



**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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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 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

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3 dependents (13·6%).⁷ In addition, the UCS covered those previously enrolled in a voluntary
4 health card (VHC) scheme (22·0%), in private health insurance (1·6%), or in a tax-based, means-
5 tested Low Income Scheme (LIS) for the poor, elderly, children and disabled (28·9%)^{7,8} as well
6 as more than one quarter (26·6%) of the population without previous insurance.⁷ The UCS was
7 rolled out to all provinces between April and October 2001.⁵ By 2005, 95·5% of the population
8 was insured, with just over 70% of the population covered by the UCS.⁷
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16 The UCS is a compulsory, tax-financed scheme with comprehensive coverage of inpatient and
17 outpatient services, including medicines on the National List of Essential Medicines (NLEM).⁵
18 Individuals must enroll in the scheme at a local Contracting Unit for Primary Care (CUP),⁵
19 primarily housed in government-owned hospitals.⁹ Each CUP receives a capitated payment per
20 registered member to provide outpatient services and medicines.⁵ CUPs served as gate-keepers
21 for secondary and tertiary hospitals. When patients were referred, payments for higher-level care
22 initially came out of the CUP's capitated payment, so CUPs had a financial disincentive to refer
23 patients.⁵
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32 Our objective was to evaluate the immediate, short-term (one year) and long-term (five year)
33 impacts of the UCS on pharmaceutical market size and composition for medicines for three non-
34 communicable diseases (NCDs): cancer, cardiovascular disease, and diabetes. We hypothesized
35 that the UCS would result in a gradual increase in sales volume, particularly of products used in
36 primary care, as enrollment into the Scheme increased, and in an immediate increase in market
37 share of less expensive generic or branded generic products and medicines on the NLEM in
38 response to capitated payment rules. We focused on medicines for NCDs since these illnesses
39 represent a large and growing health care burden in Thailand^{10–13} and other LMICs¹⁴ and most,
40 but not all, medicines for NCDs would be prescribed and dispensed in primary care settings.
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48 **Methods**

49 *Data*

50 We used data on quarterly pharmaceutical sales in Thailand from 1998 to 2006 provided by IMS
51 Health.¹⁵ The sales data are generated from reports to IMS Health by multinational
52 pharmaceutical companies and surveys of purchases by hospital and retail pharmacies. IMS
53 surveys approximately 200 hospitals (including general and specialized, public and private) and
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3 350 retail pharmacies in Thailand, and employs a stratified random sample of these facilities that
4 enables national projections. Medicines were classified according to the European
5 Pharmaceutical Research Association (EphMRA) Anatomical Therapeutic Chemical (ATC)
6 system.¹⁶
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10 11 12 **Outcomes**

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14 We used two outcome measures: total volume and percent market share. *Total volume* is the
15 number of standard units purchased per capita per quarter (i.e., “sales”). We analyzed total
16 volume by sector (i.e., retail versus hospital) and, within the hospital sector, by NLEM versus
17 non-NLEM status of medicines (based on the 1999 Thai NLEM). A standard unit, as defined by
18 IMS Health, is the smallest dose of a product, which equates to one tablet or capsule for an oral
19 dosage form, one teaspoon (5ml) for a syrup, and one ampoule or vial for an injectable product.
20 We divided total volume by size of the population over 15 years old to control for population
21 growth (using yearly population estimates from the World Bank¹⁷). We used the entire
22 population as denominator for insulins, since they are also used for Type 1 diabetes, a chronic
23 disease that affects children. *Percent market share* is the percent of total volume in four mutually
24 exclusive categories of licensing status: originator brand products, branded generic products
25 (products sold under a brand name other than the originator brand name of the molecule), generic
26 products (products that are sold under the generic molecule name), and products manufactured
27 by Thailand’s Government Pharmaceutical Organization (GPO).
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40 We analyzed total volume and market share for medicines in eight therapeutic classes: two
41 classes of diabetes products (oral antidiabetics and insulins), three classes of cardiovascular
42 disease products (antihypertensives, lipid-regulating, and cardiac therapy products) and three
43 classes of cancer products (antineoplastics, immunostimulating agents, and cytostatic hormone
44 therapy products); Table 1 in the online appendix lists all medicines by ATC code. Antidiabetic,
45 insulin, antihypertensive and lipid-lowering products are used for conditions that are typically
46 treated in primary care settings (i.e., diabetes, high blood pressure and high cholesterol), whereas
47 cardiac therapy and cancer products are used for more severe conditions that are more likely to
48 be treated by a specialist and/or in inpatient settings.
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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

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3 The majority of sales in Thailand for all cancer, cardiovascular disease and diabetes medicines
4 studied were in the hospital sector and were for medicines on the NLEM. After implementation
5 of the UCS, there was a significant increase in level of sales of insulins and a significant increase
6 in trend in sales of antidiabetic, insulin, antihypertensive, lipid regulating, and cytostatic
7 hormone products [Table 1, Figures 1 and 2]. There was a significant reduction in level of sales
8 immediately following the reforms for three medication classes: antihypertensive, cardiac
9 therapy and immunostimulating agents (although only the latter was significant in the sensitivity
10 analyses using a longer intervention period).
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19 The UCS was associated with increased sales of diabetes medicines. One year after the policy,
20 the sale of insulin was 35% (95% CI: 15%, 55%) higher and, at five years, 174% (95% CI:
21 114%-235%) higher than what would have been expected in the absence of the UCS [Table 2].
22 The increase in insulin sales was driven primarily by human insulins, which are on the NLEM
23 and marketed as branded generics by two manufacturers. The policy was associated with a 39%
24 (95% CI: 14%, 64%) increase in antidiabetic product sales five years after implementation
25 [Table 2]. This is largely due to increased sales of generic and branded generic metformin and
26 glibenclamide products, both of which are on the NLEM.
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35 Implementation of the UCS appears to have had a mixed impact on sales of cardiovascular
36 medicines. Five years after the policy, the sale of lipid lowering agents was nearly double (108%
37 increase; 95% CI: 60%, 157%) what would have been expected in the absence of the scheme
38 [Table 2]. The increase was primarily due to sales of branded generic simvastatin and
39 gemfibrozil products, which are on the NLEM, and a small but steady increase in sales of
40 originator atorvastatin products, which are not on the NLEM. For antihypertensives, the
41 significant increase in post-policy trend compensated for an initial drop in sales, resulting in a
42 slight increase in sales five years after the policy (19% increase; 95% CI: -3%, 40%). The
43 increased trend was primarily due to sales of enalapril, atenolol, and amlodipine, all of which are
44 on the NLEM and predominately sold as branded generics. The reform had no significant impact
45 on sales of cardiac therapy medicines one or five years after the policy.
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3 The results were also mixed for cancer medicines. The UCS had no significant one- or five-year
4 impact on the sale of antineoplastics or cytostatic hormones (although the latter class did
5 experience a significant post-policy increase in trend). However, the policy was associated with
6 an immediate reduction in sales of immunostimulating agents that did not recover in the post-
7 policy period. One year after implementation, the sale of immunostimulating agents was 35%
8 (95% CI: -45%, -25%) lower than expected from pre-policy trends, and 26% lower (95% CI: -
9 45%, -8%) five years post-policy. This drop is almost entirely due to a sharp reduction in sales of
10 interferon alfa-2b, a non-NLEM medicine, around the time of UCS implementation, which could
11 have been due to a co-incidental recall of an interferon alfa-2b product.²¹
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21 There was mixed evidence about the effects of the UCS on utilization of NLEM medicines. For
22 all classes that experienced a post-policy increase in trend, there was an increase in sales of both
23 NLEM medicines (except for cytostatic hormones) *and* non-NLEM products [see online
24 appendix, Table 3]. The immediate decrease in sales of cardiac therapies and immunostimulating
25 agents was largely due to a decrease in non-NLEM medicines. However, for these two classes,
26 there was no corresponding increase in NLEM medicines.
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33 Finally, as expected, the reform had little impact on sales volume in the retail sector – there were
34 few significant post-implementation changes, and the changes that were significant were small in
35 magnitude [see online appendix, Table 2].
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41 *Hospital Sector Market Share*

42 Immediately following the reform, there were significant shifts in hospital sector market share by
43 licensing status for most classes [Table 3]. The changes for antidiabetics and cardiac medicines -
44 the two therapeutic classes with the largest shifts – were due to significant increases in GPO-
45 produced medicines, primarily at the expense of branded generics and, to a lesser extent,
46 generics. There was a significant increase in GPO antidiabetic products (+16% of market; 95%
47 CI: 12%, 20%), and decreases in branded generic (-12%; 95% CI: -16%, -9%) and generic (-4%;
48 95% CI: -6%, -1%) products immediately after the policy [Figure 3]. Similarly, there was a
49 significant increase in GPO cardiac therapy products (+22%; 95% CI: 15%, 28%), and
50 significant decreases of branded generic (-14%; 95% CI: -21%, -7%) and generic (-4%; 95% CI: -
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3 6%, -2%) products immediately after the policy [Figure 4]. There was also a small decrease in
4 market share of generic antihypertensives (-6%; 95% CI: -8%, -3%), which was compensated for
5 by a marginally significant increase in GPO products.
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10 The market for lipid regulating agents experienced an immediate shift from originator products (-
11 8% market share; 95% CI: -10%, -5%) to branded generics (+8%; 95% CI: 5%, 10%). A similar
12 shift was seen for in the market for immunostimulating agents (6% decrease in originator
13 products [95% CI:-10%, -3%] and a 5% increase in branded generics [95% CI:2%, 7%]). The
14 cytostatic hormone market experienced an immediate shift from branded generic (-8%; 95% CI:-
15 12%, -4%) to generic products (+6%, 95% CI: 1%, 11%). Generic insulins experienced a slight
16 decrease in market share caused by the market exit of the sole generic manufacturer just prior to
17 the policy. There were no immediate changes in market share for antineoplastics. Aside from the
18 immediate level changes following the policy, there were few major changes in market share for
19 all classes.
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28 29 30 **Discussion**

31 The UCS was associated with long-term (i.e., 5 year) increases in hospital sector sales of
32 medicines for chronic diseases that are usually treated in primary care settings, such as diabetes,
33 high blood pressure, and high cholesterol. We hypothesized this gradual increase in volume since
34 the UCS expanded access to primary care⁷ and actual enrollment into the scheme occurred
35 gradually from implementation in 2001 until around 2005, by which time 95.5% of the
36 population had insurance coverage.⁷ The UCS, which radically changed hospital financing and
37 reimbursement, was also associated with an immediate market shift to locally produced or
38 branded generic products for most therapeutic classes.
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48 Despite these increases in access, the policy did not appear to increase sales of medicines for
49 more severe diseases like heart failure, arrhythmias, and cancer, which are often treated in
50 secondary or tertiary settings. This finding is in line with evidence that the capitated payment
51 system discouraged referrals of UCS patients to higher-level care.^{5,7,22} The UCS also appears to
52 have had a mixed impact on utilization of essential medicines. There were increases in NLEM
53 medicines, which are covered, as well as non-NLEM medicines. Similarly, given the capitated
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3 UCS payment system, we expected to see an increase in sales of generic medicines, which are
4 typically less expensive. However, the majority of sales in most classes were for branded generic
5 products, many of which had generic alternatives in the market. Interestingly, substantial market
6 share shifts occurred toward products manufactured by the Thai GPO, which by law received
7 preferential status by hospital purchasers.²³ GPO products have been noted to have higher than
8 market prices²⁴ and sometimes to be of substandard quality.²⁵

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16 Our study demonstrates the value of IMS Health market intelligence data for rigorous health
17 policy evaluation. Unlike other sources of data on pharmaceutical utilization (i.e., national health
18 surveys or ad hoc hospital surveys), IMS data represent country pharmaceutical markets
19 consistently over time and are useful for the evaluation of system-wide interventions.
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21 Nevertheless, the data pose some limitations. Aggregate national sales data do not allow us to
22 determine whether observed increases in medicines sales occurred preferentially among UCS
23 enrollees or enrollees in the SHI and CSMBS schemes, conceivably to compensate for financial
24 strain of the UCS on hospital budgets.⁵ CSMBS expenditures increased following UCS
25 implementation²⁶ and increased medicines sales among CSMBS, reimbursed on a fee-for-service
26 basis, could explain increases in non-NLEM medicines and medicines with less expensive
27 therapeutic alternatives.²⁷ However, it is unlikely that increased utilization among CSMBS
28 enrollees explains most of the observed volume changes since it would imply that one-quarter
29 (for diabetes) to one-third (for hypertension) of CSMBS members were on these treatments and
30 the change in utilization would have needed to be coincident with the initiation of the UCS.
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42 Our interpretation of the observed changes assumes that pharmaceutical sales to hospital and
43 retail pharmacies reflected total market utilization, and that hospital sales volumes included
44 utilization at affiliated primary care units. This assumption seems justified in light of the
45 estimated 91% accuracy of IMS Health data in representing the Thai pharmaceutical market.²⁸
46 For local generic products, including those produced by the GPO, IMS Health data is based on
47 pharmacy surveys only (as opposed to pharmacy surveys and manufacturer reports), so we may
48 have underestimated utilization. Finally, since we did not convert standard units of product sold
49 to defined daily doses (DDD), we do not describe sales changes in terms of average adult doses.
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3 There are also potential limitations due to study design and statistical analysis. We addressed the
4 main threat to the internal validity of the interrupted time series design - a concurrent event that
5 affects the outcome of interest - by assessing other policies or market events that occurred at the
6 time of the UCS, through literature reviews, discussions with in-country experts, and by
7 including the retail sector as a comparison. The statistical approach, segmented regression
8 analysis, usually assumes a linear trend and well-defined break point. Sensitivity analyses that
9 varied model specification and intervention duration did not change the findings. By reporting
10 results from fully-specified models, we may have underestimated the statistical significance of
11 one- and five-year change estimates.
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21 While both the context and the implementation of universal coverage in Thailand are unique, our
22 findings suggest that expanding health insurance coverage with a medicines benefit to the entire
23 population in a LMIC increased the volume of medicines sold and, by inference, improved
24 access to medicines in the primary care sector. Since the study period, Thailand has enacted
25 further policies to address pharmaceutical sector cost escalation (e.g., strict enforcement of
26 reimbursement for only NLEM medicines in the CSMBS²⁹) and to ensure appropriate access to
27 non-NLEM medicines (e.g., coverage of medicines for HIV, renal replacement therapy, and
28 mental health conditions).³⁰⁻³² In the future, it will be important for Thailand and other countries
29 to assess quality of medicines use, out-of-pocket and system expenditures, and health outcomes
30 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.

1
2
3 **Figure Index (attached in separate document):***

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

6
7 **Figure 2.** Standard Units Per Capita by Quarter: Antihypertensives (Hospital vs. Retail)

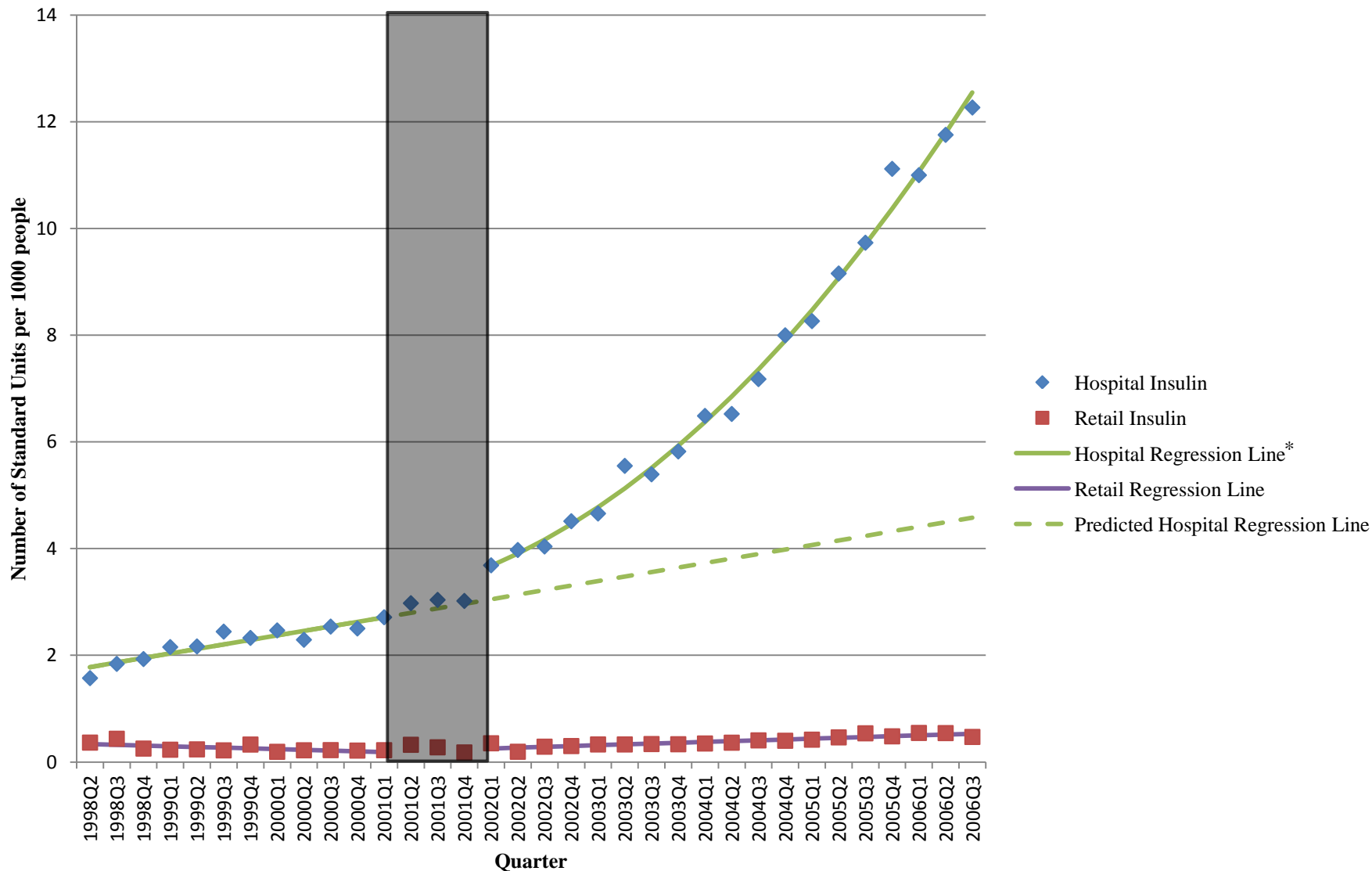
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9 **Figure 3.** Licensing Status Market Share by Quarter: Antidiabetics (Hospital Sector)

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

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

16
17 **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)

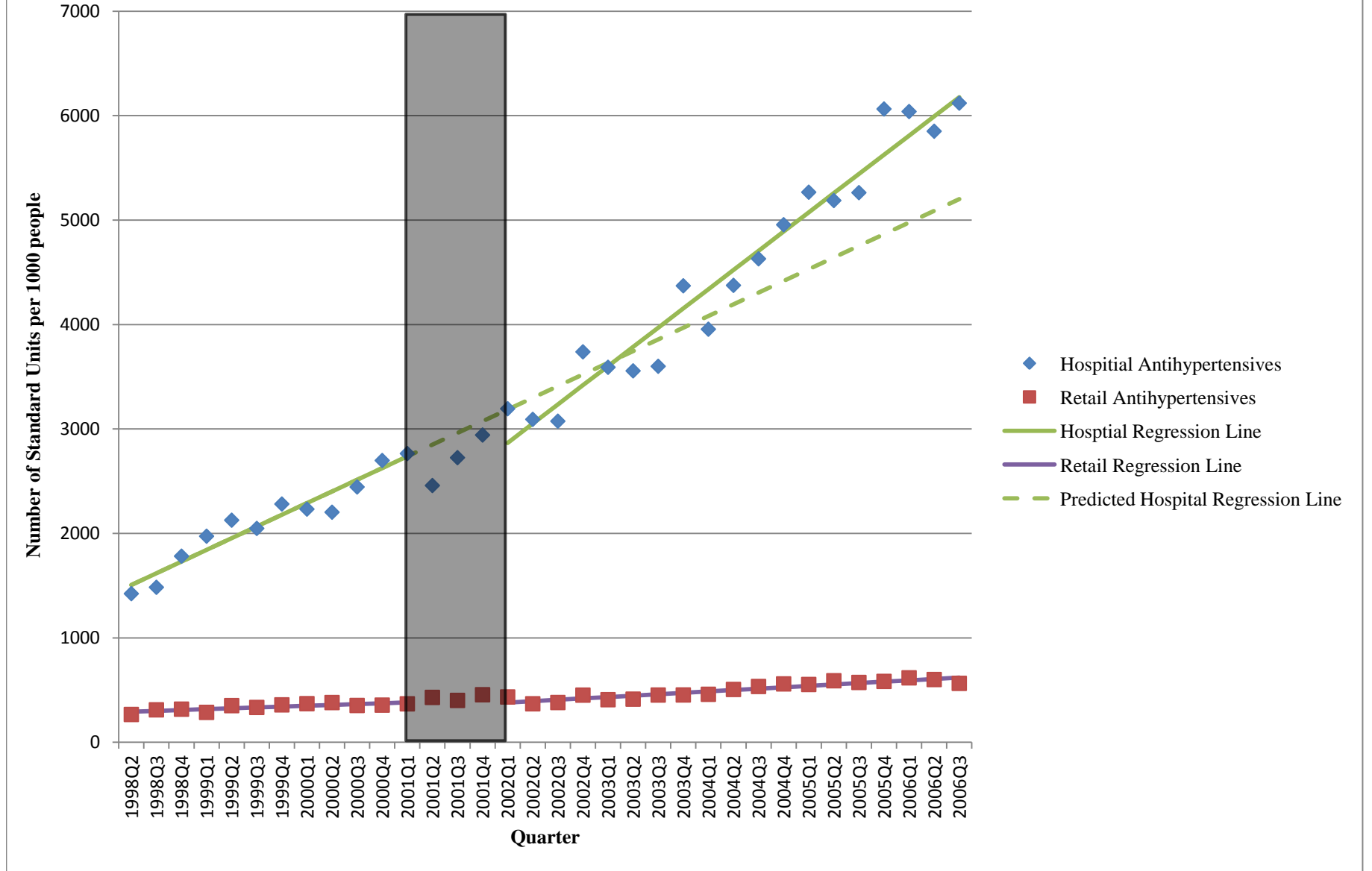


Figure 3. Licensing Status Market Share by Quarter for Antidiabetics (Hospital Pharmacies)

