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Availability, Health-Care Costs, and Utilization Patterns of Biologics in Taiwan

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ABSTRACT

Objective: To provide an overview of the use of biologics in Taiwan, including the access to new biologics, the impact of this access on the growth of health-care expenditure, and the utilization patterns. **Methods:** We first conducted a market-level analysis to investigate the availability of global biologics in Taiwan as well as the growth and concentration of aggregate spending on biologics. We then conducted a patient-level analysis to investigate the costs and utilization patterns for selected new biologics. **Results:** We found that the concentration index is such that the 20 leading biologics in Taiwan account for more than 90% of the total spending on biologics. In our patient-level study on four biologics, the annual cost of treatment per patient ranged from NT$100,000 to NT$400,000. The prevalence rate of the user was between 6.5 and 37.2 per 100,000 of population. The treatment costs were inversely related to the prevalence rate of users. We also found that physicians in larger and public hospitals were more likely to prescribe new biologics to their patients compared with their counterparts practicing in smaller and private hospitals. In addition, we found that physicians were more likely to prescribe biologics to patients with more severe diseases and higher comorbidities. **Conclusions:** We conclude that public spending on biologics in Taiwan is highly targeted toward about 20 products with higher annual expenditures and growth rates and that the utilization of these biologics is targeted at a small number of patients. In addition, the access to these costly biologics is not uniform among patients in a country with universal coverage for prescription drugs.

Keywords: access to new biologics, biologics, health-care costs, technology diffusion.

Introduction

Biologics are defined as medicines whose active substance is made from a living organism or its products and are produced by using biotechnology methods or other cutting-edge technologies. Biologics differ from chemically synthesized drugs along many dimensions, including manufacturing, the market dynamics, mode of administration, target specificity, body distribution, and half-life [1–3]. In recent years, nearly one-fourth of all new chemical entities launched in the United States and the European Union have been biologics [4]. Thus, biologics are important new health-care technologies. The market for biologics has grown more rapidly than that for general pharmaceutical products, and as a result the share of biologics in global pharmaceutical sales has increased rapidly from 4.4% in 1998 to 10.5% in 2007.

As observed in many other new technologies in medicine, the adoption of biologics is costly. Compared with chemically synthesized drugs, manufacturing biologics is much more complex. Moreover, biologics have, until recently, usually targeted small patient populations. Given these characteristics of their manufacturing and marketing, it is not surprising that the prices of many biologics are relatively high [5]. The high cost of adopting new biologics often becomes a public concern, particularly in health systems dominated by public financing where decisions about which biologics will be covered by public programs can become highly politicized. As a result, countries often face a policy dilemma between providing access to new biologics and controlling their health-care budgets.

The purpose of this article was to provide an overview of the use of biologics in Taiwan with a special focus on the accessibility and cost impacts of new biologics. On the basis of both population and sampling claims data obtained from the national health insurance (NHI) program, we performed market- and patient-level analysis to explore several issues surrounding the utilization of biologics in Taiwan. Specifically, we analyzed the access issue by comparing the lists of biologics in Taiwan's NHI formulary with the list of blockbuster biologics in the global market. In addition, we analyzed the trend of NHI spending on biologics over time. Furthermore, we performed patient-level analysis for individual biologics to analyze the costs and utilization patterns of selected new biologics.

There are several advantages in using Taiwanese data to quantify the impact of adopting new biologics on health-care costs and

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Table 1 – Launch dates of blockbuster biologics in Taiwan.

