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## 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**

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**SEDAP Research Paper No. 115**

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

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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 Pharmicare 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; Zweifel and Crivelli 1996; Anis and Wen 1998) Finally, although Pharmicare 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 Pharmicare claims data to examine Pharmicare reimbursement rates for NSAIDs, as well as prescribing patterns and Pharmicare-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, Pharmicare 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 Pharmicare 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<sup>1</sup> 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

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<sup>1</sup> 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  $\beta_j$ ,  $j=0, \dots, 5$  are unknown parameters estimated using ordinary least squares and  $\varepsilon_t$  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 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 Pharmicare 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 Pharmicare’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 Pharmicare 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 Pharmicare 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).



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

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

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

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

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.

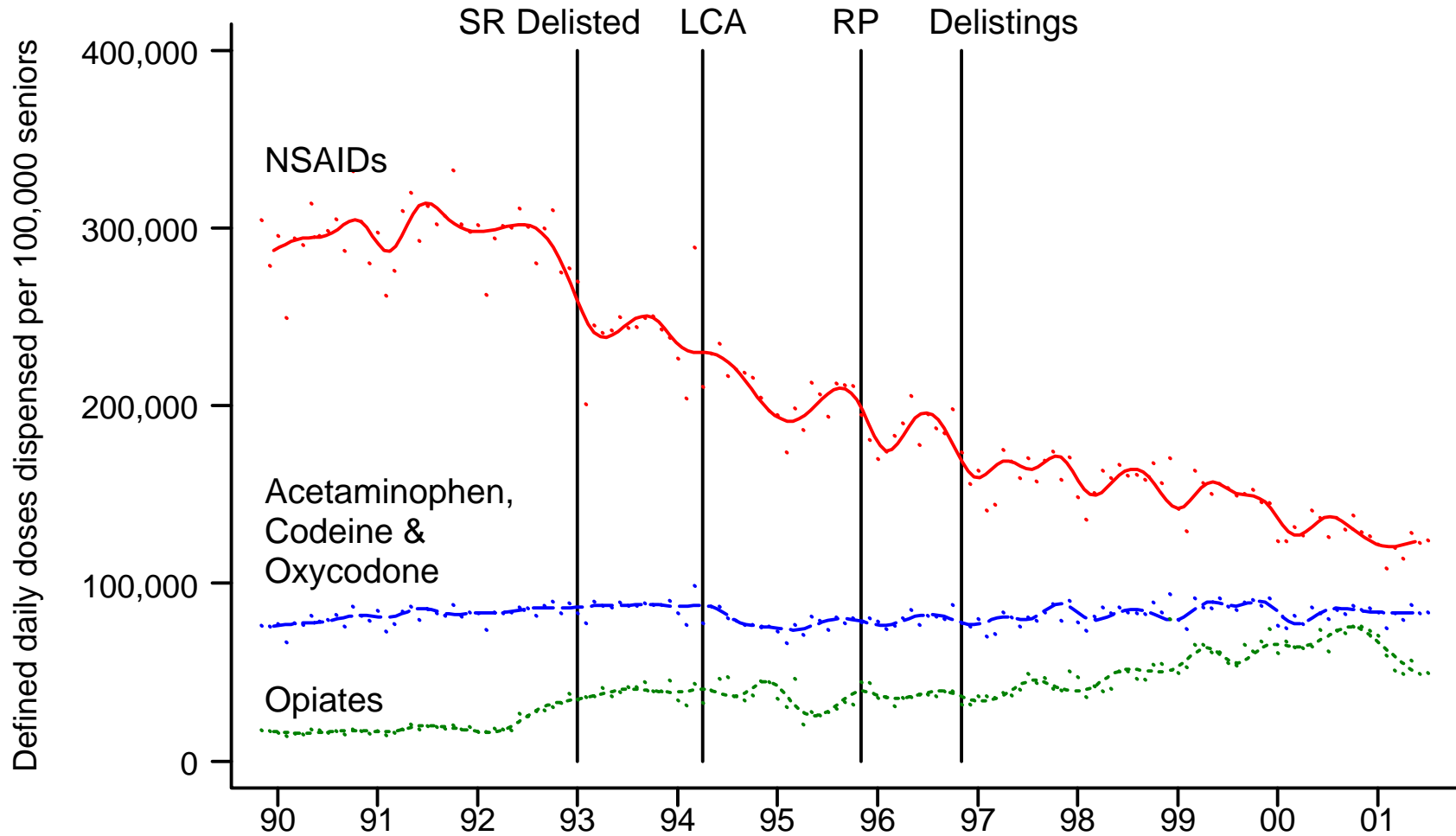


Figure 2 Defined daily doses of NSAIDs dispensed per 100,000 seniors, by NSAID reimbursement category and month

