S E D A P

A PROGRAM FOR RESEARCH ON

SOCIAL AND ECONOMIC DIMENSIONS OF AN AGING POPULATION

The Impact of Differential Cost Sharing of Non-Steroidal Anti-Inflammatory Agents on the Use and Costs of Analgesic Drugs

Paul V. Grootendorst, John K. Marshall, Anne M. Holbrook, Lisa R. Dolovich, Bernie J. O'Brien, Adrian R. Levy

SEDAP Research Paper No. 115

For further information about SEDAP and other papers in this series, see our web site:
http://socserv2.mcmaster.ca/sedap

Requests for further information may be addressed to:
Secretary, SEDAP Research Program
Kenneth Taylor Hall, Room 426
McMaster University
Hamilton, Ontario, Canada
L8S 4M4
FAX: 905 521 8232
e-mail: qsep@mcmaster.ca

THE IMPACT OF DIFFERENTIAL COST SHARING OF NON-STEROIDAL ANTI-INFLAMMATORY AGENTS ON THE USE AND COSTS OF ANALGESIC DRUGS

PAUL V. GROOTENDORST, JOHN K. MARSHALL, ANNE M. HOLBROOK, LISA R. DOLOVICH, BERNIE J. O'BRIEN, ADRIAN R. LEVY

SEDAP Research Paper No. 115

April 2004

The Program for Research on Social and Economic Dimensions of an Aging Population (SEDAP) is an interdisciplinary research program centred at McMaster University with participants at the University of British Columbia, Queen's University, Univérsité de Montréal, and the University of Toronto. It has support from the Social Sciences and Humanities Research Council of Canada under the Major Collaborative Research Initiatives Program, and further support from Statistics Canada, the Canadian Institute for Health Information, and participating universities. The SEDAP Research Paper series provides a vehicle for distributing the results of studies undertaken by those associated with the program. Authors take full responsibility for all expressions of opinion.

The impact of differential cost sharing of non-steroidal anti-inflammatory agents on the use and costs of analgesic drugs

Paul V. Grootendorst, PhD[1,2,3]
John K. Marshall, MD, MSc, FRCPC [3,4]
Anne M. Holbrook, MD, PharmD, MSc, FRCPC [3,4,6]
Lisa R. Dolovich, MSc, PharmD [1,3,5]
Bernie J. O'Brien, PhD[3,6]
Adrian R. Levy, PhD[7,8]

1. Faculty of Pharmacy, University of Toronto, Toronto ON, Canada
2. Department of Economics, McMaster University, Hamilton ON
3. Centre for Evaluation of Medicines, St. Joseph's Hospital, Hamilton ON
4. Department of Medicine, McMaster University, Hamilton ON
5. Department of Family Medicine, McMaster University
6. Department of Clinical Epidemiology and Biostatistics, McMaster University
7. Centre for Health Evaluation and Outcome Sciences, St. Paul's Hospital, Vancouver BC
8. Department of Health Care and Epidemiology, University of British Columbia

This version: March 19, 2004.

Address for correspondence:

Paul Grootendorst, Faculty of Pharmacy, University of Toronto
19 Russell St., Toronto, Ontario, Canada M5S 2S2.
Email: paul.grootendorst@utoronto.ca; Phone: 416-946-3994; Fax: 416-978-1833

Funding Source and Acknowledgements:

Support for this project from the Health Transitions Fund, Health Canada; the Canadian Health Services Research Foundation; Brogan Inc.; the BC Ministry of Health; and the Drug Information Association is acknowledged. The views expressed herein do not necessarily represent the official policy of federal, provincial or territorial governments, or the project funders. Edward Newman provided invaluable research assistance. We thank Sean Burnett, Wendy Eyres and Suzanne Solven of the BC Ministry of Health for assistance with the collection and interpretation of the data. Paul Grootendorst is supported by a career award from the Rx&D Health Research Foundation and the Canadian Institutes of Health Research (CIHR). Anne Holbrook is the recipient of a CIHR Career Investigator Award; Adrian Levy is supported by a Scholar award from the BC Michael Smith Foundation for Health Research. This paper is dedicated to the memory of our colleague Bernie O'Brien (1959-2004).

Running title: Reference pricing of NSAIDs

ABSTRACT

Objective: To estimate the effect of differential cost sharing (DCS) schemes for non-steroidal anti-inflammatory drugs (NSAIDs) on drug subsidy program and beneficiary expenditures.
Data Sources/Study Setting: Monthly aggregate claims data from Pharmacare, the public drug subsidy program for seniors in British Columbia, Canada over the period 1989-11 to 2001-06.
Study Design: DCS limits insurance reimbursement of a group of therapeutically similar drugs to the cost of the lowest priced drugs, with beneficiaries responsible for costs above the reimbursement limit. Pharmacare introduced two different forms of DCS, generic substitution (GS) and reference pricing (RP), in April 1994 and November 1995, respectively, to the NSAIDs. Under GS, generic and brand versions of the same NSAID are considered interchangeable, whereas under RP different NSAIDs are. We extrapolated average reimbursement per day of NSAID therapy over the months before GS and RP to estimate what expenditures would have been without the policies. These counterfactual predictions were compared to actual values to estimate the impact of the policies; the estimated impacts on reimbursement rates were multiplied by the post-policy volume of NSAIDS dispensed, which appeared unaffected by the policies, to estimate expenditure changes.
Data Collection: The cleaned NSAID claims data, obtained from Pharmacare's databases, were aggregated by month and by their reimbursement status under the GS and RP policies.
Principal Findings: After RP, program expenditures declined by $22.7 million, or $4 million annually, cutting expenditure by half. Most savings accrued from the substitution of low cost NSAIDs for more costly alternatives. About 20% of savings represented expenditures by seniors who elected to pay for partially-reimbursed drugs. GS produced one quarter the savings of RP.
Conclusions: RP of NSAIDs achieved its goal of reducing drug expenditures and was more effective than GS. The effects of RP on patient health and associated health care costs remain to be investigated.
Key Words: Reference pricing; generic substitution; prescription drugs; drug cost containment NSAIDs.

Introduction

Differential cost sharing has been used by both public and private drug insurance programs to limit program expenditures. Under this scheme, reimbursement of each drug in a group of 'therapeutically similar' drugs is limited to an average of the prices of the lowest cost drugs in the group. Patients wanting higher cost drugs are responsible for the difference in drug price and the reimbursement limit. Differential cost sharing programs come in two basic flavors, depending on the drugs considered therapeutically similar: (1) different brands of chemically equivalent drugs and (2) chemically distinct but therapeutically related drugs. The former flavor, often referred to as generic substitution (GS), is widely used, whereas the latter, known as reference pricing (RP), has been used less frequently and is controversial, although evidence on its effects is beginning to emerge (Lopez-Casasnovas and Puig-Junoy 2000; Grootendorst *et al.* 2001a; Schneeweiss 2002a; Schneeweiss 2002b; Hazlet and Blough 2002). Some have recommended that RP be integrated into the Medicare prescription drug benefit (Huskamp et al. 2000; Morgan, Barer, and Agnew 2003). In this paper, we compare the drug program savings realized by the application of GS and RP to the class of non-steroidal anti-inflammatory drugs (NSAIDs) by Pharmacare, the publicly funded drug subsidy program for seniors, welfare recipients and other residents of British Columbia (BC), Canada.

Given that there is more price variation between different NSAIDs than there is between different brands of the same NSAID, RP should produce greater budgetary savings than GS. As an example, an academic research group, the BC Therapeutics Initiative, reported in 1995 that the daily cost of acetylsalicylic acid (ASA) varied between $0.06 to $0.17 (depending on the amount used), whereas the daily cost of a newer NSAID, etodolac, varied from $1.79 to $3.58

(Therapeutics Initiative 1995). Critics contend, however, that RP cannot control drug costs in the longer term, for several reasons. First, physicians can apply for exemption from RP for Pharmacare beneficiaries that have failed or are likely to fail on a lower cost, fully reimbursed drug. Although they require paper work, exemption requests are usually granted. Second, physicians might substitute relatively costly analgesics that are not subject to RP (such as oxycodone) for those that are. Third, economic theory suggests that setting reimbursement rates according to the prices of a set of reference standard drugs might encourage the manufacturers of those drugs to raise prices. (Morton 1997; Zwefel and Crivelli 1996; Anis and Wen 1998) Finally, although Pharmacare saves money on those beneficiaries who elect to pay extra for the higher cost drugs, these expenditures are merely shifted – overall drug costs do not decline.

To address these issues, we used aggregated monthly Pharmacare claims data to examine Pharmacare reimbursement rates for NSAIDs, as well as prescribing patterns and Pharmacare-reimbursed expenditures for NSAIDs and other analgesic drugs and patients' out-of-pocket spending on NSAIDs, in the periods before and after introduction of GS and RP.

Methods

Pharmacare NSAID reimbursement policies

In addition to GS and RP, Pharmacare introduced several other policies during the 1990s to limit NSAID expenditures. The first of these was the delisting of selected sustained release (SR) NSAIDs in January 1993 from the formulary. This was followed by the April 1994 introduction of GS, under the auspices of the Low Cost Alternative (LCA) program. LCA limited Pharmacare reimbursement of multi-sourced drugs (i.e. different brands of drugs with the

same active ingredient, dosage form and strength) to the average of the lowest cost (typically 'generic') drugs. RP was introduced in November 1995. Under the policy, the less costly 'Unrestricted' NSAIDs, enteric coated ASA (650mg), ibuprofen and naproxen remained fully reimbursed; Pharmacare also began to reimburse acetaminophen (500mg). The decision to provide full reimbursement for acetaminophen, ASA, ibuprofen and naproxen was consistent with earlier recommendations by the BC Therapeutics Initiative that these drugs be used as first line therapy for osteoarthritis (Therapeutics Initiative 1995).

Reimbursement of the 'First Line Restricted' NSAIDs (diclofenac, diclofenac/misoprostol (Arthrotec), diflunisal, fenoprofen, flurbiprofen, indomethacin, ketoprofen, naproxen SR and enteric coated tablets, and salsalate) was initially limited to $0.45/day ($13.45 for a 30 day supply), then reduced to $0.43/day on March 1, 2001. Patients intolerant of Unrestricted NSAIDS or with specific diagnoses (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, collagen vascular disease or gout) were eligible for exemption from the policy. Exemption required that physicians submit a written request to a Pharmacare pharmacist, who would then adjudicate the request and render a decision, typically within 48 hours. All NSAID prescriptions written by rheumatologists were automatically exempted from RP. Exemption for a 'Second Line Restricted' NSAID (nabumetone, piroxicam, tenoxicam, tiaprofenic acid, tolmetin, sulindac, ketorolac or diclofenac potassium) required failure on a First Line Restricted NSAID. These Second Line drugs were delisted a year later (November 1996), but concerns expressed by physicians and pharmacists led to reinstatement of all but ketorolac and diclofenac potassium under the 'Special Authority' program in February 1997. Special Authority, also known as 'prior authorization', is similar to RP in that Pharmacare will fully

reimburse a drug only if it approves. Special Authority differs from RP in that Pharmacare will not reimburse any of the cost of targeted drugs for patients who fail to receive prior approval.

Various other NSAIDs[1] were either delisted or required special authority at various times over the sample period, but these drugs collectively accounted for less than 7% of all NSAID prescribing in the 19 months before RP. Notably, the cyclooxygenase-2 selective inhibitors (COX-2s) were also placed under special authority at the time of their introduction in September 2000. We assessed these drugs separately because they were reimbursed by Pharmacare only late into our sample period.