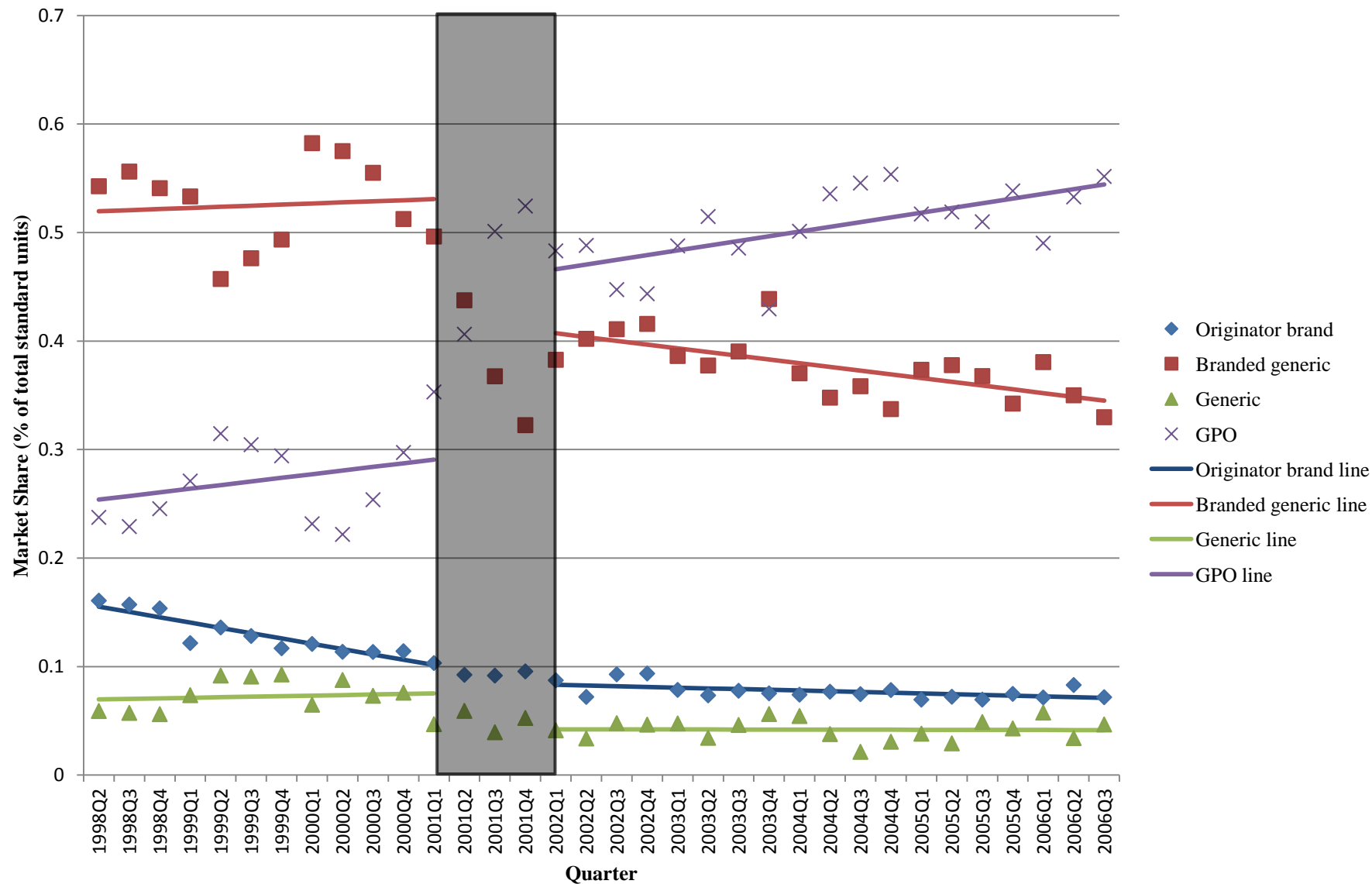
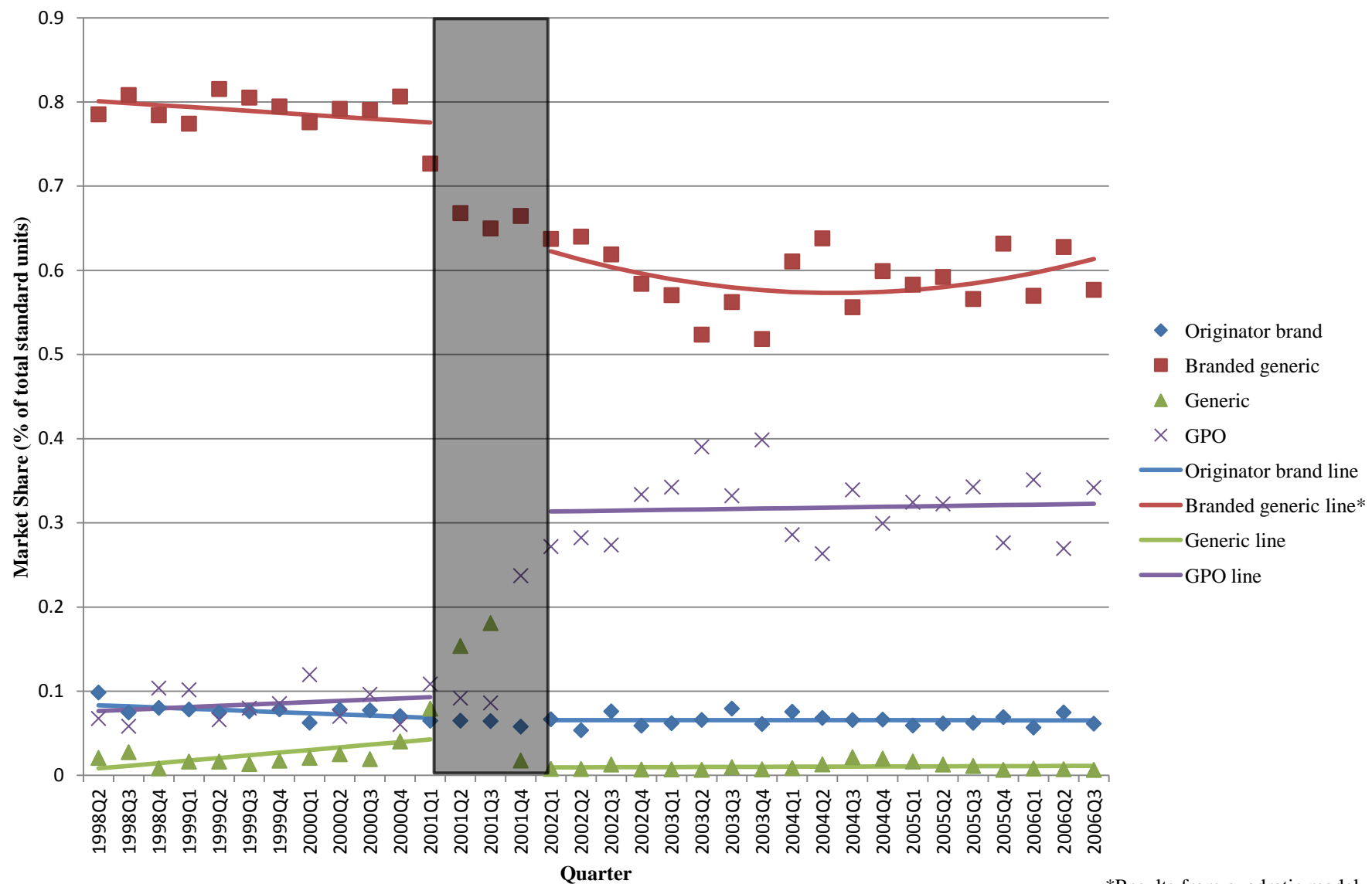


Figure 4. Licensing Status Market Share by Quarter for Cardiac Therapy Agents (Hospital Pharmacies)



*Results from quadratic model

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 personal 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 personal communication, all insulins are on NLEM
	Insulins	INSULIN DETEMIR	A10 (DRUGS USED IN DIABETES)	A10C5 (H INSUL+ANG LONG ACT)	1	according to personal communication, all insulins are on NLEM
	Insulins	INSULIN GLARGINE	A10 (DRUGS USED IN DIABETES)	A10C5 (H INSUL+ANG LONG ACT)	1	according to personal communication, all insulins are on NLEM
	Insulins	INSULIN HUMAN BASE	A10 (DRUGS USED IN DIABETES)	A10C1 (H INSUL+ANG FAST ACT)	1	according to personal 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 personal communication, all insulins are on NLEM
	Insulins	INSULIN HUMAN ISOPHANE	A10 (DRUGS USED IN DIABETES)	A10C2 (H INSUL+ANG INTERMED ACT)	1	according to personal 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 personal 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 personal communication, all insulins are on NLEM
	Insulins	INSULIN LISPRO	A10 (DRUGS USED IN DIABETES)	A10C1 (H INSUL+ANG FAST ACT)	1	according to personal 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 personal communication, all insulins are on NLEM
	Insulins	INSULIN PORCINE BASE	A10 (DRUGS USED IN DIABETES)	A10D0 (ANIMAL INSULINS)	1	according to personal communication, all insulins are on NLEM
	Insulins	INSULIN PORCINE ISOPHANE	A10 (DRUGS USED IN DIABETES)	A10D0 (ANIMAL INSULINS)	1	according to personal communication, all insulins are on NLEM
	Insulins	INSULIN PORCINE ZINC SUSPENSION (COMPOUND)	A10 (DRUGS USED IN DIABETES)	A10D0 (ANIMAL INSULINS)	1	according to personal 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 (ANTIHYPERT.PL MAINLY PERI)	0	
	Antihypertensives	CLONIDINE	C2 (ANTIHYPERTENSIVES)	C2A1 (ANTIHYPERT.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	DHYDRALAZINE	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPERT.PL MAINLY PERI)	1	
	Antihypertensives	DOXAZOSIN	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPERT.PL MAINLY PERI)	1	
	Antihypertensives	HYDRALAZINE	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPERT.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 (ANTIHYPERT.PL MAINLY PERI)	0	
	Antihypertensives	METHYLDOPA	C2 (ANTIHYPERTENSIVES)	C2A1 (ANTIHYPERT.PL MAINLY CENT)	1	
	Antihypertensives	MINOXIDIL	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPERT.PL MAINLY PERI)	1	
	Antihypertensives	NITROPRUSSIDE	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPERT.PL MAINLY PERI)	1	
	Antihypertensives	PRAZOSIN	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPERT.PL MAINLY PERI)	1	
	Antihypertensives	RESERPINE	C2 (ANTIHYPERTENSIVES)	C2C0 (RAUWOLF ALK+OTH A-HY HERB)	1	
	Antihypertensives	RILMENIDINE	C2 (ANTIHYPERTENSIVES)	C2A1 (ANTIHYPERT.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	ATENLOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS.PLAIN)	1	
	Antihypertensives	ATENLOLOL#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	

1	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
2	Antihypertensives	METOPROLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)	0
3	Antihypertensives	NEBIVOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)	0
	Antihypertensives	OXPRENOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)	0
4	Antihypertensives	PINDOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)	0
5	Antihypertensives	PROPRANOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)	1
	Antihypertensives	SOTALOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)	0
6	Antihypertensives	AMLODIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	1
	Antihypertensives	ATENOLOL#NIFEDIPINE	C8 (CALCIUM ANTAGONISTS)	C8B2 (CALC ANTAG/B BLOCKR COMB)	0
7	Antihypertensives	BARNIDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
	Antihypertensives	DILTIAZEM	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	1
8	Antihypertensives	FELODIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	1
9	Antihypertensives	GALLOPAMIL	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
10	Antihypertensives	ISRADIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
	Antihypertensives	LACIDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
11	Antihypertensives	LERCANIDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
	Antihypertensives	MANIDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
12	Antihypertensives	MIBEFRADIL	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
13	Antihypertensives	NICARDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	1
	Antihypertensives	NIFEDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	1
14	Antihypertensives	NISOLDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
15	Antihypertensives	NITRENDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	0
16	Antihypertensives	VERAPAMIL	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)	1
	Antihypertensives	AMILORIDE	C3 (DIURETICS)	C3A1 (POT SPARING AGENTS PLAIN)	0
17	Antihypertensives	AMILORIDE#HYDROCHLOROTHIAZIDE	C3 (DIURETICS)	C3A5 (POT SPARING+THIAZ COMBS)	1
18	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
19	Antihypertensives	BENDROFLUMETHIAZIDE#POTASSIUM	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)	0
20	Antihypertensives	BUMETANIDE	C3 (DIURETICS)	C3A2 (LOOP DIURETICS PLAIN)	0
21	Antihypertensives	FUROSEMIDE	C3 (DIURETICS)	C3A2 (LOOP DIURETICS PLAIN)	1
	Antihypertensives	HYDROCHLOROTHIAZIDE	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)	1
22	Antihypertensives	HYDROCHLOROTHIAZIDE#TRIAMTERENE	C3 (DIURETICS)	C3A5 (POT SPARING+THIAZ COMBS)	0
23	Antihypertensives	INDAPAMIDE	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)	0
	Antihypertensives	SPIRONOLACTONE	C3 (DIURETICS)	C3A1 (POT SPARING AGENTS PLAIN)	1
24	Antihypertensives	TORASEMIDE	C3 (DIURETICS)	C3A2 (LOOP DIURETICS PLAIN)	0
25	Antihypertensives	TRIPAMIDE	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)	0
	Antihypertensives	XIPAMIDE	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)	0
26	Antihypertensives	ALISKIREN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9X0 (OTH RENIN-ANGIOTEN AGENT)	0
27	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
28	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
29	Antihypertensives	CAPTOPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)	1
30	Antihypertensives	CILAZAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)	0
	Antihypertensives	DELAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)	0
31	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
32	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
33	Antihypertensives	HYDROCHLOROTHIAZIDE#IRBESARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D1 (AT2 ANTG COMB C2 &/O DIU)	0
34	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
35	Antihypertensives	HYDROCHLOROTHIAZIDE#QUINAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9B1 (ACE INH COMB+A-HYP/DIUR)	0
36	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
37	Antihypertensives	HYDROCHLOROTHIAZIDE#VALSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D1 (AT2 ANTG COMB C2 &/O DIU)	0
38	Antihypertensives	IMIDAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)	0
39	Antihypertensives	INDAPAMIDE#PERINDOPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9B1 (ACE INH COMB+A-HYP/DIUR)	0
40	Antihypertensives	IRBESARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)	0
	Antihypertensives	LISINAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)	0
41	Antihypertensives	LOSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)	0
42	Antihypertensives	OLMESARTAN MEDOXOMIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)	0
43	Antihypertensives	PERINDOPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)	0
	Antihypertensives	QUINAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)	0
44	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
45	Antihypertensives	VALSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)	0
46	Cardiac Therapy	ADENOSINE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	0

both ingredients listed separately, not in combo

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1	Cardiac Therapy	AMIODARONE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	1
2	Cardiac Therapy	AMRINONE	C1 (CARDIAC THERAPY)	C1F0 (POSITIVE INOTROPIC AGENT)	0
3	Cardiac Therapy	CAFFEINE#ETAMIVAN	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)	0
4	Cardiac Therapy	DIGITALIS PURPUREA	C1 (CARDIAC THERAPY)	C1A1 (CARDIAC GLYCOSIDES PLAIN)	0
5	Cardiac Therapy	DIGITOXIN	C1 (CARDIAC THERAPY)	C1A1 (CARDIAC GLYCOSIDES PLAIN)	0
6	Cardiac Therapy	DIGOXIN	C1 (CARDIAC THERAPY)	C1A1 (CARDIAC GLYCOSIDES PLAIN)	1
7	Cardiac Therapy	DISOPYRAMIDE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	0
8	Cardiac Therapy	DOBUTAMINE	C1 (CARDIAC THERAPY)	C1C2 (CARDIAC DOPAMINERG AGENT)	1
9	Cardiac Therapy	DOPAMINE	C1 (CARDIAC THERAPY)	C1C2 (CARDIAC DOPAMINERG AGENT)	1
10	Cardiac Therapy	EPINEPHRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)	1
11	Cardiac Therapy	ETAFEDRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)	0
12	Cardiac Therapy	ETILEFRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)	0
13	Cardiac Therapy	FLECAINIDE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	0
14	Cardiac Therapy	GLYCINE MAX#UBIDECARENONE	C1 (CARDIAC THERAPY)	C1X0 (ALL OTHER CARDIAC PREFS)	0
15	Cardiac Therapy	ISOPRENALINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)	0
16	Cardiac Therapy	ISOSORBIDE DINITRATE	C1 (CARDIAC THERAPY)	C1E0 (NITRITES AND NITRATES)	1
17	Cardiac Therapy	ISOSORBIDE MONONITRATE	C1 (CARDIAC THERAPY)	C1E0 (NITRITES AND NITRATES)	1
18	Cardiac Therapy	IVABRADINE	C1 (CARDIAC THERAPY)	C1D0 (CORONRY THER EXC C AN+ND)	0
19	Cardiac Therapy	LIDOCAINE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	1
20	Cardiac Therapy	MAGNESIUM#POTASSIUM#PROCAINE	C1 (CARDIAC THERAPY)	C1X0 (ALL OTHER CARDIAC PREFS)	0
21	Cardiac Therapy	METARAMINOL	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)	1
22	Cardiac Therapy	METILDIGOXIN	C1 (CARDIAC THERAPY)	C1A1 (CARDIAC GLYCOSIDES PLAIN)	0
23	Cardiac Therapy	MEXILETINE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	0
24	Cardiac Therapy	MIDODRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)	0
25	Cardiac Therapy	MILRINONE	C1 (CARDIAC THERAPY)	C1F0 (POSITIVE INOTROPIC AGENT)	0
26	Cardiac Therapy	NITROGLYCERIN	C1 (CARDIAC THERAPY)	C1E0 (NITRITES AND NITRATES)	0
27	Cardiac Therapy	NOREPINEPHRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)	0
28	Cardiac Therapy	OXYFEDRINE	C1 (CARDIAC THERAPY)	C1D0 (CORONRY THER EXC C AN+ND)	0
29	Cardiac Therapy	PENTAERYTHRITYL TETRANITRATE	C1 (CARDIAC THERAPY)	C1E0 (NITRITES AND NITRATES)	0
30	Cardiac Therapy	PROCAINAMIDE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	1
31	Cardiac Therapy	PROPAFENONE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	1
32	Cardiac Therapy	QUINIDINE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	0
33	Cardiac Therapy	TOCAINIDE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)	0
34	Cardiac Therapy	TRIMETAZIDINE	C1 (CARDIAC THERAPY)	C1D0 (CORONRY THER EXC C AN+ND)	0
35	Cardiac Therapy	UBIDECARENONE	C1 (CARDIAC THERAPY)	C1X0 (ALL OTHER CARDIAC PREFS)	0
36	Cardiac Therapy	UBIQUINONE(S)	C1 (CARDIAC THERAPY)	C1X0 (ALL OTHER CARDIAC PREFS)	0
37	Lipid Regulating	ACIPIMOX	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A9 (OTH.CHOLEST&TRIGLY.REGUL)	0
38	Lipid Regulating	ALLIUM SATIVUM	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
39	Lipid Regulating	ALLIUM SATIVUM#ARACHIS HYPOGAEA	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
40	Lipid Regulating	ALLIUM SATIVUM#SOYA LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
41	Lipid Regulating	AMLODIPINE#ATORVASTATIN	C11 (C.V. MULTITH. COMB PROD)	C11A1 (LIPREG.CV.MULT-TH.FX.COM)	0
42	Lipid Regulating	ATORVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))	0
43	Lipid Regulating	BEZAFIBRATE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A2 (FIBRATES)	0
44	Lipid Regulating	CERIVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))	0
45	Lipid Regulating	COLESTYRAMINE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A3 (ION-EXCHANGE RESINS)	0
46	Lipid Regulating	DOCOSAHEXANOIC ACID#EICOSAPENTAENOIC ACID	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
47	Lipid Regulating	DOCOSAHEXANOIC ACID#EICOSAPENTAENOIC ACID#VITAMIN E	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
48	Lipid Regulating	EZETIMIBE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A9 (OTH.CHOLEST&TRIGLY.REGUL)	0
49	Lipid Regulating	EZETIMIBE#SIMVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10C0 (LIP.REG.CO.W.OTHLIP.REG)	0
50	Lipid Regulating	FENOFIBRATE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A2 (FIBRATES)	0
51	Lipid Regulating	FISH	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
52	Lipid Regulating	FISH#SOYA LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
53	Lipid Regulating	FLUVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))	0
54	Lipid Regulating	GEMFIBROZIL	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A2 (FIBRATES)	1
55	Lipid Regulating	LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
56	Lipid Regulating	LECITHIN#SOYA LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
57	Lipid Regulating	NICOTINIC ACID	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A9 (OTH.CHOLEST&TRIGLY.REGUL)	1
58	Lipid Regulating	PITAVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))	0
59	Lipid Regulating	PRAVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))	1
60	Lipid Regulating	PROBUCOL	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A9 (OTH.CHOLEST&TRIGLY.REGUL)	0
61	Lipid Regulating	PYRICARBATE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A9 (OTH.CHOLEST&TRIGLY.REGUL)	0
62	Lipid Regulating	ROSUVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))	0
63	Lipid Regulating	SALMON	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	1
64	Lipid Regulating	SIMVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))	1
65	Lipid Regulating	SOYA LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)	0
66	CANCER				
67	Antineoplastics	ALEMTUZUMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)	0
68	Antineoplastics	ALTRETAMINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	0

only listed in combo with lidocaine

listed as "calcitonic salmon" on NLEM

1	Antineoplastics	ASPARAGINASE	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)	0
	Antineoplastics	AZACITIDINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
	Antineoplastics	BEVACIZUMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)	0
2	Antineoplastics	BLEOMYCIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)	1
3	Antineoplastics	BORTEZOMIB	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)	0
	Antineoplastics	BUSULFAN	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	1
4	Antineoplastics	CAPECITABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
5	Antineoplastics	CARBOPLATIN	L1 (ANTINEOPLASTICS)	L1X2 (PLATINUM COMPOUNDS)	1
	Antineoplastics	CARMUSTINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	1
6	Antineoplastics	CETUXIMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)	0
7	Antineoplastics	CHLORAMBUCIL	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	1
	Antineoplastics	CHLORMETHINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	0
8	Antineoplastics	CISPLATIN	L1 (ANTINEOPLASTICS)	L1X2 (PLATINUM COMPOUNDS)	1
9	Antineoplastics	CLADRIBINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
	Antineoplastics	CYCLOPHOSPHAMIDE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	1
10	Antineoplastics	CYTARABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	1
11	Antineoplastics	DACARBAZINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	0
	Antineoplastics	DACTINOMYCIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)	1
12	Antineoplastics	DASATINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)	0
13	Antineoplastics	DECITABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
	Antineoplastics	DOCETAXEL	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)	0
14	Antineoplastics	DOXORUBICIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)	1
15	Antineoplastics	EPIDRUBICIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)	1
16	Antineoplastics	ERLOTINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)	0
	Antineoplastics	ETOPOSIDE	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)	1
17	Antineoplastics	FLUDARABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
18	Antineoplastics	FLUOROURACIL	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	1
	Antineoplastics	GEFITINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)	0
19	Antineoplastics	GEMCITABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
20	Antineoplastics	HYDROXYCARBAMIDE	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)	0
	Antineoplastics	IBRITUMOMAB TIUXETAN	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)	0
21	Antineoplastics	IDARUBICIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)	1
22	Antineoplastics	IPOSFAMIDE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	1
	Antineoplastics	IMATINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)	0
23	Antineoplastics	IRINOTECAN	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)	0
24	Antineoplastics	IXABEPILONE	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)	0
	Antineoplastics	LAPATINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)	0
25	Antineoplastics	LOMUSTINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	1
26	Antineoplastics	MELPHALAN	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	1
	Antineoplastics	MERCAPTOPURINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	1
27	Antineoplastics	METHOTREXATE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	1
	Antineoplastics	MITOMYCIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)	1
28	Antineoplastics	MITOXANTRONE	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)	0
29	Antineoplastics	NILOTINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)	0
	Antineoplastics	OXALIPLATIN	L1 (ANTINEOPLASTICS)	L1X2 (PLATINUM COMPOUNDS)	0
30	Antineoplastics	PACLITAXEL	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)	1
31	Antineoplastics	PEMETREXED	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
	Antineoplastics	PROCARBAZINE	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)	1
32	Antineoplastics	RITUXIMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)	0
33	Antineoplastics	SORAFENIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)	0
	Antineoplastics	SUNITINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)	0
34	Antineoplastics	TEGAFUR	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
35	Antineoplastics	TEGAFUR#URACIL	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	1
36	Antineoplastics	TEMOZOLOMIDE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)	0
	Antineoplastics	TIOGUANINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)	0
37	Antineoplastics	TOPOTECAN	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)	0
38	Antineoplastics	TRASTUZUMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)	0
	Antineoplastics	TRETINOIN	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)	0
39	Antineoplastics	VINBLASTINE	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)	1
40	Antineoplastics	VINCRIStINE	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)	1
	Antineoplastics	VINORELBINE	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)	0
41	Cytostatic Hormones	AMINOGLUTETHIMIDE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)	0
	Cytostatic Hormones	ANASTROZOLE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)	0
42	Cytostatic Hormones	BICALUTAMIDE	L2 (CYTOSTATIC HORMONE THER)	L2B2 (CYTO ANTI-ANDROGENS)	0
43	Cytostatic Hormones	BUSERELIN	L2 (CYTOSTATIC HORMONE THER)	L2A3 (CYTO GONAD HORMON ANALOG)	1
44	Cytostatic Hormones	CYPROTERONE	L2 (CYTOSTATIC HORMONE THER)	L2B2 (CYTO ANTI-ANDROGENS)	1
	Cytostatic Hormones	EXEMESTANE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)	0
45	Cytostatic Hormones	FLUTAMIDE	L2 (CYTOSTATIC HORMONE THER)	L2B2 (CYTO ANTI-ANDROGENS)	1
46	Cytostatic Hormones	FORMESTANE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)	1

