# Impact of Universal Health Insurance Coverage in Thailand on Sales and Market Share of Medicines for Non-Communicable Diseases: An Interrupted Time Series Study

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# TITLE PAGE

## Impact of Universal Health Insurance Coverage in Thailand on Sales and Market Share of Medicines for Non-Communicable Diseases: an Interrupted Time Series Study

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**Study Design:** Observational study (interrupted time series design)

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**Author contributions:** Laura Garabedian, Dennis Ross-Degnan and Anita Wagner designed the study and developed the analytic approach. Peter Stephens assembled the data files. Laura Garabedian analyzed the data. Sauwakon Ratanawijitrasin provided the Thai national list of essential medicines and information on relevant Thai policies and context surrounding the reform. All authors participated in the interpretation of the results. Laura Garabedian wrote the first draft of the paper. All authors contributed to the writing of the manuscript.

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## Article Summary

### Article Focus

- Medicines present a key challenge to achieving universal coverage.
- Health insurance systems have the potential to improve cost-effective use of medicines, yet there is little evidence about their impact on medicine use in low and middle income countries.
- The recent implementation of universal health coverage in Thailand presents a unique opportunity to measure the impact of health insurance expansion and associated physician payment changes on utilization of medicines.

### Key Messages

- Expanding health insurance coverage with a medicines benefit to the entire Thai population increased access to medicines in primary care.
- The universal coverage scheme did not seem to have increased use of medicines for diseases that are typically treated in secondary or tertiary care settings, or increased generic market penetration.
- In the future, it will be important for countries to assess quality and equity of medicines use as they pursue policies to achieve universal coverage.

### Strengths and Limitations

- We used an interrupted time series design, the strongest quasi-experimental approach for evaluating effects of interventions, increasing internal validity.
- It is impossible to examine population subgroups in national IMS Health market data, but we are reasonably confident that universal coverage scheme enrollees are responsible for observed changes.

## ABSTRACT

***Objective:*** In 2001, Thailand implemented the Universal Coverage Scheme (UCS), a public insurance system covering primarily the poor and uninsured that aimed to achieve universal access to health care, including essential medicines, and to influence provider behavior to use resources efficiently via capitated payment. Our objective was to evaluate the impact of the UCS on utilization of medicines in Thailand for three non-communicable diseases: cancer, cardiovascular disease, and diabetes.

***Design:*** Interrupted time series design, with a non-equivalent comparison group.

***Setting:*** Thailand, 1998-2006.

***Data:*** Quarterly purchases of medicines from hospital and retail pharmacies collected by IMS Health between 1998 and 2006.

***Intervention:*** UCS implementation, April-October 2001.

***Outcome measures:*** Total pharmaceutical sales volume and percent market share by licensing status.

***Results:*** The UCS was associated with long-term increases in sales of medicines for conditions that are typically treated in outpatient primary care settings, such as diabetes, high cholesterol and high blood pressure, but not for medicines for diseases that are typically treated in secondary or tertiary care settings, such as heart failure, arrhythmias, and cancer. While the majority of increases in sales were for essential medicines, there were also significant post-policy increases in sales of non-essential medicines. Immediately following the reform, there was a significant shift in hospital sector market share by licensing status for most classes of medicines. Government-produced products often replaced branded generic or generic competitors.

***Conclusions:*** Our results suggest that expanding health insurance coverage with a medicines benefit to the entire Thai population increased access to medicines in primary care. However, our study also suggests that the UCS may have had potentially undesirable effects. Evaluations of the long-term impacts of universal health coverage on medicines utilization are urgently needed.

## MANUSCRIPT

## Introduction

### *Universal Health Coverage*

In 2005, Member States of the World Health Organization (WHO) made a commitment to work towards universal health care coverage.[1] The 2010 WHO World Health Report provides a roadmap for countries to achieve this goal.[2] Universal coverage requires the restructuring of health care and financing systems to improve access to health care services, reduce financial hardship, and increase the efficiency and equity of the health system.[2]

Medicines, which consume 25–65% of total public and private spending on health in developing countries,[3] present a key challenge to achieving universal coverage. According to the WHO, three of the top ten sources of health care inefficiency involve medicines: high medicine prices and underuse of generics; use of substandard and counterfeit medicines; and inappropriate and ineffective use of medicines.[2] Health insurance systems have several features (e.g., a defined population, access to utilization data, and financial leverage) that give them a unique advantage to reduce out-of-pocket (OOP) expenditures and improve the cost-effective use of medicines through active management strategies involving medicines selection, purchasing, contracting (e.g., physician payment) and utilization management.[4] However, there is little evidence about the impact of health insurance on access to and use of medicines in low- and middle-income countries (LMICs).[4]

The recent implementation of universal health coverage in Thailand presents a unique opportunity to measure the impact of health insurance expansion and physician payment changes (from fee-for-service to capitation) on utilization of medicines.

### *Universal Health Coverage in Thailand*

With the implementation of the UCS in 2001, Thailand became one of the first LMICs to achieve universal coverage.[5,6] The reforms preserved the formal sector workforce schemes: the Social Health Insurance (SHI) scheme for private sector employees (6·3% of the total population) and the Civil Service Medical Benefit Scheme (CSMBS) for government employees and their

dependents (13·6%).[7] In addition, the UCS covered those previously enrolled in a voluntary health card (VHC) scheme (22·0%), in private health insurance (1·6%), or in a tax-based, means-tested Low Income Scheme (LIS) for the poor, elderly, children and disabled (28·9%)[7,8] as well as more than one quarter (26·6%) of the population without previous insurance.[7] The UCS was rolled out to all provinces between April and October 2001.[5] By 2005, 95·5% of the population was insured, with just over 70% of the population covered by the UCS.[7]

The UCS is a compulsory, tax-financed scheme with comprehensive coverage of inpatient and outpatient services, including medicines on the National List of Essential Medicines (NLEM).[5] Individuals must enroll in the scheme at a local Contracting Unit for Primary Care (CUP),[5] primarily housed in government-owned hospitals.[9] Each CUP receives a capitated payment per registered member to provide outpatient services and medicines.[5] CUPs served as gate-keepers for secondary and tertiary hospitals. When patients were referred, payments for higher-level care initially came out of the CUP's capitated payment, so CUPs had a financial disincentive to refer patients.[5]

Our objective was to evaluate the immediate, short-term (one year) and long-term (five year) impacts of the UCS on pharmaceutical market size and composition for medicines for three non-communicable diseases (NCDs): cancer, cardiovascular disease, and diabetes. We hypothesized that the UCS would result in a gradual increase in sales volume, particularly of products used in primary care, as enrollment into the Scheme increased, and in an immediate increase in market share of less expensive generic or branded generic products and medicines on the NLEM in response to capitated payment rules. We focused on medicines for NCDs since these illnesses represent a large and growing health care burden in Thailand[10–13] and other LMICs[14] and most, but not all, medicines for NCDs would be prescribed and dispensed in primary care settings.

## Methods

### *Data*

We used data on quarterly pharmaceutical sales in Thailand from 1998 to 2006 provided by IMS Health.[15] The sales data are generated from reports to IMS Health by multinational pharmaceutical companies and surveys of purchases by hospital and retail pharmacies. IMS surveys approximately 200 hospitals (including general and specialized, public and private) and

350 retail pharmacies in Thailand, and employs a stratified random sample of these facilities that enables national projections. Medicines were classified according to the European Pharmaceutical Research Association (EphMRA) Anatomical Therapeutic Chemical (ATC) system.[16]

***Outcomes***

We used two outcome measures: total volume and percent market share. *Total volume* is the number of standard units purchased per capita per quarter (i.e., "sales"). We analyzed total volume by sector (i.e., retail versus hospital) and, within the hospital sector, by NLEM versus non-NLEM status of medicines (based on the 1999 Thai NLEM). A standard unit, as defined by IMS Health, is the smallest dose of a product, which equates to one tablet or capsule for an oral dosage form, one teaspoon (5ml) for a syrup, and one ampoule or vial for an injectable product. We divided total volume by size of the population over 15 years old to control for population growth (using yearly population estimates from the World Bank[17]). We used the entire population as denominator for insulins, since they are also used for Type 1 diabetes, a chronic disease that affects children. *Percent market share* is the percent of total volume in four mutually exclusive categories of licensing status: originator brand products, branded generic products (products sold under a brand name other than the originator brand name of the molecule), generic products (products that are sold under the generic molecule name), and products manufactured by Thailand's Government Pharmaceutical Organization (GPO).

We analyzed total volume and market share for medicines in eight therapeutic classes: two classes of diabetes products (oral antidiabetics and insulins), three classes of cardiovascular disease products (antihypertensives, lipid-regulating, and cardiac therapy products) and three classes of cancer products (antineoplastics, immunostimulating agents, and cytostatic hormone therapy products); Table 1 in the online appendix lists all medicines by ATC code. Antidiabetic, insulin, antihypertensive and lipid-lowering products are used for conditions that are typically treated in primary care settings (i.e., diabetes, high blood pressure and high cholesterol), whereas cardiac therapy and cancer products are used for more severe conditions that are more likely to be treated by a specialist and/or in inpatient settings.

### *Research Design*

We used an interrupted time series design, the strongest quasi-experimental approach for evaluating effects of interventions, which has been used extensively for medication use research.[18] Although we did not have an equivalent control group, we used medicines sold in the retail sector as a non-equivalent comparison group,[19] assuming that the retail market should be relatively unaffected by the reforms since UCS enrollees could only obtain covered medicines through their local, hospital-based CUP.

### *Statistical Analysis*

The intervention was the UCS roll-out from April to October 2001. We defined three distinct periods: 12 quarters pre-reform (1998Q2-2001Q1), a 3-quarter UCS roll-out period (2001Q2-2001Q4; grey box in figures), and 19 quarters post-reform (2002Q1-2006Q3). We dropped 2006Q4 from the analysis since there was a policy change at this time (the removal of an initial 30 Baht co-payment per visit) that may have impacted outcomes. In sensitivity analyses, we extended the intervention roll-out period through 2002 and through 2003 to account for potentially delayed implementation and lag of actual enrollment into the scheme.

We used segmented linear regression to measure the pre-reform trend, the immediate level change following the intervention period, and the post-reform change in trend (as compared to the pre-reform trend). We controlled for serial autocorrelation using an autoregressive error model. We retained all terms in the models, even if non-significant. We used the models to estimate absolute and relative differences (with 95% confidence intervals)[20] in observed versus predicted total volume at one year and five years post-reform. In sensitivity analyses, we included a quadratic term for the post-reform trend and used a likelihood ratio test to determine the best-fitting model. We report below results from the best-fitting model of the shortest (i.e., 3 quarter) intervention period and mention differences in model results where they existed. Results from sensitivity analyses are available upon request. We used the AUTOREG procedure in SAS 9.2 for all analyses.

## Results

### *Hospital Sector Volume*

The majority of sales in Thailand for all cancer, cardiovascular disease and diabetes medicines studied were in the hospital sector and were for medicines on the NLEM. After implementation of the UCS, there was a significant increase in level of sales of insulins and a significant increase in trend in sales of antidiabetic, insulin, antihypertensive, lipid regulating, and cytostatic hormone products [Table 1, Figures 1 and 2]. There was a significant reduction in level of sales immediately following the reforms for three medication classes: antihypertensive, cardiac therapy and immunostimulating agents (although only the latter was significant in the sensitivity analyses using a longer intervention period).

The UCS was associated with increased sales of diabetes medicines. One year after the policy, the sale of insulin was 35% (95% CI: 15%, 55%) higher and, at five years, 174% (95% CI: 114%-235%) higher than what would have been expected in the absence of the UCS [Table 2]. The increase in insulin sales was driven primarily by human insulins, which are on the NLEM and marketed as branded generics by two manufacturers. The policy was associated with a 39% (95% CI: 14%, 64%) increase in antidiabetic product sales five years after implementation [Table 2]. This is largely due to increased sales of generic and branded generic metformin and glibenclamide products, both of which are on the NLEM.

Implementation of the UCS appears to have had a mixed impact on sales of cardiovascular medicines. Five years after the policy, the sale of lipid lowering agents was nearly double (108% increase; 95% CI: 60%, 157%) what would have been expected in the absence of the scheme [Table 2]. The increase was primarily due to sales of branded generic simvastatin and gemfibrozil products, which are on the NLEM, and a small but steady increase in sales of originator atorvastatin products, which are not on the NLEM. For antihypertensives, the significant increase in post-policy trend compensated for an initial drop in sales, resulting in a slight increase in sales five years after the policy (19% increase; 95% CI: -3%, 40%). The increased trend was primarily due to sales of enalapril, atenolol, and amlodipine, all of which are on the NLEM and predominately sold as branded generics. The reform had no significant impact on sales of cardiac therapy medicines one or five years after the policy.

The results were also mixed for cancer medicines. The UCS had no significant one- or five-year impact on the sale of antineoplastics or cytostatic hormones (although the latter class did experience a significant post-policy increase in trend). However, the policy was associated with an immediate reduction in sales of immunostimulating agents that did not recover in the post-policy period. One year after implementation, the sale of immunostimulating agents was 35% (95% CI: -45%, -25%) lower than expected from pre-policy trends, and 26% lower (95% CI: -45%, -8%) five years post-policy. This drop is almost entirely due to a sharp reduction in sales of interferon alfa-2b, a non-NLEM medicine, around the time of UCS implementation, which could have been due to a co-incidental recall of an interferon alfa-2b product.[21]

There was mixed evidence about the effects of the UCS on utilization of NLEM medicines. For all classes that experienced a post-policy increase in trend, there was an increase in sales of both NLEM medicines (except for cytostatic hormones) *and* non-NLEM products [see online appendix, Table 3]. The immediate decrease in sales of cardiac therapies and immunostimulating agents was largely due to a decrease in non-NLEM medicines. However, for these two classes, there was no corresponding increase in NLEM medicines.

Finally, as expected, the reform had little impact on sales volume in the retail sector – there were few significant post-implementation changes, and the changes that were significant were small in magnitude [see online appendix, Table 2].

***Hospital Sector Market Share***

Immediately following the reform, there were significant shifts in hospital sector market share by licensing status for most classes [Table 3]. The changes for antidiabetics and cardiac medicines - the two therapeutic classes with the largest shifts – were due to significant increases in GPO-produced medicines, primarily at the expense of branded generics and, to a lesser extent, generics. There was a significant increase in GPO antidiabetic products (+16% of market; 95% CI: 12%, 20%), and decreases in branded generic (-12%; 95% CI:-16%, -9%) and generic (-4%; 95% CI: -6%,-1%) products immediately after the policy [Figure 3]. Similarly, there was a significant increase in GPO cardiac therapy products (+22%; 95% CI: 15%, 28%), and significant decreases of branded generic (-14%; 95% CI:-21%, -7%) and generic (-4%; 95% CI:-

6%, -2%) products immediately after the policy [Figure 4]. There was also a small decrease in market share of generic antihypertensives (-6%; 95% CI: -8%, -3%), which was compensated for by a marginally significant increase in GPO products.

The market for lipid regulating agents experienced an immediate shift from originator products (-8% market share; 95% CI: -10%, -5%) to branded generics (+8%; 95% CI: 5%, 10%). A similar shift was seen for in the market for immunostimulating agents (6% decrease in originator products [95% CI:-10%, -3%] and a 5% increase in branded generics [95% CI:2%, 7%]). The cytostatic hormone market experienced an immediate shift from branded generic (-8%; 95% CI:-12%, -4%) to generic products (+6%, 95% CI: 1%, 11%). Generic insulins experienced a slight decrease in market share caused by the market exit of the sole generic manufacturer just prior to the policy. There were no immediate changes in market share for antineoplastics. Aside from the immediate level changes following the policy, there were few major changes in market share for all classes.

**Discussion**

The UCS was associated with long-term (i.e., 5 year) increases in hospital sector sales of medicines for chronic diseases that are usually treated in primary care settings, such as diabetes, high blood pressure, and high cholesterol. We hypothesized this gradual increase in volume since the UCS expanded access to primary care[7] and actual enrollment into the scheme occurred gradually from implementation in 2001 until around 2005, by which time 95·5% of the population had insurance coverage.[7] The UCS, which radically changed hospital financing and reimbursement, was also associated with an immediate market shift to locally produced or branded generic products for most therapeutic classes.

Despite these increases in access, the policy did not appear to increase sales of medicines for more severe diseases like heart failure, arrhythmias, and cancer, which are often treated in secondary or tertiary settings. This finding is in line with evidence that the capitated payment system discouraged referrals of UCS patients to higher-level care.[5,7,22] The UCS also appears to have had a mixed impact on utilization of essential medicines. There were increases in NLEM medicines, which are covered, as well as non-NLEM medicines. Similarly, given the capitated

UCS payment system, we expected to see an increase in sales of generic medicines, which are typically less expensive. However, the majority of sales in most classes were for branded generic products, many of which had generic alternatives in the market. Interestingly, substantial market share shifts occurred toward products manufactured by the Thai GPO, which by law received preferential status by hospital purchasers.[23] GPO products have been noted to have higher than market prices[24] and sometimes to be of substandard quality.[25]

Our study demonstrates the value of IMS Health market intelligence data for rigorous health policy evaluation. Unlike other sources of data on pharmaceutical utilization (i.e., national health surveys or ad hoc hospital surveys), IMS data represent country pharmaceutical markets consistently over time and are useful for the evaluation of system-wide interventions. Nevertheless, the data pose some limitations. Aggregate national sales data do not allow us to determine whether observed increases in medicines sales occurred preferentially among UCS enrollees or enrollees in the SHI and CSMBS schemes, conceivably to compensate for financial strain of the UCS on hospital budgets.[5] CSMBS expenditures increased following UCS implementation[26] and increased medicines sales among CSMBS, reimbursed on a fee-for-service basis, could explain increases in non-NLEM medicines and medicines with less expensive therapeutic alternatives.[27] However, it is unlikely that increased utilization among CSMBS enrollees explains most of the observed volume changes since it would imply that one-quarter (for diabetes) to one-third (for hypertension) of CSMBS members were on these treatments and the change in utilization would have needed to be coincident with the initiation of the UCS.

Our interpretation of the observed changes assumes that pharmaceutical sales to hospital and retail pharmacies reflected total market utilization, and that hospital sales volumes included utilization at affiliated primary care units. This assumption seems justified in light of the estimated 91% accuracy of IMS Health data in representing the Thai pharmaceutical market.[28] For local generic products, including those produced by the GPO, IMS Health data is based on pharmacy surveys only (as opposed to pharmacy surveys and manufacturer reports), so we may have underestimated utilization. Finally, since we did not convert standard units of product sold to defined daily doses (DDD), we do not describe sales changes in terms of average adult doses.

There are also potential limitations due to study design and statistical analysis. We addressed the main threat to the internal validity of the interrupted time series design - a concurrent event that affects the outcome of interest - by assessing other policies or market events that occurred at the time of the UCS, through literature reviews, discussions with in-country experts, and by including the retail sector as a comparison. The statistical approach, segmented regression analysis, usually assumes a linear trend and well-defined break point. Sensitivity analyses that varied model specification and intervention duration did not change the findings. By reporting results from fully-specified models, we may have underestimated the statistical significance of one- and five-year change estimates.

While both the context and the implementation of universal coverage in Thailand are unique, our findings suggest that expanding health insurance coverage with a medicines benefit to the entire population in a LMIC increased the volume of medicines sold and, by inference, improved access to medicines in the primary care sector. Since the study period, Thailand has enacted further policies to address pharmaceutical sector cost escalation (e.g., strict enforcement of reimbursement for only NLEM medicines in the CSMBS[29]) and to ensure appropriate access to non-NLEM medicines (e.g., coverage of medicines for HIV, renal replacement therapy, and mental health conditions).[30–32] In the future, it will be important for Thailand and other countries to assess quality of medicines use, out-of-pocket and system expenditures, and health outcomes as they pursue policies to achieve universal coverage.

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## TABLES

**Table 1. Summary of the Impact of the Universal Coverage Scheme on Volume in the Hospital Sector (from segmented regression results) ***

| Therapeutic Area | Pre-policy trend | Immediate change after policy | Post-policy trend change |
|---|---|---|---|
| | | | |
| **DIABETES** | | | |
| **Antidiabetics**** | ↑ | | ↑ |
| **Insulins**** | ↑ | ↑ | ↑ |
| | | | |
| **CARDIOVASCULAR DISEASE** | | | |
| **Antihypertensives** | ↑ | ↓ | ↑ |
| **Lipid Regulating Agents**** | ↑ | | ↑ |
| **Cardiac Therapy** | ↑ | ↓ | |
| | | | |
| **CANCER** | | | |
| **Antineoplastics** | ↑ | | |
| **Cytostatic Hormones** | ↑ | | ↑ |
| **Immunostimulating Agents**** | ↑ | ↓ | |

*Arrows signify a statistically significant coefficient ($p<0.05$) from segmented regression with linear post-policy trend term, unless noted otherwise.
**Quadratic model (which has a squared post-policy trend term) fits better than linear model.
Note: See online appendix Table 2 and Figures 1-8 for regression coefficients and figures for all therapeutic areas.

**Table 2. Relative Impact of UCS on Sales of Medicines by Class (one and five years post policy)***

| Therapeutic Class | One Year Impact (in standard units) | | | Five Year Impact (in standard units) | | |
|---|---|---|---|---|---|---|
| | Predicted | Observed | Relative Change (95% CI) | Predicted | Observed | Relative Change (95% CI) |
| **Antidiabetics** | 2602·91 | 2769·79 | 6·4% (-6·9, 19·7) | 3669·13 | 5090·62 | **38·7% (13·5, 64·0)** |
| **Insulins** | 3·30 | 4·45 | **34·8% (15·1, 54·5)** | 4·58 | 12·56 | **174·4% (113·9, 235·0)** |
| **Cardiac Therapy Agents** | 699·28 | 607·27 | -13·2% (-26·9, 0·6) | 908·12 | 825·49 | -9·1% (-31·9, 13·1) |
| **Lipid Regulating Agents** | 522·34 | 504·58 | -3·4% (-19·9, 13·1) | 781·97 | 1629·11 | **108·3% (59·8, 156·9)** |
| **Antihypertensives** | 3521·47 | 3418·79 | -2·9% (-15·5, 9·7) | 5200·86 | 6177·49 | 18·8% (-2·8, 40·3)** |
| **Antineoplastics** | 35·38 | 34·21 | -3·3% (-15·4, 8·7) | 46·14 | 48·13 | 4·3% (-16·3, 24·9) |
| **Cytostatic Hormones** | 29·48 | 30·58 | 3·7% (-10·1, 17·6) | 39·82 | 47·52 | 19·3% (-5·1, 43·8) |
| **Immunostimulating Agents** | 0·65 | 0·43 | **-35·0% (-45·1, -25·0)** | 0·81 | 0·60 | **-26·3% (-45·0, -7·6)** |

***Bold** signifies that the change is statistically significant (i.e., confidence interval does not include the null value of 0).
** The *absolute* five-year difference, which is estimated using more precise method, is significant. See online appendix Table 4.

**Table 3. Immediate Impact of UCS on Hospital Sector Market Share***

| Therapeutic Area | Licensing Status | Immediate post-policy absolute change in % market share (95% CI) |
|---|---|---|
| **DIABETES** | | |
| **Antidiabetics** | Originator brand | -0·3% (-1·6, 1·0) |
| | Branded generic | **-12·3% (-16·0, -8·7)** |
| | Generic | **-3·5% (-5·8, -1·1)** |
| | GPO | **16·1% (12·0, 20·2)** |
| **Insulins*****| Originator brand** | -0·04% (-0·4, 0·3) |
| | Branded generic | **7·0% (2·9, 11·1)** |
| | Generic | **-6·2% (-10·3, -2·1)** |
| **CARDIOVASCULAR DISEASE** | | |
| **Antihypertensives** | Originator brand** | -0·1% (-2·3, 2·0) |
| | Branded generic** | -0·2% (-6·1, 1·8) |
| | Generic | **-5·7% (-8·3, -3·0)** |
| | GPO | 5·3% (-0·1, 10·6) |
| **Lipid Regulating Agents** | Originator brand** | **-7·8% (-10·2, -5·4)** |
| | Branded generic** | **7·6% (5·1, 10·0)** |
| | Generic | 0·2% (-0·4, 0·7) |
| | GPO | 0·2% (-0·3, 0·8) |
| **Cardiac Therapy** | Originator brand | 0·1% (-0·8, 1·0) |
| | Branded generic** | **-13·5% (-20·5, -6·5)** |
| | Generic | **-4·3% (-6·2, -2·4)** |
| | GPO | **21·6% (15·0, 28·1)** |
| **CANCER*****| | |
| **Antineoplastics** | Originator brand | 1·1% (-1·0, 3·2) |
| | Branded generic | -1·0% (-5·4, 3·4) |
| | Generic | 0·4% (-2·7, 3·4) |
| **Cytostatic Hormones** | Originator brand** | 0·4% (-5·4, 6·1) |
| | Branded generic** | **-7·7% (-12·0, -3·5)** |
| | Generic** | **6·0% (1·4, 10·6)** |
| **Immunostimulating Agents** | Originator brand | **-6·4% (-9·7, -3·0)** |
| | Branded generic | **4·5% (1·7, 7·3)** |
| | Generic | -0·2% (-0·3, 0·02) |

***Bold** signifies a statistically significant regression coefficient ($p<0.05$). Changes are in absolute terms (i.e., percentage point change).
**Quadratic model (which has a squared post-policy term) fits better than linear model.
***GPO did not produce any insulins or cancer medicines during the study period.
Note 1: See online appendix Table 5 and Figures 9-16 for market share regression coefficients and figures for all therapeutic areas
Note 2: Aside from the immediate level changes following the policy, there were few major changes in market share. See online appendix, Table 6 for absolute one- and five-year differences.

**Figure Index (attached in separate document):***

**Figure 1.** Standard Units Per Capita by Quarter: Insulin (Hospital vs. Retail)

**Figure 2.** Standard Units Per Capita by Quarter: Antihypertensives (Hospital vs. Retail)

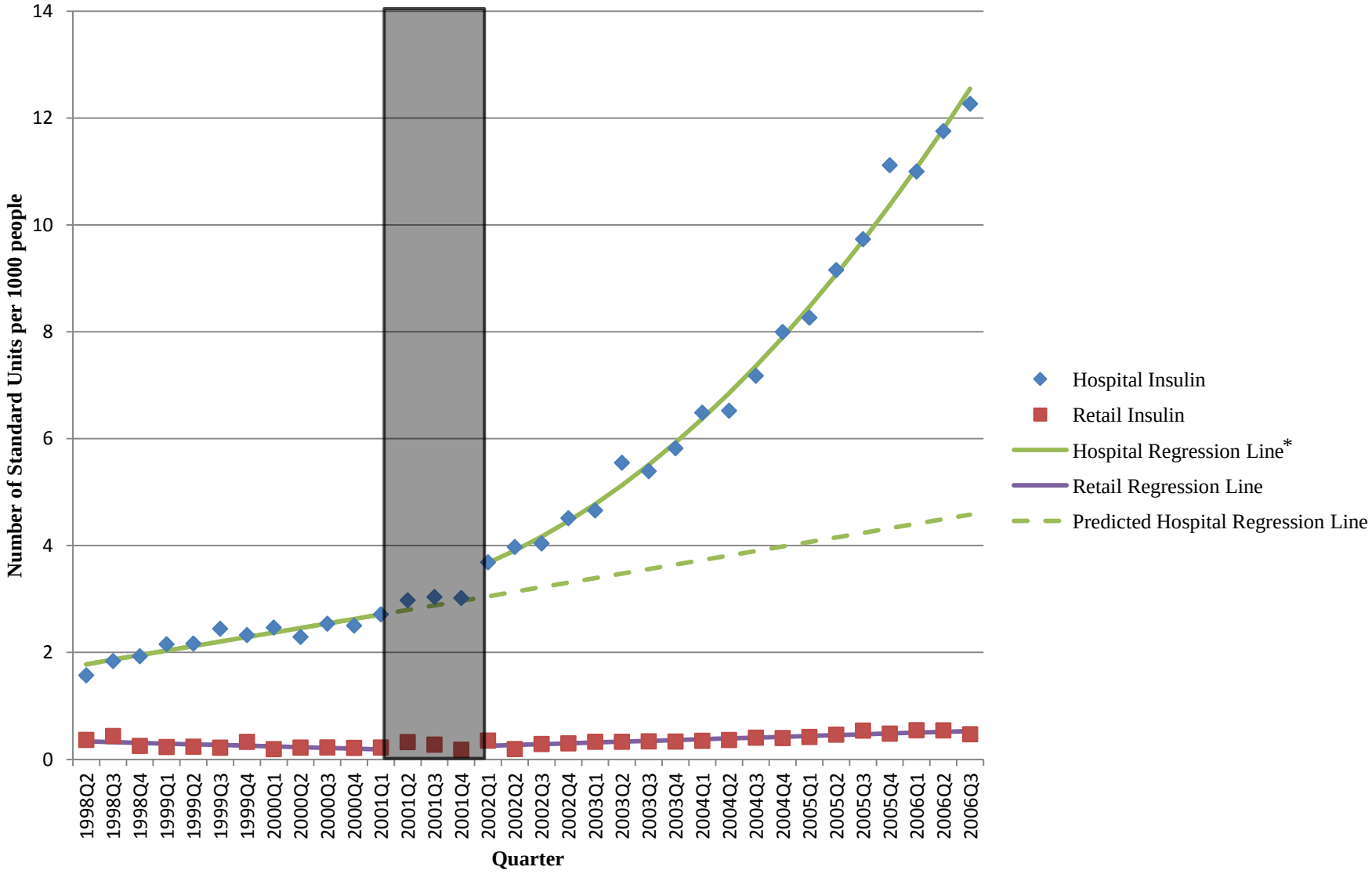
**Figure 3.** Licensing Status Market Share by Quarter: Antidiabetics (Hospital Sector)

**Figure 4.** Licensing Status Market Share by Quarter: Cardiac Therapy Products (Hospital Sector)

*The grey box in each figure represents the 3-quarter UCS roll-out period.

