Economic Consequences of Underuse of Generic Drugs: Evidence from Medicaid and Implications for Prescription Drug Benefit Plans

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Objective. To calculate the financial impact of underuse of generic medications in state Medicaid programs.

Data Sources/Study Setting. State-by-state data on Medicaid drug spending for 48 states and the District of Columbia in calendar year 2000.

Study Design. We compared the total amount paid by each state Medicaid program for brand name prescriptions with the amount that would have been paid for generic versions of the same agent, to estimate the level of unrealized savings from use of substitutable generic drugs. We also examined whether variation in prices between states represented a potential source of unrealized savings.

Principal Findings. Analysis of state-by-state Medicaid prescription drug spending in 2000 identified potential savings of $229 million that could have been realized from greater use of generic drugs. If the best available prices from each state had been used nationally, savings would have increased to $450 million. The majority of the unrealized savings were concentrated in a small group of medications, including clozapine, alprazolam, and levothyroxine.

Conclusions. Federal regulations on prescription drug reimbursement limit the excess spending on brand name drugs in the Medicaid program to a small percentage of total spending, although the absolute dollar amount is large. Further savings could be realized if lowest available prices were used nationwide. Concentrating on specific agents may be a productive way to address the unrealized savings.

Key Words. Generic medications, Medicaid, health insurance, medication costs

Prescription drugs represent a rapidly increasing percentage of total medical expenditures; covering their costs is the subject of considerable current debate. Recent estimates project the total expenditure for prescription drugs at $160.9 billion for 2002 (Health Care Financing Administration 2002). A prescription drug benefit for Medicare recipients has been actively debated, and many have raised concern about the potential cost of this benefit (U.S. Government Accounting Office 1999). For any prescription drug benefit

program to be economically viable, sources of excess spending on medications need to be identified and contained.

Brand name drugs are typically more expensive than generic versions of the same drug, which in general have identical therapeutic effects. The Food and Drug Administration (FDA) evaluates and approves the bioequivalence of generic drugs. Controversy persists about the bioequivalence of a handful of medications, but nearly all other generic drugs provide identical therapeutic benefit.

State Medicaid programs provide health care coverage to those defined as either "categorically needy," whose coverage is federally mandated, or "medically needy," as determined by each state. Medicaid coverage includes prescription drugs in every state. Since 1987, the Health Care Financing Administration has set upper limits on Medicaid payment for certain drugs which are generically available from multiple sources and have been deemed therapeutically equivalent by the FDA (Nightingale 1998). These prices are referred to as Federal Upper Limit (FUL) prices, and are aimed at encouraging use of generic drugs in state Medicaid programs. States have some discretion in how they apply these price formulas; the various state payment plans are referred to as Maximum Allowable Cost (MAC) programs (National Pharmaceutical Council 1998). For drugs with these limits, Medicaid will only reimburse the pharmacy for the MAC price, regardless of whether generic or brand name product is dispensed. There may be exceptions to these limits if the prescribing physician indicates that the brand name drug is medically necessary. Federal law also requires drug manufacturers to negotiate rebate arrangements with state Medicaid programs; these rebates are based on the average manufacturer's price for a drug and are generally slightly higher for brand name than for generic drugs (National Pharmaceutical Council 1998).

Using aggregated state-level reimbursement data from the national Medicaid program, we sought to estimate potential savings from broader use

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of generic drugs and assess differences across states in spending on brand name and generic medications.

METHODS

Data Source

State-level data on prescriptions filled and amounts paid through most state Medicaid programs were obtained from data made available by the Health Care Financing Administration (HCFA) (2000). Data for 2000 were available for 48 states and the District of Columbia. No data were available for Arizona and Rhode Island. Some states provided data for only two or three quarters; in these cases we multiplied the available data as needed to yield an annualized projection. Data classifying drugs by generic entity, therapeutic class, manufacturer, formulation, and strength were obtained from the National Drug Data File (NDDF) (First Data Bank 2000).

