinatal Care. *American Journal of Public Health, 71*(1), 38-46. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=bth&AN=4945601&site=ehost-live

Giuliani, G., Selke, G., & Garattini, L. (1998). The German experience in reference pricing. *Health Policy, 44*(1), 73-85. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851098000128

Global Burden of Disease Study 2010. (2013). Australia Global Burden of Disease Study 2010 (GBD 2010) Results 1990-2010 Seattle, United States: (Institute for Health Metrics and Evaluation (IHME)).

Goldman, D. P. (2007). Prescription drug cost sharing: associations with medication and medical utilization and spending and health. *JAMA (Chicago, Ill.), 298*(1), 61-69. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17609491

Goldman, D. P., Joyce, G. F., Escarce, J. J., & et al. (2004). Pharmacy benefits and the use of drugs by the chronically ill. *JAMA, 291*(19), 2344-2350. Retrieved from http://dx.doi.org/10.1001/jama.291.19.2344. doi:10.1001/jama.291.19.2344

Goldstein, J. L., & Brown, M. S. (2009). The LDL Receptor. *Arteriosclerosis, Thrombosis, and Vascular Biology, 29*(4), 431-438. Retrieved from http://atvb.ahajournals.org/content/29/4/431.abstract. doi:10.1161/atvbaha.108.179564

Gopinath, L. (1996, 1 November 1996). Cholesterol drug dilemma. *Chemistry World*.

Gottlieb, S. (2002). Drug companies maintain “astounding” profits. *BMJ, 324*(7345), 1054. doi:10.1136/bmj.324.7345.1054/b

Government Digital Service. (2013). *NHS charges from April 2013 announced. News story* Retrieved from https://www.gov.uk/government/news/nhs-charges-from-april-2013-announced

Green, C. J., Maclure, M., Fortin, P. M., Ramsay, C. R., Aaserud, M., & Bardal, S. (2010). Pharmaceutical policies: effects of restrictions on reimbursement. *Cochrane Database of Systematic Reviews*(8), CD008654. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20687098

Grimshaw, J., McAuley, L. M., Bero, L. A., Grilli, R., Oxman, A. D., Ramsay, C., et al. (2003). Systematic reviews of the effectiveness of quality improvement strategies and programmes. *Quality and Safety in Health Care, 12*(4), 298-303. Retrieved from http://qualitysafety.bmj.com/content/12/4/298.abstract. doi:10.1136/qhc.12.4.298

Grootendorst, P. V., Dolovich, L. R., O'Brien, B. J., Holbrook, A. M., & Levy, A. R. (2001). Impact of reference-based pricing of nitrates on the use and costs of anti-anginal drugs. *Canadian Medical Association. Journal, 165*(8), 1011-1019. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11699696

Gross, D. J., Ratner, J., Perez, J., & Glavin, S. L. (1994). International pharmaceutical spending controls: France, Germany, Sweden, and the United Kingdom. *Health care financing review, 15*(3), 127-140. Retrieved from http://search.proquest.com/docview/196956792?accountid=10382

Guillén, A. M., & Cabiedes, L. (2003). Reforming pharmaceutical policies in the European Union: a "penguin effect"? *International Journal of Health Services, 33*(1), 1-28. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12641260. doi:10.2190/1jc6-frl4-qm2l-qn6e

Håkonsen, H., Horn, A. M., & Toverud, E.-L. (2009). Price control as a strategy for pharmaceutical cost containment—What has been achieved in Norway in the period 1994–2004? *Health Policy, 90*(2–3), 277-285. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851008002200. doi:10.1016/j.healthpol.2008.09.018

Hanbury, A., Farley, K., Thompson, C., Wilson, P., Chambers, D., & Holmes, H. (2013). Immediate versus sustained effects: interrupted time series analysis of a tailored intervention. *Implementation Science, 8*(1), 130. Retrieved from http://www.implementationscience.com/content/8/1/130

Harrington, C., & Estes, C. (2008). *Health Policy: Crisis and Reform in the U.S. Health Care Delivery System*: Jones & Bartlett Learning.

Harris, A. (1994). *Economic Evaluation and the Reimbursement of Pharmaceuticals in Australia*. Victoria: Centre for Health Program Evaluation. Retrieved from http://www.buseco.monash.edu.au/centres/che/pubs/wp40.pdf

Harris, C. M., & Scrivener, G. (1996). Fundholders' prescribing costs: the first five years. *BMJ, 313*(7071), 1531-1534. doi:10.1136/bmj.313.7071.1531

Harrison, C., Britt, H., Miller, G., & Henderson, J. (2013). Prevalence of Chronic Conditions in Australia. *PLoS One, 8*(7), e67494. Retrieved from http://dx.doi.org/10.1371%2Fjournal.pone.0067494. doi:10.1371/journal.pone.0067494

Harvey, K. (2005). The Pharmaceutical Benefits Scheme 2003-2004. *Australia and New Zealand Health Policy, 2*(1), 2. Retrieved from http://www.anzhealthpolicy.com/content/2/1/2

Hazlet, T. K., & Blough, D. K. (2002). Health services utilization with reference drug pricing of histamine(2) receptor antagonists in British Columbia elderly. *Medical Care, 40*(8), 640-649. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12187178

Healy, J., Sharman, E., & Lokuge, B. (2006). *Australia: Health system review*. Retrieved from http://www.euro.who.int/__data/assets/pdf_file/0007/96433/E89731.pdf

Helfenstein, U. (1986). Box-jenkins modelling of some viral infectious diseases. *Statistics in Medicine, 5*(1), 37-47. Retrieved from http://dx.doi.org/10.1002/sim.4780050107. doi:10.1002/sim.4780050107

Herr, A., & Suppliet, M. (2011). *Co-Payment Exemptions and Reference Prices: an Empirical Study of Pharmaceutical Prices in Germany*. c. o. D. o. E. HEDG, University of York. Retrieved from http://EconPapers.repec.org/RePEc:yor:hectdg:11/18

Holmes, D. R., Becker, J. A., Granger, C. B., Limacher, M. C., Page, R. L., & Sila, C. (2011). ACCF/AHA 2011 Health Policy Statement on Therapeutic Interchange and Substitution: A Report of the American College of Cardiology Foundation Clinical Quality Committee. *Circulation, 124*(11), 1290-1310. Retrieved from http://circ.ahajournals.org/content/124/11/1290.short. doi:10.1161/CIR.0b013e31822d97d5

Hsiao, F.-Y., Tsai, Y.-W., & Huang, W.-F. (2010). Price regulation, new entry, and information shock on pharmaceutical market in Taiwan: a nationwide data-based study from 2001 to 2004. *BMC Health Services Research, 10*, 218. Retrieved from http://www.biomedcentral.com/1472-6963/10/218

Huang, S.-H., Hsu, C.-N., Yu, S.-H., & Cham, T.-M. (2012). Impact of drug price adjustments on utilization of and expenditures on angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in Taiwan. *BMC Public Health, 12*(1), 288. Retrieved from http://www.biomedcentral.com/1471-2458/12/288

Hynd, A., Roughead, E. E., Preen, D. B., Glover, J., Bulsara, M., & Semmens, J. (2008). The impact of co-payment increases on dispensings of government-subsidised medicines in Australia. *Pharmacoepidemiology and Drug Safety, 17*(11), 1091-1099. Retrieved from http://dx.doi.org/10.1002/pds.1670. doi:10.1002/pds.1670

Hynd, A., Roughead, E. E., Preen, D. B., Glover, J., Bulsara, M., & Semmens, J. (2009). Increased patient co-payments and changes in PBS-subsidised prescription medicines dispensed in Western Australia. *Australian and New Zealand Journal of Public Health, 33*(3), 246-252. Retrieved from http://dx.doi.org/10.1111/j.1753-6405.2009.00383.x. doi:10.1111/j.1753-6405.2009.00383.x

IMAP. (2001). *Pharmaceuticals & Biotech Industry Global Report*. Retrieved from http://www.imap.com/imap/media/resources/IMAP_PharmaReport_8_272B8752E0FB3.pdf

IMS Consulting Group. (2012). The Impact Global Pharma Cost Containment Measures in Asia-Pacific. *IMS Asia-Pacific Insight,* 10-13.

IMS Health Service Centre. (2009). *IMS Pharmaceutical Pricing & Reimbursement Concise Guide: Australia*. Retrieved from http://www.imshealth.com/ims/Global/Asia%20Pacific/Australia/PPR_Concise_Guide_Australia_Q209.pdf

IMS Institute for Healthcare Informatics. (2011a). *The Global Use of Medicines: Outlook Through 2015*. NJ, USA: IMS Health Incorporated. Retrieved from http://www.imshealth.com/ims/Global/Content/Insights/

IMS Institute for Healthcare Informatics. (2011b). *Top 20 Global Corporations*. NJ, USA: IMS Health Incorporated. Retrieved from http://www.imshealth.com/deployedfiles/ims/Global/Content/Corporate/

IMS Institute for Healthcare Informatics. (2012a). *The Global Use of Medicines: Outlook Through 2016*. NJ, USA: IMS Health Incorporated. Retrieved from http://www.imshealth.com/deployedfiles/ims/Global/Content/Insights

IMS Institute for Healthcare Informatics. (2012b). *Top 20 Global Products 2011*. NJ, USA: IMS Health Incorporated. Retrieved from http://www.imshealth.com/deployedfiles/ims/Global/Content/Corporate/

IMS Institute for Healthcare Informatics. (2013a). *The Global Use of Medicines: Outlook Through 2017*. NJ, USA: IMS Health Incorporated.

IMS Institute for Healthcare Informatics. (2013b). *Top 20 Global Products 2012*. NJ, USA: IMS Health Incorporated. Retrieved from http://www.imshealth.com/deployedfiles/ims/Global/Content/Corporate/

IMS Institute for Healthcare Informatics. (2014). *Top 20 Global Products 2013*. NJ, USA: IMS Health Incorporated. Retrieved from http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Corporate/

Institute of Medicine, I. (2007). *The Learning Healthcare System: Workshop Summary* (9780309133937). Washington, DC: T. N. A. Press. Retrieved from http://books.google.com.my/books?id=VWmjvCZOFjoC

Insull, W., Kafonek, S., Goldner, D., & Zieve, F. (2001). Comparison of efficacy and safety of atorvastatin (10 mg) with simvastatin (10 mg) at six weeks. *The American Journal of Cardiology, 87*(5), 554-559. Retrieved from http://www.sciencedirect.com/science/article/pii/S0002914900014302. doi:http://dx.doi.org/10.1016/S0002-9149(00)01430-2

International Federation of Pharmaceutical Manufacturers and Associations, I. (2011). *The Pharmaceutical Industry and Global Health: Facts and Figures*. Geneva. Retrieved from http://www.ifpma.org/fileadmin/content/Publication/2011/2011_The_Pharmaceutical_Industry_and_Global_Health_low_ver2.pdf

International Federation of Pharmaceutical Manufacturers and Associations, I. (2012). *The Pharmaceutical Industry and Global Health: Facts and Figures*. Geneva. Retrieved from http://www.ifpma.org/fileadmin/content/Publication/2013/IFPMA_-_Facts_And_Figures_2012_LowResSinglePage.pdf

International Monetary Fund. (2013). World Economic Outlook Database: (International Monetary Fund,).

Johnson, R. E., Campbell, W. H., & Azevedo, D. J. (1978). Examining the Drug Utilization And Expenditures of a Medically Indigent Population. *Inquiry, 15*(1), 38-44. Retrieved from http://www.jstor.org/stable/29771131. doi:10.2307/29771131

Johnson, R. E., Goodman, M. J., Hornbrook, M. C., & Eldredge, M. B. (1997). The impact of increasing patient prescription drug cost sharing on therapeutic classes of drugs received and on the health status of elderly HMO members. *Health Services Research, 32*(1), 103-122. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9108807

Jones, P. H., Davidson, M. H., Stein, E. A., Bays, H. E., McKenney, J. M., Miller, E., et al. (2003). Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR Trial). *The American Journal of Cardiology, 92*(2), 152-160. Retrieved from http://www.sciencedirect.com/science/article/pii/S0002914903005307. doi:http://dx.doi.org/10.1016/S0002-9149(03)00530-7

Joyce, G. F., Escarce, J. J., Solomon, M. D., & Goldman, D. P. (2002). Employer drug benefit plans and spending on prescription drugs. *JAMA, 288*(14), 1733-1739. Retrieved from http://dx.doi.org/10.1001/jama.288.14.1733. doi:10.1001/jama.288.14.1733

Julio López, B., & Elias, M. (2000). Pharmaceutical Expenditure in Spain: Cost and Control. *International Journal of Health Services, 30*(3), 597-616. Retrieved from http://dx.doi.org/10.2190/YL3J-QK9B-0NMQ-KMVK. doi:10.2190/yl3j-qk9b-0nmq-kmvk

Kalisch, L., Roughead, E. E., & Gilbert, A. L. (2007a). Do Pharmacists Adhere to Brand Substitution Guidelines?: The Example of Simvastatin. *Journal of Pharmacy Practice and Research, 37*(4), 292-294. Retrieved from http://search.informit.com.au.dbgw.lis.curtin.edu.au/documentSummary;dn=628726070188473;res=IELHEA

Kalisch, L., Roughead, E. E., & Gilbert, A. L. (2007b). Pharmaceutical brand substitution in Australia – are there multiple switches per prescription? *Australian and New Zealand Journal of Public Health, 31*(4), 348-352. Retrieved from

http://dx.doi.org/10.1111/j.1753-6405.2007.00085.x. doi:10.1111/j.1753-6405.2007.00085.x

Kanavos, P. (2003). Overview of pharmaceutical pricing and reimbursement regulation in Europe. *Japanese Pharmacology and Therapeutics, 31*(10), 819-838.

Kephart, G., Sketris, I. S., Bowles, S. K., Richard, M. E., & Cooke, C. A. (2005). Impact of a criteria-based reimbursement policy on the use of respiratory drugs delivered by nebulizer and health care services utilization in Nova Scotia, Canada. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 25*(9), 1248-1257. Retrieved from http://dx.doi.org/10.1592/phco.2005.25.9.1248. doi:10.1592/phco.2005.25.9.1248

Kirchgässner, G., Wolters, J., & Hassler, U. (2012). *Introduction to Modern Time Series Analysis*: Springer Berlin Heidelberg.

Kitagawa, G. (2010). Introduction and Preparatory Analysis *Introduction to Time Series Modeling.* (pp. 1-15): Chapman and Hall/CRC. Retrieved from http://dx.doi.org/10.1201/9781584889229-c1 doi:10.1201/9781584889229-c1

Kozma, C. M., Reeder, C. E., & Schulz, R. M. (1993). Economic, clinical, and humanistic outcomes: a planning model for pharmacoeconomic research. *Clinical Therapeutics, 15*(6), 1121-1132; discussion 1120. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8111809

Kozyrskyj, A. L., Mustard, C. A., Cheang, M. S., & Simons, F. E. R. (2001). Income-based drug benefit policy: Impact on receipt of inhaled corticosteroid prescriptions by Manitoba children with asthma. *Canadian Medical Association. Journal, 165*(7), 897-902. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11599328

Lagarde, M. (2012). How to do (or not to do) … Assessing the impact of a policy change with routine longitudinal data. *Health Policy and Planning, 27*(1), 76-83. Retrieved from http://heapol.oxfordjournals.org/content/27/1/76.abstract. doi:10.1093/heapol/czr004

Lameire, N., Joffe, P., & Wiedemann, M. (1999). Healthcare systems—an international review: an overview. *Nephrology Dialysis Transplantation, 14*(suppl 6), 3-9. Retrieved from http://ndt.oxfordjournals.org/content/14/suppl_6/3.abstract. doi:10.1093/ndt/14.suppl_6.3

Landsman, P. B., Yu, W., Liu, X., Teutsch, S. M., & Berger, M. L. (2005). Impact of 3-tier pharmacy benefit design and increased consumer cost-sharing on drug utilization. *The American journal of managed care, 11*(10), 621-628. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16232003

Law, M. R., Wald, N. J., & Thompson, S. G. (1994). By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? *British Medical Journal, 308*(6925), 367. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2539460/

Lee, I.-H., Bloor, K., Hewitt, C., & Maynard, A. (2012). The effects of new pricing and copayment schemes for pharmaceuticals in South Korea. *Health Policy, 104*(1), 40-49. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851011001904. doi:10.1016/j.healthpol.2011.09.003

Lee, Y.-C., Yang, M.-C., Huang, Y.-T., Liu, C.-H., & Chen, S.-B. (2006). Impacts of cost containment strategies on pharmaceutical expenditures of the National Health Insurance in Taiwan, 1996-2003. *PharmacoEconomics, 24*(9), 891-902. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16942123

Leibowitz, A., Manning, W. G., & Newhouse, J. P. (1985). The demand for prescription drugs as a function of cost-sharing. *Social Science & Medicine, 21*(10), 1063-1069. Retrieved from http://www.sciencedirect.com/science/article/pii/0277953685901613

Leopold, M. C. (2013). *Pharmaceutical policy measures implemented in response to the recession in Europe 2012/2013*. Vienna. Retrieved from http://haieurope.org/wp-content/uploads/2014/02/Christine_Leopold-Pharmaceutical_policy_measures_implemented_in_response_to_the_recession_in_Europe_2012-2013.pdf

Liu, S.-Z., & Romeis, J. C. (2003). Assessing the effect of Taiwan's outpatient prescription drug copayment policy in the elderly. *Medical Care, 41*(12), 1331-1342. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14668666

Liu, S.-Z., & Romeis, J. C. (2004). Changes in drug utilization following the outpatient prescription drug cost-sharing program—evidence from Taiwan's elderly. *Health Policy, 68*(3), 277-287. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851003002562. doi:10.1016/j.healthpol.2003.12.013

Liu, Y.-M., & Hsieh, C.-R. (2012). New drugs and the growth of health expenditure: evidence from diabetic patients in Taiwan. *Health Economics, 21*(5), 496-513. Retrieved from http://dx.doi.org/10.1002/hec.1724. doi:10.1002/hec.1724

Lofgren, H. (2009). Generic Medicines in Australia: Business Dynamics and Recent Policy Reform. *SSRN eLibrary*. Retrieved from http://ssrn.com/paper=1471687. doi:10.2139/ssrn.1471687

Longest, B. B. (2009). *Health Policymaking in the United States*: Health Administration Press.

López-Casasnovas, G., & Puig-Junoy, J. (2000). Review of the literature on reference pricing. *Health Policy, 54*(2), 87-123. Retrieved from http://www.sciencedirect.com/science/article/pii/S0168851000001007

MacCara, M. E., Sketris, I. S., Comeau, D. G., & Weerasinghe, S. D. (2001). Impact of a limited fluoroquinolone reimbursement policy on antimicrobial prescription claims. *Annals of Pharmacotherapy, 35*(7-8), 852-858. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11485132

Marais, A. D., Firth, J. C., Bateman, M. E., Byrnes, P., Martens, C., & Mountney, J. (1997). Atorvastatin: An Effective Lipid-Modifying Agent in Familial Hypercholesterolemia. *Arteriosclerosis, Thrombosis, and Vascular Biology, 17*(8), 1527-1531. Retrieved from http://atvb.ahajournals.org/content/17/8/1527.abstract. doi:10.1161/01.atv.17.8.1527

Marshall, D. A., Gough, J., Grootendorst, P., Buitendyk, M., Jaszewski, B., Simonyi, S., et al. (2006). Impact of administrative restrictions on antibiotic use and expenditure in Ontario: time series analysis. *Journal of Health Services & Research Policy, 11*(1), 13-20. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16378528

Marshall, D. A., Willison, D. J., Grootendorst, P., LeLorier, J., Maclure, M., Kulin, N. A., et al. (2007). The effects of coxib formulary restrictions on analgesic use and cost: regional evidence from Canada. *Health Policy, 84*(1), 1-13. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17570558

Marshall, J. K., Grootendorst, P. V., O'Brien, B. J., Dolovich, L. R., & et al. (2002). Impact of reference-based pricing for histamine-2 receptor antagonists and restricted access for proton pump inhibitors in British Columbia. *Canadian Medical Association.*

Journal, 166(13), 1655-1662. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12126319

Martikainen, J. E., Häkkinen, U., & Enlund, H. (2007). Adoption of new antiglaucoma drugs in Finland: Impact of changes in copayment. *Clinical Therapeutics, 29*(11), 2468-2476. Retrieved from http://www.sciencedirect.com/science/article/pii/S0149291807003621

Martin, L. R., & DiMatteo, R. (2013). *The Oxford Handbook of Health Communication, Behavior Change, and Treatment Adherence*: OUP USA.

Martindale: The Complete Drug Reference. (2010). London Pharmaceutical Press. S. C. Sweetman (Ed.). Retrieved from http://www.medicinescomplete.com.dbgw.lis.curtin.edu.au

Matowe, L. K., Leister, C. A., Crivera, C., & Korth-Bradley, J. M. (2003). Interrupted time series analysis in clinical research. *The Annals of Pharmacotherapy, 37*(7-8), 1110-1116. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12841825

Maynard, A., & Bloor, K. (2003). Dilemmas In Regulation Of The Market For Pharmaceuticals. *Health Affairs, 22*(3), 31-41. Retrieved from http://content.healthaffairs.org/content/22/3/31.abstract. doi:10.1377/hlthaff.22.3.31

McManus, P., Birkett, D. J., Dudley, J., & Stevens, A. (2001). Impact of the Minimum Pricing Policy and introduction of brand (generic) substitution into the Pharmaceutical Benefits Scheme in Australia. *Pharmacoepidemiology and Drug Safety, 10*(4), 295-300. Retrieved from http://dx.doi.org/10.1002/pds.603. doi:10.1002/pds.603

McManus, P., Donnelly, N., Henry, D., Hall, W., Primrose, J., & Lindner, J. (1996). Prescription drug utilization following patient co-payment changes in Australia. *Pharmacoepidemiology and Drug Safety, 5*(6), 385-392. Retrieved from http://dx.doi.org/10.1002/(SICI)1099-1557(199611)5:6<385::AID-PDS246>3.0.CO;2-8. doi:10.1002/(sici)1099-1557(199611)5:6<385::aid-pds246>3.0.co;2-8

Medibank Private Limited. (2014). *History.* Retrieved from http://www.medibank.com.au/About-Us/Corporate-Information/History.aspx

Medicare Australia. (2010). *Medicare Australia Annual Report 2009-2010*. Canberra: Commonwealth of Australia. Retrieved from www.medicareaustralia.gov.au

Medicare Australia. (2013). Pharmaceutical Benefits Schedule Item Reports Tuggeranong: (Department of Human Services).