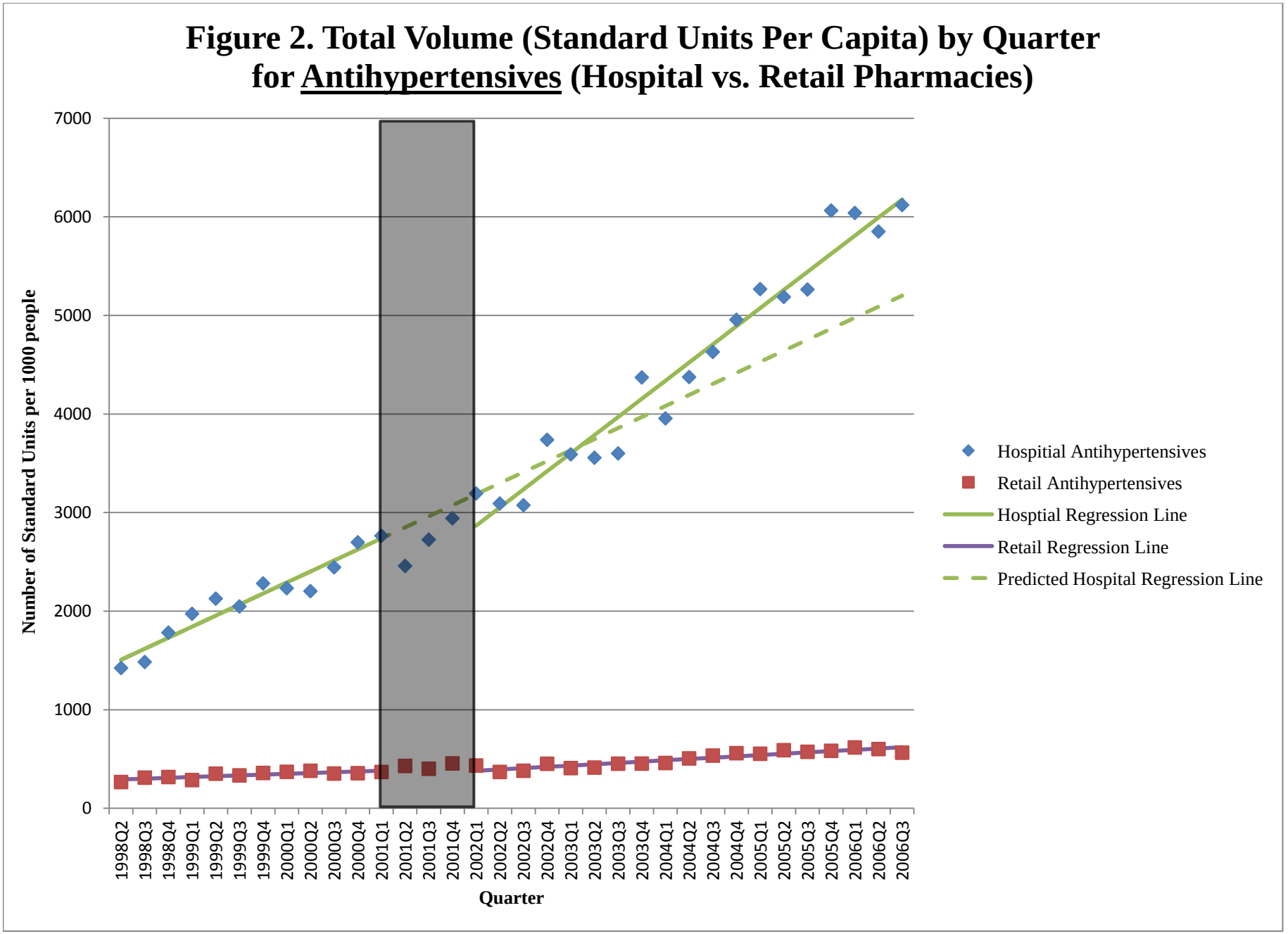
**Online appendix (attached in separate document)**

**Figure 1. Total Volume (Standard Units Per Capita) by Quarter for Insulin (Hospital vs. Retail Pharmacies)**




*Results from quadratic model

**Figure 2. Total Volume (Standard Units Per Capita) by Quarter for Antihypertensives (Hospital vs. Retail Pharmacies)**



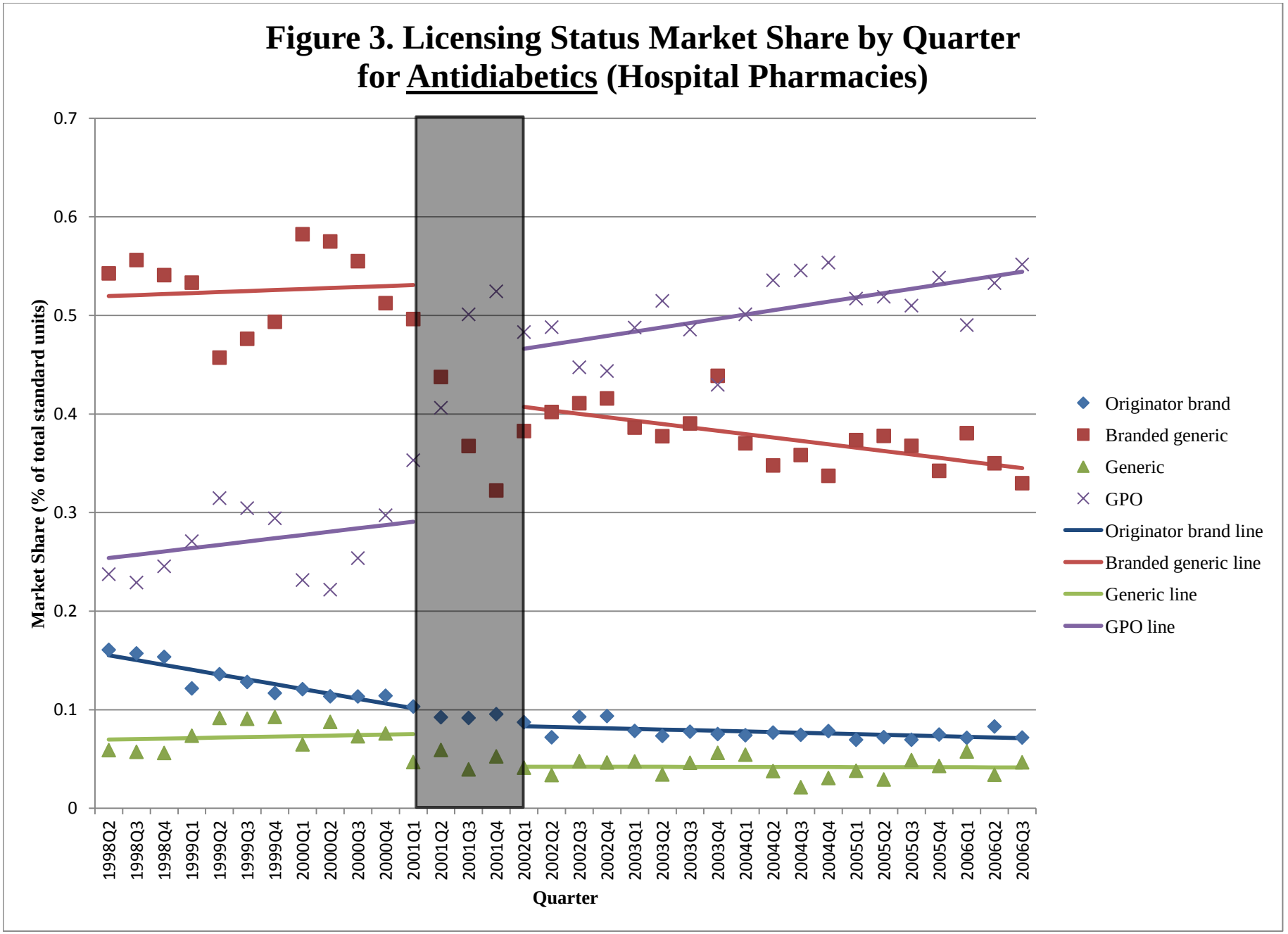
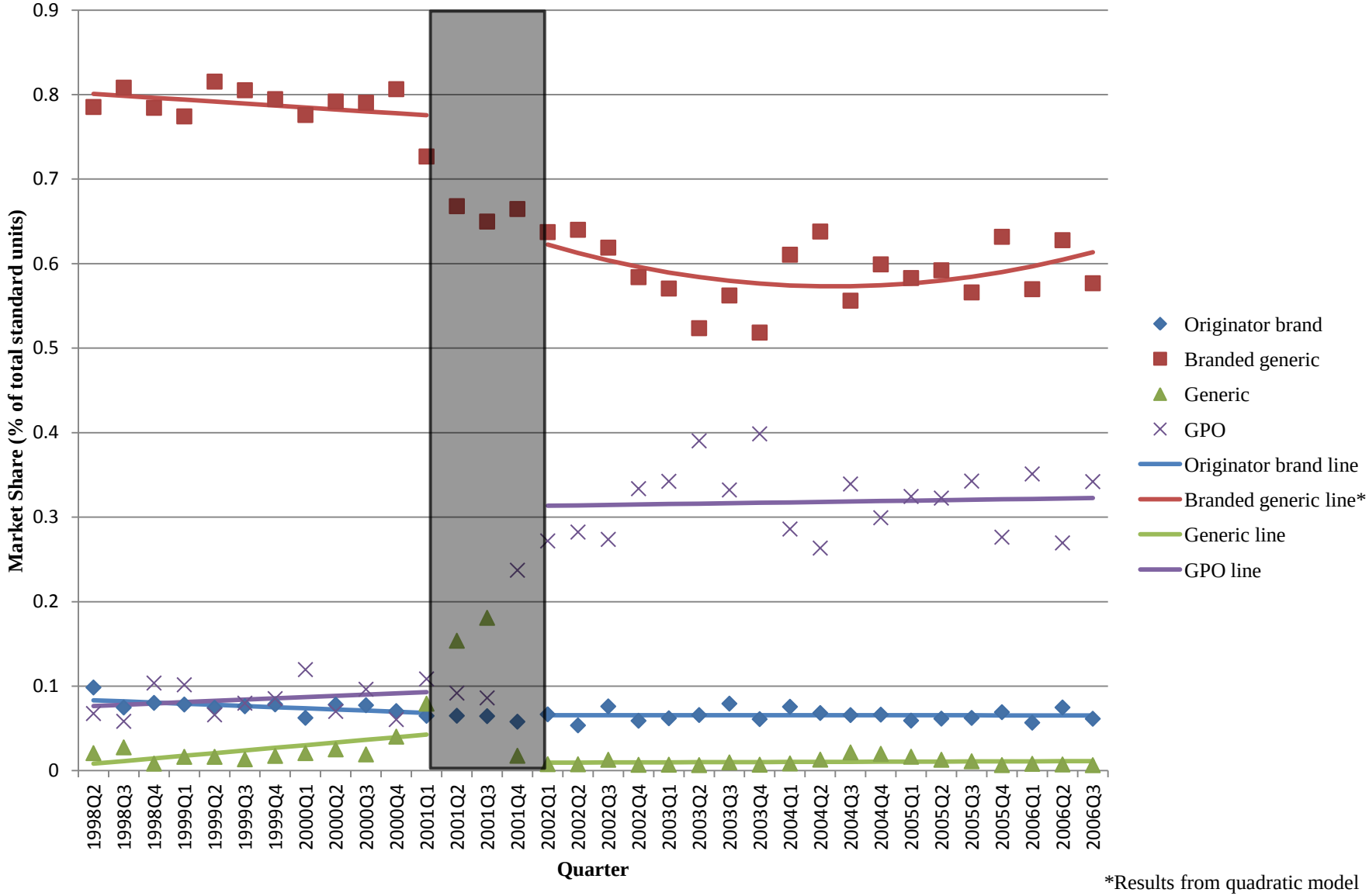


Figure 3. Licensing Status Market Share by Quarter for Antidiabetics (Hospital Pharmacies)
Market Share (% of total standard units)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Originator brand
Branded generic
Generic
GPO
Originator brand line
Branded generic line
Generic line
GPO line

**Figure 4. Licensing Status Market Share by Quarter for Cardiac Therapy Agents (Hospital Pharmacies)**



**Appendix Table 1. List of Medicines by ATC**

| Therapeutic Area | Classification for Analysis | Molecule Name | ATC2 Classification | ATC4 Classification | NLEM (1=on NLEM 1999-2004) | Note regarding NLEM |
|---|---|---|---|---|---|---|
| **DIABETES** | | | | | | |
| | Antidiabetics | ACARBOSE | A10 (DRUGS USED IN DIABETES) | A10L0 (A-GLUCOSIDASE INH A-DIAB) | 1 | |
| | Antidiabetics | BUFORMIN | A10 (DRUGS USED IN DIABETES) | A10J1 (BIGUANIDE A-DIABS PLAIN) | 0 | |
| | Antidiabetics | CHLORPROPAMIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) | 1 | |
| | Antidiabetics | EXENATIDE | A10 (DRUGS USED IN DIABETES) | A10S0 (GLP-1 AGONIST A-DIABS) | 0 | |
| | Antidiabetics | GLIBENCLAMIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS ) | 1 | |
| | Antidiabetics | GLIBENCLAMIDE#METFORMIN | A10 (DRUGS USED IN DIABETES) | A10J2 (BIGUANIDE & S-UREA COMBS) | 0 | both ingredients listed separately, not in combo |
| | Antidiabetics | GLICLAZIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) | 1 | |
| | Antidiabetics | GLICLAZIDE#METFORMIN | A10 (DRUGS USED IN DIABETES) | A10J2 (BIGUANIDE & S-UREA COMBS) | 0 | both ingredients listed separately, not in combo |
| | Antidiabetics | GLIMEPIRIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) | 0 | |
| | Antidiabetics | GLIMEPIRIDE#METFORMIN | A10 (DRUGS USED IN DIABETES) | A10J2 (BIGUANIDE & S-UREA COMBS) | 0 | |
| | Antidiabetics | GLIMEPIRIDE#ROSIGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K2 (GLITAZONE & S-UREA COMBS) | 0 | |
| | Antidiabetics | GLIPIZIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) | 1 | |
| | Antidiabetics | GLIQUIDONE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) | 0 | |
| | Antidiabetics | METFORMIN | A10 (DRUGS USED IN DIABETES) | A10J1 (BIGUANIDE A-DIABS PLAIN) | 1 | |
| | Antidiabetics | METFORMIN#PIOGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K3 (GLITAZONE & BIGUAN COMBS) | 0 | |
| | Antidiabetics | METFORMIN#ROSIGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K3 (GLITAZONE & BIGUAN COMBS) | 0 | |
| | Antidiabetics | METFORMIN#SITAGLIPTIN | A10 (DRUGS USED IN DIABETES) | A10N3 (DPP-IV INH & BIGUAN COMB) | 0 | |
| | Antidiabetics | METFORMIN#VILDAGLIPTIN | A10 (DRUGS USED IN DIABETES) | A10N3 (DPP-IV INH & BIGUAN COMB) | 0 | |
| | Antidiabetics | PIOGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K1 (GLITAZONE A-DIABS PLAIN) | 0 | |
| | Antidiabetics | REPAGLINIDE | A10 (DRUGS USED IN DIABETES) | A10M1 (GLINIDE A-DIABS PLAIN) | 0 | |
| | Antidiabetics | ROSIGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K1 (GLITAZONE A-DIABS PLAIN) | 0 | |
| | Antidiabetics | SITAGLIPTIN | A10 (DRUGS USED IN DIABETES) | A10N1 (DPP-IV INH A-DIAB PLAIN) | 0 | |
| | Antidiabetics | VILDAGLIPTIN | A10 (DRUGS USED IN DIABETES) | A10N1 (DPP-IV INH A-DIAB PLAIN) | 0 | |
| | Antidiabetics | VOGLIBOSE | A10 (DRUGS USED IN DIABETES) | A10L0 (A-GLUCOSIDASE INH A-DIAB) | 0 | |
| | Insulins | INSULIN ASPART | A10 (DRUGS USED IN DIABETES) | A10C1 (H INSUL+ANG FAST ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN ASPART#INSULIN ASPART PROTAMINE CRYSTALLINE | A10 (DRUGS USED IN DIABETES) | A10C3 (H INSUL+ANG INT+FAST ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN DETEMIR | A10 (DRUGS USED IN DIABETES) | A10C5 (H INSUL+ANG LONG ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN GLARGINE | A10 (DRUGS USED IN DIABETES) | A10C5 (H INSUL+ANG LONG ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN HUMAN BASE | A10 (DRUGS USED IN DIABETES) | A10C1 (H INSUL+ANG FAST ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN HUMAN BASE#INSULIN HUMAN ISOPHANE | A10 (DRUGS USED IN DIABETES) | A10C3 (H INSUL+ANG INT+FAST ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN HUMAN ISOPHANE | A10 (DRUGS USED IN DIABETES) | A10C2 (H INSUL+ANG INTERMED ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN HUMAN ZINC SUSPENSION (COMPOUND) | A10 (DRUGS USED IN DIABETES) | A10C4 (H INSUL+ANG INT+LONG ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN HUMAN ZINC SUSPENSION (CRYSTALLINE) | A10 (DRUGS USED IN DIABETES) | A10C5 (H INSUL+ANG LONG ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN LISPRO | A10 (DRUGS USED IN DIABETES) | A10C1 (H INSUL+ANG FAST ACT) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN LISPRO#INSULIN LISPRO PROTAMINE | A10 (DRUGS USED IN DIABETES) | A10C1 (H INSUL+ANG FAST ACT ) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN PORCINE BASE | A10 (DRUGS USED IN DIABETES) | A10D0 (ANIMAL INSULINS) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN PORCINE ISOPHANE | A10 (DRUGS USED IN DIABETES) | A10D0 (ANIMAL INSULINS) | 1 | according to pesonal communication, all insulins are on NLEM |
| | Insulins | INSULIN PORCINE ZINC SUSPENSION (COMPOUND) | A10 (DRUGS USED IN DIABETES) | A10D0 (ANIMAL INSULINS ) | 1 | according to pesonal communication, all insulins are on NLEM |
| | | | | | | |
| **CARIOVASCULAR DISEASE** | | | | | | |
| | Antihypertensives | AJMALICINE#BUTIZIDE#RESCINNAMINE#RESERPINE | C2 (ANTIHYPERTENSIVES) | C2D0 (RAUWOLF ALK+OTH COM+DIUR) | 0 | |
| | Antihypertensives | BUNAZOSIN | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) | 0 | |
| | Antihypertensives | CLONIDINE | C2 (ANTIHYPERTENSIVES) | C2A1 (ANTIHYPER.PL MAINLY CENT) | 1 | |
| | Antihypertensives | CLOPAMIDE#DIHYDROERGOCRISTINE#RESERPINE | C2 (ANTIHYPERTENSIVES) | C2D0 (RAUWOLF ALK+OTH COM+DIUR) | 0 | |
| | Antihypertensives | CLOPAMIDE#RESERPINE | C2 (ANTIHYPERTENSIVES) | C2D0 (RAUWOLF ALK+OTH COM+DIUR) | 0 | |
| | Antihypertensives | DIHYDRALAZINE | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) | 1 | |
| | Antihypertensives | DOXAZOSIN | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) | 1 | |
| | Antihypertensives | HYDRALAZINE | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) | 1 | |
| | Antihypertensives | HYDRALAZINE#HYDROCHLOROTHIAZIDE#RESERPINE | C2 (ANTIHYPERTENSIVES) | C2B2 (A-HYPERT(N V)MAINLY PERI) | 0 | all ingredients listed separately, not in combo |
| | Antihypertensives | KETANSERIN | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) | 0 | |
| | Antihypertensives | METHYLDOPA | C2 (ANTIHYPERTENSIVES) | C2A1 (ANTIHYPER.PL MAINLY CENT) | 1 | |
| | Antihypertensives | MINOXIDIL | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) | 1 | |
| | Antihypertensives | NITROPRUSSIDE | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) | 1 | |
| | Antihypertensives | PRAZOSIN | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) | 1 | |
| | Antihypertensives | RESERPINE | C2 (ANTIHYPERTENSIVES) | C2C0 (RAUWLF ALK+OTH A-HY HERB) | 1 | |
| | Antihypertensives | RILMENIDINE | C2 (ANTIHYPERTENSIVES) | C2A1 (ANTIHYPER.PL MAINLY CENT) | 0 | |
| | Antihypertensives | 1-PROPANOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) | 0 | |
| | Antihypertensives | AMILORIDE#HYDROCHLOROTHIAZIDE#TIMOLOL | C7 (BETA BLOCKING AGENTS) | C7B1 (B-BLOCK COMB HYPOT/DIURT) | 1 | |
| | Antihypertensives | ATENOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) | 1 | |
| | Antihypertensives | ATENOLOL#CHLORTALIDONE | C7 (BETA BLOCKING AGENTS) | C7B1 (B-BLOCK COMB HYPOT/DIURT) | 0 | |
| | Antihypertensives | BETAXOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) | 1 | |
| | Antihypertensives | BISOPROLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) | 0 | |
| | Antihypertensives | BISOPROLOL#HYDROCHLOROTHIAZIDE | C7 (BETA BLOCKING AGENTS) | C7B1 (B-BLOCK COMB HYPOT/DIURT) | 0 | |
| | Antihypertensives | CARVEDILOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) | 0 | |

| | | | | | |
|---|---|---|---|---|---|
| | Antihypertensives | CLOPAMIDE#PINDOLOL | C7 (BETA BLOCKING AGENTS) | C7B1 (B-BLOCK COMB HYPOT/DIURT) | 0 |
| | Antihypertensives | LABETALOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) | 0 |
| | Antihypertensives | METOPROLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) | 0 |
| | Antihypertensives | NEBIVOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN ) | 0 |
| | Antihypertensives | OXPRENOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN ) | 0 |
| | Antihypertensives | PINDOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN ) | 0 |
| | Antihypertensives | PROPRANOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN ) | 1 |
| | Antihypertensives | SOTALOL | C7 (BETA BLOCKING AGENTS | C7A0 (B-BLOCKING AGENTS,PLAIN ) | 0 |
| | Antihypertensives | AMLODIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 1 |
| | Antihypertensives | ATENOLOL#NIFEDIPINE | C8 (CALCIUM ANTAGONISTS) | C8B2 (CALC ANTAG/B BLOCKR COMB) | 0 |
| | Antihypertensives | BARNIDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | DILTIAZEM | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 1 |
| | Antihypertensives | FELODIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 1 |
| | Antihypertensives | GALLOPAMIL | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | ISRADIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | LACIDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | LERCANIDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | MANIDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | MIBEFRADIL | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | NICARDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 1 |
| | Antihypertensives | NIFEDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 1 |
| | Antihypertensives | NISOLDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | NITRENDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 0 |
| | Antihypertensives | VERAPAMIL | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) | 1 |
| | Antihypertensives | AMILORIDE | C3 (DIURETICS) | C3A1 (POT SPARING AGENTS PLAIN) | 0 |
| | Antihypertensives | AMILORIDE#HYDROCHLOROTHIAZIDE | C3 (DIURETICS) | C3A5 (POT SPARING+THIAZ COMBS ) | 1 |
| | Antihypertensives | BAROSMA BETULINA#CAPSICUM#METHYLENE BLUE#URGINEA SCIL | C3 (DIURETICS) | C3A6 (OTHER DIURETICS) | 0 |
| | Antihypertensives | BAROSMA BETULINA#HYOSCYAMUS ALBUS#POTASSIUM | C3 (DIURETICS) | C3A6 (OTHER DIURETICS) | 0 |
| | Antihypertensives | BENDROFLUMETHIAZIDE#POTASSIUM | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) | 0 |
| | Antihypertensives | BUMETANIDE | C3 (DIURETICS) | C3A2 (LOOP DIURETICS PLAIN) | 0 |
| | Antihypertensives | FUROSEMIDE | C3 (DIURETICS) | C3A2 (LOOP DIURETICS PLAIN) | 1 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) | 1 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#TRIAMTERENE | C3 (DIURETICS) | C3A5 (POT SPARING+THIAZ COMBS) | 0 |
| | Antihypertensives | INDAPAMIDE | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) | 0 |
| | Antihypertensives | SPIRONOLACTONE | C3 (DIURETICS) | C3A1 (POT SPARING AGENTS PLAIN) | 1 |
| | Antihypertensives | TORASEMIDE | C3 (DIURETICS) | C3A2 (LOOP DIURETICS PLAIN) | 0 |
| | Antihypertensives | TRIPAMIDE | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) | 0 |
| | Antihypertensives | XIPAMIDE | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) | 0 |
| | Antihypertensives | ALISKIREN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9X0 (OTH RENIN-ANGIOTEN AGENT) | 0 |
| | Antihypertensives | ALISKIREN#HYDROCHLOROTHIAZIDE | C9 (RENIN-ANGIOTEN SYS AGENT) | C9X0 (OTH RENIN-ANGIOTEN AGENT) | 0 |
| | Antihypertensives | AMLODIPINE#VALSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D3 (AT2 ANTG COMB CALC ANTAG) | 0 |
| | Antihypertensives | CANDESARTAN CILEXETIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) | 0 |
| | Antihypertensives | CANDESARTAN CILEXETIL#HYDROCHLOROTHIAZIDE | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) | 0 |
| | Antihypertensives | CAPTOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) | 1 |
| | Antihypertensives | CILAZAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) | 0 |
| | Antihypertensives | DELAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) | 0 |
| | Antihypertensives | ENALAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) | 1 |
| | Antihypertensives | EPROSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) | 0 |
| | Antihypertensives | FOSINOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) | 0 |
| | Antihypertensives | FOSINOPRIL#HYDROCHLOROTHIAZIDE | C9 (RENIN-ANGIOTEN SYS AGENT) | C9B1 (ACE INH COMB+A-HYP/DIUR) | 0 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#IRBESARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) | 0 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#LOSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) | 0 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#OLMESARTAN MEDOXOMIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) | 0 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#QUINAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9B1 (ACE INH COMB+A-HYP/DIUR) | 0 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#RAMIPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9B1 (ACE INH COMB+A-HYP/DIUR) | 0 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#TELMISARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) | 0 |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#VALSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) | 0 |
| | Antihypertensives | IMIDAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) | 0 |
| | Antihypertensives | INDAPAMIDE#PERINDOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9B1 (ACE INH COMB+A-HYP/DIUR) | 0 |
| | Antihypertensives | IRBESARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) | 0 |
| | Antihypertensives | LISINOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN ) | 0 |
| | Antihypertensives | LOSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) | 0 |
| | Antihypertensives | OLMESARTAN MEDOXOMIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) | 0 |
| | Antihypertensives | PERINDOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN ) | 0 |
| | Antihypertensives | QUINAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN ) | 0 |
| | Antihypertensives | RAMIPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) | 0 |
| | Antihypertensives | TELMISARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) | 0 |
| | Antihypertensives | VALSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) | 0 |
| | Cardiac Therapy | ADENOSINE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 0 |

both ingredients listed separately, not in combo

| | | | | | | |
|---|---|---|---|---|---|---|
| | Cardiac Therapy | AMIODARONE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 1 | |
| | Cardiac Therapy | AMRINONE | C1 (CARDIAC THERAPY) | C1F0 (POSITIVE INOTROPIC AGENT) | 0 | |
| | Cardiac Therapy | CAFFEINE#ETAMIVAN | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) | 0 | |
| | Cardiac Therapy | DIGITALIS PURPUREA | C1 (CARDIAC THERAPY) | C1A1 (CARDIAC GLYCOSIDES PLAIN) | 0 | |
| | Cardiac Therapy | DIGITOXIN | C1 (CARDIAC THERAPY) | C1A1 (CARDIAC GLYCOSIDES PLAIN) | 0 | |
| | Cardiac Therapy | DIGOXIN | C1 (CARDIAC THERAPY) | C1A1 (CARDIAC GLYCOSIDES PLAIN) | 1 | |
| | Cardiac Therapy | DISOPYRAMIDE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 0 | |
| | Cardiac Therapy | DOBUTAMINE | C1 (CARDIAC THERAPY) | C1C2 (CARDIAC DOPAMINERG AGENT) | 1 | |
| | Cardiac Therapy | DOPAMINE | C1 (CARDIAC THERAPY) | C1C2 (CARDIAC DOPAMINERG AGENT) | 1 | |
| | Cardiac Therapy | EPINEPHRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) | 1 | |
| | Cardiac Therapy | ETAFEDRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) | 0 | |
| | Cardiac Therapy | ETILEFRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) | 0 | |
| | Cardiac Therapy | FLECAINIDE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 0 | |
| | Cardiac Therapy | GLYCINE MAX#UBIDECARENONE | C1 (CARDIAC THERAPY) | C1X0 (ALL OTHER CARDIAC PREPS) | 0 | |
| | Cardiac Therapy | ISOPRENALINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) | 0 | |
| | Cardiac Therapy | ISOSORBIDE DINITRATE | C1 (CARDIAC THERAPY) | C1E0 (NITRITES AND NITRATES) | 1 | |
| | Cardiac Therapy | ISOSORBIDE MONONITRATE | C1 (CARDIAC THERAPY) | C1E0 (NITRITES AND NITRATES) | 1 | |
| | Cardiac Therapy | IVABRADINE | C1 (CARDIAC THERAPY) | C1D0 (CORONRY THER EXC C AN+NI) | 0 | |
| | Cardiac Therapy | LIDOCAINE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 1 | |
| | Cardiac Therapy | MAGNESIUM#POTASSIUM#PROCAINE | C1 (CARDIAC THERAPY) | C1X0 (ALL OTHER CARDIAC PREPS) | 0 | |
| | Cardiac Therapy | METARAMINOL | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) | 1 | |
| | Cardiac Therapy | METILDIGOXIN | C1 (CARDIAC THERAPY) | C1A1 (CARDIAC GLYCOSIDES PLAIN) | 0 | |
| | Cardiac Therapy | MEXILETINE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 0 | |
| | Cardiac Therapy | MIDODRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) | 0 | |
| | Cardiac Therapy | MILRINONE | C1 (CARDIAC THERAPY) | C1F0 (POSITIVE INOTROPIC AGENT) | 0 | |
| | Cardiac Therapy | NITROGLYCERIN | C1 (CARDIAC THERAPY) | C1E0 (NITRITES AND NITRATES) | 0 | |
| | Cardiac Therapy | NOREPINEPHRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) | 0 | only listed in combo with lidocaide |
| | Cardiac Therapy | OXYFEDRINE | C1 (CARDIAC THERAPY) | C1D0 (CORONRY THER EXC C AN+NI) | 0 | |
| | Cardiac Therapy | PENTAERYTHRITYL TETRANITRATE | C1 (CARDIAC THERAPY) | C1E0 (NITRITES AND NITRATES) | 0 | |
| | Cardiac Therapy | PROCAINAMIDE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 1 | |
| | Cardiac Therapy | PROPAFENONE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 1 | |
| | Cardiac Therapy | QUINIDINE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 0 | |
| | Cardiac Therapy | TOCAINIDE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) | 0 | |
| | Cardiac Therapy | TRIMETAZIDINE | C1 (CARDIAC THERAPY) | C1D0 (CORONRY THER EXC C AN+NI) | 0 | |
| | Cardiac Therapy | UBIDECARENONE | C1 (CARDIAC THERAPY) | C1X0 (ALL OTHER CARDIAC PREPS) | 0 | |
| | Cardiac Therapy | UBIQUINONE(S) | C1 (CARDIAC THERAPY) | C1X0 (ALL OTHER CARDIAC PREPS) | 0 | |
| | Lipid Regulating | ACIPIMOX | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) | 0 | |
| | Lipid Regulating | ALLIUM SATIVUM | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | ALLIUM SATIVUM#ARACHIS HYPOGAEA | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | ALLIUM SATIVUM#SOYA LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | AMLODIPINE#ATORVASTATIN | C11 (C.V. MULTITH. COMB PROD) | C11A1 (LIPREG.CV.MULT-TH.FX.COM) | 0 | |
| | Lipid Regulating | ATORVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) | 0 | |
| | Lipid Regulating | BEZAFIBRATE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A2 (FIBRATES) | 0 | |
| | Lipid Regulating | CERIVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) | 0 | |
| | Lipid Regulating | COLESTYRAMINE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A3 (ION-EXCHANGE RESINS) | 0 | |
| | Lipid Regulating | DOCOSAHEXANOIC ACID#EICOSAPENTAENOIC ACID | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | DOCOSAHEXANOIC ACID#EICOSAPENTAENOIC ACID#VITAMIN E | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | EZETIMIBE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) | 0 | |
| | Lipid Regulating | EZETIMIBE#SIMVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10C0 (LIP.REG.CO.W.OTH.LIP.REG) | 0 | |
| | Lipid Regulating | FENOFIBRATE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A2 (FIBRATES) | 0 | |
| | Lipid Regulating | FISH | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | FISH#SOYA LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | FLUVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED) ) | 0 | |
| | Lipid Regulating | GEMFIBROZIL | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A2 (FIBRATES) | 1 | |
| | Lipid Regulating | LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | LECITHIN#SOYA LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | Lipid Regulating | NICOTINIC ACID | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) | 1 | |
| | Lipid Regulating | PITAVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) | 0 | |
| | Lipid Regulating | PRAVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) | 1 | |
| | Lipid Regulating | PROBUCOL | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) | 0 | |
| | Lipid Regulating | PYRICARBATE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) | 0 | |
| | Lipid Regulating | ROSUVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) | 0 | |
| | Lipid Regulating | SALMON | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 1 | listed as "calcitonic salmon" on NLEM |
| | Lipid Regulating | SIMVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) | 1 | |
| | Lipid Regulating | SOYA LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) | 0 | |
| | | | | | | |
| **CANCER** | | | | | | |
| | Antineoplastics | ALEMTUZUMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) | 0 | |
| | Antineoplastics | ALTRETAMINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 0 | |

