Pharmaceutical Price Control Policy, Pharmaceutical Innovation, and Health Durability

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Abstract: *Background*: The increase in R&D and upward trend of R&D/pharmaceutical sales has occurred despite government controlled pharmaceutical price reduction in Japan. This paper identifies the effect of the government's price control policy on pharmaceutical innovation and evaluates the influence of new chemical entities (NCE) on health durability.

Method: The study employed pharmaceutical price, government approval, and new pricing adaptation policies to evaluate their influences on NCE. Quantitative and qualitative expressions of pharmaceutical innovation were analyzed to measure health durability.

Results: The results show that the government pharmaceutical price and new pricing adaptation policies may have been effective in increasing NCE in the pharmaceutical industry. In addition, our findings show that the optimum R&D adjustment rate for NCE (32%) would cause a downward influence of 0.4494 billion yen of NCE in the long run, while a full adjustment (i.e. 100%) of R&D would bring an increase of 0.709 billion yen in the long run. Finally, the aggregate effects of NCE reduce illness-caused death. The six leading illnesses share a 65.95% decrease in death caused by illness of those aged 65 years or older.

Conclusion: Pharmaceutical price control is not intended to hamper the pharmaceutical industry. It is a price reduction of the government's approved-list of pharmaceutical drugs under the national healthcare system geared toward controlling rapid and excessive growth of pharmaceutical expenditures.

Keywords: Pharmaceutical price control policy, pharmaceutical innovation, health durability.

INTRODUCTION

The development of new drugs could foster advances in the methods used to treat illnesses and reduce skyrocketing healthcare costs [1]. Innovative drugs with new chemical entities fundamentally transform the process of treatment and lead to better health results. Pharmaceutical advances that have caused considerable improvements in life expectancy and health are a result of steadily increasing investments in research. Pharmaceutical drugs have been prescribed to prevent illness, treat disease, and maintain health, so that one's quality of life is enhanced [2]. Health-related research and development is the key to the future of the pharmaceutical industry.

The Japanese government has implemented a price control scheme on pharmaceutical drugs, in order to prevent a rapid increase in drug disbursement and cost of healthcare. The ratio of prescription expenditures to national healthcare expenditures has increased from about 0.2% in 1970 to about 20% in 2007 [3]. Since the 1970s, about 800 original pharmaceutical drugs based on new chemical entities, have been launched in Japan despite the strict pharmaceutical price control policy [4]. Past studies suggest that government price control negatively influences pharmaceutical research and development (R&D) incentives [5-10]. However, the increasing outlays for R&R and upward trend of R&D/pharmaceutical sales occurred despite government controlled pharmaceutical price reduction in Japan [3]. Hara affirmed that Japanese technological innovations in the pharmaceutical industry are weak under the price policy, concluding that most pharmaceutical drugs developed by Japanese companies are only developed through modification-based innovation and lack appeal in foreign markets [11]. Grabowski and Wang [6] similarly point out that Japanese companies seem to introduce less innovative new chemical entities at higher rates into markets at home and in a few neighboring countries because of the strict government pharmaceutical price policy. Furthermore, Ekelund and Persson [12] state that price regulation

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discourages price competition among brand-name pharmaceutical drugs. Product differentiation is one way to survive in the market [13-15]. Berndt [16] and Hsieh and Sloan [17] affirm that a number of possible substitute medications in the market would lead to the differentiation of products. Price control would not necessarily reduce pharmaceutical innovation. The literature shows no evidence linking government pharmaceutical price policies to pharmaceutical innovation.

The link between pharmaceutical innovation and health has clearly been discussed by Morgan, McMahon, and Greyson [18] and Lichtenberg [19-20]. Lichtenberg [19] used the 1996 Medical Expenditure Survey to demonstrate that the effectiveness of newer medicines was also associated with less employee lost work time. He affirmed that pharmaceutical innovation, coupled with the current stock of drugs, causes an increase in cancer survival rates [20]. Based on results from fifty-two countries between 1982 and 2001, he emphasized that launches of new chemical entities had a strong positive impact on the probability of survival. The study on Australia's price policy by Morgan, McMahon, and Greyson [18] underlines the balance between health goals and government pharmaceutical price policies, which promote public health objectives without adversely affecting pharmaceutical industry size. Hsieh and Sloan [17] underscore that the estimated benefits of adopting pharmaceutical innovation generally far exceeds the costs.

BACKGROUND OF PHARMACEUTICAL PRICE REGULATION

The Ministry of Health, Labor, and Welfare of Japan, which is responsible for pharmaceutical price regulation, reports that a total of 12,423 pharmaceutical drugs (11,242 generic drugs and 1,181 brand-name pharmaceutical drugs) are approved and listed under the national health insurance system [4]. However, in terms of the utilization of drugs, brand-name pharmaceutical drug use is about 83.6%, while generics are only about 16.4% [4, 21].

There are three major characteristics that define national health insurance (NHI) in Japan. First, nearly all people are covered by some HI program under the NHI system. Second, the government uses uniform national rates to regulate the price of nearly all medical practices and prescription drugs at hospitals and clinics. Third, the NHI system follows the cost-based, fee-for-service (FFS) reimbursement system. Under the so-called "national all-coverage insurance scheme," one distinctive feature of Japanese medical expenditures is higher per capita expenditures on prescription drugs than in other industrialized nation. For example, the ratio of prescription drugs to total national healthcare expenditures in Japan is approximately 14% (about 20% when including pharmaceutical use by hospital inpatients), and the trend has noticeably increased, whereas the same ratio in the US is about 10% [4]. Another feature is that expenditures on medications and injections per episode of illness account for nearly half of the total medical expenditures on elderly outpatients in Japan.

In response to the high proportion of medication and injection costs and the increasing trend in medical expenditures, the Ministry of Health, Labor, and Welfare in Japan has advocated setting a price cap on currently regulated prices of prescription drugs. The regulated, uniform pharmaceutical price is based on the weighted-average market purchase price and the adjustment zone. The regulated pharmaceutical price is set according to the following formula: regulated price = weighted-average market purchase price before consumption tax + [1 + (1 + local consumption tax rate) x national consumption tax rate] + adjustment zone [4]. There are two methods for pricing a new pharmaceutical product [4]. A similarity- and efficacy-comparison method is a new line extension of existing molecules, and compares the innovative value (40% of additional merit), useful value (3%~10% of additional merit), and market value (3%~10% of additional merit) of a new product relative to existing pharmaceutical drugs. Another method is the original cost calculation method used for new products, and this method is based on production costs, sales/management costs, operating costs, distribution costs, and consumption taxes. Japanese government pricing for the similarity- and efficacy-comparison method and the original cost calculation method places less emphasis on short- and long-run cost perspectives [16].