Medicare Levy Amendment (DisabilityCare Australia) Bill, No. 43, Parliment Australia (2013).

Medicines Partnership of Australia. (2012). *August 2012 – Sharp drop in average cost of PBS medicines Pharmaceutical Benefits Scheme (PBS) Scorecard.* Retrieved from http://medicinespartnership.com.au/pbs-scorecards/august-2012-sharp-drop-in-average-cost-of-pbs-medicines-pharmaceutical-benefits-scheme-pbs-scorecard/

Mol, P. G. M., Wieringa, J. E., NannanPanday, P. V., Gans, R. O. B., Degener, J. E., Laseur, M., et al. (2005). Improving compliance with hospital antibiotic guidelines: a time-series intervention analysis. *Journal of Antimicrobial Chemotherapy, 55*(4), 550-557. Retrieved from http://jac.oxfordjournals.org/content/55/4/550.abstract. doi:10.1093/jac/dki037

Moreno-Torres, I. n., Puig-Junoy, J., & Raya, J. M. (2011). The impact of repeated cost containment policies on pharmaceutical expenditure: experience in Spain. *The European Journal of Health Economics, 12*(6), 563-573.

Morgan, S., Hanley, G., & Greyson, D. (2009). Comparison of tiered formularies and reference pricing policies: a systematic review. *Open Med, 3*(3), e131-139. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21603047

Mossialos, E., & Mrazek, M. (2004). Regulating pharmaceutical prices in the European Union. In E. Mossialos, M. Mrazek & T. Walley (Eds.), *Regulation Pharmaceuticals in Europe: Striving for Efficiency, Equity and Quality.* (pp. 114-129). Maidenhead, England: Open University Press.

National Commission of Audit. (2014). *Towards Responsible Government*. Canberra, ACT. Retrieved from http://www.ncoa.gov.au/report

National Heart Foundation of Australia. (2013). *High cholesterol. You & your heart* Retrieved from http://www.heartfoundation.org.au/your-heart/cardiovascular-conditions/Pages/high-cholesterol.aspx

Newey, W. K., & West, K. D. (1986). A simple, positive semi-definite, heteroskedasticity and autocorrelationconsistent covariance matrix: (National Bureau of Economic Research Cambridge, Mass., USA).

Olejaz, M., Juul Nielsen, A., Rudkjøbing, A., Okkels Birk, H., Krasnik, A., & Hernández-Quevedo, C. (2012). *Denmark: Health system review*. W. World Health Organization.

Ong, M., Catalano, R., & Hartig, T. (2003). A time-series analysis of the effect of increased copayments on the prescription of antidepressants, anxiolytics, and sedatives in Sweden from 1990 to 1999. *Clinical Therapeutics, 25*(4), 1262-1275. Retrieved from http://www.sciencedirect.com/science/article/pii/S0149291803800826. doi:10.1016/s0149-2918(03)80082-6

Organisation for Economic Co-operation and Development. (1987). Financing and Delivering Health Care. A Comparative Analysis of OECD Countries. *OECD Social Policy Studies, 4*

Organisation for Economic Co-operation and Development. (2013). OECD.StatExtracts. Retrieved 7 March 2013 http://stats.oecd.org/index.aspx?DataSetCode=HEALTH_STAT#

Ortiz, M., Simons, L. A., & Calcino, G. (2010). Generic substitution of commonly used medications: Australia-wide experience, 2007-2008. *Medical Journal of Australia, 192*(7), 370-373.

Palmer, G. R., & Short, S. D. (2000). *Health Care and Public Policy: An Australian Analysis*: Macmillan Education Australia.

Parliamentary Budget Office. (2013). *Australian Government spending*. Canberra: P. o. Australia. Retrieved from http://www.aph.gov.au/

Parvis, E. N. (2002). *The Pharmaceutical Industry: Access and Outlook*. New York: Nova Science Pub.

Pharmaceutical Benefits Pricing Authority. (1999). *Annual Report For the Year Ended 30 June 1999*. Canberra: AusInfo.

Pharmaceutical Benefits Pricing Authority. (2009). *Policies, Procedures and Methods Used In the Recommendations for Pricing of Pharmaceutical Products*. Canberra: Department of Health and Ageing. Retrieved from http://www.health.gov.au/internet/main/publishing.nsf/content/1D0AFBEEF35A185DCA2572B200015F5F/$File/PBPA-Manual-May%202009.pdf

Pharmaceutical Benefits Pricing Authority. (2010). *Annual Report For the Year Ended 30 June 2010*. Canberra, ACT: Department of Health and Ageing Retrieved from

http://www.pbs.gov.au/industry/pricing/pbs-items/historical/pbpa-pdf/pbpa-annual-report-2010.pdf.

Pichetti, S., Sorasith, C., & Sermet, C. (2011). Analysis of the impact of removing mucolytics and expectorants from the list of reimbursable drugs on prescription rates: a time-series analysis for France 1998-2010. *Health Policy, 102*(2-3), 159-169. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21802761

Pilote, L., Beck, C., Richard, H., & Eisenberg, M. J. (2002). The effects of cost-sharing on essential drug prescriptions, utilization of medical care and outcomes after acute myocardial infarction in elderly patients. *Canadian Medical Association Journal, 167*(3), 246-252. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12186169

Puig-Junoy, J., & Moreno-Torres, I. (2007). Impact of pharmaceutical prior authorisation policies: A systematic review of the literature. *PharmacoEconomics, 25*(8), 637-648. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17640106

Q1Group LLC. (2013). *2013 Medicare Part D Outlook.* Retrieved from http://www.q1medicare.com/PartD-The-2013-Medicare-Part-D-Outlook.php

Qingyue, M., Liying, J., & Beibei, Y. (2011). *Cost-sharing mechanisms in health insurance schemes: A systematic review*. W. World Health Organization. Retrieved from http://www.who.int/alliance-hpsr/projects/alliancehpsr_chinasystematicreviewcostsharing.pdf

Ramsay, C. R., Matowe, L., Grilli, R., Grimshaw, J. M., & Thomas, R. E. (2003). INTERRUPTED TIME SERIES DESIGNS IN HEALTH TECHNOLOGY ASSESSMENT: LESSONS FROM TWO SYSTEMATIC REVIEWS OF BEHAVIOR CHANGE STRATEGIES. *International Journal of Technology Assessment in Health Care, 19*(04), 613-623. Retrieved from http://dx.doi.org/10.1017/S0266462303000576. doi:doi:10.1017/S0266462303000576

Research Economics Support Team. (2011). *Factsheet - Medicare Australia data for research: an introduction.* Retrieved from http://www.chere.uts.edu.au/crest/pdfs/Factsheet-Medicare_Australia-FINAL.pdf

Rickard, M. (2002). *The Pharmaceutical Benefits Scheme : options for cost control*. Canberra: Dept. of the Parliamentary Library.

Rietveld, A. H., & Haaijer-Ruskamp, F. M. (2003). Policy options for cost containment of pharmaceuticals. In M. N. G. Dukes, F. M. Haaijer-Ruskamp, C. Joncheere & A. H. Rietveld (Eds.), *Drugs and Money - Prices, Affordability and Cost Containment.* (pp. 29–54). Amsterdam: IOS Press. Retrieved from http://apps.who.int/medicinedocs/pdf/s4912e/s4912e.pdf

Sacks, F. M., Pfeffer, M. A., Moye, L. A., Rouleau, J. L., Rutherford, J. D., Cole, T. G., et al. (1996). The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. *The New England Journal of Medicine, 335*(14), 1001-1009. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8801446. doi:10.1056/NEJM199610033351401

Samuelson, P. A., & Nordhaus, W. D. (2010). *Economics* (19 ed.): Tata McGraw Hill.

Sansom, L. (2004). The subsidy of pharmaceuticals in Australia: processes and challenges. *Australian health review : a publication of the Australian Hospital Association, 28*(2), 194-205. Retrieved from <Go to ISI>://MEDLINE:15527399

Sayer, G., Britt, H., Horn, F., Bhasale, A., McGeechan, K., Charles, J., et al. (2000). *Measures of health and health care delivery in general practice in Australia*. Canberra:

Australian Institute of Health and Welfare. Retrieved from http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=6442455926

Schneeweiss, S., Maclure, M., Carleton, B., Glynn, R. J., & Avorn, J. (2004). Clinical and economic consequences of a reimbursement restriction of nebulised respiratory therapy in adults: direct comparison of randomised and observational evaluations. *BMJ, 328*(7439), 560. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14982865

Schneeweiss, S., Maclure, M., Dormuth, C. R., Glynn, R. J., Canning, C., & Avorn, J. (2006). A therapeutic substitution policy for proton pump inhibitors: Clinical and economic consequences. *Clinical Pharmacology & Therapeutics, 79*(4), 379-388. Retrieved from http://dx.doi.org/10.1016/j.clpt.2005.12.304

Schneeweiss, S., Soumerai, S. B., Glynn, R. J., & Maclure, M. (2002). Impact of reference-based pricing for angiotensin-converting enzyme inhibitors on drug utilization. *Canadian Medical Association. Journal, 166*(6), 737-745. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11944760

Schneeweiss, S., Soumerai, S. B., Maclure, M., Dormuth, C., Walker, A. M., & Glynn, R. J. (2003). Clinical and economic consequences of reference pricing for dihydropyridine calcium channel blockers. *Clinical Pharmacology & Therapeutics, 74*(4), 388-400. Retrieved from http://dx.doi.org/10.1016/S0009-9236(03)00227-3

Schuster, H., Barter, P. J., Stender, S., Cheung, R. C., Bonnet, J., Morrell, J. M., et al. (2004). Effects of switching statins on achievement of lipid goals: measuring effective reductions in cholesterol using rosuvastatin therapy (MERCURY I) study. *American heart journal, 147*(4), 705-712. Retrieved from http://linkinghub.elsevier.com/retrieve/pii/S0002870303007105?showall=true

Scottish Intercollegiate Guidelines Network. (2008). *SIGN 50: A Guideline Developer's Handbook*. Edinburgh, UK: Scottish Intercollegiate Guidelines Network. Retrieved from http://www.sign.ac.uk/pdf/sign50.pdf

Scotton, R. B., & Macdonald, C. R. (1993). *The Making of Medibank*: School of Health Services Management, University of New South Wales.

Searles, A., Jefferys, S., Doran, E., & Henry, D. A. (2007). Reference pricing, generic drugs and proposed changes to the Pharmaceutical Benefits Scheme. *Medical Journal of Australia, 187*(4), 236-239. Retrieved from https://www.mja.com.au/journal/2007/187/4/reference-pricing-generic-drugs-and-proposed-changes-pharmaceutical-benefits

Senate Community Affairs References Committee. (2010). *Inquiry Into: Consumer Access to Pharmaceutical Benefits*. Canberra: Parliament of Australia. Retrieved from http://www.aph.gov.au/binaries/senate/committee/clac_ctte/consumer_access_pharm_benefits/submissions/sub27.pdf

Shepherd, J., Cobbe, S. M., Ford, I., Isles, C. G., Lorimer, A. R., MacFarlane, P. W., et al. (1995). Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. *The New England Journal of Medicine, 333*(20), 1301-1307. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7566020. doi:10.1056/NEJM199511163332001

Shepherd, J., Hunninghake, D. B., Barter, P., McKenney, J. M., & Hutchinson, H. G. (2003). Guidelines for lowering lipids to reduce coronary artery disease risk: a comparison of rosuvastatin with atorvastatin, pravastatin, and simvastatin for achieving lipid-lowering goals. *The American Journal of Cardiology, 91*(5, Supplement 1), 11-17.

Retrieved from http://www.sciencedirect.com/science/article/pii/S0002914903000043. doi:http://dx.doi.org/10.1016/S0002-9149(03)00004-3

Sims, C. A. (1974). Seasonality in Regression. *Journal of the American Statistical Association, 69*(347), 618-626. Retrieved from http://www.tandfonline.com/doi/abs/10.1080/01621459.1974.10480178. doi:10.1080/01621459.1974.10480178

Sloan, C. (1995). *A history of the Pharmaceutical Benefits Scheme, 1947-1992*. Canberra: Australian Govt. Pub. Service.

Smith, D. G., & Kirking, D. M. (1992). Impact of consumer fees on drug utilisation. *PharmacoEconomics, 2*(4), 335-342. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10147046

Sokol, M. C., McGuigan, K. A., Verbrugge, R. R., & Epstein, R. S. (2005). Impact of Medication Adherence on Hospitalization Risk and Healthcare Cost. *Medical Care, 43*(6), 521-530. Retrieved from http://journals.lww.com/lww-medicalcare/Fulltext/2005/06000/Impact_of_Medication_Adherence_on_Hospitalization.2.aspx

Soumerai, S. B., Ross-Degnan, D., & Kahn, J. S. (1992). Effects of Professional and Media Warnings about the Association between Aspirin Use in Children and Reye's Syndrome. *The Milbank Quarterly, 70*(1), 155-182. Retrieved from http://www.jstor.org/stable/3350088. doi:10.2307/3350088

Stafford, R. S., & Radley, D. C. (2002). The potential of pill splitting to achieve cost savings. *The American journal of managed care, 8*(8), 706-712. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12212758

StataCorp. (2013). *STATA User's Guide* (Release 13 ed.). College Station, Texas: Stata Press.

Steering Committee for the Review of Government Service Provision, S. (2014). *Report on Government Services 2014*. Canberra: P. Commission. Retrieved from http://www.pc.gov.au/__data/assets/pdf_file/0019/132346/rogs-2014-volumee-health.pdf

Stone, D. A. (2000). United states. *Journal of Health Politics, Policy & Law, 25*(5), 953-953. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=2009431881&site=ehost-live

Strandberg, T. E., Feely, J., & Sigurdsson, E. L. (2004). Twelve-week, multicenter, randomized, open-label comparisonof the effects of rosuvastatin 10 mg/d and atorvastatin 10 mg/d in high-risk adults: a DISCOVERY study. *Clinical Therapeutics, 26*(11), 1821-1833. Retrieved from http://www.sciencedirect.com/science/article/pii/0149291804803461

Sweeny, K. (2007a). *Key Aspects of the Australian Pharmaceutical Benefits Scheme*. Victoria University of Technology. Retrieved from http://www.cfses.com/documents/pharma/35-Key_aspects_of_PBS_Sweeny.pdf

Sweeny, K. (2007b). *Trends and Outcomes in the Australian Pharmaceutical Benefits Scheme*. Melbourne: Victoria University of Technology. Retrieved from http://www.cfses.com/documents/pharma/36-Trends_Outcomes_PBS_Sweeny.pdf

Sweeny, K. (2013). *The Impact of Further PBS Reform*. Melbourne: Victoria University. Retrieved from http://medicinesaustralia.com.au/files/2010/01/20130515-rep-The-Impact-of-Further-PBS-Reforms-Final-report-from-CSES.pdf

Tamblyn, R., Laprise, R., Hanley, J. A., Abrahamowicz, M., Scott, S., Mayo, N., et al. (2001). Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA, 285*(4), 421-429. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11242426

The Department of Families Housing Community Services and Indigenous Affairs. (2009). *Annual Report 2008-09*. Canberra. Retrieved from http://resources.fahcsia.gov.au/annualreport/2009/docs/ar08_09.pdf

The Department of Families Housing Community Services and Indigenous Affairs. (2012). *Annual Report 2011–12*. Canberra. Retrieved from http://www.fahcsia.gov.au/sites/default/files/documents/10_2012/fahcsia-2011-12-annual-report_0.pdf

Timonen, J., Karttunen, P., Bengtström, M., & Ahonen, R. (2009). The impact of generic substitution on the turnover and gross margin of pharmaceutical companies a survey 1 year and 5 years after the introduction of generic substitution in Finland. *Health Policy, 92*(2-3), 116-123. Retrieved from http://www.scopus.com/inward/record.url?eid=2-s2.0-69249235556&partnerID=40&md5=129182bd3d4f2ce47aa470ac15edd3d8. doi:10.1016/j.healthpol.2009.03.004

Towse, A. (2003). The Efficient Use Of Pharmaceuticals: Does Europe Have Any Lessons For A Medicare Drug Benefit? *Health Affairs, 22*(3), 42-45. Retrieved from http://content.healthaffairs.org/content/22/3/42.abstract. doi:10.1377/hlthaff.22.3.42

U.S. Food And Drug Administration. (2012a, 2 Feb 2012). *Drugs@FDA Glossary of Terms.* Retrieved from http://www.fda.gov/Drugs/informationondrugs/ucm079436.htm#G

U.S. Food And Drug Administration. (2012b). *FY 2012 Innovative Drug Approvals*. Retrieved from http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM330859.pdf

Usher, C., Tilson, L., Bennett, K., & Barry, M. (2012). Cost containment interventions introduced on the community Drugs Schemes in Ireland—Evaluation of expenditure trends using a National Prescription claims database. *Clinical Therapeutics, 34*(3), 632-639. Retrieved from http://www.sciencedirect.com/science/article/pii/S0149291812000719. doi:10.1016/j.clinthera.2012.01.025

van Driel, M. L., Vander Stichele, R., Elseviers, M., De Sutter, A., De Maeseneer, J., & Christiaens, T. (2008). Effects of an evidence report and policies lifting reimbursement restrictions for acid suppressants: analysis of the Belgian national database. *Pharmacoepidemiology and Drug Safety, 17*(11), 1113-1122. Retrieved from http://dx.doi.org/10.1002/pds.1664. doi:10.1002/pds.1664

Vogler, S., Zimmermann, N., Leopold, C., & de Joncheere, K. (2011). Pharmaceutical policies in European countries in response to the global financial crisis. *Southern med review, 4*(2), 69-79. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23093885. doi:10.5655/smr.v4i2.1004

Wagner, A. K., Soumerai, S. B., Zhang, F., & Ross-Degnan, D. (2002). Segmented regression analysis of interrupted time series studies in medication use research. *Journal of Clinical Pharmacy and Therapeutics, 27*(4), 299-309. Retrieved from http://dx.doi.org/10.1046/j.1365-2710.2002.00430.x. doi:10.1046/j.1365-2710.2002.00430.x

Wallace, L. S. (2013). A View Of Health Care Around The World. *The Annals of Family Medicine, 11*(1), 84. Retrieved from http://www.annfammed.org/content/11/1/84.1.short. doi:10.1370/afm.1484

Weir, M. C., Grimshaw, J. M., Mayhew, A., & Fergusson, D. (2012). Decisions about lumping vs. splitting of the scope of systematic reviews of complex interventions are not well justified: A case study in systematic reviews of health care professional reminders. *Journal of Clinical Epidemiology, 65*(7), 756-763. Retrieved from http://www.sciencedirect.com/science/article/pii/S0895435611003945

WHO Collaborating Centre for Drug Statistics Methodology. (2009, 17 Dec 2009). *Definition and general considerations.* Retrieved from http://www.whocc.no/ddd/definition_and_general_considera/

Willis, E., Reynolds, L., & Helen, K. (2012). *Understanding the Australian Health Care System*: Elsevier Health Sciences APAC.

Winkelmayer, W. C., Asslaber, M., Bucsics, A., Burkhardt, T., Schautzer, A., Wieninger, P., et al. (2010). Impact of reimbursement changes on statin use among patients with diabetes in Austria. *Wiener Klinische Wochenschrift, 122*(3-4), 89-94. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20213375

Wolffenbuttel, B. H. R., Mahla, G., Muller, D., Pentrup, A., & Black, D. M. (1998). Efficacy and safety of a new cholesterol synthesis inhibitor, atorvastatin, in comparison with simvastatin and pravastatin, in subjects with hypercholesterolemia. *The Netherlands Journal of Medicine, 52*(4), 131-137. Retrieved from http://www.sciencedirect.com/science/article/pii/S0300297797000922. doi:http://dx.doi.org/10.1016/S0300-2977(97)00092-2

World Health Organization, WHO International Working Group for Drug Statistics Methodology, WHO Collaborating Centre for Drug Statistics Methodology, & WHO Collaborating Centre for Drug Utilization Research and Clinical Pharmacological Services. (2003). *Introduction to drug utilization research*. Oslo, Norway. Retrieved from http://apps.who.int/medicinedocs/pdf/s4876e/s4876e.pdf

Yee, H. S., & Fong, N. T. (1998). Atorvastatin in the Treatment of Primary Hypercholesterolemia and Mixed Dyslipidemias. *Annals of Pharmacotherapy, 32*(10), 1030-1043. Retrieved from http://aop.sagepub.com/content/32/10/1030.abstract. doi:10.1345/aph.17231

Yfantopoulos, J. (2008). Pharmaceutical Pricing and Reimbursement Reforms in Greece. *The European Journal of Health Economics, 9*(1), 87-97. Retrieved from http://www.jstor.org/stable/40283700

Appendices

Table A1 Data extraction form for systematic review

SIGN	**Data extraction form**	
Study identification (*Include author, title, year of publication, journal title, pages*)		
Guideline topic:	Key Question No:	Completed by:
Study design		

This form is intended for use with studies where no comparison group has been used. These will normally constitute level 3 evidence and do not require completion of a methodology checklist. Please indicate which of the following most closely matches the design of the study covered by this form *(tick one box)*:

- **Before and after study:** (Patients are assessed once before, and once after an intervention has been applied and allowed time to work). □
- **Case series**: (A report on a series of patients with a condition and/or outcome of interest). □
- **Interrupted time series**: (A study where patients are assessed at regular intervals before, during, and after an intervention has been applied. Assessment must be made more than once post-intervention). □
- **Retrospective cohort**: (Study where data is gathered retrospectively on a defined group of patients). □
- **Single case design**: (Patients are given a treatment and their condition monitored. Treatment is then withdrawn and their condition monitored for a further period. This sequence may be repeated. Despite the name, the study may cover a number of patients but each individual patient will be assessed and reported separately). □
- **Single cohort**: (A defined group of patients is observed over a period of time during which they receive an exposure or treatment, and the results recorded. There is no comparison group. These studies are often **retrospective cohorts**). □
- **Other design**: (Please describe briefly)

Non-systematic reviews and **consensus reports** (including consensus guidelines) constitute level 4 evidence, and do not require data extraction of this kind.