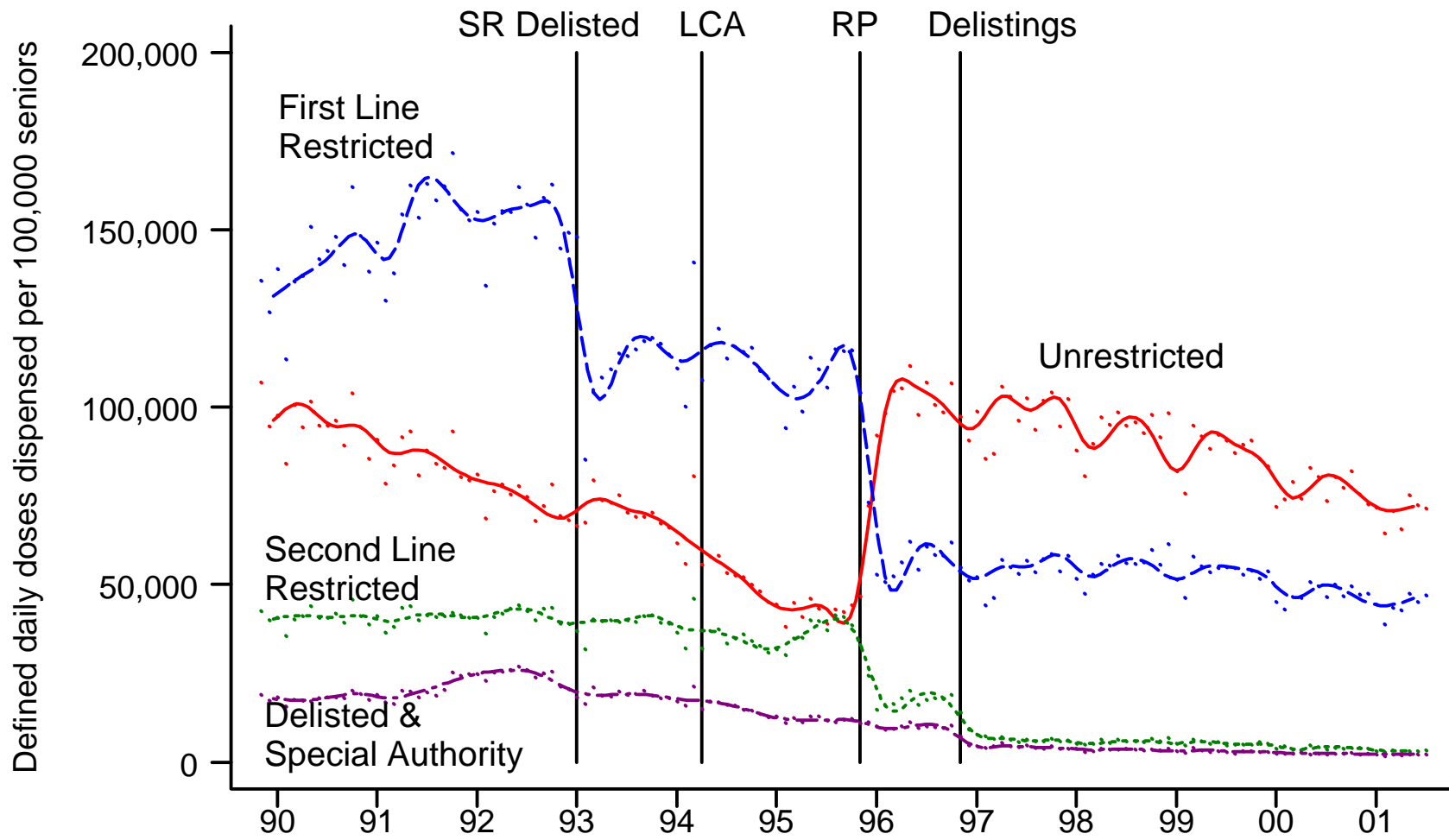




Figure 3 Average Pharmicare reimbursement per defined daily dose dispensed, by NSAID reimbursement category and month