Data

BC Pharmacare provided monthly prescribing and expenditures data on individual NSAIDs and other analgesics, for its senior (age 65+) beneficiaries for the period November 1989 to June 2001. A previous report indicated high accuracy and completeness of provincial government drug claims data. (Williams and Young 1996a, 1996b) We focused on seniors given that they are the highest per capita users of analgesics (Health Canada 2003), and the size and composition of the beneficiary population is relatively stable. For each drug group and month, we measured: (1) the number of defined daily doses (DDDs) dispensed per 100,000 seniors; (2) Pharmacare drug expenditure per DDD (equivalently, the average cost per day of therapy); (3) Pharmacare drug expenditures per 100,000 seniors; and (4) patient out-of-pocket drug ingredient expenditures per 100,000 seniors. The DDDs were constructed as the total number of mg dispensed divided by the World Health Organization estimates (World Health Organization 2000) of the typical daily maintenance dose (in mg). Data on the size of the senior population in

[1] These include etodolac, phenylbutazone, floctafenine, mefenamic, the SR and enteric coated (other than 650mg) forms of ASA, 1 gram SR form of naproxen, as well as the injectable and/or suppository forms of indometacin, naproxen, ketoprofen, diclofenac, and piroxicam.

BC were obtained from Statistics Canada (Statistics Canada 2000). Expenditures data excluded dispensing fees and are expressed in Canadian currency. In March 2004, $1CAN = $0.75US.

Statistics were produced for individual NSAIDs and also for groups categorized by their RP reimbursement status (Unrestricted, First Line Restricted, Second Line Restricted, Delisted/Special Authority). The remaining analgesics were grouped into the following broad categories: COX-2s; acetaminophen, codeine, oxycodone and combinations of these drugs; and the remaining opiates.

Estimation of policy effects

For variables (1), (2) and (4), we constructed tables of mean monthly rates during each of 5 time periods demarcated by the introduction of the 4 major Pharmacare NSAID reimbursement policies. These were: (A) the delisting of sustained release NSAIDs in January 1993; (B) the introduction of LCA in April 1994; (C) the application of RP to the NSAID drugs in November 1995; and (D) the delisting of the Second Line Restricted NSAIDs in November 1996 (most of these drugs were relisted in February 1997 but subject to Special Authority prescribing restrictions). The NSAIDs oxyphenylbutazone, diclofenac potassium and ibuprofen (200 and 400 mg capsules), and the opiates levorphanol, opium tincture, sufentanil and oxymorphone were removed from the tables due to their very low prescribing volumes.

The intended effect of RP is to reduce Pharmacare expenditures by reducing the average price paid for NSAID drugs. Regression models were therefore estimated using monthly data to assess how the slope and position of the linear trend in average Pharmacare expenditure per DDD of NSAID therapy was affected by the introduction of LCA and RP. Our identifying

assumption is that the pre-policy intervention trends would have continued into the post-policy period had the policies not been implemented. The estimating model is:

$$CostDDD_t = \beta_0 + \beta_1 t + \beta_2 LCA_t + \beta_3 LCA_t \times t + \beta_4 RP_t + \beta_5 RP_t \times t + \varepsilon_t \quad (1)$$

where $CostDDD_t$ refers to Pharmacare NSAID expenditure per DDD in month t (February 1993 to June 2001), the LCA_t indicator equals 1 in April 1994 and thereafter, and equals 0 otherwise, the RP_t indicator is equal 1 in November 1995 and thereafter, and equals 0 otherwise. The β_j, j=0, …, 5 are unknown parameters estimated using ordinary least squares and ε_t is the error term. Standard errors were estimated using the Newey-West autocorrelation consistent covariance matrix (Newey and West 1987) to ensure that hypothesis testing was valid in the presence of up to 12-period autocorrelation. Parameter estimates appear in Appendix 1.

To estimate total savings from RP, we multiplied the estimated reduction in expenditure per DDD by the number of DDDs of all NSAIDs dispensed post-RP (which appeared to be unaffected by the introduction of RP). The savings produced from LCA were estimated in analogous fashion.

Under the terms of the LCA policy, beneficiaries were responsible for any costs in excess of the average of the lowest cost (typically generic) drugs in multi-sourced drug categories. With the introduction of RP, non-exempted beneficiaries were also were responsible for any costs in excess of the reference price when using Restricted NSAIDs. We estimated the additional average monthly out-of-pocket expenditure per beneficiary and the additional beneficiary expenditure per DDD associated with the introduction of RP. To do so, we estimated linear regression models of each of these outcomes as a function of an indicator variable equal to one for the months that RP was in effect using observations from the month after introduction of LCA (May 1994) to the end of our sample period (June 2001).

Results

Prescribing

Before RP, the overall volume of NSAIDs dispensed in BC was declining – a trend established after the January 1993 delisting of the SR NSAIDs – and RP did not appear to affect this decline (Figure 1). While RP had little effect on the total volume of NSAIDs dispensed, it did have a substantial impact on the mix. In particular, rates of prescribing of Unrestricted NSAIDs doubled from 47,417 DDDs dispensed per 100,000 seniors per month during the 19 months prior to RP to 95,221 DDDs dispensed per 100,000 seniors per month during the 12 month period immediately after RP (Figure 2, Table 1). This increase was almost entirely due to the increased use of naproxen: Table 1 indicates that mean monthly prescribing rates more than tripled between the pre- and post-RP periods. Rates of ibuprofen use increased by only 25% between the same two time periods, while ASA use actually declined 28%.

Before the introduction of RP, diclofenac and diclofenac-misoprostol were the two most commonly prescribed NSAIDs; after Pharmacare restricted reimbursement of these drugs to $0.45/day, however, rates of use fell by 45% and 41% respectively. Not all drugs experienced similar declines: rates of use of indomethacin, another commonly used NSAID, declined by only 9%. Compared to the 19 months prior to RP, use of the First Line Restricted drugs dropped by 44% during the year after RP, and dropped a further 10% in the period thereafter. Use of the Second Line Restricted NSAIDs dropped by 48% in the year after RP and dropped an additional 37% after these drugs were initially delisted and then relisted under the terms of the Special

Authority program. Finally, use of the NSAIDs that were delisted or placed on special authority at various points in time eventually dropped to 35% of the pre-RP rates.

The introduction of RP was not associated with increased use of acetaminophen, codeine, or oxycodone (Figure 1). The situation is less clear-cut for fentanyl and the other higher potency opiates. While rates of use of these drugs did not increase appreciably in the year after the introduction of RP, their use did increase about a year thereafter (i.e. when the Second Line Restricted NSAIDs were delisted in November 1996). Compared to the pre-RP period, mean monthly rates of opiates use after November 1996 increased by 53% (Table 1). Moreover, with the gradual decline in NSAIDs use, the opiate share of total analgesic prescribing has increased (Figure 1). Rates of COX-2 NSAID use increased by an average monthly rate of 28% after their inclusion on the Pharmacare formulary in September 2000; as of June 2001, roughly 12,000 defined daily doses were dispensed per 100,000 seniors per month (data not shown).

Pharmacare Expenditures

During the 19 months prior to the introduction of RP, Pharmacare spent an average of $1.32 per DDD (excluding dispensing fees) on seniors taking the Delisted/Special Authority NSAIDs, $1.20 per DDD for the Second Line Restricted NSAIDs, $0.87 per DDD for the First Line Restricted and $0.16 per DDD on the Unrestricted NSAIDs (Table 2 and Figure 3). By limiting reimbursement of the Restricted drugs to non-exempted seniors to $0.45 per DDD, Pharmacare was able to reduce its cost per day by between 20-26%, depending on the Restricted drug category, in the first 12 months post-RP. (Average expenditure did not drop by a greater percentage amount because Pharmacare continued to fully reimburse the drug costs of exemptees.) Pharmacare average expenditure per DDD on all NSAIDs eventually dropped by

50%, from $0.80 to $0.40. Based on regression model (1), we estimate that RP reduced (undiscounted) NSAID expenditure by $22.7 million over the 68 month period November 1995 – June 2001, with a 95% confidence interval (CI) of $21.1 to $24.3 million. Annualized savings are $4.0 million per year (95% CI: $3.7 to $4.3 million), or 44% of the $9.1 million Pharmacare spent on NSAIDs for seniors in the 12 months prior to RP. These savings were not offset by additional expenditures on other analgesic drugs (Figure 5): While there was a gradual increase in opiate use (Figure 1), there was an offsetting decline in Pharmacare's reimbursement rates for these drugs (Figure 4). Budgetary savings produced by LCA over the 87 month period April 1994 – June 2001 were estimated to be $7.5 million (95% CI: $4.1 to $10.9 million). Annualized savings were $1.0 million (95% CI: $0.6 to 1.5 million), or 10% of the $10 million Pharmacare spent on NSAIDs for seniors in the year prior to LCA.

Patient Expenditures

Out-of-pocket NSAID expenditures across all seniors increased by an average of $798,000 annually after the introduction of RP (95% CI: $647,000 to $948,000); this represents about 20% of annual Pharmacare savings on NSAIDs (Figure 6). Average additional cost per senior was modest. During the LCA period (April 1994 to October 1995), each senior paid on average $0.02 per month to substitute brandname for generic NSAID drugs. After RP, each senior spent an additional $0.13 per month for Restricted NSAID drugs (95% CI: $0.10 to $0.15). Since not all seniors used Restricted NSAIDs post-policy, however, the cost per user was likely much higher. These figures also exclude out-of-pocket costs for those seniors who did not receive a Special Authority exemption for Second Line Restricted drugs used after

November 1996. (As Pharmacare did not pay for any portion of these drugs, data on their use and expenditures are not available.)

Discussion

The Reference Pricing policy reduced NSAID expenditure on its senior beneficiaries by about $4 million annually during the 5 years following its introduction. The policy did so by reducing average Pharmacare expenditure per day of NSAID therapy by about half; the total volume of NSAIDs dispensed was unaffected. These savings accrued despite liberal exemption criteria and the opportunity for physicians to prescribe higher potency analgesics that were not subject to reimbursement restriction. Similar relative expenditure reductions were realized after the Medicaid programs of Georgia and Tennessee implemented prior authorization programs for various higher-cost NSAIDs (Kotzan et al. 1993; Smalley et al. 1995). However, in both programs some of the expenditure reduction was due to decreased NSAID use. Application of the generic substitution policy in BC produced annualized savings of $1 million, or roughly one quarter those realized by RP. RP was able to achieve larger savings by exploiting substantial price differences between different NSAIDs; GS could only exploit price differences that existed between the different brands of multi-sourced NSAIDs.

GS and RP were also applied to Pharmacare's other beneficiary groups – residents of long-term care facilities, social assistance recipients and households whose drug costs exceed an income-contingent deductible. In 1999, Pharmacare drug expenditures on these groups were sizeable – about 86% of Pharmacare expenditures on seniors (British Columbia Ministry of

Health Services 2001). Given that per capita analgesic use is likely lower among these groups, however, RP probably generated less than proportionate budgetary savings.

Pharmacare has applied RP to several other therapeutic groups and analysts have now estimated the savings accruing to Pharmacare's seniors' drug program for each of them. The present analysis finds savings for NSAIDs to be $4 million annually. Marshall *et al.* (2002) found that the application of RP to the H2 blockers in October 1995 and the concurrent application of Special Authority to the proton pump inhibitors saved Pharmacare between $7.3 to $8.7 million annually, depending on the estimation method chosen. Grootendorst *et al.* (2001b) estimated that the application of RP to the 3 groups of cardiac drugs – the ACE inhibitors and Calcium Channel Blockers (both targeted by RP in January 1997) and nitrates (November 1995) – saved Pharmacare about $7.8 million annually. Hence combined savings are between $19.1 and $20.5 million annually; this does not include any savings on Pharmacare subsidies for non-senior beneficiaries.