Name of drug	Manufacturing firms	ATC code	Launch date
Aranesp (darbepoetin alfa)	Amgen	B03XA02	May 1, 2004
Avastin (bevacizumab)	Genentech	L01XC07	NA
Avonex (interferon beta-1a)	Biogen/IDEC	–	NA
Betaseron (interferon beta-1b)	Bayer Schering	L03AB08	March 1, 1998
Cerezyme (imiglucerase)	Genzyme	A16AB02	October 22, 1998
Enbrel (etanercept)	Amgen	L04AB01	March 1, 2003
Erbitux (cetuximab)	ImClone Systems	L01XC06	March 1, 2007
Herceptin (trastuzumab)	Genentech	L01XC03	April 1, 2002
Humalog (insulin lispro injection)	Eli Lilly	A10AD04 A10AB04 A10AC04	February 1, 2004
Humira (adalimumab)	Abbott Laboratories	L04AB04	September 1, 2004
Lantus (insulin glargine injection)	Sanofi-Aventis	A10AE04	February 1, 2004
Neulasta (pegfilgrastim)	Amgen	L03AA13	NA
Neupogen (filgrastim)	Amgen	L03AA02	1995
Novolog (insulin aspart injection)	Novo Nordisk	A10AB05 A10AD05	2003
NovoSeven (coagulation factor VIIa)	Novo Nordisk	–	NA
Pegasys (peginterferon alfa-2a)	Roche	L03AB11	November 1, 2003
Rebif (interferon beta-1a)	MerckSerono	L03AB07	April 1, 2002
Remicade (infliximab)	Centacor (J&J)	L04AB02	NA
Rituxan (rituximab)	Genentech	L01XC02	April 1, 2002
Synagis (palivizumab)	MedImmune	J06BB16	NA

Note: Blockbuster biologics indicate that their annual sales exceeded US$1 billion in 2007.
ATC, Anatomical Therapeutic Chemical classification system; NA, not available.

utilization patterns. First, Taiwan has a social insurance system providing universal insurance coverage for 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 [6]. The single-payer system allows policymakers as well as researchers to trace the impact of introducing new drugs on national health costs.

Second, about one-quarter of Taiwan's health-care expenditure is on pharmaceuticals. As compared with other developed countries, the higher spending makes it more likely for prescription drugs to become the target of cost containment. As a result, the experience of Taiwan provides a valuable insight into understanding how policymakers struggle with the conflict between increasing access to new drugs and controlling health-care costs.

Data and Methods

The data used in this study had two main sources. First, we obtained data on the aggregate expenditure on biologics from NHI population claims data. Second, we used a longitudinal data set to analyze the costs and utilization patterns of individual biologics. This data set contains 1 million individuals (about 4.35% of the total population in Taiwan) randomly selected from the registry of NHI beneficiaries in the year 2005. The sampling file was then merged with the insurance claim files that trace back all the medical utilization records of the same individuals in every year and follow their medical utilizations in subsequent years, hereafter referred to as the 2005 Longitudinal Health Insurance Database (LHID).

The 2005 LHID was made publicly available through the National Health Research Institute. This data set contains detailed records on the utilization of personal health-care services, including outpatient visits, hospital admissions, and prescription drugs. We merged the data for outpatient visits with the corresponding drugs prescribed and dispensed by using anonymous identification numbers. The advantage of this data set is that all the medical utilizations can be linked together for the same patient. As a result, the data provide information on the characteristics of patients, providers, and the drugs prescribed.

In this article, we adopted two approaches to analyze the use of biologics in Taiwan. We first conducted a market-level analysis to investigate the availability of global biologics in Taiwan as well as the growth and concentration of aggregate spending on biologics. The advantage of this approach is that it provides population-based information on the overall utilization of biologics in Taiwan. The market-level analysis, however, does not provide information on individual patients. We then conducted a patient-level analysis to provide a descriptive analysis of the costs and utilization patterns for four important biologics, namely, Enbrel, Mabthera, Herceptin, and Pegasys, which were selected on the basis of higher annual sales and higher growth rates. In the patient-level analysis, we analyzed the mean cost of treatment per patient by using the cohort data that all the prescriptions have been linked together for the same patients. By means of aggregation and four case studies, we summarize the findings of this research.

Market-Level Analysis

Taiwan has established, under its system of NHI, a national formulary that includes all pharmaceuticals subject to reimbursement by the NHI. The detailed list of drugs in the drug formulary provides a base on which to analyze the availability of biologics in Taiwan by comparing the list based on the NHI formulary with the list of important biologics in the global market.

