Adoption of Pharmaceutical Innovation and the Growth of Drug Expenditure in Taiwan: Is It Cost Effective?

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ABSTRACT

Objectives: To investigate the impact of adopting pharmaceutical innovations on the growth of pharmaceutical expenditures, focusing specifically on Taiwan’s experience.

Methods: We first provide a descriptive analysis of cost impacts of introducing new drugs into Taiwan’s national formulary using data from Taiwan. We then use a statistical method to decompose the growth of pharmaceutical expenditures during 1997–2001 into three components: 1) treatment expansion; 2) treatment substitution; and 3) price effect. By incorporating the estimated benefit from prior studies, we calculate the incremental cost-effectiveness ratio for new drugs as a whole.

Results: We find that from 1997 to 2001 public expenditures on pharmaceuticals grew 57%. The primary drivers of this expenditure growth were treatment expansion and treatment substitution. Prices declined by 18%. Cost per life-year gained resulting from introduction of new drugs was US$1053 (in 2003 dollars) from the perspective of the public payer and US$1824 from the perspective of society as a whole.

Conclusions: Overall, our analysis provides evidence with previous studies that the drug reimbursement price is not the primary driver of increased spending. Rather the introduction of new drugs into the formulary leading to expansion of treatment, expansion and substitution of the new drugs for existing drugs may increase spending. Although the adoption of pharmaceutical innovation is costly, the estimated benefit of adopting pharmaceutical innovation generally far exceeds the cost, indicating that the adoption of pharmaceutical innovation is on the whole worthwhile.

Keywords: drug expenditure, pharmaceutical innovation, treatment expansion, treatment substitution.

Introduction

Technological change in medicine has been a major cause of rising health-care expenditures in many countries [1]. A substantial amount of technological progress in medicine has taken the form of pharmaceutical innovation. Consequently, both spending on prescription drugs and the share of drug expenditure in total health-care expenditures have increased rapidly in recent years [2–4]. Around the world, governments have used a number of regulatory mechanisms to control spending on pharmaceuticals [4]. Nevertheless, there is a growing body of empirical evidence that technological advances in the form of new prescription drugs have made a substantial contribution to increased longevity and improved quality of life [5–7]. Thus, there is an inherent conflict between the regulatory goal of controlling health-care budgets and improving population health.

The purpose of this study is to use the experience of Taiwan as an example to investigate the impact of adopting pharmaceutical innovations on the growth of pharmaceutical expenditures and whether pharmaceutical innovation is worth the increased cost. There are several advantages of using Taiwanese data to quantify the impact of pharmaceutical innovation on health-care costs. First, Taiwan has a social insurance system providing universal insurance coverage. The National Health Insurance (NHI) plan offers comprehensive benefits, including physician services, hospital care, and prescription drugs. To control the cost of public insurance, the government in Taiwan regulates the price paid by the single health insurance plan for individual drugs. The single-payer system allows policymakers as well as researchers to trace the impact of introducing new drugs on national health costs.

Second, under a system of NHI, Taiwan has established a national formulary (positive list), which includes all pharmaceuticals subject to reimbursement by NHl. Because the government imposes direct price controls on pharmaceuticals by fixing the prices product by product, the numbers of drugs included in the formularies are extraordinary large. There are more than 21,000 drugs included in the NHI formularies in Taiwan. The detailed list of drug formulary allows the researcher to decompose the source of expenditure growth on prescription drugs.
Third, Taiwan spends about one quarter of health-care expenditures on pharmaceuticals. As compared to other developed countries, the higher spending makes prescription drugs be more likely to become the target of cost containment. As a result, the experience of Taiwan provides a valuable insight on understanding how policymakers struggle with the conflict between short-run cost impact and long-run health benefit.

The focal points of this article are threefold. We first briefly discuss institutional details of Taiwan’s pharmaceutical policies and describe the cost implications of introducing new prescription drugs. We then decompose the growth of pharmaceutical expenditures during 1997–2001 into three components. The first is the growth of expenditures on prescription drugs attributable to an increase in quantity of prescribed drugs—the treatment expansion effect. Second, technological change may lead to shifts in drug use within specific therapeutic category, especially to more expensive products—the treatment substitution effect. The third is the effect of price changes on pharmaceutical expenditure—pure price effect.

By incorporating the estimated benefit from the existing study into our cost measurement, we also calculate the incremental cost-effectiveness ratio for new drugs as a whole. Specifically, we compare spending on new drugs per capita with average annual increase in life expectancy attributable to new drug launches.

**Institutional Background**

**Characteristics of Pharmaceutical Market**

There are two distinguishing characteristics of health-care system that shape the structure of pharmaceutical market in Taiwan. First, physicians dispense the drugs that they prescribe. Thus, they are in a position to profit directly from the sales of prescription drugs. The government regulates the reimbursement price, i.e., the price paid on behalf of patients, but do not regulate the acquisition prices that hospitals or physicians practicing in clinics purchase drugs from the pharmaceutical manufacturers. Thus, hospitals or clinic physicians receive the profit margin between the reimbursement and the acquisition prices.

Second, the medical staff is employed by the hospital. Also, patients are free to choose their own providers; there is no gatekeeper mechanism. Under this system, except for emergencies, the main source of inpatients is the outpatient department at the same hospital. Thus, hospitals in Taiwan have a strong incentive to operate large outpatient departments to increase their inpatient flows. Larger hospitals often possess substantial bargaining power with pharmaceutical manufacturers and can obtain drugs at a lower acquisition price. In general, the profit margin between the reimbursement price and the acquisition price represents a major source of hospital revenue.