1	Cytostatic Hormones	FULVESTRANT	L2 (CYTOSTATIC HORMONE THER)	L2B9 (OTH CYTO HORMON ANTAGIST)	0
2	Cytostatic Hormones	GOSERELIN	L2 (CYTOSTATIC HORMONE THER)	L2A3 (CYTO GONAD HORMON ANALOG)	1
3	Cytostatic Hormones	LETROZOLE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)	0
4	Cytostatic Hormones	LEUPRORELIN	L2 (CYTOSTATIC HORMONE THER)	L2A3 (CYTO GONAD HORMON ANALOG)	1
5	Cytostatic Hormones	MEDROXYPROGESTERONE	L2 (CYTOSTATIC HORMONE THER)	L2A2 (CYTOSTATIC PROGESTOGENS)	0
6	Cytostatic Hormones	MEGESTROL	L2 (CYTOSTATIC HORMONE THER)	L2A2 (CYTOSTATIC PROGESTOGENS)	1
7	Cytostatic Hormones	TAMOXIFEN	L2 (CYTOSTATIC HORMONE THER)	L2B1 (CYTO ANTI-OESTROGENS)	1
8	Cytostatic Hormones	TOREMIFENE	L2 (CYTOSTATIC HORMONE THER)	L2B1 (CYTO ANTI-OESTROGENS)	0
9	Cytostatic Hormones	TRIPTORELIN	L2 (CYTOSTATIC HORMONE THER)	L2A3 (CYTO GONAD HORMON ANALOG)	0
10	Immunostimulating Agents	FILGRASTIM	L3 (IMMUNOSTIMULATING AGENTS)	L3A1 (COLONY-STIMULATING FACT.)	1
11	Immunostimulating Agents	INTERFERON ALFA	L3 (IMMUNOSTIMULATING AGENTS)	L3B1 (INTERFERONS ALPHA)	0
12	Immunostimulating Agents	INTERFERON ALFA-2A	L3 (IMMUNOSTIMULATING AGENTS)	L3B1 (INTERFERONS ALPHA)	0
13	Immunostimulating Agents	INTERFERON ALFA-2B	L3 (IMMUNOSTIMULATING AGENTS)	L3B1 (INTERFERONS ALPHA)	0
14	Immunostimulating Agents	INTERFERON ALFA-N1	L3 (IMMUNOSTIMULATING AGENTS)	L3B1 (INTERFERONS ALPHA)	0
15	Immunostimulating Agents	INTERFERON BETA-1A	L3 (IMMUNOSTIMULATING AGENTS)	L3B2 (INTERFERONS BETA)	0
16	Immunostimulating Agents	INTERFERON BETA-1B	L3 (IMMUNOSTIMULATING AGENTS)	L3B2 (INTERFERONS BETA)	0
17	Immunostimulating Agents	LENOGRASTIM	L3 (IMMUNOSTIMULATING AGENTS)	L3A1 (COLONY-STIMULATING FACT.)	1
18	Immunostimulating Agents	MOLGRAMOSTIM	L3 (IMMUNOSTIMULATING AGENTS)	L3A1 (COLONY-STIMULATING FACT.)	1
19	Immunostimulating Agents	PEGFILGRASTIM	L3 (IMMUNOSTIMULATING AGENTS)	L3A1 (COLONY-STIMULATING FACT.)	0
20	Immunostimulating Agents	TETRACHLORODECAOXIDE	L3 (IMMUNOSTIMULATING AGENTS)	L3A9 (OTH.IMMUNOSTIM.EX.INTFRN)	0
21	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					
<u>Insulins</u>					
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)	-
<u>Antidiabetics</u>					
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					
<u>Antihypertensives</u>					
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)	-
<u>Lipid Regulating Agents</u>					
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)	-
<u>Cardiac Therapy</u>					
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					
<u>Antineoplastics</u>					
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)
<u>Cytostatic Hormones</u>					
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)
<u>Immunostimulating Agents</u>					
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 better 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	TIME 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)	-
Antihypertensives (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., $p < 0.05$)

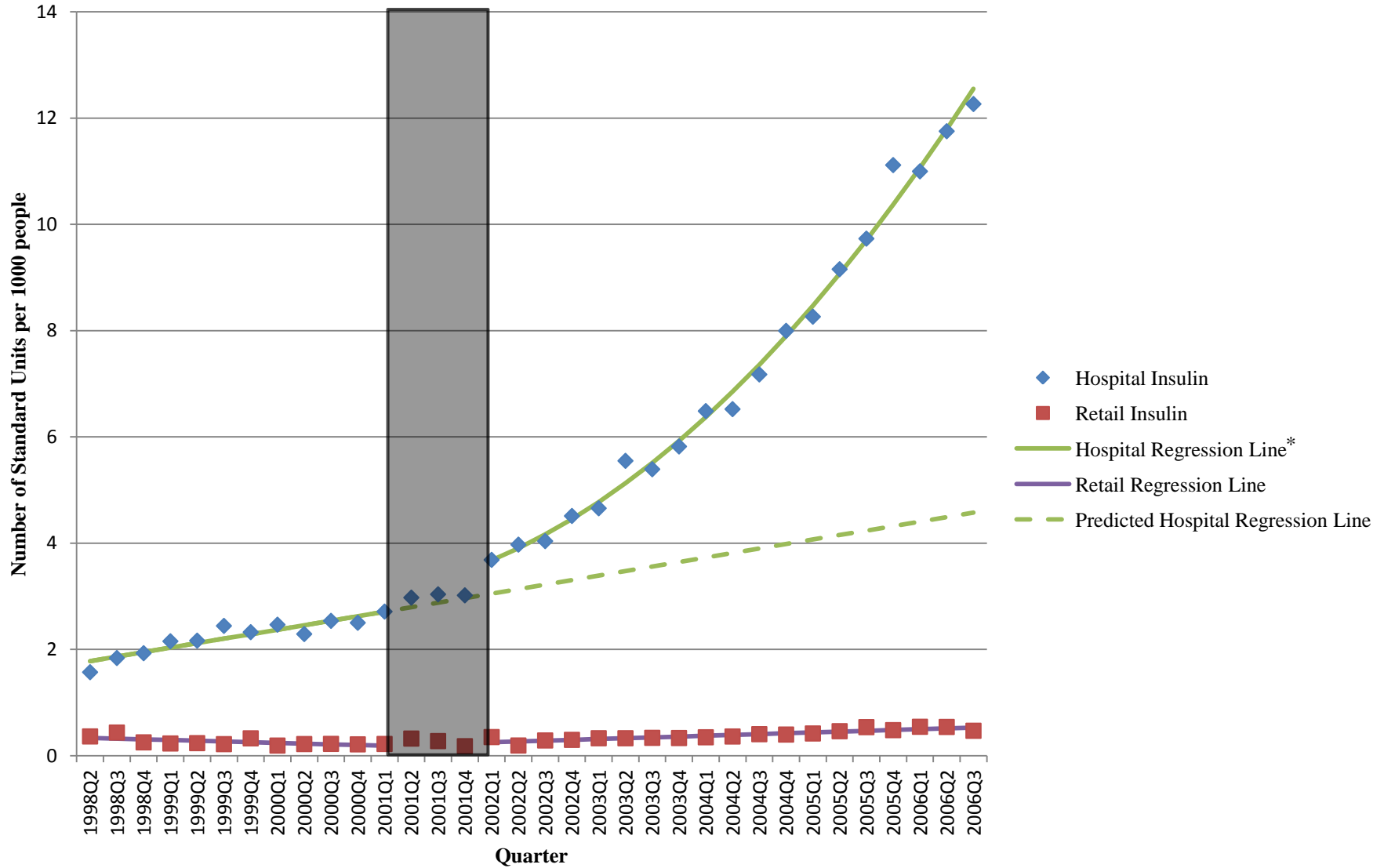
**Results from quadratic model (which has squared post-policy trend term) were included if quadratic model fits better than linear model.

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)

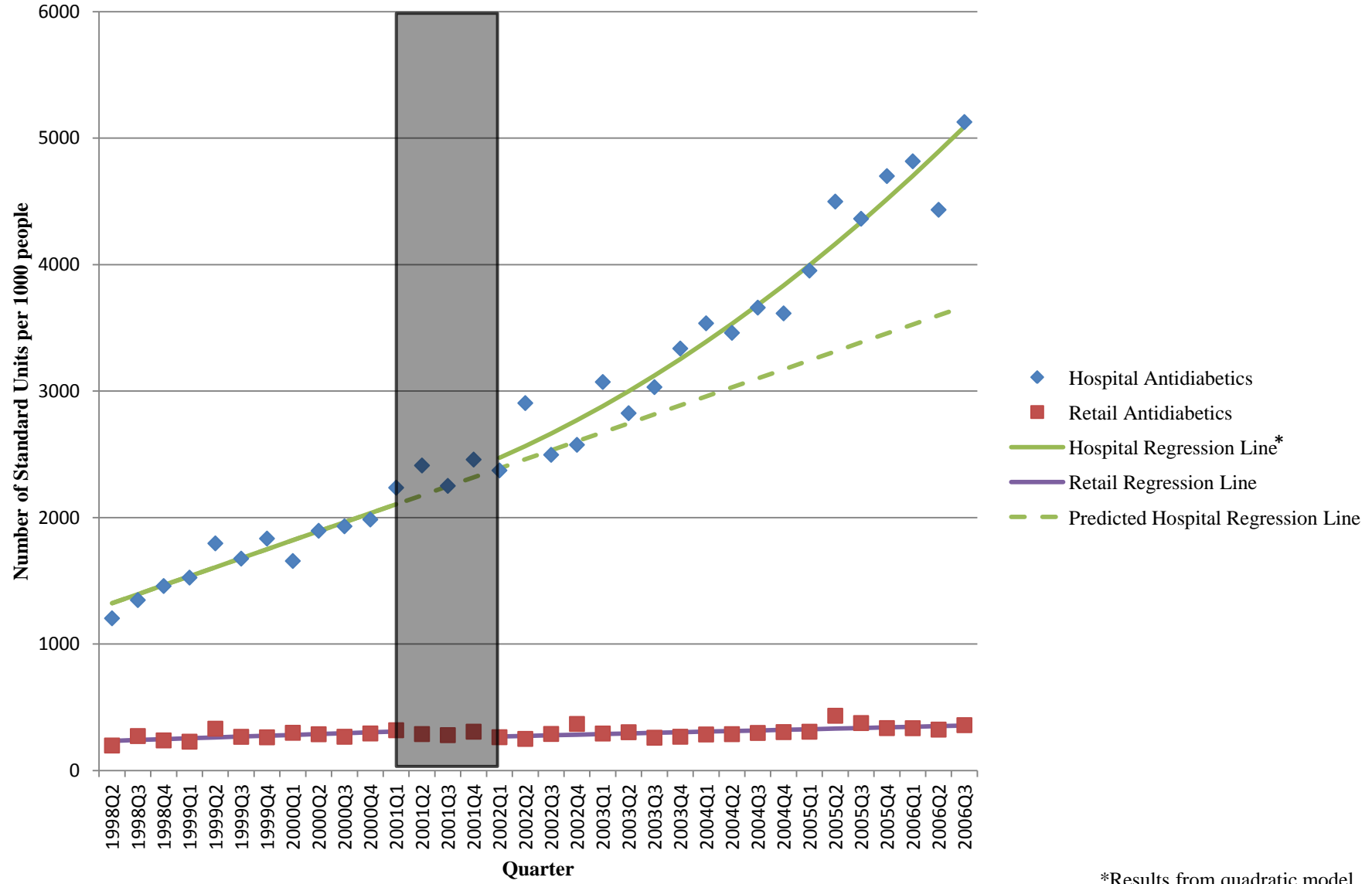
*bold signifies that change is statistically significant (i.e., confidence interval does not include the null value of 0)

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



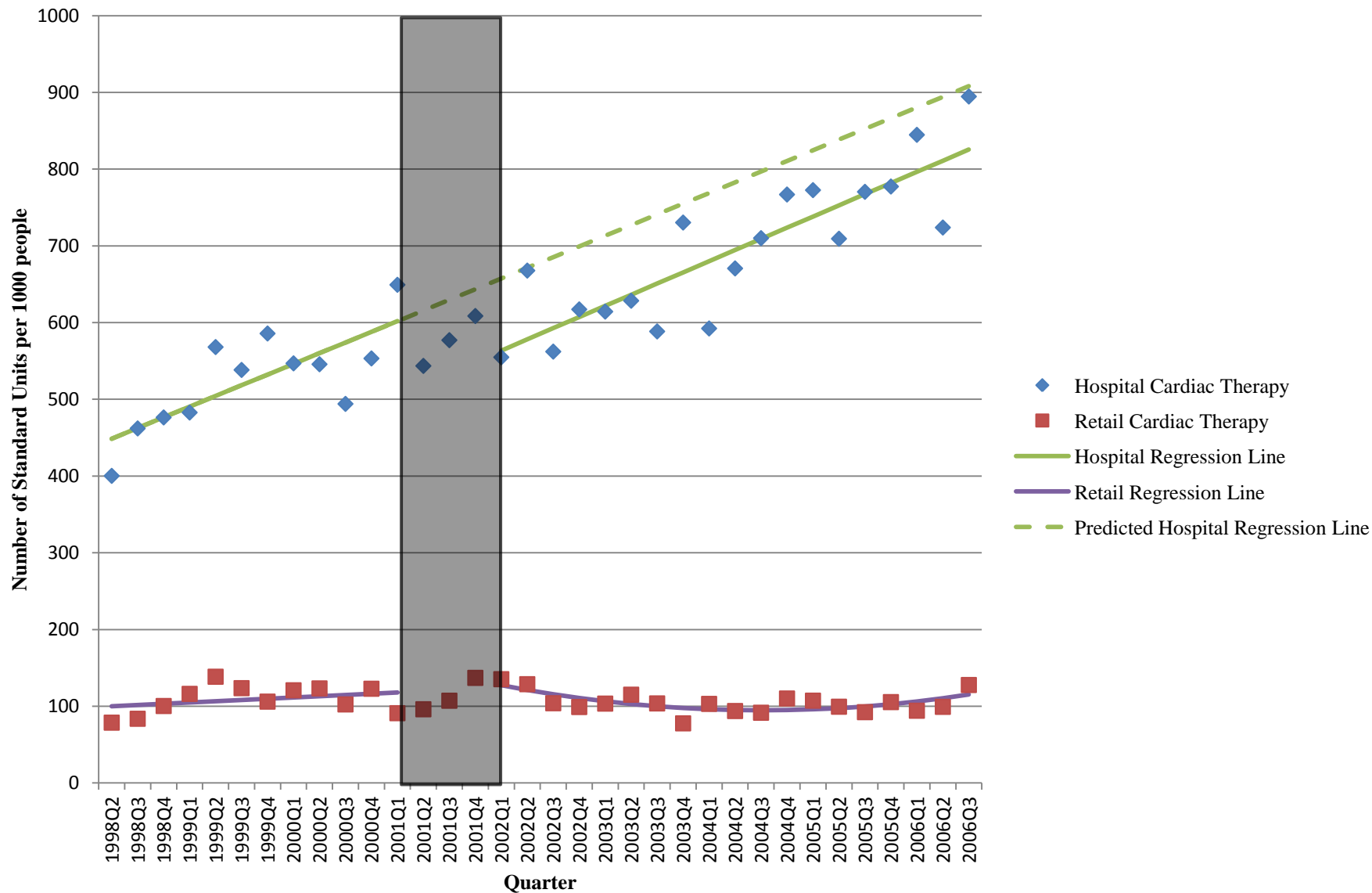
*Results from quadratic model

Appendix Figure 2. Standard Units Per Capita by Quarter Antidiabetics (Hospital vs. Retail)

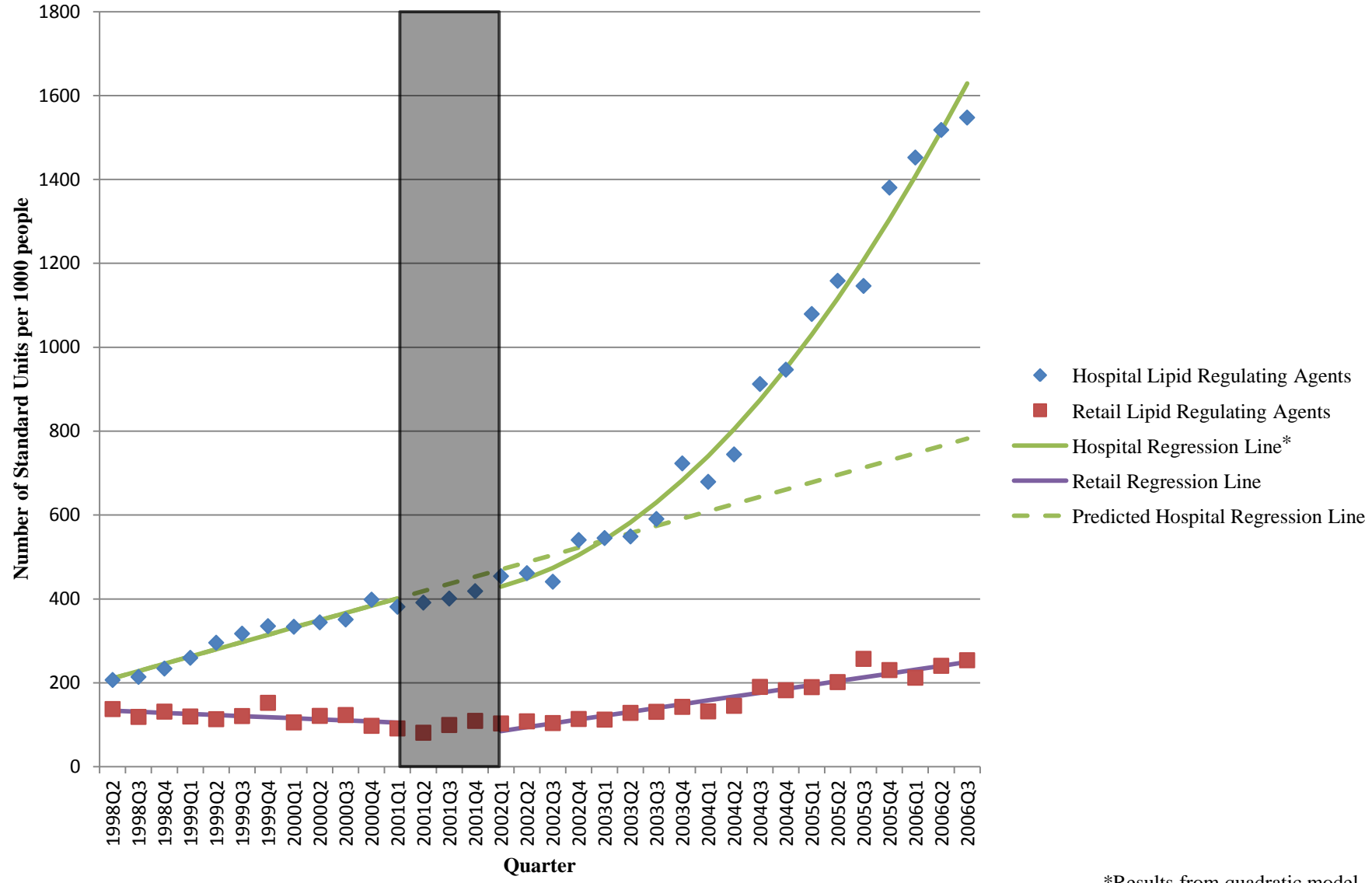


*Results from quadratic model

Appendix Figure 3. Standard Units Per Capita by Quarter
Cardiac Therapy (Hospital vs. Retail)