In the pricing formula, the weighted-average market purchase price, which is the basis of the reimbursement fee for prescription drugs, is not necessarily equal to the market-trade price of individual drugs. For hospitals and clinics, the physician's purchase price is determined through private negotiations with the pharmaceutical company or a wholesaler. If the individual purchase price is lower than the weighted-average market purchase price, it creates a price margin that will be larger than the pre-calculated adjustment zone. The adjustment zone may be negative or positive. The fundamental purpose of the adjustment zone is to restrain and discourage over-prescribing, while the secondary purpose is to stabilize and efficiently evenly distribute product over the drug market. If the price margin is equal to the adjustment zone, then the reimbursement price would be exhausted. However, the existence of the price margin makes the actual amount lower than the reimbursement price, which consequently increases hospital/clinic revenue. Since the price margin goes to the medical institutions, the larger the price margin received, the higher the margin of received reimbursement.

The Ministry of Health, Labor, and Welfare tends to set higher prices for new drugs entering the market despite close similarity in quality and effects with existent drugs in the market. This may lead to differing utilization incentives and to a negative influence on pharmaceutical producers and physicians, since the price evaluation for new drugs tends to reduce the relative regulated price of existing drugs compared to incoming ones. This reduction gives an incentive to pharmaceutical companies to produce and market marginally improved products in order to maintain profits. With the same profit-minded reasoning, physicians and pharmacists are willing to purchase newly produced drug products [22]. However, purchasing new drugs only marginally increases the net revenues for hospitals/clinics and pharmacies. This reinforcing relationship between pharmaceutical companies (or wholesalers) and physicians/pharmacists brings about overproduction and over-prescription of drugs in the medical sector, which further allows inefficient medical institutions to remain in the healthcare service industry.

Under the national healthcare system, the price control policy, which restrains rising pharmaceutical costs, does not appear to have strong negative incentives for research and development activities with rising levels of pharmaceutical technology [4]. Medical & Pharmaceutical Industry [4] reports that the new chemical entities for diseases of the cardiovascular system, alimentary system, and for metabolism have been increasing since the late 1980s, and for malignant neoplasm their number began to rise around 1993. It is unclear whether government price control on pharmaceutical drugs is associated with the rising level of new chemical entities, which are a source of longevity and health of the population.

Our current study investigates two empirical research questions. First, does government regulation of the price of pharmaceuticals adversely affect the pharmaceutical industry? If so, what are the effects of price control on pharmaceutical innovation, such as new chemical entities? Second, what are the effects of new chemical entities on health, especially on the aforementioned illnesses of the cardiovascular system, alimentary system, metabolism, malignant neoplasm, etc.?

METHODS

Empirical Specifications

Effects of the Government Price Policy on a New Chemical Entity

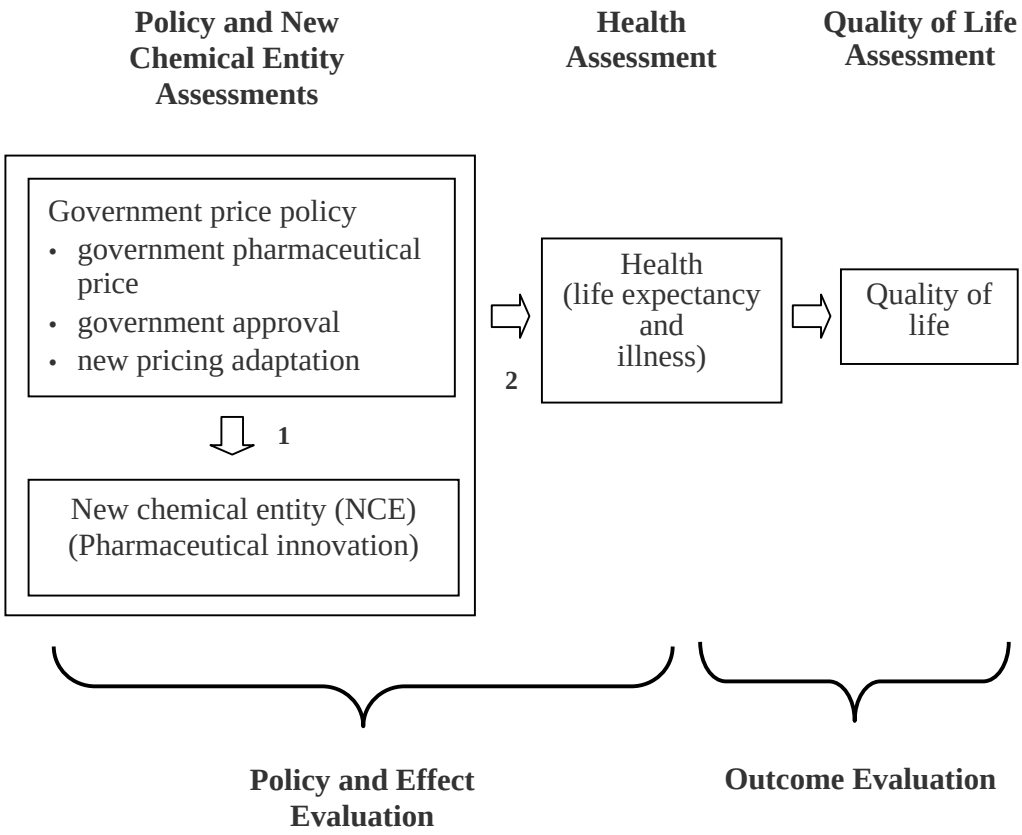
The empirical framework of the study assumes that the sales levels of a drug are attributed to its quality [6, 22]. The sales of pharmaceutical drugs not only produce individual benefits from the use of the drug, but also social benefits [9]. Pharmaceutical innovation is attributable, in part, to a quantitative expansion of drug utilization by the population. Sales consist of price and quantity, but a decrease in production cost due to economies of scale will increase the affordability of pharmaceutical drugs. One important assumption is that innovation creates a new value, causing corresponding increases in pharmaceutical prices. Thus, the social value of pharmaceutical innovation depends on the quantitative expansion of innovative drugs in the market.

Assume that the quality of pharmaceuticals reflects its price and the quantity sold. This implies that an attractive, quality oriented pharmaceutical product will increase sales, and will either increase the price or the quantity in the market, Berndt [16], who emphasizes the demand side. Although the pharmaceutical industry is not a purely competitive product market in Japan, the value of a new chemical entity is reflected in its sales, i.e. payers' marginal valuation [16, 22]. Grossman [23] notes that consumers not only increase their stock of health capital by using better pharmaceutical drugs, but also increase satisfaction levels and enjoyment of life by taking better quality oriented pharmaceutical drugs. Rational consumers utilize quality oriented products and quality oriented health investments, thereby increasing the longevity of the population [24-26].

Under government price control, the market does not determine prices and the pharmaceutical industry is not purely competitive, since price does not function as a signal of the market. The exit of unwanted products and entry of needed products are not naturally selected by the market mechanism. The competitive process that includes the exit and entry of firms does not function properly. As a natural consequence of the Japanese government's price regulation on prescription drugs, price control provides physicians with the opportunity to over-prescribe drugs to patients under the cost-based, fee-for-service (FFS) reimbursement scheme, since the regulated pricing system creates the price margin between the regulated price and the market-trade price.