In Table 1, we summarize a list of 20 important biologics in the global market whose annual sales exceeded US$1 billion in 2007. Among them, 14 biologics are available in Taiwan through the coverage of public insurance. The launch dates of these biologics range from 1998 to 2007. By 2007, six biologics—Avastin, Avonex, Neulasta, NovoSeven, Remicade, and Synagis—were not covered

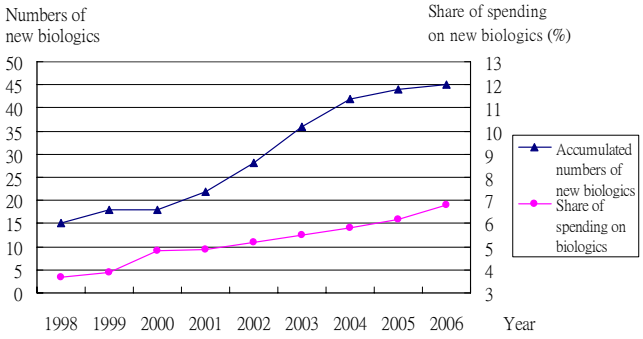

Fig. 1 – Accumulated numbers of new biologics in the NHI formulary and share of pharmaceutical spending on new biologics. From Bureau of National Health Insurance, Taipei, Taiwan. Note: New biologics are defined as those included in the NHI formulary after 1997. NHI, national health insurance.

by public insurance. This result suggests that the probability of new biologics being launched in Taiwan is 0.7. That is, for every 10 important biologics (in terms of sales) available in the global market, only 7 biologics will be launched in the Taiwan market. A plausible explanation for new drugs not being launched is a lower expected price [7].

In the global market, many new biologics have been introduced annually as a consequence of technological advances [8]. In addition to requiring that authorization be obtained to market a new biologic product, Taiwan, like other countries with direct price controls on pharmaceutical products, requires that the manufacturer of a new biologic product obtain approval for insurance coverage and a price for reimbursement by the single public payer. As a result, many new biologics as well as other chemically synthesized drugs are added to the NHI formulary annually. During the period from 1997 to 2006, the annual number of new biologics included in the NHI formulary varied year by year, ranging from 1 to 11, with the exception of the year 2000 in that no new biologic product was launched in that year.

Figure 1 shows the accumulated numbers of new biologics added to the NHI formulary over time. A new biologic product is defined here as one that was included in the formulary after 1997. By 2006, the total accumulated number of new biologics included in the NHI formulary was 45, indicating that on average about 4.5 new biologics were added to the NHI formulary annually. While the total number of biologics accounts for only about 0.3% (68 of 21,000) of the total number of products listed in the NHI formulary, as more new biologics have been included in the NHI formulary, the share of NHI pharmaceutical expenditure accounted for by the biologics has increased steadily, from 3.7% in 1998 to 6.8% in 2006. This suggests that the introduction of new biologics into the formulary is an important determinant of increased spending on prescription drugs.

Although the market share of biologics in Taiwan has increased over time, this share is lower than the mean share in the global market. In 2005, the United States had the highest biologic share (12.9%) in the world, with shares ranging between 8% and 10% among major European countries [8]. By contrast, Japan had a relatively low share of biologics in its total drug spending, that is, only 5.4%. This suggests that the current utilization rates of biologics in Taiwan are very low as compared with those in the United States and European countries, but are slightly higher than those in Japan.

In spite of the lower market share, the spending on biologics has grown more rapidly than the spending on general pharmaceutical products and health care. As shown in Table 2, the total NHI health-care expenditure increased from NT$291 billion in 1998 to NT$456 billion in 2006 (USD 1 = 32.5 NTD, 1997–2006), indicating that the mean annual growth rate during this period was 5.8%. As mentioned earlier, in Taiwan about one-quarter of the expenditure of the NHI program was accounted for by pharmaceuticals. Thus, the mean annual growth rate of pharmaceutical expenditure was almost the same as that of health-care expenditure. By contrast, the mean annual growth rate of biologics was 14.4% between 1998 and 2006, which was more than double the mean growth rate of pharmaceutical products and general health care (Table 2). This suggests that biologics are expected to account for a much more significant share of the health-care cost in the future.

Table 2 – NHI spending on biologics, pharmaceuticals, and health care in Taiwan, 1998–2006.