The following information is required to complete evidence tables facilitating cross-study comparisons. Please complete all sections for which information is available. *PLEASE PRINT CLEARLY*		
1	Where is this study carried out? *Country or state involved*	
2	What types of data source used? *Name the data source – e.g. PBS Medicare Australia (if appropriate)*	
3	How many patients are included in this study? *Please indicate number, at the time the study began, and the number of dropouts (if appropriate).*	
4	What are the main characteristics of the patient population? *Include all relevant characteristics –* • *age,* • *sex,* • *ethnic origin,* • *co-morbidity,* • *disease status*	
5	What kind of drugs included in this study?	
6	What intervention (treatment, procedure) is being investigated in this study? *List all cost containment policies covered by the study.*	
7	How long are patients followed-up in the study? *The length of time patients is followed from beginning participation in the study. Note specified end points used to decide end of follow-up (e.g. death, complete cure). Note if follow-up period is shorter than originally planned.*	

8	What outcome measure(s) are used in the study? *List all outcomes that are used to assess effectiveness of the interventions.*	
9	What size of effect is identified in the study? *List all measures of effect in the units used in the study – e.g. absolute or relative risk, NNT, etc. Include p values and any confidence intervals that are provided.*	
10	How was this study funded? *List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.*	
11	What is the limitation of this study? *List all the limitation.*	
12	Does this study help to answer your key question? *Summarise the main conclusions of the study and indicate how it relates to the key question. Include any comment on the choice of study design, likely validity of the conclusions, etc.*	

Table A2 References to studies excluded from this review

1.	Aaltonen, K., Ragupathy, R., Tordoff, J., Reith, D., & Norris, P. (2010). The impact of pharmaceutical cost containment policies on the range of medicines available and subsidized in Finland and New Zealand. *Value in health, 13*(1), 148-156.
2.	Aaserud, M., Dahlgren, A. T., Kosters, J. P., Oxman, A. D., Ramsay, C., & Sturm, H. (2006). Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. *Cochrane Database of Systematic Reviews*(2), CD005979.
3.	Abdelgawad, T., & Egbuonu-Davis, L. (2006). Preferred drug lists and Medicaid prescriptions. *Pharmacoeconomics, 24 Suppl 3*, 55-63.
4.	Almarsdóttir, A. B. A. B., & Traulsen, J. M. J. M. (2005). Cost-containment as part of pharmaceutical policy. *Pharmacy world & science : PWS, 27*(3), 144-148.
5.	Andersson, F. (1993). Methodological aspects of international drug price comparisons. *Pharmacoeconomics, 4*(4), 247-256.
6.	Angus, D. E., & Karpetz, H. M. (1998). Pharmaceutical policies in Canada. Issues and challenges. *Pharmacoeconomics, 14 Suppl 1*, 81-96.
7.	Antonanzas, F., Oliva, J., Pinillos, M., & Juarez, C. (2007). Economic aspects of the new Spanish laws on pharmaceutical preparations. *Eur J Health Econ, 8*(3), 297-300.
8.	Atella, V. (2000). Drug cost containment policies in Italy: are they really effective in the long-run?: The case of minimum reference price. *Health Policy, 50*(3), 197-218.
9.	Austvoll-Dahlgren, A., Aaserud, M., Vist, G., Ramsay, C., Oxman, A. D., Sturm, H., et al. (2008). Pharmaceutical policies: effects of cap and co-payment on rational drug use. *Cochrane Database of Systematic Reviews*(1), CD007017.
10.	Barr, C. (1994). The future research agenda. A view from the pharmaceutical industry. *Pharmacoeconomics, 6 Suppl 1*, 61-62.
11.	Barr, J. T., & Schumacher, G. E. (1994). Applying decision analysis to pharmacy management and practice decisions. *Top Hosp Pharm Manage, 13*(4), 60-71.

12. Barros, P. P., & Nunes, L. C. (2010). The impact of pharmaceutical policy measures: An endogenous structural-break approach. *Social Science & Medicine, 71*(3), 440-450.

13. Barry, D. R., & Romig, B. (2003). The cost of drugs: a policy conundrum of global proportions. *N C Med J, 64*(6), 287-288.

14. Bergen, D. C. (1997). Special report from the World Federation of Neurology. The worldwide impact of new drugs: development, distribution, and use. *Epilepsia, 38*(9), 1050-1053.

15. Bergman, D., Hoadley, J., Kaye, N., Crowley, J., & Hostetter, M. (2006). Using clinical evidence to manage pharmacy benefits: experiences of six states. *Issue Brief (Commonw Fund)*(899), 1-14.

16. Bernardi, A., & Pegoraro, R. (2003). Italian drug policy: ethical aims of essential assistance levels. *Health Care Anal, 11*(4), 279-286.

17. Berndt, E. R. (2002). Pharmaceuticals in U.S. health care: determinants of quantity and price. *J Econ Perspect, 16*(4), 45-66.

18. Bonafede, M., Dick, A., Noyes, K., Klein, J. D., & Brown, T. (2008). The effect of acupuncture utilization on healthcare utilization. *Med Care, 46*(1), 41-48.

19. Bono, J. D., & Crawford, S. Y. (2010). Impact of Medicare Part D on independent and chain community pharmacies in rural Illinois--A qualitative study. *Research in social & administrative pharmacy : RSAP, 6*(2), 110-120.

20. Boonen, L., van der Geest, S. A., Schut, F. T., & Varkevisser, M. (2010). Pharmaceutical policy in the Netherlands: from price regulation towards managed competition. *Pharmaceutical Markets and Insurance Worldwide, Advances in Health Economics and Health Services Research, 22*, 53-76.

21. Bougher, D. J. (2001). Reinventing the government role in pharmacotherapy. *Can J Clin Pharmacol, 8 Suppl A*, 45A-47A.

22. Boulet, A. P., & Tessier, G. (1997). Reference-based pricing in British Columbia: implications for cardiologists--an analysis. *Can J Cardiol, 13*(1), 46-51.

23. Bourgault, C., Elstein, E., Le Lorier, J., & Suissa, S. (1999). Reference-based pricing of prescription drugs: exploring the equivalence of angiotensin-converting-enzyme inhibitors. *Canadian Medical Association Journal, 161*(3), 255-260.

24. Breuil-Genier, P. (2000). The control of health care spending in short and long terms: notes on the French experiment (1996-1998). *Cah Sociol Demogr Med, 40*(1), 35-46.

25. Briesacher, B. A., Zhao, Y., Madden, J. M., Zhang, F., Adams, A. S., Tjia, J., et al. (2011). Medicare part D and changes in prescription drug use and cost burden: national estimates for the Medicare population, 2000 to 2007. *Medical Care, 49*(9), 834-841.

26. Brown, E. (1999). Cox-2 inhibitors. *Physician Exec, 25*(1), 74-76.

27. Buchanan, R. J., & Smith, S. R. (1994). Medicaid policies for HIV-related prescription drugs. *Health Care Financ Rev, 15*(3), 43-61.

28. Burstall, M. L. (1997). The management of the cost and utilisation of pharmaceuticals in the United Kingdom. *Health Policy, 41, Supplement*(0), S27-S43.

29. Busse, R., Schreyögg, J., & Henke, K.-D. (2005). Regulation of pharmaceutical markets in Germany: improving efficiency and controlling expenditures? *The International Journal of Health Planning and Management, 20*(4), 329-349.

30. Canton, E., & Westerhout, E. (1999). A model for the Dutch pharmaceutical market. *Health Econ, 8*(5), 391-402.

31. Carroll, J. (2002). When success sours: PBMs under scrutiny. *Manag Care, 11*(9), 20-26.

32. Castellblanch, R. (2003). Challenging pharmaceutical industry political power in Maine and Vermont. *J Health Polit Policy Law, 28*(1), 109-132.

33. Chalkidou, K., Anderson, G. F., & Faden, R. (2011). Eliminating drug price differentials across government programmes in the USA. *Health economics, policy, and law, 6*(1), 43-64.

34. Chen, L.-C., Schafheutle, E. I., & Noyce, P. R. (2009). The impact of nonreferral outpatient co-payment on medical care utilization and expenditures in Taiwan. *Research in Social and Administrative Pharmacy, 5*(3), 211-224.

35. Contoyannis, P., Hurley, J., Grootendorst, P., Jeon, S.-H., & Tamblyn, R. (2005). Estimating the price elasticity of expenditure for prescription drugs in the

presence of non-linear price schedules: an illustration from Quebec, Canada. *Health Economics, 14*(9), 909-923.

36. Cook, A. E. (1999). Strategies for containing drug costs: implications for a Medicare benefit. *Health Care Financ Rev, 20*(3), 29-37.

37. Coombes, M. E., Morgan, S. G., Barer, M. L., & Pagliccia, N. (2004). Who's the fairest of them all? Which provincial pharmacare model would best protect Canadians against catastrophic drug costs? *Healthc Q, 7*(4), suppl 13-19.

38. Cox, E. R., Jernigan, C., Coons, S. J., & Draugalis, J. L. (2001). Medicare beneficiaries' management of capped prescription benefits. *Med Care, 39*(3), 296-301.

39. Cunningham, P. J. (2002). Prescription drug access: not just a Medicare problem. *Issue Brief Cent Stud Health Syst Change*(51), 1-4.

40. Cutler, T. W., Stebbins, M. R., Lai, E., Smith, A. R., & Lipton, H. L. (2008). Problem-based learning using the online Medicare Part D Plan Finder tool. *American Journal of Pharmaceutical Education, 72*(3), 47.

41. Danzon, P., & Towse, A. (2002). The economics of gene therapy and of pharmacogenetics. *Value in Health, 5*(1), 5-13.

42. Danzon, P. M., & Ketcham, J. D. (2004). Reference pricing of pharmaceuticals for Medicare: evidence from Germany, The Netherlands, and New Zealand. *Front Health Policy Res, 7*, 1-54.

43. Data, J. L. (1998). Potential stifling effects of pharmaco-economics and regulatory policies. *Am J Cardiol, 81*(8A), 34F-35F.

44. Davidova, J., Praznovcova, L., & Lundborg, C. S. (2008). Pricing and reimbursement of pharmaceuticals in the Czech Republic and Sweden. *Pharmacy World & Science, 30*(1), 57-64.

45. Davis, P. (2004). "Tough but fair"? The active management of the New Zealand drug benefits scheme by an independent Crown agency. *Australian Health Review, 28*(2), 171-181.

46. Daw, J. R., & Morgan, S. G. (2012). Stitching the gaps in the Canadian public drug coverage patchwork?: a review of provincial pharmacare policy changes from 2000 to 2010. *Health Policy, 104*(1), 19-26.

47. de Bakker, D. H., Coffie, D. S., Heerdink, E. R., van Dijk, L., & Groenewegen, P. P. (2007). Determinants of the range of drugs prescribed in general practice: a cross-sectional analysis. *BMC Health Serv Res, 7*, 132.

48. de Wolf, P., Brouwer, W. B. F., & Rutten, F. F. H. (2005). Regulating the Dutch pharmaceutical market: improving efficiency or controlling costs? *International Journal of Health Planning & Management, 20*(4), 351-374.

49. Denis, A., Mergaert, L., Fostier, C., Cleemput, I., & Simoens, S. (2010). A comparative study of European rare disease and orphan drug markets. *Health Policy, 97*(2-3), 173-179.

50. Dhalla, I., & Laupacis, A. (2008). Moving from opacity to transparency in pharmaceutical policy. *CMAJ, 178*(4), 428-431.

51. Diaby, V., & Lachaine, J. (2011). An application of a proposed framework for formulary listing in low-income countries: the case of Cote d'Ivoire. *Applied Health Economics and Health Policy, 9*(6), 389-402.

52. Dickson, M. (1992). The pricing of pharmaceuticals: an international comparison. *Clinical Therapeutics, 14*(4), 604-610; discussion 603.

53. Domino, M. E., Martin, B. C., Wiley-Exley, E., Richards, S., Henson, A., Carey, T. S., et al. (2011). Increasing time costs and copayments for prescription drugs: an analysis of policy changes in a complex environment. *Health Services Research, 46*(3), 900-919.

54. Domino, M. E., Olinick, J., Sleath, B., Leinwand, S., Byrns, P. J., & Carey, T. (2004). Restricting patients' medication supply to one month: saving or wasting money? *American Journal of Health-System Pharmacy, 61*(13), 1375-1379.

55. Doran, E., & Robertson, J. (2009). Australia's pharmaceutical cost sharing policy: reducing waste or affordability? *Australian Health Review, 33*(2), 231-240.

56. Drummond, M., Jonsson, B., & Rutten, F. (1997). The role of economic evaluation in the pricing and reimbursement of medicines. *Health Policy, 40*(3), 199-215.

57. Drummond, M. F., & Mason, A. R. (2007). European perspective on the costs and cost-effectiveness of cancer therapies. *J Clin Oncol, 25*(2), 191-195.

58. Duckett, S. J. (2004). Drug policy down under: Australia's pharmaceutical benefits scheme. *Health care financing review, 25*(3), 55-67.

59. Dylst, P., Vulto, A., & Simoens, S. (2011). The impact of reference-pricing systems in Europe: a literature review and case studies. *Expert Review of Pharmacoeconomics & Outcomes Research, 11*(6), 729-737.

60. Ess, S. M., Schneeweiss, S., & Szucs, T. D. (2003). European Healthcare Policies for Controlling Drug Expenditure. *PharmacoEconomics, 21*(2), 89-103.

61. Fahlman, C., Stuart, B., & Zacker, C. (2001). Community pharmacist knowledge and behavior in collecting drug copayments from Medicaid recipients. *Am J Health Syst Pharm, 58*(5), 389-395.

62. Fattore, G., & Jommi, C. (1998). The new pharmaceutical policy in Italy. *Health Policy, 46*(1), 21-41.

63. Fattore, G., & Jommi, C. (2008). The last decade of Italian pharmaceutical policy: instability or consolidation? *Pharmacoeconomics, 26*(1), 5-15.

64. Federal Medicaid policy. Year end issue brief. (2008). *Issue Brief Health Policy Track Serv*, 1-50.

65. Fise, T. (2004). Medicare prescription drugs and reform: what the new law will mean to gastroenterologists and their patients. *Am J Gastroenterol, 99*(5), 775-776.

66. Flizar, G. M., Klein, S. R., & Monson, R. A. (2006). HHS moves forward with E-prescribing standards. *J Healthc Inf Manag, 20*(3), 10-12.

67. Fraeyman, J., Van Hal, G., De Loof, H., Remmen, R., De Meyer, G. R. Y., & Beutels, P. (2012). Potential impact of policy regulation and generic competition on sales of cholesterol lowering medication, antidepressants and acid blocking agents in Belgium. *Acta Clinica Belgica, 67*(3), 160-171.

68. Frank, R. G. (2001). Prescription drug prices: why do some pay more than others do? *Health Aff (Millwood), 20*(2), 115-128.

69. Frank, R. G. (2003). Government commitment and regulation of prescription drugs. *Health Affairs, 22*(3), 46-48.

70. Frank, R. G. (2004). Prescription-drug prices. *New England Journal of Medicine, 351*(14), 1375-1377.

71. Freemantle, N. (1999). Does the UK National Health Service need a fourth hurdle for pharmaceutical reimbursement to encourage the more efficient prescribing of pharmaceuticals? *Health Policy, 46*(3), 255-265.

72.	Freemantle, N., & Bloor, K. (1996). Lessons from international experience in controlling pharmaceutical expenditure. I: influencing patients. *BMJ, 312*(7044), 1469-1471.
73.	Frencher, S. K., Jr., & Glied, S. (2006). The Medicare Prescription Drug Improvement and Modernization Act: prescription drugs and academic medicine. *Acad Med, 81*(9), 812-816.
74.	Freund, D. A., Willison, D., Reeher, G., Cosby, J., Ferraro, A., & O'Brien, B. (2000). Outpatient pharmaceuticals and the elderly: policies in seven nations. *Health Affairs, 19*(3), 259-266.
75.	Galizzi, M. M., Ghislandi, S., & Miraldo, M. (2011). Effects of reference pricing in pharmaceutical markets: a review. *PharmacoEconomics, 29*(1), 17-33.
76.	Ganguli, G. (2003). Consumers devise drug cost-cutting measures: medical and legal issues to consider. *Health Care Manag (Frederick), 22*(3), 275-281.
77.	Garrison, L., & Towse, A. (2003). The Drug Budget Silo Mentality in Europe: An Overview. *Value in Health, 6*, S1-S9.
78.	Geitona, M., Zavras, D., Hatzikou, M., & Kyriopoulos, J. (2006). Generics market in Greece: the pharmaceutical industry's beliefs. *Health Policy, 79*(1), 35-48.
79.	Gellad, W. F., Schneeweiss, S., Brawarsky, P., Lipsitz, S., & Haas, J. S. (2008). What if the federal government negotiated pharmaceutical prices for seniors? An estimate of national savings. *Journal of general internal medicine, 23*(9), 1435-1440.
80.	Gemmill, M. C., Costa-Font, J., & McGuire, A. (2007). In search of a corrected prescription drug elasticity estimate: a meta-regression approach. *Health Economics, 16*(6), 627-643.
81.	Gencarelli, D. M. (2003). Medicaid prescription drug coverage: state efforts to control costs. *NHPF Issue Brief*(790), 1-17.
82.	Ghislandi, S., Krulichova, I., & Garattini, L. (2005). Pharmaceutical policy in Italy: towards a structural change? *Health Policy, 72*(1), 53-63.
83.	Gibson, T. B., Ozminkowski, R. J., & Goetzel, R. Z. (2005). The effects of prescription drug cost sharing: a review of the evidence. *The American journal of managed care, 11*(11), 730-740.

84. Ginsburg, P. B. (1993). Expenditure limits and cost containment. *Inquiry, 30*(4), 389-399.

85. Giuliani, G., Selke, G., & Garattini, L. (1998). The German experience in reference pricing. *Health Policy, 44*(1), 73-85.

86. Goetzel, R. Z., Ozminkowski, R. J., Meneades, L., Stewart, M., & Schutt, D. C. (2000). Pharmaceuticals--cost or investment? An employer's perspective. *J Occup Environ Med, 42*(4), 338-351.

87. Goldman, D. P. (2006). Varying Pharmacy Benefits with Clinical Status: The Case of Cholesterol-Lowering Therapy. *Medical Benefits, 23*(6), 3-3.

88. Grice, S. (2003). In that case: a pharmaceutical company that makes generic versions of commonly used drugs has produced a generic of a proprietary drug widely prescribed in a particular service. Response. *N Z Bioeth J, 4*(3), 22-24.

89. Griffin, M. T. (1991). AIDS drugs & the pharmaceutical industry: a need for reform. *American Journal of Law & Medicine, 17*(4), 363-410.

90. Gross, D. J., Ratner, J., Perez, J., & Glavin, S. L. (1994). International pharmaceutical spending controls: France, Germany, Sweden, and the United Kingdom. *Health care financing review, 15*(3), 127-140.

91. Guillén, A. M., & Cabiedes, L. (2003). Reforming pharmaceutical policies in the European Union: a "penguin effect"? *International Journal of Health Services, 33*(1), 1-28.

92. Hailey, D. (1997). Australian economic evaluation and government decisions on pharmaceuticals, compared to assessment of other health technologies. *Soc Sci Med, 45*(4), 563-581.

93. Harris, B. N., West, D. S., Johnson, J., Hong, S. H., & Stowe, C. D. (2004). Effects on the cost and utilization of proton pump inhibitors from adding over-the counter omeprazole to drug benefit coverage in a state employee health plan. *J Manag Care Pharm, 10*(5), 449-455.

94. Headen, A., & Masia, N. (2005). Exploring the potential link between Medicaid access restrictions, physician location, and health disparities. *Am J Manag Care, 11 Spec No*, Sp21-26.

95. Heinrich, C. J., & Hill, C. J. (2008). Role of state policies in the adoption of naltrexone for substance abuse treatment. *Health Serv Res, 43*(3), 951-970.

96. Hesselgrave, B. L. (2003). Helping to manage the high cost of rare diseases. *Manag Care Q, 11*(1), 1-6.

97. Hillman, A. L., Pauly, M. V., Escarce, J. J., Ripley, K., Gaynor, M., Clouse, J., et al. (1999). Financial incentives and drug spending in managed care. *LDI Issue Brief, 4*(1), 1-4.