These two characteristics have had several important consequences in the pharmaceutical markets in Taiwan. First, the existence of profit margins for pharmaceuticals has led to distortions in relative prices of prescription drugs and other health-care services. Compared to prescription drugs, other health-care services, such as production of diagnostic information and surgical treatment, are very labor intensive. In contrast to physical products, there is no wholesale market for services, and hence providers do not have an opportunity to earn a profit margin between the reimbursement and the acquisition prices. With a positive margin on prescription drugs, providers have a financial incentive to substitute prescription drugs for other inputs, such as time spent in diagnosis or in surgical treatment. Spending on pharmaceuticals consequently accounts for one quarter of health-care expenditures in Taiwan. In 2004, the share of health-care expenditures spent on drugs ranged from 9% to 30% among OECD countries [8]. Although many other factors also account for the international variation in the share of pharmaceutical spending, the existence of profit incentives in prescribing drugs provides a plausible explanation for the relatively higher share of drug expenditures observed in Taiwan.

Second, although reimbursement prices are fixed by government, there is price competition in the wholesale market. Given the profit that providers can earn from the sale of drugs, the profit margin between the reimbursement and the acquisition price becomes the important factor in the drug prescribing decisions. Since there are many drugs within a therapeutic group, the pharmaceutical manufacturers compete by cutting acquisition prices. Of course, the lower limit on such prices is marginal cost of manufacturing and distributing the drugs. Providers in turn only select the drugs with higher profit margins into their prescription formularies.

Price competition in the wholesale market has driven many products from the market (Table 1). Although there are 21,931 drugs listed in the Taiwan’s national formulary, only about 75% of products are actually sold in a given year. In addition, the distribution of market size (in terms of annual expenditures) by product is highly skewed. About 3700 drugs, or 17% of products listed in the national formulary, account for about 97% of expenditures on pharmaceuticals. The prescriber’s profit incentive shifts price competition from the retail to the wholesale market with the result that only about 3700 drugs remain actively sold in the market. In monetary terms, the annual market size is greater than one million Taiwan dollars (or about US$30,000).
Pricing and Cost Impact of New Drugs

New pharmaceutical products are introduced annually as a consequence of technological advances. In addition to obtaining authorization to market a new drug, Taiwan, like other countries with direct price controls on pharmaceutical products, requires that the manufacturer of a new drug obtain approval for coverage and a price for reimbursement by the Bureau of National Health Insurance (BNHI) [4,9,10]. Taiwan has not formally employed economic evaluation to establish prices for new drugs to be included on its formulary. Rather, BNHI adopts a mix of strategies to determine the reimbursement price for new drugs, including reference to existing products and to international comparisons, and the drug’s therapeutic value.

BNHI uses the median price of international comparisons to set the cap on regulated prices for branded drugs still on patent. For off-patent branded drugs, the price cap is 85% of international median prices. For generic drugs, the price cap is the mean price of the branded price in the same therapeutic group if the drug has passed a bio-equivalent test and 85% of the mean price of the branded drugs in the same therapeutic group if a bio-equivalent test is not conducted for the drug. The BNHI selects 10 countries as the reference group for international comparisons, including Australia, Belgium, Canada, France, Germany, Japan, Sweden, Switzerland, United Kingdom, and the United States [11].

Many forms of new prescription drugs are added to the national formulary annually, including new molecular entities, formulations, combinations, and indications. As a single payer, BNHI can trace all expenditures on drugs as well as other health-care services through its electronic administrative system. Table 2 summarizes the expenditure and number of new drugs included in the national formulary between 1996 and 2003. A new drug is defined here as one that was included in the national formulary after 1996.

During 1996–2003, the annual number of new drugs included in the national formulary has ranged from 13 to 75. On average, each drug cost about NT$ 21–59 million annually (1 US$ equaled about 27.5–34.6 NT$ during this period). Judging from the average market size per drug in Taiwan, the annual mean cost per new drug is very significant. For example, as shown in Table 1, there were only 717 products in Taiwan’s market (3.2% of total number of products listed in the formulary) for which annual expenditure on individual drug exceeded NT$20 million. Thus, the cost impact of introducing new drugs was substantial relative to the mean national level. Furthermore, the average annual growth rate of

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of new drugs</th>
<th>Mean annual expenditure per drug between introduction year and 2003 (in million NT dollar)</th>
<th>Mean annual growth rate of expenditure between introduction year to 2003 (%)</th>
<th>Total expenditure on new drugs (in million NT dollar)</th>
<th>Spending on new drugs as percent of total spending in pharmaceuticals</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>13</td>
<td>59</td>
<td>40</td>
<td>—</td>
<td>—</td>
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<tr>
<td>1997</td>
<td>54</td>
<td>21</td>
<td>24</td>
<td>473</td>
<td>0.99</td>
</tr>
<tr>
<td>1998</td>
<td>75</td>
<td>47</td>
<td>49</td>
<td>1,933</td>
<td>3.49</td>
</tr>
<tr>
<td>1999</td>
<td>42</td>
<td>30</td>
<td>64</td>
<td>4,063</td>
<td>6.42</td>
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<tr>
<td>2000</td>
<td>36</td>
<td>54</td>
<td>190</td>
<td>6,121</td>
<td>9.23</td>
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<tr>
<td>2001</td>
<td>73</td>
<td>40</td>
<td>229</td>
<td>8,431</td>
<td>12.45</td>
</tr>
<tr>
<td>2002</td>
<td>56</td>
<td>32</td>
<td>216</td>
<td>12,863</td>
<td>16.67</td>
</tr>
<tr>
<td>2003</td>
<td>50</td>
<td>—</td>
<td>—</td>
<td>16,694</td>
<td>20.92</td>
</tr>
</tbody>
</table>

Source: Bureau of National Health Insurance, Taipei, Taiwan.
Note: 1. The definition of new drugs includes 1) new molecular entity; 2) new formulation; 3) new combination; and 4) new indication. 2. The exchange rate of US$/NT$ was 34.42 in 2003.