While the total volume of NSAIDs dispensed did not change appreciably after RP, the mix of NSAIDs dispensed did. In particular, the use of the lower cost, fully reimbursed NSAIDs increased from 23% to 58% of total NSAID use. This was due primarily to the increased use of naproxen. The use of First Line Restricted drugs – especially diclofenac, diclofenac-misoprostol, enteric-coated and SR naproxen, and ketoprofen – dropped after the implementation of RP. When RP was introduced, acetaminophen was placed on the formulary in recognition of its importance in treating mild to moderate arthritis. However, it was not commonly prescribed. There was a moderate increase in rates of opiate use 2 years after RP was introduced; it is unclear if this was attributable to RP.

Savings generated from RP need to be compared to its potential costs. First, switching between NSAIDS to comply with the policy may have worsened symptoms. While we did not have data on patient health outcomes and individual patients commonly report better efficacy and/or tolerability with particular NSAIDs (Langman et al. 2001; Walker, Chan, and Yood 1992), we note that there is no consistent evidence of clinically significant differences in the anti-inflammatory and analgesic effect of the numerous different NSAIDs (Holbrook 2001; Brooks and Day 1991). Retrospective analyses of observational data have suggested a hierarchy among conventional NSAIDs in their potential for gastrointestinal injury, but these differences can be attributed to variations in effective dose and channeling bias (Rodriguez 1998; Henry 1996). Others have studied the effects of prior authorization programs targeting higher cost NSAIDs on the health related quality of life (Momani, Madhavan, and Nau 2002) and medical services use (Kotzan et al. 1993; Smalley et al. 1995) of chronic NSAID users enrolled in various US state Medicaid programs. None of these studies detected any deleterious effects among those who were not given Medicaid subsidies for the higher cost NSAIDs.

Second, patient expenditures increased by about 20% of Pharmacare savings, and likely more due to spending on delisted drugs and spending by patients who were denied special authority exemptions for the COX-2 NSAIDs and other analgesics. Finally, RP may have generated administrative costs. Patients taking Restricted NSAIDs likely consulted their physician about treatment options (e.g., switching to a fully reimbursed drug, applying for an exemption or paying out-of-pocket costs); those who switched were likely monitored. Physicians and especially pharmacists were observed to spend considerable uncompensated time explaining the RP policy to patients, especially when RP was first introduced (Kent 2000; Mullett and Coughlan 1998; Woollard 1996).

REFERENCES

Anis, A. and Q. Wen. 1998. "Price regulation of pharmaceuticals in Canada." *Journal of Health Economics* 17: 21-38.

British Columbia Ministry of Health Services. 2001. "Pharmacare Trends 2000. Victoria, BC": Pharmacare, British Columbia Ministry of Health Services. [accessed on December 13, 2002]. Available at: http://www.healthservices.gov.bc.ca/pharme/outgoing/PcareTrends2000.pdf

Brooks, P.M. and R. O. Day. 1991. "Nonsteroidal antiinflammatory drugs--differences and similarities." *New England Journal of Medicine* 324 (24): 1716-25.

Grootendorst, P., L. Dolovich, B. O'Brien, A. Holbrook, and A. R. Levy. 2001a. "Impact of reference-based pricing of nitrates on the use and costs of anti-anginal drugs." *Canadian Medical Association Journal* 165 (8): 1011-19.

Grootendorst, P, L. Dolovich, A. Holbrook, A. R. Levy, and B. O'Brien. 2001b. "The impact of reference pricing of cardiovascular drugs on health care costs and health outcomes." Final Report to the Health Transitions Fund. [accessed on December 13, 2002]. Available at: http://www.thecem.net/projectsframe.html

Hazlet, T. K. and D. K. Blough. 2002. "Health services utilization with reference drug pricing of histamine(2) receptor antagonists in British Columbia elderly." *Medical Care* 40 (8): 640-49.

Health Canada. 2003. Arthritis in Canada. An ongoing challenge (Cat. # H39-4/14-2003E): Ottawa, Health Canada.

Henry, D., L. L. Y. Lim, L. A. G. Rodriguez, S. P. Gutthann, J. L. Carson, Griffin M et al. 1996. "Variability in risk of gastrointestinal complications with individual non-steroidal anti-inflammatory drugs: results of a collaborative meta-analysis." *British Medical Journal* 312 (7046): 1563-66.

Holbrook, A. 2001. For the Ontario Musculoskeletal Therapy Review Panel. Medical treatment guidelines for the treatment of osteoarthritis, rheumatoid arthritis and acute musculoskeletal injury: Ontario Ministry of Health.

Huskamp, H. A., M. B. Rosenthal, R. G. Frank, and J. P. Newhouse. 2000. "The Medicare prescription drug benefit: how will the game be played?" *Health Affairs* 19: 8-23.

Kent, H. 2000. "BC's reference-based pricing stirs controversy."*Canadian Medical Association Journal* 162 (8): 1190.

Kotzan, J. A., J. McMillan, C. Jankel, and A. Foster. 1993. "Initial impact of a Medicaid prior authorization program for NSAID prescriptions." *Journal of Research in Pharmaceutical Economics* 5 (1): 25-41.

Langman, M., K. H. Kahler, S. X. Kong, Q. Zhang, E. Finch, Bentkover J. D. et al. 2001. "Drug switching patterns among patients taking non-steroidal anti- inflammatory drugs: a retrospective cohort study of a general practitioners database in the United Kingdom." *Pharmacoepidemiol Drug Saf* 10 (6): 517-24.

Lopez-Casasnovas, G. and J. Puig-Junoy. 2000. "Review of the literature on reference pricing." *Health Policy* 54: 87-123.

Marshall, J. K., P. V. Grootendorst, B. J. O'Brien, L. R. Dolovich, A. M. Holbrook, and A. R. Levy. 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): 1655-62.

Momani, A. A., S. S. Madhavan, and D. P. Nau. 2002. "Impact of NSAIDs prior authorization policy on patients' QoL." *Annals of Pharmacotherapy* 36 (11): 1686-91.

Morgan, S. G., M. L. Barer, and J. D. Agnew. 2003. "Whither senior's Pharmacare: lessons from (and for) Canada." *Health Affairs* 22: 49-59.

Morton, F. S. 1997. "The strategic response by pharmaceutical firms to the Medicaid most-favored-customer rules." *RAND Journal of Economics* 28 (2): 269-90.

Mullett, J. and R. Coughlan. 1998. "Clinicians' and seniors' views of reference based pricing: Two sides of a coin." *Journal of Applied Gerontology* 17 (3): 296-317.

Newey, W. and K. West. 1987. "A simple, positive semi-definite heteroscedasticity and autocorrelation consistent covariance matrix." *Econometrica* 55: 703-8.

Rodriguez, L. A. G. 1998. "Variability in risk of gastrointestinal complications with different nonsteroidal anti-inflammatory drugs." *American Journal of Medicine* 104: 41-2.

Schneeweiss, S., S. Soumerai, R. J. Glynn, M. Maclure, C. Dormuth, and A. M. Walker. 2002a. "Impact of reference-based pricing for angiotensin-converting enzyme inhibitors on drug utilization." *Canadian Medical Association Journal* 166 (6): 737-45.

Schneeweiss, S., A. M. Walker, R. J. Glynn, M. Maclure, C. Dormuth, and S. Soumerai. 2002b. "Outcomes of reference pricing for angiotensin-converting-enzyme inhibitors." *New England Journal of Medicine* 346 (11): 822-29.

Smalley, W.E., M. R. Griffin, R. L. Fought, L. Sullivan, and W. A. Ray. 1995. "Effect of a prior-authorization requirement on the use of nonsteroidal antiinflammatory drugs by Medicaid patients." *New England Journal of Medicine* 332 (24): 1612-17.

Statistics Canada. 2000. Canadian socio-economic information management system (data matrix 6377): Ottawa: Statistics Canada.

Therapeutics Initiative. 1995. "Should We Be Using NSAIDs for the Treatment of Osteoarthritis and Rheumatism?" [accessed on March 19, 2002]. Available at: http://www.ti.ubc.ca/pages/letter4.html

Walker, A. M., K. W. Chan, and R. A. Yood. 1992. "Patterns of interchange in the dispensing of non-steroidal anti- inflammatory drugs." *Journal of Clinical Epidemiology* 45 (2): 187-95.

Williams, J. I. and W. Young. 1996a. Inventory of studies on the accuracy of Canadian health administrative databases. Technical report: Toronto, Institute for Clinical Evaluative Sciences.

Williams, J. I. and W. Young. 1996b. "A summary of studies on the quality of health care administrative databases in Canada." In *Patterns of Health Care in Ontario,* 2nd edn, edited by V. Goel, J. I. Williams, G. Anderson, P. Blackstein-Hirsch, C. Fooks, and C.D. Naylor, pp. 339–345. Ottawa, Canadian Medical.

Woollard, R.F. 1996. "Opportunity lost: a frontline view of reference-based pricing."*Canadian Medical Association Journal* 154 (8): 1185-88.

World Health Organization. 2000. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment: Oslo, WHO.

Zweifel, P. and L. Crivelli. 1996. "Price regulation of drugs: lessons from Germany." *Journal of Regulatory Economics* 10: 257-73.

Table 1 Average monthly number of defined daily doses dispensed per 100,000 seniors, by analgesic and time period