98. Hirst, N. G., Whitty, J. A., Synnott, R. L., Eley, D. S., & Scuffham, P. A. (2011). Predictors of government subsidized pharmaceutical use in patients with diabetes or cardiovascular disease in a primary care setting: evidence from a prospective randomized trial. *Journal of medical economics, 14*(6), 698-704.

99. Hodgkin, D., Merrick, E. L., & Hiatt, D. (2012). The relationship of antidepressant prescribing concentration to treatment duration and cost. *The journal of mental health policy and economics, 15*(1), 3-11.

100. Hospital antibiotic control measures in the UK. Working Party of the British Society for Antimicrobial Chemotherapy. (1994). *J Antimicrob Chemother, 34*(1), 21-42.

101. Hu, S., Chen, W., Cheng, X., Chen, K., Zhou, H., & Wang, L. (2001). Pharmaceutical cost-containment policy: experiences in Shanghai, China. *Health Policy and Planning, 16*(suppl 2), 4-9.

102. Huskamp, H. A. (2003). Managing Psychotropic Drug Costs: Will Formularies Work? *Health Affairs, 22*(5), 84-96.

103. Huskamp, H. A. (2005). Pharmaceutical cost management and access to psychotropic drugs: the U.S. context. *Int J Law Psychiatry, 28*(5), 484-495.

104. Iglehart, J. K. (1991). Germany's health care system (2). *N Engl J Med, 324*(24), 1750-1756.

105. Iglehart, J. K. (2003). Medicare and drug pricing. *N Engl J Med, 348*(16), 1590-1597.

106. Jenkings, K. N., & Barber, N. (2004). What constitutes evidence in hospital new drug decision making? *Soc Sci Med, 58*(9), 1757-1766.

107.	Jimenez-Rubio, D., & Hernandez-Quevedo, C. (2010). Explaining the demand for pharmaceuticals in Spain: are there differences in drug consumption between foreigners and the Spanish population? *Health Policy, 97*(2-3), 217-224.
108.	Johnson, J. T., Neill, K. K., & Davis, D. A. (2011). Five-year examination of utilization and drug cost outcomes associated with benefit design changes including reference pricing for proton pump inhibitors in a state employee health plan. *Journal of managed care pharmacy : JMCP, 17*(3), 200-212.
109.	Johnson, R. E., Goodman, M. J., Hornbrook, M. C., & Eldredge, M. B. (1997). The effect of increased prescription drug cost-sharing on medical care utilization and expenses of elderly health maintenance organization members. *Med Care, 35*(11), 1119-1131.
110.	Kalish, S. C., Bohn, R. L., & Avorn, J. (1997). Policy analysis of the conversion of histamine2 antagonists to over-the-counter use. *Med Care, 35*(1), 32-48.
111.	Kammer, C. (2002). Pharmaceuticals: pharmaceutical cost control measures: year end report-2002. *Issue Brief Health Policy Track Serv*, 1-14.
112.	Kanavos, P. (1999). Financing pharmaceuticals in transition economies. *Croat Med J, 40*(2), 244-259.
113.	Kanavos, P. (2007). Do generics offer significant savings to the UK National Health Service? *Curr Med Res Opin, 23*(1), 105-116.
114.	Kanavos, P., & Reinhardt, U. (2003). Reference Pricing For Drugs: Is It Compatible With U.S. Health Care? *Health Affairs, 22*(3), 16-30.
115.	Kane, N. M. (1997). Pharmaceutical cost containment and innovation in the United States. *Health Policy, 41 Suppl*, S71-89.
116.	Kane, N. M., & Saltman, R. B. (1997). Comparative experience in home care and pharmaceutical policy. *Health Policy, 41 Suppl*, S1-7.
117.	Kelton, C. M., Rebelein, R. P., Heaton, P. C., Ferrand, Y., & Guo, J. J. (2008). Differences in the cost of antidepressants across state Medicaid programs. *J Ment Health Policy Econ, 11*(1), 33-47.
118.	Kesselheim, A. S., & Choudhry, N. K. (2008). The international pharmaceutical market as a source of low-cost prescription drugs for U.S. patients. *Ann Intern Med, 148*(8), 614-619.

119.	Kilian, J., & Stubbings, J. (2007). Medicare Part D: selected issues for pharmacists and beneficiaries in 2007. *J Manag Care Pharm, 13*(1), 59-65.
120.	King, M. A., & Roberts, M. S. (2007). The influence of the Pharmaceutical Benefits Scheme (PBS) on inappropriate prescribing in Australian nursing homes. *Pharm World Sci, 29*(1), 39-42.
121.	Kleinke, J. D. (2004). Access versus excess: value-based cost sharing for prescription drugs. *Health Aff (Millwood), 23*(1), 34-47.
122.	Kling, J. R., Mullainathan, S., Shafir, E., Vermeulen, L. C., & Wrobel, M. V. (2012). Comparison friction: experimental evidence from medicare drug plans. *The quarterly journal of economics, 127*(1), 199-235.
123.	Koopmanschap, M. A., & Rutten, F. F. H. (2003). The Drug Budget Silo Mentality: The Dutch Case. *Value in Health, 6*, S46-S51.
124.	Kosterlitz, J. (1993). Rx: higher prices. *Natl J (Wash), 25*(7), 396-399.
125.	Krcmery, V., & Gould, I. M. (1999). Antibiotic policies in Central/Eastern Europe (CEE) after 1990. *J Hosp Infect, 43 Suppl*, S269-274.
126.	Lai, C. J., Smith, A. R., Stebbins, M. R., Cutler, T. W., & Lipton, H. L. (2011). Promoting interprofessional collaboration: pharmacy students teaching current and future prescribers about Medicare Part D. *Journal of managed care pharmacy : JMCP, 17*(6), 439-448.
127.	Lamphere-Thorpe, J. A., Johnston, W. P., Kilpatrick, K. E., & Norwood, G. J. (1994). Who cares what it costs to dispense a Medicaid prescription? *Health care financing review, 15*(3), 9-24.
128.	Latham, S. R. (2003). Pharmaceutical costs: an overview and analysis of legal and policy responses by the states. *Journal of Legal Medicine, 24*(2), 141-173.
129.	Law, M. R., Lu, C. Y., Soumerai, S. B., Graves, A. J., LeCates, R. F., Zhang, F., et al. (2010). Impact of two Medicaid prior-authorization policies on antihypertensive use and costs among Michigan and Indiana residents dually enrolled in Medicaid and Medicare: results of a longitudinal, population-based study. *Clinical Therapeutics, 32*(4), 729-741; discussion 716.
130.	Law, M. R., Ystma, A., & Morgan, S. G. (2011). The short-term impact of Ontario's generic pricing reforms. *PLoS One, 6*(7), e23030.

131. Le Pen, C. (1996). Drug Pricing and Reimbursement in France: Towards a New Model? 1 [Miscellaneous]. *PharmacoEconomics, 2*, 26-36.

132. Le Pen, C. (2003). The Drug Budget Silo Mentality: The French Case. *Value in Health, 6*, S10-S19.

133. Lee, J., Fischer, M. A., Shrank, W. H., Polinski, J. M., & Choudhry, N. K. (2012). A Systematic review of reference pricing: implications for US prescription drug spending. *The American journal of managed care, 18*(11), e429-437.

134. LeLorier, J., Bell, A., Bougher, D. J., Cox, J. L., & Turpie, A. G. G. (2008). Drug reimbursement policies in Canada--need for improved access to critical therapies. *Annals of Pharmacotherapy, 42*(6), 869-873.

135. Levinson, W., & Laupacis, A. (2006). A call for fairness in formulary decisions. *Arch Intern Med, 166*(1), 16-18.

136. Levy, R. (2002). Costs and benefits of pharmaceuticals: the value equation for older Americans. *Care Manag J, 3*(3), 135-142.

137. Levy, R. A. (1992a). Clinical aspects of therapeutic substitution. *Pharmacoeconomics, 1*(Suppl 1), 41-44.

138. Levy, R. A. (1992b). Prescription Cost Sharing: Economic and Health Impacts, and Implications for Health Policy. *PharmacoEconomics, 2*(3), 219-237.

139. Liaw, S. T., Pearce, C. M., Chondros, P., McGrath, B. P., Piggford, L., & Jones, K. (2003). Doctors' perceptions and attitudes to prescribing within the Authority Prescribing System. *Med J Aust, 178*(5), 203-206.

140. Lichtenberg, F. R. (2011). Pharmaceutical companies' variation of drug prices within and among countries can improve long-term social well-being. *Health Affairs, 30*(8), 1539-1544.

141. Light, D. W., & Lexchin, J. (2004). Will lower drug prices jeopardize drug research? A policy fact sheet. *Am J Bioeth, 4*(1), W1-4.

142. Liu, Y. M., & Hsieh, C. R. (2012). New drugs and the growth of health expenditure: evidence from diabetic patients in Taiwan. *Health Economics, 21*(5), 496-513.

143. Ljungkvist, M. O., Andersson, D., & Gunnarsson, B. (1997). Cost and utilisation of pharmaceuticals in Sweden. *Health Policy, 41 Suppl*, S55-69.

144.	Lofgren, H. (1998). The Pharmaceutical Benefits Scheme and the shifting paradigm of welfare policy. *Australian Health Review, 21*(2), 111-123.
145.	Lofgren, H. (2004). Generic drugs: international trends and policy developments in Australia. *Australian Health Review, 27*(1), 39-48.
146.	López-Casasnovas, G., & Puig-Junoy, J. (2000). Review of the literature on reference pricing. *Health Policy, 54*(2), 87-123.
147.	MacEachern, L. (2003). Pharmaceuticals issue brief: managed care drug formularies: year end report-2003. *Issue Brief Health Policy Track Serv*, 1-8.
148.	Maclure, M., Carleton, B., & Schneeweiss, S. (2007). Designed delays versus rigorous pragmatic trials: lower carat gold standards can produce relevant drug evaluations. *Med Care, 45*(10 Supl 2), S44-49.
149.	Mapelli, V., & Lucioni, C. (2003). Spending on Pharmaceuticals in Italy: Macro Constraints with Local Autonomy. *Value in Health, 6*, S31-S45.
150.	Mariko, M. (1991). Drugs: towards sound prescribing and pricing. *World Health Forum, 12*(1), 34-37.
151.	Marwaha, A. (2002). Exploring the rise in American pharmaceutical prices. *Pharos of Alpha Omega Alpha Honor Medical Society, 65*(2), 11-15.
152.	Mason, J., Freemantle, N., Nazareth, I., Eccles, M., Haines, A., & Drummond, M. (2001). When is it cost-effective to change the behavior of health professionals? *Jama, 286*(23), 2988-2992.
153.	Masso, A. R., & O'Hara, J. (1993). State legislation inhibiting the operation of managed care pharmacy programs increases costs. *Benefits Q, 9*(3), 46-51.
154.	Maynard, A., & Bloor, K. (2003). Dilemmas In Regulation Of The Market For Pharmaceuticals. *Health Affairs, 22*(3), 31-41.
155.	Mays, G. P., Hurley, R. E., & Grossman, J. M. (2001). Consumers face higher costs as health plans seek to control drug spending. *Issue Brief Cent Stud Health Syst Change*(45), 1-4.
156.	McKeon, E. (2003). Prescription drug access: the ANA adopts principles to evaluate congressional Medicare proposals. *Am J Nurs, 103*(9), 106.

157. Mendelson, D., Ramchand, R., Abramson, R., & Tumlinson, A. (2002). Prescription drugs in nursing homes: managing costs and quality in a complex environment. *NHPF Issue Brief*(784), 1-18.

158. Menkes, D. B., & Woodall, A. A. (2003). In that case: a pharmaceutical company that makes generic versions of commonly used drugs has produced a generic of a proprietary drug widely prescribed in a particular service. Response. *N Z Bioeth J, 4*(3), 22, 24-25.

159. Merkur, S., & Mossialos, E. (2007). A pricing policy towards the sourcing of cheaper drugs in Cyprus. *Health Policy, 81*(2-3), 368-375.

160. Metge, C., Black, C., Peterson, S., & Kozyrskyj, A. L. (1999). The population's use of pharmaceuticals. *Med Care, 37*(6 Suppl), Js42-59.

161. Meyer, P. R. (1996). Towards a research agenda for pharmaceutical issues. *Pharmacoeconomics, 10 Suppl 2*, 130-134; discussion 135-138.

162. Miller, M. P., Furberg, C. D., Small, R. H., Millman, F. M., Ambrosius, W. T., Harshbarger, J. S., et al. (2007). Controlling prescription drug expenditures: a report of success. *American Journal of Managed Care, 13*(8), 473-480.

163. Milligan, C. J., Jr. (2005). Impact of the Medicare prescription drug benefit on home- and community-based services waiver programs. *Issue Brief (Commonw Fund)*(815), 1-8.

164. Mitton, C. R., McMahon, M., Morgan, S., & Gibson, J. (2006). Centralized drug review processes: are they fair? *Soc Sci Med, 63*(1), 200-211.

165. Moran, A., & Goldman, L. (2008). Eliminating out-of-pocket drug costs may improve outcomes after myocardial infarction--but at what cost to Medicare? *Nature clinical practice. Cardiovascular medicine, 5*(10), 606-607.

166. Morgan, S., Bassett, K., & Mintzes, B. (2004). An outcomes-based approach to decisions about drug coverage policies in British Columbia. *Psychiatr Serv, 55*(11), 1230-1232.

167. Morgan, S., Hanley, G., & Greyson, D. (2009). Comparison of tiered formularies and reference pricing policies: a systematic review. *Open Med, 3*(3), e131-139.

168.	Morgan, S. G. (2002). Quantifying components of drug expenditure inflation: the British Columbia seniors' drug benefit plan. *Health Services Research, 37*(5), 1243-1266.
169.	Morgan, S. G. (2006). Prescription drug expenditures and population demographics. *Health Serv Res, 41*(2), 411-428.
170.	Morgan, S. G., Agnew, J. D., & Barer, M. L. (2004). Seniors' prescription drug cost inflation and cost containment: evidence from British Columbia. *Health Policy, 68*(3), 299-307.
171.	Mossinghoff, G. J. (1994). The need for health care reform. *Health Syst Rev, 27*(3), 5-6.
172.	Motheral, B. R. (2011). Pharmaceutical step-therapy interventions: a critical review of the literature. *Journal of managed care pharmacy : JMCP, 17*(2), 143-155.
173.	Mott, D. A., Thorpe, J. M., Thorpe, C. T., Kreling, D. H., & Gadkari, A. S. (2010). Effects of Medicare Part D on drug affordability and use: Are seniors with prior high out-of-pocket drug spending affected more? *Research in social & administrative pharmacy : RSAP, 6*(2), 90-99.
174.	Mucha, L., Masia, N. A., & Axelsen, K. J. (2006). Per-patient-per-month drug costs in Medicare Part D protected classes. *PharmacoEconomics, 24 Suppl 3*, 79-84.
175.	Munnich, F. E., & Sullivan, K. (1994). The impact of recent legislative change in Germany. *Pharmacoeconomics, 6 Suppl 1*, 22-27.
176.	Narciso, S. (2005). Retailing policies for generic medicines. *Int J Health Care Finance Econ, 5*(2), 165-190.
177.	Narine, L., Senathirajah, M., & Smith, T. (1999). Evaluating reference-based pricing: initial findings and prospects. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne, 161*(3), 286-288.
178.	Neugut, A. I., Subar, M., Wilde, E. T., Stratton, S., Brouse, C. H., Hillyer, G. C., et al. (2011). Association between prescription co-payment amount and compliance with adjuvant hormonal therapy in women with early-stage breast cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 29*(18), 2534-2542.

179. Neumann, P. J., Lin, P. J., Greenberg, D., Berger, M., Teutsch, S., Mansley, E., et al. (2006). Do drug formulary policies reflect evidence of value? *Am J Manag Care, 12*(1), 30-36.

180. Okunade, A. A. (1998). Financing structure dynamics and other determinants of Medicaid pharmaceutical expenditures, 1993-1996. *Journal of Health Care Finance, 25*(1), 59-71.

181. Okunade, A. A. (2001). The impact of 1990 Medicaid drug rebates policy on access to prescriptions. *Journal of Health & Social Policy, 12*(3), 33-51.

182. Oliver, A. J., Ikegami, N., & Ikeda, S. (1997). Japan's aging population. Implications for healthcare. *Pharmacoeconomics, 11*(4), 306-318.

183. Oliver, A. J., Ikegami, N., & Ikeda, S. (1999). Effect of Japanese government policy on hospital pharmaceutical profit levels. *J Health Serv Res Policy, 4*(1), 27-32.

184. Olson, B. M., Armstrong, E. P., Grizzle, A. J., & Nichter, M. A. (2003). Industry's perception of presenting pharmacoeconomic models to managed care organizations. *J Manag Care Pharm, 9*(2), 159-167.

185. Ortolon, K. (2000). Prescribing a cure. Texas lawmakers look to reduce prescription drug spending. *Tex Med, 96*(12), 54-59.

186. Page, R. L., 2nd, Barton, P., & Nair, K. (2008). Effect of cost-sharing for prescription medications on health outcomes in older adults: a critical review of the literature and potential implications for managed care. *Consult Pharm, 23*(1), 44-54.

187. Palumbo, F. B., Schondelmeyer, S. W., Miller, D. W., & Speedie, S. M. (1992). Battered bottom lines: the impact of eroding pharmaceutical discounts on health-care institutions. *Am J Hosp Pharm, 49*(5), 1177-1185.

188. Patel, U. D., & Davis, M. M. (2006). Falling into the doughnut hole: drug spending among beneficiaries with end-stage renal disease under Medicare Part D plans. *J Am Soc Nephrol, 17*(9), 2546-2553.

189. Pavcnik, N. (2002). Do Pharmaceutical Prices Respond to Potential Patient Out-of-Pocket Expenses? *The RAND Journal of Economics, 33*(3), 469-487.

190. Pearce, M. J., & Begg, E. J. (1992). A Review of Limited Lists and Formularies: Are They Cost-Effective? [Review]. *PharmacoEconomics, 1*(3), 191-202.

191. Pelc, A., & Castan, J. P. (1994). New developments in pricing and drug reimbursement in France. *Pharmacoeconomics, 6 Suppl 1*, 28-35.

192. Pelton, L. E., Strutton, D., & Smith, M. C. (1993). Future pharmacists and public initiatives to control retail drug prices: a political economy framework. *Health Mark Q, 10*(3-4), 241-259.

193. Peters, C. P. (2010). Medicaid payment for generic drugs: achieving savings and access. *Issue Brief*(839), 1-16.

194. Pitaknetinan, K., Tangcharoensathien, V., Supachutikul, A., Bennett, S., & Mills, A. (1999). Profit, payment and pharmaceutical practices: perspectives from hospitals in Bangkok. *Health Policy, 46*(3), 179-194.

195. Pracht, E. E., & Moore, W. J. (2003). Interest groups and state Medicaid drug programs. *Journal of Health Politics, Policy & Law, 28*(1), 9-39.

196. Probyn, A. J. (2004). Some drugs more equal than others: pseudo-generics and commercial practice. *Australian health review : a publication of the Australian Hospital Association, 28*(2), 207-217.

197. Puig-Junoy, J. (2010). Impact of European Pharmaceutical Price Regulation on Generic Price Competition: A Review. *PharmacoEconomics, 28*(8), 649-663.

198. Qingyue, M., Liying, J., & Beibei, Y. (2011). *Cost-sharing mechanisms in health insurance schemes: A systematic review*. W. World Health Organization. Retrieved from http://www.who.int/alliance-hpsr/projects/alliancehpsr_chinasystematicreviewcostsharing.pdf

199. Rabbani, A., & Alexander, G. C. (2009). Cost savings associated with filling a 3-month supply of prescription medicines. *Applied Health Economics and Health Policy, 7*(4), 255-264.

200. Ratanawijitrasin, S., Soumerai, S. B., & Weerasuriya, K. (2001). Do national medicinal drug policies and essential drug programs improve drug use?: a review of experiences in developing countries. *Social Science & Medicine, 53*(7), 831-844.

201. Reinhardt, U. E. (2001). Perspectives on the pharmaceutical industry. *Health Aff (Millwood), 20*(5), 136-149.

202.	Reutzel, T. J. (1993). The nature and consequences of policies intended to contain costs in outpatient drug insurance programs. *Clinical Therapeutics, 15*(4), 752-764.
203.	Rigter, H. (1994). Recent public policies in The Netherlands to control pharmaceutical pricing and reimbursement. *PharmacoEconomics, 6 Suppl 1*, 15-21.
204.	Rocchi, F., Addis, A., & Martini, N. (2004). Current national initiatives about drug policies and cost control in Europe: the Italy example. *Journal of Ambulatory Care Management, 27*(2), 127-131.
205.	Roe, C. M., McNamara, A. M., & Motheral, B. R. (2002). Use of chronic medications among a large, commercially-insured US population. *Pharmacoepidemiol Drug Saf, 11*(4), 301-309.
206.	Rosen, Y., Yachelevich, N., Benedek, P., Grotto, I., Goldberg, A., Morad, Y., et al. (2004). No need to tax the sick: clinical guidelines for rofecoxib as an alternative effective method to the copayment policy in the advent of increasing pharmaceutical expenditures. *Mil Med, 169*(11), 932-936.
207.	Ross, E. A., & Bellamy, F. B. (2010). Reducing patient financial liability for hospitalizations: the physician role. *Journal of hospital medicine, 5*(3), 160-162.
208.	Roy, S., & Madhavan, S. S. (2009). Cluster analysis of state Medicaid prescription drug benefit programs based on potential determinants of per capita drug expenditure. *Research in social & administrative pharmacy : RSAP, 5*(1), 51-62.
209.	Rubino, M., Summers, K. H., Puenpatom, A., Fu, C., Ohsfeldt, R. L., & Ben-Joseph, R. H. (2011). A comparison of daily average consumption (DACON) of oxycodone and oxymorphone long-acting oral tablets. *Journal of managed care pharmacy : JMCP, 17*(5), 367-376.
210.	Sasso, A. T., Lurie, I. Z., Lee, J. U., & Lindrooth, R. C. (2006). The effects of expanded mental health benefits on treatment costs. *J Ment Health Policy Econ, 9*(1), 25-33.
211.	Scherer, F. M. (2004). The pharmaceutical industry--prices and progress. *New England Journal of Medicine, 351*(9), 927-932.