The empirical study by Lu and Comanor [27] affirms that prices of pharmaceuticals generally reflect their therapeutic prices, which are associated with more effective, new pharmaceuticals. Vernon [9] explicitly states that the R&D intensity is expressed as a function of the expected return to R&D and pre-tax pharmaceutical profit through which price regulation may exert an influence on R&D. Similarly, Grabowski and Vernon [28] emphasize expected return, cash flow, and regulatory controls. We underscore that innovations will be affected by government regulations, including price control. Grabowski and Wang [6] underlined the historical trend of high new chemical entities (NCE) between the unregulated U.S. pharmaceutical market and low NCE by regulated European and Japanese markets. However, in this study our approach is slightly different from previous studies on government regulations of pharmaceutical innovation [6, 9, 28, 29] and on health by Morgan, McMahon, and Greyson [18], Lichtenberg [19-20], and Cutler [2]. The uniqueness of our focus is the evaluation of specific government price controls, not regulation in general, and on the association of new chemical entities to the health of the population by a production function approach [23].

This study utilizes a simplified PRECEDE-PROCEED approach (hereafter referred to as SPP) to examine the effects of the Japanese government's pharmaceutical price control policy on pharmaceutical innovation and health (life expectancy and illness) [30-33]. The SPP model is used to assess policies and programs, and observes decision-making behavior and its influential policy/program factors [31, 32]. In Fig. (**1**), the SPP shows five phases, that include three phases of assessment and two phases of evaluation. Policy and new chemical entity assessments in Fig. (**1**) represent the assessment of government price policy (pharmaceutical price, government approval, and new pricing adaption) on new chemical entities. In this specification, NCE represent an innovation that is expressed in two ways. One way is to quantitatively express the innovation as the number of new chemical entities launched in a year, and the second way is to qualitatively express it as the total sales of pharmaceutical drugs divided by the new chemical entities launched, which is deflated by the pharmaceutical drug price index [22]. Thus, the quality of a new chemical entity is the value of the new chemical entity associated with sales in the pharmaceutical market as a whole. We explicitly focus on three government price policies: pharmaceutical price, government approved-listed pharmaceutical drugs, and new pricing adaptation to evaluate the policy influence on new chemical entities (innovation) in this study. We note that the regulated pricing under the FFS reimbursement scheme has retarded the increase in the rate of separation between prescribing and dispensing drugs at different medical institutions, and that this rate still remains about 50% in Japan. The FFS reimbursement scheme and the large,



Source: Green and Kreuter [32].

Fig. (1). Simplified PRECEDE-PROCEED approach for the assessment and evaluation of government price policy, pharmaceutical innovation, and health.

positive price margin between government regulated prices of prescription drugs and market-trade prices have kept drug prescription and dispensation at the same level. However, our specification does not include this type of government regulation about the historical trend of separation between prescribing and dispensing pharmaceutical drugs because the specification may obfuscate some of the key behavior relationships that this study seeks to identify.

Based on the aforementioned discussion, we specify the regression model for the first estimation that is required to evaluate the effects of the government pharmaceutical price policy on a new chemical entity as pharmaceutical innovation in pathway 1 of Fig. (**1**).

$$NCE = f\,(\text{Government price policy}, NCE(-t), X) + \upsilon, \qquad (1)$$

where υ is an unobserved error, generally assumed to satisfy $E(\upsilon|\ \text{Government price policy}, NCE(-t), X) = 0$. NCE stands for a new chemical entity and represents pharmaceutical innovation. Our estimation for the NCE activities is the total sales of pharmaceutical drugs divided by the new chemical entities launched that are deflated by the pharmaceutical drug price index to reflect the value of a new chemical entity on the pharmaceutical market [22]. X is a vector of other covariates (pharmaceutical R&D expenditures, pharmaceutical technology level, other economic factors, etc.) in Table **1**. The study assumes that the number of cases of pharmaceutical technology exports and imports represents the pharmaceutical technology levels of pharmaceutical products/production, and the pharmaceutical technology level is not directly inherited from the number of new chemical entities approved [29]. The estimation for equation (1) also encapsulates the alternative view of the determinants of economic factors. The equation considers factors such as pharmaceutical expenses of health insurance cases in the national healthcare allotment of prescriptions, which decline as the dependency ratio of the aging population with national health insurance and elderly prescriptions increases. Other economic factors are the ratio of pharmaceutical production sales to GDP as the pharmaceutical industry size [13-15], and number of people engaged in medical care institutions (except clerks and other administrative workers) as a supply side control factor. We inclusion medical workers because medication is assigned a certain number of points for reimbursement; it induces more prescriptions per patient; and it induces overuse of prescription drugs under the FFS reimbursement scheme. Thus, the regulated drug price reflects the reimbursement fee from the government's insurance agency, which depends on drugs the physicians choose. Therefore, physicians tend to choose drugs with larger price margins because of the added net revenue to hospitals and clinics. A detailed definition of each variable is shown in Table **1**.

Table 1. Definition of the Variables for Influences of Pharmaceutical Price Control Policy on Pharmaceutical Innovation and Health Durability

Variables	Definition
Health (Illness)	Illness caused death at age 65 years or older of males and females in Table **3**. (m=582,370). Death caused by each type of illness is in Table **4** and each mean (m) value is also included in Table **4**.
Government Price Policy	
Government Pharmaceutical Price	A change in drug price standard for pharmaceutical base by the government (%). (m=see Table **2**).
Government Approvals	Number of government approved-listed pharmaceutical drugs.
New Pricing Adaptation	Market oriented weighted average adjustment method for calculating regulated pharmaceutical price (=1 since 1992, =0 before 1992).
Innovation	
NCE	Total sales of pharmaceutical drugs divided by new chemical entities launched that are deflated by the pharmaceutical drug CPI (base year 2000) in 0.1 billion yen. (m=270.866 billion yen).
NCE(-t)	Total sales of pharmaceutical drugs divided by new chemical entities launched that are deflated by the pharmaceutical drug CPI (base year 2000) in 0.1 billion yen. "t" indicates a lag year. (m=see Table **2**).
QNCE	Number of new chemical entities launched in a year. (m=see Table **3**).
QNCE(-t)	Number of new chemical entities launched in a year. "t" indicates a lag year.
Pharmaceutical R&D	
R&D	Real values of R&D expenses by the pharmaceutical industry deflated by the GDP deflator (base year 1995) in million yen. (m=see Table **2**).
R&D(-t)	Real values of R&D expenses by the pharmaceutical industry deflated by the GDP deflator (base year 1995) in million yen. "t" indicates a lag year.
Pharmaceutical Technology Level	
Export	Number of cases of pharmaceutical technology export. (m=see Table **2**).
Import	Number of cases of pharmaceutical technology import. (m=see Table **2**).
Other Economic Factors	
Pharmaceuticals Cases	Ratio of pharmaceutical expenses of health insurance cases in national healthcare expenditures (x100=%). (m=see Table **2**).
Elderly Prescriptions	Number of prescriptions in 10,000 divided by the dependency ratio of the aged population [(population aged 65 or older /population aged 15-64)x100]
Pharmaceutical Market Size	Share of pharmaceutical sales in GDP. (m=see Table **2**).
Medical Workers	Number of persons engaged in medical care institutions except clerks and other administrative workers. (m=see Table **2**).