Description of Variables

The HCFA data on state-level Medicaid drug spending were provided by state, year, and quarter. For each state Medicaid program, the data were categorized by the National Drug Code (NDC) and included the total number of prescriptions filled, units of medication dispensed, and amount paid by the state's Medicaid program for each distinct product. The NDC numbers were used to link the records to drug-specific information from the NDDF, such as the ingredient(s) in a given drug, formulation (e.g. standard tablet, timed-release capsule, transdermal patch), strength, manufacturer, and the package size from which the medication was dispensed. An additional variable categorized whether a given NDC number represented a generic drug or a brand name drug.

Calculation of Generic Prices and Potential Savings

Calculation of generic prices and potential savings was limited to medications dispensed as pills, tablets, or capsules. For drugs available in both short-acting and long-acting forms, brand name drugs were included in the substitution calculation only if there were generic drugs available in the identical form. To ensure that substitutions were clinically reasonable, drugs were grouped by ingredient(s), formulation, strength, and package size. Package size was included because some generic medications are dispensed in very large packages of several thousand units while brand name medications are

generally dispensed in much smaller packages. This difference in package size might magnify the difference in per-unit price calculated beyond the disparity between the costs of the medications themselves.

For brand name prescriptions with identical generic alternatives that met the above criteria, we calculated the reimbursement per unit (i.e., the price for a single tablet, pill, or capsule) for a comparable generic product, based on the lowest cost generic NDC code that was in common use in that state. Although we did not have direct access to each state's MAC prices, the lowest commonly used generic price per unit should provide a good approximation of the MAC price.

We then calculated the potential savings for each brand name NDC that met our substitution criteria. Multiplying the number of units dispensed in all the prescriptions for the brand name NDC by the price per unit of the generic alternative yielded the cost that would have applied if available generic drugs had been dispensed instead of brand name preparations of the same medication. We had in our data the amount reimbursed and the units dispensed for brand and generic NDCs. Using these variables, we calculated the potential savings from more consistent use of generic drugs for each individual medication in the following way:

$$\textit{Price per unit}_{generic} = \textit{Amount reimbursed}_{generic} \div \textit{Units dispensed}_{generic} \quad (1)$$

$$\textit{Potential savings}_{brand} = \textit{Amount reimbursed}_{brand} - (\textit{Units dispensed}_{brand} \times \textit{Price per unit}_{generic}) \quad (2)$$

Some generic medications, such as enalapril and sotalol, first became available during the 2000 calendar year. For these medications we prorated the calculated potential savings, reducing the potential savings by the fraction of the year during which the generic version was not yet available. We did not incorporate manufacturer rebates into these calculations.

We performed an additional analysis to calculate the potential savings if the best MAC prices from a given state had been available nationwide. For each generic entity, we compared costs across all states to find the lowest per-unit price for all generic drugs in common use. We then repeated the calculation of potential savings as shown above, using the lowest per-unit MAC price across all states instead of the lowest generic per-unit price from within the state.

RESULTS

For 2000, the total amount reimbursed by Medicaid nationally in the 49 studied states was slightly over $20.9 billion. Of that total, about $4.3 billion (18.0 percent) was for medications that were available in both brand name and generic forms. In these 49 Medicaid programs, we identified potential savings of $229 million from use of generic drugs, representing 6.1 percent of expenditure on drugs available in both generic and branded forms and 1.1 percent of total drug spending. There was considerable variation among states, from a low potential savings of 3.3 percent of spending on such generically available drugs to a high of 10.3 percent of spending on generically available drugs. Table 1 lists the spending on generically available drugs and the calculated potential savings by state for 2000.