Year	Total health-care expenditure (billion NT$)	Total pharmaceutical expenditure (billion NT$)	Total spending on biologics (billion NT$)	Share of drug spending in total NHI spending (%)	Share of biologics spending in total drug spending (%)
1998	290.9	73.0	2.7	25.1	3.7
1999	316.6	81.3	3.2	25.7	3.9
2000	326.0	84.1	4.0	25.8	4.8
2001	341.7	85.1	4.2	24.9	4.9
2002	370.9	92.2	4.8	24.9	5.2
2003	383.9	96.3	5.3	25.1	5.5
2004	438.8	111.1	6.4	25.3	5.8
2005	452.4	113.9	7.1	25.2	6.2
2006	456.4	116.4	7.9	25.5	6.8
Mean annual growth rate between 1998 and 2006 (%)	5.8	6.0	14.4	0.2	7.9

Source: Bureau of National Health Insurance, Taipei, Taiwan; calculated by authors.
Note:
1. The average exchange rate was around 1 US$ to 32.5 NT$ in 1998–2006.
2. Total pharmaceutical expenditure includes the expenditure on kidney dialysis.
NHI, national health insurance.

Table 3 – The concentration index in terms of spending on biologics in 2006.

ATC code	Name of ingredients	Effective launch year in NHI formulary	Annual sales (in million NT$)	Share of total NHI spending on biologics (%)	Cumulative percentage of NHI spending on biologics (%)
B03XA01	Erythropoietin	1997	1875	23.69	23.69
B02BD02	Factor VIII	1998	1168	14.76	38.45
B05AA01	Albumin	1995	708	8.95	47.40
H01AC01	Somatotropin human (growth hormone)	1996	431	5.45	52.85
L04AA11	Etanercept	2003	385	4.87	57.71
L03AA02	Filgrastin	1995	332	4.20	61.91
A10AB05	Insulin aspart	2003	316	3.99	65.89
L01XC02	Rituximab	2002	284	3.58	69.48
L01XC03	Trastuzumab	2002	265	3.35	72.83
L03AB11	Peginterferon-alfa-2a	2003	245	3.10	75.93
J06BB04	Immunoglobulin	1997	197	2.49	78.42
A16AB02	Imiglucerase	1999	187	2.36	80.78
L03AB10	Peginterferon-alpha-2b	2003	160	2.02	82.81
A10AD01	Insulin human	1997	133	1.69	84.49
B02BD09	Gamma-fix (nonacog alfa)	2004	131	1.66	86.15
A10AC01	Insulin human	1997	121	1.52	87.67
J06BA02	Immunoglobulin	1995	118	1.49	89.16
L03AA10	Lenograstim	1998	113	1.43	90.59
A10AE04	Insulin glargine	2004	106	1.34	91.93
B02BD03	Human plasma protein with a factor VIII inhibitor	2004	80	1.01	92.94

Data Source: Bureau of National Health Insurance, Taipei, Taiwan; calculated by authors.
Note:
1. The average exchange rate was around US$1 to NT$32.5 in 1998–2006.
2. Effective launch year indicates the timing that the biologics begin to be used in Taiwan's hospitals after the biologics have been included in the NHI formulary.
ATC, Anatomical Therapeutic Chemical classification system; NHI, national health insurance.

Table 3 shows the concentration index in terms of spending on biologics. By 2006, the NHI formulary included 68 biologics. The aggregate spending on biologics, however, has been highly concentrated among a few selected biologics. The best-selling biologic product, erythropoietin, accounts for nearly one-quarter of spending on all biologics. The concentration index among the top four biologics (in terms of sales) is more than 50%. The concentration index among the 10 leading biologics in Taiwan is about 75%. The 20 leading biologics account for more than 90% of the total spending on biologics in Taiwan. The annual sales of these 20 biologics range from NT$80 million to NT$1.8 billion. This result suggests that spending on biologics in Taiwan is highly targeted at specific therapeutic classes, such as insulins and analogues, antihemorrhagics, antianemic preparations, as well as antineoplastic and immunomodulating agents.

In addition to a higher expenditure, most of the important biologics (in terms of sales) have experienced a very high growth rate. Table 4 lists 20 leading biologics in terms of high growth rates between the effective launch year and 2006. For example, for the insulin aspart, which was included in the NHI formulary in 2003, the mean annual growth rate of spending between 2003 and 2006 was more than 4000%. Other products with a mean annual growth rate exceeding 100% include peginterferon-alfa-2a, insulin glargin, botulinum toxin type a, etanercept, and gamma-fix. Among the 20 biologics listed in Table 3, 15 biologics are also listed in Table 4, suggesting that most biologics with larger market size also experienced a higher growth rate in terms of their sales. Together, Tables 3 and 4 suggest that spending on biologics in Taiwan is highly targeted toward about 20 products with higher annual expenditures and growth rates.