| | | | | | |
|---|---|---|---|---|---|
| | Antineoplastics | ASPARAGINASE | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) | 0 |
| | Antineoplastics | AZACITIDINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | BEVACIZUMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) | 0 |
| | Antineoplastics | BLEOMYCIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) | 1 |
| | Antineoplastics | BORTEZOMIB | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) | 0 |
| | Antineoplastics | BUSULFAN | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 1 |
| | Antineoplastics | CAPECITABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | CARBOPLATIN | L1 (ANTINEOPLASTICS) | L1X2 (PLATINUM COMPOUNDS) | 1 |
| | Antineoplastics | CARMUSTINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 1 |
| | Antineoplastics | CETUXIMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) | 0 |
| | Antineoplastics | CHLORAMBUCIL | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 1 |
| | Antineoplastics | CHLORMETHINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS ) | 0 |
| | Antineoplastics | CISPLATIN | L1 (ANTINEOPLASTICS) | L1X2 (PLATINUM COMPOUNDS) | 1 |
| | Antineoplastics | CLADRIBINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | CYCLOPHOSPHAMIDE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 1 |
| | Antineoplastics | CYTARABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 1 |
| | Antineoplastics | DACARBAZINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 0 |
| | Antineoplastics | DACTINOMYCIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) | 1 |
| | Antineoplastics | DASATINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) | 0 |
| | Antineoplastics | DECITABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | DOCETAXEL | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS ) | 0 |
| | Antineoplastics | DOXORUBICIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) | 1 |
| | Antineoplastics | EPIRUBICIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) | 1 |
| | Antineoplastics | ERLOTINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) | 0 |
| | Antineoplastics | ETOPOSIDE | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) | 1 |
| | Antineoplastics | FLUDARABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | FLUOROURACIL | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 1 |
| | Antineoplastics | GEFITINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) | 0 |
| | Antineoplastics | GEMCITABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | HYDROXYCARBAMIDE | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) | 0 |
| | Antineoplastics | IBRITUMOMAB TIUXETAN | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) | 0 |
| | Antineoplastics | IDARUBICIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) | 1 |
| | Antineoplastics | IFOSFAMIDE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 1 |
| | Antineoplastics | IMATINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) | 0 |
| | Antineoplastics | IRINOTECAN | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) | 0 |
| | Antineoplastics | IXABEPILONE | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) | 0 |
| | Antineoplastics | LAPATINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) | 0 |
| | Antineoplastics | LOMUSTINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 1 |
| | Antineoplastics | MELPHALAN | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 1 |
| | Antineoplastics | MERCAPTOPURINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 1 |
| | Antineoplastics | METHOTREXATE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 1 |
| | Antineoplastics | MITOMYCIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) | 1 |
| | Antineoplastics | MITOXANTRONE | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) | 0 |
| | Antineoplastics | NILOTINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) | 0 |
| | Antineoplastics | OXALIPLATIN | L1 (ANTINEOPLASTICS) | L1X2 (PLATINUM COMPOUNDS) | 0 |
| | Antineoplastics | PACLITAXEL | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) | 1 |
| | Antineoplastics | PEMETREXED | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | PROCARBAZINE | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) | 1 |
| | Antineoplastics | RITUXIMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) | 0 |
| | Antineoplastics | SORAFENIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) | 0 |
| | Antineoplastics | SUNITINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) | 0 |
| | Antineoplastics | TEGAFUR | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | TEGAFUR#URACIL | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 1 |
| | Antineoplastics | TEMOZOLOMIDE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) | 0 |
| | Antineoplastics | TIOGUANINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) | 0 |
| | Antineoplastics | TOPOTECAN | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) | 0 |
| | Antineoplastics | TRASTUZUMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) | 0 |
| | Antineoplastics | TRETINOIN | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) | 0 |
| | Antineoplastics | VINBLASTINE | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) | 1 |
| | Antineoplastics | VINCRISTINE | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) | 1 |
| | Antineoplastics | VINORELBINE | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) | 0 |
| | Cytostatic Hormones | AMINOGLUTETHIMIDE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) | 0 |
| | Cytostatic Hormones | ANASTROZOLE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) | 0 |
| | Cytostatic Hormones | BICALUTAMIDE | L2 (CYTOSTATIC HORMONE THER) | L2B2 (CYTO ANTI-ANDROGENS) | 0 |
| | Cytostatic Hormones | BUSERELIN | L2 (CYTOSTATIC HORMONE THER) | L2A3 (CYTO GONAD HORMON ANALOG) | 1 |
| | Cytostatic Hormones | CYPROTERONE | L2 (CYTOSTATIC HORMONE THER) | L2B2 (CYTO ANTI-ANDROGENS) | 1 |
| | Cytostatic Hormones | EXEMESTANE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) | 0 |
| | Cytostatic Hormones | FLUTAMIDE | L2 (CYTOSTATIC HORMONE THER) | L2B2 (CYTO ANTI-ANDROGENS) | 1 |
| | Cytostatic Hormones | FORMESTANE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) | 1 |

| | | | | | |
|---|---|---|---|---|---|
| | Cytostatic Hormones | FULVESTRANT | L2 (CYTOSTATIC HORMONE THER) | L2B9 (OTH CYTO HORMON ANTAGIST) | 0 |
| | Cytostatic Hormones | GOSERELIN | L2 (CYTOSTATIC HORMONE THER) | L2A3 (CYTO GONAD HORMON ANALOG) | 1 |
| | Cytostatic Hormones | LETROZOLE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) | 0 |
| | Cytostatic Hormones | LEUPRORELIN | L2 (CYTOSTATIC HORMONE THER) | L2A3 (CYTO GONAD HORMON ANALOG) | 1 |
| | Cytostatic Hormones | MEDROXYPROGESTERONE | L2 (CYTOSTATIC HORMONE THER) | L2A2 (CYTOSTATIC PROGESTOGENS ) | 0 |
| | Cytostatic Hormones | MEGESTROL | L2 (CYTOSTATIC HORMONE THER) | L2A2 (CYTOSTATIC PROGESTOGENS ) | 1 |
| | Cytostatic Hormones | TAMOXIFEN | L2 (CYTOSTATIC HORMONE THER) | L2B1 (CYTO ANTI-OESTROGENS) | 1 |
| | Cytostatic Hormones | TOREMIFENE | L2 (CYTOSTATIC HORMONE THER) | L2B1 (CYTO ANTI-OESTROGENS) | 0 |
| | Cytostatic Hormones | TRIPTORELIN | L2 (CYTOSTATIC HORMONE THER) | L2A3 (CYTO GONAD HORMON ANALOG) | 0 |
| | Immunostimulating Agents | FILGRASTIM | L3 (IMMUNOSTIMULATING AGENTS) | L3A1 (COLONY-STIMULATING FACT.) | 1 |
| | Immunostimulating Agents | INTERFERON ALFA | L3 (IMMUNOSTIMULATING AGENTS) | L3B1 (INTERFERONS ALPHA) | 0 |
| | Immunostimulating Agents | INTERFERON ALFA-2A | L3 (IMMUNOSTIMULATING AGENTS) | L3B1 (INTERFERONS ALPHA) | 0 |
| | Immunostimulating Agents | INTERFERON ALFA-2B | L3 (IMMUNOSTIMULATING AGENTS) | L3B1 (INTERFERONS ALPHA) | 0 |
| | Immunostimulating Agents | INTERFERON ALFA-N1 | L3 (IMMUNOSTIMULATING AGENTS) | L3B1 (INTERFERONS ALPHA) | 0 |
| | Immunostimulating Agents | INTERFERON BETA-1A | L3 (IMMUNOSTIMULATING AGENTS) | L3B2 (INTERFERONS BETA) | 0 |
| | Immunostimulating Agents | INTERFERON BETA-1B | L3 (IMMUNOSTIMULATING AGENTS) | L3B2 (INTERFERONS BETA) | 0 |
| | Immunostimulating Agents | LENOGRASTIM | L3 (IMMUNOSTIMULATING AGENTS) | L3A1 (COLONY-STIMULATING FACT.) | 1 |
| | Immunostimulating Agents | MOLGRAMOSTIM | L3 (IMMUNOSTIMULATING AGENTS) | L3A1 (COLONY-STIMULATING FACT.) | 1 |
| | Immunostimulating Agents | PEGFILGRASTIM | L3 (IMMUNOSTIMULATING AGENTS) | L3A1 (COLONY-STIMULATING FACT.) | 0 |
| | Immunostimulating Agents | TETRACHLORODECAOXIDE | L3 (IMMUNOSTIMULATING AGENTS) | L3A9 (OTH.IMMUNOSTIM.EX.INTFRN) | 0 |
| | Immunostimulating Agents | THYMALFASIN | L3 (IMMUNOSTIMULATING AGENTS) | L3A9 (OTH.IMMUNOSTIM.EX.INTFRN) | 0 |

**Appendix Table 2. Segmented Regression Coefficients: Total Volume***

| | INTERCEPT | TIME | INTERVENTION | TIME AFTER INTERVENTION | TIME AFTER INTERVENTION SQUARED** |
|---|---|---|---|---|---|
| | Beta | Beta (Std. Err.) | Beta (Std. Err.) | Beta (Std. Err.) | Beta (Std. Err.) |
| **DIABETES** | | | | | |
| **Insulins** | | | | | |
| **Hospital** | 1.6941 | **0.0848 (0.0185)** | **0.5151 (0.2400)** | **0.0961 (0.0432)** | **0.0156 (0.0019)** |
| **Retail** | 0.3485 | **-0.0134 (0.0041)** | 0.0902 (0.0445) | **0.0288 (0.0046)** | - |
| | | | | | |
| **Antidiabetics** | | | | | |
| **Hospital** | 1252.37 | **71.08 (12.05)** | 66.40 (167.31) | 12.80 (26.17) | **3.08 (1.24)** |
| **Retail** | 228.87 | **6.67 (3.01)** | -63.98 (32.56) | -1.88 (3.37) | - |
| | | | | | |
| **CARDIOVASCULAR DISEASE** | | | | | |
| **Antihypertensives** | | | | | |
| **Hospital** | 1394.24 | **111.96 (17.14)** | **-390.49 (185.18)** | **71.95 (19.17)** | - |
| **Retail** | 284.98 | **8.12 (2.24)** | -39.71 (24.19) | **5.20 (2.50)** | - |
| | | | | | |
| **Lipid Regulating Agents** | | | | | |
| **Hospital** | 193.47 | **17.31 (3.33)** | -37.98 (43.19) | -6.02 (7.78) | **2.77 (0.34)** |
| **Retail** | 136.25 | -2.59 (1.31) | -21.37 (14.18) | **11.72 (1.47)** | - |
| | | | | | |
| **Cardiac Therapy** | | | | | |
| **Hospital** | 434.75 | **13.92 (4.11)** | **-94.51 (44.37)** | 0.63 (4.59) | - |
| **Retail** | 98.32 | 1.63 (1.18) | 11.50 (15.31) | **-8.80 (2.76)** | **0.32 (0.12)** |
| | | | | | |
| **CANCER** | | | | | |
| **Antineoplastics** | | | | | |
| **Hospital** | 21.75 | **0.72 (0.16)** | -2.02 (1.78) | 0.21 (0.18) | - |
| **Retail** | 0.26 | 0.004 (0.02) | 0.18 (0.37) | 0.05 (0.06) | -0.005 (0.002) |
| | | | | | |
| **Cytostatic Hormones** | | | | | |
| **Hospital** | 16.38 | **0.69 (0.15)** | -0.66 (1.60) | **0.44 (0.17)** | - |
| **Retail** | 0.3538 | **-0.03 (0.01)** | **0.53 (0.13)** | -0.03 (0.02) | **0.004 (0.001)** |
| | | | | | |
| **Immunostimulating Agents** | | | | | |
| **Hospital** | 0.45 | **0.01 (0.004)** | **-0.18 (0.05)** | -0.02 (0.008) | 0.0007 (0.0004) |
| **Retail** | 0.0000066 | -0.0000005 (0.000001) | 0.0000003 (0.000007) | 0.0000005 (0.0000007) | - |

* **Bold** signifies statistically significant coefficient (i.e., $p<0.05$)

**Results from quadratic model (which has squared post-policy trend term) were included if quadratic model fits better than linear model.

**Appendix Table 3. Summary of Hospital Sector Volume Regression Results by NLEM***

| Therapeutic Area | Pre-policy trend | Immediate change after policy | Post-policy trend change |
|---|---|---|---|
| | | | |
| **DIABETES** | | | |
| **Antidiabetics** | | | |
| NLEM** | ↑ | | ↑ |
| non-NLEM** | ↑ | | ↑ |
| **Insulins *** ** | | | |
| NLEM** | ↑ | ↑ | ↑ |
| non-NLEM | | | |
| | | | |
| **CARDIOVASCULAR DISEASE** | | | |
| **Antihypertensives** | | | |
| NLEM | ↑ | | ↑ |
| non-NLEM** | ↑ | | ↑ |
| **Lipid Regulating Agents** | | | |
| NLEM** | ↑ | | ↑ |
| non-NLEM** | ↑ | ↓ | ↑ |
| **Cardiac Therapy** | | | |
| NLEM | ↑ | | |
| non-NLEM** | ↑ | ↓ | |
| | | | |
| **CANCER** | | | |
| **Antineoplastics** | | | |
| NLEM | ↑ | | |
| non-NLEM** | ↑ | | |
| **Cytostatic Hormones** | | | |
| NLEM | ↑ | | |
| non-NLEM** | ↑ | ↑ | ↑ |
| **Immunostimulating Agents** | | | |
| NLEM** | ↑ | | |
| non-NLEM | | ↓ | ↓ |

*Arrows signify a statistically significant coefficient ($p<0.05$) from segmented regression. Volume is population adjusted - denominator is entire population for insulins and over-15 population for rest of therapeutic areas.

**Quadratic model (which has a squared time-after term) fits beter than linear model.

Details: - Both after and after-squared terms were significant for insulins, non-NLEM antidiabetics, non-NLEM antihypertensives

- Only after-squared term was significant for NLEM antidiabetics and NLEM lipid regulators

- Only linear after term was significant for non-NLEM immunostimulating agents

- The linear after term for nonNLEM antidiabetics and nonNLEM lipid reg was negative, but the positive after-squared term meant a long-term increase in trend

***All insulins are classified as NLEM medicines

**Appendix Table 4. Absolute Impact of the Reform on Sales of Medicines by Class (one and five years post-policy)***

| Therapeutic Class | One Year Impact (in standard units) | | | Five Year Impact (in standard units) | | |
|---|---|---|---|---|---|---|
| | Predicted | Observed | Absolute Change (95% CI) | Predicted | Observed | Absolute Change (95% CI) |
| **Antidiabetics** | 2602.91 | 2769.79 | 166.87 (-160.98, 494.73) | 3669.13 | 5090.62 | **1421.49 (739.57, 2103.42)** |
| **Insulins** | 3.30 | 4.45 | **1.15 (0.66, 1.64)** | 4.58 | 12.56 | **7.98 (6.94, 9.02)** |
| **Cardiac Therapy Agents** | 699.28 | 607.27 | -92.01 (-201.38, 17.36) | 908.12 | 825.49 | -82.63 (-309.66, 144.40) |
| **Lipid Regulating Agents** | 522.34 | 504.58 | -17.76 (-106.50, 70.97) | 781.97 | 1629.11 | **847.14 (659.98, 1034.30)** |
| **Antihypertensives** | 3521.47 | 3418.79 | -102.68 (-559.16, 353.80) | 5200.86 | 6177.49 | **976.62 (29.03, 1924.22)** |
| **Antineoplastics** | 35.38 | 34.21 | -1.17 (-5.56, 3.22) | 46.14 | 48.13 | 1.99 (-7.13, 11.11) |
| **Cytostatic Hormones** | 29.48 | 30.58 | 1.10 (-2.85, 5.05) | 39.82 | 47.52 | 7.70 (-0.50, 15.89) |
| **Immunostimulating Agents** | 0.65 | 0.43 | **-0.23 (-0.32, -0.13)** | 0.81 | 0.60 | **-0.21 (-0.42, -0.01)** |

***bold** signifies that change is statistically significant (i.e., confidence interval does not include the null value of 0)

**Appendix Table 5. Segmented Regression Coefficients: Hospital Market Share***

| | INTERCEPT | TIME | INTERVENTION | TIME AFTER INTERVENTION | IME AFTER INTERVENTION SQUARED** |
|---|---|---|---|---|---|
| | Beta | Beta (Std. Err.) | Beta (Std. Err.) | Beta (Std. Err.) | Beta (Std. Err.) |
| **Insulins (Hospital)** | | | | | |
| Originator Brand | -0.0017 | **0.0005 (0.0001)** | -0.0004 (0.0017) | -0.0003 (0.0003) | **0.0001 (0.0000002)** |
| Branded Generic | 0.8934 | 0.0026 (0.0019) | **0.0697 (0.0200)** | **-0.0048 (0.0021)** | - |
| Generic | 0.1083 | -0.0030 (0.0019) | **-0.0624 (0.0200)** | 0.0031 (0.0021) | - |
| | | | | | |
| **Antidiabetics (Hospital)** | | | | | |
| Originator Brand | 0.1601 | **-0.0049 (0.0006)** | -0.0028 (0.0064) | **0.0042 (0.0007)** | - |
| Branded Generic | 0.5178 | 0.0010 (0.0016) | **-0.1233 (0.0178)** | **-0.0045 (0.0017)** | - |
| Generic | 0.0692 | 0.0005 (0.0011) | **-0.0345 (0.0116)** | -0.000545 (0.0012) | - |
| GPO | 0.2505 | 0.0034 (0.0018) | **0.1610 (0.0200)** | 0.000992 (0.0019) | - |
| | | | | | |
| **Antihypertentives (Hospital)** | | | | | |
| Originator Brand | 0.296 | **-0.0066 (0.0008)** | -0.0014 (0.0105) | 0.0034 (0.0019) | **0.0002 (0.00008)** |
| Branded Generic | 0.4491 | **0.0056 (0.0015)** | -0.0214 (0.0191) | **0.0092 (0.0034)** | **-0.0006 (0.0002)** |
| Generic | 0.041 | **0.0033 (0.0012)** | **-0.0567 (0.0130)** | **-0.0030 (0.0013)** | - |
| GPO | 0.211 | -0.0020 (0.0024) | 0.0525 (0.0259) | -0.0022 (0.0027) | - |
| | | | | | |
| **Lipid Regulating Agents (Hospital)** | | | | | |
| Originator Brand | 0.5657 | **-0.0092 (0.0008)** | **-0.0776 (0.0116)** | **-0.0061 (0.0116)** | **0.0003 (0.00009)** |
| Branded Generic | 0.427 | **0.0096 (0.0008)** | **0.0755 (0.0118)** | **0.0055 (0.0017)** | **-0.0003 (0.00009)** |
| Generic | 0.004897 | -0.0003 (0.0002) | 0.0015 (0.0025) | 0.0002 (0.0003) | - |
| GPO | -0.000482 | 0.0001 (0.0003) | 0.0023 (0.0028) | -0.0003 (0.0003) | - |
| | | | | | |
| **Cardiac Therapy (Hospital)** | | | | | |
| Originator Brand | 0.0847 | **-0.0014 (0.0004)** | 0.0013 (0.0044) | **0.0014 (0.0004)** | |
| Branded Generic | 0.8032 | -0.0023 (0.0026) | **-0.1351 (0.0340)** | -0.0093 (0.0061) | **0.0006 (0.0003)** |
| Generic | 0.005095 | **0.0031 (0.0009)** | **-0.0426 (0.0093)** | **-0.0030 (0.0010)** | - |
| GPO | 0.0751 | 0.0015 (0.0030) | **0.2155 (0.0319)** | -0.0010 (0.0033) | - |
| | | | | | |
| **Antineoplastics (Hospital)** | | | | | |
| Originator Brand | 0.1554 | 0.0015 (0.0009) | 0.0110 (0.0103) | -0.0014 (0.0010) | - |
| Branded Generic | 0.5518 | -0.0011 (0.0020) | -0.0100 (0.0216) | 0.0011 (0.0022) | - |
| Generic | 0.2862 | -0.0004 (0.0014) | 0.0037 (0.0149) | 0.0002 (0.0015) | - |
| | | | | | |
| **Cytostatic Hormones (Hospital)** | | | | | |
| Originator Brand | 0.4664 | -0.0032 (0.0022) | 0.0038 (0.0280) | **-0.0127 (0.0050)** | **0.0007 (0.0002)** |
| Branded Generic | 0.5141 | **0.0036 (0.0015)** | **-0.0773 (0.0206)** | **0.0195 (0.0035)** | **-0.0013 (0.0002)** |
| Generic | 0.0144 | 0.0004 (0.0017) | **0.0600 (0.0224)** | -0.0060 (0.0040) | **0.0005 (0.0002)** |
| | | | | | |
| **Immunostimulating Agents (Hospital)** | | | | | |
| Originator Brand | 0.9742 | 0.0007 (0.0015) | **-0.0636 (0.0162)** | **-0.0113 (0.0017)** | - |
| Branded Generic | -0.000536 | 0.0001 (0.0013) | **0.0450 (0.0137)** | **0.0108 (0.0014)** | - |
| Generic | -0.000986 | **0.0002 (0.0001)** | -0.0016 (0.0009) | **-0.0003 (0.00009)** | - |

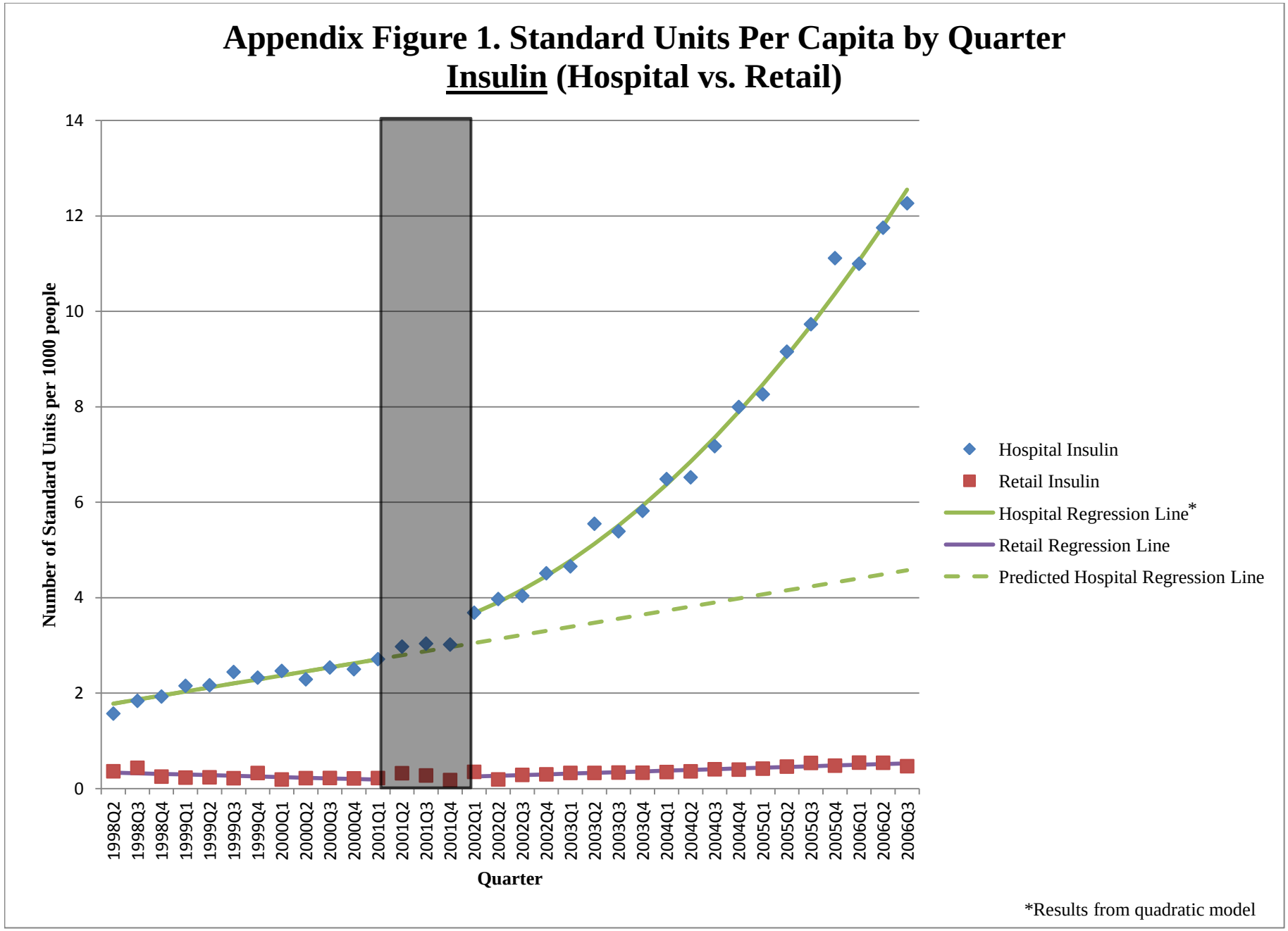
* **Bold** signifies statistically significant coefficient (i.e., p<0.05)

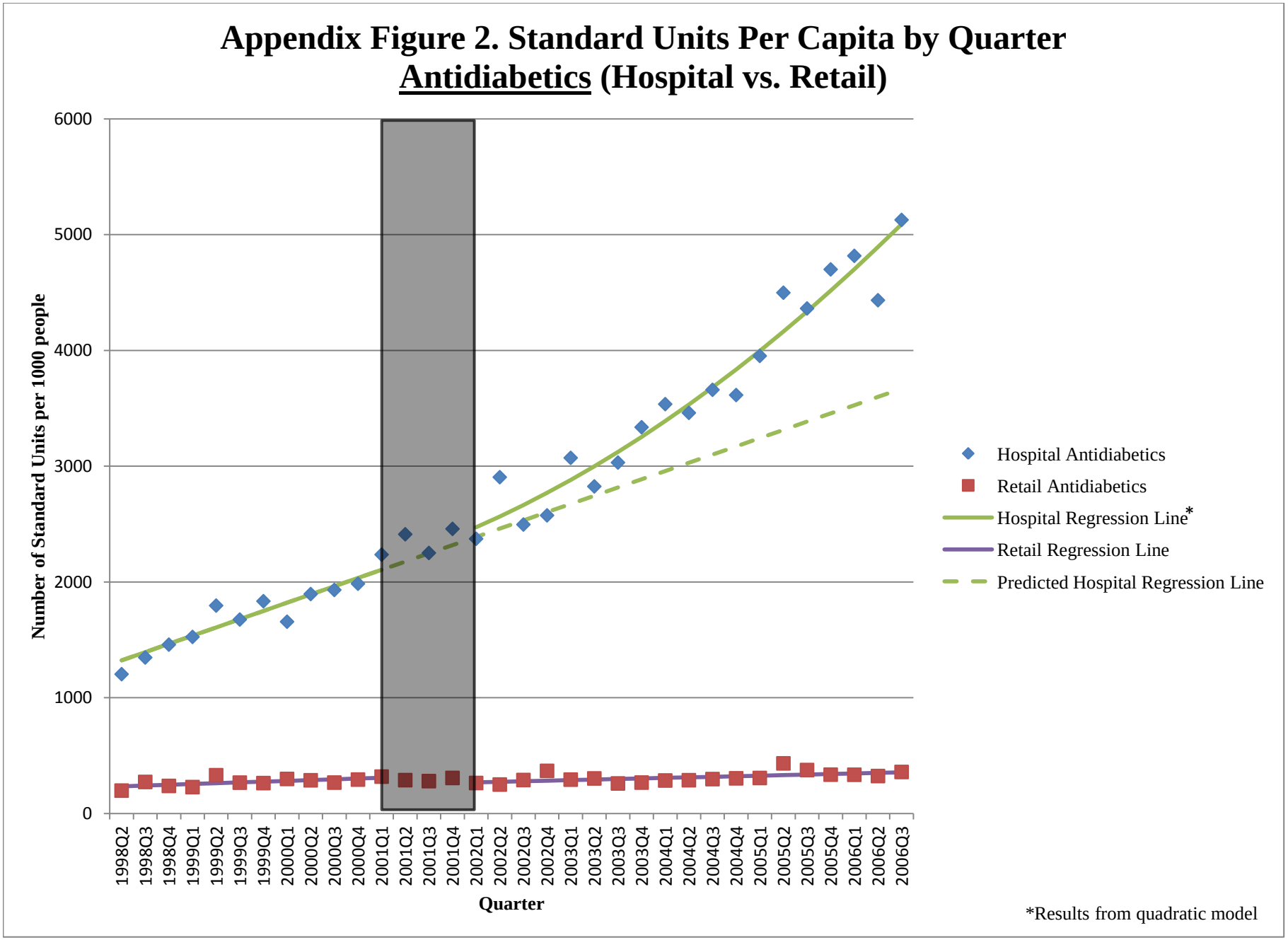
**Results from quadratic model (which has squared post-policy trend term) were included if quadratic model fits better than linear model.