Analgesic Category		Time Period				
		Historical Nov 89 - Dec 92	SR Delisted Jan 93 - Mar 94	LCA Apr 94 - Oct 95	RP NSAIDs Nov 95 - Oct 96	Delistings Nov 96 - Jun 01
NSAIDS						
Unrestricted	asa ect 650mg tab	42,922 **219**	31,408 **160**	19,622 **100**	14,071 **72**	7,779 **40**
	ibuprofen tab	14,835 **170**	11,721 **134**	8,737 **100**	10,906 **125**	11,221 **128**
	naproxen tab	27,966 **147**	26,693 **140**	19,058 **100**	70,244 **369**	68,206 **358**
	Subtotal	*85,723* ***181***	*69,822* ***147***	*47,417* ***100***	*95,221* ***201***	*87,206* ***184***
First Line Restricted	diclofenac	81,432 **214**	54,985 **145**	37,995 **100**	20,328 **54**	16,968 **45**
	diclofenac/misoprostol		12,725 **48**	26,248 **100**	15,552 **59**	15,994 **61**
	diflunisal	3,729 **253**	2,120 **144**	1,474 **100**	692 **47**	446 **30**
	fenoprofen	852 **220**	541 **140**	387 **100**	199 **51**	128 **33**
	flurbiprofen	5,611 **224**	3,805 **152**	2,501 **100**	1,207 **48**	838 **34**
	indometacin	18,508 **160**	13,622 **118**	11,555 **100**	10,545 **91**	9,636 **83**
	ketoprofen	27,252 **277**	16,185 **165**	9,836 **100**	5,580 **57**	3,241 **33**
	naproxen ect & sr	11,186 **53**	11,956 **57**	20,982 **100**	7,772 **37**	4,308 **21**
	salsalate			288 **100**	276 **96**	138 **48**
	Subtotal	*148,570* ***134***	*115,939* ***104***	*111,266* ***100***	*62,151* ***56***	*51,697* ***46***
Second Line Restricted	sulindac	8,492 **203**	5,762 **138**	4,189 **100**	2,048 **49**	598 **14**
	nabumetone			5,749 **100**	5,714 **99**	2,146 **37**
	piroxicam cap	12,006 **193**	8,830 **142**	6,215 **100**	3,034 **49**	672 **11**
	tenoxicam	5,251 **54**	9,431 **97**	9,724 **100**	3,259 **34**	660 **7**
	tiaprofenic acid	15,404 **160**	12,761 **133**	9,613 **100**	4,445 **46**	993 **10**
	tolmetin	3,119 **206**	2,183 **144**	1,514 **100**	882 **58**	424 **28**
	Subtotal	*44,272* ***120***	*38,967* ***105***	*37,004* ***100***	*19,382* ***52***	*5,493* ***15***
Delisted/Special Auth.	ketorolac tromethamine inj	17 **100**	16 **94**	17 **100**	8 **47**	8 **47**
	ketorolac tromethamine tab	6,243 **170**	4,701 **128**	3,668 **100**	1,623 **44**	48 **1**
	etodolac			28 **100**	132 **471**	41 **146**
	indometacin sup	2,686 **172**	2,154 **138**	1,565 **100**	1,362 **87**	1,003 **64**
	mefenamic	206 **147**	166 **119**	140 **100**	118 **84**	96 **69**
	naproxen sup/inj	1,256 **196**	905 **141**	640 **100**	658 **103**	504 **79**
	naproxen 1 gram sr	4,242 **140**	4,288 **142**	3,025 **100**	2,967 **98**	1,396 **46**
	phenylbutazone	276 **223**	178 **144**	124 **100**	98 **79**	74 **60**
	ketoprofen sup	1,172 **234**	801 **160**	500 **100**	316 **63**	177 **35**
	diclofenac sup	1,863 **137**	1,650 **121**	1,361 **100**	1,184 **87**	1,038 **76**
	piroxicam sup	704 **146**	550 **114**	482 **100**	324 **67**	47 **10**
	floctafenine	1,150 **203**	969 **171**	566 **100**	348 **61**	185 **33**
	asa ect tab, sr tab/cap	3,862 **249**	2,446 **158**	1,551 **100**	1,195 **77**	209 **13**
	Subtotal	*23,677* ***173***	*18,824* ***138***	*13,667* ***100***	*10,333* ***76***	*4,826* ***35***
	All NSAIDs	***302,242 144***	***243,552 116***	***209,354 100***	***187,087 89***	***149,222 71***
COX-2 NSAIDS						7,199
ACETAMINOPHEN & MILD OPIATES	acetaminophen				3,012	4,472
	codeine	1,183 **115**	1,027 **100**	1,032 **100**	1,105 **107**	1,931 **187**
	codeine/acetaminophen	71,455 **101**	78,555 **111**	70,694 **100**	70,277 **99**	70,937 **100**
	codeine/asa	7,476 **159**	5,883 **125**	4,692 **100**	4,234 **90**	3,469 **74**
	oxycodone/acetaminophen	1,565 **109**	1,520 **106**	1,436 **100**	1,643 **114**	2,327 **162**
	All Acetam./Mild Opiates	***81,679 105***	***86,985 112***	***77,854 100***	***80,271 103***	***83,136 107***
OPIATES	fentanyl	7,330 **42**	20,558 **117**	17,636 **100**	17,924 **102**	30,189 **171**
	hydromorphone	4,746 **88**	5,467 **101**	5,414 **100**	6,360 **117**	13,130 **243**
	meperidine	361 **98**	358 **98**	367 **100**	363 **99**	412 **112**
	morphine	6,129 **82**	7,339 **98**	7,499 **100**	8,881 **118**	9,795 **131**
	propoxyphene	5,009 **137**	4,250 **116**	3,662 **100**	3,405 **93**	325 **9**
	anileridine	471 **97**	489 **101**	485 **100**	540 **111**	552 **114**
	pentazocine	923 **181**	695 **137**	509 **100**	490 **96**	159 **31**
	All Opiates	***24,969 70***	***39,156 110***	***35,572 100***	***37,963 107***	***54,562 153***

Notes: the bolded values indicate period-specific average monthly rates relative to rates in the LCA period.

Table 2 Average Pharmacare expenditure per defined daily dose, by analgesic and time period

Analgesic Category		Time Period				
		Historical Nov 89 - Dec 92	SR Delisted Jan 93 - Mar 94	LCA Apr 94 - Oct 95	RP NSAIDs Nov 95 - Oct 96	Delistings Nov 96 - Jun 01
NSAIDS						
Unrestricted	asa ect 650mg tab	0.23 **173**	0.22 **167**	0.13 **100**	0.12 **91**	0.12 **91**
	ibuprofen tab	0.25 **217**	0.20 **173**	0.11 **100**	0.11 **96**	0.11 **93**
	naproxen tab	0.32 **143**	0.27 **122**	0.22 **100**	0.22 **97**	0.21 **95**
	Subtotal	*0.26* ***158***	*0.23* ***143***	*0.16* ***100***	*0.19* ***115***	*0.19* ***115***
First Line Restricted	diclofenac	1.19 **140**	1.05 **123**	0.85 **100**	0.63 **74**	0.59 **69**
	diclofenac/misoprostol		1.24 **101**	1.23 **100**	1.01 **82**	0.90 **73**
	diflunisal	1.04 **121**	1.12 **131**	0.85 **100**	0.64 **75**	0.64 **75**
	fenoprofen	1.12 **95**	1.20 **101**	1.18 **100**	0.89 **75**	0.95 **80**
	flurbiprofen	1.31 **155**	1.23 **146**	0.84 **100**	0.63 **75**	0.61 **72**
	indometacin	0.89 **206**	0.52 **121**	0.43 **100**	0.40 **94**	0.35 **81**
	ketoprofen	1.05 **189**	0.92 **167**	0.55 **100**	0.46 **84**	0.42 **75**
	naproxen ect & sr	0.94 **111**	0.84 **99**	0.85 **100**	0.59 **70**	0.49 **57**
	salsalate			1.44 **100**	1.24 **86**	1.14 **79**
	Subtotal	*1.11* ***127***	*0.98* ***112***	*0.87* ***100***	*0.67* ***77***	*0.62* ***72***
Second Line Restricted	sulindac	1.27 **121**	1.27 **121**	1.04 **100**	0.83 **79**	1.00 **96**
	nabumetone			1.48 **100**	1.24 **84**	1.29 **87**
	piroxicam cap	1.03 **128**	1.01 **126**	0.81 **100**	0.64 **79**	0.73 **90**
	tenoxicam	1.36 **102**	1.36 **102**	1.34 **100**	1.07 **80**	1.09 **82**
	tiaprofenic acid	1.43 **115**	1.46 **118**	1.24 **100**	0.80 **65**	0.94 **76**
	tolmetin	1.03 **105**	1.10 **112**	0.98 **100**	0.79 **80**	0.90 **92**
	Subtotal	*1.25* ***105***	*1.29* ***108***	*1.20* ***100***	*0.95* ***80***	*1.07* ***89***
Delisted/Special Auth.	ketorolac tromethamine inj	5.64 **116**	4.94 **102**	4.84 **100**	4.62 **96**	4.83 **100**
	ketorolac tromethamine tab	1.87 **97**	1.90 **99**	1.93 **100**	0.93 **48**	1.34 **70**
	etodolac			1.01 **100**	0.97 **97**	0.85 **84**
	indometacin sup	1.46 **105**	1.58 **114**	1.39 **100**	1.23 **89**	1.04 **75**
	mefenamic	2.02 **83**	2.40 **99**	2.43 **100**	2.39 **98**	1.65 **68**
	naproxen sup/inj	1.36 **115**	1.46 **123**	1.19 **100**	1.00 **84**	0.92 **77**
	naproxen 1 gram sr	0.93 **142**	0.89 **135**	0.66 **100**	0.64 **97**	0.64 **98**
	phenylbutazone	0.52 **737**	0.35 **501**	0.07 **100**	0.05 **77**	0.06 **82**
	ketoprofen sup	2.30 **114**	2.40 **119**	2.01 **100**	1.86 **93**	1.59 **79**
	diclofenac sup	1.45 **93**	1.54 **99**	1.56 **100**	1.40 **90**	1.14 **73**
	piroxicam sup	1.68 **91**	1.86 **100**	1.85 **100**	1.76 **95**	1.41 **76**
	floctafenine	1.66 **94**	1.74 **99**	1.76 **100**	1.73 **99**	1.71 **98**
	asa ect tab, sr tab/cap	0.38 **104**	0.36 **98**	0.36 **100**	0.39 **108**	0.38 **104**
	Subtotal	*1.35* ***102***	*1.38* ***105***	*1.32* ***100***	*0.98* ***74***	*0.96* ***73***
	All NSAIDs	***0.91 114***	***0.85 106***	***0.80 100***	***0.47 59***	***0.40 50***
COX-2 NSAIDS						0.98
ACETAMINOPHEN & MILD OPIATES	acetaminophen				0.14	0.11
	codeine	0.45 **104**	0.48 **111**	0.43 **100**	0.38 **87**	0.36 **84**
	codeine/acetaminophen	0.17 **147**	0.18 **149**	0.12 **100**	0.12 **98**	0.13 **110**
	codeine/asa	0.78 **97**	0.90 **113**	0.80 **100**	0.83 **104**	0.81 **101**
	oxycodone/acetaminophen	2.64 **254**	3.10 **298**	1.04 **100**	0.87 **84**	0.86 **82**
	All Acetam./Mild Opiates	***0.28 155***	***0.28 155***	***0.18 100***	***0.17 96***	***0.18 102***
OPIATES	fentanyl	0.21 **102**	0.20 **99**	0.21 **100**	0.20 **97**	0.19 **93**
	hydromorphone	0.47 **145**	0.39 **122**	0.32 **100**	0.33 **104**	0.39 **123**
	meperidine	1.47 **96**	1.55 **102**	1.53 **100**	1.48 **97**	1.44 **94**
	morphine	2.85 **94**	3.04 **101**	3.02 **100**	2.89 **96**	2.52 **83**
	propoxyphene	0.83 **97**	0.87 **102**	0.86 **100**	0.84 **98**	0.84 **98**
	anileridine	4.45 **97**	4.60 **100**	4.58 **100**	4.45 **97**	4.31 **94**
	pentazocine	1.43 **93**	1.53 **100**	1.53 **100**	1.49 **97**	1.44 **94**
	All Opiates	***1.17 119***	***0.93 95***	***0.98 100***	***1.00 102***	***0.72 73***

Notes: the bolded values indicate period-specific average monthly rates relative to rates in the LCA period.