212. Schneeweiss, S. (2007). Reference drug programs: Effectiveness and policy implications. *Health Policy, 81*(1), 17-28.

213. Schneeweiss, S., Maclure, M., Dormuth, C., & Avorn, J. (2002). Pharmaceutical cost containment with reference-based pricing: time for refinements. *CMAJ, 167*(11), 1250-1251.

214. Schneeweiss, S., Maclure, M., & Soumerai, S. B. (2002). Prescription duration after drug copay changes in older people: methodological aspects. *Journal of the American Geriatrics Society, 50*(3), 521-525.

215. Schneeweiss, S., Maclure, M., Walker, A. M., Grootendorst, P., & Soumerai, S. B. (2001). On the evaluation of drug benefits policy changes with longitudinal claims data: the policy maker's versus the clinician's perspective. *Health Policy, 55*(2), 97-109.

216. Schneeweiss, S., Patrick, A. R., Maclure, M., Dormuth, C. R., & Glynn, R. J. (2007). Adherence to statin therapy under drug cost sharing in patients with and without acute myocardial infarction: a population-based natural experiment. *Circulation, 115*(16), 2128-2135.

217. Schneeweiss, S., Schöffski, O., & Selke, G. W. (1998). What is Germany's experience on reference based drug pricing and the etiology of adverse health outcomes or substitution? *Health Policy, 44*(3), 253-260.

218. Schneider, M. (1991). Health care cost containment in the Federal Republic of Germany. *Health care financing review, 12*(3), 87-101.

219. Schoffski, O., & Graf von der Schulenburg, J. M. (1997). Unintended effects of a cost-containment policy: results of a natural experiment in Germany. *Soc Sci Med, 45*(10), 1537-1539.

220. Searing, A. (2003). Prescription drug pricing: the consumer perspective. *N C Med J, 64*(6), 300-302.

221. Searles, A. (2009). The PBS in a globalised world: free trade and reference pricing. *Australian health review : a publication of the Australian Hospital Association, 33*(2), 186-191.

222. Seay, M. (2004). Pharmaceuticals issue brief: pharmaceutical assistance programs: year end report--2004. *Issue Brief Health Policy Track Serv*, 1-26.

223. Semin, S., & Guldal, D. (1996). The growing dependency in health care. Recent changes in medical technology imports and exports in Turkey. *Int J Technol Assess Health Care, 12*(4), 752-754.

224. Shea, D. G., Stuart, B. C., & Briesacher, B. (2003). Participation and crowd-out in a Medicare drug benefit: simulation estimates. *Health Care Financ Rev, 25*(2), 47-61.

225. Shulman, S. R. (1992). The reimbursement factor in pharmaceutical regulation: rebates, cost-effectiveness, and practice guidelines. *Pharmacoeconomics, 1*(Suppl 1), 21-27.

226. Shulman, S. R. (1994). The Canadian Patented Medicine Prices Review Board. New rules and new status. *Pharmacoeconomics, 6 Suppl 1*, 71-79.

227. Siegel, S. (2004). An introduction to the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. *Health Care Law Monthly*, 3-14.

228. Simoens, S. (2009). Developing competitive and sustainable Polish generic medicines market. *Croatian medical journal, 50*(5), 440-448.

229. Simoens, S. (2011). Pricing and reimbursement of orphan drugs: the need for more transparency. *Orphanet journal of rare diseases, 6*, 42.

230. Smith, A. J. (1991). Prescription charges and the evaluation of health policies. *Med J Aust, 154*(5), 303-304.

231. Soon, J. A., Meckley, L. M., Levine, M., Marciante, K. D., Fielding, D. W., & Ensom, M. H. (2007). Modelling costs and outcomes of expanded availability of emergency contraceptive use in British Columbia. *Can J Clin Pharmacol, 14*(3), e326-338.

232. Sorget, K. (2004). Pharmaceutical reimportation: economic and policy implications. *Manag Care, 13*(3 Suppl), 41-42.

233. Soumerai, S. B., Ross-Degnan, D., Fortess, E. E., & Abelson, J. (1993). A Critical Analysis of Studies of State Drug Reimbursement Policies: Research in Need of Discipline. *The Milbank Quarterly, 71*(2), 217-252.

234. Soumerai, S. B., Ross-Degnan, D., Fortess, E. E., & Walser, B. L. (1997). Determinants of change in Medicaid pharmaceutical cost sharing: does evidence affect policy? *Milbank Q, 75*(1), 11-34.

235. Speir, A. M., Rich, J. B., Crosby, I., & Fonner, E., Jr. (2009). Regional collaboration as a model for fostering accountability and transforming health care. *Seminars in thoracic and cardiovascular surgery, 21*(1), 12-19.

236. Stargardt, T. (2010). The impact of reference pricing on switching behaviour and healthcare utilisation: the case of statins in Germany. *The European journal of health economics : HEPAC : health economics in prevention and care, 11*(3), 267-277.

237. Steiner, D. J. (2012). Pharmaceuticals and medical devices: cost savings. Issue brief. *Issue Brief*, 1-33.

238. Stuart, B., & Grana, J. (1995). Are prescribed and over-the-counter medicines economic substitutes? A study of the effects of health insurance on medicine choices by the elderly. *Med Care, 33*(5), 487-501.

239. Stuart, B., & Zacker, C. (1999). Who bears the burden of Medicaid drug copayment policies? *Health Affairs, 18*(2), 201-212.

240. Summer, L., Nemore, P., & Finberg, J. (2008). Medicare Part D: how do vulnerable beneficiaries fare? *Issue Brief (Commonw Fund), 35*, 1-11.

241. Swann, R. A., & Clark, J. (1994). Antibiotic policies--relevance to general practitioner prescribing. Family Health Services Authority, Great Britain. *J Antimicrob Chemother, 33 Suppl A*, 131-135.

242. Sweeny, K. (2009). The impact of copayments and safety nets on PBS expenditure. *Australian Health Review, 33*(2), 215-230.

243. Szalay, T., Pazitny, P., Szalayova, A., Frisova, S., Morvay, K., Petrovic, M., et al. (2011). Slovakia health system review. *Health systems in transition, 13*(2), v-xxiii, 1-174.

244. Tamblyn, R. M. (2005). Prescription drug coverage: an essential service or a fringe benefit? *CMAJ, 173*(11), 1343-1344.

245. Tao, G., Kassler, W. J., & Rein, D. B. (2000). Medical care expenditures for genital herpes in the United States. *Sex Transm Dis, 27*(1), 32-38.

246. Thomas, L. G., 3rd. (1994). Pricing, regulation, and competitiveness. Lessons for the US from the Japanese pharmaceutical industry. *Pharmacoeconomics, 6 Suppl 1*, 67-70.

247. Towse, A. (2003). The Efficient Use Of Pharmaceuticals: Does Europe Have Any Lessons For A Medicare Drug Benefit? *Health Affairs, 22*(3), 42-45.

248. von der Schulenburg, J. M. G. (1997). Management of cost and utilization of pharmaceuticals in Germany. *Health Policy, 41, Supplement*(0), S45-S53.

249. Wall Street comes to Washington: market watchers and policy analysts evaluate the health care system. (2001). *Issue Brief Cent Stud Health Syst Change*(43), 1-4.

250. Walley, T., Mrazek, M., & Mossialos, E. (2005). Regulating pharmaceutical markets: improving efficiency and controlling costs in the UK. *The International Journal of Health Planning and Management, 20*(4), 375-398.

251. Watanabe, A. M., Dollens, R. W., Malatestinic, W. N., & Browne, R. A. (2004). Is a paradigm shift in US healthcare reimbursement inevitable? *Circulation, 109*(12), 1456-1459.

252. Watts, J. J., & Segal, L. (2009). Market failure, policy failure and other distortions in chronic disease markets. *BMC Health Services Research, 9*, 102.

253. Weinberg, M. (2009). Reforming patient assistance programs: perfect world meets real world. *Health Affairs, 28*(3), 839-842.

254. Werling, K., Abraham, S., & Strelec, J. (2007). The 340B Drug Pricing Program: an opportunity for savings, if covered entities such as disproportionate share hospitals and federally qualified health centers know how to interpret the regulations. *J Health Care Finance, 34*(2), 57-70.

255. Werner, P., & Vered, I. (2002). Women's willingness to pay out-of-pocket for drug treatment for osteoporosis before and after the enactment of regulations providing public funding: evidence from a natural experiment in Israel. *Osteoporos Int, 13*(3), 228-234.

256. Willison, D. J. (2002). More of the same is not enough. *Healthc Pap, 3*(1), 47-55; discussion 87-94.

257. Wilson, C. N. (1993). Health reform costly to hospital pharmacies. *Hosp Pharm, 28*(6), 554, 556, 559-560.

258. Wonder, M. J., Neville, A. M., & Parsons, R. (2006). Are Australians Able to Access New Medicines on the Pharmaceutical Benefits Scheme in a More

or Less Timely Manner? An Analysis of Pharmaceutical Benefits Advisory Committee Recommendations, 1999–2003. *Value in Health, 9*(4), 205-212.

259. Work, D. R., & Domino, M. E. (2003). The cost of prescription drugs: rising concerns over equity, fairness and access to essential care. *North Carolina Medical Journal, 64*(6), 270-274.

260. Yoongthong, W., Hu, S., Whitty, J. A., Wibulpolprasert, S., Sukantho, K., Thienthawee, W., et al. (2012). National drug policies to local formulary decisions in Thailand, China, and Australia: drug listing changes and opportunities. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research, 15*(1 Suppl), S126-131.

261. Yu, X., Li, C., Shi, Y., & Yu, M. (2010). Pharmaceutical supply chain in China: current issues and implications for health system reform. *Health Policy, 97*(1), 8-15.

262. Zeber, J. E., Grazier, K. L., Valenstein, M., Blow, F. C., & Lantz, P. M. (2007). Effect of a medication copayment increase in veterans with schizophrenia. *Am J Manag Care, 13*(6 Pt 2), 335-346.

263. Zechnich, A. D., Greenlick, M., Haxby, D., & Mullooly, J. (1998). Elimination of over-the-counter medication coverage in the Oregon Medicaid population: the impact on program costs and drug use. *Medical Care, 36*(8), 1283-1294.

264. Zhang, S., Doucette, W. R., Urmie, J. M., Xie, Y., & Brooks, J. M. (2010). Factors associated with independent pharmacy owners' satisfaction with Medicare Part D contracts. *Research in social & administrative pharmacy : RSAP, 6*(2), 121-129.

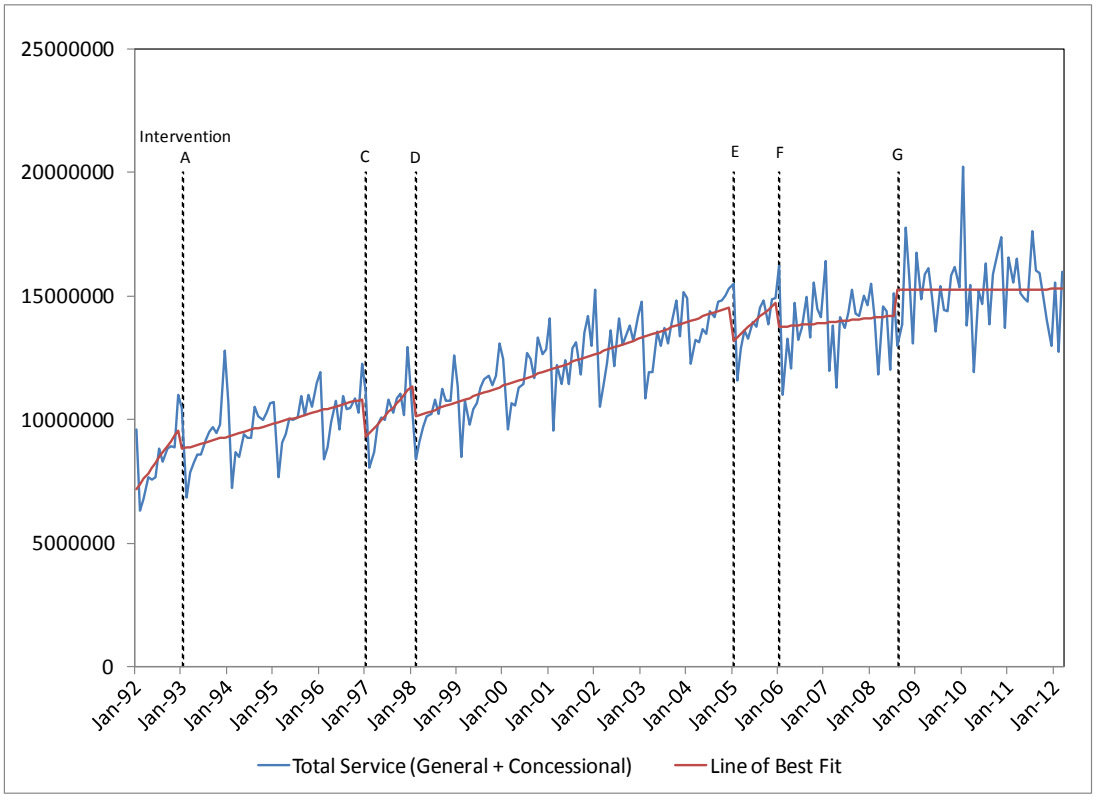


Figure A3 Number of services for general beneficiaries and concessional beneficiaries before and after interventions for all ATC main drug groups, January 1992 to March 2012

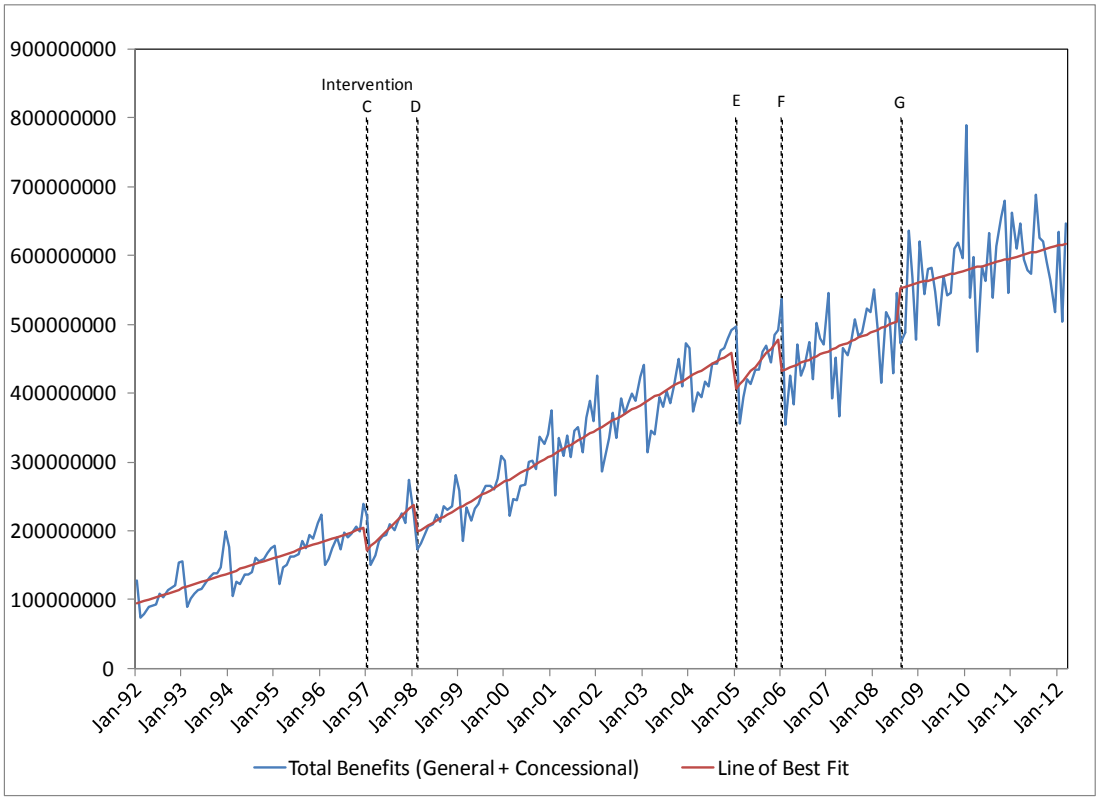
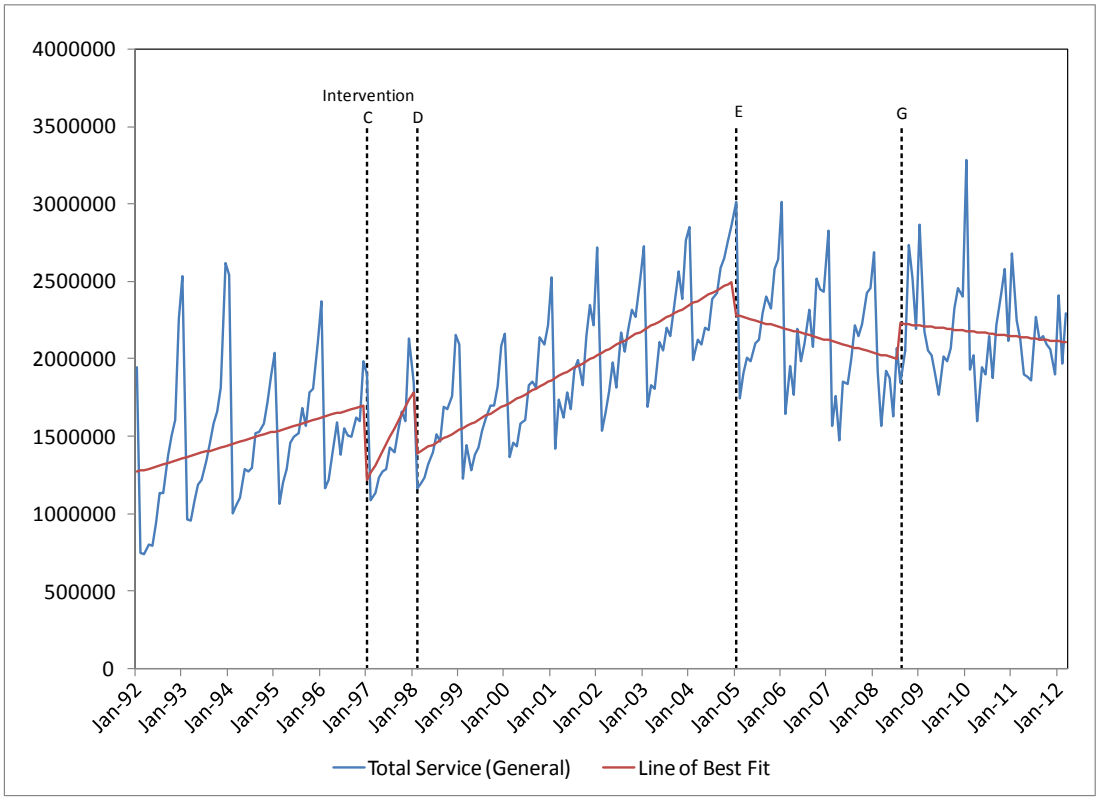


Figure A4 Total benefits for general beneficiaries and concessional beneficiaries before and after interventions for all ATC main drug groups, January 1992 to March 2012



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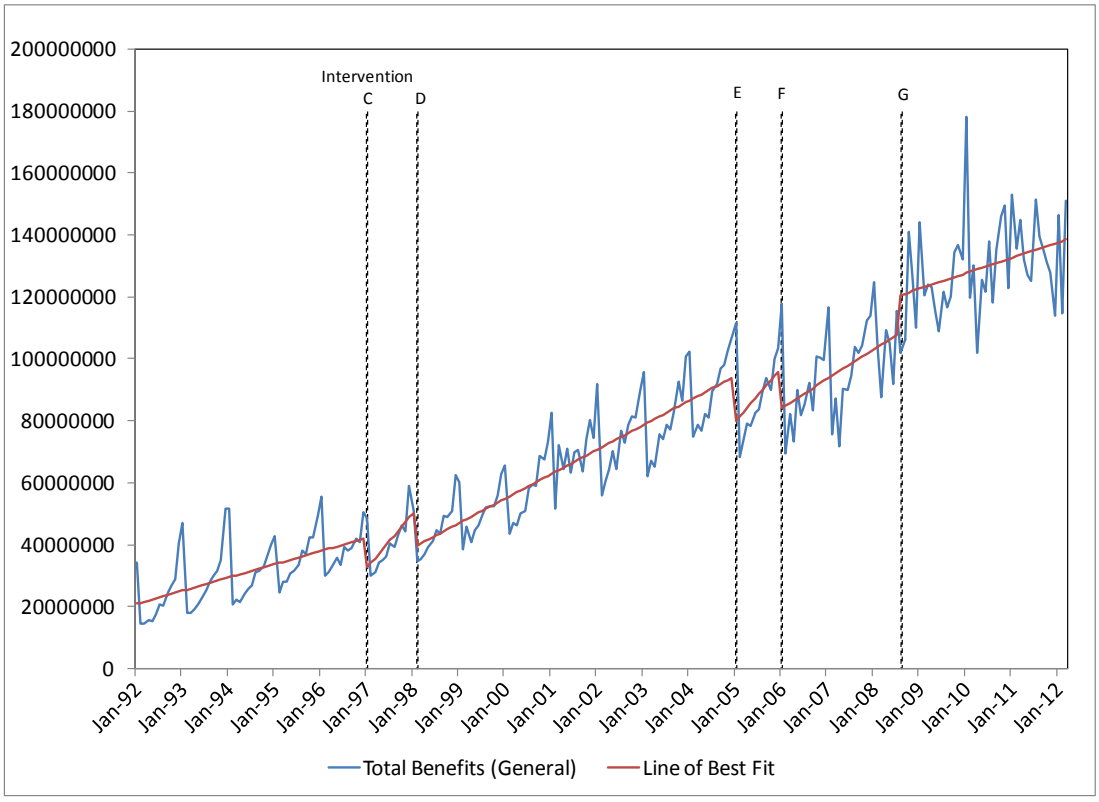