Table 1: National Potential Savings in State Medicaid Programs from Greater Use of Generic Drugs, 2000 (Data for All States Except Arizona and Rhode Island)

State	*Spending on Generically Available Medications*	*Potential Savings*	*% Savings*	*Total Spending*
WI	$ 64,110,566	$ 6,600,405	10.3	$ 351,553,590
NJ	106,525,601	10,977,037	10.3	566,785,748
MD	28,667,535	2,897,346	10.1	204,735,050
OH	116,337,456	11,398,550	9.8	918,942,521
VT	2,486,781	237,622	9.6	14,602,938
MN	39,951,389	3,668,052	9.2	228,524,845
ND	7,126,850	615,864	8.6	38,449,378
AK	8,478,325	710,848	8.4	56,848,157
TX	211,029,943	17,355,530	8.2	1,116,359,395
WY	4,514,704	369,585	8.2	27,495,933
MT	11,544,009	924,024	8.0	61,292,615
MA	116,207,084	9,239,299	8.0	691,277,148
NH	9,464,188	745,329	7.9	59,537,376
NY	422,587,439	33,144,095	7.8	2,430,950,057
KS	27,207,185	2,005,216	7.4	169,688,825
CT	47,221,757	3,395,149	7.2	265,756,253
SD	7,137,897	473,530	6.6	40,843,402
NE	22,863,734	1,476,625	6.5	143,018,192
NM	9,695,621	605,292	6.2	51,409,847
VA	76,595,719	4,733,567	6.2	385,198,076
ID	12,304,077	757,432	6.2	76,248,223
SC	69,859,578	4,291,274	6.1	399,827,981
MS	52,123,805	3,022,874	5.8	360,533,973

continued

Table 1: Continued

State	Spending on Generically Available Medications	Potential Savings	% Savings	Total Spending
DE	10,073,820	582,995	5.8	66,172,361
AR	37,157,851	2,120,714	5.7	213,878,765
NV	9,922,226	566,092	5.7	53,891,037
IA	41,242,082	2,287,557	5.5	208,450,635
NC	160,050,579	8,633,327	5.4	817,583,061
GA	109,458,138	5,855,185	5.3	570,631,752
UT	16,605,476	866,919	5.2	99,854,310
OK	37,427,880	1,944,410	5.2	187,402,622
ME	28,841,055	1,476,806	5.1	179,854,841
CO	27,089,032	1,362,262	5.0	149,711,592
KY	97,845,135	4,855,973	5.0	506,642,019
IN	100,889,655	5,003,461	5.0	513,548,253
FL	205,876,475	10,128,361	4.9	1,341,039,784
IL	161,113,117	7,825,117	4.9	833,504,735
MO	114,934,880	5,463,079	4.8	618,155,467
PA	107,936,551	5,043,211	4.7	625,978,737
LA	98,293,808	4,547,088	4.6	491,789,978
MI	84,686,369	3,909,251	4.6	454,639,922
CA	506,437,048	23,357,318	4.6	2,554,354,967
HI	8,519,185	378,429	4.4	56,742,338
OR	28,961,226	1,286,056	4.4	174,600,044
AL	60,660,080	2,558,940	4.2	344,846,214
TN	122,693,092	4,834,312	3.9	562,189,891
WV	42,466,920	1,623,389	3.8	218,511,602
WA	69,308,569	2,598,054	3.7	391,846,510
DC	6,606,411	219,678	3.3	46,380,312
Total	3,769,137,903	228,972,529	6.1	20,942,081,272

Our analysis of the potential savings using the best MAC price available across states is summarized in Table 2. The total potential savings almost double, to a total of $450 million dollars, representing 11.9 percent of spending on drugs available in both brand and generic forms and 2.1 percent of total drug expenditures. The amount by which the potential savings increase varied from state to state. For example, the potential savings in Ohio increased by 29.6 percent ($3.4 million in absolute terms) while the amount in California more than doubled (absolute increase of $31.7 million).