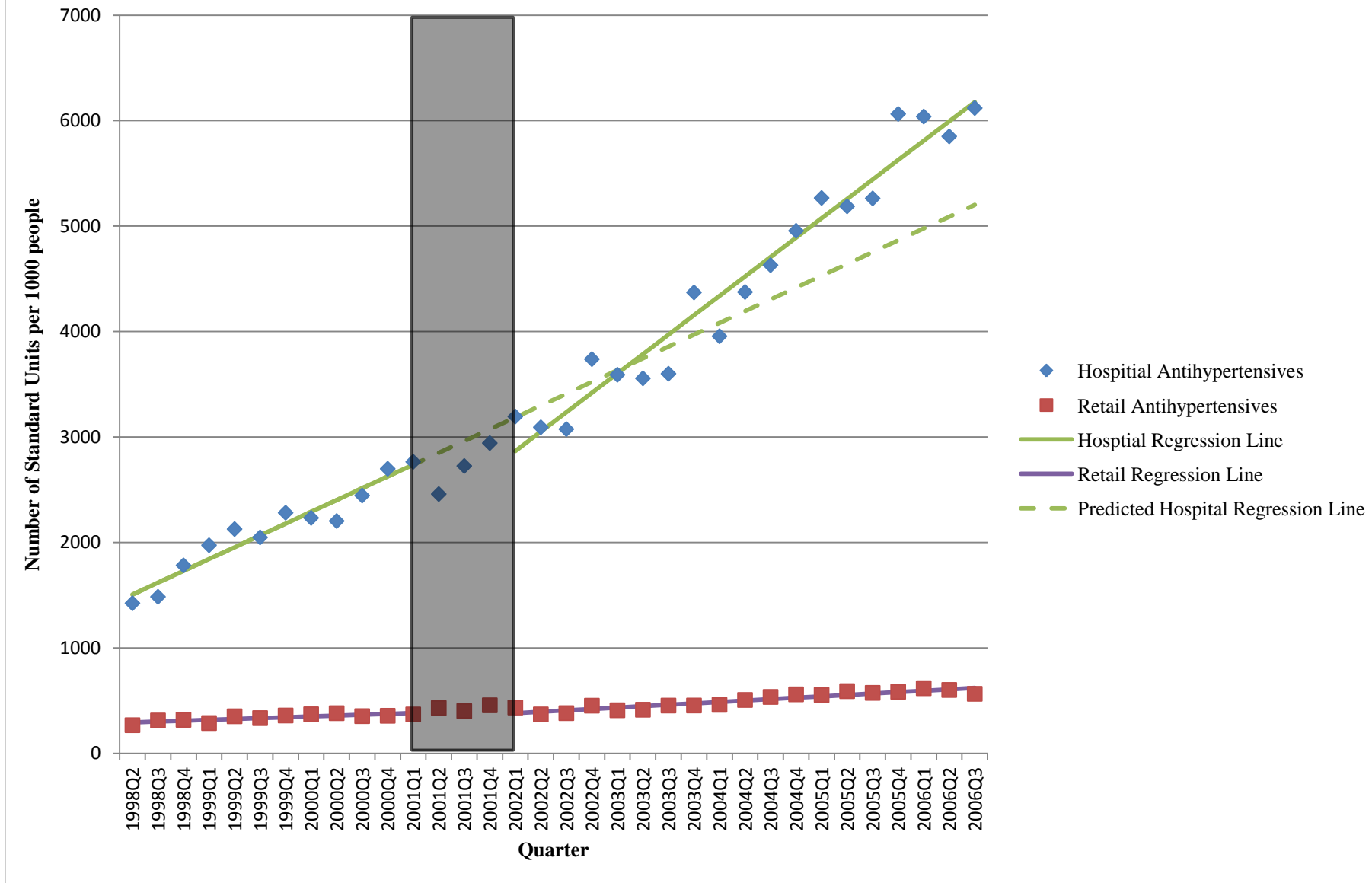


Appendix Figure 4. Standard Units Per Capita by Quarter Lipid Regulating Agents (Hospital vs. Retail)

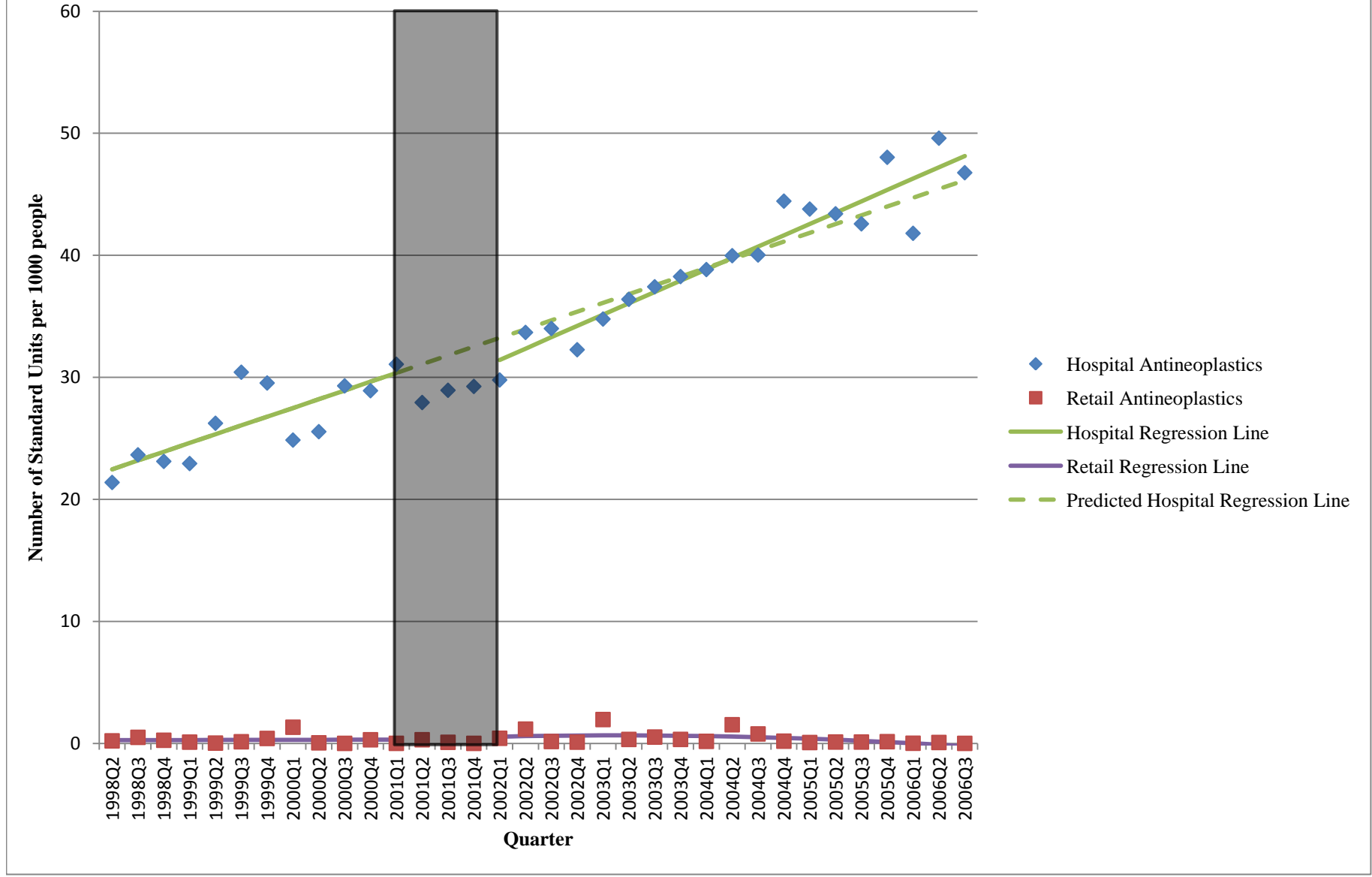


*Results from quadratic model

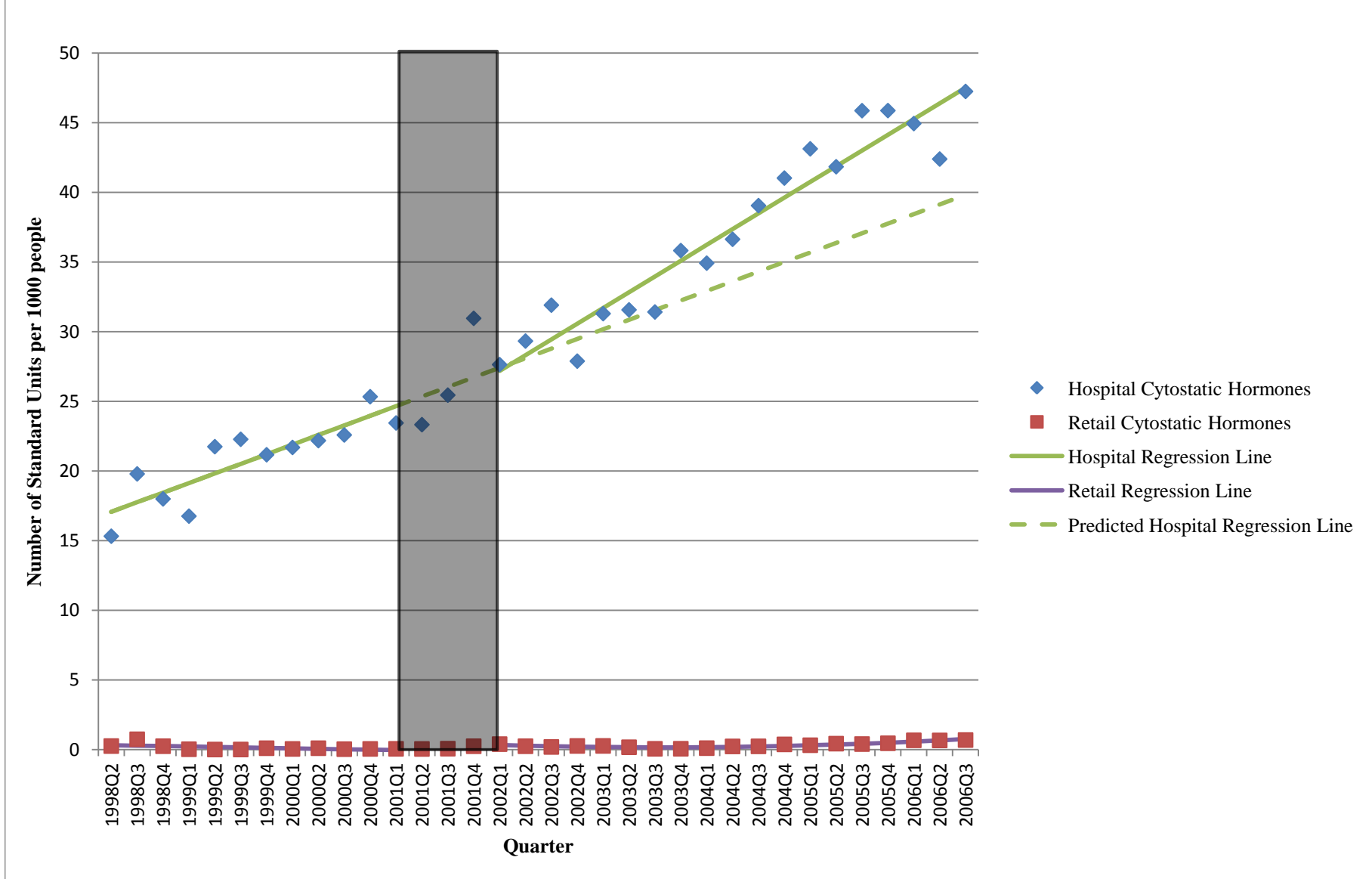
Appendix Figure 5. Standard Units Per Capita by Quarter
Antihypertensives (Hospital vs. Retail)



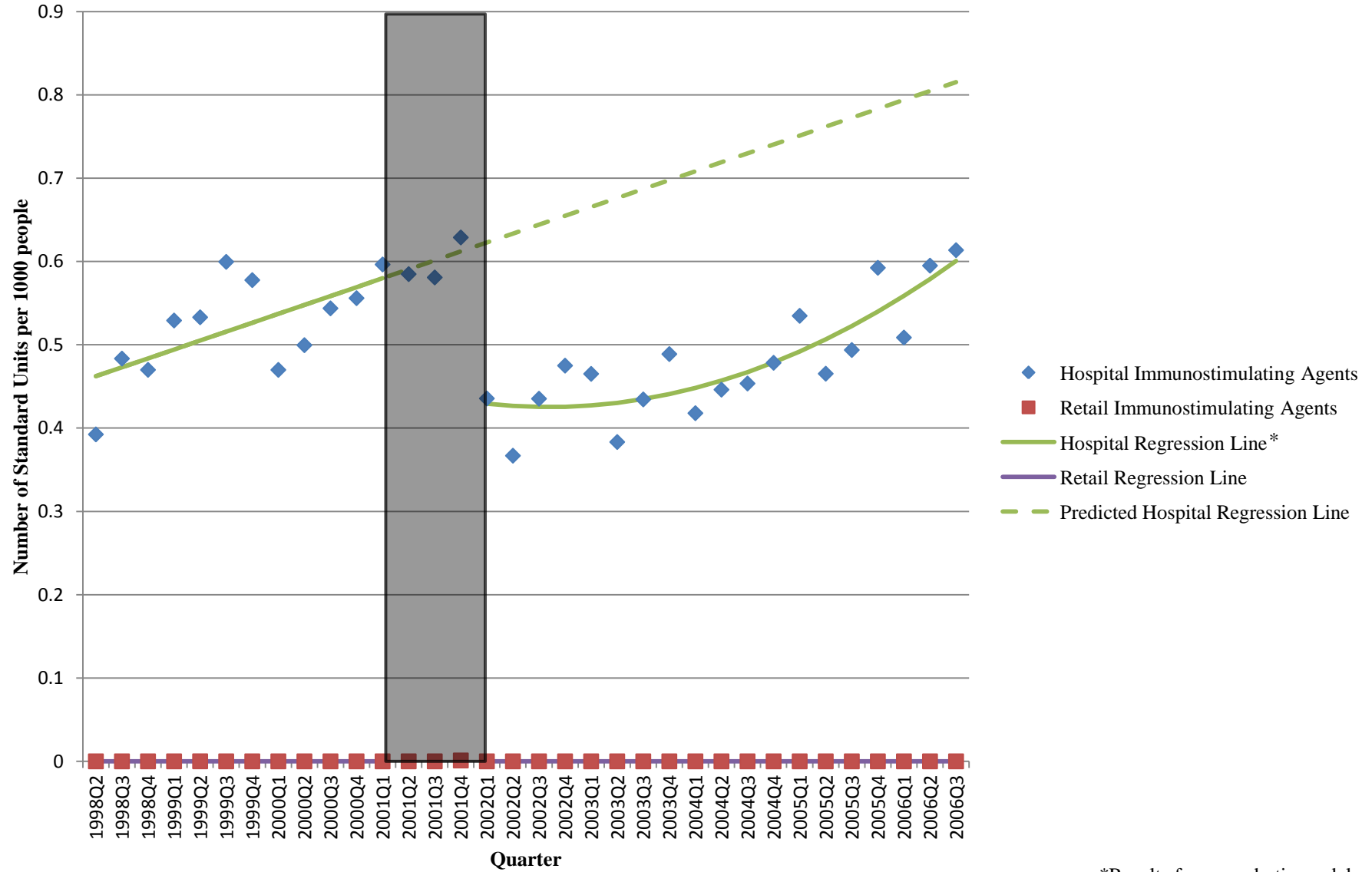
Appendix Figure 6. Standard Units Per Capita by Quarter Antineoplastics (Hospital vs. Retail)



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

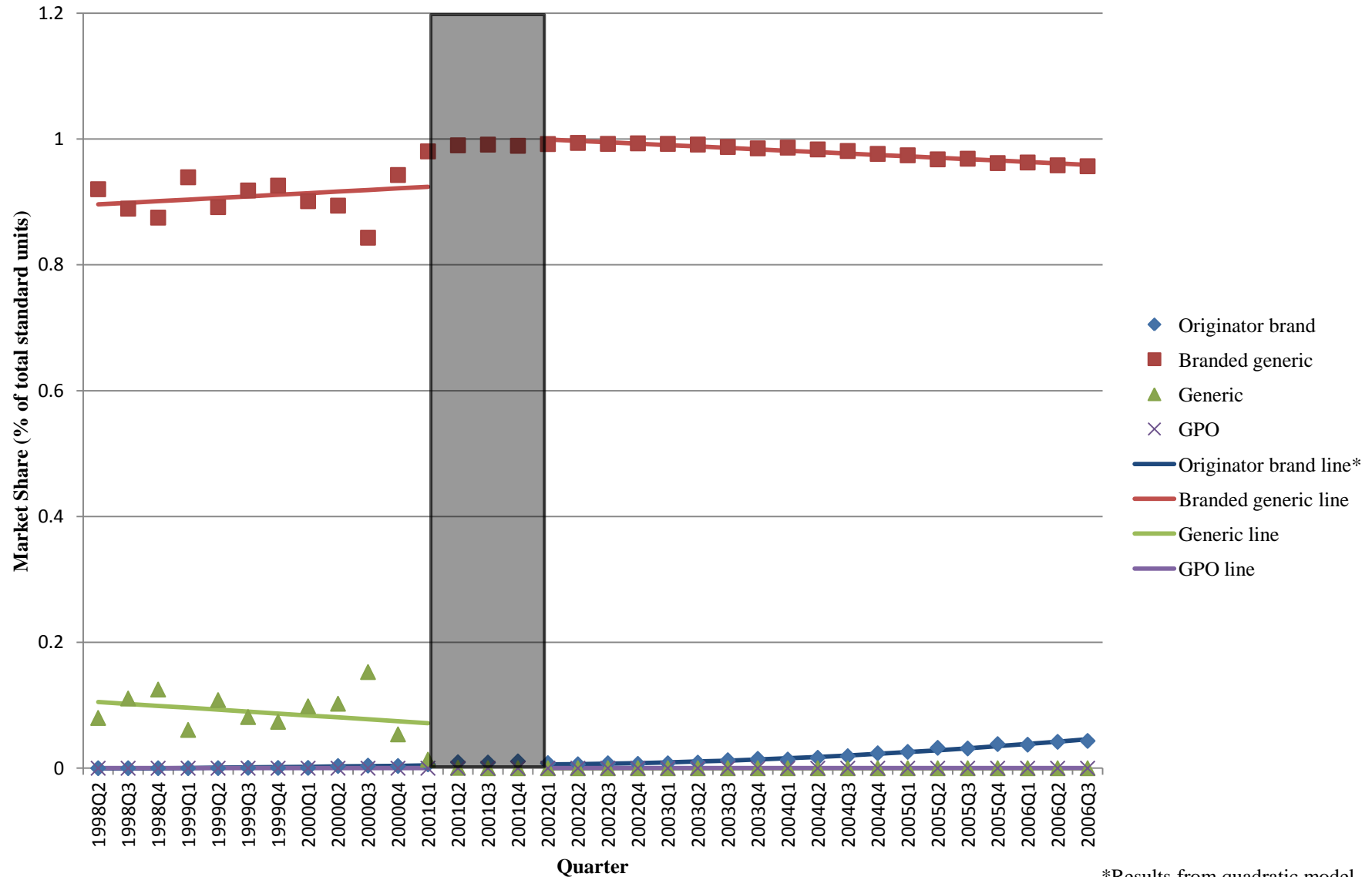


Appendix Figure 8. Standard Units Per Capita by Quarter Immunostimulating Agents (Hospital vs. Retail)



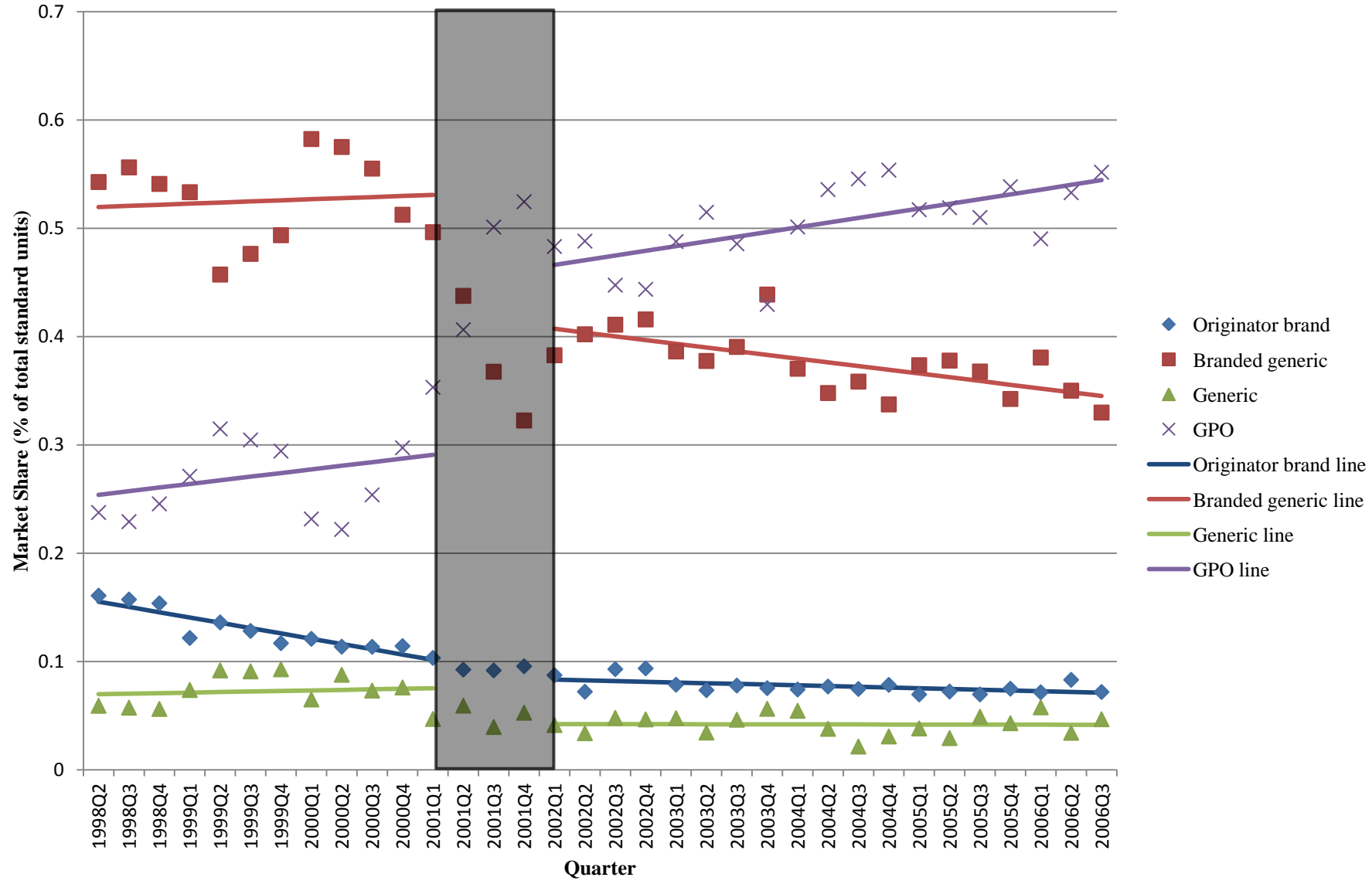
*Results from quadratic model

Appendix Figure 9. Licensing Status Market Share by Quarter
Insulin (Hospital Sector)