Table 1 The distribution of pharmaceutical spending by market size

<table>
<thead>
<tr>
<th>Market size in 2001 (NT dollar)</th>
<th>Number of drugs</th>
<th>Percentage of total number of drug (%)</th>
<th>Pharmaceutical spending (in million NT dollar)</th>
<th>Percentage of total pharmaceutical spending (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than 100 million</td>
<td>129</td>
<td>0.59</td>
<td>25,666</td>
<td>37.90</td>
</tr>
<tr>
<td>50–100 million</td>
<td>178</td>
<td>0.81</td>
<td>12,230</td>
<td>18.06</td>
</tr>
<tr>
<td>20–50 million</td>
<td>410</td>
<td>1.87</td>
<td>12,780</td>
<td>18.75</td>
</tr>
<tr>
<td>10–20 million</td>
<td>474</td>
<td>2.16</td>
<td>6,617</td>
<td>10.38</td>
</tr>
<tr>
<td>1–10 million</td>
<td>2,536</td>
<td>11.56</td>
<td>9,005</td>
<td>13.49</td>
</tr>
<tr>
<td>Less than 1 million</td>
<td>12,684</td>
<td>57.84</td>
<td>1,382</td>
<td>2.07</td>
</tr>
<tr>
<td>0 (no sale)</td>
<td>5,520</td>
<td>25.17</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>21,931</td>
<td>100.00</td>
<td>66,730</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Source: Bureau of National Health Insurance, Taipei, Taiwan.
Note: The exchange rate of US$/NT$ was 34.42 in 2003.
drug expenditure for new products between the years of introduction to 2003 ranged form 24% to 229% (Table 2). A shorter observational period was associated with a higher growth rate. This suggests that the introduction of new drug is not only costly in the short run, but also in the longer run. For example, in 1998, 75 new drugs were included into the formulary and the mean annual growth rate of expenditure was 49% from 1998 to 2003, substantially more than the mean annual growth rate of overall expenditures on pharmaceuticals (6.4%). By 2003, total spending on 399 new drugs introduced into the national formulary after 1996 was about NT$17 billion, accounting for 21% of total drug expenditures in that year. This indicates that on average introducing a new drug into the formulary costs about NT$42 million (17,000/399) per year.

As suggested by Cutler and McClellan [12], new technology in medicine affects the cost of health care through the two channels: a treatment substitution effect and a treatment expansion effect. In the context of pharmaceuticals, a treatment substitution effect describes substitution of new drugs for older ones for treating established patients. Because of the high costs of pharmaceutical innovation which is partly reflected in high prices because of the patent system, the price of new drug is higher than for older drugs, at least some of which are no longer patented. Thus, the treatment substitution effect always leads to increased pharmaceutical expenditures [13,14]. The treatment expansion effect indicates that the introduction of new drugs into the formulary leads more people to be treated for disease. Hence, the treatment expansion effect also leads to increased pharmaceutical expenditure. In the next section, we will use a statistical method to decompose the growth of pharmaceutical expenditure into treatment substitution effect and expansion effect.

**Decomposition of the Source of Expenditure Growth**

**Previous Studies**

The rapid increase in pharmaceutical expenditure has led to a search for the primary determinants of this increase. By definition, pharmaceutical expenditures are the product of prices and demand (quantity of prescription pharmaceuticals consumed). The demand for drug in turn depends on several factors, such as drug insurance benefit coverage, income, the incidence and duration of chronic diseases, and technological advances in medicine.

In practice, the relative importance of the above-mentioned factors varies with country-specific aspects of the health-care system and pharmaceutical policy in each country. For example, in a country in which government does not regulate pharmaceutical prices directly, such as the United States, price increases may have a relatively important role in accounting for expenditure growth. There is evidence that some pharmaceutical manufacturers adopt a penetration strategy to launch their new drugs that leads to an upward sloping price curve over time [15].

By contrast, in some countries in which governments impose direct controls on product prices, such as Japan and Sweden, price-cap regulation rules out the use of penetration strategies [16,17]. Real (relative to a consumer price index for all goods and services) prices of drugs often fall over time as a result of government regulation and price-cutting. In these countries, price increases have not been an important cause of increased expenditures. Similarly, the introduction of insurance coverage for prescription drugs is an important factor in accounting for expenditure growth in countries in which private and/or public drug insurance benefit coverage has gradually been added. For example, in 1965, only 3.5% of the US prescription drug expenditure was paid by private insurance. By 1998, the private plus Medicaid insurance share increased to 69.8% [3]. The empirical evidence shows that the growth in the US pharmaceutical expenditure closely paralleled this expanded drug insurance coverage [18]. But health insurance is not the primary driver of increased spending in countries that insurance coverage for prescription drugs had remained constant over time, such as Japan and Taiwan.

Given that the major cause or causes of increased spending varies across countries and over time, several studies have sought to identify the underlying drivers of spending trends by decomposing the sources of expenditure growth [2,3,19,20]. Dubois et al. [2] used large claims databases from managed care and the employer-sponsored health benefit plans in the United States to disaggregate the growth of drug spending between 1994 and 1998 into several price and volume factors. They decomposed the change in price into three components: 1) pure inflation (measuring by an index of change in actual transaction prices); 2) price change because of the change in dosage strength and therapeutic mix; and 3) change in mean price per day on account of the introduction of new drugs. For volume, they calculated these three measures: 1) changes in the number of prescriptions per person; 2) changes in the number of days supplied per prescription; and 3) changes in the number of users and potential users of prescription drugs per thousand plan members, which they used as a measure of prevalence of the disease. In their study, users were defined as patients treated with a particular drug and potential users were defined as patients with a diagnosis corresponding to an approved indication for that drug but no drug use. They found that change in volume was the primary driver of increased spending for the seven diseases they studied. In particular, increase in disease prevalence and in the number of prescriptions per patient for new drugs were the two most important
factors accounting for the growth in pharmaceutical expenditures.