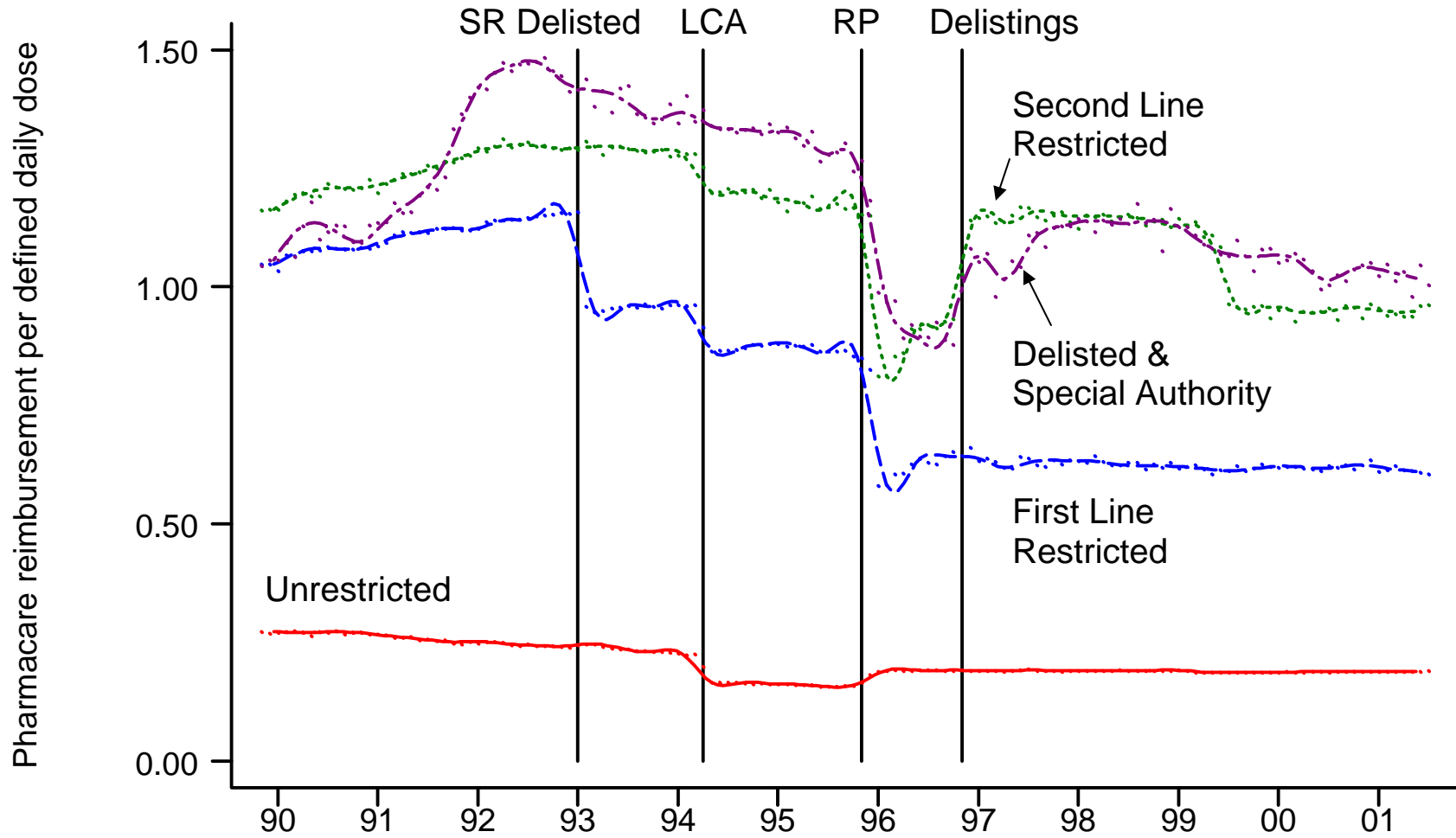


Figure 4 Average Pharmicare reimbursement per defined daily dose dispensed, by analgesic category and month