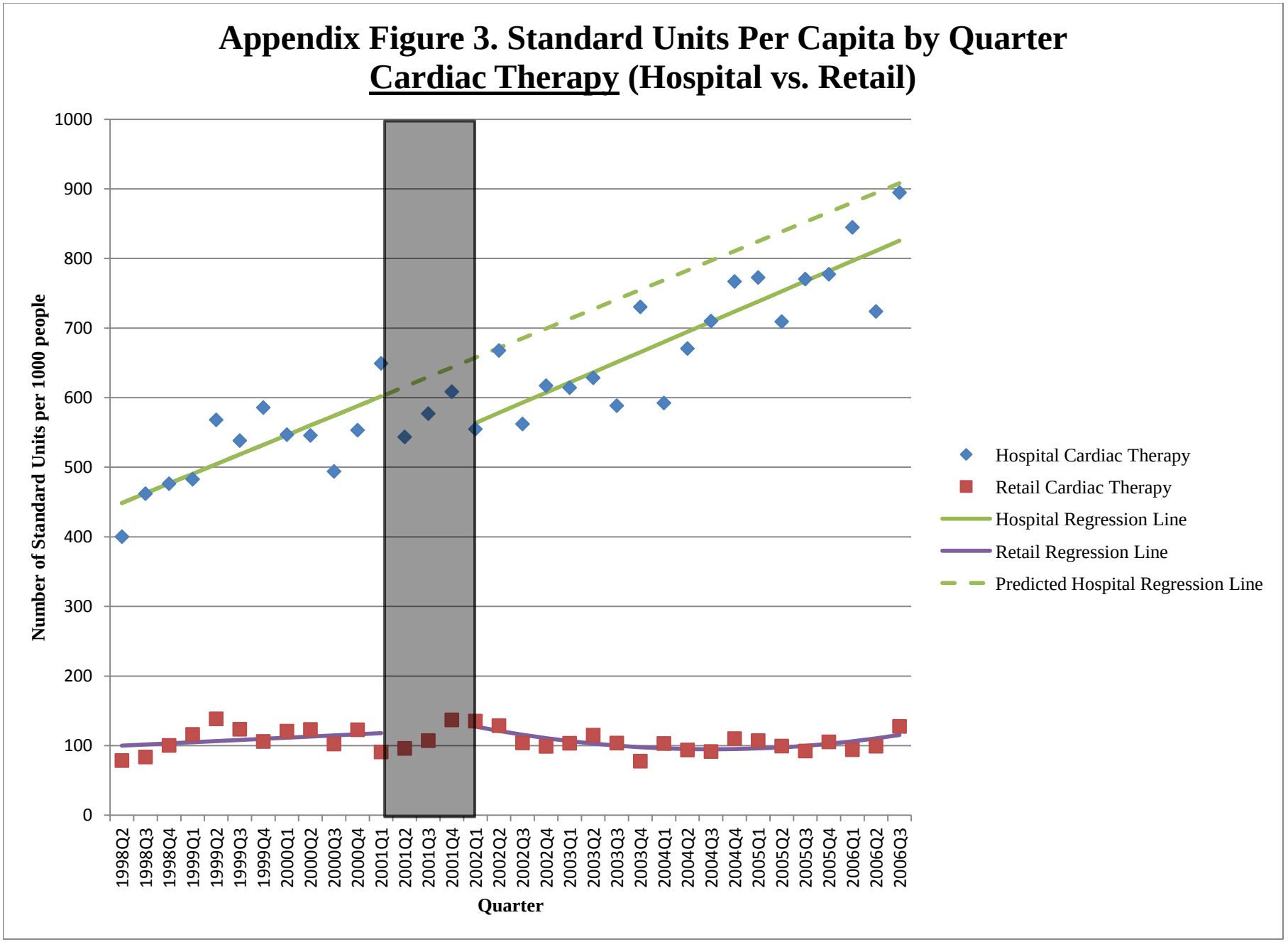
**Appendix Table 6. Absolute Impact of the Reform on Sales of Licensing Status Market Share by Class (one and five years post-policy)***

| Therapeutic Class | One Year Impact (in % market share) | | | Five Year Impact (in % market share) | | |
|---|---|---|---|---|---|---|
| | Predicted | Observed | Relative Change (95% CI) | Predicted | Observed | Relative Change (95% CI) |
| **Antidiabetics** | | | | | | |
| Original/Licensed | 0.0672 | 0.0813 | 0.0140 (-0.0016, 0.0297) | -0.0061 | 0.0712 | **0.0773 (0.0448, 0.1098)** |
| Other | 0.5371 | 0.3960 | **-0.1412 (-0.1851, -0.0972)** | 0.5524 | 0.3443 | **-0.2080 (-0.2966, -0.1195)** |
| Unbranded | 0.0788 | 0.0421 | **-0.0367 (-0.0652, -0.0082)** | 0.0864 | 0.0415 | -0.0449 (-0.1041, 0.0144) |
| GPO | 0.3142 | 0.4792 | **0.1649 (0.1156, 0.2143)** | 0.3645 | 0.5444 | **0.1798 (0.0805, 0.2792)** |
| | | | | | | |
| **Insulins** | | | | | | |
| Originator Brand | 0.0079 | 0.0081 | 0.0002 (-0.0035, 0.0038) | 0.0156 | 0.0461 | **0.0305 (0.0228, 0.0382)** |
| Branded Generic | 0.9419 | 0.9925 | **0.0505 (0.0010, 0.1000)** | 0.9802 | 0.9590 | -0.0212 (-0.1240, 0.0815) |
| Generic | 0.0501 | 0.0000 | **-0.0501 (-0.0994, -0.0008)** | 0.0042 | 0.0000 | -0.0042 (-0.1065, 0.0982) |
| | | | | | | |
| **Antihypertensives** | | | | | | |
| Originator Brand | 0.1697 | 0.1850 | 0.0153 (-0.0063, 0.0368) | 0.0700 | 0.2010 | **0.1310 (0.0854, 0.1765)** |
| Branded Generic | 0.5557 | 0.5619 | 0.0062 (-0.0330, 0.0454) | 0.6398 | 0.5890 | -0.0507 (-0.1333, 0.0319) |
| Generic | 0.1029 | 0.0341 | **-0.0688 (-0.1009, -0.0368)** | 0.1519 | 0.0373 | **-0.1145 (-0.1811, -0.0480)** |
| GPO | 0.1725 | 0.2160 | 0.0435 (-0.0203, 0.1074) | 0.1420 | 0.1520 | 0.0100 (-0.1225, 0.1425) |
| | | | | | | |
| **Cardiac Therapy** | | | | | | |
| Originator Brand | 0.0588 | 0.0656 | 0.0068 (-0.0041, 0.0176) | 0.0384 | 0.0655 | **0.0271 (0.0049, 0.0493)** |
| Branded Generic | 0.7594 | 0.5961 | **-0.1633 (-0.2332, -0.0935)** | 0.7594 | 0.5961 | **-0.1633 (-0.2332, -0.0935)** |
| Generic | 0.1116 | 0.0113 | **-0.1002 (-0.1477, -0.0528)** | 0.1116 | 0.0113 | **-0.1002 (-0.1477, -0.0528)** |
| GPO | 0.1034 | 0.3149 | **0.2115 (0.1329, 0.2901)** | 0.1034 | 0.3149 | **0.2115 (0.1329, 0.2901)** |
| | | | | | | |
| **Lipid Regulators** | | | | | | |
| Originator Brand | 0.3905 | 0.2942 | **-0.0963 (-0.1187, -0.0739)** | 0.2522 | 0.1838 | **-0.0684 (-0.1158, -0.0210)** |
| Branded Generic | 0.6086 | 0.7010 | **0.0924 (0.0697, 0.1151)** | 0.7519 | 0.8159 | **0.0640 (0.0160, 0.1119)** |
| Generic | -0.0009 | 0.0015 | 0.0024 (-0.0038, 0.0085) | -0.0054 | 0.0004 | 0.0058 (-0.0070, 0.0186) |
| GPO | 0.0022 | 0.0033 | 0.0011 (-0.0058, 0.0079) | 0.0044 | 0.0008 | -0.0035 (-0.0177, 0.0106) |
| | | | | | | |
| **Antineoplastics** | | | | | | |
| Originator Brand | 0.1840 | 0.1894 | 0.0054 (-0.0201, 0.0308) | 0.2066 | 0.1908 | -0.0158 (-0.0675, 0.0359) |
| Branded Generic | 0.5308 | 0.5252 | -0.0056 (-0.0587, 0.0476) | 0.5142 | 0.5252 | 0.0110 (-0.0993, 0.1214) |
| Generic | 0.2783 | 0.2827 | 0.0044 (-0.0323, 0.0412) | 0.2721 | 0.2793 | 0.0072 (-0.0690, 0.0835) |
| | | | | | | |
| **Cytostatic Hormones** | | | | | | |
| Originator Brand | 0.4058 | 0.3704 | -0.0353 (-0.0928, 0.0222) | 0.3579 | 0.3803 | 0.0224 (-0.0988, 0.1437) |
| Branded Generic | 0.5821 | 0.5626 | -0.0195 (-0.0609, 0.0218) | 0.6358 | 0.4764 | **-0.1595 (-0.2463, -0.0727)** |
| Generic | 0.0221 | 0.0653 | 0.0432 (-0.0029, 0.0893) | 0.0282 | 0.1393 | **0.1112 (0.0140, 0.2083)** |
| | | | | | | |
| **Immunostimulating Agents** | | | | | | |
| Originator Brand | 0.9875 | 0.8787 | **-0.1087 (-0.1488, -0.0687)** | 0.9979 | 0.7198 | **-0.2781 (-0.3612, -0.1951)** |
| Branded Generic | 0.0018 | 0.0902 | **0.0884 (0.0546, 0.1221)** | 0.0037 | 0.2546 | **0.2509 (0.1808, 0.3210)** |
| Generic | 0.0036 | 0.0007 | **-0.0028 (-0.0050, -0.0007)** | 0.0071 | -0.0003 | **-0.0074 (-0.0120, -0.0029)** |

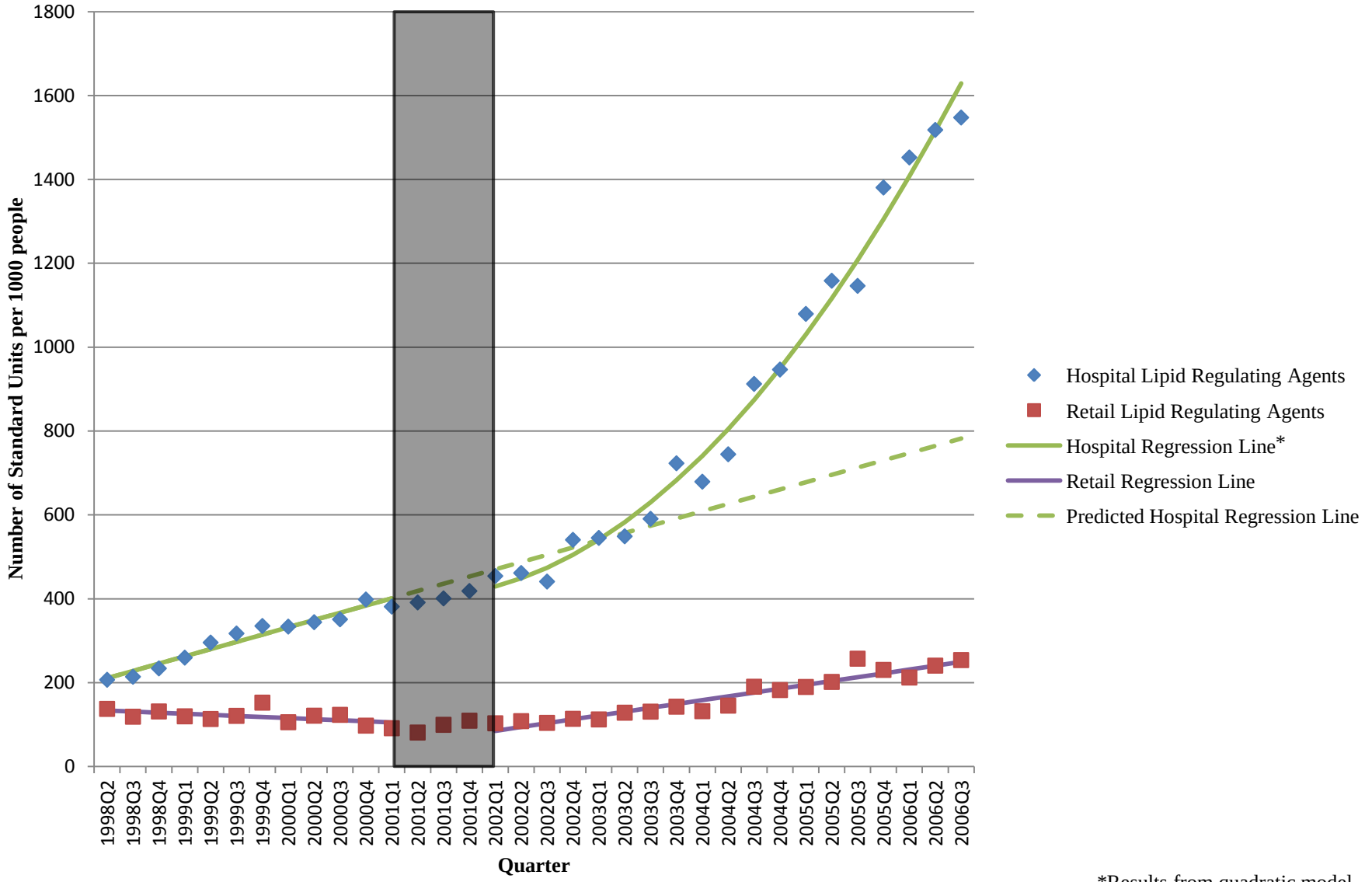
***bold** signifies that change is statistically significant (i.e., confidence interval does not include the null value of 0)


Appendix Figure 1. Standard Units Per Capita by Quarter
Insulin (Hospital vs. Retail)
Number of Standard Units per 1000 people
0
2
4
6
8
10
12
14
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Hospital Insulin
Retail Insulin
Hospital Regression Line*
Retail Regression Line
Predicted Hospital Regression Line
*Results from quadratic model

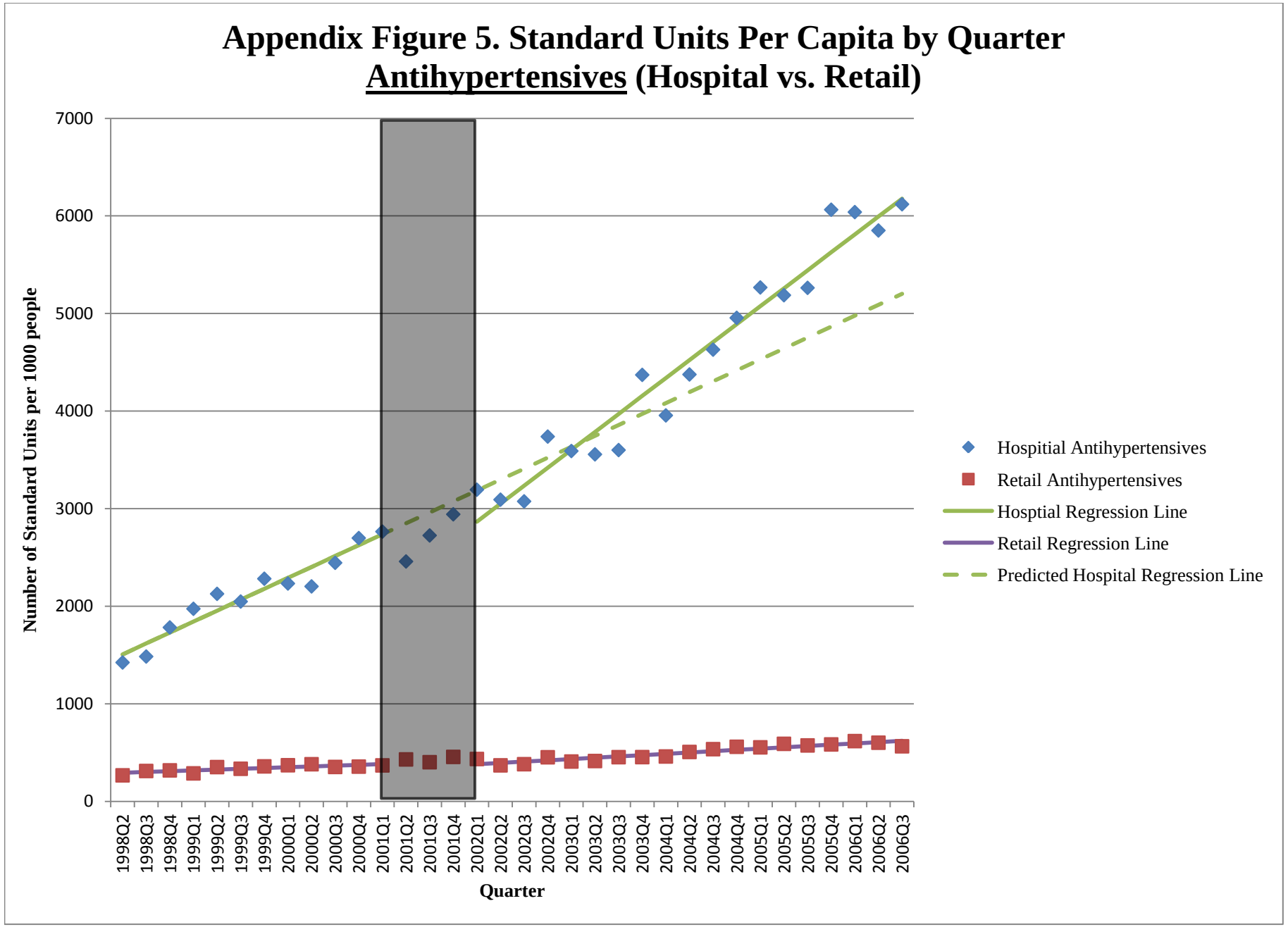

Appendix Figure 2. Standard Units Per Capita by Quarter
Antidiabetics (Hospital vs. Retail)
Number of Standard Units per 1000 people
6000
5000
4000
3000
2000
1000
0
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Hospital Antidiabetics
Retail Antidiabetics
Hospital Regression Line*
Retail Regression Line
Predicted Hospital Regression Line
*Results from quadratic model

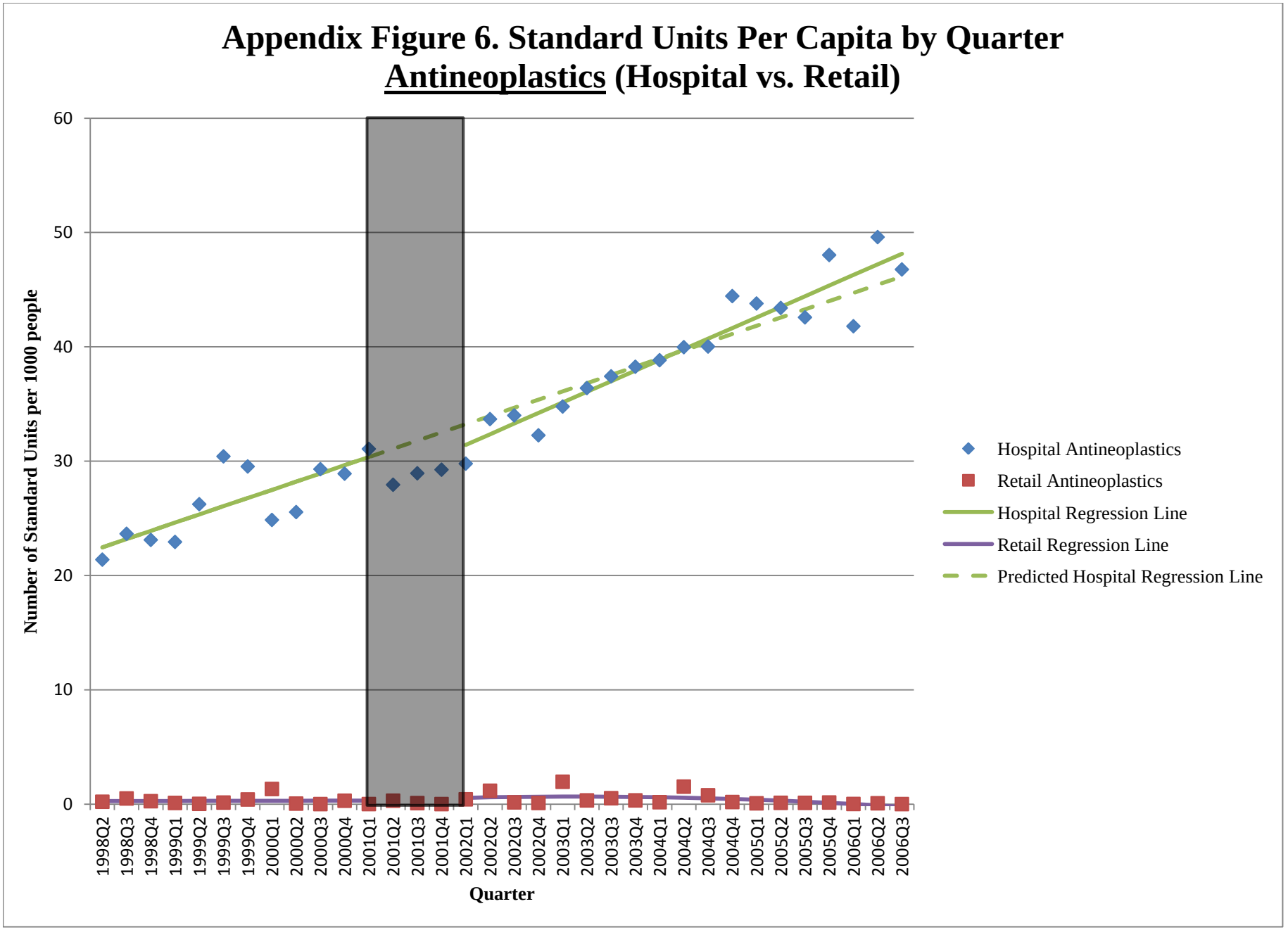

Appendix Figure 3. Standard Units Per Capita by Quarter
Cardiac Therapy (Hospital vs. Retail)
Number of Standard Units per 1000 people
1000
900
800
700
600
500
400
300
200
100
0
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Hospital Cardiac Therapy
Retail Cardiac Therapy
Hospital Regression Line
Retail Regression Line
Predicted Hospital Regression Line

# Appendix Figure 4. Standard Units Per Capita by Quarter
## Lipid Regulating Agents (Hospital vs. Retail)

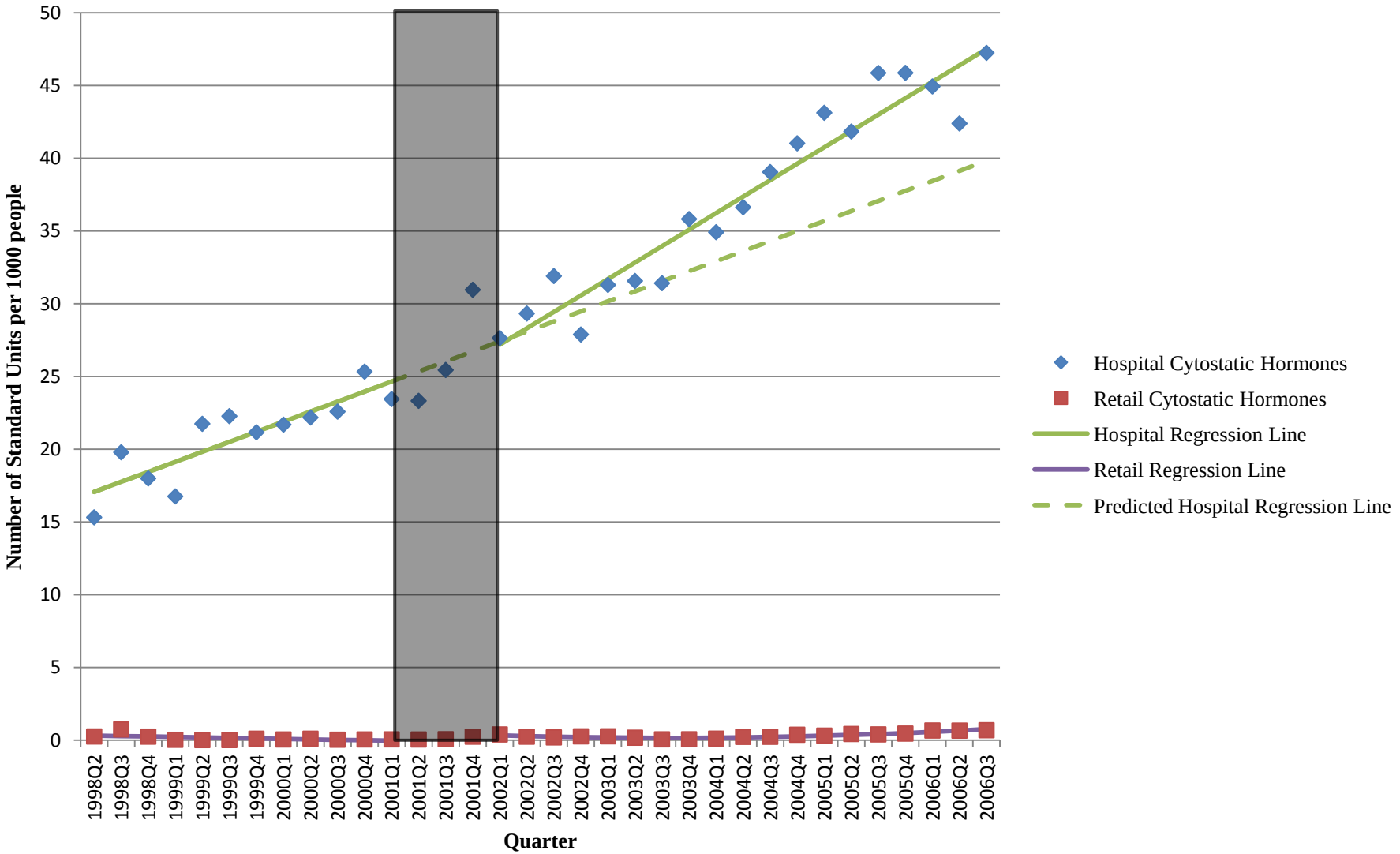



*Results from quadratic model

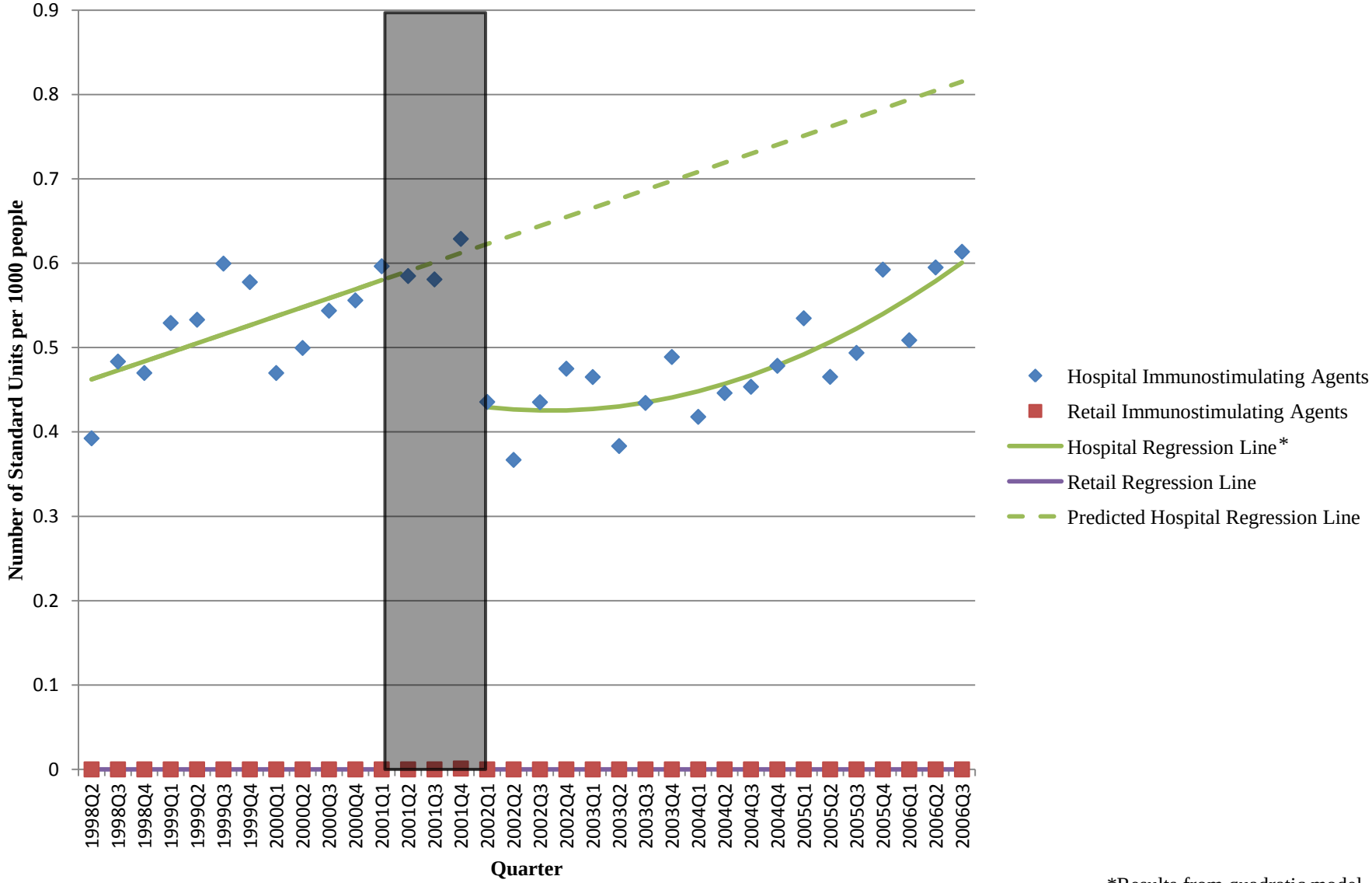

Appendix Figure 5. Standard Units Per Capita by Quarter
Antihypertensives (Hospital vs. Retail)
Number of Standard Units per 1000 people
7000
6000
5000
4000
3000
2000
1000
0
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Hospitial Antihypertensives
Retail Antihypertensives
Hosptial Regression Line
Retail Regression Line
Predicted Hospital Regression Line


Appendix Figure 6. Standard Units Per Capita by Quarter
Antineoplastics (Hospital vs. Retail)
Number of Standard Units per 1000 people
60
50
40
30
20
10
0
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Hospital Antineoplastics
Retail Antineoplastics
Hospital Regression Line
Retail Regression Line
Predicted Hospital Regression Line

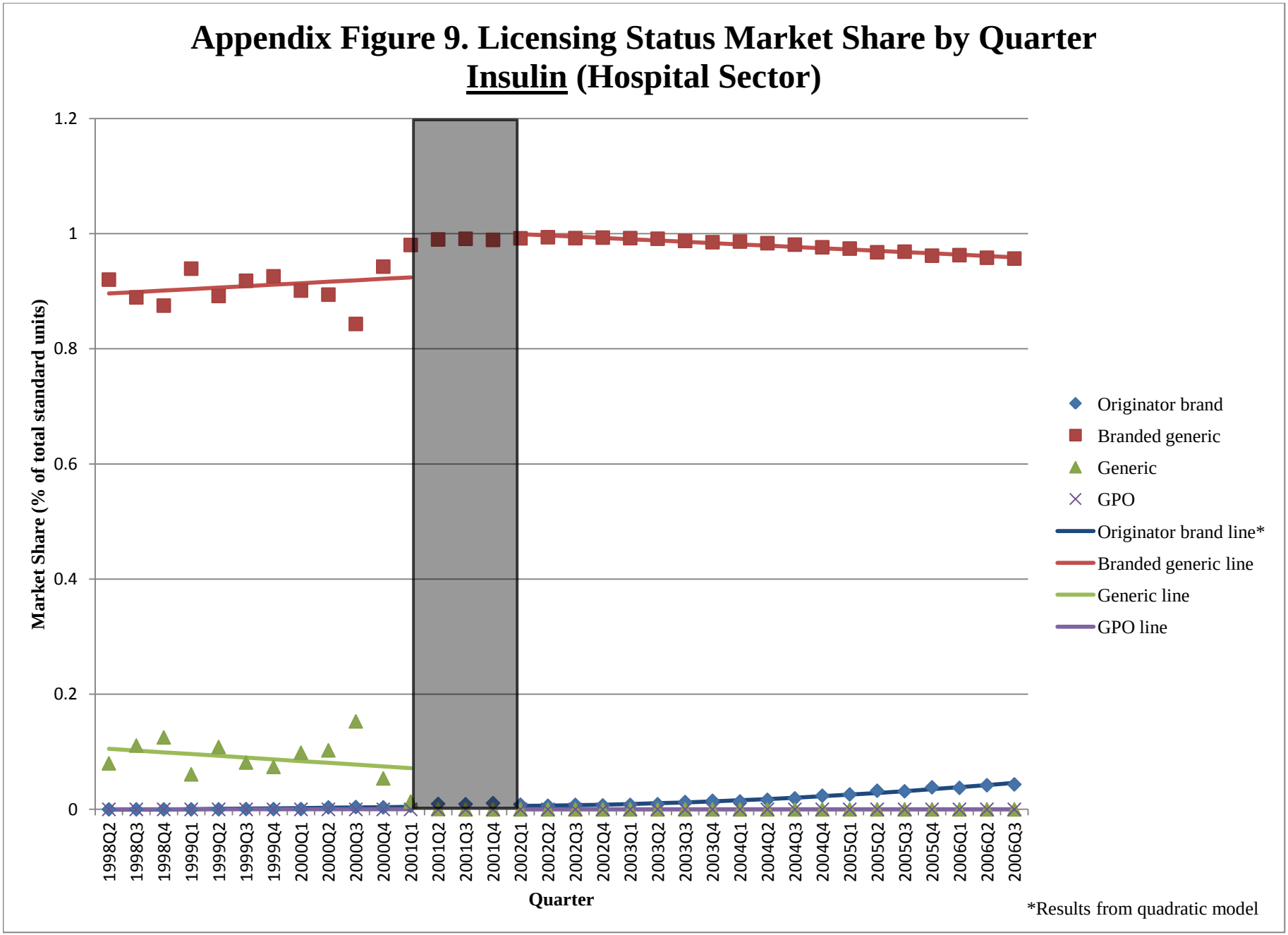
# Appendix Figure 7. Standard Units Per Capita by Quarter
## Cytostatic Hormones (Hospital vs. Retail)