Berndt [3] used aggregate sales data to decompose pharmaceutical expenditure growth in the USA into three components: 1) price growth of incumbent products; 2) quantity growth of incumbent products; and 3) expenditures on new products. Between 1987 and 1994, price growth of incumbent products accounted for about half of the total expenditure growth. Nevertheless, from 1994 through 2000, price growth accounted for only 20% of expenditure growth. The remaining 80% was attributable to quantity growth of incumbent drugs and expenditures on new drugs. His finding suggests that price increases have become a relatively less important factor in explaining the growth of the US pharmaceutical expenditures since the mid-1990s. Rather, quantity growth, either from increased demand for incumbent or new drugs, has become the primary determinant of expenditure growth, which is consistent with the studies by Dubois et al. [2]. Berndt’s analysis further indicated that this quantity growth was driven by increased drug insurance benefit coverage and enhanced marketing efforts, especially direct-to-consumer advertising.

Morgan [19] used Canadian data to decompose the change in per capita prescription drug expenditures from 1985 to 1999 into four components: 1) the pattern of exposure to drugs across therapeutic categories; 2) the mix of drugs used within therapeutic categories; 3) the price of unchanged products; and 4) the rate of generic drug product selection. He found that the above-mentioned first three factors worked together to lead to a per capita expenditure growth from $49 to $150 per quarter over the period of study. Nevertheless, generic substitution resulted in a saving in per capita spending of $14 per quarter during the study’s observational period.

Thus, net increased spending was $87 per quarter. For the expenditure growth of $101 which was driven by increases in both price and quantity, the increase in price accounted for 22% of increased spending, indicating that price increases have also had a relatively minor role in explaining growth of pharmaceutical expenditure in Canada. Rather the primary cause of increased spending was quantity growth, a result consistent with other studies [2,3]. Morgan emphasized that the major economic forces behind the quantity growth were an increase in the rate of exposure to a given therapeutic category of drugs and changes in the mix of drugs used within therapeutic categories with these factors being of almost equal importance and together accounting for 78% of the expenditure growth in Canada.

Addis and Magrini [20] used data from Italy to decompose the growth of pharmaceutical expenditures into three components: 1) quantity (expressed in term of defined daily doses, DDDs); 2) price; and 3) a change in product mix, a change in expenditures because of the shift within the same therapeutic group of drugs toward more or less expensive products. In Italy, drug expenditure increased 13.5% from 2000 to 2001. Their decomposition of this growth rate showed that the increase in quantity of prescription drugs consumed (measured by DDDs) led to a 9.5% increase in expenditure and mix effects led to the expenditure growth by 4.8%. Price changes led to a decrease in drug expenditure of 1%.

In spite of the wide variation in statistical methods and data sources, existing studies provide fairly consistent evidence that price is not the primary determinant of increased spending in prescription drugs, but rather the quantity growth is. Existing studies also have identified several common factors underlying quantity growth, including an increase in disease prevalence, an increase in drug utilization, and a change in the drug mix within therapeutic categories, both working to expand treatment and to substitute drug therapy for other forms of therapy.

Method

For this study, we employed the concepts of treatment expansion and substitution effects and the statistical method developed by Addis and Magrini [20] to decompose the growth of pharmaceutical expenditure in Taiwan. The growth of pharmaceutical expenditures from the base period (0) to the current period (1) can be expressed as:

\[
\frac{\sum P_i^1 Q_i^1}{\sum P_i^0 Q_i^0} = \frac{\sum Q_i^1}{\sum Q_i^0} \times \frac{\sum P_i^1 Q_i^0}{\sum P_i^0 Q_i^0} \times \frac{\sum P_i^1 Q_i^1}{\sum Q_i^1} \tag{1}
\]

In equation 1, \(Q_i^1\) and \(Q_i^0\) represent quantities of the \(r\)th prescription drug dispensed in periods 1 and 0 respectively, measured in terms of DDD. As mentioned, the government in Taiwan regulates reimbursement prices product by product. Thus, our analysis classified drugs by brand name. Drugs with the same ingredient but produced by different manufacturers are treated as different products. \(P_i\) and \(P_i^0\) represent the prices of the \(r\)th drug per DDD in periods 1 and 0, respectively. Summing the product of prices by quantities for all drugs yields the total expenditure on prescription drugs. The left hand side of equation 1 therefore represents the growth in pharmaceutical expenditures from the base period (0) to the current period (1).

Expenditure growth can be decomposed into three components on the right side of equation 1. The first ratio on the right side is an index of quantity growth between two periods. We used the DDD as the standard unit of prescription drug and hence the quantities of prescription drugs could be summed and compared.
across different drugs and time periods. The growth of the pure quantity of drug consumed represents the treatment expansion effect that arises from more people being treated or the increase in treatment intensity for the same group of treated patients, such as occurs when prescriptions per patient and/or days per prescription increased.

The second ratio represents the Laspeyres price index, using quantities of drugs consumed in the base year as weights. This index measures the pure price change between current period (1) and base period (0).

The third ratio represents an index for the mix effect, which equals the ratio of two weighted average prices per DDD in the current period. The numerator of this ratio uses the quantity of drug consumed at current period (1) as the weight to calculate the mean price per DDD. By contrast, the denominator of this ratio uses the quantity of drug consumed in base period (0) as the weight to calculate the mean price per DDD. The third ratio is not equal to 1 as long as the quantity mixes of all drugs used in current period \(Q^1\) are different to those of the base period \(Q^0\). Since the drug prices within the same therapeutic group is not uniform in Taiwan, the drug substitution that physicians prescribe different brands of drugs for treating the same disease would lead to a change in price per DDD. Thus, this ratio represents the change in the mean price per DDD from shifts within the same therapeutic groups of drugs toward more or less expensive products. If the ratio is greater than 1, it indicates that there is an increase in mean price per DDD resulting from the change in the mix of quantities between the current period and the base period. Thus, this index represents expenditure growth because of treatment substitution.