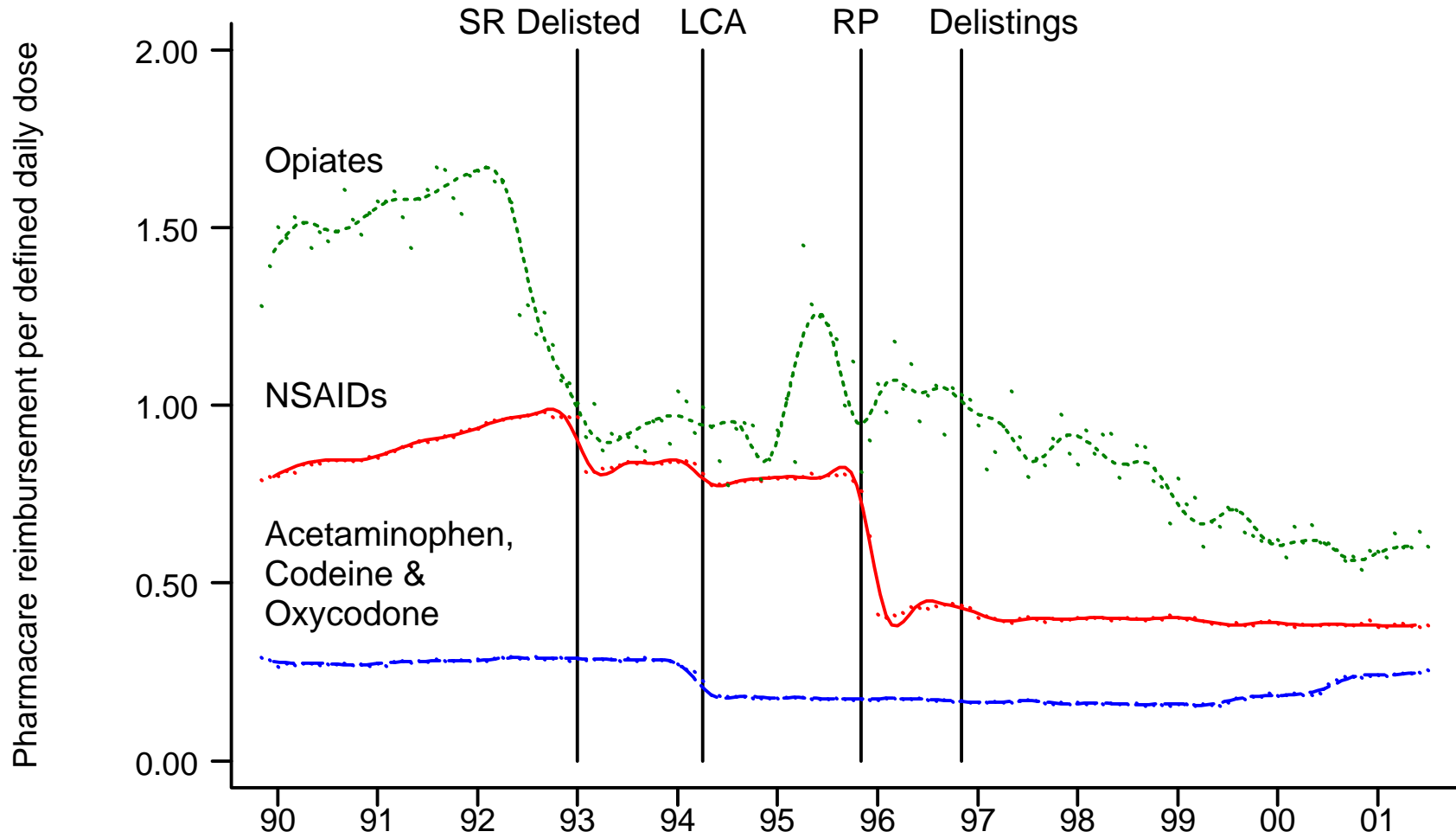


Figure 5 Pharmacare drug expenditures on analgesics per 100,000 seniors, by analgesic category and month