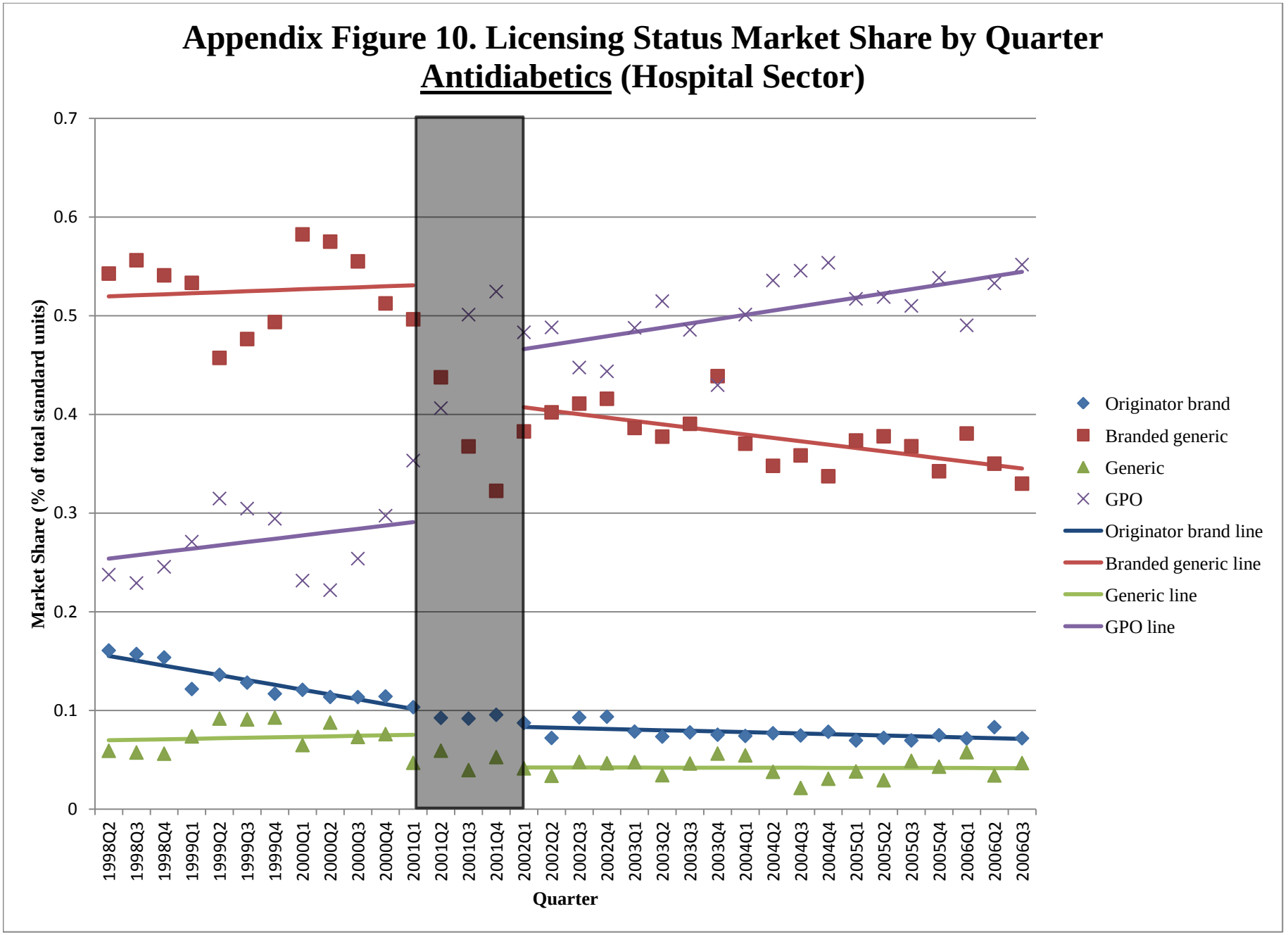


# Appendix Figure 8. Standard Units Per Capita by Quarter
## Immunostimulating Agents (Hospital vs. Retail)

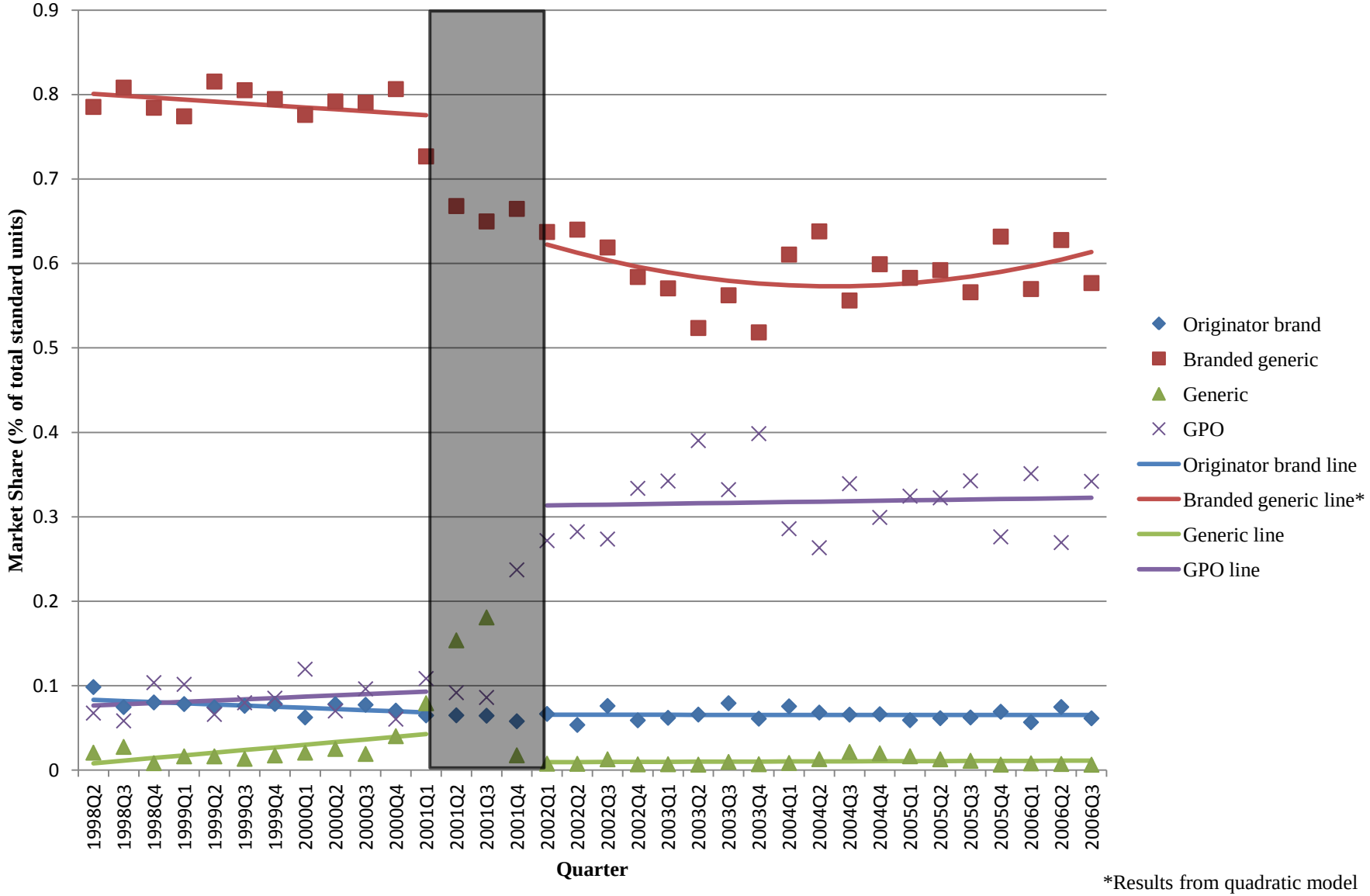


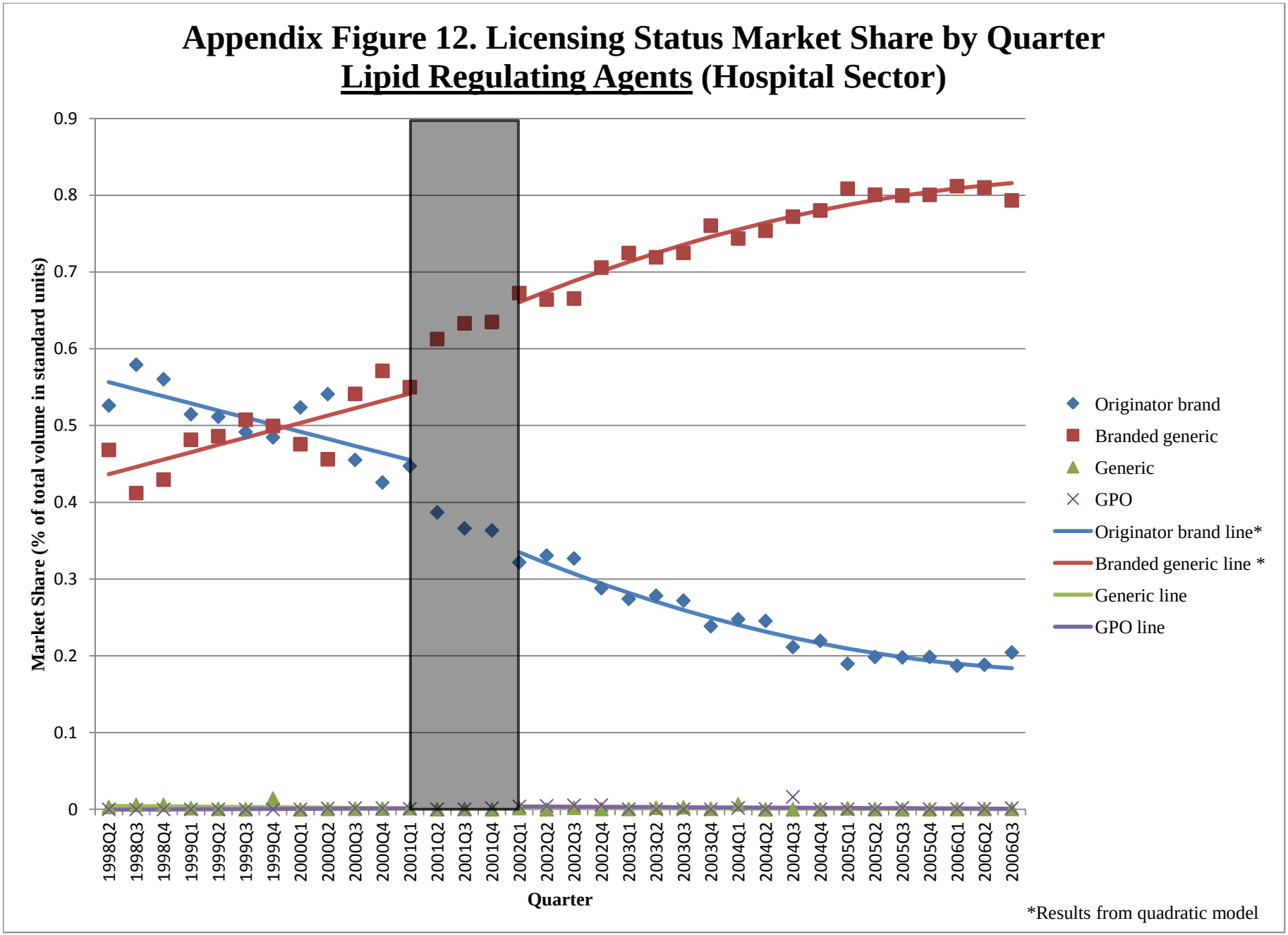

*Results from quadratic model


Appendix Figure 9. Licensing Status Market Share by Quarter
Insulin (Hospital Sector)
Market Share (% of total standard units)
1.2
1
0.8
0.6
0.4
0.2
0
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Originator brand
Branded generic
Generic
GPO
Originator brand line*
Branded generic line
Generic line
GPO line
*Results from quadratic model

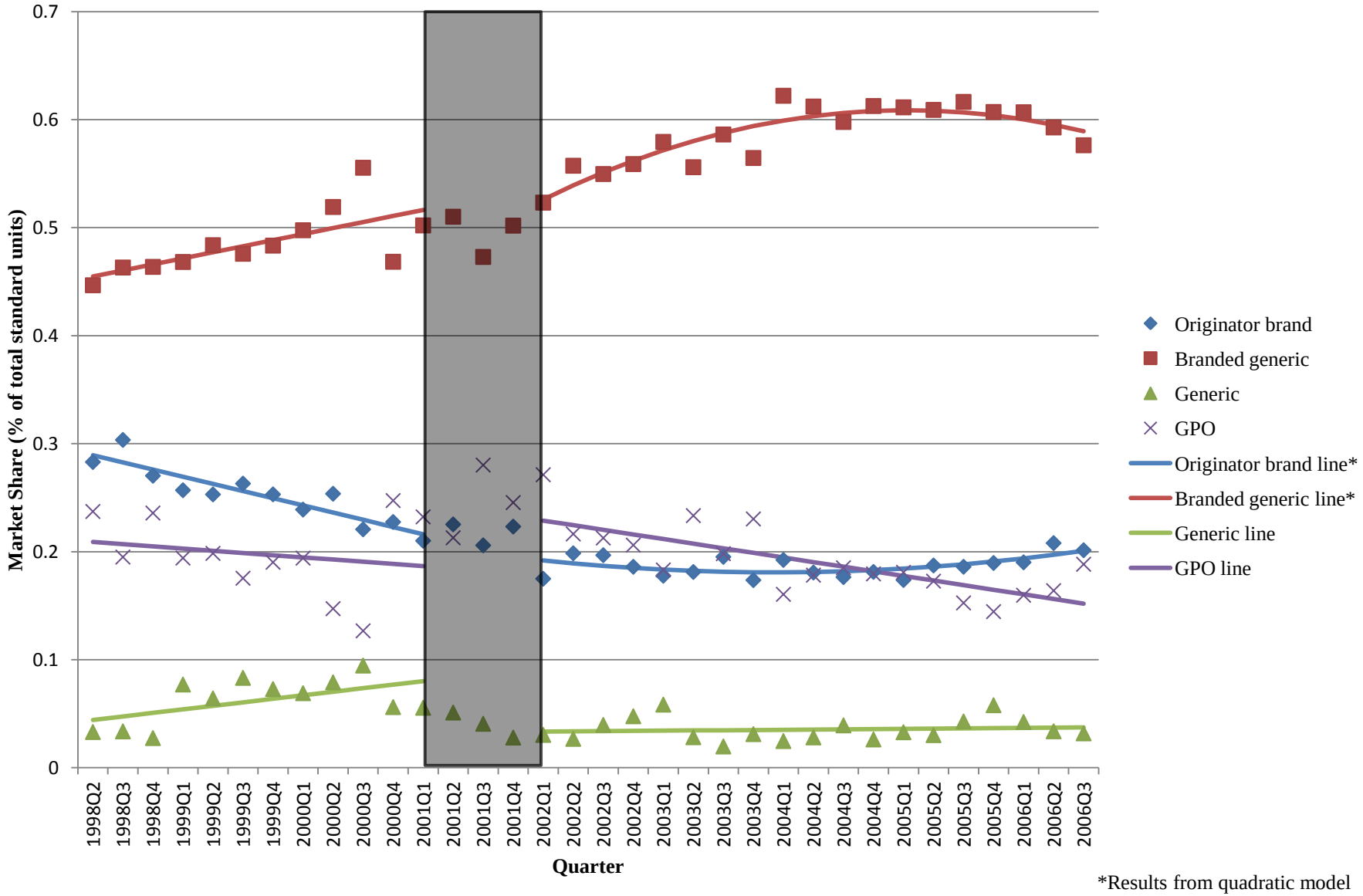

Appendix Figure 10. Licensing Status Market Share by Quarter
Antidiabetics (Hospital Sector)
Market Share (% of total standard units)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Originator brand
Branded generic
Generic
GPO
Originator brand line
Branded generic line
Generic line
GPO line

# Appendix Figure 11. Licensing Status Market Share by Quarter
## Cardiac Therapy Agents (Hospital Sector)

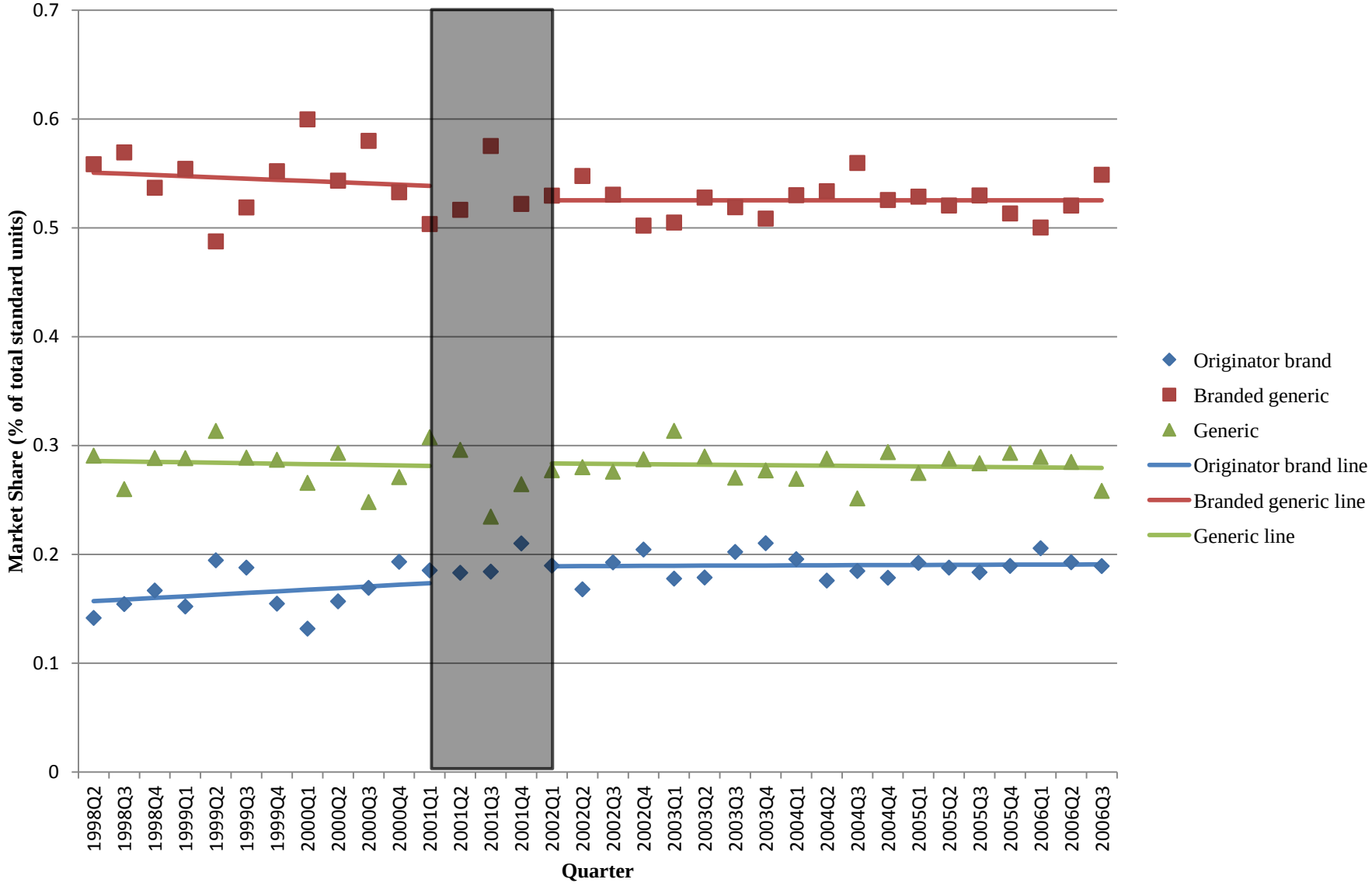



Appendix Figure 12. Licensing Status Market Share by Quarter
Lipid Regulating Agents (Hospital Sector)
Market Share (% of total volume in standard units)
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1998Q2
1998Q3
1998Q4
1999Q1
1999Q2
1999Q3
1999Q4
2000Q1
2000Q2
2000Q3
2000Q4
2001Q1
2001Q2
2001Q3
2001Q4
2002Q1
2002Q2
2002Q3
2002Q4
2003Q1
2003Q2
2003Q3
2003Q4
2004Q1
2004Q2
2004Q3
2004Q4
2005Q1
2005Q2
2005Q3
2005Q4
2006Q1
2006Q2
2006Q3
Quarter
Originator brand
Branded generic
Generic
GPO
Originator brand line*
Branded generic line *
Generic line
GPO line
*Results from quadratic model

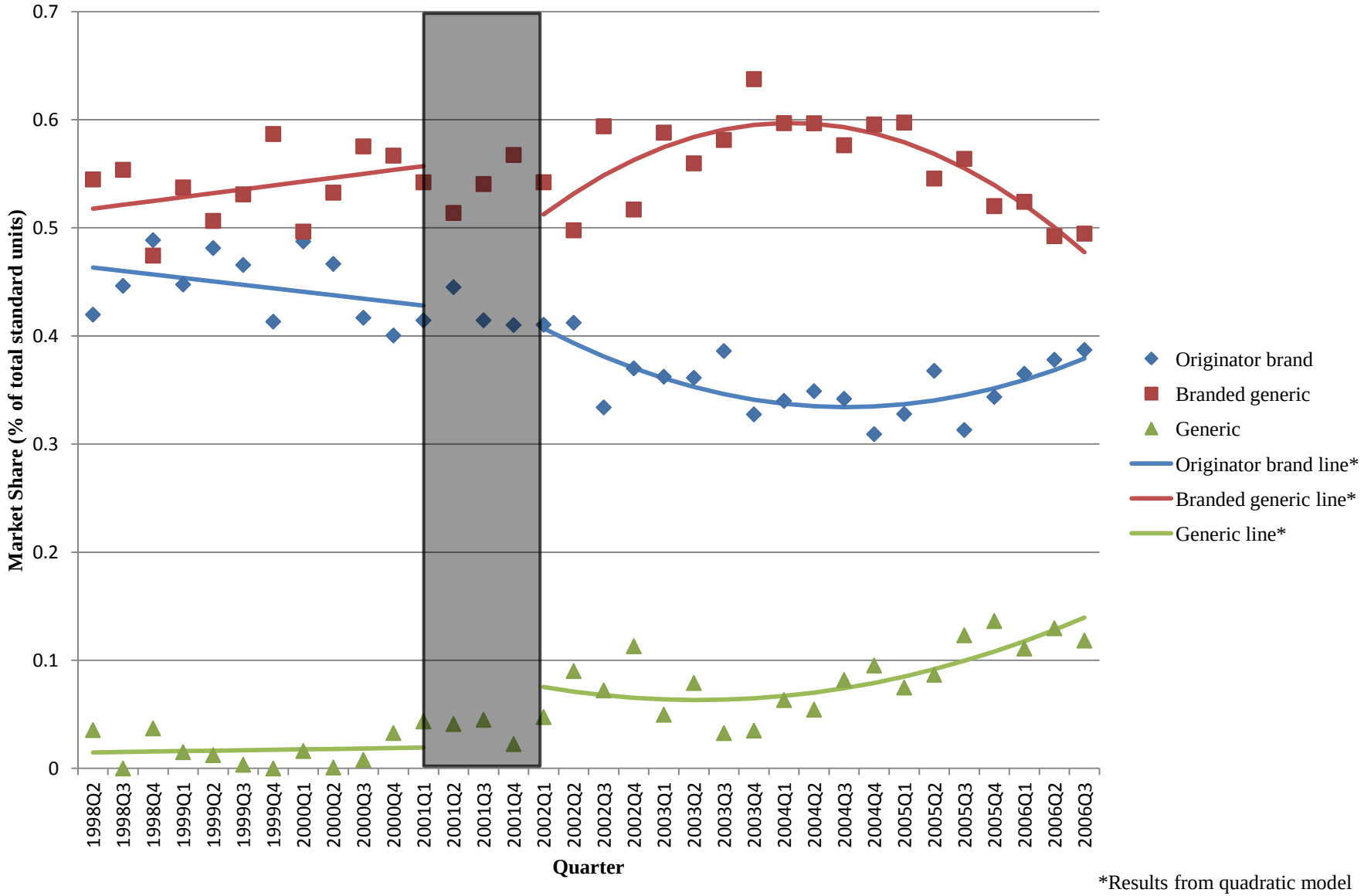
# Appendix Figure 13. Licensing Status Market Share by Quarter
## Antihypertensives (Hospital Sector)



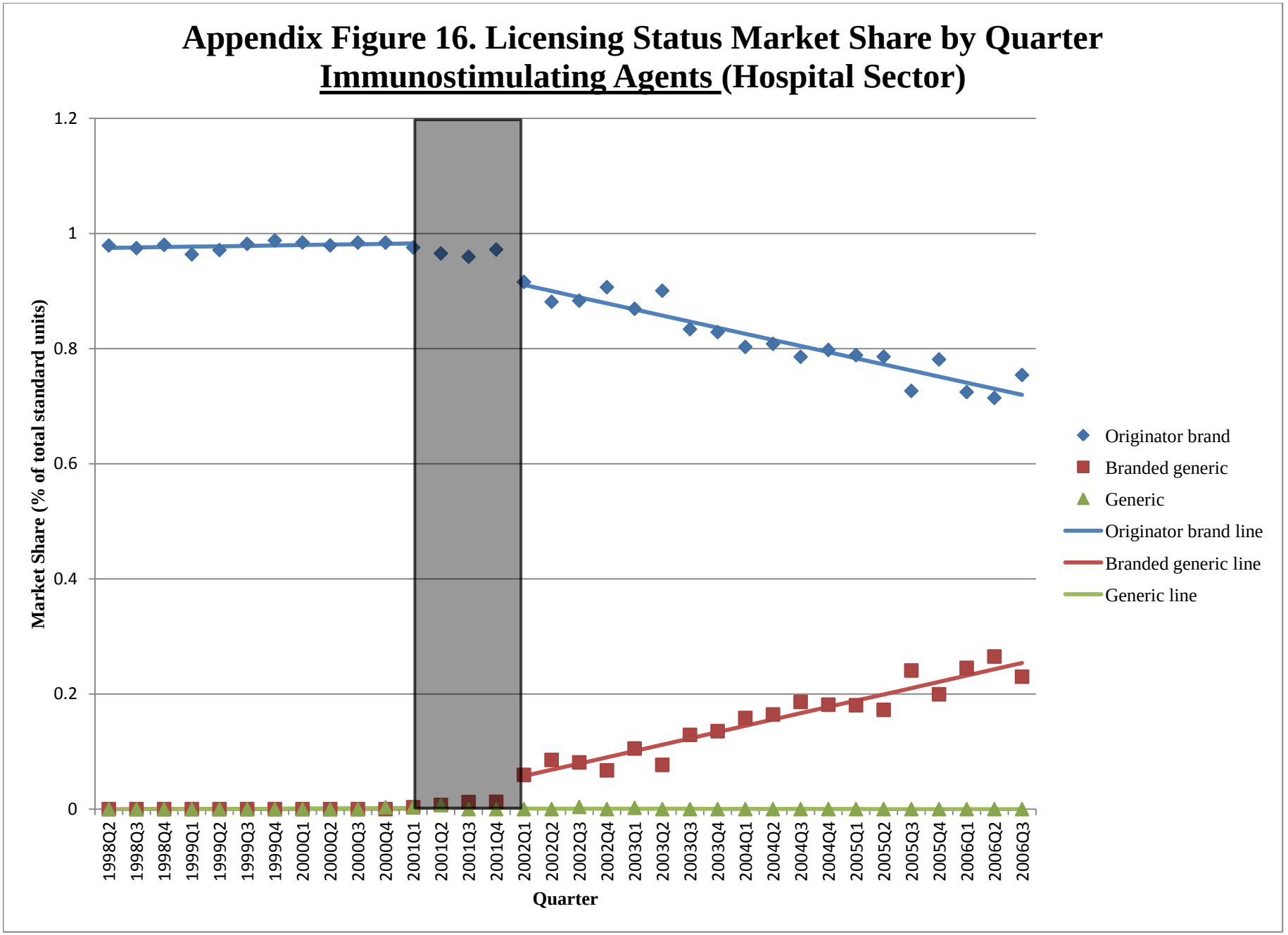
# Appendix Figure 14. Licensing Status Market Share by Quarter
## Antineoplastics (Hospital Sector)



# Appendix Figure 15. Licensing Status Market Share by Quarter
## Cytostatic Hormones (Hospital Sector)




*Results from quadratic model



# STROBE Checklist: Impact of Universal Health Coverage in Thailand on Sales and Market Share of Medicines for Non-Communicable Diseases

STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1✓ | (*a*) Indicate the study's design with a commonly used term in the title or the abstract |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** | | |
| Background/rationale | 2✓ | Explain the scientific background and rationale for the investigation being reported |
| Objectives | 3✓ | State specific objectives, including any prespecified hypotheses |
| **Methods** | | |
| Study design | 4✓ | Present key elements of study design early in the paper<br>**NOTE: We use an interrupted time series design, which is a robust longitudinal observational design.** |
| Setting | 5✓ | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants | 6 ✓ | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case<br>**NOTE: We explain the data source and methods of selection (i.e., hospital vs. pharmacy sales data – the latter serves as a non-equivalent comparison group) and give the rationale for the choice of therapeutic classes and date range.** |
| Variables | 7✓ | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/ measurement | 8*✓ | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias | 9✓ | Describe any efforts to address potential sources of bias |
| Study size | 10✓ | Explain how the study size was arrived at |
| Quantitative variables | 11✓ | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods | 12✓ | (*a*) Describe all statistical methods, including those used to control for confounding |
| | | (*b*) Describe any methods used to examine subgroups and interactions |
| | | (*c*) Explain how missing data were addressed |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed |

| | |
|---|---|
| | *Case-control study*—If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy |
| | (*e*) Describe any sensitivity analyses |

Continued on next page

| | | |
|---|---|---|
| **Results** | | |
| Participants | 13*NA | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| | | (b) Give reasons for non-participation at each stage |
| | | (c) Consider use of a flow diagram |
| Descriptive data | 14*✓ | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount)<br>**NOTE: We give the characteristics of the therapeutic classes (i.e., number subclasses, medicines within each subclass).** |
| Outcome data | 15*✓ | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures<br>**NOTE: We report numbers of outcome events over time.** |
| Main results | 16✓ | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (*b*) Report category boundaries when continuous variables were categorized |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Other analyses | 17✓ | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | | |
| Key results | 18✓ | Summarise key results with reference to study objectives |
| Limitations | 19✓ | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Interpretation | 20✓ | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalisability | 21✓ | Discuss the generalisability (external validity) of the study results |
| **Other information** | | |
| Funding | 22✓ | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

# Impact of Universal Health Insurance Coverage in Thailand on Sales and Market Share of Medicines for Non-Communicable Diseases: An Interrupted Time Series Study

| | |
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| Primary Subject Heading: | Global health |
| Secondary Subject Heading: | Health policy, Health economics, Health services research, Pharmacology and therapeutics, Public health |
| Keywords: | Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Essential Medicines, CARDIOLOGY, DIABETES & ENDOCRINOLOGY, ONCOLOGY |
| | |

# TITLE PAGE

## Impact of Universal Health Insurance Coverage in Thailand on Sales and Market Share of Medicines for Non-Communicable Diseases: an Interrupted Time Series Study

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**Study Design:** Observational study (interrupted time series design)

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**Author contributions:** Laura Garabedian, Dennis Ross-Degnan and Anita Wagner designed the study and developed the analytic approach. Peter Stephens assembled the data files. Laura Garabedian analyzed the data. Sauwakon Ratanawijitrasin provided the Thai national list of essential medicines and information on relevant Thai policies and context surrounding the

reform. All authors participated in the interpretation of the results. Laura Garabedian wrote the first draft of the paper. All authors contributed to the writing of the manuscript.

Opinions expressed are solely those of the authors and not of the institutions they represent.

**Competing Interest Statement:** All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: LFG had financial support from Harvard Medical School and Harvard University, AW and DRD were supported in part by a grant from the Novartis Foundation for Sustainable Development, PS is an employee of IMS Health; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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**IRB Approval:** Harvard Pilgrim Health Care Institute Office of Sponsored Programs



**Data Sharing Statement:** Data available upon request, at the approval of IMS Institute for Healthcare Informatics.

## Article Summary

### Article Focus

- Medicines present a key challenge to achieving universal coverage.
- Health insurance systems have the potential to improve cost-effective use of medicines, yet there is little evidence about their impact on medicine use in low- and middle-income countries.
- The rapid implementation of universal health coverage in Thailand presents a unique opportunity to measure the impact of health insurance expansion and capitated payment on utilization of medicines.

### Key Messages

- Expanding health insurance coverage with a medicines benefit to the entire Thai population increased access to medicines in primary care.
- The universal coverage scheme did not seem to have increased use of medicines for diseases that are typically treated in secondary or tertiary care settings, or increased generic market penetration.
- In the future, it will be important for countries to assess quality and equity of medicines use as they pursue policies to achieve universal coverage.

### Strengths and Limitations

- We used an interrupted time series design, the strongest quasi-experimental approach for evaluating effects of interventions, increasing internal validity.
- It is impossible to examine population subgroups in national IMS Health market data, but we are reasonably confident that universal coverage scheme enrollees are responsible for observed changes.

## ABSTRACT

***Objective:*** In 2001, Thailand implemented the Universal Coverage Scheme (UCS), a public insurance system that aimed to achieve universal access to health care, including essential medicines, and to influence primary care centers and hospitals to use resources efficiently, via capitated payment for outpatient services and other payment policies for inpatient care. Our objective was to evaluate the impact of the UCS on utilization of medicines in Thailand for three non-communicable diseases: cancer, cardiovascular disease, and diabetes.

***Design:*** Interrupted time series design, with a non-equivalent comparison group.

***Setting:*** Thailand, 1998-2006.

***Data:*** Quarterly purchases of medicines from hospital and retail pharmacies collected by IMS Health between 1998 and 2006.

***Intervention:*** UCS implementation, April-October 2001.

***Outcome measures:*** Total pharmaceutical sales volume and percent market share by licensing status and National Essential Medicine List (NEML) status.