Several medications had particularly high amounts of potential savings from generic substitution. In 2000, use of generic clozapine would have yielded potential savings of $23.1 million (11.4 percent of reimbursement for that product); levothyroxine would have produced potential savings of

Table 2: National Potential Savings in State Medicaid Programs Using Best MAC Price, 2000 (Data for All States Except Arizona and Rhode Island)

State	*Spending on Generically Available Medications*	*Potential Savings*	*% Savings*	*Total Spending*
NJ	$ 106,525,601	$ 19,719,420	18.5	$ 566,785,748
ND	7,126,850	1,294,888	18.2	38,449,378
AK	8,478,325	1,535,151	18.1	56,848,157
VT	2,486,781	444,813	17.9	14,602,938
NH	9,464,188	1,647,537	17.4	59,537,376
WY	4,514,704	781,125	17.3	27,495,933
MD	28,667,535	4,894,855	17.1	204,735,050
CT	47,221,757	7,463,057	15.8	265,756,253
WI	64,110,566	10,098,003	15.8	351,553,590
SD	7,137,897	1,111,845	15.6	40,843,402
ID	12,304,077	1,895,587	15.4	76,248,223
NY	422,587,439	64,473,249	15.3	2,430,950,057
MN	39,951,389	6,034,570	15.1	228,524,845
IA	41,242,082	5,819,220	14.1	208,450,635
NM	9,695,621	1,358,078	14.0	51,409,847
MT	11,544,009	1,611,971	14.0	61,292,615
HI	8,519,185	1,189,021	14.0	56,742,338
KS	27,207,185	3,611,025	13.3	169,688,825
OH	116,337,456	14,768,118	12.7	918,942,521
UT	16,605,476	2,086,190	12.6	99,854,310
TX	211,029,943	26,450,426	12.5	1,116,359,395
CO	27,089,032	3,381,261	12.5	149,711,592
AR	37,157,851	4,607,006	12.4	213,878,765
NE	22,863,734	2,819,844	12.3	143,018,192
MS	52,123,805	6,301,376	12.1	360,533,973
IL	161,113,117	19,429,516	12.1	833,504,735
SC	69,859,578	8,392,133	12.0	399,827,981
WA	69,308,569	8,316,030	12.0	391,846,510
NV	9,922,226	1,180,418	11.9	53,891,037
MA	116,207,084	13,776,296	11.9	691,277,148
DE	10,073,820	1,187,478	11.8	66,172,361
VA	76,595,719	9,009,344	11.8	385,198,076
OK	37,427,880	4,148,420	11.1	187,402,622
CA	506,437,048	55,026,686	10.9	2,554,354,967
MO	114,934,880	12,352,295	10.7	618,155,467
PA	107,936,551	11,492,783	10.6	625,978,737
ME	28,841,055	3,069,213	10.6	179,854,841
KY	97,845,135	10,150,074	10.4	506,642,019
MI	84,686,369	8,781,068	10.4	454,639,922
NC	160,050,579	16,160,579	10.1	817,583,061
OR	28,961,226	2,890,481	10.0	174,600,044
IN	100,889,655	9,862,246	9.8	513,548,253
LA	98,293,808	9,553,891	9.7	491,789,978

continued

Table 2: Continued

State	Spending on Generically Available Medications	Potential Savings	% Savings	Total Spending
TN	122,693,092	11,836,222	9.6	562,189,891
DC	6,606,411	614,826	9.3	46,380,312
FL	205,876,475	18,554,261	9.0	1,341,039,784
AL	60,660,080	5,427,407	8.9	344,846,214
GA	109,458,138	9,530,766	8.7	570,631,752
WV	42,466,920	3,647,127	8.6	218,511,602
Total	3,769,137,903	449,787,196	11.9	20,942,081,272

Table 3: National Potential Savings in State Medicaid Programs from Greater Use of Generic Drugs, Specific Agents, 2000