Note: Data sources are from (a) Medical & Pharmaceutical Industry, Jihou, 2002, 2004, and 2007, Tokyo; (b) Drug Approved and Licensing Procedures in Japan, Society of Japanese Pharmacopoeia, 1982-2006, Tokyo; (c) Vital Statistics, Statistics, and Information Department, the MHLW, 1970-2006; and (d) Japan Statistical Yearbook, Ministry of Public Management, Japan Statistical Association, 1970-2006, Roujin Iryou Jigyou Nenpou, Health Insurance Bureau, MHLW, 1990-2006.

For this study, we used several approaches to increase the reliability of the estimation in order to evaluate the effects of the pricing policy on new chemical entities: pharmaceutical price, a government approved list of a number of pharmaceutical drugs, and a new pricing adaptation policy. A drug with a new chemical entity may attract market sales, which may in turn lead to R&D activities. The benefits of a new pharmaceutical chemical entity with new products are longevity, quality of life, and a healthy work effort relating to labor productivity. Research and development activities will increase levels of innovative pharmaceutical drugs. Thus, new chemical entities and activities of research and development are endogenously associated. The economic theory underlying the above discussion implies that a specification error leads to the simultaneity problem in this model. We consider three estimation issues: serial correlation, specification, and exogeneity/endogeneity tests [33, 34]. Our study generalizes the basic setup to establish a link between government price policy, current new chemical entities, and R&D activities.

First, we follow Acemoglu and Linn [14] and include lagged NCE in the current new chemical entity equation and perform the specification test. Equation (1) contains a lag of dependent variables and new chemical entities to examine the effect of past new chemical entities. The study obtained the residual variable from the ordinary least squares (OLS) regression and created the lagged residual variable. The result of the "t" statistics for the null hypothesis shows that ρ^*, which is the estimate of the first-order serial correlation estimation of ρ, is not significantly different from 0. Thus, the first-order serial correlation is not presented in the NCE estimation equation (1).

Second, this study assumes that R&D costs become fixed or sunk, once a new pharmaceutical drug is developed and ready to be marketed [16]. It is necessary to investigate the relationship between pharmaceutical R&D and pharmaceutical innovation. Yabuki and Morisawa [35] emphasized that R&D expenses are associated with the values of new drugs. Given the Japanese government's price control policy, the pharmaceutical industry in Japan is not a purely competitive product market. Given price control, product differentiation will be necessary for the sales of drugs with new chemical entities. The economic theory underlying the above discussion states that there would be an upward bias of the estimate of the true impact of R&D if it were omitted [33, 34]. The results of Hausman's specification test show that the endogeneity and exogeneity test $\hat{u}_1$ ($t_1 = 0.602$; a regression error term from the equation of R&D) and $\hat{u}_2$ ($t_2 = -0.865$; a regression error term from the government pharmaceutical price policy) are not statistically significant, and indicate no simultaneity problem for this specification. Both R&D and government price policy variables can be treated as exogenous [33, 34] for this estimation.

Third, the study generalizes the basic setup to establish a link between a current new chemical entity and a government price policy. Recalling that the government pharmaceutical price policy will affect pharmaceutical drug innovation [9, 12], the new chemical entities and government price policies may be associated with each other. Thus, we exploit Hausman's specification test for endogenoity and exogeneity for the equation (1). The results of the regression error term from the equation of the government price $\hat{u}_1$ ($t_1 = 1.603$) and the regression error term from the equation of the new chemical entity $\hat{u}_2$($t_2 = 0.031$) are not statistically significant. The results indicate that there is no simultaneity problem for the specification by including a new chemical entity and government price policy factors.

Effects of Pharmaceutical Innovations on Health

The probable reasons for the Japanese government's price regulation of pharmaceuticals are twofold. The first reason is related to the public goods concept, which is that pharmaceutical drugs generate positive externalities through consumption of pharmaceuticals to improve the health of the population [23, 36]. Improvement of health does not only increase a person's own health status, but also raises the health of others through improvements and externalities such as preventative care and resistance to transmitted diseases [37-39]. Second, from an equity point of view, easy access to pharmaceutical drugs satisfies basic healthcare needs [18, 40]. In this section, our health measure is similar to life expectancy by Lichtenberg [20], mortality by Lichtenberg [19, 41], and cancer survivability by Lichtenberg [42]. Our approach is similar to those prior approaches. In this study, we use crude measures of health: illness-caused deaths per year for those aged 65 years or older and death caused by the six leading illnesses (of the cardiovascular system, alimentary system, metabolism, malignant neoplasm, respiratory system, and urogenital system) of those aged 65 years or older. The reason for choosing these illnesses is that the deaths caused by the alimentary system and metabolism have been rapidly rising since 1970 relative to the cardiovascular system and malignant neoplasm in Japan. Along with the rapid increase in leading deaths, for the past two decades the leading NCEs have been systematically used in cardiovascular, metabolic, anti-malignant tumor, and alimentary system medicines, including peptic ulcer medicine, by Japanese pharmaceutical companies. In addition, the Japanese pharmaceutical companies recently imposed efforts on the NCE of antibiotic and chemotherapy medicine. Thus, to evaluate the effects of pharmaceutical innovations on health, the second equation is pathway 2 in Fig. (**1**). Based on the previous discussion and equations (1), we consider that health depends on pharmaceutical innovation and government price policy.

$$\text{Health} = f\,(\text{QNCE, Government price policy, X}) + \omega, \qquad (2)$$

where ω is an unobserved error, generally assumed to satisfy $E(\omega \mid \text{QNCE, Government price policy, X}) = 0$ and QNCE stands for innovation. In equation 2, health represents the aforementioned two crude measures: illness-caused deaths and the six leading illnesses (in the cardiovascular system, alimentary system, metabolism, malignant neoplasm, respiratory system, and urogenital system). It is noteworthy to infer from some recent past work on coronary intervention by Hochman *et al.* [43], on acute myocardial infarction treatment by Cutler [2], and on the treatment of heart attacks by Chandra and Staiger [44] because of the lack of availability of micro-level Japanese data which is relevant to specific illness and which is associated with our crude measures of empirical study on Japan. However, we specifically focus on Japanese government price policy using two different health measures to understand the effects of NCE on the health of the population to avoid obfuscating the key price policy implication. The measurement of government price policy is the same as we specified in the previous regression model of the first estimation on NCE in (1). We employ three types of the government price policy for the estimation: pharmaceutical price, government approval, and new pricing adaptation in regression model (2). X is a vector of other covariates (pharmaceutical technology level, other economic factors, etc.).

Our objective is to examine the influence of NCE on health gain, and our structural model (2) does not include improvement of environmental factors, nutrition, and other important developments of modern civilization. In the past thirty years, widespread diseases such as malaria, tuberculosis, diphtheria, and cholera, have mainly been confined to areas of Africa, Asia, and Latin America, as shown in Healthy People 2010 [45]. Other causes may have led to improved health by a variety of influences on health of the population. For example, Ross [46] discussed national healthcare policy and superior health outcomes, DuBard and Gizlice [47] surveyed barriers of access to healthcare services and preventive care in health status in the U.S., Cutler [2] examined costs and benefits of quality adjusted life expectancy by revascularization, Grossman [23] emphasized effects of health education on improved health stocks, and Durkin, Biener, and Wakefield [48] surveyed the effect of mass media antismoking messages on smokers.