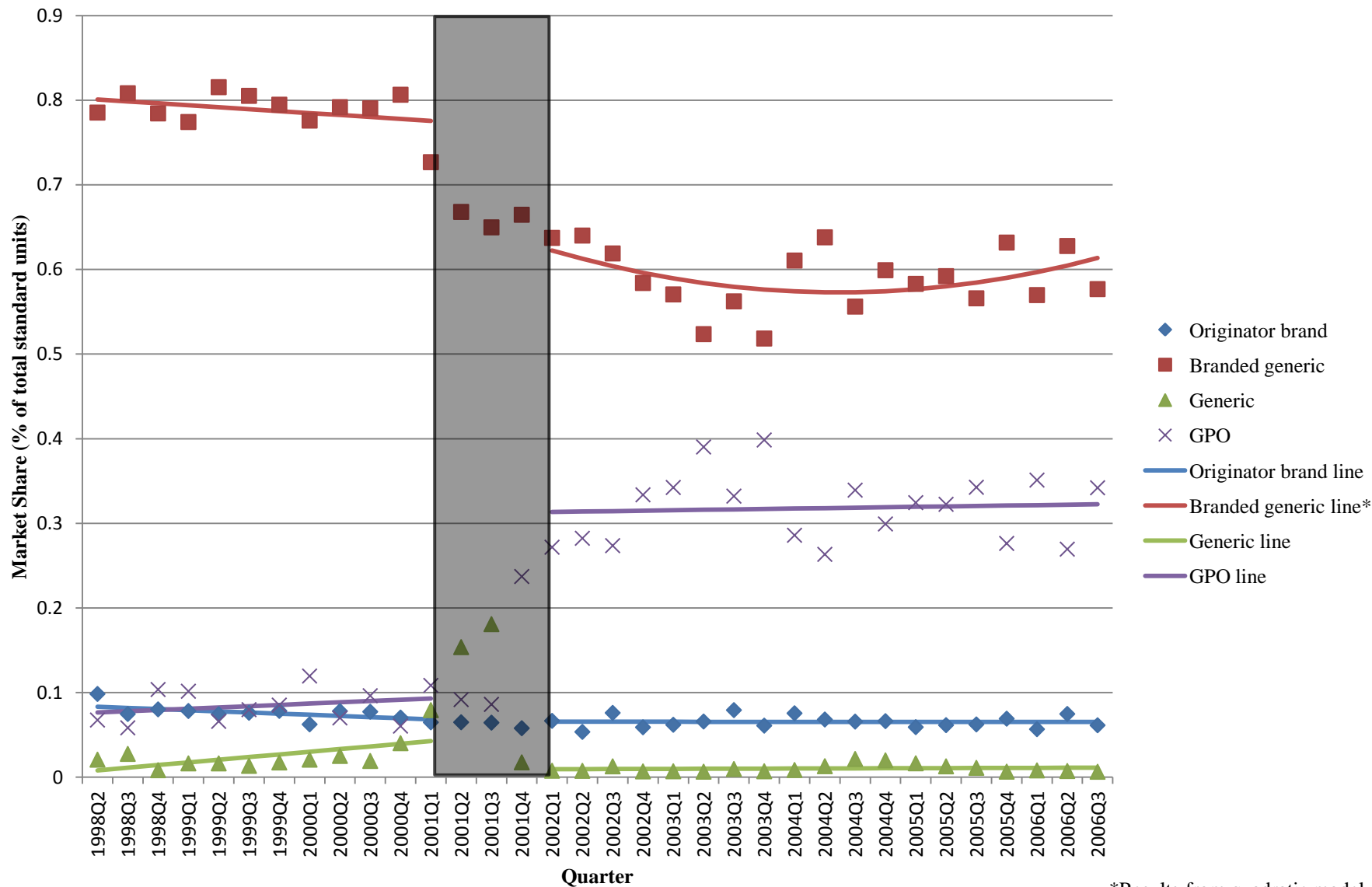


*Results from quadratic model

Appendix Figure 10. Licensing Status Market Share by Quarter
Antidiabetics (Hospital Sector)

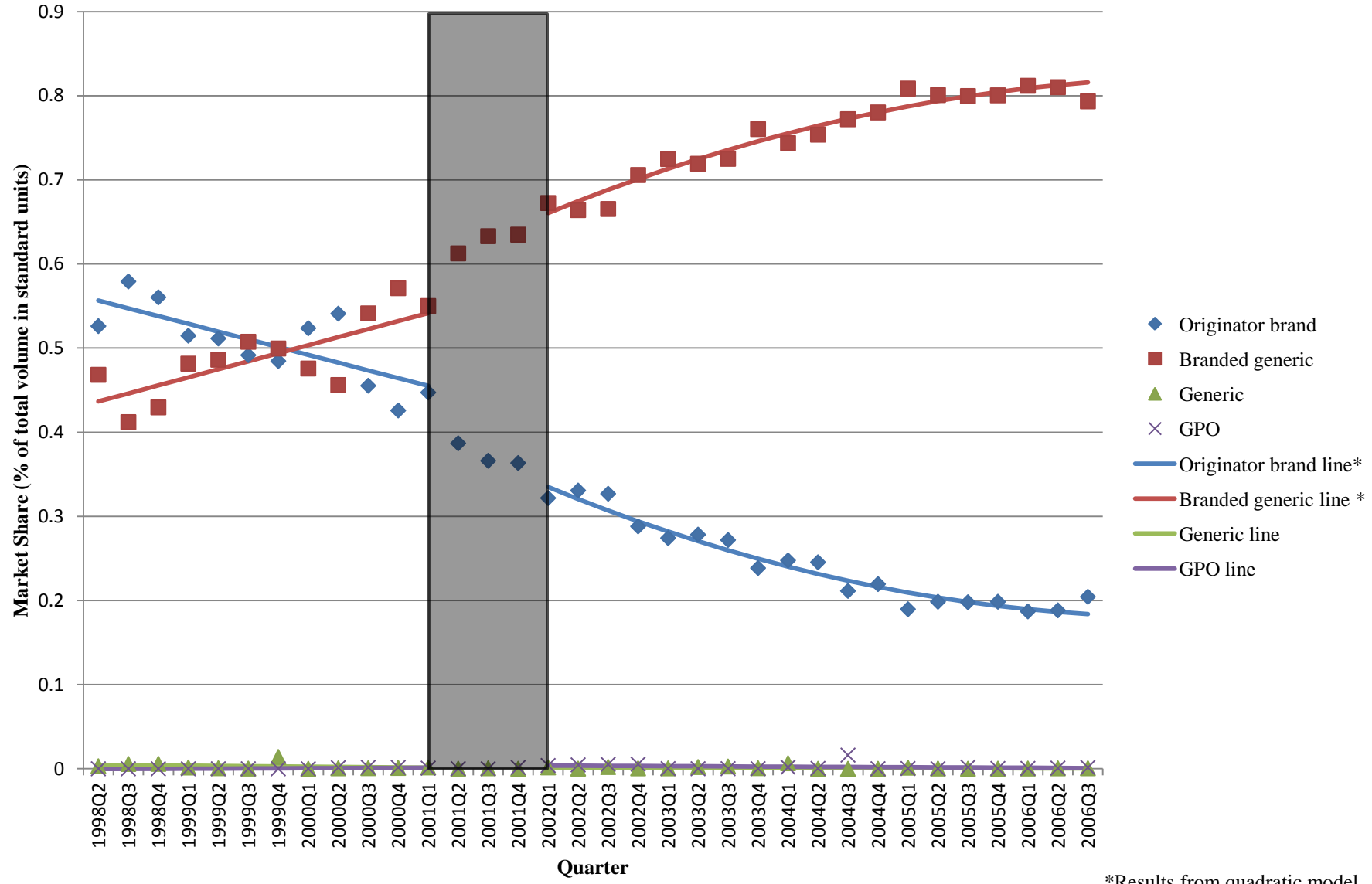


Appendix Figure 11. Licensing Status Market Share by Quarter
Cardiac Therapy Agents (Hospital Sector)



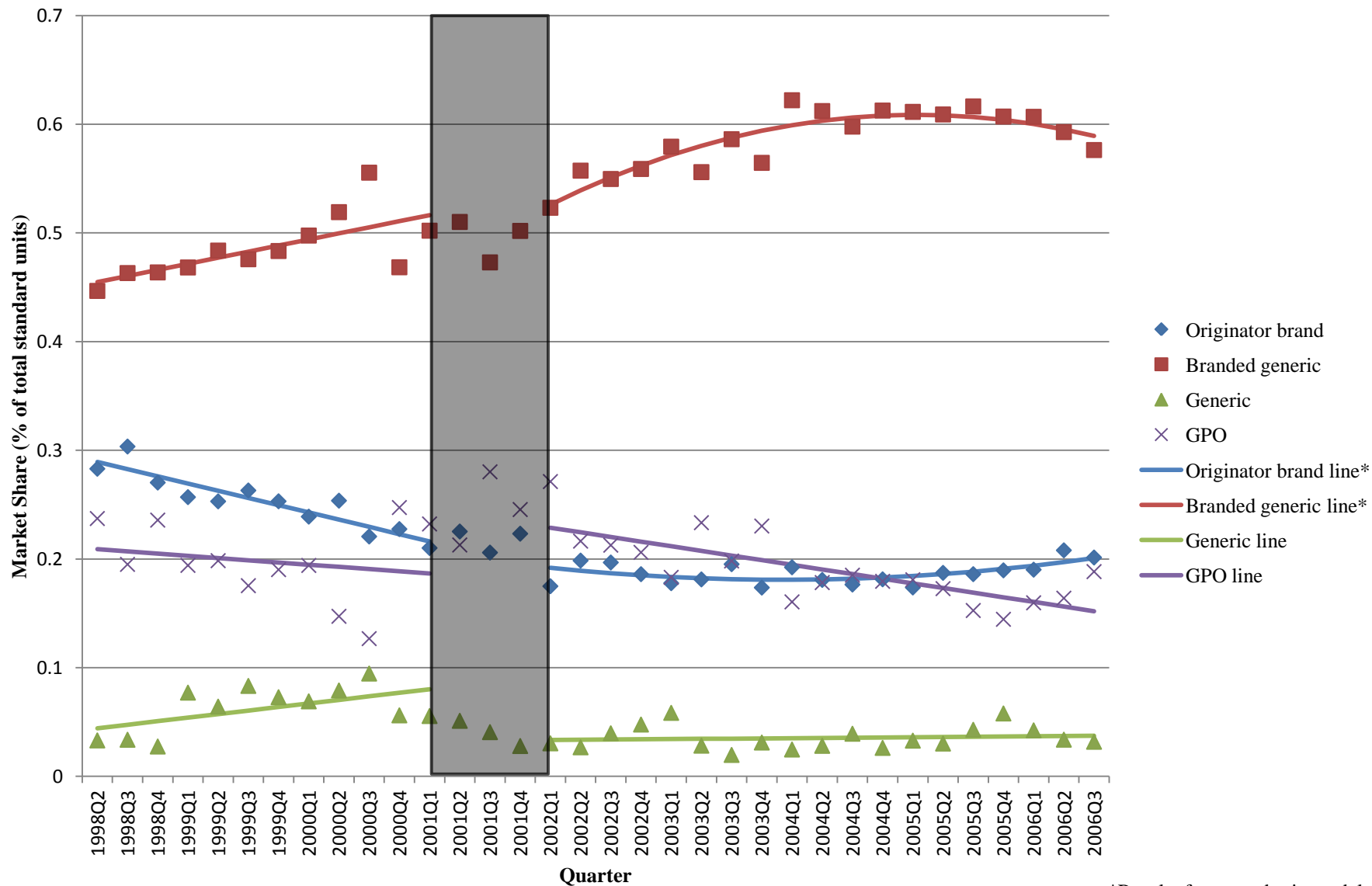
*Results from quadratic model

Appendix Figure 12. Licensing Status Market Share by Quarter Lipid Regulating Agents (Hospital Sector)



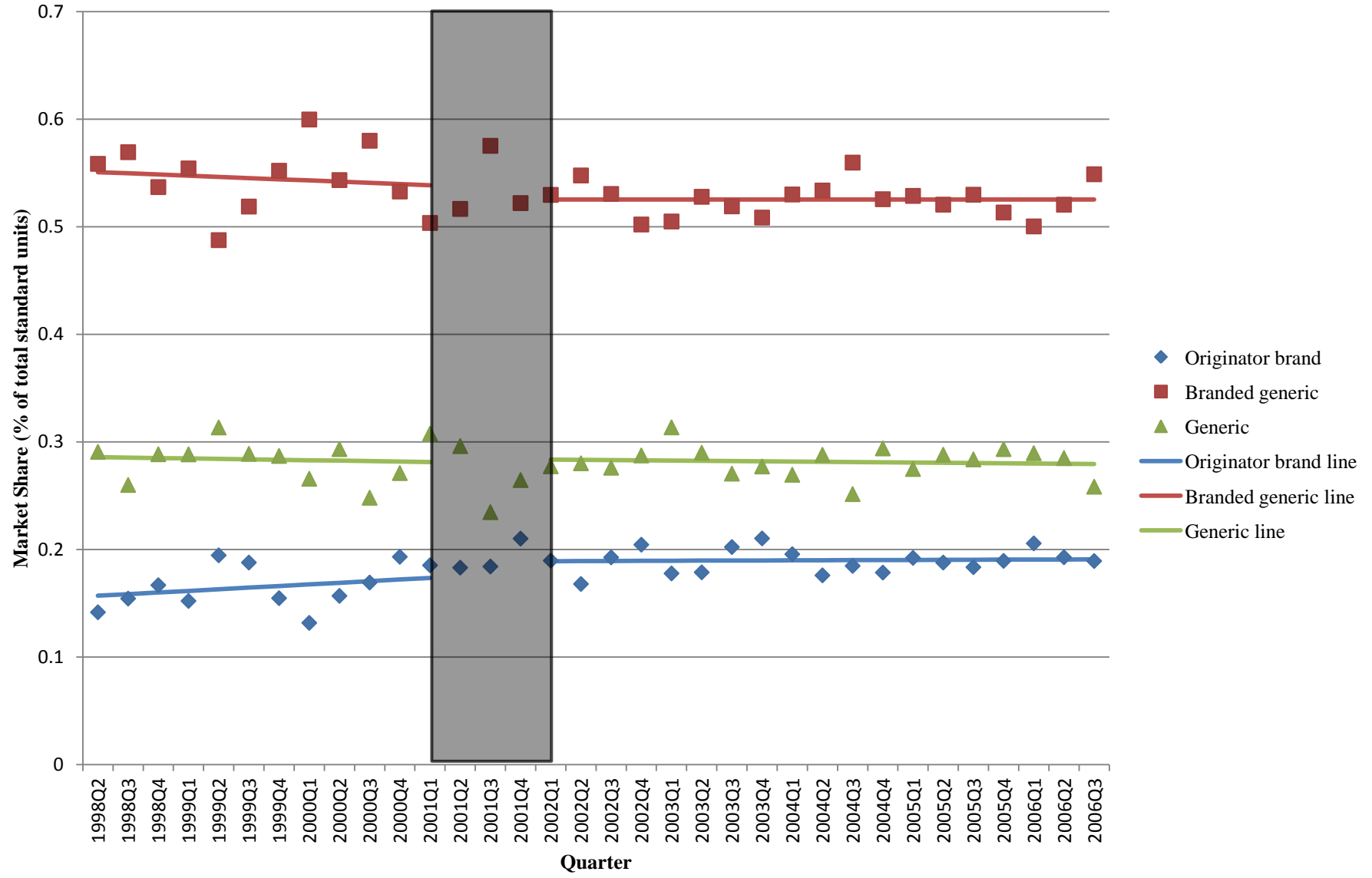
*Results from quadratic model

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

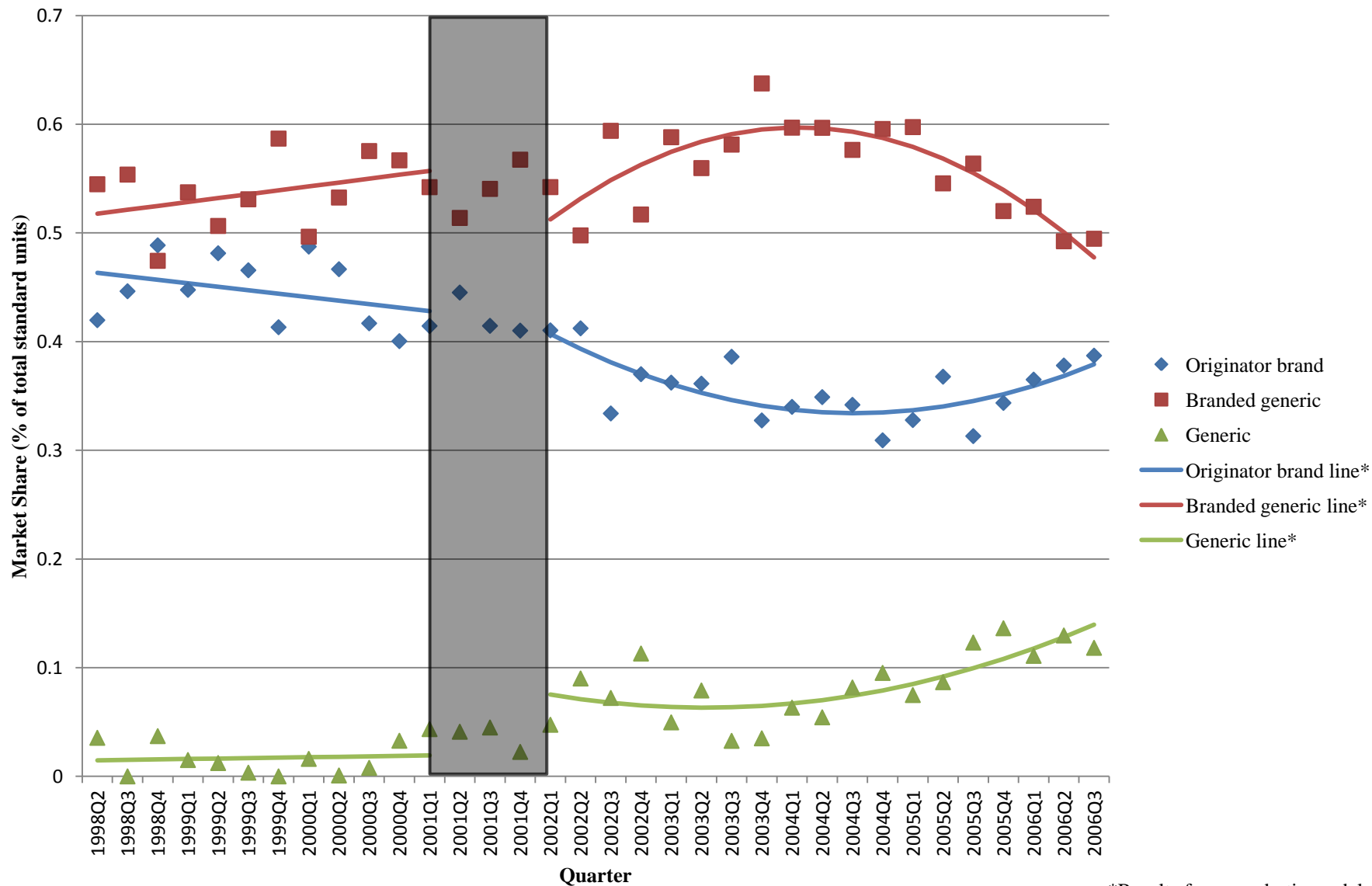


*Results from quadratic model

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

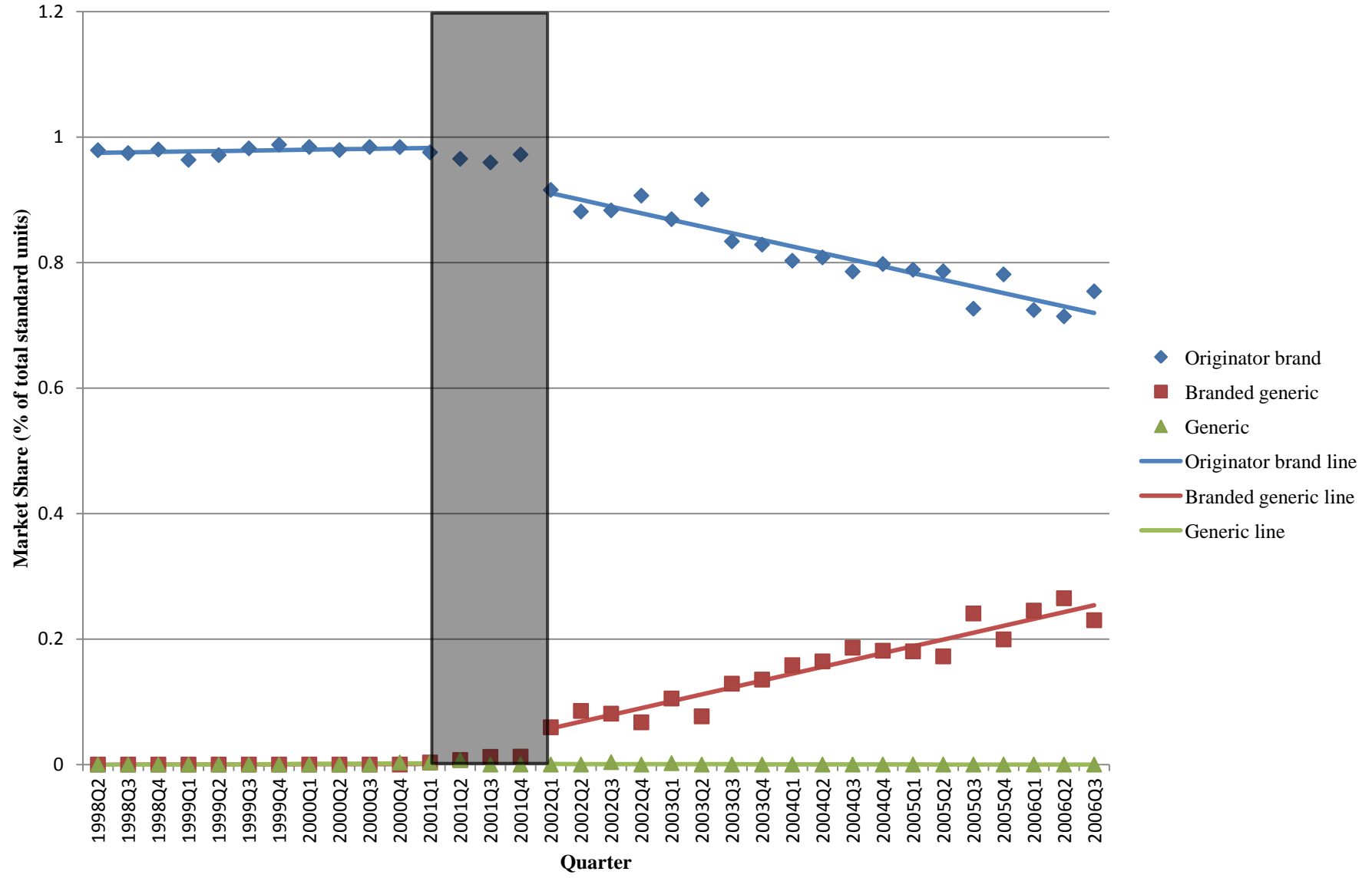


Appendix Figure 15. Licensing Status Market Share by Quarter
Cytostatic Hormones (Hospital Sector)



*Results from quadratic model

Appendix Figure 16. Licensing Status Market Share by Quarter
Immunostimulating Agents (Hospital Sector)



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 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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case 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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed

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Case-control study—If applicable, explain how matching of cases and controls was addressed

Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy

(e) Describe any sensitivity analyses

Continued on next page

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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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount) NOTE: We give the characteristics of the therapeutic classes (i.e., number subclasses, medicines within each subclass).
Outcome data	15*✓	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures 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-
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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

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

3
4 Opinions expressed are solely those of the authors and not of the institutions they represent.