		Primary Analysis		Best MAC-Price Analysis	
	Total Reimbursed	Potential Savings	% Savings	Potential Savings	% Savings
Clozapine	$ 202,761,006	$ 23,098,582	11.4	$ 67,821,868	33.4
Levothyroxine	68,802,671	17,726,624	25.8	28,157,885	40.9
Alprazolam	35,308,683	11,028,311	31.2	11,628,543	32.9
Enalapril	122,126,165	10,530,374	8.6	31,134,625	25.5
Carbamazepine	84,814,301	10,275,413	12.1	14,077,999	16.6
Digoxin	38,781,930	10,075,230	26.0	17,768,745	45.8
Amylase/Lipase/ Protease	37,087,356	7,655,759	20.6	10,011,224	27.0
Warfarin	78,612,618	7,316,279	9.3	20,484,740	26.1
Phenytoin extended	64,340,706	5,899,264	9.2	11,337,251	17.6
Ranitidine	176,288,934	5,876,778	3.3	9,455,660	5.4
Total of selected drugs	908,924,370	109,482,614	12.0	221,878,540	24.4

$17.7 million (25.8 percent of reimbursement). Table 3 lists the ten medications with the highest amount of unrealized savings in 2000 in the first three columns. The combined potential savings for these 10 medications was over $109 million, or 47.8 percent of the total potential savings from all medications. The last two columns of Table 3 show the potential savings for these ten medications in the analysis using the best MAC price available. As with the state level results shown in Tables 1 and 2, the changes are not uniform across drugs, so that the potential savings for clozapine and enalapril increase more than 150 percent while the potential savings for alprazolam are almost unchanged.

DISCUSSION

At a time that Medicaid programs nationally are severely pressed to afford their current drug benefits, these findings demonstrate a source of potential savings from increased use of generic medications. Although the potential savings from the two scenarios presented range between a quarter billion dollars and almost a half billion dollars, formidable amounts for programs that are seeking to contain costs in any way possible, they represent a modest proportion of total Medicaid spending on prescription drugs. The data provide some important insights for the design of a prescription drug benefit for the elderly, either under Medicare or in a private insurance context.

Much of the excess costs found result from prescriptions for which the physician specifically requested a brand name drug as "medically necessary." The pharmacologic rationale for such a decision in most cases is dubious. One method of reducing excess spending on brand name drugs is to target physician behavior in this regard.

Prior research has shown considerable variation in physician beliefs and practices regarding generic substitution, as well as poor understanding among physicians of the FDA regulations for generic products (Banahan and Kolassa 1997; Murphy 1999). Physicians may be influenced by marketing information to believe that brand name drugs are somehow more effective or are held to a higher manufacturing standard, even in the absence of data supporting this belief. The important role of the physician in the decision to use a brand name or a generic drug has been described previously (Hellerstein 1998), and some interventions have attempted to target physician behavior directly (Ahluwalia et al.). Nevertheless, given that Medicaid already has financial regulations favoring the use of generic drugs (by limiting payment for the brand name version), this portion of potential savings may be difficult to achieve through reimbursement policy and may require additional changes in physician prescribing practices. One important limitation of our analysis was our inability to incorporate manufacturer rebates into the calculations. The rebates are calculated based on the average manufacturer's price for a drug (National Pharmaceutical Council 1998); that price is not easily available and was not practical to use as part of this analysis.

Variations in MAC price levels are also an important source of unrealized savings. The drug-by-drug analysis (Table 3) demonstrates that most potential savings come from a small number of medications. Indeed, in the main analysis, clozapine alone accounts for over 10 percent of the potential savings. The best MAC price available analysis provides evidence that some

states are more successful at controlling costs for specific medications. The large increase in potential savings for some of the medications implies that much lower prices for these medications are available in some states than others. There is considerable heterogeneity among states in the proportion of drug spending which could have been saved by greater use of generic medications (Table 2). Variation in how states implement their MAC programs for prescription drug price limits may account for such differences. Future research comparing the details and operationalization of MAC programs across states may provide important information for the design of a Medicare prescription drug benefit and could help realize some of the potential savings. Policy efforts that target specific medications may be able to address areas of excess spending in an efficient manner.