Patient-Level Study

Costs and utilization patterns

Enbrel (etanercept) is one of the antitumor necrosis factor drugs that have been shown to be effective in the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, and ankylosing spondylitis [9]. This drug was introduced into the NHI formulary on March 1, 2003. During the period between 2003 and 2007, we identified 78 patients who had used Enbrel to treat their diseases (Table 5). Because the sampling data set contains 1 million persons, this suggests that the prevalence rate of Enbrel users over a 5-year period is 7.8 per 100,000 population. Among the 78 patients we observed, 72% were female. The ages of these users ranged from 25 to 77, with the mean age being 52.91. On average, these patients received treatment using Enbrel for 2.31 years and each received about 11 prescriptions per year. The mean cost per prescription was NT$25,513, and the mean annual cost of drug treatment per patient was NT$278,458. Overall, the results suggest that the treatment cost using Enbrel is extremely high compared with the treatment costs of common chronic diseases such as hepatitis B and diabetes [10,11].

Following the same approach, we also conducted patient-level analysis for Mabthera (rituximab), Herceptin (trastuzumab), and Pegasys (peginterferon-alfa-2A). The utilization patterns of these three biologics are similar to that of Enbrel. On the basis of our analysis of Table 5, we conclude that the utilization of these four biologics was concentrated among a smaller number of patients and that the annual cost of treatment per patient was high, ranging from NT$100,000 to NT$400,000. The prevalence rate of the

Table 4 – Mean annual growth rate of important biologics in Taiwan.

ATC code	Name of ingredients	Effective launch year in NHI formulary	Sales in 2006 (in million NT$)	Mean annual growth rate in sales between effective launch year and 2006 (%)
A10AB05	Insulin aspart	2003	316	4007.08
L03AB11	Peginterferon-alfa-2a	2003	245	234.74
A10AE04	Insulin glargine	2004	106	225.33
M03AX01	Botulinum toxin type a	1999	50	203.64
L04AA11	Etanercept	2003	385	196.15
B02BD09	Gamma-fix (nonacog alfa)	2001	131	131.72
J06BB04	Immunoglobulin	1997	197	87.64
L03AB10	Peginterferon-alpha-2b	2003	160	86.56
L03AB08	Interferon beta-1b	1998	21	71.05
B02BD03	Human plasma protein with a factor VIII inhibitor	2004	80	70.71
L01XC02	Rituximab	2002	284	69.89
L03AC01	Aldesleukin	2001	58	54.08
L01XC03	Trastuzumab	2002	265	38.61
A16AB02	Imiglucerase	1999	187	18.29
L03AA10	Lenograstim	1998	113	15.58
A10AD01	Insulin human	1997	133	13.96
J06BB09	Immunoglobulin	1995	42	10.66
L04AA04	Immunoglobulin	1995	32	10.59
B02BD02	Factor VIII	1998	1168	10.09
H01AC01	Somatotropin human (growth hormone)	1996	431	9.22

Data Source: Bureau of National Health Insurance, Taipei, Taiwan; calculated by authors.
Note:
1. The average exchange rate was around US$1 to NT$32.5 in 1998–2006.
2. Effective launch year indicates the timing that the biologics begin to be used in Taiwan's hospitals after the biologics have been included in the NHI formulary.
ATC, Anatomical Therapeutic Chemical classification system; NHI, national health insurance.

user was between 6.5 and 37.2 per 100,000 population, and the associated costs were inversely related to the prevalence rate of drug users. A plausible explanation for this result is that the public payer tends to impose a stronger restriction on the reimbursement guideline if the treatment cost per patient is higher. Thus, high-cost biologics are associated with a lower number of users.

Pattern of technology diffusion

Figures 2 and 3 analyze the pattern of technology diffusion by examining the market shares of four individual biologics across providers. In Taiwan, the regulatory agency classifies hospitals into three accreditation levels: 1) medical center, 2) metropolitan hospital, and 3) community hospital. The accreditation level is positively associated with the size of the hospitals. In addition, the delivery of health-care services is dominated by the private sector, which accounts for about 70% of health-care services.