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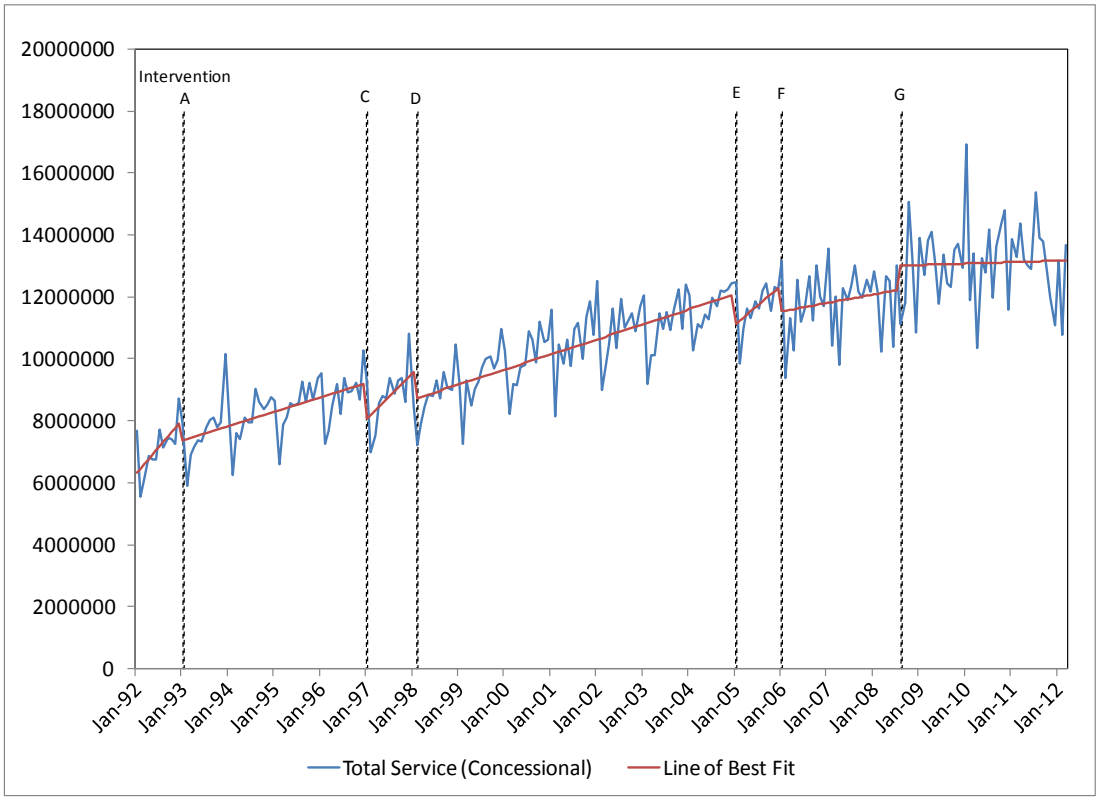

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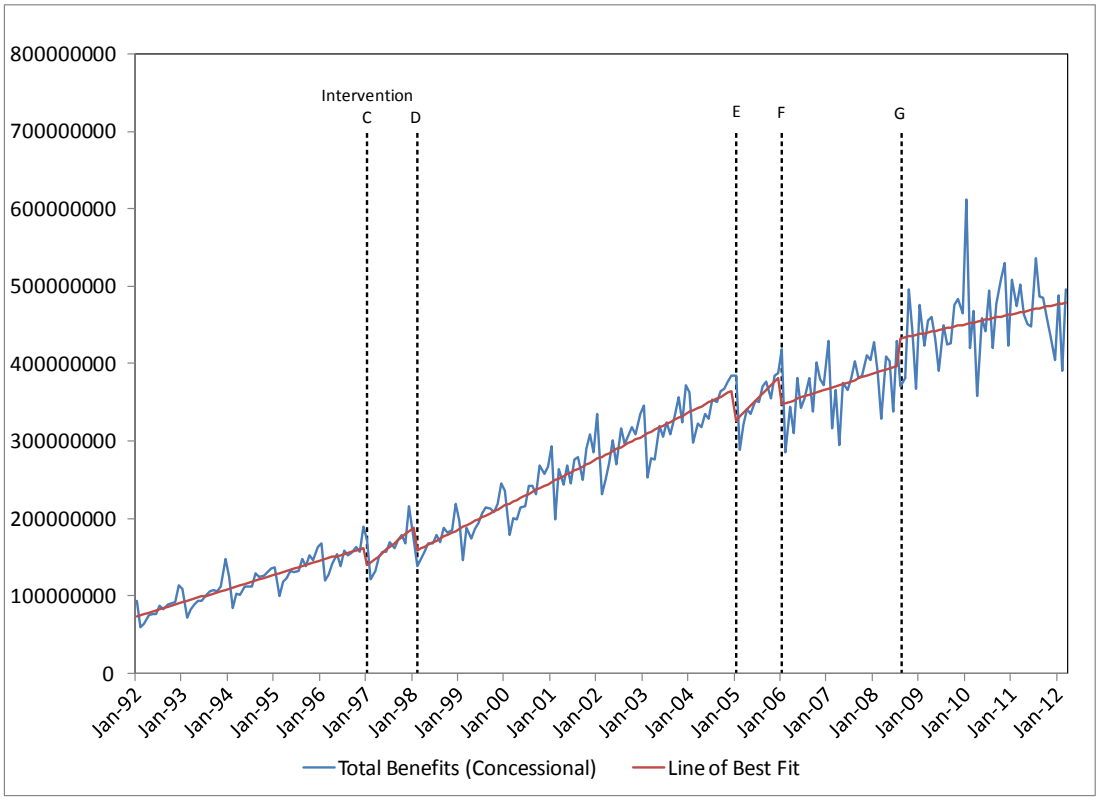

Figure A8 Total benefits for concessional beneficiaries before and after interventions for all ATC main drug groups, January 1992 to March 2012

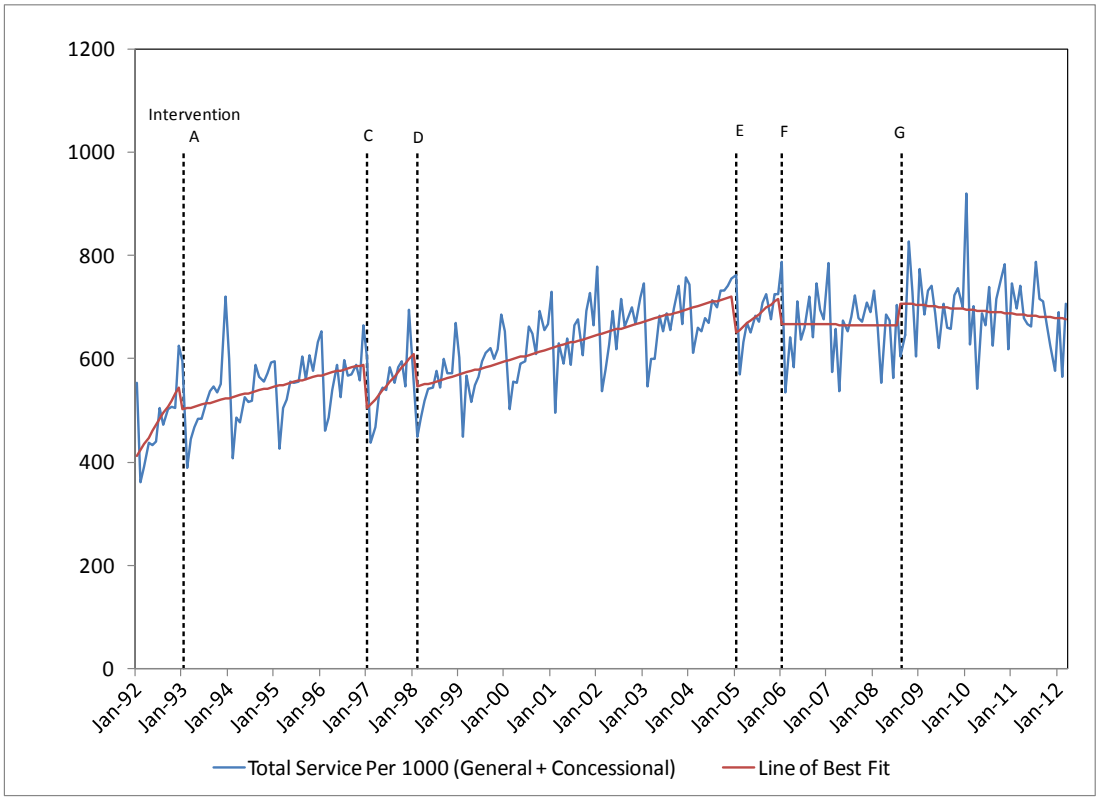

Figure A9 Number of services per 1000 general and concessional beneficiaries before and after interventions for all ATC main drug groups, January 1992 to March 2012

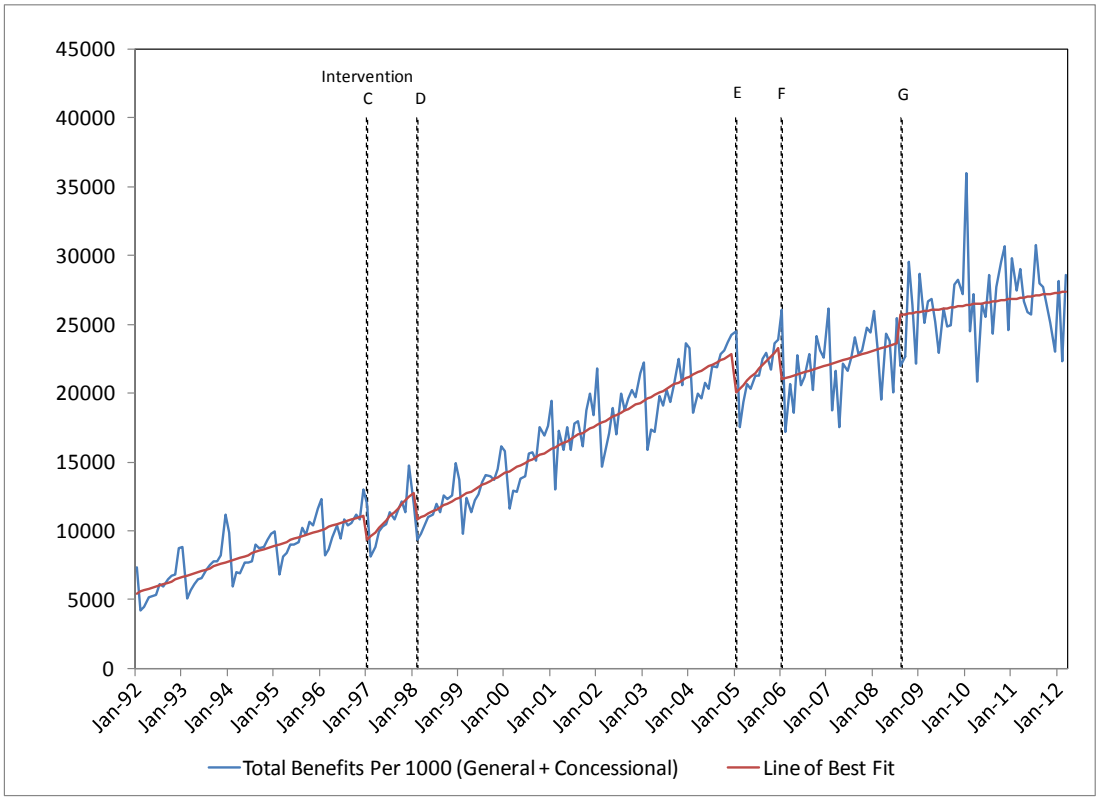

Figure A10 Total benefits per 1000 general and concessional beneficiaries before and after interventions for all ATC main drug groups, January 1992 to March 2012

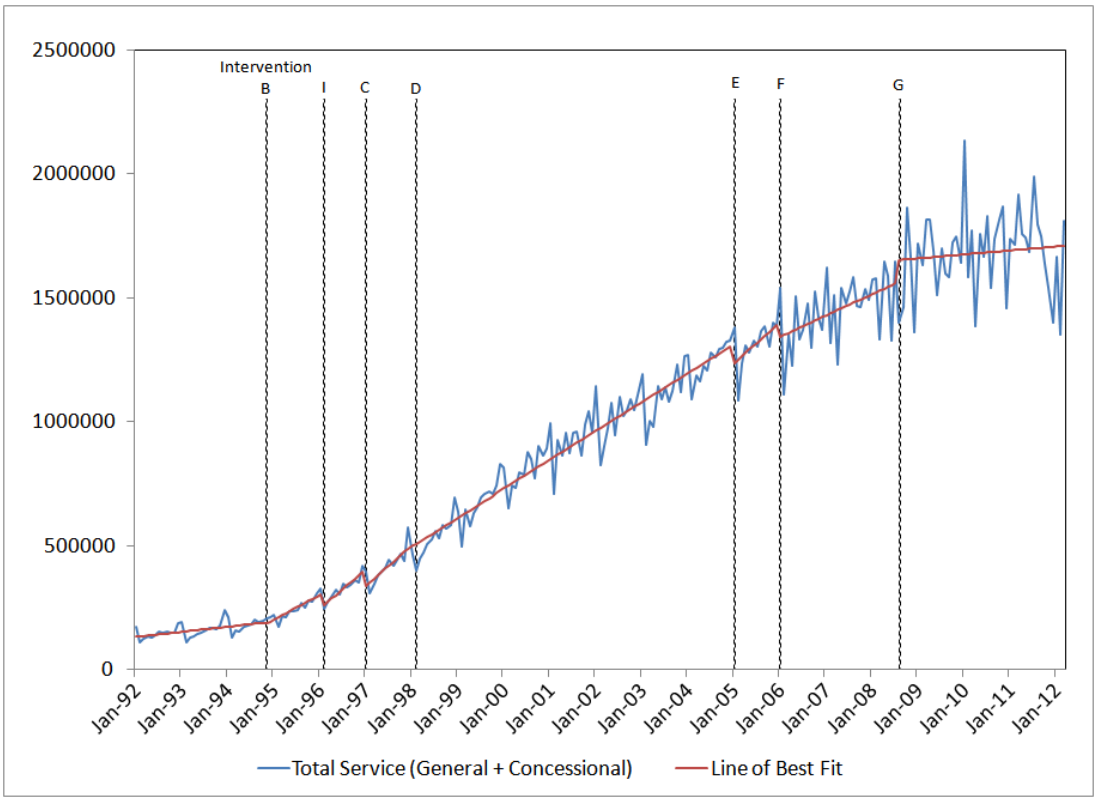

Figure A11 Number of services for general beneficiaries and concessional beneficiaries before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

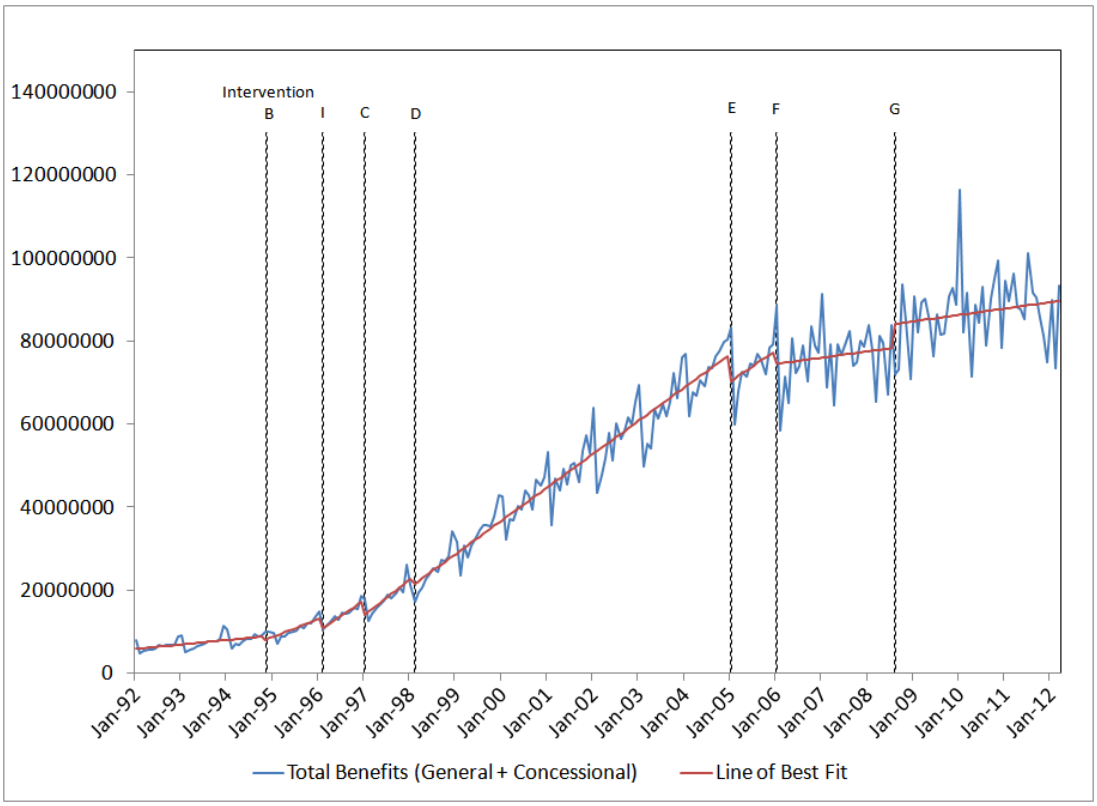

Figure A12 Number of benefits for general beneficiaries and concessional beneficiaries before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

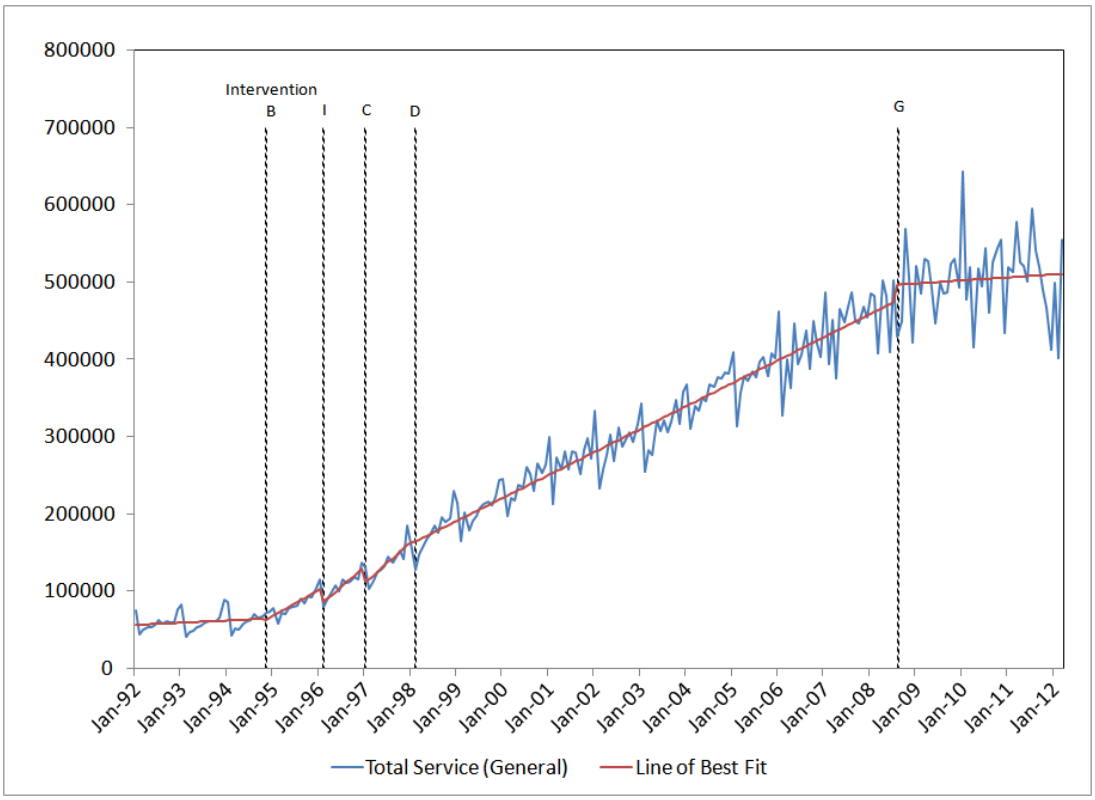

Figure A13 Number of services for general beneficiaries before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