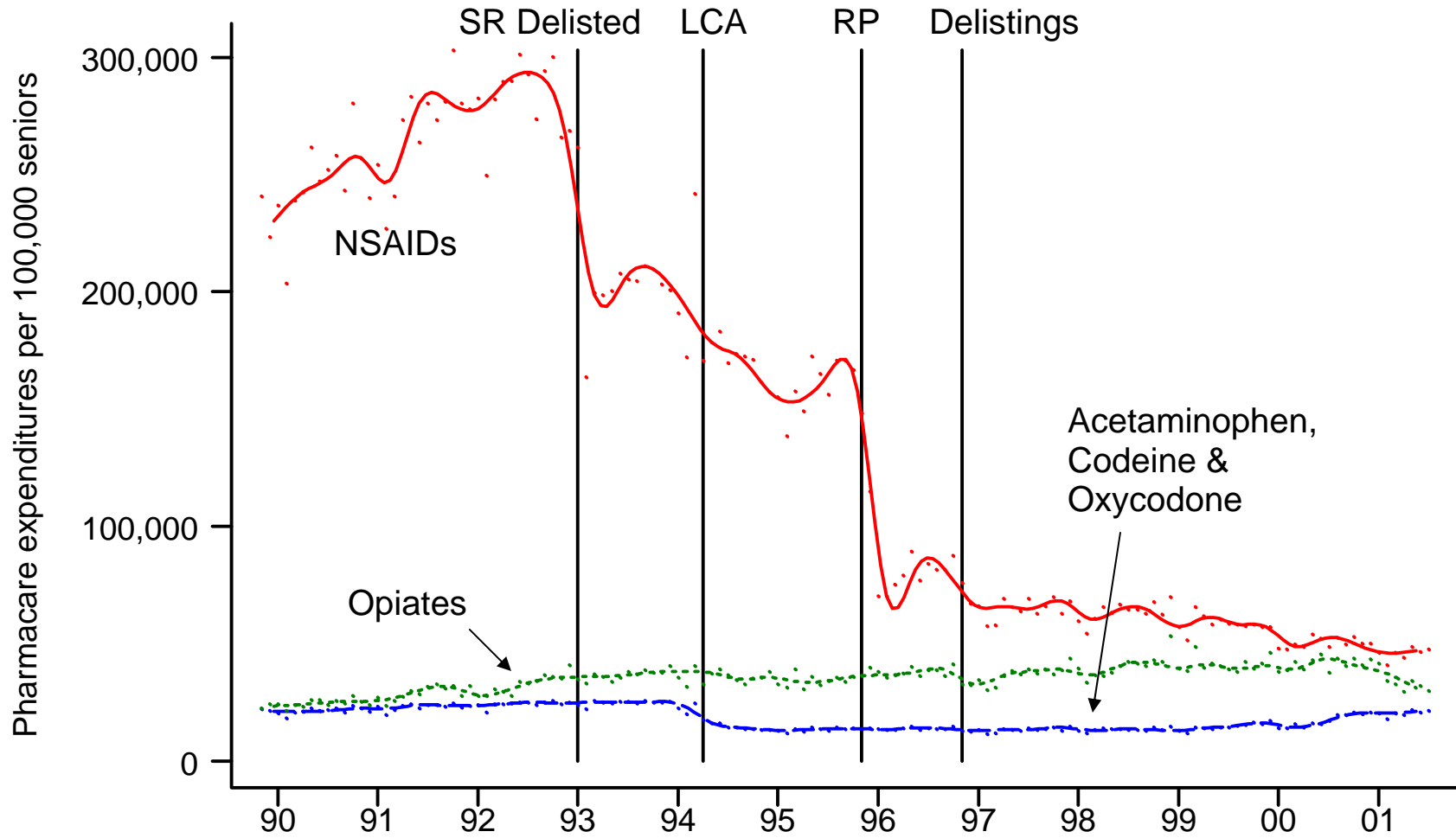
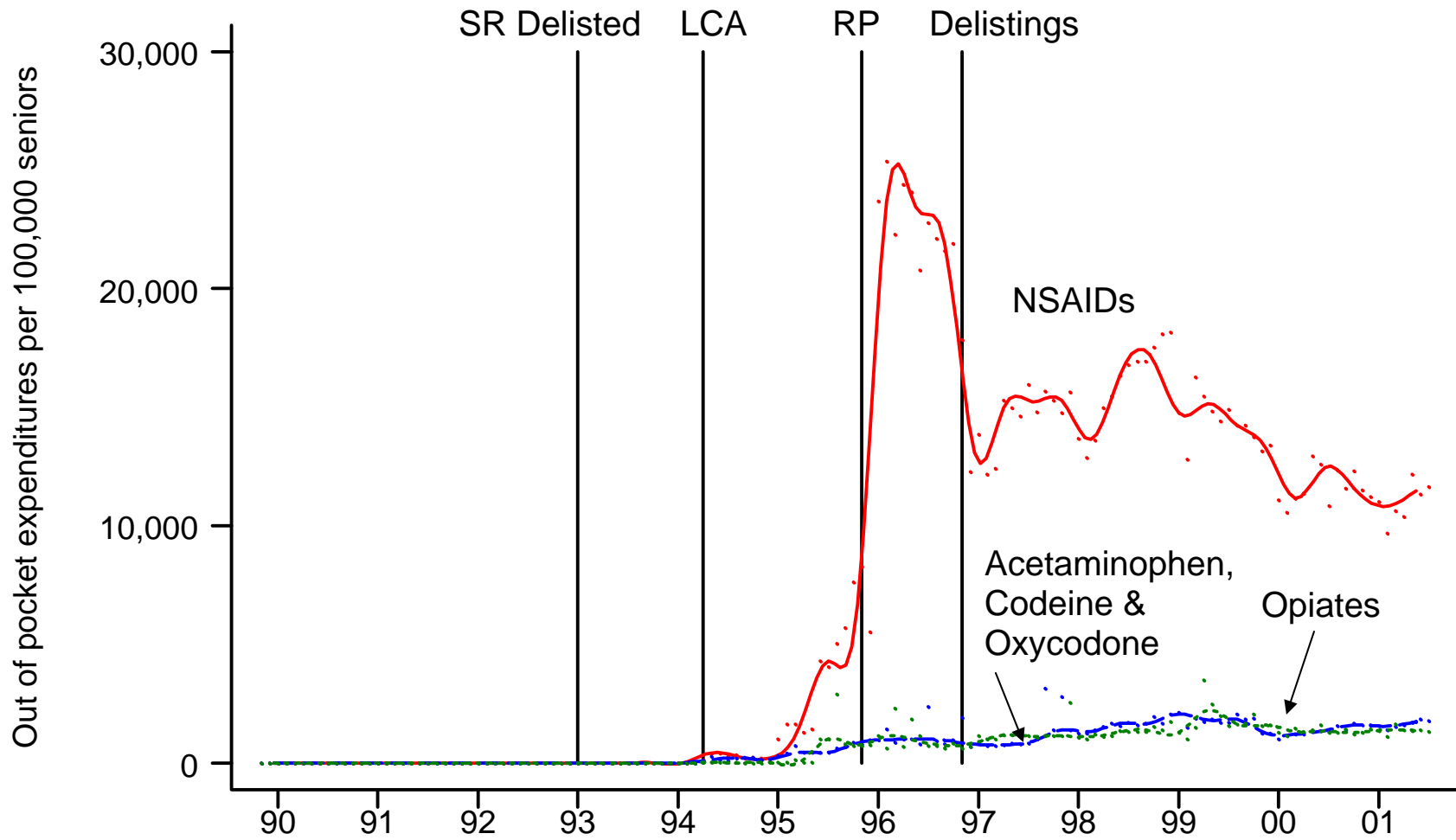


Figure 6 Patient out-of-pocket drug expenditures per 100,000 seniors, by therapeutic category and month



Appendix 1 Parameter estimates

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

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

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

<b>Covariate</b>	<b>coefficient</b>	<b>t-ratio</b>	<b>p-value</b>
<i>RP</i>	0.130	9.34	<0.001
<i>Constant</i>	0.020	1.96	0.053

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

<b>Covariate</b>	<b>coefficient</b>	<b>t-ratio</b>	<b>p-value</b>
<i>RP</i>	66,461.200	10.54	<0.001
<i>Constant</i>	9,488.796	1.95	0.054

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