Table 3 Average monthly beneficiary out-of-pocket expenditure per 100,000 seniors, by analgesic and time period

Analgesic Category		Time Period				
		Historical Nov 89 - Dec 92	SR Delisted Jan 93 - Mar 94	LCA Apr 94 - Oct 95	RP NSAIDs Nov 95 - Oct 96	Delistings Nov 96 - Jun 01
NSAIDS						
Unrestricted	asa ect 650mg tab	0 **0**	0 **0**	66 **100**	127 **192**	91 **138**
	ibuprofen tab	0 **0**	0 **0**	22 **100**	80 **364**	93 **423**
	naproxen tab	0 **0**	0 **0**	32 **100**	286 **894**	463 **1,447**
	Subtotal	*0* ***0***	*0* ***0***	*120* ***100***	*493* ***411***	*647* ***539***
First Line Restricted	diclofenac	0 **0**	0 **0**	342 **100**	5,449 **1,593**	4,918 **1,438**
	diclofenac/misoprostol	**0**	0 **0**	170 **100**	3,401 **2,001**	4,693 **2,761**
	diflunisal	0 **0**	0 **0**	19 **100**	155 **816**	96 **505**
	fenoprofen	0 **0**	0 **0**	4 **100**	58 **1,450**	26 **650**
	flurbiprofen	0 **0**	0 **0**	30 **100**	286 **953**	234 **780**
	indometacin	0 **0**	0 **0**	132 **100**	905 **686**	522 **395**
	ketoprofen	0 **0**	0 **0**	308 **100**	1,014 **329**	623 **202**
	naproxen ect & sr	0 **0**	0 **0**	141 **100**	1,965 **1,394**	1,517 **1,076**
	salsalate	**0**	0 **0**	6 **100**	59 **983**	42 **700**
	Subtotal	*0* ***0***	*0* ***0***	*1,152* ***100***	*13,292* ***1,154***	*12,671* ***1,100***
Second Line Restricted	sulindac	0 **0**	0 **0**	31 **100**	528 **1,703**	20 **65**
	nabumetone	**0**	**0**	105 **100**	1,424 **1,356**	128 **122**
	piroxicam cap	0 **0**	0 **0**	48 **100**	534 **1,113**	23 **48**
	tenoxicam	0 **0**	0 **0**	60 **100**	732 **1,220**	39 **65**
	tiaprofenic acid	0 **0**	0 **0**	252 **100**	1,119 **444**	47 **19**
	tolmetin	0 **0**	0 **0**	41 **100**	135 **329**	12 **29**
	Subtotal	*0* ***0***	*0* ***0***	*537* ***100***	*4,472* ***833***	*269* ***50***
Delisted/Special Auth.	ketorolac tromethamine inj	0	0	0	1	2
	ketorolac tromethamine tab	0 **0**	0 **0**	29 **100**	1,643 **5,666**	27 **93**
	etodolac			0	0	0
	indometacin sup	0 **0**	0 **0**	23 **100**	118 **513**	59 **257**
	mefenamic	0 **0**	0 **0**	1 **100**	3 **300**	8 **800**
	naproxen sup/inj	0 **0**	0 **0**	24 **100**	28 **117**	18 **75**
	naproxen 1 gram sr	0 **0**	0 **0**	9 **100**	29 **322**	14 **156**
	phenylbutazone	0	0	0	0	0
	ketoprofen sup	0 **0**	0 **0**	20 **100**	26 **130**	15 **75**
	diclofenac sup	0 **0**	0 **0**	5 **100**	91 **1,820**	89 **1,780**
	piroxicam sup	0	0	0	14	2
	floctafenine	0 **0**	0 **0**	3 **100**	10 **333**	8 **267**
	asa ect tab, sr tab/cap	0 **0**	0 **0**	3 **100**	11 **367**	9 **300**
	Subtotal	*0* ***0***	*0* ***0***	*117* ***100***	*1,974* ***1,687***	*251* ***215***
	All NSAIDs	***0 0***	***0 0***	***1,926 100***	***20,231 1,050***	***13,838 718***
COX-2 NSAIDS						74
ACETAMINOPHEN & MILD OPIATES	acetaminophen	0	0	0	145	207
	codeine	0 **0**	0 **0**	4 **100**	31 **775**	39 **975**
	codeine/acetaminophen	0 **0**	0 **0**	133 **100**	225 **169**	452 **340**
	codeine/asa	0 **0**	0 **0**	83 **100**	156 **188**	285 **343**
	oxycodone/acetaminophen	0 **0**	0 **0**	151 **100**	523 **346**	521 **345**
	All Acetam./Mild Opiates	***0 0***	***0 0***	***371 100***	***1,080 291***	***1,504 405***
OPIATES	fentanyl	0 **0**	0 **0**	2 **100**	0 **0**	95 **4,750**
	hydromorphone	0 **0**	0 **0**	23 **100**	60 **261**	122 **530**
	meperidine	0 **0**	0 **0**	2 **100**	9 **450**	22 **1,100**
	morphine	0 **0**	0 **0**	296 **100**	748 **253**	1,061 **358**
	propoxyphene	0 **0**	0 **0**	17 **100**	45 **265**	9 **53**
	anileridine	0 **0**	0 **0**	18 **100**	48 **267**	81 **450**
	pentazocine	0 **0**	0 **0**	2 **100**	104 **5,200**	4 **200**
	All Opiates	***0 0***	***0 0***	***360 100***	***1,014 282***	***1,394 387***

Notes: the bolded values indicate period-specific average monthly rates relative to rates in the LCA period.

Figure 1 Defined daily doses of analgesics dispensed per 100,000 seniors, by analgesic category and month

Notes: We fit a moving average trend line through the data points.
The vertical lines indicate the introduction of the 4 major NSAID cost control policies in the 1990s; see text for details of these policies.

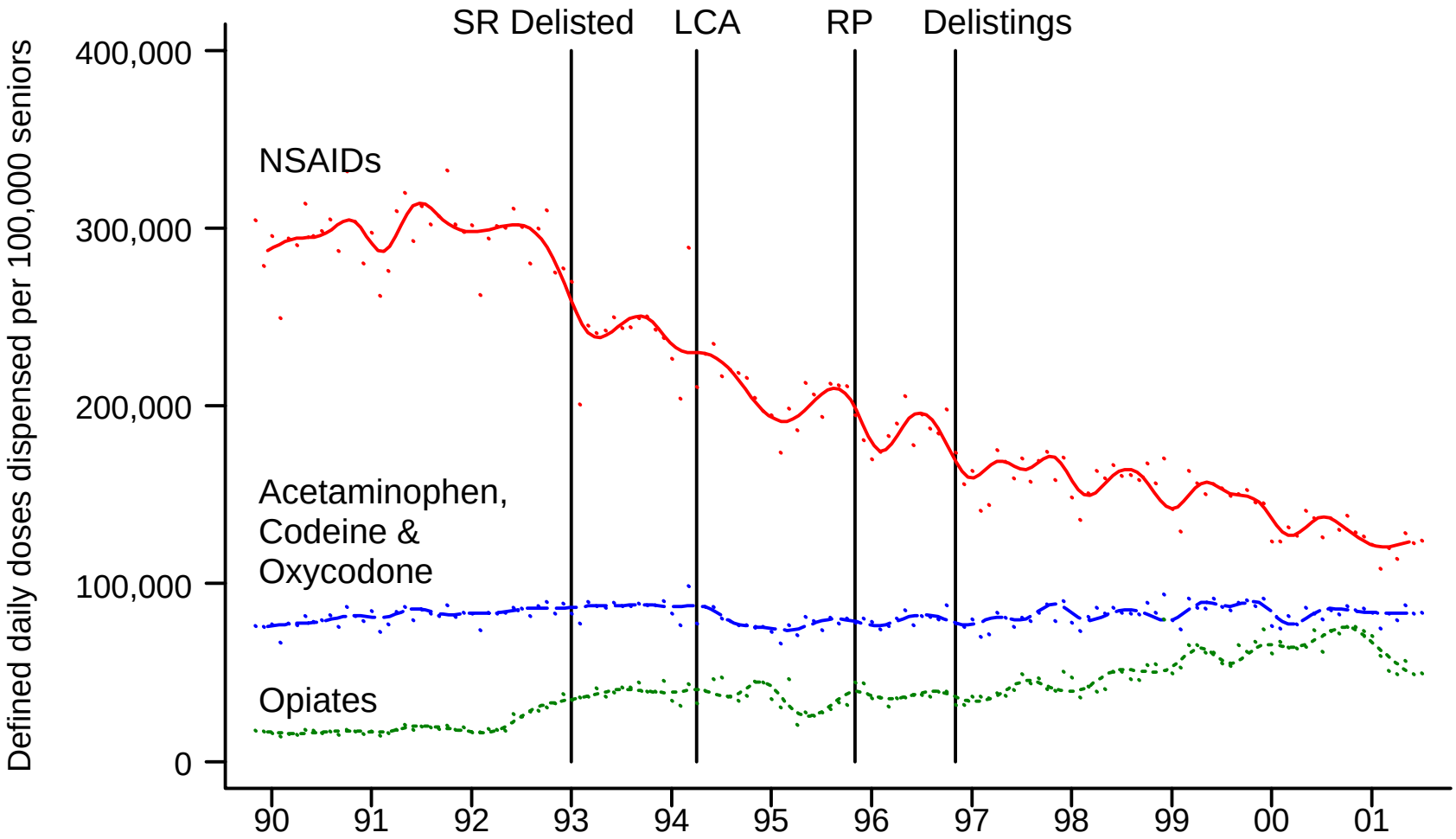


Figure 2 Defined daily doses of NSAIDs dispensed per 100,000 seniors, by NSAID reimbursement category and month

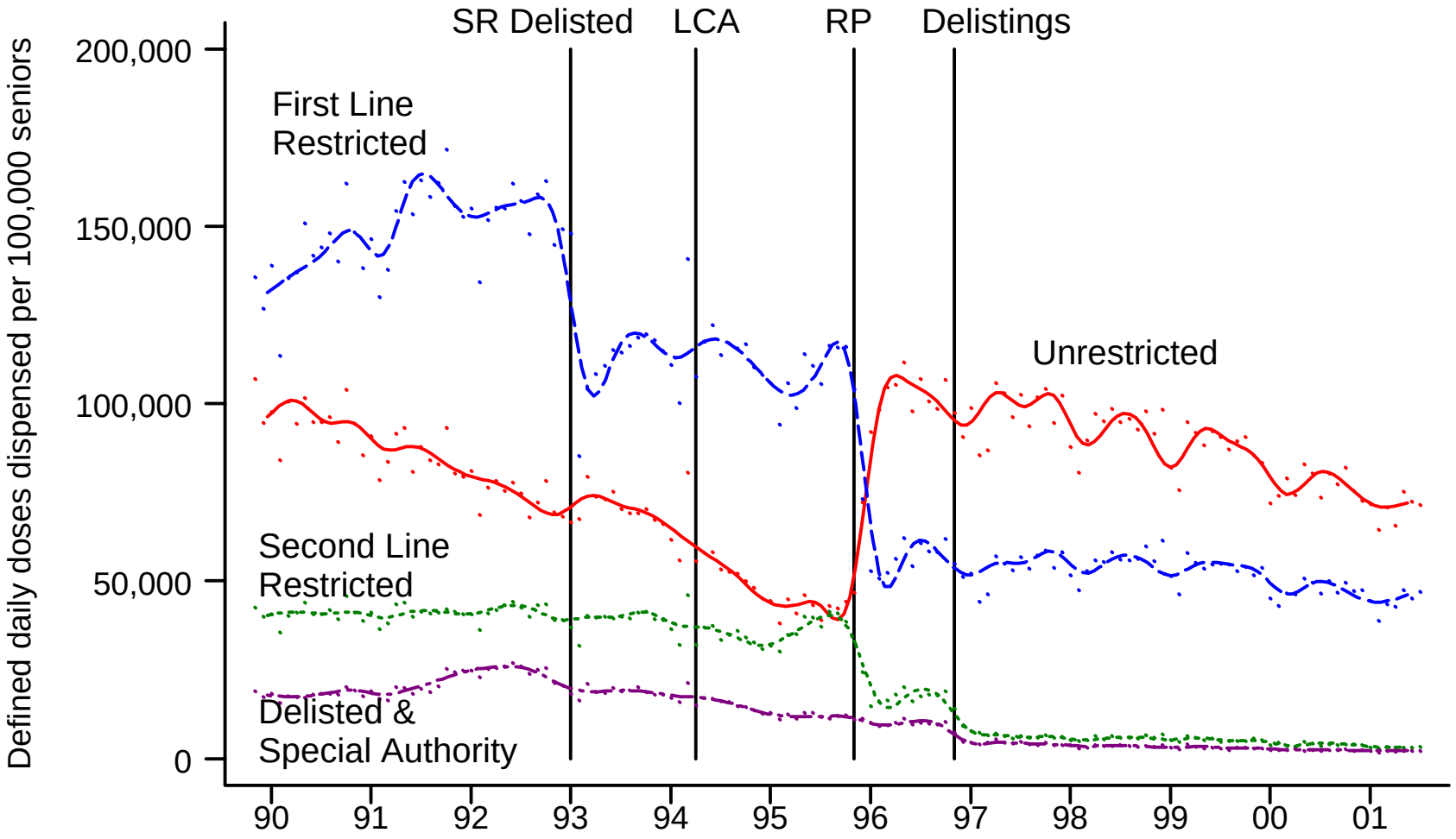


Figure 3 Average Pharmacare reimbursement per defined daily dose dispensed, by NSAID reimbursement category and month