In our specification, we hypothesize that the new chemical entities will increase health durability. The approach in this study is based on an assessment of the aggregate contribution of new chemical entities, which is expressed as innovation. The innovation is quantitatively

represented as the number of new chemical entities launched in a year (QNCE), as we discussed in the previous section, and QNCE is defined in Table **1**. In addition, the effects of new chemical entities take three years to fully impact disease survival rates [20]. Thus, in developing the second estimation, it's important to consider the 3-year lag (i.e. t-1, t-2, and t-3) in order to examine the effectiveness of new chemical entities, since excluding a relevant variable would lead to biased estimates. Thus, a change in the structural model requires consideration of the estimation procedure for specification tests for the model estimation and endogeneity/exogeneity tests.

Concerning the test for the structural stability of the regression model, the F test (= 2.78) is greater than the critical value (= 2.42). The statistics test for the null hypothesis is rejected and the lag variables of new chemical entities, t-1, t-2, and t-3, should be included for the estimation of equation 2 in the SPP framework, as shown in pathway 2 of Fig. (**1**). For Hausman's exogeneity/endogeneity test, the residuals of government price and the new chemical entity reduced form are included in the structural form. The results present "t" statistic coefficient residuals for both new chemical entities (t= -0.684) and the price of drugs under government control (t= -0.446) in the structural form. The instrumental variables for this evaluation are expenses for research and development for the new chemical entity and the number of people engaged in providing medical care, except for clerks and other administrative workers. The results imply that both factors can be treated exogenously.

Data

The Japanese government has approved and introduced new chemical entities into the pharmaceutical market. Drugs based on new chemical entities have been manufactured in Japan and other foreign countries. The aggregate time series, from 1970 to 2004, includes 800 original new drugs that are based on new chemical entities. Four hundred and ninety eight (498) of the 800 new drugs have been launched by Japanese pharmaceutical companies. The number of NCEs in the early 1970s is underreported, and it's possible that the data does not report foreign NCEs precisely. The NCEs in this study are obtained from two sources: one is the Medical & Pharmaceutical Industry published by Jiho in 2002, 2004, and 2007 in Tokyo; the other is the Drug Approved and Licensing Procedures in Japan published by the Society of Japanese Pharmacopoeia from 1982 to 2006, in Tokyo.

The cross-sectional and time-series data, from 1970 to 2004, categorize twenty-two new chemical entities. A lack of data sources for new chemical entities has generated missing values in the data series and prevented statistical procedures from maintaining observations for the regression analysis, such as the new chemical entities of febrifuge, analgesic and antiphlogistic medicine, and nervous system peripheriсum medicine. The new chemical entities for hormone, radiopharmaceutical, antibiotic, and biomedical medicine are not included in the illness-specific assessment. For two measures of illness, we use illness-caused deaths per year at age 65 years or older and death caused by six leading illnesses (in the cardiovascular system, alimentary system, metabolism, malignant neoplasm, respiratory system, and urogenital system) of those aged 65 years or older. The leading causes of death with respect to the age classification are based on Vital Statistics, Statistics and Information Department, Ministry of Health, Labor and Welfare; and the Japan Statistical Yearbook, 1970-2006, Statistics Bureau, Ministry of Public Management, Japan Statistical Association, Tokyo. The cause of death classifications are obtained from the Vital Statistics of Japan, which conforms to the 10th Revision of International Statistical Classification of Diseases and Related Health Problems.

The sources of government price policy and other macro-level statistics come from the Japan Statistical Yearbook, 1980-2006, Statistics Bureau, Ministry of Public Management, Japan Statistical Association, in Tokyo. The data on national healthcare expenditures and health insurance related statistics are based on Roujinn Iryou Jigyo Nenpou 1990-2006, Health Insurance Bureau, Minister of Health, Labor, and Welfare, Tokyo. The pharmaceutical production data comes from the Medical & Pharmaceutical Industry 2002 and 2007, Ministry of Health, Labor, and Welfare, Jiho, Tokyo. A detailed definition of each variable is shown in Table **1**.

RESULTS

Government Price Policy on New Chemical Entities

The estimation results of equation (1), which explains the influence of the government price policy on new chemical entities, is shown in Table **2** and in pathway 1 in Fig. (**1**). Government price policy is related to three measures: pharmaceutical price, namely price reduction of listed pharmaceutical drugs; the number of government approved-listed pharmaceutical drugs; and the new pricing adaptation (see Definition of the Variables in Table **1**). Recall that price is not market-determined, but rather is determined by the Japanese government. However, the price may reflect the actual market to some extent since the regulated price is always higher than the average price. The formula for the regulated price is based on the market oriented, weighted average adjustment method. The adjustment is equal to 2% of the price before the revision. In Table **2**, the positive coefficients of the government pharmaceutical price and the new pricing adaptation show that both policies may have affected pharmaceutical company's decisions to increase new chemical entities. The positive coefficients of the government price policy show that the purpose of government regulation of pharmaceutical prices seems to target the pharmaceutical industry and its growth and development, but rather intends to control the rapid rise of healthcare expenditures, i.e. pharmaceutical use.

For an innovation variable, the purpose of NCE is to examine the effect of the past marketed NCE(-1): the total sales of pharmaceutical drugs divided by new chemical entities launched, which is deflated by the pharmaceutical drug CPI, on the current activity of innovation [35]. The result clearly reveals the influence of older, marketed chemical entities on recently launched new chemical entities. The estimation of equation (1) demonstrates interesting results in Table **2**. Using the elasticity concept, a 1 percent increase in NCE(-1) leads to a 0.6% increase in the value of new chemical entities (see definition Table **1**). By applying elasticity, the monetary impact of NCE(-1), 2.6 billion yen,

Table 2. Effects of Government Price Policy on New Chemical Entity (NCE: Innovation)

Parameter	Marginal	t-Statistics	P-Value	Means
Government Price Policy				
Government Pharmaceutical Price	90.193	2.525	0.023	-6.123
Government Approvals	-0.055	-0.446	0.662	12400.00
New Pricing Adaptation	1946.34	2.281	0.037	0.30
Innovation				
NCE(-1)	0.677	3.342	0.004	2648.66
Pharmaceutical R&D				
R&D	-2.290	-2.032	0.059	4907.50
R&D(-1)	-2.192	-2.304	0.035	4621.95
R&D(-2)	-0.012	-0.014	0.989	4359.58
Pharmaceutical Technology Level				
Technology Export	33.833	2.566	0.021	255.25
Technology Import	0.682	0.119	0.907	184.55
Other Economic Factors				
Pharmaceuticals Cases	234E+3	3.076	0.007	0.029
Elderly Prescriptions	-16.550	-3.038	0.008	888.034
Pharmaceutical Market Size	293E+3	1.306	0.210	0.015
Medical Workers	0.032	2.865	0.011	947088.00
Intercept	-15356.0	-2.853	-0.012	
Number of observations	35			
R-squared	0.687			
F-statistics	2.706			
Durbin-Watson *	2.185*			

Notes: * The Durbin h test is not valid with a negative value of $\sqrt{\frac{T}{1-T[Var(\hat{\beta})]}}$ in Var($\hat{\beta}$) $h=\left(1-\frac{DW}{2}\right)\sqrt{\frac{T}{1-T[Var(\hat{\beta})]}}$. Thus, the study estimated the following equation, $\hat{\varepsilon_t}=\alpha+\rho^{*}\hat{\varepsilon}_{t-1}+\beta^{*}Y_{t-1}+\gamma^{*}X_t+u_t$, and tested that ρ^{*} is not significantly different from 0. The first-order serial correlation is not present in the NCE estimation.