5
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17 access to medicines using IMS Health data for presentation at the Third International Conference
18 for Improving Use of Medicines.

19
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30 located; and, vi) licence any third party to do any or all of the above.

31
32 **Data Sharing Statement:** Data available upon request, at the approval of IMS Institute for
33 Healthcare Informatics.

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3 1 **Article Summary**
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5 2 **Article Focus**
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- 7 3 • Medicines present a key challenge to achieving universal coverage.
8 4 • Health insurance systems have the potential to improve cost-effective use of medicines,
9 5 yet there is little evidence about their impact on medicine use in low- and middle-income
10 6 countries.
11 7 • The rapid implementation of universal health coverage in Thailand presents a unique
12 8 opportunity to measure the impact of health insurance expansion and capitated payment
13 9 on utilization of medicines.
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16
17 10 **Key Messages**
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- 19 11 • Expanding health insurance coverage with a medicines benefit to the entire Thai
20 12 population increased access to medicines in primary care.
21 13 • The universal coverage scheme did not seem to have increased use of medicines for
22 14 diseases that are typically treated in secondary or tertiary care settings, or increased
23 15 generic market penetration.
24 16 • In the future, it will be important for countries to assess quality and equity of medicines
25 17 use as they pursue policies to achieve universal coverage.
26
27

28 18 **Strengths and Limitations**
29

- 30 19 • We used an interrupted time series design, the strongest quasi-experimental approach for
31 20 evaluating effects of interventions, increasing internal validity.
32 21 • It is impossible to examine population subgroups in national IMS Health market data, but
33 22 we are reasonably confident that universal coverage scheme enrollees are responsible for
34 23 observed changes.
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3 **1 ABSTRACT**
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5 **2 Objective:** In 2001, Thailand implemented the Universal Coverage Scheme (UCS), a public
6 insurance system that aimed to achieve universal access to health care, including essential
7 medicines, and to influence primary care centers and hospitals to use resources efficiently, via
8 capitated payment for outpatient services and other payment policies for inpatient care. Our
9 objective was to evaluate the impact of the UCS on utilization of medicines in Thailand for three
10 non-communicable diseases: cancer, cardiovascular disease, and diabetes.
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12

13 **3 Design:** Interrupted time series design, with a non-equivalent comparison group.
14

15 **4 Setting:** Thailand, 1998-2006.
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17 **5 Data:** Quarterly purchases of medicines from hospital and retail pharmacies collected by IMS
18 Health between 1998 and 2006.
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20 **6 Intervention:** UCS implementation, April-October 2001.
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22 **7 Outcome measures:** Total pharmaceutical sales volume and percent market share by licensing
23 status and National Essential Medicine List (NEML) status.
24

25 **8 Results:** The UCS was associated with long-term increases in sales of medicines for conditions
26 that are typically treated in outpatient primary care settings, such as diabetes, high cholesterol
27 and high blood pressure, but not for medicines for diseases that are typically treated in secondary
28 or tertiary care settings, such as heart failure, arrhythmias, and cancer. While the majority of
29 increases in sales were for essential medicines, there were also post-policy increases in sales of
30 non-essential medicines. Immediately following the reform, there was a significant shift in
31 hospital sector market share by licensing status for most classes of medicines. Government-
32 produced products often replaced branded generic or generic competitors.
33

34 **9 Conclusions:** Our results suggest that expanding health insurance coverage with a medicines
35 benefit to the entire Thai population increased access to medicines in primary care. However, our
36 study also suggests that the UCS may have had potentially undesirable effects. Evaluations of the
37 long-term impacts of universal health coverage on medicines utilization are urgently needed.
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3 1 **MANUSCRIPT**
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6 2 **Introduction**
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8 3 *Universal Health Coverage*
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10 4 In 2005, Member States of the World Health Organization (WHO) made a commitment to work
11 5 towards universal health care coverage.¹ The 2010 WHO World Health Report provides a
12 6 roadmap for countries to achieve this goal.² Universal coverage requires the restructuring of
13 7 health care and financing systems to improve access to health care services, reduce financial
14 8 hardship, and increase the efficiency and equity of the health system.²
15 9

16 10 Medicines, which consume 25%–65% of total public and private spending on health in
17 11 developing countries,³ present a key challenge to achieving universal coverage. The high
18 12 spending on, and inefficient use of, medicines threaten the financial sustainability of a universal
19 13 coverage scheme. According to the WHO, three of the top ten sources of health care inefficiency
20 14 involve medicines: high medicine prices and underuse of generics; use of substandard and
21 15 counterfeit medicines; and inappropriate and ineffective use of medicines.² Health insurance
22 16 systems have several features (e.g., a defined population, access to utilization data, and financial
23 17 leverage) that give them a unique advantage to reduce out-of-pocket (OOP) expenditures and
24 18 improve the cost-effective use of medicines through active management strategies involving
25 19 medicines selection, purchasing, contracting (e.g., physician payment) and utilization
26 20 management.⁴ However, there is little evidence about the impact of health insurance on access to
27 21 and use of medicines in low- and middle-income countries (LMICs).⁴
28 22

29 23 The recent implementation of universal health coverage in Thailand presents a unique
30 24 opportunity to measure the impact of health insurance expansion and hospital payment changes
31 25 (the majority of the population is now covered under a closed-ended payment scheme⁵) on
32 26 utilization of medicines.
33 27

34 28 *Universal Health Coverage in Thailand*
35 29

36 30 With the implementation of the UCS in 2001, Thailand became one of the first LMICs to achieve
37 31 universal coverage.^{6,7} The reform preserved the formal sector workforce schemes: the Social
38 32 Health Insurance (SHI) scheme for private sector employees (7.2% of the total population in
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3 1 2001) and the Civil Service Medical Benefit Scheme (CSMBS) for government employees and
4 their dependents (8.5%).⁸ The UCS covered those previously enrolled in a voluntary health card
5 (VHC) scheme (20.8%), in private health insurance (2.1%), or in a tax-based, means-tested Low
6 Income Scheme (LIS) for the poor, elderly, children and disabled (32.4%)^{8,9} as well as more than
7 one quarter (29.0%) of the population without previous insurance.⁸ The UCS was rolled out to all
8 provinces between April and October 2001.⁶ By 2004, 95.5% of the population was insured, with
9 three-quarters (75.2%) of the population covered by the UCS.⁶

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12 9 In addition to coverage expansion, the reform also dramatically altered the mechanism for
13 hospital payment. Before the reform, hospitals were accustomed to fee-for-service (FFS)
14 payments from most insurance schemes, aside from SSI, and the uninsured, who paid OOP per
15 service (i.e., user fees).¹⁰ The majority of user fee spending was on medicines.¹¹ After the
16 reform, FFS payment only applied to CSMBS patients and for the majority of patients, now UCS
17 enrollees, hospitals were paid on a closed-ended basis⁵ for all covered services, including
18 medicines.

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21 17 The UCS is a compulsory, tax-financed scheme with comprehensive coverage of inpatient and
22 outpatient services, including medicines on the National List of Essential Medicines (NLEM).⁶
23 Individuals must enroll in the scheme at a local Contracting Unit for Primary Care (CUP),⁶
24 primarily housed in government-owned hospitals.¹² Each CUP receives a capitated payment per
25 registered member to provide outpatient services and medicines.⁶ CUPs initially served as gate-
26 keepers for secondary and tertiary hospitals. At the beginning of the scheme, when patients were
27 referred, diagnosis-related payments (DRG) for higher-level care had to come out of the CUP's
28 capitated payment, so CUPs had a financial disincentive to refer patients.⁶ Shortly after the
29 reform was implemented, a separate fund (i.e., a global budget) for inpatient services was
30 created, which likely reduced disincentives to refer created by the capitated payment scheme.⁶ A
31 capitated payment also creates financial incentives for use of lower cost medicines (e.g., generics
or less expensive therapeutic alternatives).

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55 30 Our objective was to evaluate the immediate, short-term (one year) and long-term (five year)
56 impacts of the UCS on pharmaceutical market size and composition for medicines for three non-
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1 communicable diseases (NCDs): cancer, cardiovascular disease, and diabetes. We hypothesized
2 that the UCS would result in a gradual increase in sales volume, particularly of products used in
3 primary care, as enrollment into the scheme increased and likely made access to health services
4 and medicines more affordable for the majority of the population. We also hypothesized that
5 there would be an immediate shift in market share from more expensive brand name to less
6 expensive generic or branded generic products and to medicines on the NLEM in response to
7 closed-ended budget rules. We focused on medicines for NCDs since these illnesses represent a
8 large and growing health care burden in Thailand¹³⁻¹⁶ and other LMICs¹⁷ and most, but not all,
9 medicines for NCDs would be prescribed and dispensed in primary care settings.

10 **Methods**

11 ***Data***

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

22 ***Outcomes***

23 We used two outcome measures: total volume and percent market share. *Total volume* is the
24 number of standard units purchased per capita per quarter (i.e., “sales”). We analyzed total
25 volume by sector (i.e., retail versus hospital). A standard unit, as defined by IMS Health, is the
26 smallest dose of a product, which equates to one tablet or capsule for an oral dosage form, one
27 teaspoon (5ml) for a syrup, and one ampoule or vial for an injectable product. For the total
28 volume analyses, we divided total volume by size of the population over 15 years old to control
29 for population growth (using yearly population estimates from the World Bank²⁰). We used the
30 entire population as denominator for insulins, since they are also used for Type 1 diabetes, a
31 chronic disease that affects children. *Percent market share* is the percent of total volume in four

1 mutually exclusive categories of licensing status: originator brand products, branded generic
2 products (products sold under a brand name other than the originator brand name of the
3 molecule), generic products (products that are sold under the generic molecule name), and
4 products manufactured by Thailand's Government Pharmaceutical Organization (GPO). We also
5 assessed percent market share by NLEM status (based on the 1999 and 2004 Thai NLEM).
6

7 We analyzed total volume and market share for medicines in eight therapeutic classes: two
8 classes of diabetes products (oral antidiabetics and insulins), three classes of cardiovascular
9 disease products (antihypertensives, lipid-regulating, and cardiac therapy products) and three
10 classes of cancer products (antineoplastics, immunostimulating agents, and cytostatic hormone
11 therapy products); Table 1 in the online appendix lists all medicines by ATC code. We assigned
12 each therapeutic class to one of two categories: medicines usually used to treat primary care
13 health conditions and medicines usually used to treat more complicated conditions, typically in
14 secondary/tertiary, often inpatient care, settings. Antidiabetic, insulin, antihypertensive and lipid-
15 lowering products are usually used for primary care conditions (i.e., diabetes, high blood
16 pressure and high cholesterol), whereas cardiac therapy and cancer products are usually used for
17 more severe conditions that more likely require treatment by a specialist and/or in an inpatient
18 setting.
19

20 ***Research Design***

21 We used an interrupted time series design, the strongest quasi-experimental approach for
22 evaluating effects of interventions, which has been used extensively for medication use
23 research.²¹ Although we did not have an equivalent control group, we used medicines sold in the
24 retail sector as a non-equivalent comparison group,²² assuming that the retail market should be
25 relatively unaffected by the reforms since UCS enrollees could only obtain covered medicines
26 through their local, hospital-based CUP.
27

28 ***Statistical Analysis***

29 The intervention was the UCS roll-out from April to October 2001. We defined three distinct
30 periods: 12 quarters pre-reform (1998Q2-2001Q1), a 3-quarter UCS roll-out period (2001Q2-
31 2001Q4; grey box in figures), and 19 quarters post-reform (2002Q1-2006Q3). We ended analysis
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1 prior to 2006Q4 since there was a policy change at that time (the removal of an initial 30 Baht
2 co-payment per visit) which may have impacted outcomes. In sensitivity analyses, we extended
3 the intervention roll-out period through 2002 and through 2003 to account for potentially delayed
4 implementation and lag of actual enrollment into the scheme.

5
6 We used segmented linear regression to measure the pre-reform trend, the immediate level
7 change following the intervention period, and the post-reform change in trend (as compared to
8 the pre-reform trend). For the NLEM analysis, we reclassified NLEM status in 2005Q1 (when
9 the 2004 list was implemented) and included a pre-post term (“NLEM”) in the model to account
10 for possible discontinuity due to the reclassification. We report two estimates from the
11 segmented regression models – the post-reform change in trend and the immediate level change
12 following the reform. We controlled for serial autocorrelation using an autoregressive error
13 model. We retained all terms in the models, even if non-significant. We used the models to
14 estimate absolute and relative differences (with 95% confidence intervals)²³ in observed versus
15 predicted total volume at one year and five years post-reform. In sensitivity analyses, we
16 included a quadratic term for the post-reform trend and used a likelihood ratio test to determine
17 the best-fitting model. We report below results from the best-fitting model of the shortest (i.e., 3
18 quarter) intervention period and mention differences in model results where they existed. Results
19 from sensitivity analyses are available upon request. We used the AUTOREG procedure in SAS
20 9.3 for all analyses.

21 22 **Results**

23 24 ***Hospital Sector Volume***

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

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3 1 therapy and immunostimulating agents (although only the latter was significant in the sensitivity
4 analyses using a longer intervention period) [Table 1, Figures 1 and 2].
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9 4 The UCS was associated with increased sales of diabetes medicines. One year after the policy,
10 the sale of insulin was 35% (95% CI: 15%, 55%) higher and, at five years, 174% (95% CI:
11 114%-235%) higher than what would have been expected in the absence of the UCS [Table 2].
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13 6 The increase in insulin sales was driven primarily by human insulins, which are on the NLEM
14 and marketed as branded generics by two manufacturers. The policy was associated with a 39%
15 (95% CI: 14%, 64%) increase in antidiabetic product sales five years after implementation
16 [Table 2]. This was largely due to increased sales of generic and branded generic metformin and
17 glibenclamide products, both of which are on the NLEM.
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25 13 Implementation of the UCS appears to have had a mixed impact on sales of cardiovascular
26 medicines. Five years after the policy, the sale of lipid lowering agents was nearly double (108%
27 increase; 95% CI: 60%, 157%) what would have been expected in the absence of the scheme
28 [Table 2]. The increase was primarily due to sales of branded generic simvastatin and
29 gemfibrozil products, which are on the NLEM, and a small but steady increase in sales of
30 originator atorvastatin products, which were not on the NLEM until 2004. For antihypertensives,
31 the significant increase in post-policy trend compensated for an initial drop in sales, resulting in a
32 slight increase in sales five years after the policy (19% increase; 95% CI: -3%, 40%). The
33 increased trend was primarily due to sales of enalapril, atenolol, and amlodipine, all of which are
34 on the NLEM and predominately sold as branded generics. The reform had no significant impact
35 on sales of cardiac therapy medicines one or five years after the policy.
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46 25 The results were also mixed for cancer medicines. The UCS had no significant one- or five-year
47 impact on the sale of antineoplastics or cytostatic hormones (although the latter class did
48 experience a significant post-policy increase in trend). However, the policy was associated with
49 an immediate reduction in sales of immunostimulating agents that did not recover in the post-
50 policy period. One year after implementation, the sale of immunostimulating agents was 35%
51 (95% CI: -45%, -25%) lower than expected from pre-policy trends, and 26% lower (95% CI: -
52 45%, -8%) five years post-policy. This drop is almost entirely due to a sharp reduction in sales of
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3 1 interferon alfa-2b, a non-NLEM medicine, around the time of UCS implementation, which could
4 have been due to a coincidental recall of an interferon alfa-2b product.²⁴
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9 4 Finally, as expected, the reform had little impact on sales volume in the retail sector – there were
10 few significant post-implementation changes, and the changes that were significant were small in
11 magnitude [see online appendix, Table 2].
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15 7 16 8 *Hospital Sector Market Share*

17 9 Immediately following the reform, there were significant shifts in hospital sector market share by
18 licensing status for most classes [Table 3]. The changes for antidiabetics and cardiac medicines -
19 the two therapeutic classes with the largest shifts – were due to significant increases in GPO-
20 produced medicines, primarily at the expense of branded generics and, to a lesser extent,
21 generics. There was a significant increase in GPO antidiabetic products (+16% of market; 95%
22 CI: 12%, 20%), and decreases in branded generic (-12%; 95% CI: -16%, -9%) and generic (-4%;
23 95% CI: -6%, -1%) products immediately after the policy [Figure 3]. Similarly, there was a
24 significant increase in GPO cardiac therapy products (+22%; 95% CI: 15%, 28%), and
25 significant decreases of branded generic (-14%; 95% CI: -21%, -7%) and generic (-4%; 95% CI: -
26 6%, -2%) products immediately after the policy [Figure 4]. There was also a small decrease in
27 market share of generic antihypertensives (-6%; 95% CI: -8%, -3%), which was compensated for
28 by a marginally significant increase in GPO products.
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33 22 The market for lipid regulating agents experienced an immediate shift from originator products (-
34 8% market share; 95% CI: -10%, -5%) to branded generics (+8%; 95% CI: 5%, 10%). A similar
35 shift was seen for in the market for immunostimulating agents (6% decrease in originator
36 products [95% CI: -10%, -3%] and a 5% increase in branded generics [95% CI: 2%, 7%]). The
37 cytostatic hormone market experienced an immediate shift from branded generic (-8%; 95% CI: -
38 12%, -4%) to generic products (+6%, 95% CI: 1%, 11%). Generic insulins experienced a slight
39 decrease in market share caused by the market exit of the sole generic manufacturer just prior to
40 the policy. There were no immediate changes in market share for antineoplastics. Aside from the
41 immediate level changes following the policy, there were few major changes in market share for
42 all classes.
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1 The UCS did not have a major impact on NLEM market share, likely because the share of
2 NLEM medicines was already quite high [see online appendix Table 6 and Figure 17]. The only
3 notable level change, for immunostimulating agents, was likely due to the coincidental recall of a
4 non-NLEM interferon alfa-2b product.²⁴ While all medicine classes had significant post-reform
5 trends, these trends were small in magnitude and NLEM market share remained fairly stable over
6 the study period until the 2004 NLEM was introduced. There were large changes in NLEM
7 market share for three classes – antihypertensives, lipid regulating agents and cytostatic
8 hormones – at the time of the 2004 NLEM implementation in 2005Q1 [see online appendix
9 Table 6 and Figure 17]. Given the increase in post-reform volume for many medicine classes, a
10 stable NLEM market share in the short-term (i.e., pre-2005) following the UCS implementation
11 suggests a post-reform increase in both NLEM and non-NLEM medicines.

13 Discussion

14 The UCS was associated with long-term (i.e., 5 year) increases in hospital sector sales of
15 medicines for chronic diseases that are usually treated in primary care settings, such as diabetes,
16 high blood pressure, and high cholesterol. We hypothesized this gradual increase in volumes
17 since the UCS expanded access to primary care²⁵ and actual enrollment into the scheme occurred
18 gradually from implementation in 2001 until around 2004, by which time 95.5% of the
19 population had insurance coverage.⁶ The UCS, which radically changed hospital financing and
20 reimbursement, was also associated with an immediate market shift to locally produced or
21 branded generic products for most therapeutic classes.

22
23 Despite these increases in access, the policy did not appear to increase sales of medicines for
24 more severe diseases like heart failure, arrhythmias, and cancer, which are often treated in
25 secondary or tertiary settings. This finding is consistent with evidence that the capitated payment
26 system initially discouraged referrals of UCS patients to higher-level care.^{6,25,26} The UCS also
27 appears to have had a mixed impact on utilization of essential medicines. There were increases in
28 NLEM medicines, which are covered, as well as non-NLEM medicines. Similarly, given the
29 capitated UCS payment system, we expected to see an increase in sales of generic medicines,
30 which are typically less expensive. However, the majority of sales in most classes were for
31 branded generic products, many of which had generic alternatives in the market. Interestingly,

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3 1 substantial market share shifts occurred toward products manufactured by the Thai GPO, which
4 have been noted to have higher than market prices.²⁷ By law, GPO products received preferential
5 status by hospital purchasers,²⁸ which negates the incentive to prescribe cheaper alternatives
6 under the capitated payment system. While the increase in GPO products and the UCS
7 implementation may be a coincidence in timing, it is noteworthy that the GPO expanded its
8 product line at a time when the UCS policy expanded the market of people who could afford
9 medicines.

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9 Our study demonstrates the value of IMS Health market intelligence data for rigorous health
10 policy evaluation. Unlike other sources of data on pharmaceutical utilization (i.e., national health
11 surveys or ad hoc hospital surveys), IMS data represent country pharmaceutical markets
12 consistently over time and are useful for the evaluation of system-wide interventions.
13 Nevertheless, the data pose some limitations. Aggregate national sales data do not allow us to
14 determine whether observed increases in medicines sales occurred preferentially among UCS
15 enrollees or enrollees in the SHI and CSMBS schemes, conceivably to compensate for financial
16 strain of the UCS on hospital budgets.⁶ CSMBS expenditures increased following UCS
17 implementation²⁹ and increased medicines sales among CSMBS enrollees, reimbursed on a fee-
18 for-service basis, could explain increases in non-NLEM medicines and medicines with less
19 expensive therapeutic alternatives.⁵ However, it is unlikely that increased utilization among
20 CSMBS enrollees explains most of the observed volume changes since this would imply that
21 one-half (for diabetes) to three-quarters (for hypertension) of CSMBS members (7.1% of the
22 total population in 2004⁶) were on these treatments in 2004. Even the CSMBS and SSI schemes
23 combined (20.3% of the total population in 2004⁶) are unlikely to be responsible for the observed
24 changes since this would imply that one-quarter (for diabetes) and one-third (for hypertension) of
25 enrollees in the two schemes were on these treatments in 2004. These estimates are much higher
26 than the national prevalence (6.7% for diabetes³⁰ and 22.0% for hypertension³¹ in 2004) and
27 unlikely in the civil servant and private sector workforce populations, which are likely to be
28 healthier and wealthier than the national average.