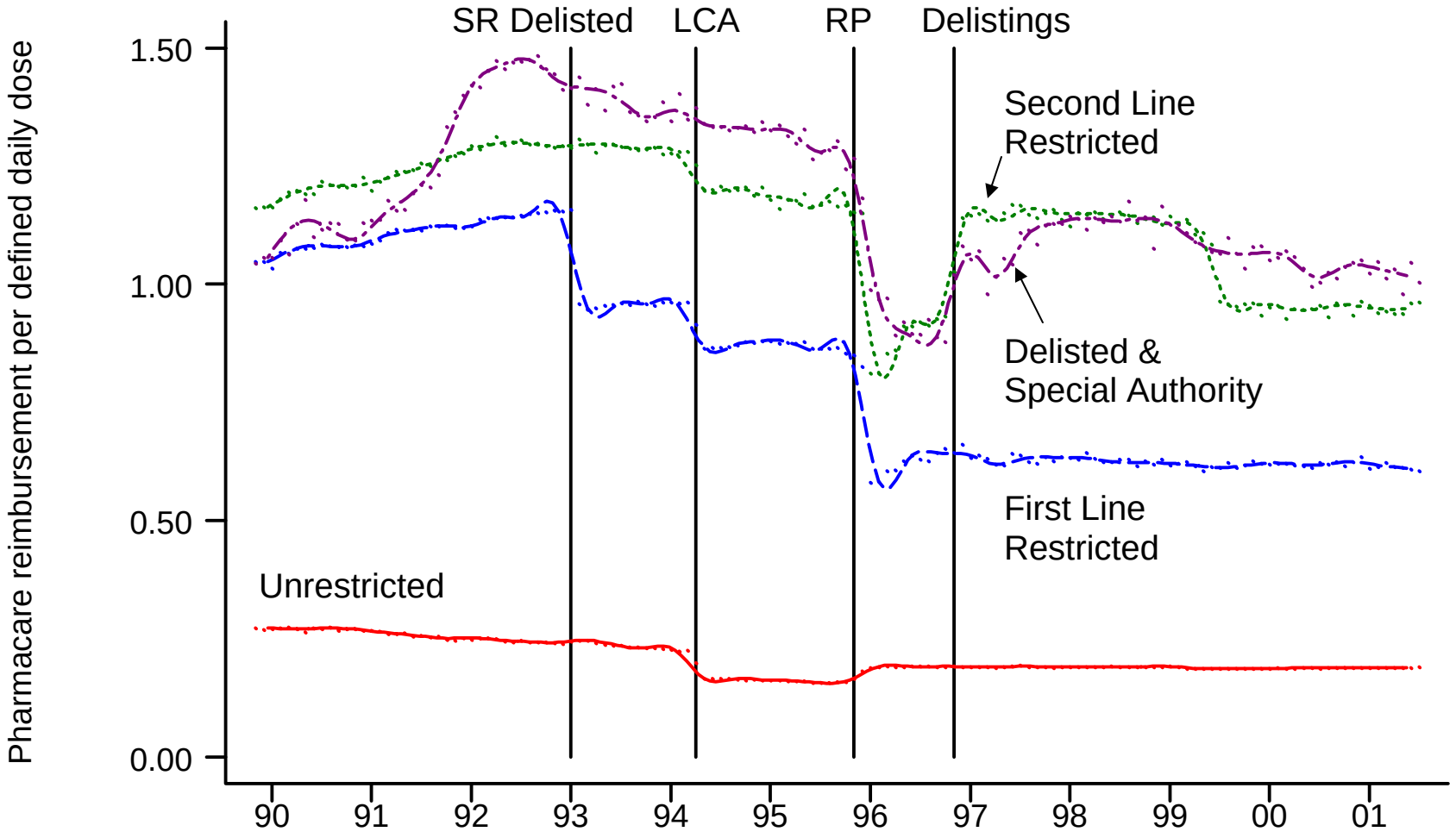


Figure 4 Average Pharmacare reimbursement per defined daily dose dispensed, by analgesic category and month

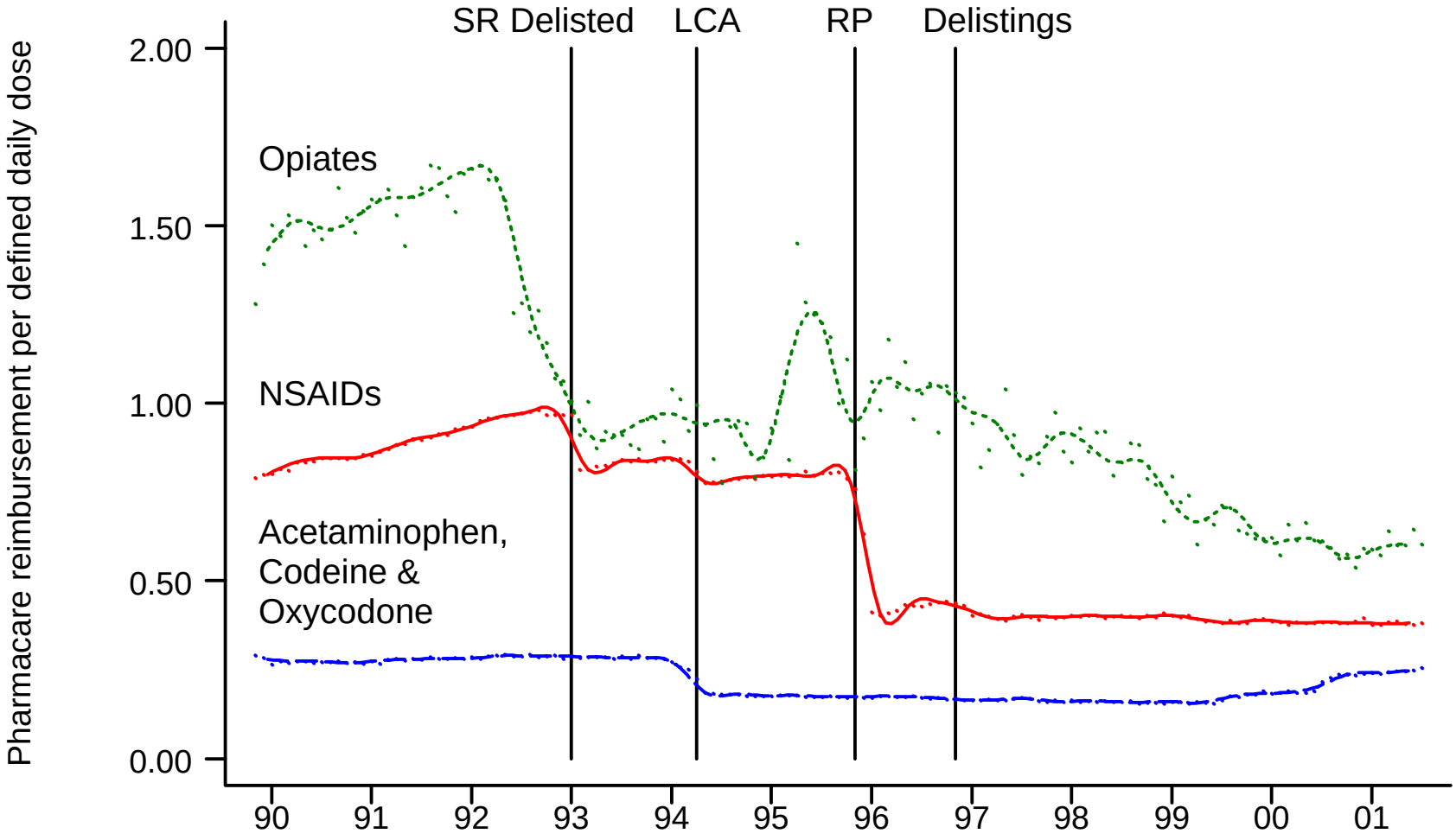


Figure 5 Pharmacare drug expenditures on analgesics per 100,000 seniors, by analgesic category and month