There has been controversy about generic substitution for some of the drugs listed in Table 3, notably warfarin (DeCara, Croze, and Falk 1998; Wittkowsky 1998; Benson and Vance-Bryan 1998; Haines 1998) digoxin (Weintraub et al. 1979; Reissell et al. 1974; Lindenbaum et al. 1971; Jounela and Sothmann 1973), and levothyroxine (Rennie 1997; Dong et al. 1997). Newer evidence argues that generic versions of these drugs are appropriate, although increased monitoring may be required when converting from brand name to generic medication (Rennie 1997; Dong et al. 1997; Baker et al. 1988; Hendeles et al. 1995; Kanthawatana et al. 1994; Kramer 1989). The persistent controversy and potential transition costs may limit the potential savings from these three drugs.

In important ways, the data presented above represent a conservative estimate of the potential savings from more widespread use of generic drugs. By limiting the savings calculation to tablets and capsules, we assumed that there were no potential savings for inhaled medications, topical medications, transdermal patches, and several other classes of widely used drugs.

There has been much interest in more aggressive substitution of different drugs within a class (McAlister et al. 1999), (therapeutic substitution, e.g., switching one ACE inhibitor for another), and this practice is currently mandated in many private insurance plans. A recent study of a reference-pricing system under which a health plan would only pay for lower priced ACE inhibitors demonstrated cost reductions without adverse effects on patients or other health care expenditures (Schneeweiss et al. 2002). We did not attempt to incorporate this source of savings into our analysis; all potential savings described here result from the replacement of a brand name product with a generic drug of identical chemical composition and duration of action.

One important question that has been addressed in prior research (Bae 1997; Stolberg and Gerth 2000) is the pattern over time of market entry and prescribing of generic drugs after a medication goes off patent. Our research examined unrealized savings only for drugs for which generics were already in the marketplace. More information on the patterns of adoption of generic alternatives as they become available would help clarify one cause of the excess costs from use of brand name drugs described above. The rate at which physicians begin writing for generic names of drugs or stop invoking medical necessity for brand name drugs will likely correlate with the extent and effectiveness of marketing of the original brand name drugs. Further research is also needed on the causes of delays in commercial availability of generic alternatives after patents have expired on the original brand name products (Stolberg and Gerth 2000).

These findings provide evidence that important savings could be realized in the Medicaid drug program through more widespread use of generic medications. The estimates presented are conservative, and the true potential savings is likely larger. As both public and private insurers struggle to accommodate increases in the cost of drug coverage, multiple strategies will be needed to control expenditures. This analysis points to one area in which excess expense can be avoided with no compromise in clinical outcomes.

REFERENCES

Ahluwalia, J. S., M. L. Weisenberger, A. M. Bernard, and S. E. McNagny. 1996. "Changing Physician Prescribing Behavior: A Low-Cost Administrative Policy that Reduced the Use of Brand-Name Nonsteroidal Anti-inflammatory Drugs." *Preventive Medicine* 25 (6): 668–72.

Bae, J. 1997. "Drug Patent Expirations and the Speed of Generic Entry." *Health Services Research* 32 (1): 87–101.

Baker, J. J., H. Moessner, U. Gonzalez, J. Grabenstein, R. Renard, T. DeNapoli, R. Jummers, and B. Schuster. 1988. "Clinical Relevance of the Substitution of Different Brands of Sustained-Release Theophylline." *Journal of Allergy and Clinical Immunology* 81 (4): 664–73.

Banahan, B. F. I., and E. Kolassa. 1997. "A Physician Survey on Generic Drugs and Substitution of Critical Dose Medications." *Archives of Internal Medicine* 157 (18): 2080–8.

Benson, S., and K. Vance-Bryan. 1998. "In Favor of Coumadin over Generic Warfarin." *American Journal of Health System Pharmacy* 55 (7): 727–9.

DeCara, J., S. Croze, and R. Falk. 1998. "Generic Warafrin: A Cost-Effective Alternative to Brand-name Drug or a Clinical Wild Card?" *Chest* 113 (2): 261–3.

Dong, B. J., W. W. Huack, J. G. Gambertoglio, L. Gee, J. R. White, J. L. Bupb, and F. J. Greenspan. 1997. "Bioequivalence of Generic and Brand-name Levothyroxine Products in the Treatment of Hypothyroidism." *Journal of the American Medical Association* 277 (15): 1205–13.