**Data Sources**

Data for this study came from two sources. First, data on the utilization of prescription drugs came from insurance claim files obtained from Taiwan’s BNHI (hereafter referred to as NHI claims data). After NHI was implemented in March 1995, and ever since, the BNHI has maintained a national, population-based claims database. The NHI claims data contain detailed records on utilization of personal health-care services, including outpatient visits, hospital admissions, and prescription drugs. The data on prescription drugs provide information identifying the drug (drug ID), the anatomical therapeutic chemical (ATC) classification system, the reimbursement price, quantity of utilization, total spending, and such drug characteristics as ingredient name, brand name, dosage, and manufacturers for all items of drugs listed in NHI formulary. We used NHI claims data for prescription drugs during 1997–2001 to investigate the sources of expenditure growth between these two periods.

Second, data on DDD came from Kao et al. [21]. In that study, DDD for prescription drugs used in Taiwan was classified according to the guidelines developed by the World Health Organization (WHO) Collaborating Center for Drug Statistics Methodology [22]. The DDD is defined as the assumed mean maintenance dose per day for a drug used for its main indication in adults [22]. This provided a standard unit of measurement invariant to price and formulation. Nevertheless, DDDs are not established for all drugs. There are no DDDs for certain drugs, such as topical products, sera, vaccines, antineoplastic agents, allergen extracts, general and local anesthetics and contrast media [22]. Thus, we only included drugs with a DDD assignment into our analysis. Among 21,931 items of drugs (in brand names) listed in NHI formulary, Kao et al. [21] assigned DDDs for 13,295 drugs.

After merging NHI claims data with DDD data by individual drug ID, we first transformed the quantity of drug consumption in terms of DDD according to the following equation:

\[
Q_i = q_i / \text{DDD}_i
\] (2)

where \(q_i\) indicates the quantity of drug utilization for the \(i\)th drug (by brand name) in terms of its package unit obtained from NHI claims data, and \(Q_i\) indicates the quantity of drug utilization for the \(i\)th drug expressed in terms of DDD; using the concept of DDD, we could aggregate across drugs. We then calculated price per DDD using

\[
P_i = E_i / Q_i
\] (3)

where \(E_i\) indicates the expenditure for the \(i\)th drug obtained from NHI claims data, and \(P_i\) represents the price per DDD for the \(i\)th drug.

After computing quantity and price expressed in terms of DDD, we applied the method depicted in equation 1 to decompose the sources of expenditure growth into three components: 1) price; 2) quantity; and 3) mix effects. In our analysis, the base period refers to 1997 and the current period refers to 2001.

**Results**

Table 3 shows our results. For simplicity, we set the index of base year (1997) equal 1. For all drugs, the index of drug expenditure grew to 1.56 in 2001, indicating that nominal pharmaceutical expenditures increased 56% during the 5-year period or, equivalently, an average annual rate of growth of 11.86%. This growth rate far exceeded the annual growth rate of overall health-care expenditures and gross domestic product in Taiwan during this period.

The decomposition reveals that the price index decreased from 1 in 1997 to 0.82 in 2001 or an 18% decrease in the price per DDD. As mentioned above,
Taiwan adopted a system of direct controls on reimbursement prices for pharmaceuticals. During our study period, the BNHI cut the reimbursement price twice (in 1999 and 2001) for nearly 10,000 drug products [11]. BNHI had two justifications for its policy: 1) to offset increasing expenditures from adding new drugs to its formulary; and 2) to reduce profit margins earned by providers. Therefore, it is not surprising that prices decreased.

In contrast to the decreases in prices, the quantity index increased from 1 in 1997 to 1.2 in 2001, implying that the quantity of prescription drugs consumed (measured in terms of DDD) increased 20% during our study period. This quantity growth comes from two sources: 1) incumbent products; and 2) new products. Nevertheless, the approach we used could not separate these two sources.

Further, as seen in Table 3, the mix effect was 1.59 in 2001, suggesting that the weighted average price per DDD increased 59% during 1997–2001 as a result of drug substitution within therapeutic groups of drugs. Thus, the treatment substitution effect is the dominant driver of increased spending in Taiwan.

There are two major factors that led to treatment substitution. First, during the study period, the BNHI cut the reimbursement price twice for selected drugs. The reduction in reimbursement prices for selected products in turn led to a change in profit margin earned by the provider and hence created an incentive for providers to change the prescription formulary or to renegotiate the acquisition price with the manufacturers. To increase profit margins, providers have an incentive to substitute the incumbent drugs with higher reimbursement prices for those with lower reimbursement prices, other things being equal. This substitution may occur within the same ingredient but different brands. In addition, it may occur among products with different ingredients but within the same therapeutic category. Our approach could not separate these two types of substitution effect. Second, the provider also substituted new drugs for the incumbent drugs after the new drugs were added to the formulary.

As Addis and Magrini [20] noted, the approach we used does not take into account the impact of introducing new drugs. Thus, we cannot know how much that the treatment expansion (quantity growth) and treatment substitution (mix effect) came from this source. For this reason, we further decomposed the source of expenditure growth by drug vintage and ATC classification. First, we categorize drugs into two groups: old and new with new drugs being those included on the formulary after 1996. As shown in Table 3, among 13,295 drugs in our analysis, 13,068 drugs are old and 227 drugs are new. The index of overall expenditure grew from 1 in 1997 to 25.22 in 2001 for new drugs. By contrast, during the same period, the overall expenditure only increased 38% for old drugs that were included in the national formulary before 1996.