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

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

9
10 There are also potential limitations due to study design and statistical analysis. We addressed the
11 main threat to the internal validity of the interrupted time series design – a concurrent event that
12 affects the outcome of interest – by assessing other policies or market events that occurred at the
13 time of the UCS, through literature reviews, discussions with in-country experts, and by
14 including the retail sector as a comparison. The statistical approach, segmented regression
15 analysis, usually assumes a linear trend and well-defined break point. Sensitivity analyses that
16 varied model specification and intervention duration did not change the findings. By reporting
17 results from fully-specified models, we may have underestimated the statistical significance of
18 one- and five-year change estimates.

19
20 While both the context and the implementation of universal coverage in Thailand are unique and
21 not necessarily generalizable to other LMICs, our findings suggest that expanding health
22 insurance coverage with a medicines benefit to the entire population, together with changes in
23 the payment system and increased local manufacturing, increased the per capita volume of
24 medicines sold and, by inference, improved access to medicines in the primary care sector in
25 Thailand, presumably by making medicines more affordable. Since the study period, Thailand
26 has enacted further policies to address pharmaceutical sector cost escalation (e.g., strict
27 enforcement of reimbursement for only NLEM medicines in the CSMBS³³) and to ensure
28 appropriate access to non-NLEM medicines (e.g., coverage of medicines for HIV, renal
29 replacement therapy, and mental health conditions).^{34–36} In the future, it will be important for
30 Thailand and other countries to assess equity in access to and quality of use of medicines,

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

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TABLES

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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.

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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.

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1 **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)

2 ***Bold** signifies a statistically significant regression coefficient ($p < 0.05$). Changes are in absolute terms (i.e., percentage point change).

3 **Quadratic model (which has a squared post-policy term) fits better than linear model.

4 ***GPO did not produce any insulins or cancer medicines during the study period.

5 Note 1: See online appendix Table 4 and Figures 9-16 for market share regression coefficients and figures for all therapeutic areas

6 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.

1
2
3 **Figure Index (attached in separate document):***

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

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

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

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

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

12
13 **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)
CAROVASCULAR 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)

1	Antihypertensives	DIHYDRALAZINE	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPER.PL MAINLY PERI)
2	Antihypertensives	DOXAZOSIN	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPER.PL MAINLY PERI)
3	Antihypertensives	HYDRALAZINE	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPER.PL MAINLY PERI)
4	Antihypertensives	HYDRALAZINE#HYDROCHLOROTHIAZIDE#RESERPINE	C2 (ANTIHYPERTENSIVES)	C2B2 (A-HYPERT(N V)MAINLY PERI)
5	Antihypertensives	KETANSERIN	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPER.PL MAINLY PERI)
6	Antihypertensives	METHYLDOPA	C2 (ANTIHYPERTENSIVES)	C2A1 (ANTIHYPER.PL MAINLY CENT)
7	Antihypertensives	MINOXIDIL	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPER.PL MAINLY PERI)
8	Antihypertensives	NITROPRUSSIDE	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPER.PL MAINLY PERI)
9	Antihypertensives	PRAZOSIN	C2 (ANTIHYPERTENSIVES)	C2A2 (ANTIHYPER.PL MAINLY PERI)
10	Antihypertensives	RESERPINE	C2 (ANTIHYPERTENSIVES)	C2C0 (RAUWLF ALK+OTH A-HY HERB)
11	Antihypertensives	RILMENIDINE	C2 (ANTIHYPERTENSIVES)	C2A1 (ANTIHYPER.PL MAINLY CENT)
12	Antihypertensives	1-PROPANOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
13	Antihypertensives	AMILORIDE#HYDROCHLOROTHIAZIDE#TIMOLOL	C7 (BETA BLOCKING AGENTS)	C7B1 (B-BLOCK COMB HYPOT/DIURT)
14	Antihypertensives	ATENOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
15	Antihypertensives	ATENOLOL#CHLORTALIDONE	C7 (BETA BLOCKING AGENTS)	C7B1 (B-BLOCK COMB HYPOT/DIURT)
16	Antihypertensives	BETAXOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
17	Antihypertensives	BISOPROLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
18	Antihypertensives	BISOPROLOL#HYDROCHLOROTHIAZIDE	C7 (BETA BLOCKING AGENTS)	C7B1 (B-BLOCK COMB HYPOT/DIURT)
19	Antihypertensives	CARVEDILOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
20	Antihypertensives	CLOPAMIDE#PINDOLOL	C7 (BETA BLOCKING AGENTS)	C7B1 (B-BLOCK COMB HYPOT/DIURT)
21	Antihypertensives	LABETALOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
22	Antihypertensives	METOPROLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
23	Antihypertensives	NEBIVOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
24	Antihypertensives	OPRENOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
25	Antihypertensives	PINDOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
26	Antihypertensives	PROPRANOLOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
27	Antihypertensives	SOTALOL	C7 (BETA BLOCKING AGENTS)	C7A0 (B-BLOCKING AGENTS,PLAIN)
28	Antihypertensives	AMLODIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
29	Antihypertensives	ATENOLOL#NIFEDIPINE	C8 (CALCIUM ANTAGONISTS)	C8B2 (CALC ANTAG/B BLOCKR COMB)
30	Antihypertensives	BARNIDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
31	Antihypertensives	DILTIAZEM	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
32	Antihypertensives	FELODIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
33	Antihypertensives	GALLOPAMIL	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
34	Antihypertensives	ISRADIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
35	Antihypertensives	LACIDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
36	Antihypertensives	LERCANIDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
37	Antihypertensives	MANIDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
38	Antihypertensives	MIBEFRADIL	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
39	Antihypertensives	NICARDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
40	Antihypertensives	NIFEDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
41	Antihypertensives	NISOLDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
42	Antihypertensives	NITRENDIPINE	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
43	Antihypertensives	VERAPAMIL	C8 (CALCIUM ANTAGONISTS)	C8A0 (CALCIUM ANTAGONIST PLAIN)
44	Antihypertensives	AMILORIDE	C3 (DIURETICS)	C3A1 (POT SPARING AGENTS PLAIN)
45	Antihypertensives	AMILORIDE#HYDROCHLOROTHIAZIDE	C3 (DIURETICS)	C3A5 (POT SPARING+THIAZ COMBS)
46	Antihypertensives	BAROSMA BETULINA#CAPSICUM#METHYLENE BLUE#URGINEA SCIL	C3 (DIURETICS)	C3A6 (OTHER DIURETICS)
47	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)

1	Antihypertensives	HYDROCHLOROTHIAZIDE	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)
2	Antihypertensives	HYDROCHLOROTHIAZIDE#TRIAMTERENE	C3 (DIURETICS)	C3A5 (POT SPARING+THIAZ COMBS)
3	Antihypertensives	INDAPAMIDE	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)
4	Antihypertensives	SPIRONOLACTONE	C3 (DIURETICS)	C3A1 (POT SPARING AGENTS PLAIN)
5	Antihypertensives	TORASEMIDE	C3 (DIURETICS)	C3A2 (LOOP DIURETICS PLAIN)
6	Antihypertensives	TRIPAMIDE	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)
7	Antihypertensives	XIPAMIDE	C3 (DIURETICS)	C3A3 (THIAZIDE+ANALOGUE PLAIN)
8	Antihypertensives	ALISKIREN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9X0 (OTH RENIN-ANGIOTEN AGENT)
9	Antihypertensives	ALISKIREN#HYDROCHLOROTHIAZIDE	C9 (RENIN-ANGIOTEN SYS AGENT)	C9X0 (OTH RENIN-ANGIOTEN AGENT)
10	Antihypertensives	AMLODIPINE#VALSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D3 (AT2 ANTG COMB CALC ANTAG)
11	Antihypertensives	CANDESARTAN CILEXETIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)
12	Antihypertensives	CANDESARTAN CILEXETIL#HYDROCHLOROTHIAZIDE	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D1 (AT2 ANTG COMB C2 &/O DIU)
13	Antihypertensives	CAPTOPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
14	Antihypertensives	CILAZAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
15	Antihypertensives	DELAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
16	Antihypertensives	ENALAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
17	Antihypertensives	EPROSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)
18	Antihypertensives	FOSINOPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
19	Antihypertensives	FOSINOPRIL#HYDROCHLOROTHIAZIDE	C9 (RENIN-ANGIOTEN SYS AGENT)	C9B1 (ACE INH COMB+A-HYP/DIUR)
20	Antihypertensives	HYDROCHLOROTHIAZIDE#IRBESARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D1 (AT2 ANTG COMB C2 &/O DIU)
21	Antihypertensives	HYDROCHLOROTHIAZIDE#LOSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D1 (AT2 ANTG COMB C2 &/O DIU)
22	Antihypertensives	HYDROCHLOROTHIAZIDE#OLMESARTAN MEDOXOMIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D1 (AT2 ANTG COMB C2 &/O DIU)
23	Antihypertensives	HYDROCHLOROTHIAZIDE#QUINAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9B1 (ACE INH COMB+A-HYP/DIUR)
24	Antihypertensives	HYDROCHLOROTHIAZIDE#RAMIPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9B1 (ACE INH COMB+A-HYP/DIUR)
25	Antihypertensives	HYDROCHLOROTHIAZIDE#TELMISARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D1 (AT2 ANTG COMB C2 &/O DIU)
26	Antihypertensives	HYDROCHLOROTHIAZIDE#VALSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9D1 (AT2 ANTG COMB C2 &/O DIU)
27	Antihypertensives	IMIDAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
28	Antihypertensives	INDAPAMIDE#PERINDOPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9B1 (ACE INH COMB+A-HYP/DIUR)
29	Antihypertensives	IRBESARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)
30	Antihypertensives	LISINOPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
31	Antihypertensives	LOSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)
32	Antihypertensives	OLMESARTAN MEDOXOMIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)
33	Antihypertensives	PERINDOPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
34	Antihypertensives	QUINAPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
35	Antihypertensives	RAMIPRIL	C9 (RENIN-ANGIOTEN SYS AGENT)	C9A0 (ACE INHIBITORS PLAIN)
36	Antihypertensives	TELMISARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)
37	Antihypertensives	VALSARTAN	C9 (RENIN-ANGIOTEN SYS AGENT)	C9C0 (ANGIOTEN-II ANTAG, PLAIN)
38	Cardiac Therapy	ADENOSINE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
39	Cardiac Therapy	AMIODARONE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
40	Cardiac Therapy	AMRINONE	C1 (CARDIAC THERAPY)	C1F0 (POSITIVE INOTROPIC AGENT)
41	Cardiac Therapy	CAFFEINE#ETAMIVAN	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)
42	Cardiac Therapy	DIGITALIS PURPUREA	C1 (CARDIAC THERAPY)	C1A1 (CARDIAC GLYCOSIDES PLAIN)
43	Cardiac Therapy	DIGITOXIN	C1 (CARDIAC THERAPY)	C1A1 (CARDIAC GLYCOSIDES PLAIN)
44	Cardiac Therapy	DIGOXIN	C1 (CARDIAC THERAPY)	C1A1 (CARDIAC GLYCOSIDES PLAIN)
45	Cardiac Therapy	DISOPYRAMIDE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
46	Cardiac Therapy	DOBUTAMINE	C1 (CARDIAC THERAPY)	C1C2 (CARDIAC DOPAMINERG AGENT)
47	Cardiac Therapy	DOPAMINE	C1 (CARDIAC THERAPY)	C1C2 (CARDIAC DOPAMINERG AGENT)
48	Cardiac Therapy	EPINEPHRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)
49	Cardiac Therapy	ETAFEDRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)
50	Cardiac Therapy	ETILEFRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)

1	Cardiac Therapy	FLECAINIDE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
2	Cardiac Therapy	GLYCINE MAX#UBIDECARENONE	C1 (CARDIAC THERAPY)	C1X0 (ALL OTHER CARDIAC PREPS)
3	Cardiac Therapy	ISOPRENALINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)
4	Cardiac Therapy	ISOSORBIDE DINITRATE	C1 (CARDIAC THERAPY)	C1E0 (NITRITES AND NITRATES)
5	Cardiac Therapy	ISOSORBIDE MONONITRATE	C1 (CARDIAC THERAPY)	C1E0 (NITRITES AND NITRATES)
6	Cardiac Therapy	IVABRADINE	C1 (CARDIAC THERAPY)	C1D0 (CORONRY THER EXC C AN+NI)
7	Cardiac Therapy	LIDOCAINE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
8	Cardiac Therapy	MAGNESIUM#POTASSIUM#PROCAINE	C1 (CARDIAC THERAPY)	C1X0 (ALL OTHER CARDIAC PREPS)
9	Cardiac Therapy	METARAMINOL	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)
10	Cardiac Therapy	METILDIGOXIN	C1 (CARDIAC THERAPY)	C1A1 (CARDIAC GLYCOSIDES PLAIN)
11	Cardiac Therapy	MEXILETINE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
12	Cardiac Therapy	MIDODRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)
13	Cardiac Therapy	MILRINONE	C1 (CARDIAC THERAPY)	C1F0 (POSITIVE INOTROPIC AGENT)
14	Cardiac Therapy	NITROGLYCERIN	C1 (CARDIAC THERAPY)	C1E0 (NITRITES AND NITRATES)
15	Cardiac Therapy	NOREPINEPHRINE	C1 (CARDIAC THERAPY)	C1C1 (CARDIAC STM EX DOPAM AGT)
16	Cardiac Therapy	OXYFEDRINE	C1 (CARDIAC THERAPY)	C1D0 (CORONRY THER EXC C AN+NI)
17	Cardiac Therapy	PENTAERYTHRITYL TETRANITRATE	C1 (CARDIAC THERAPY)	C1E0 (NITRITES AND NITRATES)
18	Cardiac Therapy	PROCAINAMIDE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
19	Cardiac Therapy	PROPAFENONE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
20	Cardiac Therapy	QUINIDINE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
21	Cardiac Therapy	TOCAINIDE	C1 (CARDIAC THERAPY)	C1B0 (ANTIARRHYTHMICS)
22	Cardiac Therapy	TRIMETAZIDINE	C1 (CARDIAC THERAPY)	C1D0 (CORONRY THER EXC C AN+NI)
23	Cardiac Therapy	UBIDECARENONE	C1 (CARDIAC THERAPY)	C1X0 (ALL OTHER CARDIAC PREPS)
24	Cardiac Therapy	UBIQUINONE(S)	C1 (CARDIAC THERAPY)	C1X0 (ALL OTHER CARDIAC PREPS)
25	Lipid Regulating	ACIPIMOX	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A9 (OTH.CHOLEST&TRIGLY.REGUL)
26	Lipid Regulating	ALLIUM SATIVUM	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
27	Lipid Regulating	ALLIUM SATIVUM#ARACHIS HYPOGAEA	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
28	Lipid Regulating	ALLIUM SATIVUM#SOYA LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
29	Lipid Regulating	AMLODIPINE#ATORVASTATIN	C11 (C.V. MULTITH. COMB PROD)	C11A1 (LIPREG.CV.MULT-TH.FX.COM)
30	Lipid Regulating	ATORVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))
31	Lipid Regulating	BEZAFIBRATE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A2 (FIBRATES)
32	Lipid Regulating	CERIVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))
33	Lipid Regulating	COLESTYRAMINE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A3 (ION-EXCHANGE RESINS)
34	Lipid Regulating	DOCOSAHEXANOIC ACID#EICOSAPENTAENOIC ACID	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
35	Lipid Regulating	DOCOSAHEXANOIC ACID#EICOSAPENTAENOIC ACID#VITAMIN E	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
36	Lipid Regulating	EZETIMIBE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A9 (OTH.CHOLEST&TRIGLY.REGUL)
37	Lipid Regulating	EZETIMIBE#SIMVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10C0 (LIP.REG.CO.W.OTH.LIP.REG)
38	Lipid Regulating	FENOFIBRATE	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A2 (FIBRATES)
39	Lipid Regulating	FISH	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
40	Lipid Regulating	FISH#SOYA LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
41	Lipid Regulating	FLUVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))
42	Lipid Regulating	GEMFIBROZIL	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A2 (FIBRATES)
43	Lipid Regulating	LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
44	Lipid Regulating	LECITHIN#SOYA LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
45	Lipid Regulating	NICOTINIC ACID	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A9 (OTH.CHOLEST&TRIGLY.REGUL)
46	Lipid Regulating	PITAVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))
47	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))

	Lipid Regulating	SALMON	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
1	Lipid Regulating	SIMVASTATIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10A1 (STATINS (HMG-COA RED))
2	Lipid Regulating	SOYA LECITHIN	C10 (LIP.REG./ANTI-ATH. PREPS)	C10B0 (ANTI-ATHEROMA NATRL ORIG)
3				
4	CANCER			
5	Antineoplastics	ALEMTUZUMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)
6	Antineoplastics	ALTRETAMINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
7	Antineoplastics	ASPARAGINASE	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)
8	Antineoplastics	AZACITIDINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
9	Antineoplastics	BEVACIZUMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)
10	Antineoplastics	BLEOMYCIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)
11	Antineoplastics	BORTEZOMIB	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)
12	Antineoplastics	BUSULFAN	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
13	Antineoplastics	CAPECITABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
14	Antineoplastics	CARBOPLATIN	L1 (ANTINEOPLASTICS)	L1X2 (PLATINUM COMPOUNDS)
15	Antineoplastics	CARMUSTINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
16	Antineoplastics	CETUXIMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)
17	Antineoplastics	CHLORAMBUCIL	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
18	Antineoplastics	CHLORMETHINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
19	Antineoplastics	CISPLATIN	L1 (ANTINEOPLASTICS)	L1X2 (PLATINUM COMPOUNDS)
20	Antineoplastics	CLADRIBINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
21	Antineoplastics	CYCLOPHOSPHAMIDE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
22	Antineoplastics	CYTARABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
23	Antineoplastics	DACARBAZINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
24	Antineoplastics	DACTINOMYCIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)
25	Antineoplastics	DASATINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)
26	Antineoplastics	DECITABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
27	Antineoplastics	DOCETAXEL	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)
28	Antineoplastics	DOXORUBICIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)
29	Antineoplastics	EPIRUBICIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)
30	Antineoplastics	ERLOTINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)
31	Antineoplastics	ETOPOSIDE	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)
32	Antineoplastics	FLUDARABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
33	Antineoplastics	FLUOROURACIL	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
34	Antineoplastics	GEFITINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)
35	Antineoplastics	GEMCITABINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
36	Antineoplastics	HYDROXYCARBAMIDE	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)
37	Antineoplastics	IBRITUMOMAB TIUXETAN	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)
38	Antineoplastics	IDARUBICIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)
39	Antineoplastics	IFOSFAMIDE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
40	Antineoplastics	IMATINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)
41	Antineoplastics	IRINOTECAN	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)
42	Antineoplastics	IXABEPILONE	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)
43	Antineoplastics	LAPATINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)
44	Antineoplastics	LOMUSTINE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
45	Antineoplastics	MELPHALAN	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
46	Antineoplastics	MERCAPTOPYRINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
47	Antineoplastics	METHOTREXATE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
	Antineoplastics	MITOMYCIN	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)
	Antineoplastics	MITOXANTRONE	L1 (ANTINEOPLASTICS)	L1D0 (ANTINEOPLAS. ANTIBIOTICS)

1	Antineoplastics	NILOTINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)
2	Antineoplastics	OXALIPLATIN	L1 (ANTINEOPLASTICS)	L1X2 (PLATINUM COMPOUNDS)
3	Antineoplastics	PACLITAXEL	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)
4	Antineoplastics	PEMETREXED	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
5	Antineoplastics	PROCARBAZINE	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)
6	Antineoplastics	RITUXIMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)
7	Antineoplastics	SORAFENIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)
8	Antineoplastics	SUNITINIB	L1 (ANTINEOPLASTICS)	L1X4 (A-NEO PROTEIN KINASE INH)
9	Antineoplastics	TEGAFUR	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
10	Antineoplastics	TEGAFUR#URACIL	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
11	Antineoplastics	TEMOZOLOMIDE	L1 (ANTINEOPLASTICS)	L1A0 (ALKYLATING AGENTS)
12	Antineoplastics	TIOGUANINE	L1 (ANTINEOPLASTICS)	L1B0 (ANTIMETABOLITES)
13	Antineoplastics	TOPOTECAN	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)
14	Antineoplastics	TRASTUZUMAB	L1 (ANTINEOPLASTICS)	L1X3 (ANTINEOPLASTIC MABS)
15	Antineoplastics	TRETINOIN	L1 (ANTINEOPLASTICS)	L1X9 (ALL OTH. ANTINEOPLASTICS)
16	Antineoplastics	VINBLASTINE	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)
17	Antineoplastics	VINCRISTINE	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)
18	Antineoplastics	VINORELBINE	L1 (ANTINEOPLASTICS)	L1C0 (VINCA ALKALOIDS)
19	Cytostatic Hormones	AMINOGLUTETHIMIDE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)
20	Cytostatic Hormones	ANASTROZOLE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)
21	Cytostatic Hormones	BICALUTAMIDE	L2 (CYTOSTATIC HORMONE THER)	L2B2 (CYTO ANTI-ANDROGENS)
22	Cytostatic Hormones	BUSERELIN	L2 (CYTOSTATIC HORMONE THER)	L2A3 (CYTO GONAD HORMON ANALOG)
23	Cytostatic Hormones	CYPROTERONE	L2 (CYTOSTATIC HORMONE THER)	L2B2 (CYTO ANTI-ANDROGENS)
24	Cytostatic Hormones	EXEMESTANE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)
25	Cytostatic Hormones	FLUTAMIDE	L2 (CYTOSTATIC HORMONE THER)	L2B2 (CYTO ANTI-ANDROGENS)
26	Cytostatic Hormones	FORMESTANE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)
27	Cytostatic Hormones	FULVESTRANT	L2 (CYTOSTATIC HORMONE THER)	L2B9 (OTH CYTO HORMON ANTAGIST)
28	Cytostatic Hormones	GOSERELIN	L2 (CYTOSTATIC HORMONE THER)	L2A3 (CYTO GONAD HORMON ANALOG)
29	Cytostatic Hormones	LETROZOLE	L2 (CYTOSTATIC HORMONE THER)	L2B3 (CYTOSTAT AROMATASE INHIB)
30	Cytostatic Hormones	LEUPRORELIN	L2 (CYTOSTATIC HORMONE THER)	L2A3 (CYTO GONAD HORMON ANALOG)
31	Cytostatic Hormones	MEDROXYPROGESTERONE	L2 (CYTOSTATIC HORMONE THER)	L2A2 (CYTOSTATIC PROGESTOGENS)
32	Cytostatic Hormones	MEGESTROL	L2 (CYTOSTATIC HORMONE THER)	L2A2 (CYTOSTATIC PROGESTOGENS)
33	Cytostatic Hormones	TAMOXIFEN	L2 (CYTOSTATIC HORMONE THER)	L2B1 (CYTO ANTI-OESTROGENS)
34	Cytostatic Hormones	TOREMIFENE	L2 (CYTOSTATIC HORMONE THER)	L2B1 (CYTO ANTI-OESTROGENS)
35	Cytostatic Hormones	TRIPTORELIN	L2 (CYTOSTATIC HORMONE THER)	L2A3 (CYTO GONAD HORMON ANALOG)
36	Immunostimulating Agents	FILGRASTIM	L3 (IMMUNOSTIMULATING AGENTS)	L3A1 (COLONY-STIMULATING FACT.)
37	Immunostimulating Agents	INTERFERON ALFA	L3 (IMMUNOSTIMULATING AGENTS)	L3B1 (INTERFERONS ALPHA)
38	Immunostimulating Agents	INTERFERON ALFA-2A	L3 (IMMUNOSTIMULATING AGENTS)	L3B1 (INTERFERONS ALPHA)
39	Immunostimulating Agents	INTERFERON ALFA-2B	L3 (IMMUNOSTIMULATING AGENTS)	L3B1 (INTERFERONS ALPHA)
40	Immunostimulating Agents	INTERFERON ALFA-N1	L3 (IMMUNOSTIMULATING AGENTS)	L3B1 (INTERFERONS ALPHA)
41	Immunostimulating Agents	INTERFERON BETA-1A	L3 (IMMUNOSTIMULATING AGENTS)	L3B2 (INTERFERONS BETA)
42	Immunostimulating Agents	INTERFERON BETA-1B	L3 (IMMUNOSTIMULATING AGENTS)	L3B2 (INTERFERONS BETA)
43	Immunostimulating Agents	LENOGRASTIM	L3 (IMMUNOSTIMULATING AGENTS)	L3A1 (COLONY-STIMULATING FACT.)
44	Immunostimulating Agents	MOLGRAMOSTIM	L3 (IMMUNOSTIMULATING AGENTS)	L3A1 (COLONY-STIMULATING FACT.)
45	Immunostimulating Agents	PEGFILGRASTIM	L3 (IMMUNOSTIMULATING AGENTS)	L3A1 (COLONY-STIMULATING FACT.)
46	Immunostimulating Agents	TETRACHLORODECAOXIDE	L3 (IMMUNOSTIMULATING AGENTS)	L3A9 (OTH.IMMUNOSTIM.EX.INTFRN)
47	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 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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case 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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed

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2 *Case-control study*—If applicable, explain how matching of cases and controls was
3 addressed

4 *Cross-sectional study*—If applicable, describe analytical methods taking account of
5 sampling strategy
6

7 (e) Describe any sensitivity analyses
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9 Continued on next page
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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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount) NOTE: We give the characteristics of the therapeutic classes (i.e., number subclasses, medicines within each subclass).
Outcome data	15*✓	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures 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
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*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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1 | reform. All authors participated in the interpretation of the results. -Laura Garabedian wrote the
2 | first draft of the paper. All authors contributed to the writing of the manuscript.