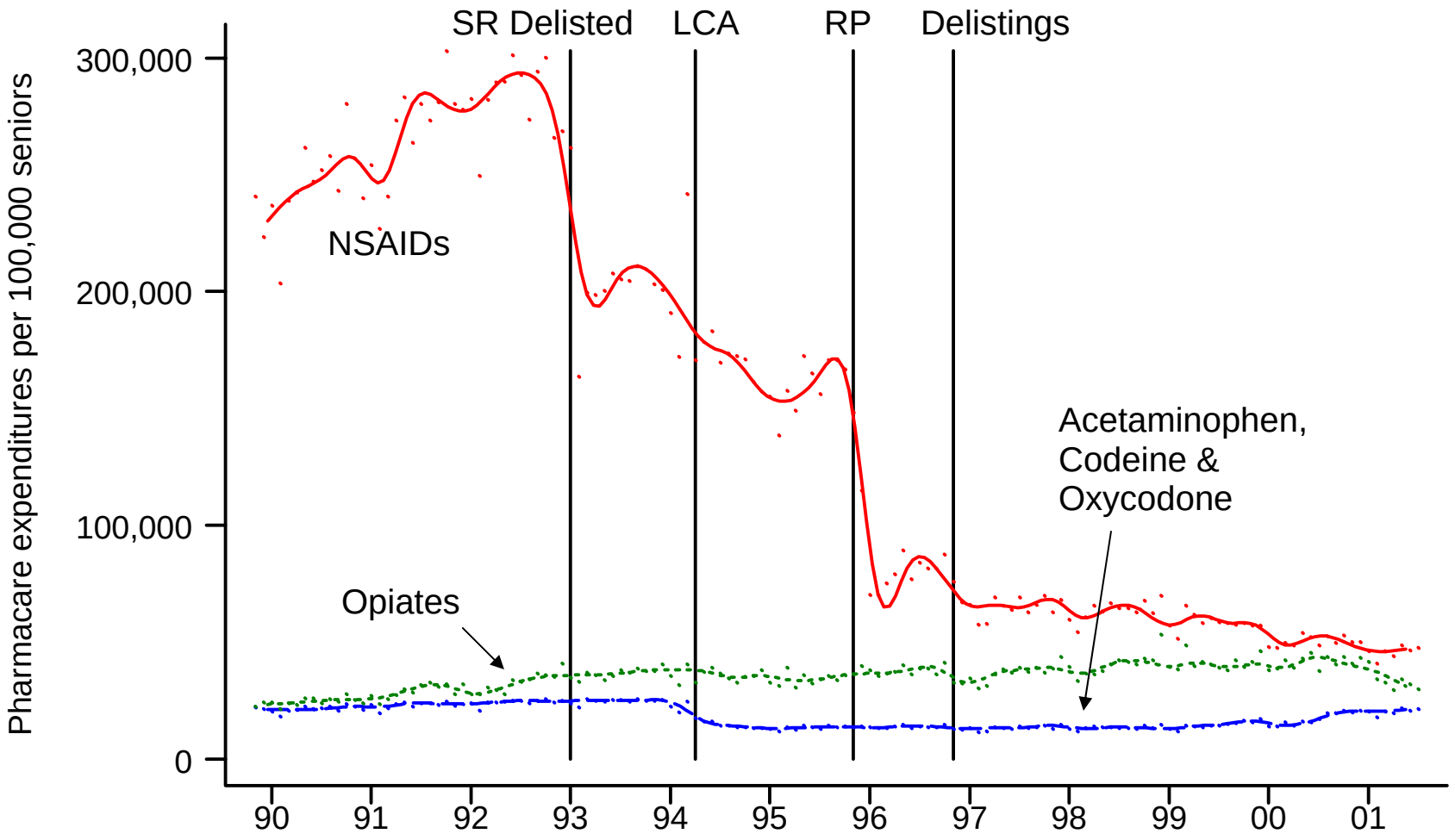
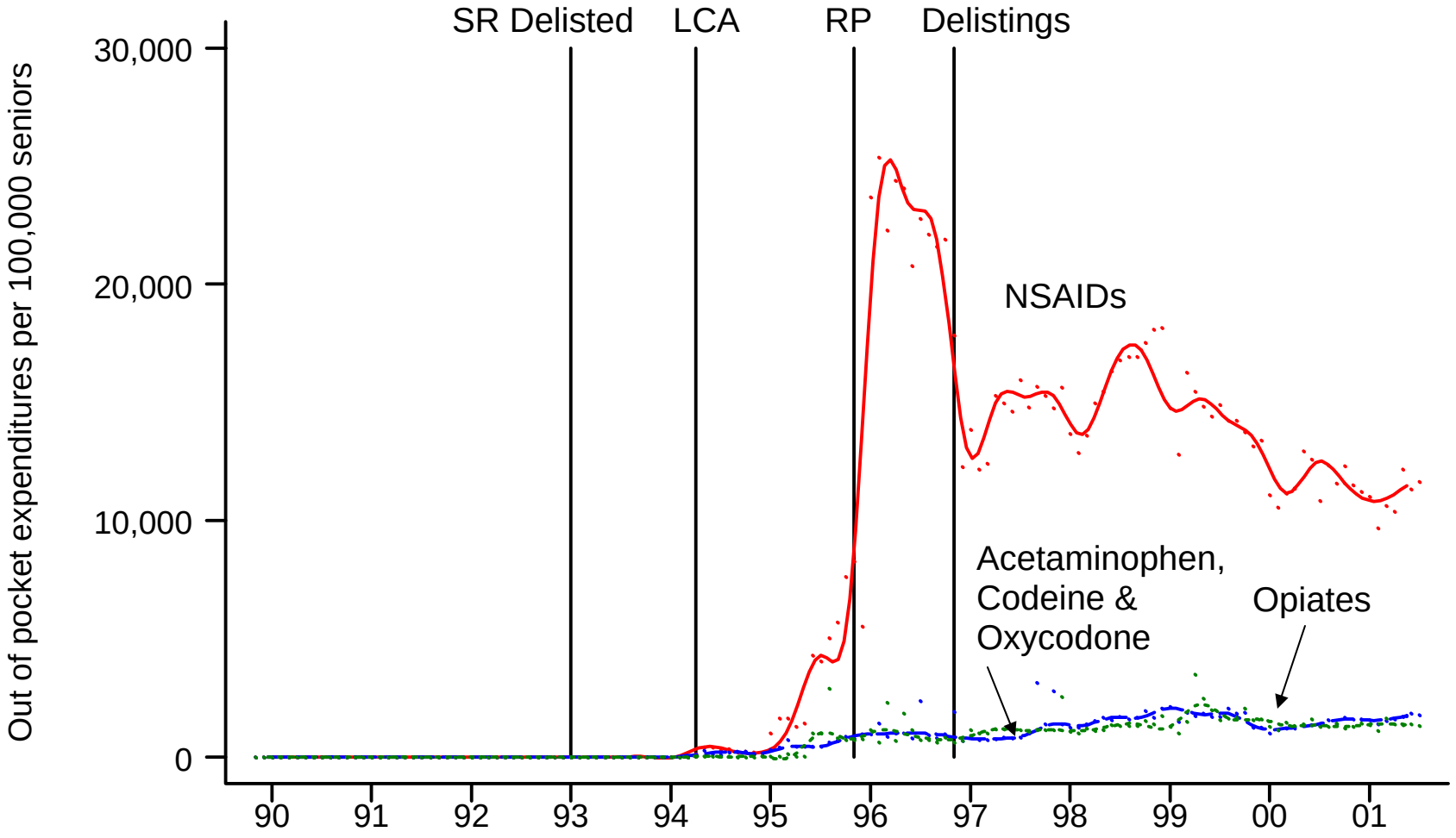


Figure 6 Patient out-of-pocket drug expenditures per 100,000 seniors, by therapeutic category and month



Appendix 1 Parameter estimates

outcome: Pharmacare reimbursement per defined daily dose NSAID therapy
estimation period: February 1993 - June 2001 (*n*=101)

Covariate	**coefficient**	**t-ratio**	**p-value**
t	0.002	3.97	<0.001
LCA	0.368	1.74	0.086
LCA×*t*	-0.001	-2.01	0.048
RP	0.658	2.52	0.013
RP×*t*	-0.002	-4.20	<0.001
Constant	0.029	0.14	0.886

outcome: beneficiary reimbursement per defined daily dose NSAID therapy
estimation period: May 1994 – June 2001 (*n*=86)

Covariate	**coefficient**	**t-ratio**	**p-value**
RP	0.130	9.34	<0.001
Constant	0.020	1.96	0.053

outcome: beneficiary expenditure on NSAIDs
estimation period: May 1994 - June 2001 (n=86)

Covariate	**coefficient**	**t-ratio**	**p-value**
RP	66,461.200	10.54	<0.001
Constant	9,488.796	1.95	0.054

SEDAP RESEARCH PAPERS

Number	Title	Author(s)
No. 1:	Population Aging and Its Economic Costs: A Survey of the Issues and Evidence	F.T. Denton B.G. Spencer
No. 2:	How Much Help Is Exchanged in Families? Towards an Understanding of Discrepant Research Findings	C.J. Rosenthal L.O. Stone
No. 3:	Did Tax Flattening Affect RRSP Contributions?	M.R. Veall
No. 4:	Families as Care-Providers Versus Care-Managers? Gender and Type of Care in a Sample of Employed Canadians	C.J. Rosenthal A. Martin-Matthews
No. 5:	Alternatives for Raising Living Standards	W. Scarth
No. 6:	Transitions to Retirement: Determinants of Age of Social Security Take Up	E. Tompa
No. 7:	Health and Individual and Community Characteristics: A Research Protocol	F. Béland S. Birch G. Stoddart
No. 8:	Disability Related Sources of Income and Expenses: An Examination Among the Elderly in Canada	P. Raina S. Dukeshire M. Denton L.W. Chambers A. Scanlan A. Gafni S. French A. Joshi C. Rosenthal
No. 9:	The Impact of Rising 401(k) Pension Coverage on Future Pension Income	W.E. Even D.A. Macpherson
No. 10:	Income Inequality as a Canadian Cohort Ages: An Analysis of the Later Life Course	S.G. Prus
No. 11:	Are Theories of Aging Important? Models and Explanations in Gerontology at the Turn of the Century	V.L. Bengtson C.J. Rice M.L. Johnson
No. 12:	Generational Equity and the Reformulation of Retirement	M.L. Johnson
No. 13:	Long-term Care in Turmoil	M.L. Johnson L. Cullen D. Patsios
No. 14:	The Effects of Population Ageing on the Canadian Health Care System	M.W. Rosenberg

Number	Title	Author(s)
No. 15:	Projections of the Population and Labour Force to 2046: Canada	F.T. Denton C.H. Feaver B.G. Spencer
No. 16:	Projections of the Population and Labour Force to 2046: The Provinces and Territories	F.T. Denton C.H. Feaver B.G. Spencer
No. 17:	Location of Adult Children as an Attraction for Black and White Elderly Migrants in the United States	K.-L. Liaw W.H. Frey J.-P. Lin
No. 18:	The Nature of Support from Adult *Sansei* (Third Generation) Children to Older *Nisei* (Second Generation) Parents in Japanese Canadian Families	K.M. Kobayashi
No. 19:	The Effects of Drug Subsidies on Out-of-Pocket Prescription Drug Expenditures by Seniors: Regional Evidence from Canada	T.F. Crossley P. Grootendorst S. Korkmaz M.R. Veall
No. 20:	Describing Disability among High and Low Income Status Older Adults in Canada	P. Raina M. Wong L.W. Chambers M. Denton A. Gafni
No. 21:	Parental Illness and the Labour Supply of Adult Children	P.T.Léger
No. 22:	Some Demographic Consequences of Revising the Definition of Old to Reflect Future Changes in Life Table Probabilities	F.T. Denton B.G. Spencer
No. 23:	Geographic Dimensions of Aging: The Canadian Experience 1991-1996	E.G. Moore D. McGuinness M.A. Pacey M.W. Rosenberg
No. 24:	The Correlation Between Husband's and Wife's Education: Canada, 1971-1996	L. Magee J. Burbidge L. Robb
No. 25:	The Effect of Marginal Tax Rates on Taxable Income: A Panel Study of the 1988 Tax Flattening in Canada	M.-A. Sillamaa M.R. Veall
No. 26:	The Stability of Self Assessed Health Status	T.F. Crossley S. Kennedy

Number	Title	Author(s)
No. 27:	How Do Contribution Limits Affect Contributions to Tax-Preferred Savings Accounts?	K. Milligan
No. 28:	The Life Cycle Model of Consumption and Saving	M. Browning T.F. Crossley
No. 29:	Population Change and the Requirements for Physicians: The Case of Ontario	F.T. Denton A. Gafni B.G. Spencer
No. 30:	Nonparametric Identification of Latent Competing Risks and Roy Duration Models	G. Colby P. Rilstone
No. 31:	Simplified Estimation of Multivariate Duration Models with Unobserved Heterogeneity	G. Colby P. Rilstone
No. 32:	Structural Estimation of Psychiatric Hospital Stays	G. Colby P. Rilstone
No. 33:	Have 401(k)s Raised Household Saving? Evidence from the Health and Retirement Study	G.V. Engelhardt
No. 34:	Health and Residential Mobility in Later Life: A New Analytical Technique to Address an Old Problem	L.M. Hayward
No. 35:	2 ½ Proposals to Save Social Security	D. Fretz M.R. Veall
No. 36:	The Consequences of Caregiving: Does Employment Make a Difference	C.L. Kemp C.J. Rosenthal
No. 37:	Fraud in Ethnocultural Seniors' Communities	P.J.D. Donahue
No. 38:	Social-psychological and Structural Factors Influencing the Experience of Chronic Disease: A Focus on Individuals with Severe Arthritis	P.J. Ballantyne G.A. Hawker D. Radoeva
No. 39:	The Extended Self: Illness Experiences of Older Married Arthritis Sufferers	P.J. Ballantyne G.A. Hawker D. Radoeva
No. 40:	A Comparison of Alternative Methods to Model Endogeneity in Count Models. An Application to the Demand for Health Care and Health Insurance Choice	M. Schellhorn
No. 41:	Wealth Accumulation of US Households: What Do We Learn from the SIPP Data?	V. Hildebrand
No. 42:	Pension Portability and Labour Mobility in the United States. New Evidence from SIPP Data.	V. Andrietti V. Hildebrand