1. Hausman's specification test show that $\hat{u}_1$ (t_1 = 0.602; a regression error term from the R&D) and $\hat{u}_2$ (t_2 = -0.865; a regression error term from the government pharmaceutical price policy) are not statistically significant, and indicate no simultaneity problem for this specification.
2. Both R&D and the government price policy variables are treated as exogenous for the estimation of Equation 1.
3. Hausman's specification test for equation (1) shows that the equation of the government price $\hat{u}_1$ (t_1 = 1.603) and the equation of the new chemical entity $\hat{u}_2$ (t_2 = 0.031). Both regression error terms are not statistically significant. There are no simultaneity problems.

leads to about a 1.6 billion yen increase in the current value of NCE per year.

For pharmaceutical R&D on the other hand in Table **2**, a 1% (0.05 billion yen) increase in the current R&D expenses would lead to a 0.04% (0.1 billion yen) decrease in the current value of NCE. Using the definition of current value of NCE based on Yabuki and Morisawa [35], an increase in current R&D activities devalues the value of existing innovative products. The result implies that the current optimum R&D adjustment rate for the NCE by Japanese pharmaceutical companies is 32.3% (Appendix A). In other words, Japanese companies will adapt their NCE expectations in light of past experiences with R&D. The negative signs of all R&D coefficients are added by our specification test. Thus, the long-run effect of R&D on the value of NCE is a decline of 0.4494(=2.290+2.192+0.012=4.494, see Table **1** for the unit of value) billion yen. The adjustment of 32.3% would cause a downward influence of 0.4494 billion yen of NCE in the long run, while a full adjustment (i.e. 100%) of R&D would bring an increase of 0.709 billion yen in the long run [33, 34].

The aforementioned result can be explained through logical reasoning. An increase in R&D raises NCE and also raises the quality of pharmaceutical drugs. However, the price of pharmaceutical drugs declines because of the Japanese government's pricing policy, as shown by the mean price reduction of the pharmaceutical price (m= -6.123) in Table **2**. What is so intriguing about the empirical result is that the coefficient of the pharmaceutical price under the government policy raises the value of NCE by roughly 9 billion yen, which is a one percentage decrease in price of listed pharmaceutical drugs using the average of 2004 values. A new pricing adaptation raises the value of NCE by 194.634 billion yen in Table **2**.

Table 3. Effects of New Chemical Entity (QNCE, i.e. Innovation) on Health (Illness-Caused Deaths)

Parameter	Marginal	t-Statistics	P-Value	Means
Innovation				
QNCE	-5863.26	-2.245	0.038	24.254
QNCE(-1)	1655.31	0.622	0.542	24.827
QNCE(-2)	-3388.27	-1.042	0.312	24.379
QNCE(-3)	6998.58	2.705	0.015	23.517
Government price policy				
Government Pharmaceutical Price	-5162.77	-1.235	0.233	-6.123
Government Pharmaceutical Price (-1)	-7629.43	-1.744	0.099	-4.181
Government Approvals	7.381	0.638	0.532	12400.20
Government Approvals(-1)	-24.079	-1.904	0.074	12253.79
Pharmaceutical technology level				
Technology Export	2812.63	3.295	0.004	255.250
Technology Export(-1)	-2465.82	-2.481	0.024	272.828
Other economic factors				
Pharmaceuticals Cases	-25891.6	-2.552	0.021	0.028
Elderly Prescriptions	2.254	2.299	0.034	835.428
Intercept	598518.0	5.673	-0.000	
Number of observations	35			
R-squared	0.876			
F-statistics	10.003			
Durbin-Watson*	2.863*			

Notes: *Berenblutt-Webb test of the hypothesis that ρ=1 and the result of "g" test show g = 0.9678 with d_L = 0.577 and d_U = 2.592. The serial correlation is inconclusive.
1. QNCE is the absolute number of new chemical entities launched in a year, and QNCE(t) means time lags.
2. Concerning the test for the structural stability of the regression model, the F test (=2.78) is greater than the critical value (=2.42). The statistics test for the null hypothesis is rejected and the lag variables of new chemical entities, t-1, t-2, and t-3, should be included for the estimation of equation (3).
3. Hausman's exogeneity/endogeneity test presents "t" statistic coefficient residuals for both new chemical entities (t = -0.684) and the price of drugs under government control (t = -0.446) in the structural form. The results imply that both factors can be treated exogenously.

Pharmaceutical Innovation and Government Price Policy on Illness

In Table **3**, the results of efforts to decrease levels of illness-caused deaths by introducing new chemical entities appear in the estimation equation (2) and are shown in Fig. (**1**). Pathway 2 in Fig. (**1**) represents this estimation. Using the coefficients of innovation variables and applying the Koyck approach to the distributed lag estimation, the long-term effect of new chemical entities on death caused by illness is about a decrease in 4,343 people per unit increase for new chemical entities (Appendix B). The result is the influence of new chemical entities launched in a year, QNCE, on illness-caused deaths per year of people at age 65 years or older. In Table **3**, the average mean of QNCEs is about 25 new chemical entities. When we multiply this mean of 25 new chemical entities by about 4,343 elderly people saved per chemical entity introduction, we can see that QNCEs lead to a decline of illness-caused deaths by approximately 108,600 people per year. This figure is about 18.6% of illness-caused deaths in the elderly population aged 65 years or older. Therefore, this policy has a large impact on illness. A one percent increase in the lagged price of pharmaceutical drugs will reduce illness-caused deaths by about 7,600 people, aged 65 years or older.