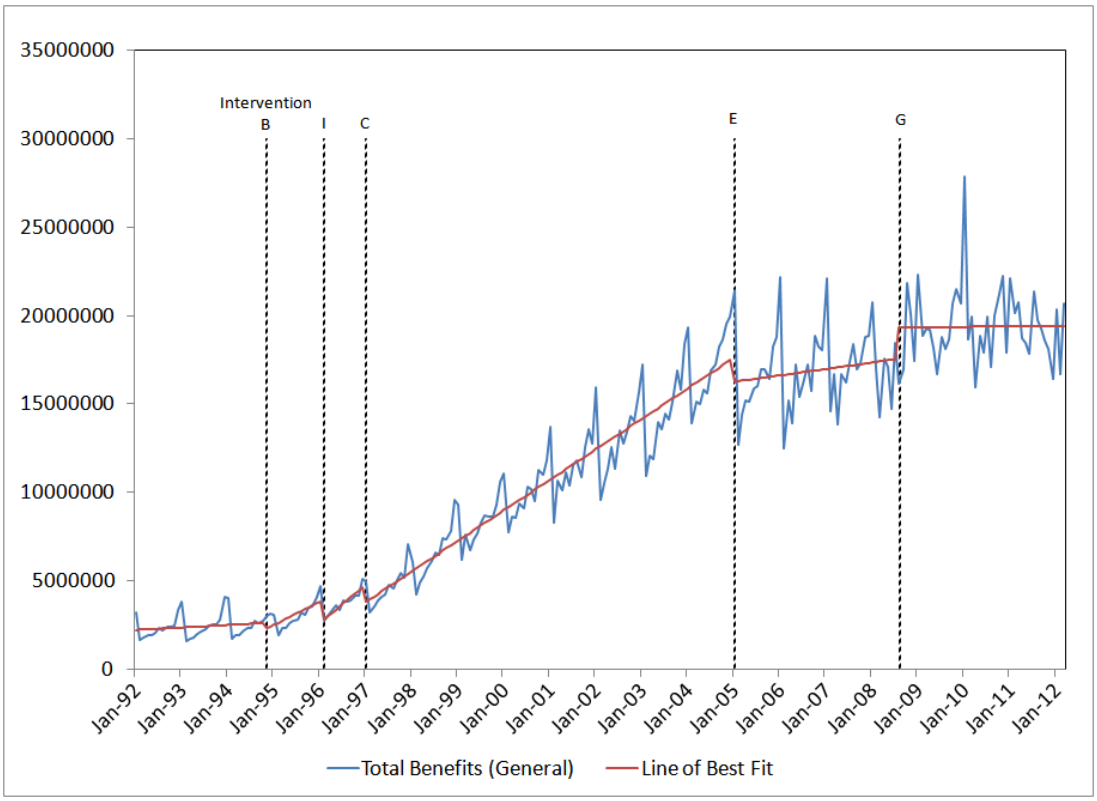

Figure A14 Number of benefits for general beneficiaries before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

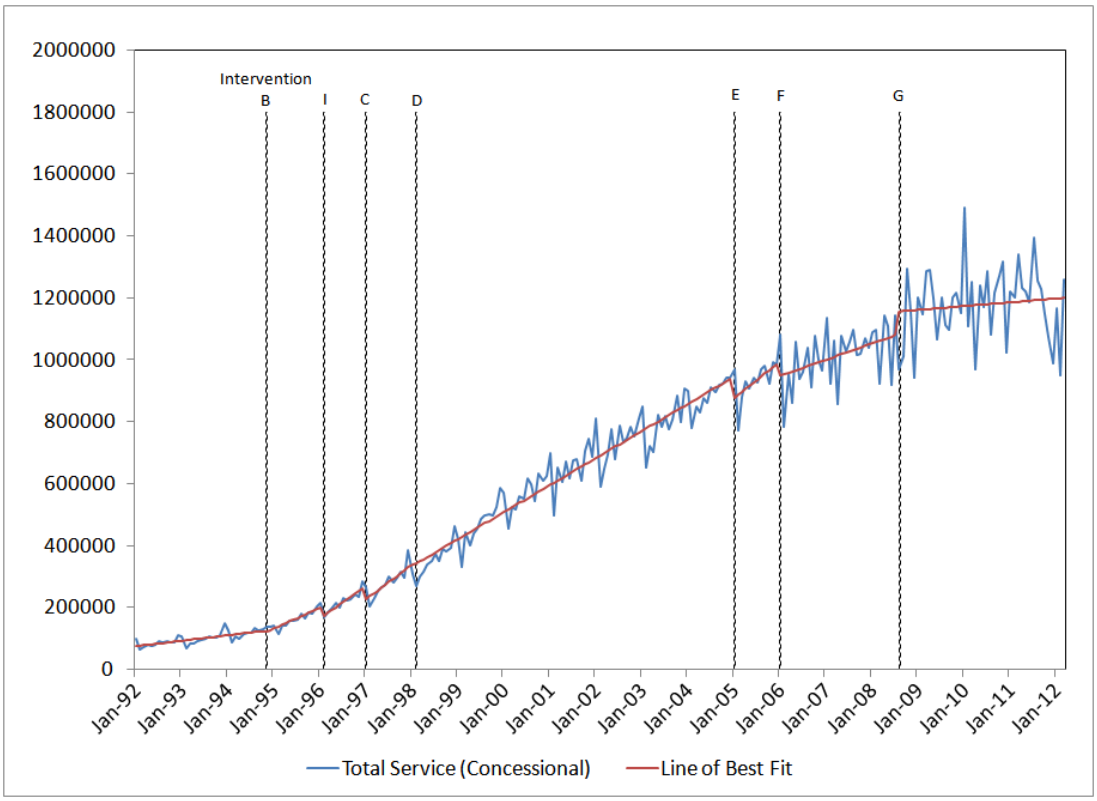

Figure A15 Number of services for concessional beneficiaries before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

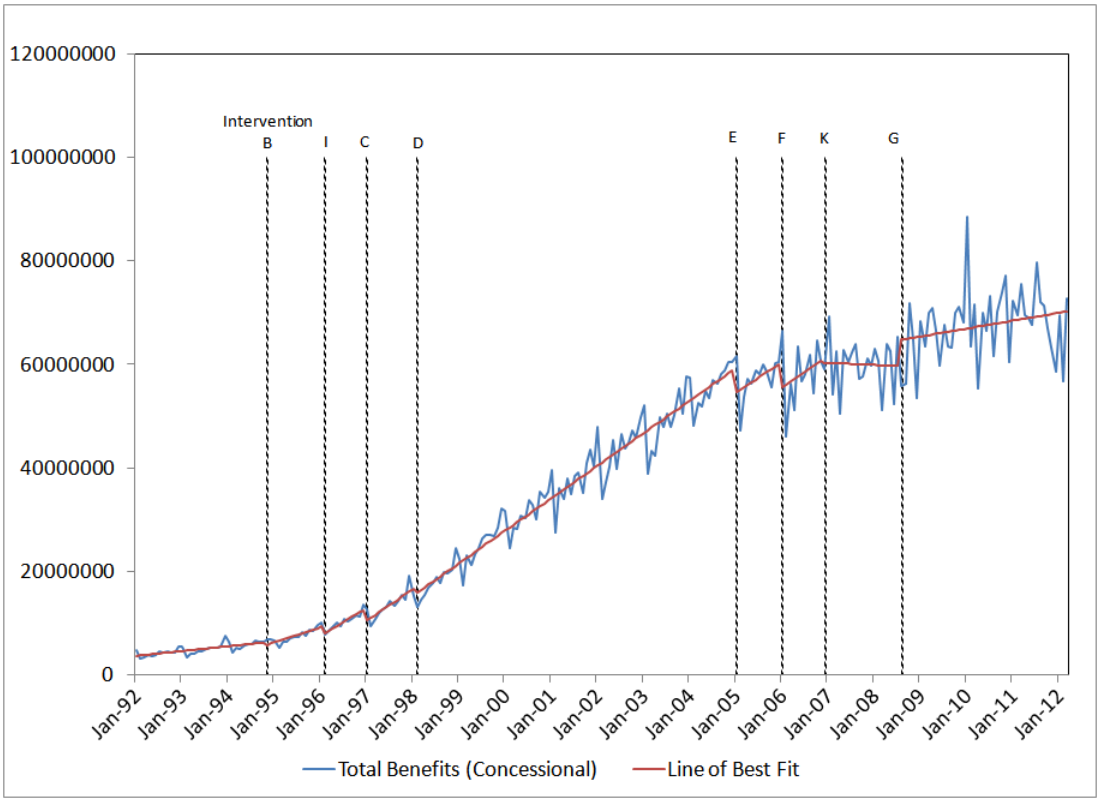

Figure A16 Number of benefits for concessional beneficiaries before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

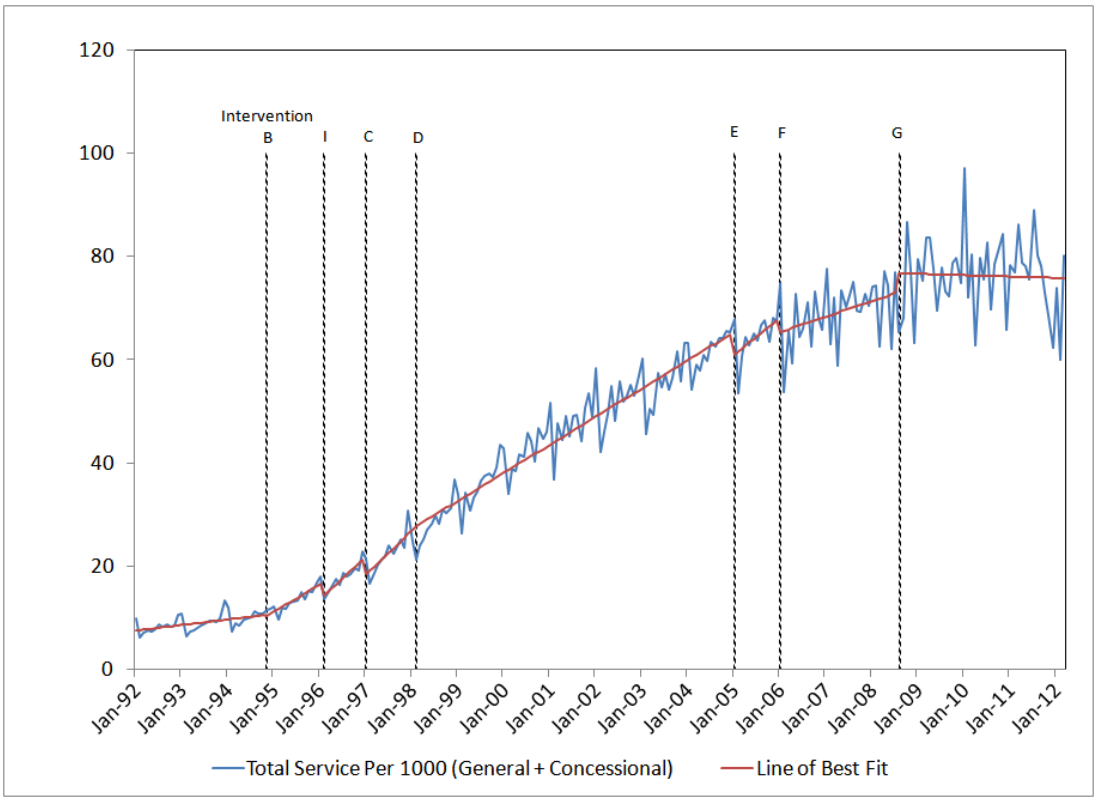

Figure A17 Total services per 1000 general and concessional beneficiaries before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

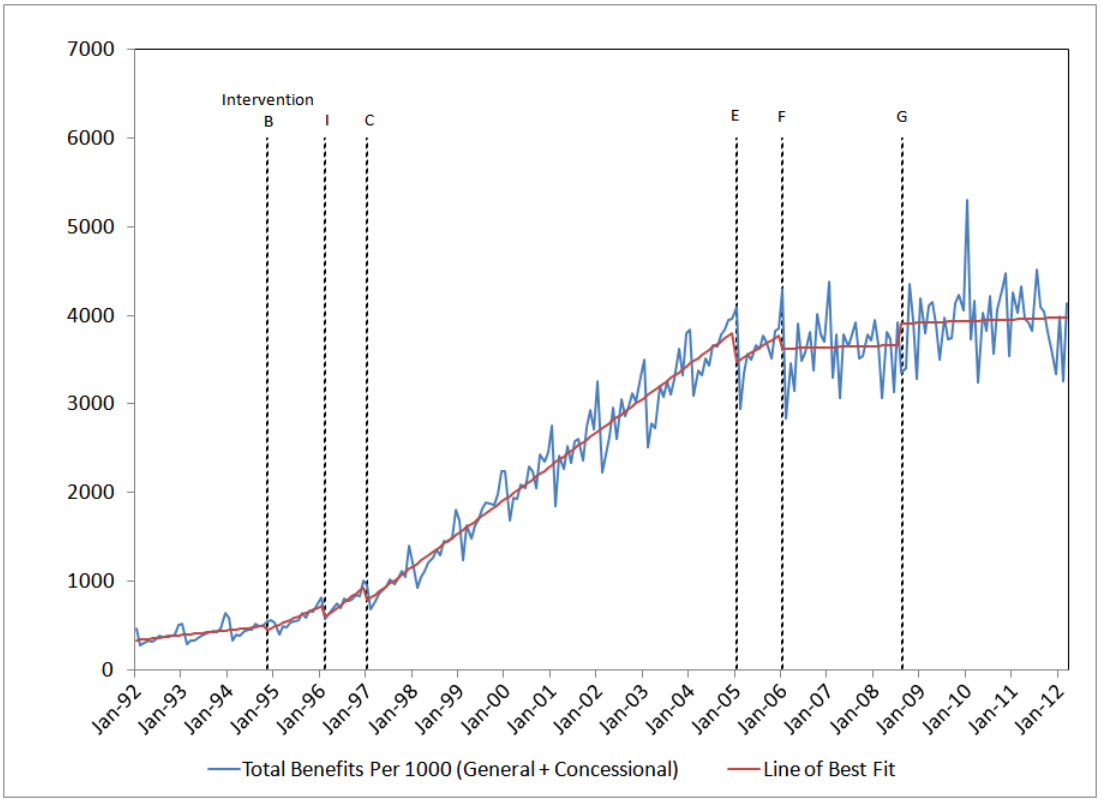

Figure A18 Total benefits per 1000 general and concessional beneficiaries before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

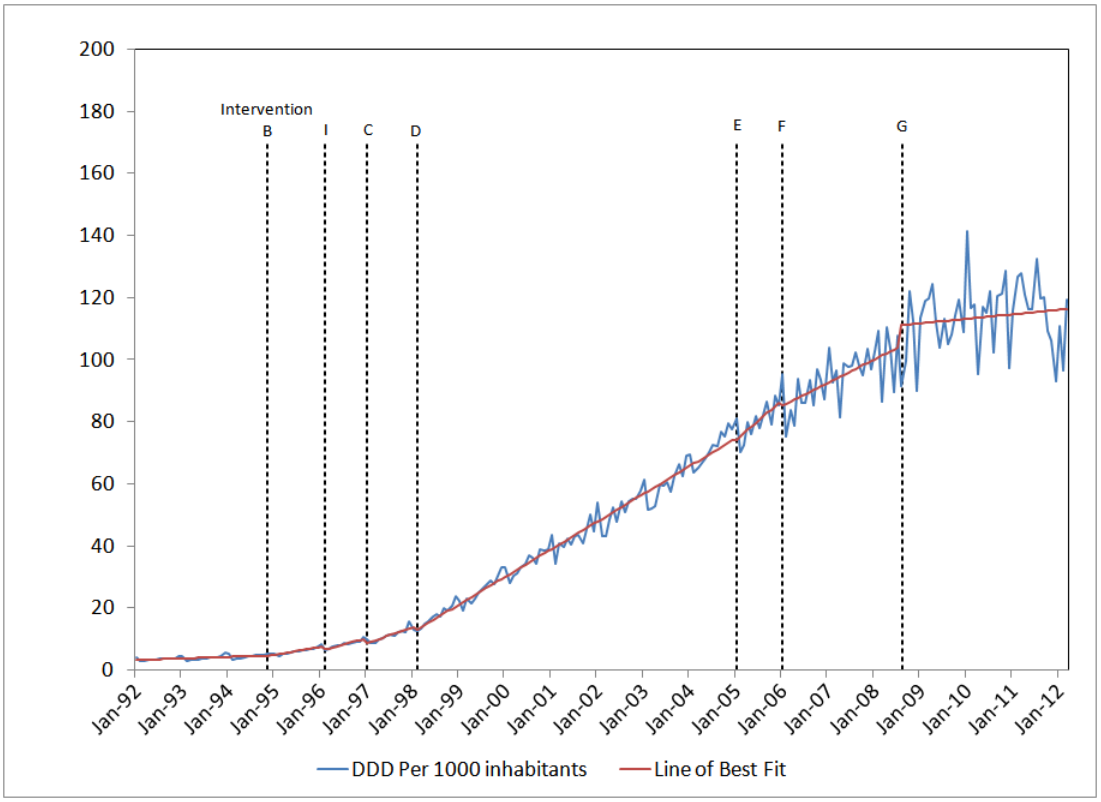

Figure A19 Total DDD per 1000 inhabitants before and after interventions for all HMG-CoA reductase inhibitor drug groups, January 1992 to March 2012

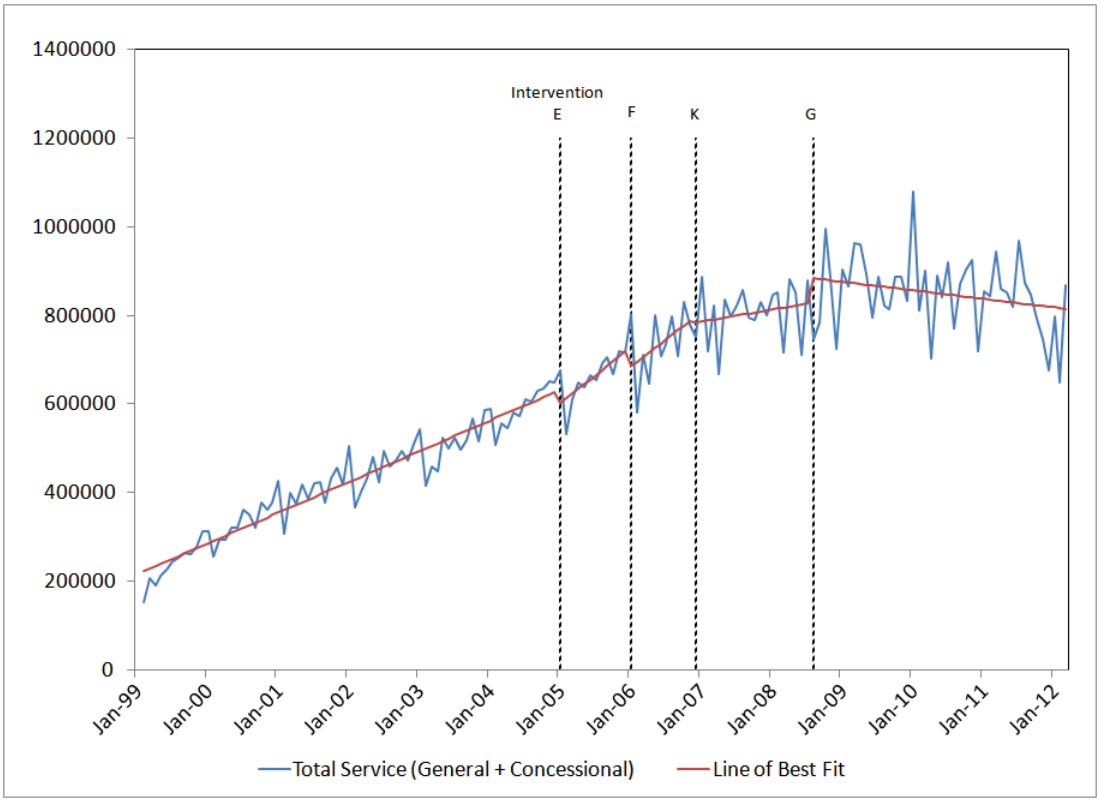

Figure A20 Number of services for general beneficiaries and concessional beneficiaries before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012

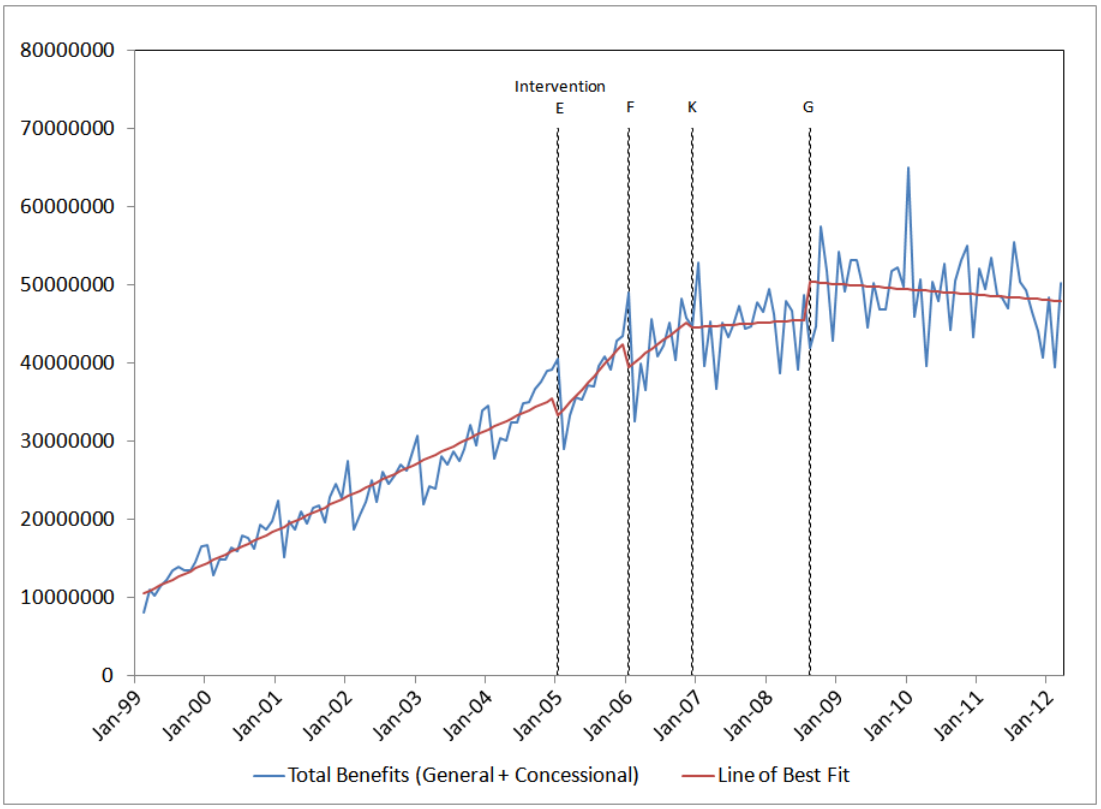

Figure A21 Number of benefits for general beneficiaries and concessional beneficiaries before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012