***Results:*** The UCS was associated with long-term increases in sales of medicines for conditions that are typically treated in outpatient primary care settings, such as diabetes, high cholesterol and high blood pressure, but not for medicines for diseases that are typically treated in secondary or tertiary care settings, such as heart failure, arrhythmias, and cancer. While the majority of increases in sales were for essential medicines, there were also post-policy increases in sales of non-essential medicines. Immediately following the reform, there was a significant shift in hospital sector market share by licensing status for most classes of medicines. Government-produced products often replaced branded generic or generic competitors.

***Conclusions:*** Our results suggest that expanding health insurance coverage with a medicines benefit to the entire Thai population increased access to medicines in primary care. However, our study also suggests that the UCS may have had potentially undesirable effects. Evaluations of the long-term impacts of universal health coverage on medicines utilization are urgently needed.

# MANUSCRIPT

## Introduction

### *Universal Health Coverage*

In 2005, Member States of the World Health Organization (WHO) made a commitment to work towards universal health care coverage.[1] The 2010 WHO World Health Report provides a roadmap for countries to achieve this goal.[2] Universal coverage requires the restructuring of health care and financing systems to improve access to health care services, reduce financial hardship, and increase the efficiency and equity of the health system.[2]

Medicines, which consume 25%–65% of total public and private spending on health in developing countries,[3] present a key challenge to achieving universal coverage. The high spending on, and inefficient use of, medicines threaten the financial sustainability of a universal coverage scheme. According to the WHO, three of the top ten sources of health care inefficiency involve medicines: high medicine prices and underuse of generics; use of substandard and counterfeit medicines; and inappropriate and ineffective use of medicines.[2] Health insurance systems have several features (e.g., a defined population, access to utilization data, and financial leverage) that give them a unique advantage to reduce out-of-pocket (OOP) expenditures and improve the cost-effective use of medicines through active management strategies involving medicines selection, purchasing, contracting (e.g., physician payment) and utilization management.[4] However, there is little evidence about the impact of health insurance on access to and use of medicines in low- and middle-income countries (LMICs).[4]

The recent implementation of universal health coverage in Thailand presents a unique opportunity to measure the impact of health insurance expansion and hospital payment changes (the majority of the population is now covered under a closed-ended payment scheme[5]) on utilization of medicines.

### *Universal Health Coverage in Thailand*

With the implementation of the UCS in 2001, Thailand became one of the first LMICs to achieve universal coverage.[6,7] The reform preserved the formal sector workforce schemes: the Social Health Insurance (SHI) scheme for private sector employees (7·2% of the total population in

2001) and the Civil Service Medical Benefit Scheme (CSMBS) for government employees and their dependents (8·5%).[8] The UCS covered those previously enrolled in a voluntary health card (VHC) scheme (20·8%), in private health insurance (2·1%), or in a tax-based, means-tested Low Income Scheme (LIS) for the poor, elderly, children and disabled (32·4%)[8,9] as well as more than one quarter (29·0%) of the population without previous insurance.[8] The UCS was rolled out to all provinces between April and October 2001.[6] By 2004, 95·5% of the population was insured, with three-quarters (75.2%) of the population covered by the UCS.[6]

In addition to coverage expansion, the reform also dramatically altered the mechanism for hospital payment. Before the reform, hospitals were accustomed to fee-for-service (FFS) payments from most insurance schemes, aside from SSI, and the uninsured, who paid OOP per service (i.e., user fees).[10] The majority of user fee spending was on medicines.[11] After the reform, FFS payment only applied to CSMBS patients and for the majority of patients, now UCS enrollees, hospitals were paid on a closed-ended basis[5] for all covered services, including medicines.

The UCS is a compulsory, tax-financed scheme with comprehensive coverage of inpatient and outpatient services, including medicines on the National List of Essential Medicines (NLEM).[6] Individuals must enroll in the scheme at a local Contracting Unit for Primary Care (CUP),[6] primarily housed in government-owned hospitals.[12] Each CUP receives a capitated payment per registered member to provide outpatient services and medicines.[6] CUPs initially served as gate-keepers for secondary and tertiary hospitals. At the beginning of the scheme, when patients were referred, diagnosis-related payments (DRG) for higher-level care had to come out of the CUP's capitated payment, so CUPs had a financial disincentive to refer patients.[6] Shortly after the reform was implemented, a separate fund (i.e., a global budget) for inpatient services was created, which likely reduced disincentives to refer created by the capitated payment scheme.[6] A capitated payment also creates financial incentives for use of lower cost medicines (e.g., generics or less expensive therapeutic alternatives).

Our objective was to evaluate the immediate, short-term (one year) and long-term (five year) impacts of the UCS on pharmaceutical market size and composition for medicines for three non-

communicable diseases (NCDs): cancer, cardiovascular disease, and diabetes. We hypothesized that the UCS would result in a gradual increase in sales volume, particularly of products used in primary care, as enrollment into the scheme increased and likely made access to health services and medicines more affordable for the majority of the population. We also hypothesized that there would be an immediate shift in market share from more expensive brand name to less expensive generic or branded generic products and to medicines on the NLEM in response to closed-ended budget rules. We focused on medicines for NCDs since these illnesses represent a large and growing health care burden in Thailand[13–16] and other LMICs[17] and most, but not all, medicines for NCDs would be prescribed and dispensed in primary care settings.

## Methods

### *Data*

We used data on quarterly pharmaceutical sales in Thailand from 1998 to 2006 provided by IMS Health.[18] The sales data are generated from reports to IMS Health by multinational pharmaceutical companies and surveys of purchases by hospital and retail pharmacies. IMS surveys approximately 200 hospitals (including general and specialized, public and private) and 350 retail pharmacies in Thailand. These facilities constitute a stratified random sample of the over 1,100 hospitals and 14,000 retail pharmacies in Thailand to enable national projections. Documentation on the IMS data collection and validation process is available upon request from the authors. Medicines were classified according to the European Pharmaceutical Research Association (EphMRA) Anatomical Therapeutic Chemical (ATC) system.[19]

### *Outcomes*

We used two outcome measures: total volume and percent market share. *Total volume* is the number of standard units purchased per capita per quarter (i.e., "sales"). We analyzed total volume by sector (i.e., retail versus hospital). A standard unit, as defined by IMS Health, is the smallest dose of a product, which equates to one tablet or capsule for an oral dosage form, one teaspoon (5ml) for a syrup, and one ampoule or vial for an injectable product. For the total volume analyses, we divided total volume by size of the population over 15 years old to control for population growth (using yearly population estimates from the World Bank[20]). We used the entire population as denominator for insulins, since they are also used for Type 1 diabetes, a chronic disease that affects children. *Percent market share* is the percent of total volume in four

mutually exclusive categories of licensing status: originator brand products, branded generic products (products sold under a brand name other than the originator brand name of the molecule), generic products (products that are sold under the generic molecule name), and products manufactured by Thailand's Government Pharmaceutical Organization (GPO). We also assessed percent market share by NLEM status (based on the 1999 and 2004 Thai NLEM).

We analyzed total volume and market share for medicines in eight therapeutic classes: two classes of diabetes products (oral antidiabetics and insulins), three classes of cardiovascular disease products (antihypertensives, lipid-regulating, and cardiac therapy products) and three classes of cancer products (antineoplastics, immunostimulating agents, and cytostatic hormone therapy products); Table 1 in the online appendix lists all medicines by ATC code. We assigned each therapeutic class to one of two categories: medicines usually used to treat primary care health conditions and medicines usually used to treat more complicated conditions, typically in secondary/tertiary, often inpatient care, settings. Antidiabetic, insulin, antihypertensive and lipid-lowering products are usually used for primary care conditions (i.e., diabetes, high blood pressure and high cholesterol), whereas cardiac therapy and cancer products are usually used for more severe conditions that more likely require treatment by a specialist and/or in an inpatient setting.

***Research Design***

We used an interrupted time series design, the strongest quasi-experimental approach for evaluating effects of interventions, which has been used extensively for medication use research.[21] Although we did not have an equivalent control group, we used medicines sold in the retail sector as a non-equivalent comparison group,[22] assuming that the retail market should be relatively unaffected by the reforms since UCS enrollees could only obtain covered medicines through their local, hospital-based CUP.

***Statistical Analysis***

The intervention was the UCS roll-out from April to October 2001. We defined three distinct periods: 12 quarters pre-reform (1998Q2-2001Q1), a 3-quarter UCS roll-out period (2001Q2-2001Q4; grey box in figures), and 19 quarters post-reform (2002Q1-2006Q3). We ended analysis

prior to 2006Q4 since there was a policy change at that time (the removal of an initial 30 Baht co-payment per visit) which may have impacted outcomes. In sensitivity analyses, we extended the intervention roll-out period through 2002 and through 2003 to account for potentially delayed implementation and lag of actual enrollment into the scheme.

We used segmented linear regression to measure the pre-reform trend, the immediate level change following the intervention period, and the post-reform change in trend (as compared to the pre-reform trend). For the NLEM analysis, we reclassified NLEM status in 2005Q1 (when the 2004 list was implemented) and included a pre-post term ("NLEM") in the model to account for possible discontinuity due to the reclassification. We report two estimates from the segmented regression models – the post-reform change in trend and the immediate level change following the reform. We controlled for serial autocorrelation using an autoregressive error model. We retained all terms in the models, even if non-significant. We used the models to estimate absolute and relative differences (with 95% confidence intervals)[23] in observed versus predicted total volume at one year and five years post-reform. In sensitivity analyses, we included a quadratic term for the post-reform trend and used a likelihood ratio test to determine the best-fitting model. We report below results from the best-fitting model of the shortest (i.e., 3 quarter) intervention period and mention differences in model results where they existed. Results from sensitivity analyses are available upon request. We used the AUTOREG procedure in SAS 9.3 for all analyses.

## Results

### *Hospital Sector Volume*

The majority of sales in Thailand for all cancer, cardiovascular disease and diabetes medicines studied were in the hospital sector and were for medicines on the NLEM. After implementation of the UCS, there was a significant increase in *level* of sales of insulins and a significant increase in *trend* in sales of antidiabetic, insulin, antihypertensive, lipid regulating, and cytostatic hormone products [Table 1, Figures 1 and 2]. There was a significant reduction in *level* of sales immediately following the reforms for three medication classes: antihypertensive, cardiac

therapy and immunostimulating agents (although only the latter was significant in the sensitivity analyses using a longer intervention period) [Table 1, Figures 1 and 2].

The UCS was associated with increased sales of diabetes medicines. One year after the policy, the sale of insulin was 35% (95% CI: 15%, 55%) higher and, at five years, 174% (95% CI: 114%-235%) higher than what would have been expected in the absence of the UCS [Table 2]. The increase in insulin sales was driven primarily by human insulins, which are on the NLEM and marketed as branded generics by two manufacturers. The policy was associated with a 39% (95% CI: 14%, 64%) increase in antidiabetic product sales five years after implementation [Table 2]. This was largely due to increased sales of generic and branded generic metformin and glibenclamide products, both of which are on the NLEM.

Implementation of the UCS appears to have had a mixed impact on sales of cardiovascular medicines. Five years after the policy, the sale of lipid lowering agents was nearly double (108% increase; 95% CI: 60%, 157%) what would have been expected in the absence of the scheme [Table 2]. The increase was primarily due to sales of branded generic simvastatin and gemfibrozil products, which are on the NLEM, and a small but steady increase in sales of originator atorvastatin products, which were not on the NLEM until 2004. For antihypertensives, the significant increase in post-policy trend compensated for an initial drop in sales, resulting in a slight increase in sales five years after the policy (19% increase; 95% CI: -3%, 40%). The increased trend was primarily due to sales of enalapril, atenolol, and amlodipine, all of which are on the NLEM and predominately sold as branded generics. The reform had no significant impact on sales of cardiac therapy medicines one or five years after the policy.

The results were also mixed for cancer medicines. The UCS had no significant one- or five-year impact on the sale of antineoplastics or cytostatic hormones (although the latter class did experience a significant post-policy increase in trend). However, the policy was associated with an immediate reduction in sales of immunostimulating agents that did not recover in the post-policy period. One year after implementation, the sale of immunostimulating agents was 35% (95% CI: -45%, -25%) lower than expected from pre-policy trends, and 26% lower (95% CI: -45%, -8%) five years post-policy. This drop is almost entirely due to a sharp reduction in sales of

interferon alfa-2b, a non-NLEM medicine, around the time of UCS implementation, which could have been due to a coincidental recall of an interferon alfa-2b product.[24]

Finally, as expected, the reform had little impact on sales volume in the retail sector – there were few significant post-implementation changes, and the changes that were significant were small in magnitude [see online appendix, Table 2].

***Hospital Sector Market Share***

Immediately following the reform, there were significant shifts in hospital sector market share by licensing status for most classes [Table 3]. The changes for antidiabetics and cardiac medicines - the two therapeutic classes with the largest shifts – were due to significant increases in GPO-produced medicines, primarily at the expense of branded generics and, to a lesser extent, generics. There was a significant increase in GPO antidiabetic products (+16% of market; 95% CI: 12%, 20%), and decreases in branded generic (-12%; 95% CI:-16%, -9%) and generic (-4%; 95% CI: -6%,-1%) products immediately after the policy [Figure 3]. Similarly, there was a significant increase in GPO cardiac therapy products (+22%; 95% CI: 15%, 28%), and significant decreases of branded generic (-14%; 95% CI:-21%, -7%) and generic (-4%; 95% CI:-6%, -2%) products immediately after the policy [Figure 4]. There was also a small decrease in market share of generic antihypertensives (-6%; 95% CI: -8%, -3%), which was compensated for by a marginally significant increase in GPO products.

The market for lipid regulating agents experienced an immediate shift from originator products (-8% market share; 95% CI:-10%, -5%) to branded generics (+8%; 95% CI:5%, 10%). A similar shift was seen for in the market for immunostimulating agents (6% decrease in originator products [95% CI:-10%, -3%] and a 5% increase in branded generics [95% CI:2%, 7%]). The cytostatic hormone market experienced an immediate shift from branded generic (-8%; 95% CI:-12%, -4%) to generic products (+6%, 95% CI: 1%, 11%). Generic insulins experienced a slight decrease in market share caused by the market exit of the sole generic manufacturer just prior to the policy. There were no immediate changes in market share for antineoplastics. Aside from the immediate level changes following the policy, there were few major changes in market share for all classes.

The UCS did not have a major impact on NLEM market share, likely because the share of NLEM medicines was already quite high [see online appendix Table 6 and Figure 17]. The only notable level change, for immunostimulating agents, was likely due to the coincidental recall of a non-NLEM interferon alfa-2b product.[24] While all medicine classes had significant post-reform trends, these trends were small in magnitude and NLEM market share remained fairly stable over the study period until the 2004 NLEM was introduced. There were large changes in NLEM market share for three classes – antihypertensives, lipid regulating agents and cytostatic hormones – at the time of the 2004 NLEM implementation in 2005Q1 [see online appendix Table 6 and Figure 17]. Given the increase in post-reform volume for many medicine classes, a stable NLEM market share in the short-term (i.e., pre-2005) following the UCS implementation suggests a post-reform increase in both NLEM and non-NLEM medicines.

## Discussion

The UCS was associated with long-term (i.e., 5 year) increases in hospital sector sales of medicines for chronic diseases that are usually treated in primary care settings, such as diabetes, high blood pressure, and high cholesterol. We hypothesized this gradual increase in volumes since the UCS expanded access to primary care[25] and actual enrollment into the scheme occurred gradually from implementation in 2001 until around 2004, by which time 95·5% of the population had insurance coverage.[6] The UCS, which radically changed hospital financing and reimbursement, was also associated with an immediate market shift to locally produced or branded generic products for most therapeutic classes.

Despite these increases in access, the policy did not appear to increase sales of medicines for more severe diseases like heart failure, arrhythmias, and cancer, which are often treated in secondary or tertiary settings. This finding is consistent with evidence that the capitated payment system initially discouraged referrals of UCS patients to higher-level care.[6,25,26] The UCS also appears to have had a mixed impact on utilization of essential medicines. There were increases in NLEM medicines, which are covered, as well as non-NLEM medicines. Similarly, given the capitated UCS payment system, we expected to see an increase in sales of generic medicines, which are typically less expensive. However, the majority of sales in most classes were for branded generic products, many of which had generic alternatives in the market. Interestingly,

substantial market share shifts occurred toward products manufactured by the Thai GPO, which have been noted to have higher than market prices.[27] By law, GPO products received preferential status by hospital purchasers,[28] which negates the incentive to prescribe cheaper alternatives under the capitated payment system. While the increase in GPO products and the UCS implementation may be a coincidence in timing, it is noteworthy that the GPO expanded its product line at a time when the UCS policy expanded the market of people who could afford medicines.

Our study demonstrates the value of IMS Health market intelligence data for rigorous health policy evaluation. Unlike other sources of data on pharmaceutical utilization (i.e., national health surveys or ad hoc hospital surveys), IMS data represent country pharmaceutical markets consistently over time and are useful for the evaluation of system-wide interventions. Nevertheless, the data pose some limitations. Aggregate national sales data do not allow us to determine whether observed increases in medicines sales occurred preferentially among UCS enrollees or enrollees in the SHI and CSMBS schemes, conceivably to compensate for financial strain of the UCS on hospital budgets.[6] CSMBS expenditures increased following UCS implementation[29] and increased medicines sales among CSMBS enrollees, reimbursed on a fee-for-service basis, could explain increases in non-NLEM medicines and medicines with less expensive therapeutic alternatives.[5] However, it is unlikely that increased utilization among CSMBS enrollees explains most of the observed volume changes since this would imply that one-half (for diabetes) to three-quarters (for hypertension) of CSMBS members (7.1% of the total population in 2004[6]) were on these treatments in 2004. Even the CSMBS and SSI schemes combined (20.3% of the total population in 2004[6]) are unlikely to be responsible for the observed changes since this would imply that one-quarter (for diabetes) and one-third (for hypertension) of enrollees in the two schemes were on these treatments in 2004. These estimates are much higher than the national prevalence (6.7% for diabetes[30] and 22.0% for hypertension[31] in 2004) and unlikely in the civil servant and private sector workforce populations, which are likely to be healthier and wealthier than the national average.

Our interpretation of the observed changes assumes that pharmaceutical sales to hospital and retail pharmacies reflected total market utilization, and that hospital sales volumes included

utilization at affiliated primary care units. This assumption seems justified in light of the estimated 91% accuracy of IMS Health data in representing the Thai pharmaceutical market.[32] For local generic products, including those produced by the GPO, IMS Health data are based on pharmacy surveys only (as opposed to pharmacy surveys and manufacturer reports), so we may have underestimated utilization. However, unless this systematic underestimation changed at the point of the UCS implementation, it would not have impacted our results. Finally, since we did not convert standard units of product sold to defined daily doses (DDD), we do not describe sales changes in terms of average adult doses.

There are also potential limitations due to study design and statistical analysis. We addressed the main threat to the internal validity of the interrupted time series design – a concurrent event that affects the outcome of interest – by assessing other policies or market events that occurred at the time of the UCS, through literature reviews, discussions with in-country experts, and by including the retail sector as a comparison. The statistical approach, segmented regression analysis, usually assumes a linear trend and well-defined break point. Sensitivity analyses that varied model specification and intervention duration did not change the findings. By reporting results from fully-specified models, we may have underestimated the statistical significance of one- and five-year change estimates.

While both the context and the implementation of universal coverage in Thailand are unique and not necessarily generalizable to other LMICs, our findings suggest that expanding health insurance coverage with a medicines benefit to the entire population, together with changes in the payment system and increased local manufacturing, increased the per capita volume of medicines sold and, by inference, improved access to medicines in the primary care sector in Thailand, presumably by making medicines more affordable. Since the study period, Thailand has enacted further policies to address pharmaceutical sector cost escalation (e.g., strict enforcement of reimbursement for only NLEM medicines in the CSMBS[33]) and to ensure appropriate access to non-NLEM medicines (e.g., coverage of medicines for HIV, renal replacement therapy, and mental health conditions).[34–36] In the future, it will be important for Thailand and other countries to assess equity in access to and quality of use of medicines,

availability of medicines in health centers and hospitals, out-of-pocket and system expenditures and affordability, and health outcomes as they pursue policies to achieve universal coverage.

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# TABLES

**Table 1. Summary of the Impact of the Universal Coverage Scheme on Volume in the Hospital Sector (from segmented regression results) ***

| Therapeutic Area | Pre-policy trend | Immediate change after policy | Post-policy trend change |
|---|---|---|---|
| | | | |
| **DIABETES** | | | |
| **Antidiabetics**** | ↑ | | ↑ |
| **Insulins**** | ↑ | ↑ | ↑ |
| | | | |
| **CARDIOVASCULAR DISEASE** | | | |
| **Antihypertensives** | ↑ | ↓ | ↑ |
| **Lipid Regulating Agents**** | ↑ | | ↑ |
| **Cardiac Therapy** | ↑ | ↓ | |
| | | | |
| **CANCER** | | | |
| **Antineoplastics** | ↑ | | |
| **Cytostatic Hormones** | ↑ | | ↑ |
| **Immunostimulating Agents**** | ↑ | ↓ | |

*Arrows signify a statistically significant coefficient ($p<0.05$) from segmented regression with linear post-policy trend term, unless noted otherwise.
**Quadratic model (which has a squared post-policy trend term) fits better than linear model.
Note: See online appendix Table 2 and Figures 1-8 for regression coefficients and figures for all therapeutic areas.

**Table 2. Relative Impact of UCS on Sales of Medicines by Class (one and five years post policy)***

| Therapeutic Class | One Year Impact (in standard units) | | | Five Year Impact (in standard units) | | |
|---|---|---|---|---|---|---|
| | Predicted | Observed | Relative Change (95% CI) | Predicted | Observed | Relative Change (95% CI) |
| **Antidiabetics** | 2602·91 | 2769·79 | 6·4% (-6·9, 19·7) | 3669·13 | 5090·62 | **38·7% (13·5, 64·0)** |
| **Insulins** | 3·30 | 4·45 | **34·8% (15·1, 54·5)** | 4·58 | 12·56 | **174·4% (113·9, 235·0)** |
| **Cardiac Therapy Agents** | 699·28 | 607·27 | -13·2% (-26·9, 0·6) | 908·12 | 825·49 | -9·1% (-31·9, 13·1) |
| **Lipid Regulating Agents** | 522·34 | 504·58 | -3·4% (-19·9, 13·1) | 781·97 | 1629·11 | **108·3% (59·8, 156·9)** |
| **Antihypertensives** | 3521·47 | 3418·79 | -2·9% (-15·5, 9·7) | 5200·86 | 6177·49 | 18·8% (-2·8, 40·3)** |
| **Antineoplastics** | 35·38 | 34·21 | -3·3% (-15·4, 8·7) | 46·14 | 48·13 | 4·3% (-16·3, 24·9) |
| **Cytostatic Hormones** | 29·48 | 30·58 | 3·7% (-10·1, 17·6) | 39·82 | 47·52 | 19·3% (-5·1, 43·8) |
| **Immunostimulating Agents** | 0·65 | 0·43 | **-35·0% (-45·1, -25·0)** | 0·81 | 0·60 | **-26·3% (-45·0, -7·6)** |

*Bold signifies that the change is statistically significant (i.e., confidence interval does not include the null value of 0).
**The *absolute* five-year difference, which is estimated using more precise method, is significant. See online appendix Table 3.

**Table 3. Immediate Impact of UCS on Hospital Sector Market Share***

| Therapeutic Area | Licensing Status | Immediate post-policy absolute change in % market share (95% CI) |
|---|---|---|
| **DIABETES** | | |
| **Antidiabetics** | Originator brand | -0·3% (-1·6, 1·0) |
| | Branded generic | **-12·3% (-16·0, -8·7)** |
| | Generic | **-3·5% (-5·8, -1·1)** |
| | GPO | **16·1% (12·0, 20·2)** |
| **Insulins*** ** | Originator brand** | -0·04% (-0·4, 0·3) |
| | Branded generic | **7·0% (2·9, 11·1)** |
| | Generic | **-6·2% (-10·3, -2·1)** |
| **CARDIOVASCULAR DISEASE** | | |
| **Antihypertensives** | Originator brand** | -0·1% (-2·3, 2·0) |
| | Branded generic** | -0·2% (-6·1, 1·8) |
| | Generic | **-5·7% (-8·3, -3·0)** |
| | GPO | 5·3% (-0·1, 10·6) |
| **Lipid Regulating Agents** | Originator brand** | **-7·8% (-10·2, -5·4)** |
| | Branded generic** | **7·6% (5·1, 10·0)** |
| | Generic | 0·2% (-0·4, 0·7) |
| | GPO | 0·2% (-0·3, 0·8) |
| **Cardiac Therapy** | Originator brand | 0·1% (-0·8, 1·0) |
| | Branded generic** | **-13·5% (-20·5, -6·5)** |
| | Generic | **-4·3% (-6·2, -2·4)** |
| | GPO | **21·6% (15·0, 28·1)** |
| **CANCER*** ** | | |
| **Antineoplastics** | Originator brand | 1·1% (-1·0, 3·2) |
| | Branded generic | -1·0% (-5·4, 3·4) |
| | Generic | 0·4% (-2·7, 3·4) |
| **Cytostatic Hormones** | Originator brand** | 0·4% (-5·4, 6·1) |
| | Branded generic** | **-7·7% (-12·0, -3·5)** |
| | Generic** | **6·0% (1·4, 10·6)** |
| **Immunostimulating Agents** | Originator brand | **-6·4% (-9·7, -3·0)** |
| | Branded generic | **4·5% (1·7, 7·3)** |
| | Generic | -0·2% (-0·3, 0·02) |

***Bold** signifies a statistically significant regression coefficient ($p<0.05$). Changes are in absolute terms (i.e., percentage point change).
**Quadratic model (which has a squared post-policy term) fits better than linear model.
***GPO did not produce any insulins or cancer medicines during the study period.
Note 1: See online appendix Table 4 and Figures 9-16 for market share regression coefficients and figures for all therapeutic areas
Note 2: Aside from the immediate level changes following the policy, there were few major changes in market share. See online appendix, Table 5 for absolute one- and five-year differences.

**Figure Index (attached in separate document):***

**Figure 1.** Standard Units Per Capita by Quarter: Insulin (Hospital vs. Retail)

**Figure 2.** Standard Units Per Capita by Quarter: Antihypertensives (Hospital vs. Retail)

**Figure 3.** Licensing Status Market Share by Quarter: Antidiabetics (Hospital Sector)

**Figure 4.** Licensing Status Market Share by Quarter: Cardiac Therapy Products (Hospital Sector)

*The grey box in each figure represents the 3-quarter UCS roll-out period.

**Online appendix (attached in separate document)**

**Appendix Table 1. List of Medicines by ATC**

| Therapeutic Area | Classification for Analysis | Molecule Name | ATC2 Classification | ATC4 Classification |
|---|---|---|---|---|
| **DIABETES** | | | | |
| | Antidiabetics | ACARBOSE | A10 (DRUGS USED IN DIABETES) | A10L0 (A-GLUCOSIDASE INH A-DIAB) |
| | Antidiabetics | BUFORMIN | A10 (DRUGS USED IN DIABETES) | A10J1 (BIGUANIDE A-DIABS PLAIN) |
| | Antidiabetics | CHLORPROPAMIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) |
| | Antidiabetics | EXENATIDE | A10 (DRUGS USED IN DIABETES) | A10S0 (GLP-1 AGONIST A-DIABS) |
| | Antidiabetics | GLIBENCLAMIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS ) |
| | Antidiabetics | GLIBENCLAMIDE#METFORMIN | A10 (DRUGS USED IN DIABETES) | A10J2 (BIGUANIDE & S-UREA COMBS) |
| | Antidiabetics | GLICLAZIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) |
| | Antidiabetics | GLICLAZIDE#METFORMIN | A10 (DRUGS USED IN DIABETES) | A10J2 (BIGUANIDE & S-UREA COMBS) |
| | Antidiabetics | GLIMEPIRIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) |
| | Antidiabetics | GLIMEPIRIDE#METFORMIN | A10 (DRUGS USED IN DIABETES) | A10J2 (BIGUANIDE & S-UREA COMBS) |
| | Antidiabetics | GLIMEPIRIDE#ROSIGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K2 (GLITAZONE & S-UREA COMBS) |
| | Antidiabetics | GLIPIZIDE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) |
| | Antidiabetics | GLIQUIDONE | A10 (DRUGS USED IN DIABETES) | A10H0 (SULPHONYLUREA A-DIABS) |
| | Antidiabetics | METFORMIN | A10 (DRUGS USED IN DIABETES) | A10J1 (BIGUANIDE A-DIABS PLAIN) |
| | Antidiabetics | METFORMIN#PIOGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K3 (GLITAZONE & BIGUAN COMBS) |
| | Antidiabetics | METFORMIN#ROSIGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K3 (GLITAZONE & BIGUAN COMBS) |
| | Antidiabetics | METFORMIN#SITAGLIPTIN | A10 (DRUGS USED IN DIABETES) | A10N3 (DPP-IV INH & BIGUAN COMB) |
| | Antidiabetics | METFORMIN#VILDAGLIPTIN | A10 (DRUGS USED IN DIABETES) | A10N3 (DPP-IV INH & BIGUAN COMB) |
| | Antidiabetics | PIOGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K1 (GLITAZONE A-DIABS PLAIN) |
| | Antidiabetics | REPAGLINIDE | A10 (DRUGS USED IN DIABETES) | A10M1 (GLINIDE A-DIABS PLAIN) |
| | Antidiabetics | ROSIGLITAZONE | A10 (DRUGS USED IN DIABETES) | A10K1 (GLITAZONE A-DIABS PLAIN) |
| | Antidiabetics | SITAGLIPTIN | A10 (DRUGS USED IN DIABETES) | A10N1 (DPP-IV INH A-DIAB PLAIN) |
| | Antidiabetics | VILDAGLIPTIN | A10 (DRUGS USED IN DIABETES) | A10N1 (DPP-IV INH A-DIAB PLAIN) |
| | Antidiabetics | VOGLIBOSE | A10 (DRUGS USED IN DIABETES) | A10L0 (A-GLUCOSIDASE INH A-DIAB) |
| | Insulins | INSULIN ASPART | A10 (DRUGS USED IN DIABETES) | A10C1 (H INSUL+ANG FAST ACT) |
| | Insulins | INSULIN ASPART#INSULIN ASPART PROTAMINE CRYSTALLINE | A10 (DRUGS USED IN DIABETES) | A10C3 (H INSUL+ANG INT+FAST ACT) |
| | Insulins | INSULIN DETEMIR | A10 (DRUGS USED IN DIABETES) | A10C5 (H INSUL+ANG LONG ACT) |
| | Insulins | INSULIN GLARGINE | A10 (DRUGS USED IN DIABETES) | A10C5 (H INSUL+ANG LONG ACT) |
| | Insulins | INSULIN HUMAN BASE | A10 (DRUGS USED IN DIABETES) | A10C1 (H INSUL+ANG FAST ACT) |
| | Insulins | INSULIN HUMAN BASE#INSULIN HUMAN ISOPHANE | A10 (DRUGS USED IN DIABETES) | A10C3 (H INSUL+ANG INT+FAST ACT) |
| | Insulins | INSULIN HUMAN ISOPHANE | A10 (DRUGS USED IN DIABETES) | A10C2 (H INSUL+ANG INTERMED ACT) |
| | Insulins | INSULIN HUMAN ZINC SUSPENSION (COMPOUND) | A10 (DRUGS USED IN DIABETES) | A10C4 (H INSUL+ANG INT+LONG ACT) |
| | Insulins | INSULIN HUMAN ZINC SUSPENSION (CRYSTALLINE) | A10 (DRUGS USED IN DIABETES) | A10C5 (H INSUL+ANG LONG ACT) |
| | Insulins | INSULIN LISPRO | A10 (DRUGS USED IN DIABETES) | A10C1 (H INSUL+ANG FAST ACT) |
| | Insulins | INSULIN LISPRO#INSULIN LISPRO PROTAMINE | A10 (DRUGS USED IN DIABETES) | A10C1 (H INSUL+ANG FAST ACT ) |
| | Insulins | INSULIN PORCINE BASE | A10 (DRUGS USED IN DIABETES) | A10D0 (ANIMAL INSULINS) |
| | Insulins | INSULIN PORCINE ISOPHANE | A10 (DRUGS USED IN DIABETES) | A10D0 (ANIMAL INSULINS) |
| | Insulins | INSULIN PORCINE ZINC SUSPENSION (COMPOUND) | A10 (DRUGS USED IN DIABETES) | A10D0 (ANIMAL INSULINS ) |
| | | | | |
| **CARIOVASCULAR DISEASE** | | | | |
| | Antihypertensives | AJMALICINE#BUTIZIDE#RESCINNAMINE#RESERPINE | C2 (ANTIHYPERTENSIVES) | C2D0 (RAUWOLF ALK+OTH COM+DIUR) |
| | Antihypertensives | BUNAZOSIN | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) |
| | Antihypertensives | CLONIDINE | C2 (ANTIHYPERTENSIVES) | C2A1 (ANTIHYPER.PL MAINLY CENT) |
| | Antihypertensives | CLOPAMIDE#DIHYDROERGOCRISTINE#RESERPINE | C2 (ANTIHYPERTENSIVES) | C2D0 (RAUWOLF ALK+OTH COM+DIUR) |
| | Antihypertensives | CLOPAMIDE#RESERPINE | C2 (ANTIHYPERTENSIVES) | C2D0 (RAUWOLF ALK+OTH COM+DIUR) |