In Table **4**, another aspect of equation (2) also explains the effect of new chemical entities (QNCE) on death caused by specific illness. It is associated with pathway 2 in Fig. (**1**). The coefficients of all $QNCE_t$ variables in the specific illness equations are statistically significant. The negative signs imply that current and lagged QNCEs reduce each specific death caused by illness. The current quantity of $QNCE_t$ generally has a larger impact on death caused by illness than the lagged $QNEC_{t-1}$ and $QNCE_{t-2}$. The results show that the flow of the time-path does not indicate a systematic, quantitative size of flow and diffusion after launching. These six leading illnesses share a 65.95% decrease in death caused by illness of those aged 65 years or older. The trends of new chemical entities of the cardiovascular system and malignant neoplasm have recently risen rapidly relative to other new chemical entities [4]. The cardiovascular system and malignant neoplasm together demonstrate about a 1,066 marginal decrease by a unit increase in drug-based new chemical entities and about 43.7% of the marginal share by these illnesses together. The results present clear evidence of the large marginal contribution to a decrease in the

Table 4. Effects of New Chemical Entities (QNCE, i.e. Innovation) on Health (Deaths Caused by Each Illness)

Illness Type (Dependent Variable)	$QNCE_t$ (m=31.54)	$QNCE_{t-1}$ (m=31.77)	$QNCE_{t-2}$ (m=32.01)	F Statistics	R^2	N
Total Illness (m=282.3E+3)	-2436.863 (-2.49$_b$)	-1066.721 (-1.04)	-1695.693 (-1.68$_c$)	15.66	0.511	68
Cardiovascular system (m=696.74E+3)	-529.217 (-2.30b)	-289.735 (-1.20)	313.960 (-1.32)	19.36	0.563	68
Malignant neoplasm (m=673.87E+3)	-536.535 (-2.90a)	-312.608 (-1.61)	-409.256 (-2.15b)	40.35	0.729	68
Alimentary system (m=136.51E+3)	-235.665 (-3.33a)	-127.833 (-1.72c)	-136.910 (-1.87b)	18.13	0.547	68
Metabolism (m=7266.54)	-59.354 (-2.95a)	-28.839 (-1.37)	-38.503 (-2.65c)	59.14	0.798	68
Respiratory system (m=315.97E+3)	-144.860 (-1.98c)	-110.634 (-1.45)	-232.115 (-3.08a)	72.72	0.829	68
Urogenital system (m=6294.06)	-104.429 (-2.65b)	-40.583 (-0.99)	-43.443 (-1.09)	6.58	0.422	68

Notes:
1. N stands for the number of observations. An increase in observations is based on the data which are combined by male and female illness. We controlled population and income. Missing values reduced the number of observations.
2. F stands for F statistics and R^2 stands for adjusted R^2.
3. t statistics are in parentheses. a: significant at 1%. b: significant at 5%. c: significant at 10%.
4. m in parentheses indicates mean statistics.

aforementioned two leading illnesses attributable to a rapid rise in new drug launches.

CONCLUSIONS AND IMPLICATIONS

Pharmaceutical price control as a containment policy for ever expanding healthcare expenditures is intended to sustain the national health insurance system. The policy clearly reflects the lack of price competition of pharmaceutical drugs, while the expenses of health insurance prescription per capita during three consecutive decades rose 183 times, during which the Japanese population was stable. Price control of pharmaceuticals by the Japanese government is not intended to strangle the pharmaceutical industry. Price control is actually a price reduction of the government's approved-list of pharmaceutical drugs under the national healthcare system. The policy is a byproduct of a healthcare policy that attempts to constrain a rapid increase in pharmaceutical expenditures in an aging society under the national healthcare system.

This paper identifies the effect of the government's price control policy on pharmaceutical innovation and evaluates the influence of new chemical entities on health, i.e. health durability. As the empirical evidence indicates, the overall contribution of new chemical entities to longevity provides noteworthy results. Our empirical results underline that the pharmaceutical industry is not a primary target for the government price policy on pharmaceuticals and the government price policy appears to be derived from a healthcare policy intended to control an increase in pharmaceutical healthcare expenditures. The results demonstrate that the policy induces pharmaceutical innovation, i.e. new chemical entities, which in turn raise health durability.

Abbott [7], Santerre and Vernon [8], and Vernon [9] state that government price control has adverse effects on R&D efforts and in turn, new chemical entities. The decline in the expected return from R&D activities leads to less quality-oriented innovations. Unlike findings in past work, the Japanese pharmaceutical industry shows different perspectives about the relationship between pricing regulation and NCE activities. Our empirical study provides new evidence that the market prices of existing drugs induce new drug development [10], and the Japanese pharmaceutical industry seems to introduce high rates of less world level and less innovative new chemical entities in a large home market and those of neighboring countries as Grabowski and Wang noted [6]. Our empirical results show that both variables - pharmaceutical price and new pricing adaptation by the government price policy - raise the monetary value of new chemical entities. As Eqelund and Persson [12] and Berndt [16] state, price regulation depresses competition among brand-name pharmaceutical drugs and leads to product differentiation through innovative products. The empirical results verify that government price control in Japan does not necessarily decrease pharmaceutical innovation activities beside world level innovative chemical entities [6]. Statistical evidence strongly suggest that the government price policy on pharmaceutical prices seems to be a cost containment policy for a rapid increase in pharmaceutical expenditures under the government oriented healthcare system, and is not intended to hamper the pharmaceutical industry. The effect of government price control seems to be a derivative of healthcare policies. Although Grabowski and Wang [6] state that a market-oriented pricing approach leads to the production a more innovative and global level of products than the government controlled pricing approach, the competitive and innovative position of the Japanese pharmaceutical industry ranks third in the world, preceded by the U.S. and the U.K., and for innovative policy and system environments Japan is fifth, preceded by the U.S., the U.K., Germany and France [49]. In a large pharmaceutical

market with an aging population, as in Japan, pharmaceutical innovation is also influenced by the size of the pharmaceutical market structure [14, 50].

Japanese pharmaceutical companies have become more global in international partnership arrangements, marketing, research/development, exporting pharmaceutical technology, licensing, etc. than in the past [51]. However, the major concern is a decrease in the global level of new chemical entities in the long run under the government's current pharmaceutical price policy. A periodic reduction in the reimbursement price of existing drugs on the government approved list will basically influence the market price of new drugs, leading to a reduction in profit for pharmaceutical producers. Japanese pharmaceutical producers may mitigate a reduction in profits by quickly producing less innovative drugs with modification-based innovation.

Our finding has two implications for healthcare policies. First, the pharmaceutical price has fallen by 80% since 1969 because of the government price policy. The policy clearly reflects the lack of an increase in the price of prescription drugs, only 1.75 times since 1970, while the expenses of health insurance prescription per capita during three consecutive decades rose 183 times [3-4]. During those three decades, the Japanese population was relatively stable, while the dependency ratio of the elderly population rose about threefold. The government has shown concern over a rapid increase in health insurance expenses, which is due in part to the utilization of price-regulated prescription drugs. Prescription drug prices, which are correspondingly set higher than the market-trade price, create an excess price margin. The rapid increase in the expenses of health insurance prescriptions also stems from the low figure of the rate of separation between prescribing and dispensing, i.e. 50% currently. If the government needs to maintain the pharmaceutical price policy for the concept of public goods and accessibility to pharmaceutical drugs to satisfy basic healthcare needs, a viable policy option would be for the government to implement a strong initiative in promoting the separation between prescribing and dispensing that may possibly and partially deter a rapid increase in the expenses of health insurance prescriptions.