The results reported in Figure 2 indicate that the likelihood of adopting these high-cost biologics is positively correlated with the size of the hospitals. With a few exceptions in the case of Pegasys, the majority of the biologic treatments are provided by larger hospitals, such as medical centers and metropolitan hospitals. In most cases, medical centers always act as a leader in the adoption of new biologics. Medical centers account for more than half the market for biologics when we combine the four biologics together. This suggests that physicians in larger hospitals were more likely to prescribe new biologics as compared with their counterparts practicing in clinics and smaller hospitals. This result is consistent with the finding in the adoption of new antidiabetic drugs [12].

Table 5 – The mean costs and utilization patterns of four selected biologics.

Variable	Enbrel	Mabthera	Herceptin	Pegasys
Number of users	78	75	65	372
Characteristics of users				
Gender (percentage of female users)	72%	52%	100%	40%
Age	52.91	63.48	53.79	50.63
Mean costs and utilization patterns				
Length of treatment (y)*	2.31	1.11	1.45	1.21
Annual number of prescriptions per patient	10.94	7.00	5.97	7.20
Cost per prescription (NT$)	25,513	58,431	73,736	13,583
Annual cost of treatment per patient (NT$)	278,458	236,243	407,843	100,993

Data Source: 2005 Longitudinal Health Insurance Database, calculated by authors.
* We count the length of treatment as 1 year if the duration of the treatment is less than 1 year.

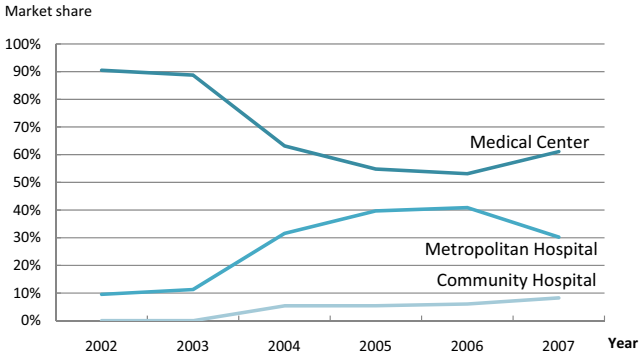

Fig. 2 – The market share (in terms of NHI spending) of four selected biologics based on the accreditation level of hospitals. From 2005 Longitudinal Health Insurance Database, calculated by authors. NHI, national health insurance.

Figure 3 shows that the ownership forms of medical providers matter in the utilization pattern of biologics. When we combine these four biologics together, the results reveal a clear pattern in that the public hospitals account for a larger market share at the entry of new technology, while the private hospitals increased the ratio of their share of the biologics market to their share of the market for general health care as treatment using new biologics became more mature.

The burden of disease

In Table 6, we provide information on the burden of the disease treated with biologics. We measured the burden of the disease by the following four indicators: 1) total health expenditure, 2) total drug expenditure, 3) the share of total health expenditure spent on drugs, and 4) Charlson's comorbidity index [13].

Because the majority of users of Enbrel were patients with rheumatoid arthritis, we focus our discussion on these patients (International Classification of Disease, 9th Revision, Clinical Modification [ICD-9-CM] 714.0). On the basis of the 2005 LHID, we identified 15,697 patients with rheumatoid arthritis during the period 2003 to 2007. Among them, 78 patients had used Enbrel (users) and the rest of them had never used Enbrel (nonusers). The results show that the mean annual total expenditure for the biologics user was NT$771,140, which was about twice as large as the total expenditure of the nonuser. Drug cost, which includes that for Enbrel and all other drugs, accounted for about half of the total health expenditure for the biologics user. By contrast, this figure was only about 14% for nonusers of biologics. Charlson's comorbidity index was 1.73 for the user and 1.68 for the nonuser. The major indication of Mabthera is non-Hodgkin's lymphoma, and thus the analysis of the prevalence and the burden of disease for Mabthera is focused on non-Hodgkin's lymphoma (ICD-9-CM 200 and 202). On the basis of 2005 LHID, we identified 635 patients with non-Hodgkin's lymphoma during the period 2003 to 2007. Among them, 75 patients had previously used Mabthera (users) and the rest of them had never used Mabthera (nonusers). The results show that the mean annual total expenditure for the biologics user was NT$4,513,605, which was about three times as high as the total expenditure for the nonuser. Drug cost, which includes that for Mabthera and all other drugs, accounted for about half of the total health expenditure for the biologics user. By contrast, this figure was only about one-third for the nonuser of biologics. Charlson's comorbidity index was 7.94 for the user and 7.04 for the nonuser.