First Data Bank. 2000. *National Drug Data File.* San Bruno, CA: Hearst Corporation.

Haines, S. 1998. "Reflections on Generic Warfarin." *American Journal of Health System Pharmacy* 55 (7): 729–33.

Health Care Financing Administration. 2002. *National Health Care Expenditure Projections: 2001–2011.* Washington, DC: Health Care Financing Administration.

———. 2000. *State Drug Utilization Data.* Washington, DC: Health Care Financing Administration.

Hellerstein, J. K. 1998. "The Importance of the Physician in the Generic versus Trade-name Prescription Decision." *RAND Journal of Economics* 29 (1): 108–36.

Hendeles, L., A. Breton, R. Beaty, and E. Harman. 1995. "Therapeutic Equivalence of Generic Slow-Release Theophylline Tablet." *Pharmacotherapy* 15 (3): 26–35.

Jounela, A., and A. Sothmann. 1973. "Bioavailability of Digoxin." *Lancet* 1 (7796): 202–3.

Kanthawatana, S., R. Ahrens, M. McCubbin, E. Bronsky, K. Blake, and L. Hendeles. 1994. "Bioequivalence of Generic Slow-Release Theophylline Tablet in Children." *Journal of Pediatrics* 125 (6, part 1): 987–91.

Kramer, P. 1989. "Slow-Release Theophylline: Substitute Only AB-Rated Products." *American Pharmacy* (3) NS29: 23–4.

Lindenbaum, J., M. Mellow, M. Blackstone, and V. J. Butler. 1971. "Variation in Biologic Availability of Digoxin from Four Preparations." *New England Journal of Medicine* 285 (24): 1344–7.

McAlister, F. A., A. Laupacis, G. A. Wells, and D. L. Sackett. 1999. "For the Evidence-Based Medicine Working Group. Users' Guides to the Medical Literature, XIX: Applying Clinical Trial Results, B: Guidelines for Determining Whether a Drug is Exerting (More Than) a Class Effect." *Journal of the American Medical Association* 282 (14): 1371–7.

Murphy, J. 1999. "Generic Substitution and Optimal Patient Care." *Archives of Internal Medicine* 159 (5): 429–33.

National Pharmaceutical Council. 1998. *Pharmaceutical Benefits under State Medical Assistance Programs.* Reston, VA: National Pharmaceutical Council.

Nightingale, S. L. 1998. "Generic Substitution." *Journal of the American Medical Association* 279 (9): 645.

Reissell, P., V. Manninen, K. Ojala, and J. Karjalainen. 1974. "Non-equivalence of Digoxin Tablets." *Annals of Clinical Research* 6 (11, supplement): 4–8.

Rennie, D. 1997. "Thyroid Storm." *Journal of the American Medical Association* 277 (15): 1238–43.

Schneeweiss, S., A. M. Walker, R. J. Glynn, M. Maclure, C. Dormuth, and S. B. Soumerai. 2002. "Outcome of Reference Pricing for Angiotensin-Converting-Enzyme Inhibitors." *New England Journal of Medicine* 346 (11): 822–9.

Stolberg, S. G., and J. Gerth. 2000. "How Companies Stall Generics and Keep Themselves Healthy." *New York Times* 23 July, 1, 12.

U.S. Government Accounting Office. 1999. *Medicare: Considerations for Adding a Prescription Drug Benefit.* Report no. GAO/T-HEHS-99-153. Washington, DC: U. S. Government Accounting Office.

Weintraub, M., F. Karch, J. Morgan, N. Trabert, A. Sorensen, L. A. Becker, and L. Lasagna. 1979. "Digoxin-Prescribing: Mostly Good News." *Journal of the American Medical Association* 242 (5): 445–8.

Wittkowsky, A. 1998. "Generic Warfarin: Implications for Patient Care." *Pharmacotherapy* 17 (4): 640–3.