The decomposition reveals that the quantity index for 227 new drugs increased from 1 in 1997 to 315 in 2001, representing a 314 fold increase in quantity of consumption. Although one would expect that the increase for new drugs would be high, it is extremely high. Since our base period is 1997, some of the 227 new drugs reported in Table 3 may not be introduced on the formulary at that time. In this case, the quantities of consumption (in terms of DDD) for those drugs in 1997 were zero. Thus, the very large number of quantity index for new drugs reported in Table 3

<table>
<thead>
<tr>
<th>Classification of drugs</th>
<th>Number of items</th>
<th>Total spending</th>
<th>Decomposition of increased spending</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Price</td>
</tr>
<tr>
<td>All drugs</td>
<td>13,295</td>
<td>1.56</td>
<td>0.82</td>
</tr>
<tr>
<td>By anatomical therapeutic chemical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alimentary tract and metabolism</td>
<td>2,108</td>
<td>1.39</td>
<td>0.81</td>
</tr>
<tr>
<td>Blood and blood forming organs</td>
<td>637</td>
<td>1.71</td>
<td>0.82</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>1,454</td>
<td>1.88</td>
<td>0.80</td>
</tr>
<tr>
<td>Dermatologicals</td>
<td>48</td>
<td>2.09</td>
<td>0.76</td>
</tr>
<tr>
<td>Genito-urinary system and sex hormones</td>
<td>618</td>
<td>1.66</td>
<td>0.90</td>
</tr>
<tr>
<td>Systemic hormonal preparations, excl. sex hormones and insulins</td>
<td>653</td>
<td>1.83</td>
<td>0.92</td>
</tr>
<tr>
<td>Antiinfectives for systemic use</td>
<td>2,540</td>
<td>1.25</td>
<td>0.81</td>
</tr>
<tr>
<td>Antineoplastic and immunomodulating agents</td>
<td>120</td>
<td>2.39</td>
<td>0.88</td>
</tr>
<tr>
<td>Musculo-skeletal system</td>
<td>1,424</td>
<td>1.39</td>
<td>0.77</td>
</tr>
<tr>
<td>Nervous system</td>
<td>1,795</td>
<td>1.76</td>
<td>0.85</td>
</tr>
<tr>
<td>Antiparasitic products, insecticides and repellents</td>
<td>198</td>
<td>1.42</td>
<td>0.48</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>1,568</td>
<td>1.34</td>
<td>0.86</td>
</tr>
<tr>
<td>Sensory organs</td>
<td>98</td>
<td>1.61</td>
<td>0.99</td>
</tr>
<tr>
<td>Various</td>
<td>34</td>
<td>3.10</td>
<td>0.56</td>
</tr>
<tr>
<td>By drug vintage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Old</td>
<td>13,068</td>
<td>1.38</td>
<td>0.82</td>
</tr>
<tr>
<td>New*</td>
<td>227</td>
<td>25.22</td>
<td>0.91</td>
</tr>
</tbody>
</table>

*New drugs indicate those included in the NHI formulary after 1996.
NHI, National Health Insurance.

Table 3 Index of NHI pharmaceutical expenditures in 2001 (base year 1997 = 1)
not only reflects the growth of quantity for the existing new drugs in 1997 but also includes the effect of adding more new drugs on the formulary between 1998 and 2001. It is apparent that the introduction of new drugs led to a very rapid increase in pharmaceutical expenditures and expenditure growth of new drugs mainly came from quantity growth.

Second, we categorize drugs into 14 groups by ATC classification. The results for subgroup analysis consistently indicate that treatment expansion and substitution effects were the major causes of increased pharmaceutical expenditures. In particular, the growth rate of expenditure for antineoplastic and immunomodulating agents was the highest among 14 subgroups, except for the group of various. Other groups with relatively high rates of growth in expenditures were drugs for cardiovascular system and nervous system. These three groups of drugs share two common characteristics: 1) they are for chronic diseases; and 2) there was relatively more pharmaceutical innovation in these subgroups. These two factors are important for the treatment expansion and substitution effects to occur. As population ages, prevalence rate of several chronic diseases, such as cancer, hypertension, heart disease, and depressant, increase. The introduction of new drugs leads more people to be treated for these diseases. Also, the relatively quick introduction of new drugs within these disease categories is more likely to induce a drug substitution in treating established patients.

Overall, our decomposition clearly demonstrates that the primary driver of increased spending in pharmaceuticals is not price. Rather, treatment expansion and substitution effects are the major determinants of expenditure growth. Because of the limitation of our approach, we are unable to provide the direct evidence to show the extent of the treatment expansion and substitution effects that is induced by pharmaceutical innovation. Nevertheless, the decomposition of our subgroup analysis shows that the adoption of pharmaceutical innovation is the primary driver for treatment expansion and substitution effects. As reported in Table 3, the quantity index is extremely large for the subgroup of new drugs. Also, Table 3 shows that quantity indexes are relatively higher for those drugs with more pharmaceutical innovation in recent years, such as for cardiovascular diseases, cancer, and mental health. Therefore, our results provide a strong indication that pharmaceutical innovation is the main underlying cause of increased spending on pharmaceuticals.

**Comparing Costs and Benefits**

To the extent that innovation is the major cause of the expenditure increase, the next question is: Was the innovation worth the increased cost?

To answer this question, we must quantify the benefits of new drugs. Compared to costs, benefits are more difficult to quantify. First, benefits are multidimensional, including at least the following four components: 1) reductions in mortality; 2) reductions in disability and morbidity; 3) improved quality of life, i.e., reduced pain and suffering; and 4) improved labor force productivity. Second, many potential health benefits of prescription drugs accrue in the long run. For example, a drug for reducing blood cholesterol may reduce heart disease prevalence several decades hence. Therefore, the long-run effects of drugs cannot fully be assessed until many years after such drugs are introduced.