3
4 | Opinions expressed are solely those of the authors and not of the institutions they represent.

5
6 | **Competing Interest Statement:** All authors have completed the Unified Competing Interest
7 | form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author)
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18 | for Improving Use of Medicines.

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

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9 **1 MANUSCRIPT**

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11 **2 Introduction**

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14 **4 *Universal Health Coverage***

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

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

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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 scheme⁵) on utilization of medicines.

49 *Universal Health Coverage in Thailand*

30 With the implementation of the UCS in 2001, Thailand became one of the first LMICs to achieve
31 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 (~~6.37.2%~~ 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 (~~22.020.8%~~), 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 (~~26.629.0%~~) of the population without previous insurance.^{7,8} The UCS was rolled out to all provinces between April and October 2001.⁵⁶ By ~~20052004~~, 95.5% of the population was insured, with ~~just over 70%~~ three-quarters (75.2%) of the population covered by the UCS.⁷⁶

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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 basis⁵ 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).⁵⁶ Individuals must enroll in the scheme at a local Contracting Unit for Primary Care (CUP),⁵⁶ primarily housed in government-owned hospitals.^{9,12} Each CUP receives a capitated payment per registered member to provide outpatient services and medicines.⁵⁶ CUPs initially served as gatekeepers 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.⁵⁶ 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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9 1 Our objective was to evaluate the immediate, short-term (one year) and long-term (five year)
10 2 impacts of the UCS on pharmaceutical market size and composition for medicines for three non-
11 3 communicable diseases (NCDs): cancer, cardiovascular disease, and diabetes. We hypothesized
12 4 that the UCS would result in a gradual increase in sales volume, particularly of products used in
13 5 primary care, as enrollment into the ~~Schemescheme~~ increased, and ~~unlikely made access to health~~
14 6 ~~services and medicines more affordable for the majority of the population. We also hypothesized~~
15 7 ~~that there would be~~ an immediate ~~increaseshift~~ in market share ~~offrom more expensive brand~~
16 8 ~~name to~~ less expensive generic or branded generic products and ~~to~~ medicines on the NLEM in
17 9 response to ~~capitated-paymentclosed-ended budget~~ rules. We focused on medicines for NCDs
18 10 since these illnesses represent a large and growing health care burden in ~~Thailand¹⁰⁻¹³Thailand¹³⁻~~
19 11 ~~16~~ and other ~~LMICs¹⁴LMICs¹⁷~~ and most, but not all, medicines for NCDs would be prescribed
20 12 and dispensed in primary care settings.

13 **Methods**

14 **Data**

15 We used data on quarterly pharmaceutical sales in Thailand from 1998 to 2006 provided by IMS
16 16 Health.^{15,18} The sales data are generated from reports to IMS Health by multinational
17 17 pharmaceutical companies and surveys of purchases by hospital and retail pharmacies.- IMS
18 18 surveys approximately 200 hospitals (including general and specialized, public and private) and
19 19 350 retail pharmacies in Thailand, ~~and employs. These facilities constitute~~ a stratified random
20 20 sample of ~~these facilities that enables~~ the over 1,100 hospitals and 14,000 retail pharmacies in
21 21 ~~Thailand to enable~~ national projections. ~~Documentation on the IMS data collection and~~
22 22 ~~validation process is available upon request from the authors.~~ Medicines were classified
23 23 according to the European Pharmaceutical Research Association (EphMRA) Anatomical
24 24 Therapeutic Chemical (ATC) system.¹⁶⁻¹⁹

26 **Outcomes**

27 We used two outcome measures: total volume and percent market share. *Total volume* is the
28 28 number of standard units purchased per capita per quarter (i.e., “sales”). We analyzed total
29 29 volume by sector (i.e., retail versus hospital) ~~and, within the hospital sector, by NLEM versus~~
30 30 ~~non-NLEM status of medicines (based on the 1999 Thai NLEM).~~ A standard unit, as defined by
31 31 IMS Health, is the smallest dose of a product, which equates to one tablet or capsule for an oral

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dosage form, one teaspoon (5ml) for a syrup, and one ampoule or vial for an injectable product.

WeFor 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 Bank¹⁷Bank²⁰). 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).

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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.¹⁸²¹ Although we did not have an equivalent control group, we used medicines sold in the retail sector as a non-equivalent comparison group,¹⁹²² assuming that the retail market should

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9 be relatively unaffected by the reforms since UCS enrollees could only obtain covered medicines
10 through their local, hospital-based CUP.
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12 13 *Statistical Analysis*

14 The intervention was the UCS roll-out from April to October 2001. We defined three distinct
15 periods: 12 quarters pre-reform (1998Q2-2001Q1), a 3-quarter UCS roll-out period (2001Q2-
16 2001Q4; grey box in figures), and 19 quarters post-reform (2002Q1-2006Q3). We ~~dropped~~
17 ~~2006Q4 from the~~ended analysis prior to 2006Q4 since there was a policy change at ~~this~~that time
18 (the removal of an initial 30 Baht co-payment per visit) ~~that~~which may have impacted outcomes.
19 In sensitivity analyses, we extended the intervention roll-out period through 2002 and through
20 2003 to account for potentially delayed implementation and lag of actual enrollment into the
21 scheme.
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27 We used segmented linear regression to measure the pre-reform trend, the immediate level
28 change following the intervention period, and the post-reform change in trend (as compared to
29 the pre-reform trend). ~~For the NLEM analysis, we reclassified NLEM status in 2005Q1 (when~~
30 ~~the 2004 list was implemented) and included a pre-post term ("NLEM") in the model to account~~
31 ~~for possible discontinuity due to the reclassification. We report two estimates from the~~
32 ~~segmented regression models – the post-reform change in trend and the immediate level change~~
33 ~~following the reform.~~ We controlled for serial autocorrelation using an autoregressive error
34 model. We retained all terms in the models, even if non-significant. We used the models to
35 estimate absolute and relative differences (with 95% confidence intervals)²⁰²³ in observed versus
36 predicted total volume at one year and five years post-reform. In sensitivity analyses, we
37 included a quadratic term for the post-reform trend and used a likelihood ratio test to determine
38 the best-fitting model. ~~We report below results from the best-fitting model of the shortest (i.e., 3~~
39 ~~quarter) intervention period and mention differences in model results where they existed. Results~~
40 ~~from sensitivity analyses are available upon request. We used the AUTOREG procedure in SAS~~
41 ~~9.23~~ for all analyses. ~~▲~~
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50 51 **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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9 1 The results were also mixed for cancer medicines. The UCS had no significant one- or five-year
10 2 impact on the sale of antineoplastics or cytostatic hormones (although the latter class did
11 3 experience a significant post-policy increase in trend). However, the policy was associated with
12 4 an immediate reduction in sales of immunostimulating agents that did not recover in the post-
13 5 policy period. One year after implementation, the sale of immunostimulating agents was 35%
14 6 (95% CI: -45%, -25%) lower than expected from pre-policy trends, and 26% lower (95% CI: -
15 7 45%, -8%) five years post-policy. This drop is almost entirely due to a sharp reduction in sales of
16 8 interferon alfa-2b, a non-NLEM medicine, around the time of UCS implementation, which could
17 9 have been due to a ~~co-incident~~coincidental recall of an interferon alfa-2b product.^{21, 24}

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

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

22 **Hospital Sector Market Share**

23 Immediately following the reform, there were significant shifts in hospital sector market share by
24 licensing status for most classes [Table 3]. The changes for antidiabetics and cardiac medicines –
25 the two therapeutic classes with the largest shifts – were due to significant increases in GPO-
26 produced medicines, primarily at the expense of branded generics and, to a lesser extent,
27 generics. There was a significant increase in GPO antidiabetic products (+16% of market; 95%
28 CI: 12%, 20%), and decreases in branded generic (-12%; 95% CI: -16%, -9%) and generic (-4%;
29 95% CI: -6%, -1%) products immediately after the policy [Figure 3]. Similarly, there was a
30 significant increase in GPO cardiac therapy products (+22%; 95% CI: 15%, 28%), and
31 significant decreases of branded generic (-14%; 95% CI: -21%, -7%) and generic (-4%; 95% CI: -

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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 ~~volume~~ volumes since the UCS expanded access to primary ~~care~~ care²⁵ and actual enrollment into

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9 1 the scheme occurred gradually from implementation in 2001 until around ~~2005~~2004, by which
10 2 time 95.5% of the population had insurance coverage.⁷⁶ The UCS, which radically changed
11 3 hospital financing and reimbursement, was also associated with an immediate market shift to
12 4 locally produced or branded generic products for most therapeutic classes.
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16 6 Despite these increases in access, the policy did not appear to increase sales of medicines for
17 7 more severe diseases like heart failure, arrhythmias, and cancer, which are often treated in
18 8 secondary or tertiary settings. This finding is ~~in-line~~consistent with evidence that the capitated
19 9 payment system initially discouraged referrals of UCS patients to higher-level care.^{5,7,22,6,25,26} The
20 10 UCS also appears to have had a mixed impact on utilization of essential medicines. There were
21 11 increases in NLEM medicines, which are covered, as well as non-NLEM medicines. Similarly,
22 12 given the capitated UCS payment system, we expected to see an increase in sales of generic
23 13 medicines, which are typically less expensive. However, the majority of sales in most classes
24 14 were for branded generic products, many of which had generic alternatives in the market.
25 15 Interestingly, substantial market share shifts occurred toward products manufactured by the Thai
26 16 GPO, which ~~by law received preferential status by hospital purchasers.~~²³ ~~GPO products have~~
27 17 ~~been noted to have higher than market prices²⁴ and sometimes to be of substandard quality.~~²⁵ have
28 18 been noted to have higher than market prices.²⁷ By law, GPO products received preferential
29 19 status by hospital purchasers,²⁸ which negates the incentive to prescribe cheaper alternatives
30 20 under the capitated payment system. While the increase in GPO products and the UCS
31 21 implementation may be a coincidence in timing, it is noteworthy that the GPO expanded its
32 22 product line at a time when the UCS policy expanded the market of people who could afford
33 23 medicines.
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43 25 Our study demonstrates the value of IMS Health market intelligence data for rigorous health
44 26 policy evaluation. Unlike other sources of data on pharmaceutical utilization (i.e., national health
45 27 surveys or ad hoc hospital surveys), IMS data represent country pharmaceutical markets
46 28 consistently over time and are useful for the evaluation of system-wide interventions.
47 29 Nevertheless, the data pose some limitations. Aggregate national sales data do not allow us to
48 30 determine whether observed increases in medicines sales occurred preferentially among UCS
49 31 enrollees or enrollees in the SHI and CSMBS schemes, conceivably to compensate for financial
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strain of the UCS on hospital budgets.⁵⁶ CSMBS expenditures increased following UCS implementation²⁶ implementation²⁹ 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 2004⁶) were on these treatments in 2004. Even the CSMBS and SSI schemes combined (20.3% of the total population in 2004⁶) 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 diabetes³⁰ and 22.0% for hypertension³¹ 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

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9 1 time of the UCS, through literature reviews, discussions with in-country experts, and by
10 2 including the retail sector as a comparison. The statistical approach, segmented regression
11 3 analysis, usually assumes a linear trend and well-defined break point. Sensitivity analyses that
12 4 varied model specification and intervention duration did not change the findings. -By reporting
13 5 results from fully-specified models, we may have underestimated the statistical significance of
14 6 one- and five-year change estimates.
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19 8 While both the context and the implementation of universal coverage in Thailand are unique and
20 9 not necessarily generalizable to other LMICs, our findings suggest that expanding health
21 10 insurance coverage with a medicines benefit to the entire population, together with changes in a
22 11 LMIC the payment system and increased the local manufacturing, increased the per capita volume
23 12 of medicines sold and, by inference, improved access to medicines in the primary care sector in
24 13 Thailand, presumably by making medicines more affordable. Since the study period, Thailand
25 14 has enacted further policies to address pharmaceutical sector cost escalation (e.g., strict
26 15 enforcement of reimbursement for only NLEM medicines in the CSMBS²⁹ CSMBS³³) and to
27 16 ensure appropriate access to non-NLEM medicines (e.g., coverage of medicines for HIV, renal
28 17 replacement therapy, and mental health conditions). ^{30-32,34-36} In the future, it will be important for
29 18 Thailand and other countries to assess equity in access to and quality of use of medicines use,
30 19 availability of medicines in health centers and hospitals, out-of-pocket and system expenditures
31 20 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.

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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).

**If the absolute five-year difference, which is estimated using more precise method, is significant. See online appendix Table 4.3.

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

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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 54 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

65 for absolute one- and five-year differences.

Figure Index (attached in separate document):*

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

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

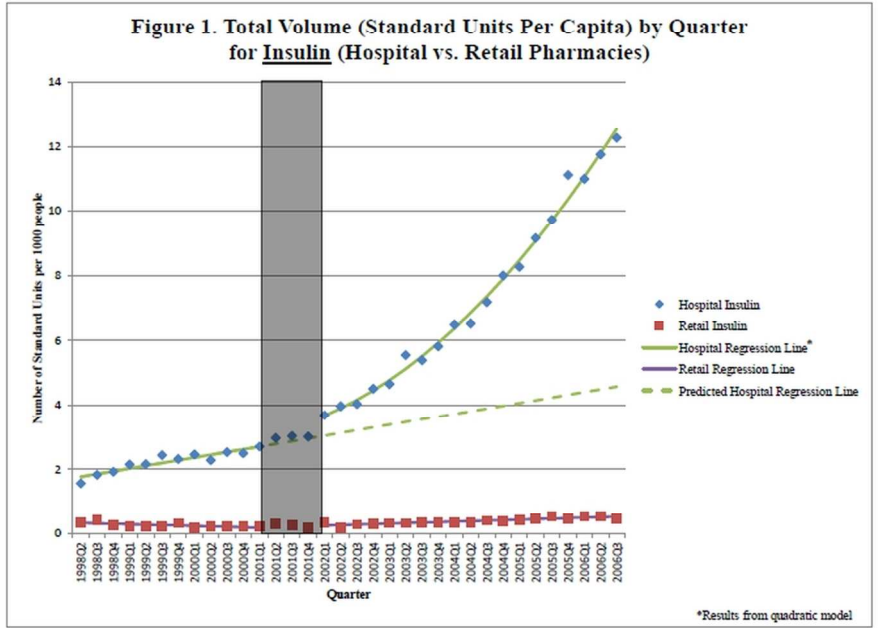
11 | **Figure 3.** Licensing Status Market Share by Quarter: Antidiabetics (Hospital Sector)

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

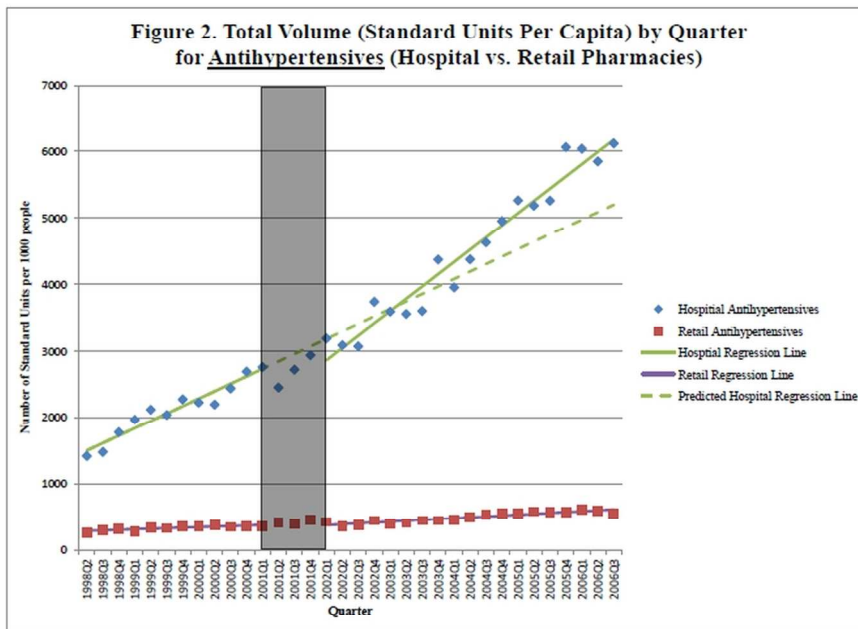
13 | *The grey box in each figure represents the 3-quarter UCS roll-out period.

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

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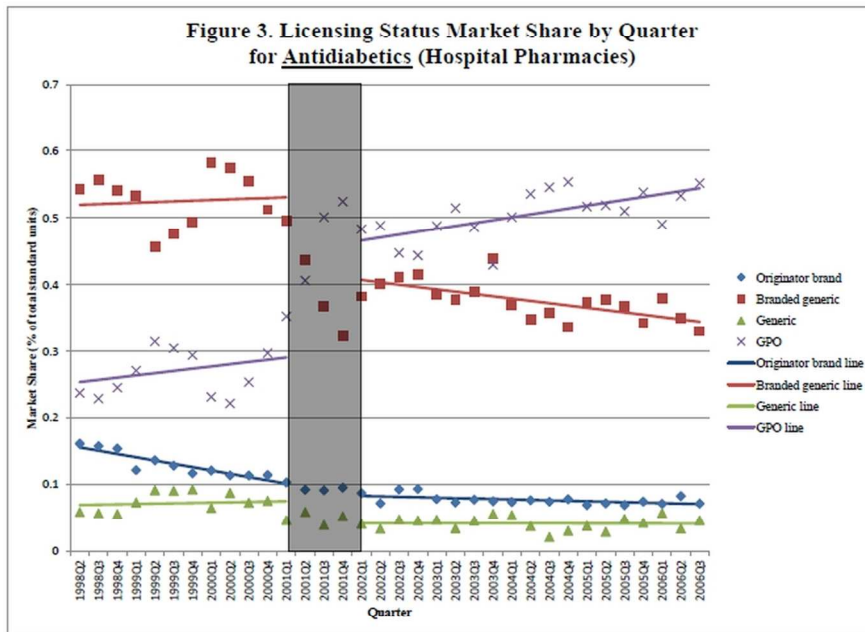
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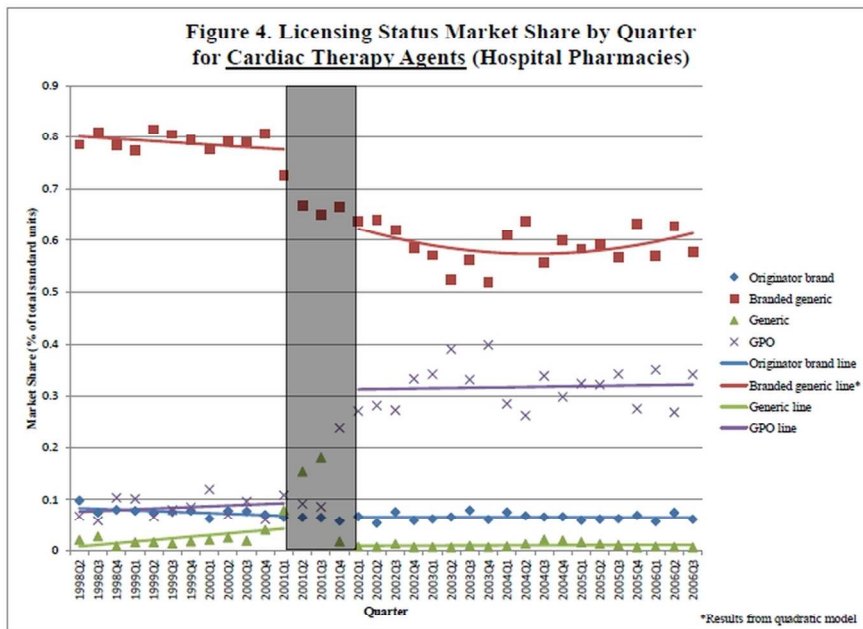
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