The fourth column of Table 6 reports the prevalence and burden of the malignant neoplasm of the female breast (ICD-9-CM 174), the major indication for Herceptin. On the basis of 2005 LHID, we identified 3704 patients with malignant neoplasm of the female breast during the period 2003 to 2007. Among them, 65 patients had used Herceptin (users) and the rest of them had never used Herceptin (nonusers). The results show that the mean annual total expenditure for the biologics user was NT$3,016,309, which was more than four times as large as the total expenditure for the nonuser. Drug cost, which includes that for Herceptin and all other drugs, accounted for about 57% of the total health expenditure for the biologics user. By contrast, this figure was only about 21% for the nonuser of biologics. Charlson's comorbidity index was 15.74 for the user and 4.81 for the nonuser.

The last column of Table 6 reports the prevalence and burden of chronic liver disease, cirrhosis, and hepatitis B and C (ICD-9-CM 571, 070.3, 070.5), which are the major indications for Pegasys [14]. On the basis of 2005 LHID, we identified 127,484 patients with chronic liver disease, cirrhosis, and hepatitis B and C during the period 2003 to 2007. Among them, 372 patients had used Pegasys (users) and the rest of them had never used Pegasys (nonusers). The results show that the mean annual total expenditure for the biologics user was NT$617,102, which was more than twice as large as the total expenditure for the nonuser. Drug cost, which includes that for Pegasys and all other drugs, accounted for about 26% of the total health expenditure for the biologics user. By contrast, this figure was only about 16% for the nonuser of biologics. Charlson's comorbidity index was 1.86 for the user and 0.97 for the nonuser.

Overall, these results provide a consistent pattern showing that the burden of the diseases for patients treated with biologics was significantly higher than that for patients without treatment involving biologics. This result suggests that biologics were more likely to be used in patients with a higher severity of diseases and higher comorbidities.

Discussion

This article explored several issues surrounding the use of biologics in Taiwan, including the accessibility, health-care costs, and utilization patterns. On the dimension of accessibility, we found that the probability of launching a new and important biologic product in Taiwan was 0.7, that is, for every 10 important biologics prevailing in the global market, only 7 will be introduced into the NHI formulary in Taiwan. This suggests that the public health insurance in Taiwan is not "affordable" for every new technology available in the global market: only about two-third of new biologics are available through public health insurance and the remaining one-third are "unavailable." To what extent the unavailable new technologies in Taiwan's public health insurance program

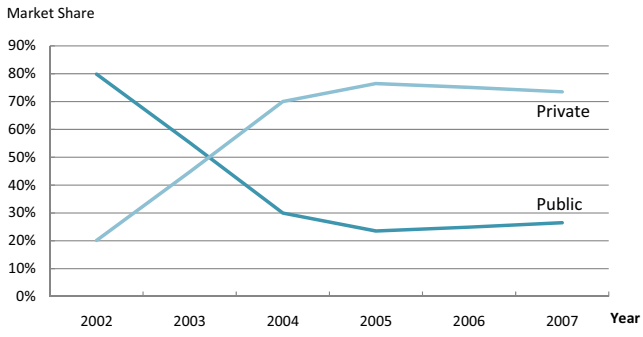

Fig. 3 – The market share (in terms of NHI spending) of four selected biologics based on the ownership form of hospitals. From 2005 Longitudinal Health Insurance Database, calculated by authors. NHI, national health insurance.

Table 6 – The prevalence and the burden of disease for four selected biologics.

Items	Rheumatoid arthritis (Enbrel)	Non-Hodgkin's lymphoma (Mabthera)	Malignant neoplasm of female breast (Herceptin)	Chronic liver disease and cirrhosis, hepatitis B and C (Pegasys)
User of biologics				
Number of patients	78	75	65	372
Annual total expenditure (NT$)	771,140	4,513,605	3,016,309	617,102
Annual drug expenditure (NT$)	383,670	2,304,515	1,729,403	162,408
Percentage of drug spending in total expenditure	49.75	51.06	57.34	26.32
CCI*	1.73	7.94	15.74	1.86
Nonuser of biologics				
Number of patients	15,619	560	3,639	127,112
Annual total expenditure (NT$)	368,712	1,675,581	720,779	252,770
Annual drug expenditure (NT$)	52,400	558,433	153,439	40,442
Percentage of drug spending in total expenditure	14.21	33.33	21.29	16.00
CCI*	1.68	7.04	4.81	0.97
All				
Number of patients	15,697	635	3,704	127,484
Percentage of biologics user	0.49	11.81	1.75	0.29

Data Source: 2005 Longitudinal Health Insurance Database, calculated by authors.
* CCI indicates Charlson's comorbidity index [13].

are due to cost concerns is an important avenue for future research.