| | | | | |
|---|---|---|---|---|
| | Antihypertensives | DIHYDRALAZINE | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) |
| | Antihypertensives | DOXAZOSIN | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) |
| | Antihypertensives | HYDRALAZINE | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) |
| | Antihypertensives | HYDRALAZINE#HYDROCHLOROTHIAZIDE#RESERPINE | C2 (ANTIHYPERTENSIVES) | C2B2 (A-HYPERT(N V)MAINLY PERI) |
| | Antihypertensives | KETANSERIN | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) |
| | Antihypertensives | METHYLDOPA | C2 (ANTIHYPERTENSIVES) | C2A1 (ANTIHYPER.PL MAINLY CENT) |
| | Antihypertensives | MINOXIDIL | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) |
| | Antihypertensives | NITROPRUSSIDE | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) |
| | Antihypertensives | PRAZOSIN | C2 (ANTIHYPERTENSIVES) | C2A2 (ANTIHYPER.PL MAINLY PERI) |
| | Antihypertensives | RESERPINE | C2 (ANTIHYPERTENSIVES) | C2C0 (RAUWLF ALK+OTH A-HY HERB) |
| | Antihypertensives | RILMENIDINE | C2 (ANTIHYPERTENSIVES) | C2A1 (ANTIHYPER.PL MAINLY CENT) |
| | Antihypertensives | 1-PROPANOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) |
| | Antihypertensives | AMILORIDE#HYDROCHLOROTHIAZIDE#TIMOLOL | C7 (BETA BLOCKING AGENTS) | C7B1 (B-BLOCK COMB HYPOT/DIURT) |
| | Antihypertensives | ATENOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) |
| | Antihypertensives | ATENOLOL#CHLORTALIDONE | C7 (BETA BLOCKING AGENTS) | C7B1 (B-BLOCK COMB HYPOT/DIURT) |
| | Antihypertensives | BETAXOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) |
| | Antihypertensives | BISOPROLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) |
| | Antihypertensives | BISOPROLOL#HYDROCHLOROTHIAZIDE | C7 (BETA BLOCKING AGENTS) | C7B1 (B-BLOCK COMB HYPOT/DIURT) |
| | Antihypertensives | CARVEDILOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) |
| | Antihypertensives | CLOPAMIDE#PINDOLOL | C7 (BETA BLOCKING AGENTS) | C7B1 (B-BLOCK COMB HYPOT/DIURT) |
| | Antihypertensives | LABETALOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) |
| | Antihypertensives | METOPROLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN) |
| | Antihypertensives | NEBIVOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN ) |
| | Antihypertensives | OXPRENOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN ) |
| | Antihypertensives | PINDOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN ) |
| | Antihypertensives | PROPRANOLOL | C7 (BETA BLOCKING AGENTS) | C7A0 (B-BLOCKING AGENTS,PLAIN ) |
| | Antihypertensives | SOTALOL | C7 (BETA BLOCKING AGENTS | C7A0 (B-BLOCKING AGENTS,PLAIN ) |
| | Antihypertensives | AMLODIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | ATENOLOL#NIFEDIPINE | C8 (CALCIUM ANTAGONISTS) | C8B2 (CALC ANTAG/B BLOCKR COMB) |
| | Antihypertensives | BARNIDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | DILTIAZEM | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | FELODIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | GALLOPAMIL | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | ISRADIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | LACIDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | LERCANIDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | MANIDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | MIBEFRADIL | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | NICARDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | NIFEDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | NISOLDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | NITRENDIPINE | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | VERAPAMIL | C8 (CALCIUM ANTAGONISTS) | C8A0 (CALCIUM ANTAGONIST PLAIN) |
| | Antihypertensives | AMILORIDE | C3 (DIURETICS) | C3A1 (POT SPARING AGENTS PLAIN) |
| | Antihypertensives | AMILORIDE#HYDROCHLOROTHIAZIDE | C3 (DIURETICS) | C3A5 (POT SPARING+THIAZ COMBS ) |
| | Antihypertensives | BAROSMA BETULINA#CAPSICUM#METHYLENE BLUE#URGINEA SCIL | C3 (DIURETICS) | C3A6 (OTHER DIURETICS) |
| | Antihypertensives | BAROSMA BETULINA#HYOSCYAMUS ALBUS#POTASSIUM | C3 (DIURETICS) | C3A6 (OTHER DIURETICS) |
| | Antihypertensives | BENDROFLUMETHIAZIDE#POTASSIUM | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) |
| | Antihypertensives | BUMETANIDE | C3 (DIURETICS) | C3A2 (LOOP DIURETICS PLAIN) |
| | Antihypertensives | FUROSEMIDE | C3 (DIURETICS) | C3A2 (LOOP DIURETICS PLAIN) |

| | | | | |
|---|---|---|---|---|
| | Antihypertensives | HYDROCHLOROTHIAZIDE | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#TRIAMTERENE | C3 (DIURETICS) | C3A5 (POT SPARING+THIAZ COMBS) |
| | Antihypertensives | INDAPAMIDE | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) |
| | Antihypertensives | SPIRONOLACTONE | C3 (DIURETICS) | C3A1 (POT SPARING AGENTS PLAIN) |
| | Antihypertensives | TORASEMIDE | C3 (DIURETICS) | C3A2 (LOOP DIURETICS PLAIN) |
| | Antihypertensives | TRIPAMIDE | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) |
| | Antihypertensives | XIPAMIDE | C3 (DIURETICS) | C3A3 (THIAZIDE+ANALOGUE PLAIN) |
| | Antihypertensives | ALISKIREN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9X0 (OTH RENIN-ANGIOTEN AGENT) |
| | Antihypertensives | ALISKIREN#HYDROCHLOROTHIAZIDE | C9 (RENIN-ANGIOTEN SYS AGENT) | C9X0 (OTH RENIN-ANGIOTEN AGENT) |
| | Antihypertensives | AMLODIPINE#VALSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D3 (AT2 ANTG COMB CALC ANTAG) |
| | Antihypertensives | CANDESARTAN CILEXETIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) |
| | Antihypertensives | CANDESARTAN CILEXETIL#HYDROCHLOROTHIAZIDE | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) |
| | Antihypertensives | CAPTOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) |
| | Antihypertensives | CILAZAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) |
| | Antihypertensives | DELAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) |
| | Antihypertensives | ENALAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) |
| | Antihypertensives | EPROSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) |
| | Antihypertensives | FOSINOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) |
| | Antihypertensives | FOSINOPRIL#HYDROCHLOROTHIAZIDE | C9 (RENIN-ANGIOTEN SYS AGENT) | C9B1 (ACE INH COMB+A-HYP/DIUR) |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#IRBESARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#LOSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#OLMESARTAN MEDOXOMIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#QUINAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9B1 (ACE INH COMB+A-HYP/DIUR) |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#RAMIPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9B1 (ACE INH COMB+A-HYP/DIUR) |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#TELMISARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) |
| | Antihypertensives | HYDROCHLOROTHIAZIDE#VALSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9D1 (AT2 ANTG COMB C2 &/O DIU) |
| | Antihypertensives | IMIDAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) |
| | Antihypertensives | INDAPAMIDE#PERINDOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9B1 (ACE INH COMB+A-HYP/DIUR) |
| | Antihypertensives | IRBESARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) |
| | Antihypertensives | LISINOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN ) |
| | Antihypertensives | LOSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) |
| | Antihypertensives | OLMESARTAN MEDOXOMIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) |
| | Antihypertensives | PERINDOPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN ) |
| | Antihypertensives | QUINAPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN ) |
| | Antihypertensives | RAMIPRIL | C9 (RENIN-ANGIOTEN SYS AGENT) | C9A0 (ACE INHIBITORS PLAIN) |
| | Antihypertensives | TELMISARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) |
| | Antihypertensives | VALSARTAN | C9 (RENIN-ANGIOTEN SYS AGENT) | C9C0 (ANGIOTEN-II ANTAG, PLAIN) |
| | Cardiac Therapy | ADENOSINE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | AMIODARONE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | AMRINONE | C1 (CARDIAC THERAPY) | C1F0 (POSITIVE INOTROPIC AGENT) |
| | Cardiac Therapy | CAFFEINE#ETAMIVAN | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) |
| | Cardiac Therapy | DIGITALIS PURPUREA | C1 (CARDIAC THERAPY) | C1A1 (CARDIAC GLYCOSIDES PLAIN) |
| | Cardiac Therapy | DIGITOXIN | C1 (CARDIAC THERAPY) | C1A1 (CARDIAC GLYCOSIDES PLAIN) |
| | Cardiac Therapy | DIGOXIN | C1 (CARDIAC THERAPY) | C1A1 (CARDIAC GLYCOSIDES PLAIN) |
| | Cardiac Therapy | DISOPYRAMIDE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | DOBUTAMINE | C1 (CARDIAC THERAPY) | C1C2 (CARDIAC DOPAMINERG AGENT) |
| | Cardiac Therapy | DOPAMINE | C1 (CARDIAC THERAPY) | C1C2 (CARDIAC DOPAMINERG AGENT) |
| | Cardiac Therapy | EPINEPHRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) |
| | Cardiac Therapy | ETAFEDRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) |
| | Cardiac Therapy | ETILEFRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) |

| | | | | |
|---|---|---|---|---|
| | Cardiac Therapy | FLECAINIDE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | GLYCINE MAX#UBIDECARENONE | C1 (CARDIAC THERAPY) | C1X0 (ALL OTHER CARDIAC PREPS) |
| | Cardiac Therapy | ISOPRENALINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) |
| | Cardiac Therapy | ISOSORBIDE DINITRATE | C1 (CARDIAC THERAPY) | C1E0 (NITRITES AND NITRATES) |
| | Cardiac Therapy | ISOSORBIDE MONONITRATE | C1 (CARDIAC THERAPY) | C1E0 (NITRITES AND NITRATES) |
| | Cardiac Therapy | IVABRADINE | C1 (CARDIAC THERAPY) | C1D0 (CORONRY THER EXC C AN+NI) |
| | Cardiac Therapy | LIDOCAINE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | MAGNESIUM#POTASSIUM#PROCAINE | C1 (CARDIAC THERAPY) | C1X0 (ALL OTHER CARDIAC PREPS) |
| | Cardiac Therapy | METARAMINOL | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) |
| | Cardiac Therapy | METILDIGOXIN | C1 (CARDIAC THERAPY) | C1A1 (CARDIAC GLYCOSIDES PLAIN) |
| | Cardiac Therapy | MEXILETINE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | MIDODRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) |
| | Cardiac Therapy | MILRINONE | C1 (CARDIAC THERAPY) | C1F0 (POSITIVE INOTROPIC AGENT) |
| | Cardiac Therapy | NITROGLYCERIN | C1 (CARDIAC THERAPY) | C1E0 (NITRITES AND NITRATES) |
| | Cardiac Therapy | NOREPINEPHRINE | C1 (CARDIAC THERAPY) | C1C1 (CARDIAC STM EX DOPAM AGT) |
| | Cardiac Therapy | OXYFEDRINE | C1 (CARDIAC THERAPY) | C1D0 (CORONRY THER EXC C AN+NI) |
| | Cardiac Therapy | PENTAERYTHRITYL TETRANITRATE | C1 (CARDIAC THERAPY) | C1E0 (NITRITES AND NITRATES) |
| | Cardiac Therapy | PROCAINAMIDE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | PROPAFENONE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | QUINIDINE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | TOCAINIDE | C1 (CARDIAC THERAPY) | C1B0 (ANTIARRHYTHMICS) |
| | Cardiac Therapy | TRIMETAZIDINE | C1 (CARDIAC THERAPY) | C1D0 (CORONRY THER EXC C AN+NI) |
| | Cardiac Therapy | UBIDECARENONE | C1 (CARDIAC THERAPY) | C1X0 (ALL OTHER CARDIAC PREPS) |
| | Cardiac Therapy | UBIQUINONE(S) | C1 (CARDIAC THERAPY) | C1X0 (ALL OTHER CARDIAC PREPS) |
| | Lipid Regulating | ACIPIMOX | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) |
| | Lipid Regulating | ALLIUM SATIVUM | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | ALLIUM SATIVUM#ARACHIS HYPOGAEA | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | ALLIUM SATIVUM#SOYA LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | AMLODIPINE#ATORVASTATIN | C11 (C.V. MULTITH. COMB PROD) | C11A1 (LIPREG.CV.MULT-TH.FX.COM) |
| | Lipid Regulating | ATORVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) |
| | Lipid Regulating | BEZAFIBRATE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A2 (FIBRATES) |
| | Lipid Regulating | CERIVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) |
| | Lipid Regulating | COLESTYRAMINE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A3 (ION-EXCHANGE RESINS) |
| | Lipid Regulating | DOCOSAHEXANOIC ACID#EICOSAPENTAENOIC ACID | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | DOCOSAHEXANOIC ACID#EICOSAPENTAENOIC ACID#VITAMIN E | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | EZETIMIBE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) |
| | Lipid Regulating | EZETIMIBE#SIMVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10C0 (LIP.REG.CO.W.OTH.LIP.REG) |
| | Lipid Regulating | FENOFIBRATE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A2 (FIBRATES) |
| | Lipid Regulating | FISH | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | FISH#SOYA LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | FLUVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED) ) |
| | Lipid Regulating | GEMFIBROZIL | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A2 (FIBRATES) |
| | Lipid Regulating | LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | LECITHIN#SOYA LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | NICOTINIC ACID | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) |
| | Lipid Regulating | PITAVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) |
| | Lipid Regulating | PRAVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) |
| | Lipid Regulating | PROBUCOL | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) |
| | Lipid Regulating | PYRICARBATE | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A9 (OTH.CHOLEST&TRIGLY.REGUL) |
| | Lipid Regulating | ROSUVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) |

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|---|---|---|---|---|
| | Lipid Regulating | SALMON | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | Lipid Regulating | SIMVASTATIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10A1 (STATINS (HMG-COA RED)) |
| | Lipid Regulating | SOYA LECITHIN | C10 (LIP.REG./ANTI-ATH. PREPS) | C10B0 (ANTI-ATHEROMA NATRL ORIG) |
| | | | | |
| **CANCER** | | | | |
| | Antineoplastics | ALEMTUZUMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) |
| | Antineoplastics | ALTRETAMINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | ASPARAGINASE | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) |
| | Antineoplastics | AZACITIDINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | BEVACIZUMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) |
| | Antineoplastics | BLEOMYCIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) |
| | Antineoplastics | BORTEZOMIB | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) |
| | Antineoplastics | BUSULFAN | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | CAPECITABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | CARBOPLATIN | L1 (ANTINEOPLASTICS) | L1X2 (PLATINUM COMPOUNDS) |
| | Antineoplastics | CARMUSTINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | CETUXIMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) |
| | Antineoplastics | CHLORAMBUCIL | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | CHLORMETHINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS ) |
| | Antineoplastics | CISPLATIN | L1 (ANTINEOPLASTICS) | L1X2 (PLATINUM COMPOUNDS) |
| | Antineoplastics | CLADRIBINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | CYCLOPHOSPHAMIDE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | CYTARABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | DACARBAZINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | DACTINOMYCIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) |
| | Antineoplastics | DASATINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) |
| | Antineoplastics | DECITABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | DOCETAXEL | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS ) |
| | Antineoplastics | DOXORUBICIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) |
| | Antineoplastics | EPIRUBICIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) |
| | Antineoplastics | ERLOTINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) |
| | Antineoplastics | ETOPOSIDE | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) |
| | Antineoplastics | FLUDARABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | FLUOROURACIL | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | GEFITINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) |
| | Antineoplastics | GEMCITABINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | HYDROXYCARBAMIDE | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) |
| | Antineoplastics | IBRITUMOMAB TIUXETAN | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) |
| | Antineoplastics | IDARUBICIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) |
| | Antineoplastics | IFOSFAMIDE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | IMATINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) |
| | Antineoplastics | IRINOTECAN | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) |
| | Antineoplastics | IXABEPILONE | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) |
| | Antineoplastics | LAPATINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) |
| | Antineoplastics | LOMUSTINE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | MELPHALAN | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | MERCAPTOPURINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | METHOTREXATE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | MITOMYCIN | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) |
| | Antineoplastics | MITOXANTRONE | L1 (ANTINEOPLASTICS) | L1D0 (ANTINEOPLAS. ANTIBIOTICS) |

| | | | | |
|---|---|---|---|---|
| | Antineoplastics | NILOTINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) |
| | Antineoplastics | OXALIPLATIN | L1 (ANTINEOPLASTICS) | L1X2 (PLATINUM COMPOUNDS) |
| | Antineoplastics | PACLITAXEL | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) |
| | Antineoplastics | PEMETREXED | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | PROCARBAZINE | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) |
| | Antineoplastics | RITUXIMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) |
| | Antineoplastics | SORAFENIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) |
| | Antineoplastics | SUNITINIB | L1 (ANTINEOPLASTICS) | L1X4 (A-NEO PROTEIN KINASE INH) |
| | Antineoplastics | TEGAFUR | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | TEGAFUR#URACIL | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | TEMOZOLOMIDE | L1 (ANTINEOPLASTICS) | L1A0 (ALKYLATING AGENTS) |
| | Antineoplastics | TIOGUANINE | L1 (ANTINEOPLASTICS) | L1B0 (ANTIMETABOLITES) |
| | Antineoplastics | TOPOTECAN | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) |
| | Antineoplastics | TRASTUZUMAB | L1 (ANTINEOPLASTICS) | L1X3 (ANTINEOPLASTIC MABS) |
| | Antineoplastics | TRETINOIN | L1 (ANTINEOPLASTICS) | L1X9 (ALL OTH. ANTINEOPLASTICS) |
| | Antineoplastics | VINBLASTINE | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) |
| | Antineoplastics | VINCRISTINE | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) |
| | Antineoplastics | VINORELBINE | L1 (ANTINEOPLASTICS) | L1C0 (VINCA ALKALOIDS) |
| | Cytostatic Hormones | AMINOGLUTETHIMIDE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) |
| | Cytostatic Hormones | ANASTROZOLE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) |
| | Cytostatic Hormones | BICALUTAMIDE | L2 (CYTOSTATIC HORMONE THER) | L2B2 (CYTO ANTI-ANDROGENS) |
| | Cytostatic Hormones | BUSERELIN | L2 (CYTOSTATIC HORMONE THER) | L2A3 (CYTO GONAD HORMON ANALOG) |
| | Cytostatic Hormones | CYPROTERONE | L2 (CYTOSTATIC HORMONE THER) | L2B2 (CYTO ANTI-ANDROGENS) |
| | Cytostatic Hormones | EXEMESTANE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) |
| | Cytostatic Hormones | FLUTAMIDE | L2 (CYTOSTATIC HORMONE THER) | L2B2 (CYTO ANTI-ANDROGENS) |
| | Cytostatic Hormones | FORMESTANE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) |
| | Cytostatic Hormones | FULVESTRANT | L2 (CYTOSTATIC HORMONE THER) | L2B9 (OTH CYTO HORMON ANTAGIST) |
| | Cytostatic Hormones | GOSERELIN | L2 (CYTOSTATIC HORMONE THER) | L2A3 (CYTO GONAD HORMON ANALOG) |
| | Cytostatic Hormones | LETROZOLE | L2 (CYTOSTATIC HORMONE THER) | L2B3 (CYTOSTAT AROMATASE INHIB) |
| | Cytostatic Hormones | LEUPRORELIN | L2 (CYTOSTATIC HORMONE THER) | L2A3 (CYTO GONAD HORMON ANALOG) |
| | Cytostatic Hormones | MEDROXYPROGESTERONE | L2 (CYTOSTATIC HORMONE THER) | L2A2 (CYTOSTATIC PROGESTOGENS ) |
| | Cytostatic Hormones | MEGESTROL | L2 (CYTOSTATIC HORMONE THER) | L2A2 (CYTOSTATIC PROGESTOGENS ) |
| | Cytostatic Hormones | TAMOXIFEN | L2 (CYTOSTATIC HORMONE THER) | L2B1 (CYTO ANTI-OESTROGENS) |
| | Cytostatic Hormones | TOREMIFENE | L2 (CYTOSTATIC HORMONE THER) | L2B1 (CYTO ANTI-OESTROGENS) |
| | Cytostatic Hormones | TRIPTORELIN | L2 (CYTOSTATIC HORMONE THER) | L2A3 (CYTO GONAD HORMON ANALOG) |
| | Immunostimulating Agents | FILGRASTIM | L3 (IMMUNOSTIMULATING AGENTS) | L3A1 (COLONY-STIMULATING FACT.) |
| | Immunostimulating Agents | INTERFERON ALFA | L3 (IMMUNOSTIMULATING AGENTS) | L3B1 (INTERFERONS ALPHA) |
| | Immunostimulating Agents | INTERFERON ALFA-2A | L3 (IMMUNOSTIMULATING AGENTS) | L3B1 (INTERFERONS ALPHA) |
| | Immunostimulating Agents | INTERFERON ALFA-2B | L3 (IMMUNOSTIMULATING AGENTS) | L3B1 (INTERFERONS ALPHA) |
| | Immunostimulating Agents | INTERFERON ALFA-N1 | L3 (IMMUNOSTIMULATING AGENTS) | L3B1 (INTERFERONS ALPHA) |
| | Immunostimulating Agents | INTERFERON BETA-1A | L3 (IMMUNOSTIMULATING AGENTS) | L3B2 (INTERFERONS BETA) |
| | Immunostimulating Agents | INTERFERON BETA-1B | L3 (IMMUNOSTIMULATING AGENTS) | L3B2 (INTERFERONS BETA) |
| | Immunostimulating Agents | LENOGRASTIM | L3 (IMMUNOSTIMULATING AGENTS) | L3A1 (COLONY-STIMULATING FACT.) |
| | Immunostimulating Agents | MOLGRAMOSTIM | L3 (IMMUNOSTIMULATING AGENTS) | L3A1 (COLONY-STIMULATING FACT.) |
| | Immunostimulating Agents | PEGFILGRASTIM | L3 (IMMUNOSTIMULATING AGENTS) | L3A1 (COLONY-STIMULATING FACT.) |
| | Immunostimulating Agents | TETRACHLORODECAOXIDE | L3 (IMMUNOSTIMULATING AGENTS) | L3A9 (OTH.IMMUNOSTIM.EX.INTFRN) |
| | Immunostimulating Agents | THYMALFASIN | L3 (IMMUNOSTIMULATING AGENTS) | L3A9 (OTH.IMMUNOSTIM.EX.INTFRN) |

# STROBE Checklist: Impact of Universal Health Coverage in Thailand on Sales and Market Share of Medicines for Non-Communicable Diseases

STROBE Statement—checklist of items that should be included in reports of observational studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1✓ | (*a*) Indicate the study's design with a commonly used term in the title or the abstract |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** | | |
| Background/rationale | 2✓ | Explain the scientific background and rationale for the investigation being reported |
| Objectives | 3✓ | State specific objectives, including any prespecified hypotheses |
| **Methods** | | |
| Study design | 4✓ | Present key elements of study design early in the paper<br>**NOTE: We use an interrupted time series design, which is a robust longitudinal observational design.** |
| Setting | 5✓ | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants | 6 ✓ | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case<br>**NOTE: We explain the data source and methods of selection (i.e., hospital vs. pharmacy sales data – the latter serves as a non-equivalent comparison group) and give the rationale for the choice of therapeutic classes and date range.** |
| Variables | 7✓ | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/ measurement | 8*✓ | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias | 9✓ | Describe any efforts to address potential sources of bias |
| Study size | 10✓ | Explain how the study size was arrived at |
| Quantitative variables | 11✓ | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods | 12✓ | (*a*) Describe all statistical methods, including those used to control for confounding |
| | | (*b*) Describe any methods used to examine subgroups and interactions |
| | | (*c*) Explain how missing data were addressed |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed |

| | |
|---|---|
| | *Case-control study*—If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy |
| | (*e*) Describe any sensitivity analyses |

Continued on next page

| | | |
|---|---|---|
| **Results** | | |
| Participants | 13*NA | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| | | (b) Give reasons for non-participation at each stage |
| | | (c) Consider use of a flow diagram |
| Descriptive data | 14*✓ | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount)<br>**NOTE: We give the characteristics of the therapeutic classes (i.e., number subclasses, medicines within each subclass).** |
| Outcome data | 15*✓ | *Cohort study*—Report numbers of outcome events or summary measures over time |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures<br>**NOTE: We report numbers of outcome events over time.** |
| Main results | 16✓ | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (*b*) Report category boundaries when continuous variables were categorized |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Other analyses | 17✓ | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | | |
| Key results | 18✓ | Summarise key results with reference to study objectives |
| Limitations | 19✓ | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Interpretation | 20✓ | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalisability | 21✓ | Discuss the generalisability (external validity) of the study results |
| **Other information** | | |
| Funding | 22✓ | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

# TITLE PAGE

## Impact of Universal Health Insurance Coverage in Thailand on Sales and Market Share of Medicines for Non-Communicable Diseases: an Interrupted Time Series Study

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**Study Design:** Observational study (interrupted time series design)

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**Author contributions:** Laura Garabedian, Dennis Ross-Degnan and Anita Wagner designed the study and developed the analytic approach. Peter Stephens assembled the data files. Laura Garabedian analyzed the data. Sauwakon Ratanawijitrasin provided the Thai national list of essential medicines and information on relevant Thai policies and context surrounding the

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reform. All authors participated in the interpretation of the results. -Laura Garabedian wrote the first draft of the paper. All authors contributed to the writing of the manuscript.

Opinions expressed are solely those of the authors and not of the institutions they represent.

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**Data Sharing Statement:** Data available upon request, at the approval of IMS Institute for Healthcare Informatics.

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## Article Summary

### Article Focus

- Medicines present a key challenge to achieving universal coverage.
- Health insurance systems have the potential to improve cost-effective use of medicines, yet there is little evidence about their impact on medicine use in low- and middle-income countries.
- The ~~recent~~rapid implementation of universal health coverage in Thailand presents a unique opportunity to measure the impact of health insurance expansion and ~~associated physician~~capitated payment ~~changes~~ on utilization of medicines.

### Key Messages

- Expanding health insurance coverage with a medicines benefit to the entire Thai population increased access to medicines in primary care.
- The universal coverage scheme did not seem to have increased use of medicines for diseases that are typically treated in secondary or tertiary care settings, or increased generic market penetration.
- In the future, it will be important for countries to assess quality and equity of medicines use as they pursue policies to achieve universal coverage.

### Strengths and Limitations

- We used an interrupted time series design, the strongest quasi-experimental approach for evaluating effects of interventions, increasing internal validity.
- It is impossible to examine population subgroups in national IMS Health market data, but we are reasonably confident that universal coverage scheme enrollees are responsible for observed changes.

## ABSTRACT

***Objective:*** In 2001, Thailand implemented the Universal Coverage Scheme (UCS), a public insurance system ~~covering primarily the poor and uninsured~~ that aimed to achieve universal access to health care, including essential medicines, and to influence ~~provider behavior~~primary care centers and hospitals to use resources efficiently, via capitated payment for outpatient services and other payment policies for inpatient care. Our objective was to evaluate the impact of the UCS on utilization of medicines in Thailand for three non-communicable diseases: cancer, cardiovascular disease, and diabetes.

***Design:*** Interrupted time series design, with a non-equivalent comparison group.

***Setting:*** Thailand, 1998-2006.

***Data:*** Quarterly purchases of medicines from hospital and retail pharmacies collected by IMS Health between 1998 and 2006.

***Intervention:*** UCS implementation, April-October 2001.

***Outcome measures:*** Total pharmaceutical sales volume and percent market share by licensing status- and National Essential Medicine List (NEML) status.

***Results:*** The UCS was associated with long-term increases in sales of medicines for conditions that are typically treated in outpatient primary care settings, such as diabetes, high cholesterol and high blood pressure, but not for medicines for diseases that are typically treated in secondary or tertiary care settings, such as heart failure, arrhythmias, and cancer. While the majority of increases in sales were for essential medicines, there were also ~~significant~~ post-policy increases in sales of non-essential medicines. Immediately following the reform, there was a significant shift in hospital sector market share by licensing status for most classes of medicines. Government-produced products often replaced branded generic or generic competitors.

***Conclusions:*** Our results suggest that expanding health insurance coverage with a medicines benefit to the entire Thai population increased access to medicines in primary care. However, our study also suggests that the UCS may have had potentially undesirable effects. Evaluations of the long-term impacts of universal health coverage on medicines utilization are urgently needed.


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## Introduction

### *Universal Health Coverage*

In 2005, Member States of the World Health Organization (WHO) made a commitment to work towards universal health care coverage.[1] The 2010 WHO World Health Report provides a roadmap for countries to achieve this goal.[2] Universal coverage requires the restructuring of health care and financing systems to improve access to health care services, reduce financial hardship, and increase the efficiency and equity of the health system.[2]

Medicines, which consume 25–%–65% of total public and private spending on health in developing countries,[3] present a key challenge to achieving universal coverage. The high spending on, and inefficient use of, medicines threaten the financial sustainability of a universal coverage scheme. According to the WHO, three of the top ten sources of health care inefficiency involve medicines: high medicine prices and underuse of generics; use of substandard and counterfeit medicines; and inappropriate and ineffective use of medicines.[2] Health insurance systems have several features (e.g., a defined population, access to utilization data, and financial leverage) that give them a unique advantage to reduce out-of-pocket (OOP) expenditures and improve the cost-effective use of medicines through active management strategies involving medicines selection, purchasing, contracting (e.g., physician payment) and utilization management.[4] However, there is little evidence about the impact of health insurance on access to and use of medicines in low- and middle-income countries (LMICs).[4]

The recent implementation of universal health coverage in Thailand presents a unique opportunity to measure the impact of health insurance expansion and ~~physician~~hospital payment changes (~~from fee-for-service to capitation~~the majority of the population is now covered under a closed-ended payment scheme[5]) on utilization of medicines.

### *Universal Health Coverage in Thailand*

With the implementation of the UCS in 2001, Thailand became one of the first LMICs to achieve universal coverage.[5,6,7] The ~~reforms~~reform preserved the formal sector workforce schemes: the

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Social Health Insurance (SHI) scheme for private sector employees (~~6·3~~7·2% of the total population in 2001) and the Civil Service Medical Benefit Scheme (CSMBS) for government employees and their dependents (~~13·6%).[7] In addition, the~~8·5%).[8] The UCS covered those previously enrolled in a voluntary health card (VHC) scheme (~~22·0~~20·8%), in private health insurance (2·1~~·6~~%), or in a tax-based, means-tested Low Income Scheme (LIS) for the poor, elderly, children and disabled (~~28·~~32·4%)[8,9]~~%)~~[7,8] as well as more than one quarter (~~26·6~~29·0%) of the population without previous insurance.[7,8] The UCS was rolled out to all provinces between April and October 2001.[5,6] By ~~2005~~2004, 95·5% of the population was insured, with ~~just over 70%~~three-quarters (75.2%) of the population covered by the UCS.[7,6]

In addition to coverage expansion, the reform also dramatically altered the mechanism for hospital payment. Before the reform, hospitals were accustomed to fee-for-service (FFS) payments from most insurance schemes, aside from SSI, and the uninsured, who paid OOP per service (i.e., user fees).[10] The majority of user fee spending was on medicines.[11] After the reform, FFS payment only applied to CSMBS patients and for the majority of patients, now UCS enrollees, hospitals were paid on a closed-ended basis[5] for all covered services, including medicines.