In spite of these difficulties, but given the importance of the topic, several studies have quantified health benefits of prescription drugs [6,23]. In part reflecting lack of data on other outcomes, most studies have focused on health benefits from reduced mortality [23]. To calculate benefits from longevity gains, one needs to estimate how much of the increase in life expectancy is attributable to the introduction of new drugs. Lichtenberg [6] investigated this issue by using an indirect two-step approach. First, he estimated the average effect of change in pharmaceutical innovation on the change in probability of survival to age 65 from a disease-specific panel database. Specifically, he tested the hypothesis that diseases for which there has relatively more pharmaceutical innovation have experienced more improvements in health outcomes than have outcomes for other diseases for which technological progress has lagged. Second, he estimated the mean effect of change in the probability of survival to 65 for the whole population on the change in life expectancy at birth using time series data. By multiplying these two estimates, he obtained the mean effect of change in pharmaceutical innovation on the change in life expectancy at birth. His results showed that, between 1986 and 2000, mean life expectancy of the entire population in his sample increased by 1.96 years. The launch of new drugs accounted for 0.79 years, 40% of the 1986–2000 increase in longevity, implying the mean annual increase in life expectancy from the introduction of new drugs for the period 1986–2000 is about three weeks (52 x 0.79/14).

Hsieh et al. [24] used a disease-specific panel database obtained from Taiwan for the period 1985–2002 and a similar approach to estimate the effect of new drug launches on longevity in that country. They found that a 10% increase in the cumulative number of new molecular entities was associated with an increase in life expectancy at birth of approximately 0.1%. They reported that the cumulative number of new molecular entities increased about 50%, from 548 in 1996 to 821 in 2002, which in turn increased life expectancy by 0.5%. In 1996, the Taiwanese life expectancies for males and females were 71.89 and 77.77, respectively.
Table 4 The incremental cost effectiveness ratio of new drug launches in Taiwan

<table>
<thead>
<tr>
<th>Perspective of measuring cost</th>
<th>Cost (spending on new drug per capita) (NT$)</th>
<th>Effectiveness (average annual increase in life expectancy attributable to new drug launches)</th>
<th>Cost-effectiveness ratio (cost per life-year gained, NT$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public insurer (BNHI)</td>
<td>725 (US$21.06)</td>
<td>0.06</td>
<td>12,083 (US$351)</td>
</tr>
<tr>
<td>Society as a whole</td>
<td>1,256 (US$36.49)</td>
<td>0.06</td>
<td>20,933 (US$608)</td>
</tr>
</tbody>
</table>

Note: The exchange rate of US$/NT$ was 34.42 in 2003. Number in parenthesis is cost expressed in terms of US$.

BNHI, Bureau of National Health Insurance.

[25]. Thus, the predicted longevity gains resulting from new drug launches were 0.36 (71.89 × 0.005) and 0.39 (77.77 × 0.005) years for males and females, respectively. During 1996–2002, the actual increase in life expectancy was 1.33 years for males and 1.17 years for females [25]. These results imply that new drug launches accounted for about 27% (0.36/1.33) to 33% (0.39/1.17) of the longevity gain in Taiwan. The mean annual increase in life expectancy of the Taiwanese population resulting from new drug launches was about three weeks (52 × 0.36/6), similar to Lichtenberg’s [6] estimates.

Used the estimated longevity gains from the introduction of new drugs, together with the cost impact of introducing new drugs into the formulary described above, we computed the incremental cost-effectiveness ratio for new drugs (Table 4). Since the estimate of the effectiveness came from another study, the observational period is not exactly consistent with this study. In spite of this difference in timing, the existing estimate of health benefit obtained from the period of 1996–2002 serves as a good proxy for the benefit of the subsequent year in 2003. As indicated above, the BNHI, a single public payer, spent NT$16,694 million on new drugs in 2003 (see Table 2). Thus, from the perspective of public insurer, expenditure of new drugs per capita was NT$725—total BNHI spending on new drugs divided by total population in Taiwan, 23 million. The mean annual increase in life expectancy of the entire male population resulting from the introduction of new drugs was 0.06 years (0.36/6). The ratio of these two number is about NT$12,083 (or about US$351 in 2003 dollars), indicating that the cost per life-year gained resulting from the launch of new drugs is extremely low as compared to most estimates of the statistical value of a life-year [7,26,27].

Although Taiwan has NHI, only about two-thirds of health-care expenditure is financed by the public sector. Private sector expenditures, either from out-of-pocket payments or private supplemental health insurance, account for the remaining one-third of such expenditures. Thus, it is necessary to account for private payments for new drugs, such as spending on new drugs not listed in NHI formulary, if one is to measure cost from a societal perspective. As shown in Table 2, spending on new drugs accounted for about 21% of total pharmaceutical expenditure paid by BNHI. Assuming that the private sector also spent this share on new drugs and multiplying per capita pharmaceutical expenditure by 21% yields national spending on new drug per capita as a measure of cost on new drugs from the perspective of society as a whole. In 2003, per capita pharmaceutical expenditure in Taiwan was NT$5980 [28]. Thus, national spending on new drugs per capita was NT$1256 (5980 × 0.21). Dividing this number by the longevity gain attributable to new drug launches, the cost per life-year gained was NT$20,933 (or US$608 in 2003 dollars) from a societal perspective.