Number	Title	Author(s)
No. 43:	Exploring the Effects of Population Change on the Costs of Physician Services	F.T. Denton A. Gafni B.G. Spencer
No. 44:	Reflexive Planning for Later Life: A Conceptual Model and Evidence from Canada	M.A. Denton S. French A. Gafni A. Joshi C. Rosenthal S. Webb
No. 45:	Time Series Properties and Stochastic Forecasts: Some Econometrics of Mortality from the Canadian Laboratory	F.T. Denton C.H. Feaver B.G. Spencer
No. 46:	Linear Public Goods Experiments: A Meta-Analysis	J. Zelmer
No. 47:	Local Planning for an Aging Population in Ontario: Two Case Studies	L.M. Hayward
No. 48:	Management Experience and Diversity in an Ageing Organisation: A Microsimulation Analysis	T. Wannell M. Gravel
No. 49:	Resilience Indicators of Post Retirement Well-Being	E. Marziali P. Donahue
No. 50:	Continuity or Change? Older People in Three Urban Areas	J. Phillips M. Bernard C. Phillipson J. Ogg
No. 51:	Intracohort Income Status Maintenance: An Analysis of the Later Life Course	S.G. Prus
No. 52:	Tax-Preferred Savings Accounts and Marginal Tax Rates: Evidence on RRSP Participation	K. Milligan
No. 53:	Cohort Survival Analysis is Not Enough: Why Local Planners Need to Know More About the Residential Mobility of the Elderly	L.M. Hayward N.M. Lazarowich
No. 54:	Unemployment and Health: Contextual Level Influences on the Production of Health in Populations	F. Béland S. Birch G. Stoddart

Number	Title	Author(s)
No. 55:	The Timing and Duration of Women's Life Course Events: A Study of Mothers With At Least Two Children	K.M. Kobayashi A. Martin-Matthews C.J. Rosenthal S. Matthews
No. 56:	Age-Gapped and Age-Condensed Lineages: Patterns of Intergenerational Age Structure Among Canadian Families	A. Martin-Matthews K. M. Kobayashi C.L. Rosenthal S.H. Matthews
No. 57:	The Relationship between Age, Socio-Economic Status, and Health among Adult Canadians	S.G. Prus
No. 58:	Measuring Differences in the Effect of Social Resource Factors on the Health of Elderly Canadian Men and Women	S.G. Prus E. Gee
No. 59:	APOCALYPSE NO: Population Aging and the Future of Health Care Systems	R.G. Evans K.M. McGrail S.G. Morgan M.L. Barer C. Hertzman
No. 60:	The Education Premium in Canada and the United States	J.B. Burbidge L. Magee A.L. Robb
No. 61:	Student Enrolment and Faculty Recruitment in Ontario: The Double Cohort, the Baby Boom Echo, and the Aging of University Faculty	B.G. Spencer
No. 62:	The Social and Demographic Contours of Contemporary Grandparenthood: Mapping Patterns in Canada and the United States	C.L. Kemp
No. 63:	Changing Income Inequality and the Elderly in Canada 1991-1996: Provincial Metropolitan and Local Dimensions	E.G. Moore M.A. Pacey
No. 64:	Mid-life Patterns and the Residential Mobility of Older Men	L.M. Hayward
No. 65:	The Retirement Incentive Effects of Canada’s Income Security Programs	M. Baker J. Gruber K. Milligan
No. 66:	The Economic Well-Being of Older Women Who Become Divorced or Separated in Mid and Later Life	S. Davies M. Denton

Number	Title	Author(s)
No. 67:	Alternative Pasts, Possible Futures: A "What If" Study of the Effects of Fertility on the Canadian Population and Labour Force	F.T. Denton C.H. Feaver B.G. Spencer
No. 68:	Baby-Boom Aging and Average Living Standards	W. Scarth M. Souare
No. 69:	The Invisible Retirement of Women	L. McDonald
No. 70:	The Impact of Reference Pricing of Cardiovascular Drugs on Health Care Costs and Health Outcomes: Evidence from British Columbia – Volume I: Summary	P.V. Grootendorst L.R. Dolovich A.M. Holbrook A.R. Levy B.J. O'Brien
No. 71:	The Impact of Reference Pricing of Cardiovascular Drugs on Health Care Costs and Health Outcomes: Evidence from British Columbia – Volume II: Technical Report	P.V. Grootendorst L.R. Dolovich A.M. Holbrook A.R. Levy B.J. O'Brien
No. 72:	The Impact of Reference Pricing of Cardiovascular Drugs on Health Care Costs and Health Outcomes: Evidence from British Columbia – Volume III: ACE and CCB Literature Review	L.R. Dolovich A.M. Holbrook M. Woodruff
No. 73:	Do Drug Plans Matter? Effects of Drug Plan Eligibility on Drug Use Among the Elderly, Social Assistance Recipients and the General Population	P. Grootendorst M. Levine
No. 74:	Living Alone and Living with Children: The Living Arrangements of Canadian and Chinese-Canadian Seniors	M.A. Pacey
No. 75:	Student Enrolment and Faculty Recruitment in Ontario: The Double Cohort, the Baby Boom Echo, and the Aging of University Faculty (Revised and updated version of No. 61)	B.G. Spencer
No. 76:	Gender Differences in the Influence of Economic, Lifestyle, and Psychosocial Factors on Later-life Health	S.G. Prus E. Gee
No. 77:	Asking Consumption Questions in General Purpose Surveys	M. Browning T.F. Crossley G. Weber
No. 78:	A Longitudinal Study of the Residential Mobility of the Elderly in Canada	Y. Ostrovsky
No. 79:	Health Care in Rural Communities: Exploring the Development of Informal and Voluntary Care	M.W. Skinner M.W. Rosenberg

Number	Title	Author(s)
No. 80:	Does Cognitive Status Modify the Relationship Between Education and Mortality? Evidence from the Canadian Study of Health and Aging	J.C. Brehaut P. Raina J. Lindsay
No. 81:	Agreement Between Self-Reported and Routinely Collected Health Care Utilisation Data Among Seniors	P. Raina V. Torrance-Rynard M. Wong C. Woodward
No. 82:	Age, Retirement and Expenditure Patterns: An Econometric Study of Older Canadian Households	F.T. Denton D.C. Mountain B.G. Spencer
No. 83:	Understanding the Relationship between Income Status and the Restrictions in Instrumental Activities of Daily Living among Disabled Older Adults	P. Raina M. Wong
No. 84:	Location of Adult Children as an Attraction for Black and White Elderly *Return* and *Onward* Migrants in the United States: Application of a Three-level Nested Logit Model with Census Data	K-L. Liaw W.H. Frey
No. 85:	Changing Income Inequality and Immigration in Canada 1980-1995	E.G. Moore M.A. Pacey
No. 86:	The Dynamics of Food Deprivation and Overall Health: Evidence from the Canadian National Population Health Survey	L. McLeod M.R. Veall
No. 87:	Quebec's Lackluster Performance in Interprovincial Migration and Immigration: How, Why, and What Can Be Done?	K-L. Liaw L. Xu M. Qi
No. 88:	Out-of-Pocket Prescription Drug Expenditures and Public Prescription Drug Programs	S. Alan T.F. Crossley P. Grootendorst M.R. Veall
No. 89:	The Wealth and Asset Holdings of U.S.-Born and Foreign-Born Households: Evidence from SIPP Data	D.A. Cobb-Clark V. Hildebrand
No. 90:	Population Aging, Productivity, and Growth in Living Standards	W. Scarth
No. 91:	A Life-course Perspective on the Relationship between Socio-economic Status and Health: Testing the Divergence Hypothesis	S.G. Prus
No. 92:	Immigrant Mental Health and Unemployment	S. Kennedy
No. 93:	The Relationship between Education and Health in Australia and Canada	S. Kennedy

Number	Title	Author(s)
No. 94:	The Transition from Good to Poor Health: An Econometric Study of the Older Population	N.J. Buckley F.T. Denton A.L. Robb B.G. Spencer
No. 95:	Using Structural Equation Modeling to Understand the Role of Informal and Formal Supports on the Well-being of Caregivers of Persons with Dementia	P. Raina C. McIntyre B. Zhu I. McDowell L. Santaguida B. Kristjansson A. Hendricks L.W. Chambers
No. 96:	Helping to Build and Rebuild Secure Lives and Futures: Intergenerational Financial Transfers from Parents to Adult Children and Grandchildren	J. Ploeg L. Campbell M. Denton A. Joshi S. Davies
No. 97:	Geographic Dimensions of Aging in Canada 1991-2001	E.G. Moore M.A. Pacey
No. 98:	Examining the “Healthy Immigrant Effect” in Later Life: Findings from the Canadian Community Health Survey	E.M. Gee K.M. Kobayashi S.G. Prus
No. 99:	The Evolution of High Incomes in Canada, 1920-2000	E. Saez M.R. Veall
No. 100:	Macroeconomic Implications of Population Aging and Public Pensions	M. Souare
No. 101:	How Do Parents Affect the Life Chances of Their Children as Adults? An Idiosyncratic Review	J. Ermisch
No. 102:	Population Change and Economic Growth: The Long-Term Outlook	F.T. Denton B.G. Spencer
No. 103:	Use of Medicines by Community Dwelling Elderly in Ontario	P.J. Ballantyne J.A. Marshman P.J. Clarke J.C. Victor
No. 104:	The Economic Legacy of Divorced and Separated Women in Old Age	L. McDonald A.L. Robb

Number	Title	Author(s)
No. 105:	National Catastrophic Drug Insurance Revisited: Who Would Benefit from Senator Kirby's Recommendations?	T.F. Crossley P.V. Grootendorst M.R. Veall
No. 106:	WAGES in CANADA: SCF, SLID, LFS and the Skill Premium	A.L Robb L. Magee J.B. Burbidge
No. 107:	A Synthetic Cohort Analysis of Canadian Housing Careers	T.F. Crossley Y. Ostrovsky
No. 108:	The Policy Challenges of Population Ageing	A. Walker
No. 109:	Social Transfers and Income Inequality in Old-age: A Multi-national Perspective	R.L. Brown S.G. Prus
No. 110:	Organizational Change and the Health and Well-Being of Home Care Workers	M. Denton I.U. Zeytinoglu S. Davies
No. 111:	Stasis Amidst Change: Canadian Pension Reform in an Age of Retrenchment	D. Béland J. Myles
No. 112:	Socioeconomic Aspects of Healthy Aging: Estimates Based on Two Major Surveys	N.J. Buckley F.T. Denton A.L. Robb B.G. Spencer
No. 113:	An Invitation to Multivariate Analysis: An Example About the Effect of Educational Attainment on Migration Propensities in Japan	A. Otomo K-L. Liaw
No. 114:	The Politics of Protest Avoidance: Policy Windows, Labor Mobilization, and Pension Reform in France	D. Béland P. Marier
No. 115:	The Impact of Differential Cost Sharing of Non-Steroidal Anti-Inflammatory Agents on the Use and Costs of Analgesic Drugs	P.V. Grootendorst J.K. Marshall A.M. Holbrook L.R. Dolovich B.J. O'Brien A.R. Levy