The UCS is a compulsory, tax-financed scheme with comprehensive coverage of inpatient and outpatient services, including medicines on the National List of Essential Medicines (NLEM).[5,6] Individuals must enroll in the scheme at a local Contracting Unit for Primary Care (CUP),[5,6] primarily housed in government-owned hospitals.[9,12] Each CUP receives a capitated payment per registered member to provide outpatient services and medicines.[5,6] CUPs initially served as gate-keepers for secondary and tertiary hospitals. ~~When~~ At the beginning of the scheme, when patients were referred, diagnosis-related payments (DRG) for higher-level care ~~initially came~~had to come out of the CUP's capitated payment, so CUPs had a financial disincentive to refer patients.[5,6] Shortly after the reform was implemented, a separate fund (i.e., a global budget) for inpatient services was created, which likely reduced disincentives to refer created by the capitated payment scheme.[6] A capitated payment also creates financial incentives for use of lower cost medicines (e.g., generics or less expensive therapeutic alternatives).

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Our objective was to evaluate the immediate, short-term (one year) and long-term (five year) impacts of the UCS on pharmaceutical market size and composition for medicines for three non-communicable diseases (NCDs): cancer, cardiovascular disease, and diabetes. We hypothesized that the UCS would result in a gradual increase in sales volume, particularly of products used in primary care, as enrollment into the ~~Scheme~~scheme increased~~,~~ and ~~in~~likely made access to health services and medicines more affordable for the majority of the population. We also hypothesized that there would be an immediate ~~increase~~shift in market share ~~of~~from more expensive brand name to less expensive generic or branded generic products and to medicines on the NLEM in response to ~~capitated payment~~closed-ended budget rules. We focused on medicines for NCDs since these illnesses represent a large and growing health care burden in ~~Thailand~~[10–13]Thailand[13–16] and other ~~LMICs~~[14]LMICs[17] and most, but not all, medicines for NCDs would be prescribed and dispensed in primary care settings.

## Methods

### *Data*

We used data on quarterly pharmaceutical sales in Thailand from 1998 to 2006 provided by IMS Health.[15–18] The sales data are generated from reports to IMS Health by multinational pharmaceutical companies and surveys of purchases by hospital and retail pharmacies. IMS surveys approximately 200 hospitals (including general and specialized, public and private) and 350 retail pharmacies in Thailand~~, and employs~~. These facilities constitute a stratified random sample of ~~these facilities that enables~~the over 1,100 hospitals and 14,000 retail pharmacies in Thailand to enable national projections. Documentation on the IMS data collection and validation process is available upon request from the authors. Medicines were classified according to the European Pharmaceutical Research Association (EphMRA) Anatomical Therapeutic Chemical (ATC) system.[16–19]

### *Outcomes*

We used two outcome measures: total volume and percent market share. *Total volume* is the number of standard units purchased per capita per quarter (i.e., "sales"). We analyzed total volume by sector (i.e., retail versus hospital~~) and, within the hospital sector, by NLEM versus non-NLEM status of medicines (based on the 1999 Thai NLEM).~~). A standard unit, as defined by IMS Health, is the smallest dose of a product, which equates to one tablet or capsule for an oral

dosage form, one teaspoon (5ml) for a syrup, and one ampoule or vial for an injectable product. ~~We~~For the total volume analyses, we divided total volume by size of the population over 15 years old to control for population growth (using yearly population estimates from the World ~~Bank[17]~~Bank[20]). We used the entire population as denominator for insulins, since they are also used for Type 1 diabetes, a chronic disease that affects children. *Percent market share* is the percent of total volume in four mutually exclusive categories of licensing status: originator brand products, branded generic products (products sold under a brand name other than the originator brand name of the molecule), generic products (products that are sold under the generic molecule name), and products manufactured by Thailand's Government Pharmaceutical Organization (GPO). We also assessed percent market share by NLEM status (based on the 1999 and 2004 Thai NLEM).

We analyzed total volume and market share for medicines in eight therapeutic classes: two classes of diabetes products (oral antidiabetics and insulins), three classes of cardiovascular disease products (antihypertensives, lipid-regulating, and cardiac therapy products) and three classes of cancer products (antineoplastics, immunostimulating agents, and cytostatic hormone therapy products); Table 1 in the online appendix lists all medicines by ATC code. We assigned each therapeutic class to one of two categories: medicines usually used to treat primary care health conditions and medicines usually used to treat more complicated conditions, typically in secondary/tertiary, often inpatient care, settings. Antidiabetic, insulin, antihypertensive and lipid-lowering products are usually used for ~~conditions that are typically treated in~~ primary care ~~settings~~conditions (i.e., diabetes, high blood pressure and high cholesterol), whereas cardiac therapy and cancer products are usually used for more severe conditions that ~~are~~ more likely ~~to be treated~~require treatment by a specialist and/or in an inpatient ~~settings.~~setting.

***Research Design***

We used an interrupted time series design, the strongest quasi-experimental approach for evaluating effects of interventions, which has been used extensively for medication use research.[~~18~~21] Although we did not have an equivalent control group, we used medicines sold in the retail sector as a non-equivalent comparison group,[~~19~~22] assuming that the retail market should

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be relatively unaffected by the reforms since UCS enrollees could only obtain covered medicines through their local, hospital-based CUP.

***Statistical Analysis***

The intervention was the UCS roll-out from April to October 2001. We defined three distinct periods: 12 quarters pre-reform (1998Q2-2001Q1), a 3-quarter UCS roll-out period (2001Q2-2001Q4; grey box in figures), and 19 quarters post-reform (2002Q1-2006Q3). We ~~dropped 2006Q4 from the~~ended analysis prior to 2006Q4 since there was a policy change at ~~this~~that time (the removal of an initial 30 Baht co-payment per visit) ~~that~~which may have impacted outcomes. In sensitivity analyses, we extended the intervention roll-out period through 2002 and through 2003 to account for potentially delayed implementation and lag of actual enrollment into the scheme.

We used segmented linear regression to measure the pre-reform trend, the immediate level change following the intervention period, and the post-reform change in trend (as compared to the pre-reform trend). For the NLEM analysis, we reclassified NLEM status in 2005Q1 (when the 2004 list was implemented) and included a pre-post term ("NLEM") in the model to account for possible discontinuity due to the reclassification. We report two estimates from the segmented regression models – the post-reform change in trend and the immediate level change following the reform. We controlled for serial autocorrelation using an autoregressive error model. We retained all terms in the models, even if non-significant. We used the models to estimate absolute and relative differences (with 95% confidence intervals)[~~20~~23] in observed versus predicted total volume at one year and five years post-reform. In sensitivity analyses, we included a quadratic term for the post-reform trend and used a likelihood ratio test to determine the best-fitting model. We report below results from the best-fitting model of the shortest (i.e., 3 quarter) intervention period and mention differences in model results where they existed. Results from sensitivity analyses are available upon request. We used the AUTOREG procedure in SAS 9.~~2~~3 for all analyses.

**Results**

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***Hospital Sector Volume***

The majority of sales in Thailand for all cancer, cardiovascular disease and diabetes medicines studied were in the hospital sector and were for medicines on the NLEM. After implementation of the UCS, there was a significant increase in *level* of sales of insulins and a significant increase in *trend* in sales of antidiabetic, insulin, antihypertensive, lipid regulating, and cytostatic hormone products [Table 1, Figures 1 and 2]. There was a significant reduction in *level* of sales immediately following the reforms for three medication classes: antihypertensive, cardiac therapy and immunostimulating agents (although only the latter was significant in the sensitivity analyses using a longer intervention period~~).~~ ) [Table 1, Figures 1 and 2].

The UCS was associated with increased sales of diabetes medicines. One year after the policy, the sale of insulin was 35% (95% CI: 15%, 55%) higher and, at five years, 174% (95% CI: 114%-235%) higher than what would have been expected in the absence of the UCS [Table 2]. The increase in insulin sales was driven primarily by human insulins, which are on the NLEM and marketed as branded generics by two manufacturers. The policy was associated with a 39% (95% CI: 14%, 64%) increase in antidiabetic product sales five years after implementation [Table 2]. This ~~is~~was largely due to increased sales of generic and branded generic metformin and glibenclamide products, both of which are on the NLEM.

Implementation of the UCS appears to have had a mixed impact on sales of cardiovascular medicines. Five years after the policy, the sale of lipid lowering agents was nearly double (108% increase; 95% CI: 60%, 157%) what would have been expected in the absence of the scheme [Table 2]. The increase was primarily due to sales of branded generic simvastatin and gemfibrozil products, which are on the NLEM, and a small but steady increase in sales of originator atorvastatin products, which ~~are~~were not on the NLEM until 2004. For antihypertensives, the significant increase in post-policy trend compensated for an initial drop in sales, resulting in a slight increase in sales five years after the policy (19% increase; 95% CI: -3%, 40%). The increased trend was primarily due to sales of enalapril, atenolol, and amlodipine, all of which are on the NLEM and predominately sold as branded generics. The reform had no significant impact on sales of cardiac therapy medicines one or five years after the policy.

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The results were also mixed for cancer medicines. The UCS had no significant one- or five-year impact on the sale of antineoplastics or cytostatic hormones (although the latter class did experience a significant post-policy increase in trend). However, the policy was associated with an immediate reduction in sales of immunostimulating agents that did not recover in the post-policy period. One year after implementation, the sale of immunostimulating agents was 35% (95% CI: -45%, -25%) lower than expected from pre-policy trends, and 26% lower (95% CI: -45%, -8%) five years post-policy. This drop is almost entirely due to a sharp reduction in sales of interferon alfa-2b, a non-NLEM medicine, around the time of UCS implementation, which could have been due to a ~~co-incidental~~coincidental recall of an interferon alfa-2b product.[~~21~~ 24]

~~There was mixed evidence about the effects of the UCS on utilization of NLEM medicines. For all classes that experienced a post-policy increase in trend, there was an increase in sales of both NLEM medicines (except for cytostatic hormones) *and* non-NLEM products [see online appendix, Table 3]. The immediate decrease in sales of cardiac therapies and immunostimulating agents was largely due to a decrease in non-NLEM medicines. However, for these two classes, there was no corresponding increase in NLEM medicines.~~

Finally, as expected, the reform had little impact on sales volume in the retail sector – there were few significant post-implementation changes, and the changes that were significant were small in magnitude [see online appendix, Table 2].

***Hospital Sector Market Share***

Immediately following the reform, there were significant shifts in hospital sector market share by licensing status for most classes [Table 3]. The changes for antidiabetics and cardiac medicines - the two therapeutic classes with the largest shifts – were due to significant increases in GPO-produced medicines, primarily at the expense of branded generics and, to a lesser extent, generics. There was a significant increase in GPO antidiabetic products (+16% of market; 95% CI: 12%, 20%), and decreases in branded generic (-12%; 95% CI:-16%, -9%) and generic (-4%; 95% CI: -6%,-1%) products immediately after the policy [Figure 3]. Similarly, there was a significant increase in GPO cardiac therapy products (+22%; 95% CI: 15%, 28%), and significant decreases of branded generic (-14%; 95% CI:-21%, -7%) and generic (-4%; 95% CI:-

6%, -2%) products immediately after the policy [Figure 4]. There was also a small decrease in market share of generic antihypertensives (-6%; 95% CI: -8%, -3%), which was compensated for by a marginally significant increase in GPO products.

The market for lipid regulating agents experienced an immediate shift from originator products (-8% market share; 95% CI: -10%, -5%) to branded generics (+8%; 95% CI:-5%, 10%). A similar shift was seen for in the market for immunostimulating agents (6% decrease in originator products [95% CI:-10%, -3%] and a 5% increase in branded generics [95% CI:2%, 7%]). The cytostatic hormone market experienced an immediate shift from branded generic (-8%; 95% CI:-12%, -4%) to generic products (+6%, 95% CI: 1%, 11%). Generic insulins experienced a slight decrease in market share caused by the market exit of the sole generic manufacturer just prior to the policy. There were no immediate changes in market share for antineoplastics. Aside from the immediate level changes following the policy, there were few major changes in market share for all classes.

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The UCS did not have a major impact on NLEM market share, likely because the share of NLEM medicines was already quite high [see online appendix Table 6 and Figure 17]. The only notable level change, for immunostimulating agents, was likely due to the coincidental recall of a non-NLEM interferon alfa-2b product.[24] While all medicine classes had significant post-reform trends, these trends were small in magnitude and NLEM market share remained fairly stable over the study period until the 2004 NLEM was introduced. There were large changes in NLEM market share for three classes – antihypertensives, lipid regulating agents and cytostatic hormones – at the time of the 2004 NLEM implementation in 2005Q1 [see online appendix Table 6 and Figure 17]. Given the increase in post-reform volume for many medicine classes, a stable NLEM market share in the short-term (i.e., pre-2005) following the UCS implementation suggests a post-reform increase in both NLEM and non-NLEM medicines.

## Discussion

The UCS was associated with long-term (i.e., 5 year) increases in hospital sector sales of medicines for chronic diseases that are usually treated in primary care settings, such as diabetes, high blood pressure, and high cholesterol. We hypothesized this gradual increase in ~~volume~~volumes since the UCS expanded access to primary ~~care~~[7]care[25] and actual enrollment into

the scheme occurred gradually from implementation in 2001 until around ~~2005~~2004, by which time 95·5% of the population had insurance coverage.[~~7~~6] The UCS, which radically changed hospital financing and reimbursement, was also associated with an immediate market shift to locally produced or branded generic products for most therapeutic classes.

Despite these increases in access, the policy did not appear to increase sales of medicines for more severe diseases like heart failure, arrhythmias, and cancer, which are often treated in secondary or tertiary settings. This finding is ~~in line~~consistent with evidence that the capitated payment system initially discouraged referrals of UCS patients to higher-level care.[~~5,7,22~~6,25,26] The UCS also appears to have had a mixed impact on utilization of essential medicines. There were increases in NLEM medicines, which are covered, as well as non-NLEM medicines. Similarly, given the capitated UCS payment system, we expected to see an increase in sales of generic medicines, which are typically less expensive. However, the majority of sales in most classes were for branded generic products, many of which had generic alternatives in the market. Interestingly, substantial market share shifts occurred toward products manufactured by the Thai GPO, which ~~by law received preferential status by hospital purchasers.[23] GPO products have been noted to have higher than market prices[24] and sometimes to be of substandard quality.[25]~~have been noted to have higher than market prices.[27] By law, GPO products received preferential status by hospital purchasers,[28] which negates the incentive to prescribe cheaper alternatives under the capitated payment system. While the increase in GPO products and the UCS implementation may be a coincidence in timing, it is noteworthy that the GPO expanded its product line at a time when the UCS policy expanded the market of people who could afford medicines.

Our study demonstrates the value of IMS Health market intelligence data for rigorous health policy evaluation. Unlike other sources of data on pharmaceutical utilization (i.e., national health surveys or ad hoc hospital surveys), IMS data represent country pharmaceutical markets consistently over time and are useful for the evaluation of system-wide interventions. Nevertheless, the data pose some limitations. Aggregate national sales data do not allow us to determine whether observed increases in medicines sales occurred preferentially among UCS enrollees or enrollees in the SHI and CSMBS schemes, conceivably to compensate for financial

strain of the UCS on hospital budgets.[5,6] CSMBS expenditures increased following UCS ~~implementation~~[26]implementation[29] and increased medicines sales among CSMBS enrollees, reimbursed on a fee-for-service basis, could explain increases in non-NLEM medicines and medicines with less expensive therapeutic alternatives.[27,5] However, it is unlikely that increased utilization among CSMBS enrollees explains most of the observed volume changes since ~~it would imply that one-quarter (for diabetes) to one-third (for hypertension) of CSMBS members were on these treatments and the change in utilization would have needed to be coincident with the initiation of the UCS.~~this would imply that one-half (for diabetes) to three-quarters (for hypertension) of CSMBS members (7.1% of the total population in 2004[6]) were on these treatments in 2004. Even the CSMBS and SSI schemes combined (20.3% of the total population in 2004[6]) are unlikely to be responsible for the observed changes since this would imply that one-quarter (for diabetes) and one-third (for hypertension) of enrollees in the two schemes were on these treatments in 2004. These estimates are much higher than the national prevalence (6.7% for diabetes[30] and 22.0% for hypertension[31] in 2004) and unlikely in the civil servant and private sector workforce populations, which are likely to be healthier and wealthier than the national average.

Our interpretation of the observed changes assumes that pharmaceutical sales to hospital and retail pharmacies reflected total market utilization, and that hospital sales volumes included utilization at affiliated primary care units. This assumption seems justified in light of the estimated 91% accuracy of IMS Health data in representing the Thai pharmaceutical market.[28,32] For local generic products, including those produced by the GPO, IMS Health data ~~is~~are based on pharmacy surveys only (as opposed to pharmacy surveys and manufacturer reports), so we may have underestimated utilization. However, unless this systematic underestimation changed at the point of the UCS implementation, it would not have impacted our results. Finally, since we did not convert standard units of product sold to defined daily doses (DDD), we do not describe sales changes in terms of average adult doses.

There are also potential limitations due to study design and statistical analysis. We addressed the main threat to the internal validity of the interrupted time series design ~~–~~ a concurrent event that affects the outcome of interest ~~–~~ by assessing other policies or market events that occurred at the

time of the UCS, through literature reviews, discussions with in-country experts, and by including the retail sector as a comparison. The statistical approach, segmented regression analysis, usually assumes a linear trend and well-defined break point. Sensitivity analyses that varied model specification and intervention duration did not change the findings. ~~-~~By reporting results from fully-specified models, we may have underestimated the statistical significance of one- and five-year change estimates.

While both the context and the implementation of universal coverage in Thailand are unique and not necessarily generalizable to other LMICs, our findings suggest that expanding health insurance coverage with a medicines benefit to the entire population, together with changes in ~~a~~ ~~LMIC~~the payment system and increased ~~the~~local manufacturing, increased the per capita volume of medicines sold and, by inference, improved access to medicines in the primary care sector in Thailand, presumably by making medicines more affordable. Since the study period, Thailand has enacted further policies to address pharmaceutical sector cost escalation (e.g., strict enforcement of reimbursement for only NLEM medicines in the ~~CSMBS~~[29]CSMBS[33]) and to ensure appropriate access to non-NLEM medicines (e.g., coverage of medicines for HIV, renal replacement therapy, and mental health conditions).[30–32~~34–36~~] In the future, it will be important for Thailand and other countries to assess equity in access to and quality of use of medicines ~~use~~, availability of medicines in health centers and hospitals, out-of-pocket and system expenditures and affordability, and health outcomes as they pursue policies to achieve universal coverage.

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**TABLES**

**Table 1. Summary of the Impact of the Universal Coverage Scheme on Volume in the Hospital Sector (from segmented regression results) ***

| Therapeutic Area | Pre-policy trend | Immediate change after policy | Post-policy trend change |
|---|---|---|---|
| | | | |
| **DIABETES** | | | |
| **Antidiabetics**** | ↑ | | ↑ |
| **Insulins**** | ↑ | ↑ | ↑ |
| | | | |
| **CARDIOVASCULAR DISEASE** | | | |
| **Antihypertensives** | ↑ | ↓ | ↑ |
| **Lipid Regulating Agents**** | ↑ | | ↑ |
| **Cardiac Therapy** | ↑ | ↓ | |
| | | | |
| **CANCER** | | | |
| **Antineoplastics** | ↑ | | |
| **Cytostatic Hormones** | ↑ | | ↑ |
| **Immunostimulating Agents**** | ↑ | ↓ | |

*Arrows signify a statistically significant coefficient ($p<0.05$) from segmented regression with linear post-policy trend term, unless noted otherwise.
**Quadratic model (which has a squared -post-policy trend- term) fits better than linear model.
Note: See online appendix Table 2 and Figures 1-8 for regression coefficients and figures for all therapeutic areas.

**Table 2. Relative Impact of UCS on Sales of Medicines by Class (one and five years post policy)***

| Therapeutic Class | One Year Impact (in standard units) | | | Five Year Impact (in standard units) | | |
|---|---|---|---|---|---|---|
| | Predicted | Observed | Relative Change (95% CI) | Predicted | Observed | Relative Change (95% CI) |
| **Antidiabetics** | 2602·91 | 2769·79 | 6·4% (-6·9, 19·7) | 3669·13 | 5090·62 | **38·7% (13·5, 64·0)** |
| **Insulins** | 3·30 | 4·45 | **34·8% (15·1, 54·5)** | 4·58 | 12·56 | **174·4% (113·9, 235·0)** |
| **Cardiac Therapy Agents** | 699·28 | 607·27 | -13·2% (-26·9, 0·6) | 908·12 | 825·49 | -9·1% (-31·9, 13·1) |
| **Lipid Regulating Agents** | 522·34 | 504·58 | -3·4% (-19·9, 13·1) | 781·97 | 1629·11 | **108·3% (59·8, 156·9)** |
| **Antihypertensives** | 3521·47 | 3418·79 | -2·9% (-15·5, 9·7) | 5200·86 | 6177·49 | 18·8% (-2·8, 40·3)** |
| **Antineoplastics** | 35·38 | 34·21 | -3·3% (-15·4, 8·7) | 46·14 | 48·13 | 4·3% (-16·3, 24·9) |
| **Cytostatic Hormones** | 29·48 | 30·58 | 3·7% (-10·1, 17·6) | 39·82 | 47·52 | 19·3% (-5·1, 43·8) |
| **Immunostimulating Agents** | 0·65 | 0·43 | **-35·0% (-45·1, -25·0)** | 0·81 | 0·60 | **-26·3% (-45·0, -7·6)** |

*Bold signifies that the change is statistically significant (i.e., confidence interval does not include the null value of 0).
**The *absolute* five-year difference, which is estimated using more precise method, is significant. See online appendix Table 43.

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**Table 3. Immediate Impact of UCS on Hospital Sector Market Share***

| Therapeutic Area | Licensing Status | Immediate post-policy absolute change in % market share (95% CI) |
|---|---|---|
| **DIABETES** | | |
| **Antidiabetics** | Originator brand | -0·3% (-1·6, 1·0) |
| | Branded generic | **-12·3% (-16·0, -8·7)** |
| | Generic | **-3·5% (-5·8, -1·1)** |
| | GPO | **16·1% (12·0, 20·2)** |
| **Insulins*** ** | Originator brand** | -0·04% (-0·4, 0·3) |
| | Branded generic | **7·0% (2·9, 11·1)** |
| | Generic | **-6·2% (-10·3, -2·1)** |
| **CARDIOVASCULAR DISEASE** | | |
| **Antihypertensives** | Originator brand** | -0·1% (-2·3, 2·0) |
| | Branded generic** | -0·2% (-6·1, 1·8) |
| | Generic | **-5·7% (-8·3, -3·0)** |
| | GPO | 5·3% (-0·1, 10·6) |
| **Lipid Regulating Agents** | Originator brand** | **-7·8% (-10·2, -5·4)** |
| | Branded generic** | **7·6% (5·1, 10·0)** |
| | Generic | 0·2% (-0·4, 0·7) |
| | GPO | 0·2% (-0·3, 0·8) |
| **Cardiac Therapy** | Originator brand | 0·1% (-0·8, 1·0) |
| | Branded generic** | **-13·5% (-20·5, -6·5)** |
| | Generic | **-4·3% (-6·2, -2·4)** |
| | GPO | **21·6% (15·0, 28·1)** |
| **CANCER*** ** | | |
| **Antineoplastics** | Originator brand | 1·1% (-1·0, 3·2) |
| | Branded generic | -1·0% (-5·4, 3·4) |
| | Generic | 0·4% (-2·7, 3·4) |
| **Cytostatic Hormones** | Originator brand** | 0·4% (-5·4, 6·1) |
| | Branded generic** | **-7·7% (-12·0, -3·5)** |
| | Generic** | **6·0% (1·4, 10·6)** |
| **Immunostimulating Agents** | Originator brand | **-6·4% (-9·7, -3·0)** |
| | Branded generic | **4·5% (1·7, 7·3)** |
| | Generic | -0·2% (-0·3, 0·02) |

***Bold** signifies a statistically significant regression coefficient ($p<0.05$). Changes are in absolute terms (i.e., percentage point change).
**Quadratic model (which has a squared post-policy term) fits better than linear model.
***GPO did not produce any insulins or cancer medicines during the study period.
Note 1: See online appendix Table ~~5~~4 and Figures 9-16 for market share regression coefficients and figures for all therapeutic areas
Note 2: Aside from the immediate level changes following the policy, there were few major changes in market share. See online appendix, Table ~~6~~5 for absolute one- and five-year differences.

**Figure Index (attached in separate document):***

**Figure 1.** Standard Units Per Capita by Quarter: Insulin (Hospital vs. Retail)

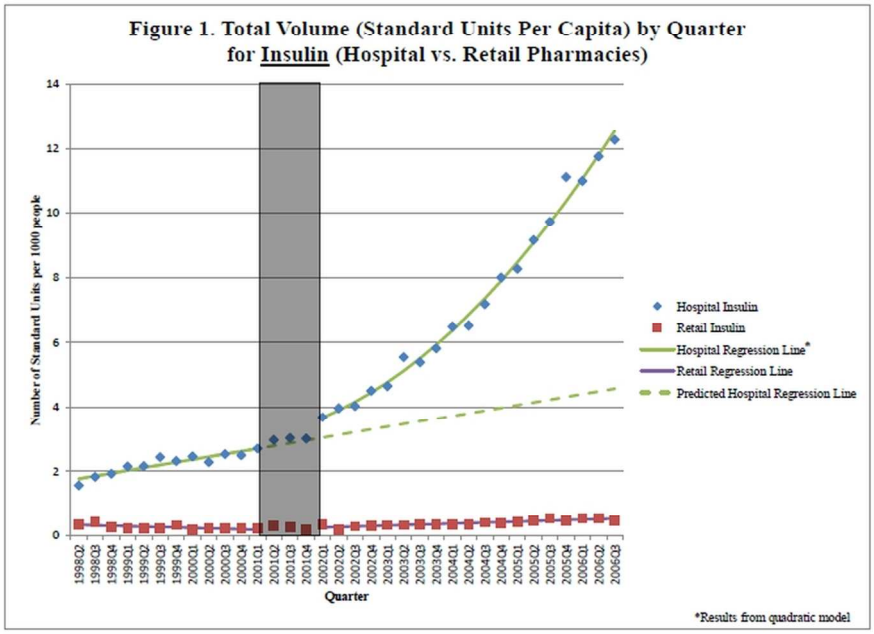
**Figure 2.** Standard Units Per Capita by Quarter: Antihypertensives (Hospital vs. Retail)

**Figure 3.** Licensing Status Market Share by Quarter: Antidiabetics (Hospital Sector)

**Figure 4.** Licensing Status Market Share by Quarter: Cardiac Therapy Products (Hospital Sector)

*The grey box in each figure represents the 3-quarter UCS roll-out period.

**Online appendix (attached in separate document)**

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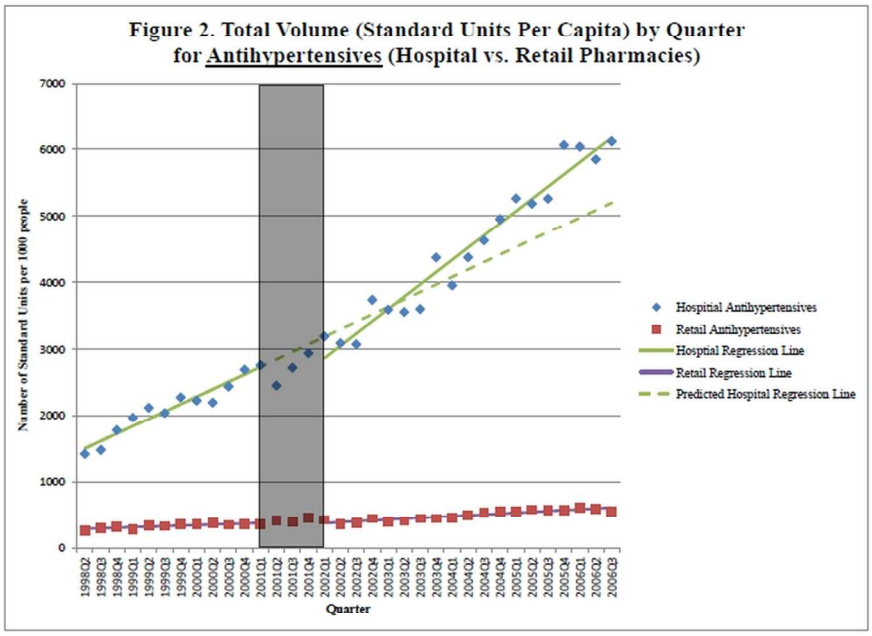


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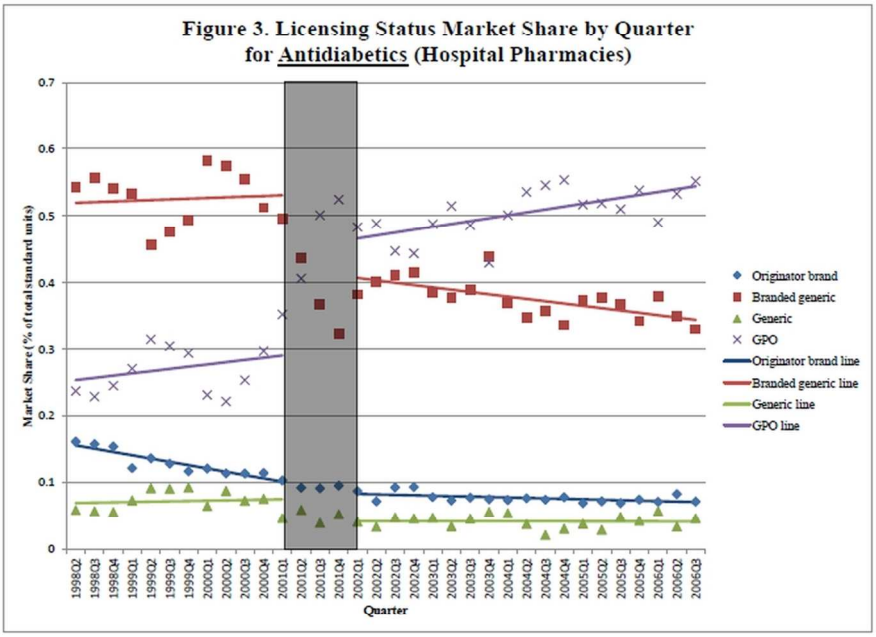


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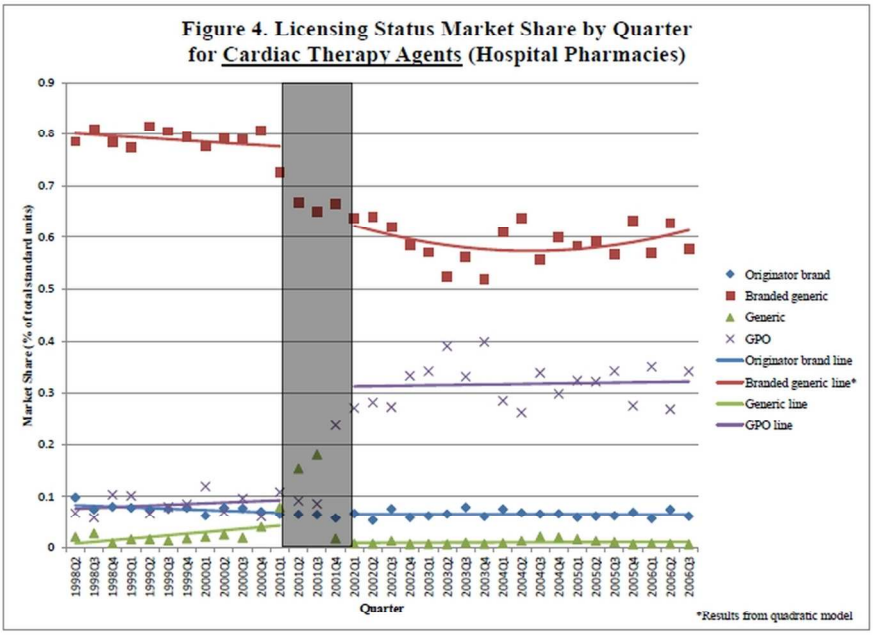


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