Second, for the current pricing policy of a new pharmaceutical product in Japan, the similarity- and efficacy-comparison method by the government, which is a new line extension of existing molecules on the market, is to refer to prices of drugs that have long been on the market [3]. Thus, the new pharmaceutical price may not reflect the actual value of the new product under the government price policy. An innovation incentive for the pharmaceutical industry is the government's referral of prices of the latest drugs on the market not only to the domestic market, but also to foreign markets. Under the national health insurance system, government price policy on different therapeutic categories does not differ. The Japanese government bases the original cost calculation method on production cost. Berndt [16] notes that the price of a new (innovative) pharmaceutical product should consider not only material on marginal manufacturing costs, but also the demand side of marginal valuation of the new pharmaceutical product.

Pharmaceutical price control generally brings up the issue of fair introductory prices, which affect an investment in R&D by pharmaceutical companies and ends up hurting the consumer's welfare (Vernon) [9]. Although there are some negative externalities caused by pharmaceutical drugs from side-effects of medications, including health deterioration caused by over-utilization of medicine [37-39], the argument is that the government intends to increase accessibility to pharmaceutical products for basic healthcare needs and to maintain the national health insurance system. Our study offers a compelling argument for the effects of the government pharmaceutical price policy on health durability. It is, however, important to put the results presented in this empirical study into appropriate perspective because of the caveats associated with the results. Since, in the literature of health economics, determinants of health durability are associated with education (including health education), income, lifestyle (smoking, drinking, physical activities, diet/nutrition, etc.) and environmental health, our results may overestimate the effect of new chemical entities on a declining death rate caused by illness for people aged 65 years or older.

Since little research to date has focused on government pharmaceutical policy, including pricing policy and its link to new chemical entity based drugs and health durability, we shed light on these issues. The study recognizes that the aggregate effect of new chemical entities reduces the illness-caused deaths by about 108,600 people per year, and one new chemical entity saves about 4,340 people per year, aged 65 years or older. More specifically, new chemical entities prevent about 66% of death caused by the six leading illnesses (in the cardiovascular system, alimentary system, metabolism, malignant neoplasm, respiratory system, and urogenital system) among those aged 65 years or older. The cardiovascular system and malignant neoplasm together demonstrate about a 1,066 marginal decrease in illness-caused deaths by a unit increase in drug-based new chemical entities. The study offers a compelling argument for the government pharmaceutical price policy on reducing illness-caused deaths, i.e. health durability, through new chemical entities. The government price policy with regulations may not only increase the affordability of pharmaceutical drugs at a lower price, but may also offer incentives to pharmaceutical companies to develop and introduce innovative pharmaceutical drugs with new chemical entities [18].

The results of this study suggest that new chemical entities and pharmaceutical innovation would decrease the mortality of specific illnesses in the elderly population. Pharmaceutical innovation is a noteworthy source of health outcome. New chemical entities appear to account for a significant, important factor in the long run, increasing health durability in the sample as a whole. Furthermore, we need further study in this field to find additional evidence for a clear-cut influence of the government price policy on pharmaceutical innovation and the precise impacts of new chemical entities on illness.

We need to add some additional issues to the government price policy. Medication in Japan is assigned a certain number of points for reimbursement; it induces more prescription per patient and it induces overuse of prescription drugs under the fee-for-service reimbursement scheme. The regulated drug price reflects the reimbursement fee from the

government's insurance agency, which depends on drugs the physicians choose. Therefore, physicians tend to choose drugs with larger price margins because of the added net revenue to hospitals and clinics. Although the Ministry of Health, Labor, and Welfare of Japan has instituted a series of reductions in regulated pharmaceutical prices that would discourage the moral hazard among physicians of over-dispensing drugs to patients, the consequences are still ambiguous and unclear. Prescription drug overuse is reinforced by the fact that out-of-pocket expenses for prescription drugs by patients are kept low by the national health insurance system. The increase in shares of medication and injections in total medical expenditures has caused the Ministry of Health, Labor, and Welfare to institute a modified cost-based reimbursement scheme, capitation, which shows to some extent a promising sign in curbing increases in total medical expenditures. However, its application continues to be limited to elderly inpatients at specially accredited hospitals. Presently, the regulated pharmaceutical pricing system and the low rate of separation contribute to the misallocation of human resources at hospitals, both of which create inefficiency in the health care system in Japan.

There are two limitations of this study. The first limitation is the availability of micro-level data in the Japanese study. To accurately and effectively investigate pharmaceutical use and its effect on longevity and health, it is essential to use micro-level data for analysis, which would generate a more valuable policy implication. Unlike macroeconomic fiscal and financial data, health related micro-level data is not yet well documented, and is restricted from public availability in Japan. The researchers' objectives would be diverted due to the lack of data sources. We hope that the present study will lead to the Japanese government making micro-level data more readily available. The second limitation of the study is that there are unobservable information sets that hospitals or clinics use at the critical decision time to bring more characteristics of supply side factors to evaluate illness. We had to estimate this using the information parameters. It is our hope that it would bring more promising, robust results by focusing on one specific illness with the NCE by including more relevant factors with individual level data.

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APPENDIX A

Based on the adaptive expectation model on pp.596-598 by Gujarati [33], $NCE_t = \beta_0 + \beta_1 R\&D^*_t + u_t$, where $R\&D^*_t$ is not directly observable, and expectations are formed by the following, $R\&D^*_t - R\&D^*_{t-1} = \gamma(R\&D_t - R\&D^*_{t-1})$ and then $R\&D^*_t = \gamma R\&D_t - (1-\gamma)R\&D^*_{t-1}$, where γ is the coefficient of expectation. To find γ, we have the following equation, $NCE_t = \gamma\beta_0 + \gamma\beta_1 R\&D_t + (1-\gamma)NCE_{t-1} + v_t$, where $v_t = u_t - (1-\gamma)u_{t-1}$. We have $(1-\gamma)NCE_{t-1}$ which leads us to find the marginal coefficient $(1-\gamma) = 0.677$ which is the coefficient of NCE(-1) in Table **2**. Thus, $\gamma = 0.323$ (=1-0.677). We also have $\gamma\beta_1 R\&D_t$ which leads us to find $\gamma\beta_1 = -2.29$ in Table **2**. $\gamma\beta_1$ measures the average response of NCE to a unit change in the actual or observed value of R&D. Thus, $\beta_1 = -2.29/\gamma = -2.29/0.323 = -7.09$ (=0.709 billion yen). β_1 measures the average response of NCE to a unit change in the expected long-run value of R&D.

APPENDIX B

The long-term effect of QNCE on the illness caused deaths of males and females, aged 65 years or older is estimated by using the Koyck approach to distributed-lag model as shown in Table **3**. $Illness_t = \alpha + \beta_0 QNCE_{t-1} + \beta_0\lambda QNCE_{t-2} + \beta_0\lambda^2 QNCE_{t-3} + \ldots + u_{t-1}$. By rearranging the equation, we get $Illness_t = \alpha(1-\lambda) + \beta_0 QNCE_{t-1} + \lambda(Illness_{t-1}) + v_t$. Following this, we obtain $\lambda = -0.35$. By using the coefficient of QNCE in innovation in Table **3**, the long-tern effect of QNCE on illness caused death is $\Sigma\beta_{0(k=0\rightarrow\infty)} = \beta_0[1/(1-\lambda)] = -5863[1/(1-(-0.35))] = -4{,}342.96$. (The unit of value is number of persons).

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