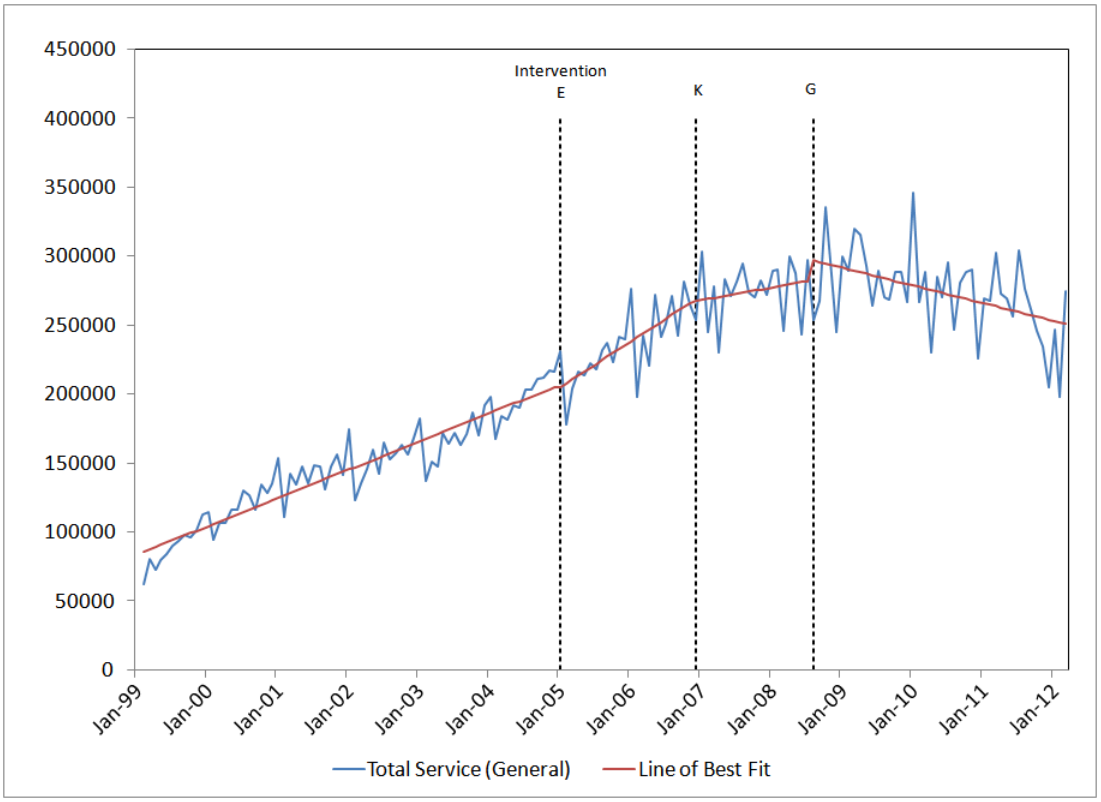

Figure A22 Number of services for general beneficiaries before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012

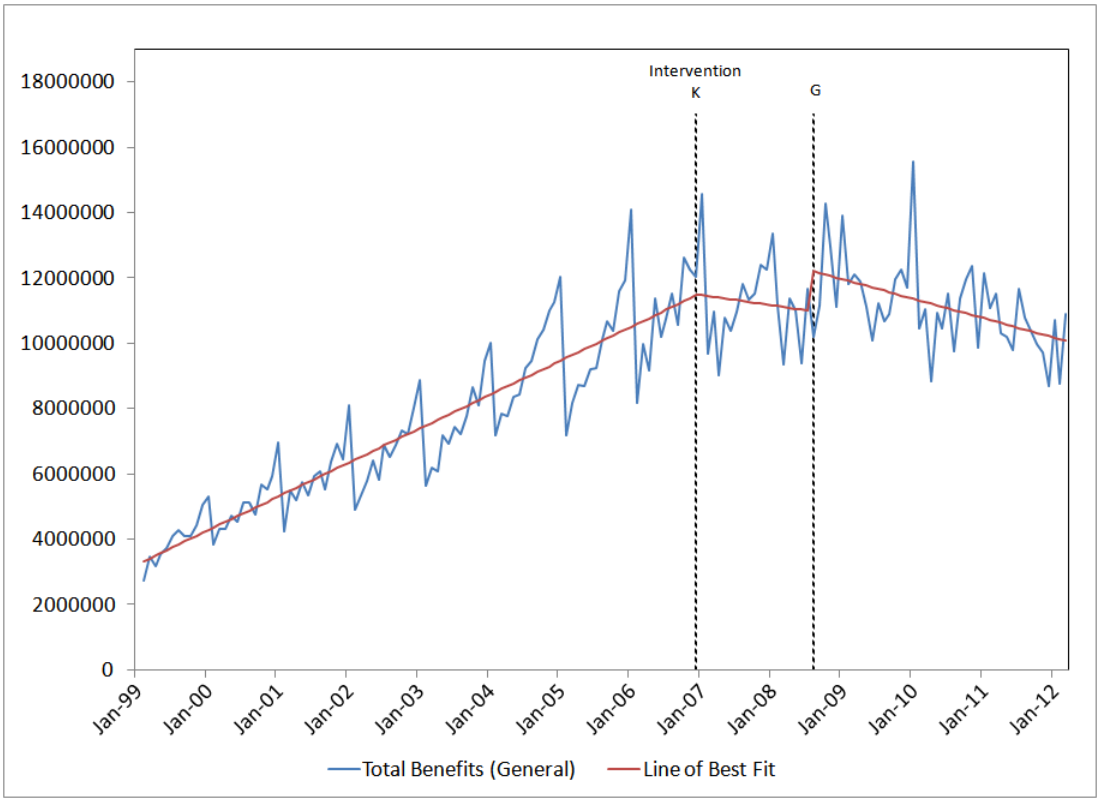

Figure A23 Number of benefits for general beneficiaries before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012

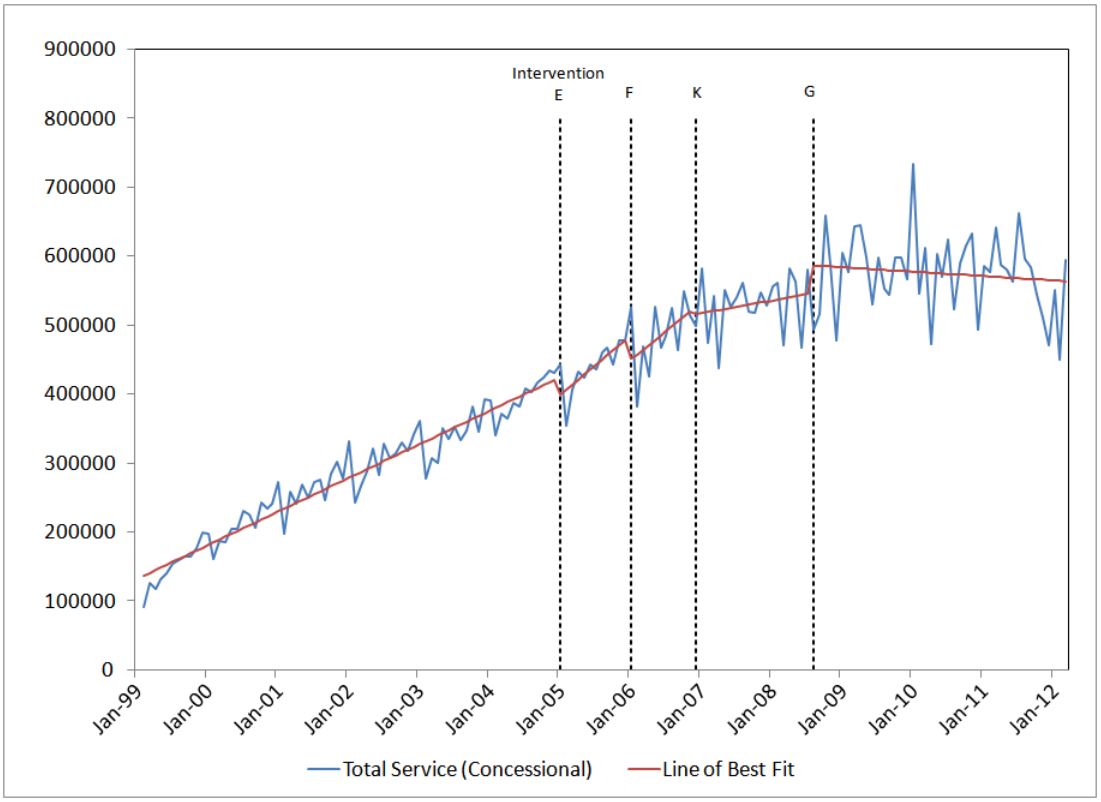

Figure A24 Number of services for concessional beneficiaries before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012

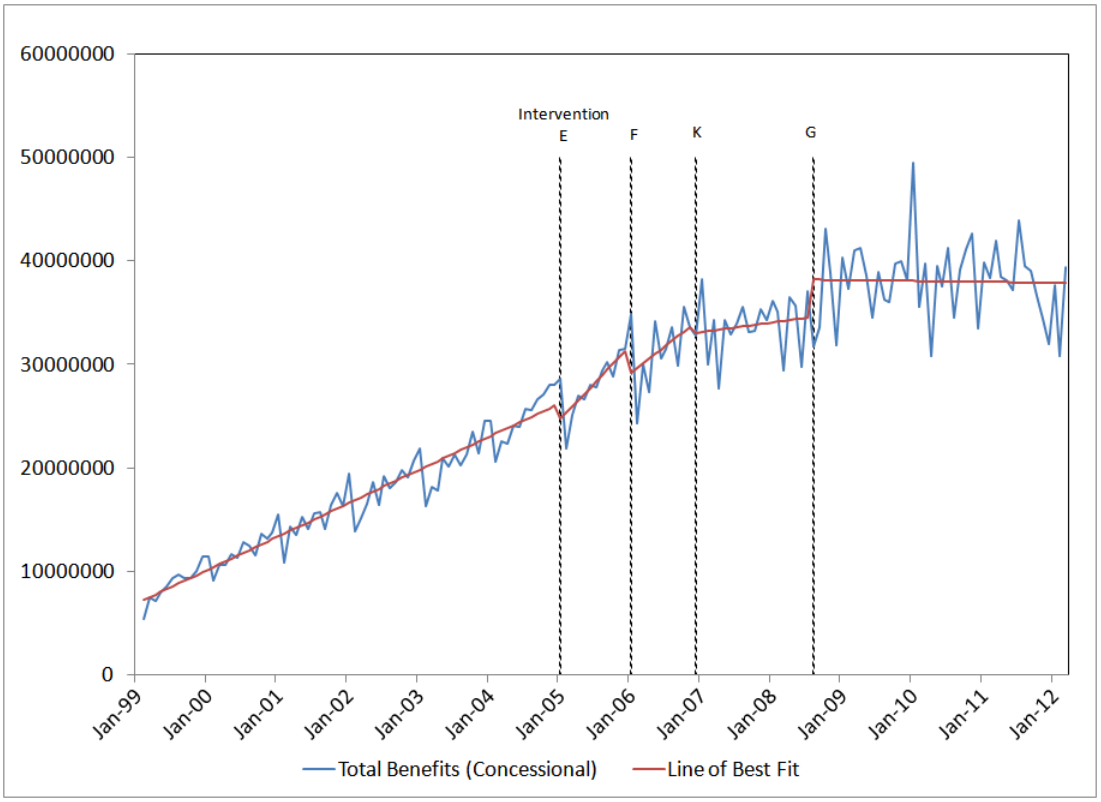

Figure A25 Number of benefits for concessional beneficiaries before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012

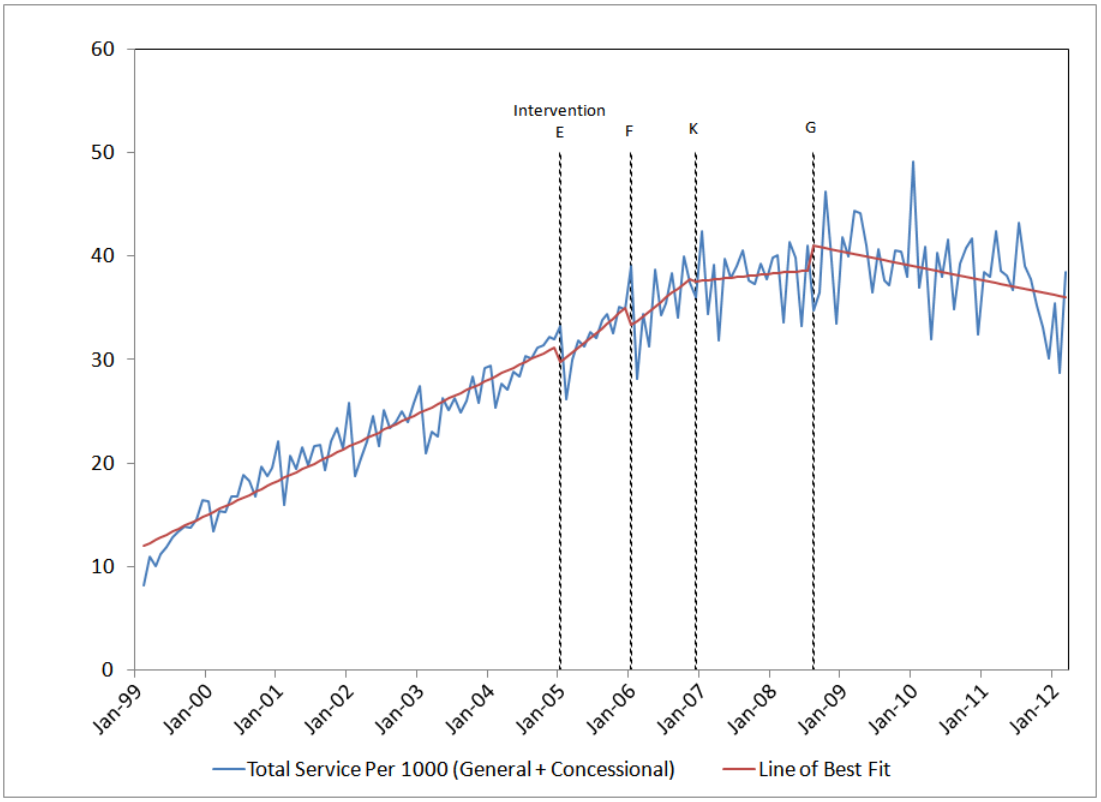

Figure A26 Total services per 1000 general and concessional beneficiaries before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012

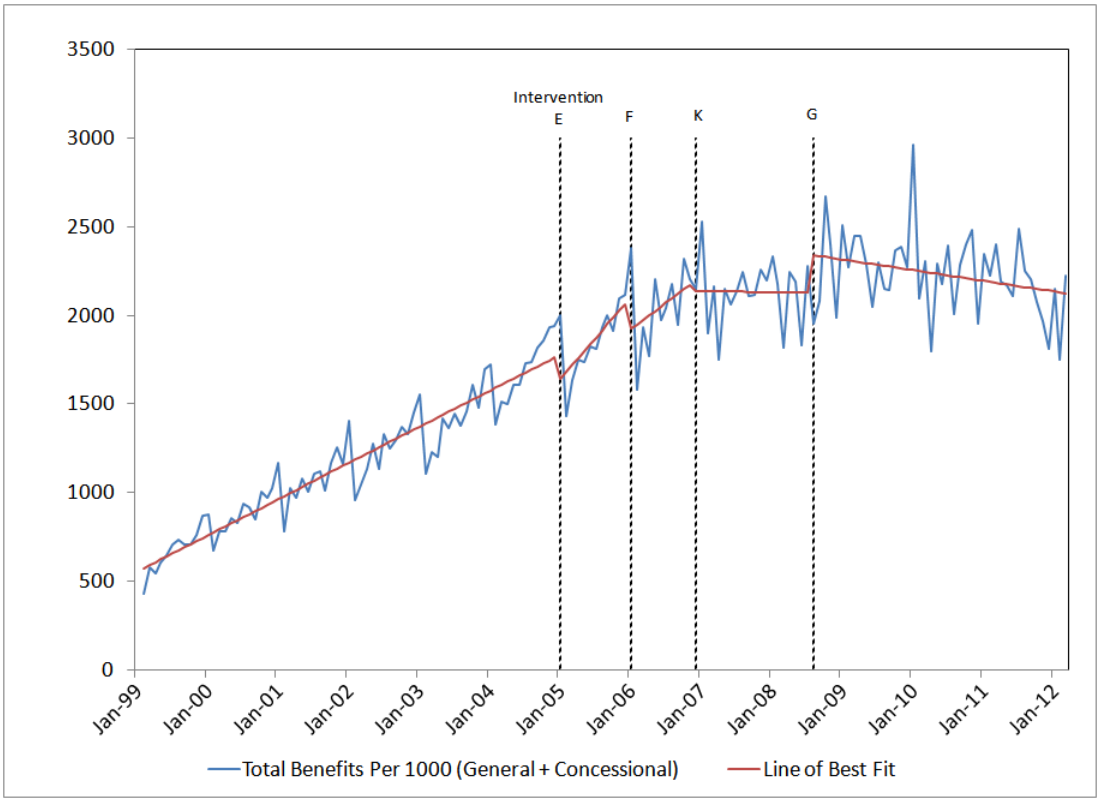

Figure A27 Total benefits per 1000 general and concessional beneficiaries before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012

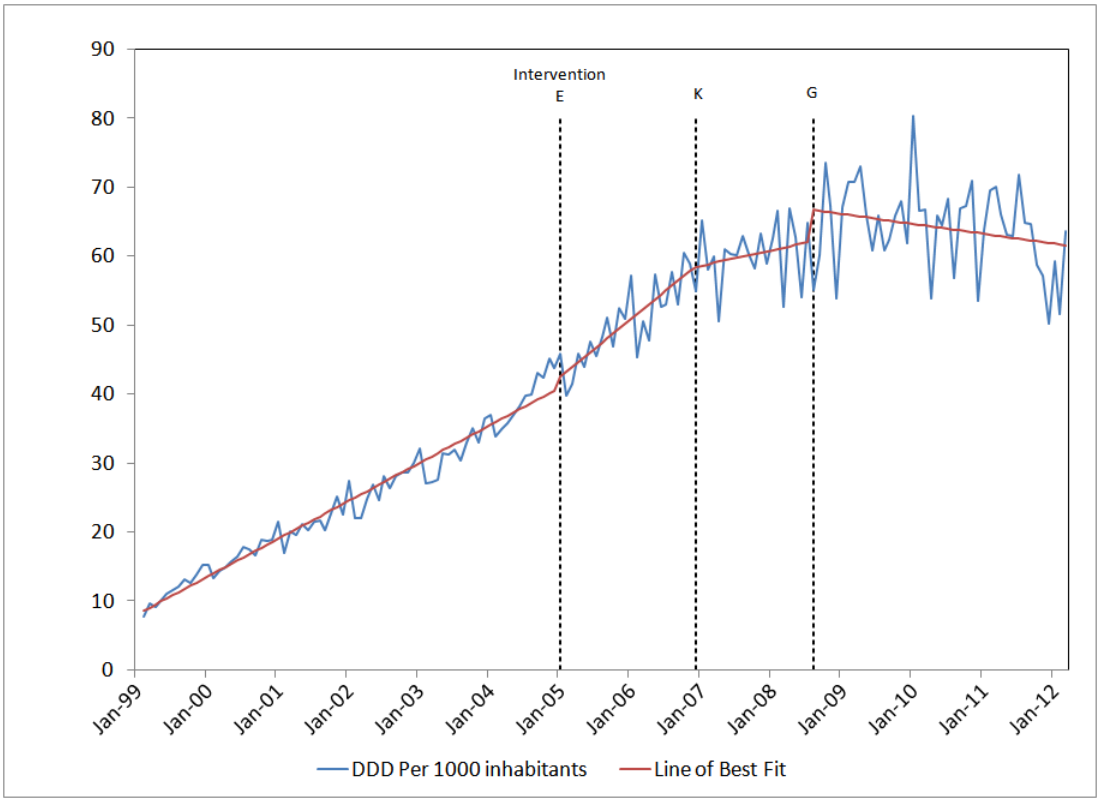

Figure A28 Total DDD per 1000 inhabitants before and after interventions for all Atorvastatin drug groups, February 1999 to March 2012