As noted by Pauly [29], there are debates on correct measurement of drug costs from a societal perspective. Most researchers used average wholesale price (AWP) as the measure of cost from a societal perspective. Nevertheless, this practice is controversial because AWP may include the excess profit of the pharmaceutical manufactures which is a transfer payment instead of true “cost” to the society. Moreover, as mentioned, providers in Taiwan earn the profit margin between the reimbursement and the acquisition prices. Thus, the per capita pharmaceutical expenditure may overestimate the true cost from a societal perspective. Because of the lack of reliable data on the profit margin, the result reported in Table 4 overestimates the cost on new drugs from the perspective of society as a whole.

Similarly, the measurement of benefits reported in Table 4 is subjected to estimate biased. Since we only considered benefits in the form of mortality reductions and excluded other benefits of new drugs, such as improved quality of life and labor force productivity, our cost-effectiveness calculation underestimated the benefit of including new drugs on the formulary. By contrast, we may have overestimated the benefit of longevity gains resulting from the launches of new drugs given that the determinants of mortality reduction are a very complex [30]. Although, as Hsieh et al. [24] acknowledged, they only partially controlled for other determinants of mortality reduction with the fixed-effects and random-effects models, there may still be unobservable characteristics not accounted for in their analysis. In particular, Lichtenberg [6] noted that other technological advances other than in the pharmaceutical sphere may have co-occurred and were not explicitly captured by the analysis. Thus, the longevity gain resulting from new drug launches may be overes-
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timated if the researcher simply uses the cumulative number of drug approved with new molecular entities as a measure of pharmaceutical innovation.

To correct the potential bias in quantifying benefits, Lichtenberg [6] took only one-third of the estimated effect of new drugs on longevity gain to calculate the cost per life-year gained from the launch of new drugs. This correction was based on the evidence that US pharmaceutical R&D expenditure accounts for about one-third of national health R&D expenditure. Thus, it is plausible that the remaining two-thirds of estimated effect of new drugs on longevity gain may be attributable to other medical innovations.

Using the same approach by dividing mean annual increase in life expectancy by three yields a cost per life-year gained resulting from new drug launches of US$1053 from the perspective of public insurer and US$1824 from the societal perspective. These estimates are still far lower than most estimates of the value of a statistical life-year. Also, our estimates on cost per life-year gained resulting from the launches of new drugs are lower than that estimated by Lichtenberg [6] (US$6750). Health benefits of new drug launches in Taiwan are almost the same as in other countries, but the per capita pharmaceutical expenditure in Taiwan was lower than that for the USA used in Lichtenberg’s calculations.

Conclusion

This study used two different approaches to investigate the effect of adopting pharmaceutical innovation on the growth of drug expenditure. First, we described the growth of public expenditure resulting from the introducing new drugs into the formulary. Our analysis indicates that during 1996–2003, the single public insurer in Taiwan added 399 new drugs to the national formulary. In 2003, total expenditure on these 399 new drugs was NT$16,694 million, accounting for 21% of total public spending in pharmaceuticals. Second, we employed a statistical method to decompose the growth of public pharmaceutical expenditures into three components: 1) quantity (treatment expansion); 2) mix (treatment substitution); and 3) pure price effects. We found that during the period from 1997 to 2001 the public expenditure on pharmaceuticals grew about 57%. The primary determinants of this expenditure growth were treatment expansion and treatment substitution. Prices of pharmaceuticals declined during this period.

Overall, our analysis provides evidence consistent with existing literature, namely that price is not the primary driver of increased spending [2,3,19,20]. Rather the introduction of new drugs onto the formulary leads to treatment expansion and substitution, which in turn boosts spending. We therefore further compared the cost and benefit of introducing new drugs into the formulary. Combining an estimated benefit from an existing study with our estimate of cost, we found that cost per life-year gained resulting from the introduction of new drugs was US$1053 from the perspective of public insurer and US$1824 from the societal perspective, far lower than estimates of the value of a statistical life-year.

Our findings have three implications for public policy. First, price regulation is not an effective approach for controlling pharmaceutical expenditures. Although our study shows that the direct regulation on reimbursement prices did reduce the rise of prices below that which would have otherwise occurred, it did not reduce overall pharmaceutical expenditure. By contrast, there are many side effects of using price regulation for cost containment, including the launch delay for new drug and disincentive for innovation [10,16]. Furthermore, in a health-care system in which providers are in a position to profit directly from prescribing drugs, cost containment by cutting regulated prices often alters profit margins between the reimbursement and acquisition prices. This in turn creates an incentive to substitute drugs toward products with higher profit margins. From a clinical viewpoint, the unjustified substitution between drugs may adversely affect quality of care, a potential adverse side effect we did not measure.

Second, overall adoption of pharmaceutical innovations is worth the increased cost of new drugs. Although introducing new drugs on the national formulary increased public outlays on pharmaceuticals, adoption of pharmaceutical innovations also increases longevity. Our conservative estimate suggests that cost per life-year gained resulting from the introduction of new drugs from the societal perspective was US$1,824, only about 1.8% of value of a statistical life-year at US$100,000 widely used in literature [7].

Third, although the adoption of pharmaceutical innovation as a whole is cost-effective, all new drugs are not equally beneficial relative to their costs, as noted by Skinner et al. [31] that technological change in medicine is not always worth it. This study presents an average effect and does not imply that every new drug is cost-effective. Our analysis has documented that the cost impact of introducing a new drug into the formulary is very significant. Facing substantial budgetary pressures, policymakers often postpone the introduction of new drugs or reduce the prices of the new drugs at introduction. Our results suggest that such strategies are likely to be unwise as an overall strategy. An effective solution for the policy dilemma between controlling health-care budget and improving the health of population is a systematic analysis of the costs versus benefits of each new drug before introduction. Some governments throughout the world have used the method of economic evaluation to systematically
evaluate the value of new drugs before including them into the formulary [32]. By contrast, Taiwan has not yet formally implemented this approach. Such evaluation represents a promising approach for boosting the value of public spending still further.

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References