With regard to health-care costs, we found that the growth rate of spending on biologics significantly exceeded the growth rate of spending on all prescription drugs. As a result, the share of biologic spending in NHI pharmaceutical expenditure increased rapidly, from 3.7% in 1998 to 6.8% in 2006. However, this share was less than the corresponding share observed in the United States and other European countries. This suggests that policymakers in Taiwan face a trade-off between increasing access to new biologics and controlling health-care costs.

With regard to the utilization patterns of biologics, our major findings are summarized as follows. First, although there are 68 biologics included in the NHI formulary, the spending on these biologics was highly concentrated. The concentration index among the 20 leading biologics was more than 90% of the total biologic spending.

Second, we found that the utilization of biologics was concentrated among a smaller number of patients and that the annual cost of treatment per patient was high. In our study on four individual biologics, the annual cost of treatment per patient ranged from NT$100,000 to NT$400,000. The prevalence rate of the user ranged from 6.5 to 37.2 per 100,000 population. We also found that the treatment costs were inversely related to the prevalence rate of drug users. That is, the higher the mean treatment cost per patient, the smaller the number of users will be.

Third, we found that the size and ownership forms of medical providers matter in the adoption of new biologics in Taiwan. Overall, we found that public hospitals and larger hospitals, such as medical centers, were the leaders in technology adoption, while other hospitals were the followers. We found that physicians in larger hospitals as well as those in public hospitals were more likely to prescribe new biologics to their patients as compared with their counterparts practicing in smaller and private hospitals, which might result from the fact that some new biologics must be prescribed by a number of specialists and large hospitals.

Finally, we found that the burden of the diseases was significantly higher for the user of the biologics than for the nonuser. This suggests that physicians are more likely to prescribe biologics to patients with more severe diseases and higher comorbidities, indicating that the clinical factor also plays an important role in guiding the physicians' decisions in biologic treatment.

There are two limitations to our study. First, the insurance claims data do not contain any information on clinical indicators. The lack of such data restricted us from further evaluating whether the use of biologics in Taiwan was appropriate. That is, the lack of clinical data limited us from answering the question as to whether biologics were "underused" or "overused" in Taiwan. Second, the insurance claims data do not contain information on the health outcome, either. This, in turn, further restricted us from comparing the health-care costs of biologics with their potential benefits.

Conclusion

In this article, we first investigated the access and cost issues in the use of biologics in Taiwan by means of a market-level analysis that analyzed the aggregate expenditure of important biologics. We then performed a patient-level analysis to analyze the utilization patterns of selected biologics. On the basis of these findings, we conclude that spending on biologics is highly concentrated in a small number of biologics and that the utilization of these biologics is targeted at a small number of patients. As a result, the use of biologics is very costly. In addition, we find that the determinants of the use of biologics include not only clinical factors, such as disease severity, but also economic factors, such as the size and ownership forms of hospitals.

Our results have two important policy implications. First, given the evidence that the use of biologics is costly, it is important to compare the gains from biologics treatment in terms of the health outcome with the increase in health expenditure to achieve an efficient allocation of health-care resources. It is not a wise strategy to restrict the introduction of new biologics into the NHI formulary for the purpose of saving money, but neither is writing a blank check for all new biologics. Thus, careful, but expeditious, analysis of the costs versus benefits of individual new biologics before their introduction represents a promising approach for boosting the value of public spending.

Second, given the evidence that the probability of receiving biologics treatment varies across the size and ownership forms of

hospitals, our findings imply that access to costly biologics is not uniform among patients in a country with universal coverage for prescription drugs. Many nonclinical factors such as physicians' financial incentives may also play an important role in the physicians' prescription decisions, which, in turn, may create an access barrier in the use of new biologics in Taiwan, even though the new biologics are included in the NHI formulary.

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