# The impact of new drug launches on premature mortality, medical procedure utilization, and medical expenditure in Colombia, 2003-2015

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## Abstract

This study provides econometric evidence about the impact of new drug launches on premature mortality, medical procedure utilization, and medical expenditure in Colombia during the period 2003-2015. A "triple-differences" research design—an analysis of premature mortality from 39 diseases in 8 Latin American countries during the period 2003-2013—is used, enabling me to control for all determinants of mortality decline that were invariant across diseases within a country, and for all determinants that were invariant across countries within a disease.

Overall, the estimates are highly consistent with the hypothesis that the greater the relative number of drugs for a disease launched in a country, the greater the subsequent relative decline in premature mortality from that disease. The estimates are somewhat larger and more significant when a lower age threshold is used for measuring premature mortality; this suggests that pharmaceutical innovation reduced mortality more at lower ages than it did at higher ages. One estimate indicates that a 10% increase in the number of drugs ever launched resulted in a 3.9% reduction in the number of years of potential life lost before age 55 three years later. A specific analysis of cancer mortality indicates that the number of years of potential life lost from cancer before ages 65, 60, and 55 is inversely related to the number of drugs for treating cancer that had been launched 3-4 years earlier.

The estimates indicate that a decade of pharmaceutical innovation reduced the number of years of potential life lost before age 70 from all natural causes in 2013 by 142,318. Estimated expenditure on new drugs per life-year below age 70 gained from the drugs was $US 4734. According to the standards of the WHO's *Choosing Interventions that are Cost–Effective* project, new drugs launched in Colombia were very cost–effective overall, even if they hadn't reduced other medical costs or increased productivity.

But the evidence strongly suggests that new drugs launched in Colombia *did* reduce other medical costs and increase productivity. The growth in the number of medical procedures performed in Colombia was inversely correlated across diseases with the growth in the number of drugs that had ever been launched 2-3 years earlier. The estimates indicate that new drugs launched in Colombia during 2006-2012 reduced the number of medical procedures in 2015 by 13.9%. Also, a previous study based on U.S. data showed that about 25% of new drug cost is offset by reduced expenditure on old drugs, so the *net* increase in pharmaceutical expenditure per life-year before age 70 gained may have been $US 3550, and that pharmaceutical innovation resulted in substantial reductions in work-loss and school-loss days.

## I. Introduction

The life expectancy of residents of Colombia has been increasing. Between 1990 and 2015, life expectancy at birth increased by 5.9 years, from 68.3 years to 74.2 years. As shown in Figure 1, life expectancy increased even during a period of negative economic growth, 1997-1999.

Previous research based on other countries (e.g. Lichtenberg (2016, 2017)) has demonstrated that pharmaceutical innovation—the introduction and use of new drugs—has been an important source of longevity increase. In this study, I will attempt to measure the contribution that pharmaceutical innovation has made to longevity increase in Colombia during the period 2003-2013. In particular, I will estimate the number of life-years gained in 2013 from drugs previously launched in Colombia. I will also estimate expenditure on these drugs in 2013. By combining these two estimates, I can calculate the overall cost-effectiveness of (or cost per life-year gained from) pharmaceutical innovation in Colombia. I will also provide estimates of the effect that new drug launches had on utilization of medical procedures in Colombia.

This study will employ a "triple-differences," or difference-in-difference-in-differences, research design: I will estimate the impact that new drug launches had on premature mortality[1] from 39 diseases in 8 Latin American countries during the period 2003-2013.[2] This design enables me to control for all determinants of mortality decline that are invariant across diseases within a country, and for all determinants that are invariant across countries within a disease. Pischke (2005, p. 11) observed that "triple differences may allow for a more credible analysis" than a difference-in-differences ("double difference") analysis. Similarly, Berck and Villas-Boas (2015) argued that "the difference-in-difference model measures the effect of policy by removing the effects of time and place. When the outcome variable is determined by policy, time, place

[1] Premature mortality will be measured by the number of years of potential life lost (YPLL) before ages 70, 65, 60, and 55. YPLL is the number of years *not* lived by an individual who died before that age, e.g. a person who died at age 50 was deprived of 5 years of potential life before age 55 and 20 years of potential life before age 70. Previous authors have argued that "reducing premature mortality is a crucial public health objective" (Renard, Tafforeau, and Deboosere (2014)). Statistics of YPLL are published by the World Health Organization, the OECD, and government agencies of the U.S. and other countries. Burnet et al (2005) argue that YPLL "should be considered when allocating research funds."

[2] The 8 countries for which the necessary data are available are: Argentina, Brazil, Chile, Colombia, Ecuador, Mexico, Peru, and Venezuela.

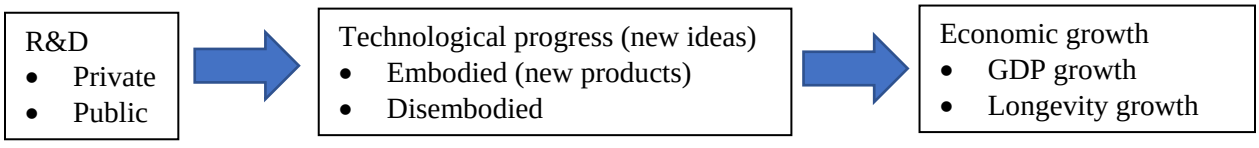
and yet another variable, a triple difference strategy may reduce the bias in the estimate of the effect of the policy change."

Figure 2 shows the number of new chemical entities (NCEs) launched in 8 Latin American countries during the period 1982-2015. Three of these countries had more drug launches than Colombia; one country (Chile) had approximately the same number, and three countries had significantly fewer. The triple-difference methodology is feasible because the *relative* number of drugs launched to treat different diseases has varied across countries. This variation is illustrated by Figure 3, which shows the difference between the number of NCEs launched in Colombia and Chile for 7 diseases during 1982-2013. Colombia had at least 2 more drug launches than Chile did for four diseases (e.g. prostate cancer), but at least 2 fewer drug launches for three other diseases (e.g. breast cancer). I hypothesize that Colombia's difference between the decline in mortality from the first 4 diseases and the decline in mortality from the latter 3 diseases should be larger than Chile's difference. Instead of performing the analysis using just these 14 observations (7 diseases * 2 countries), I will perform the analysis on about 312 observations (39 diseases * 8 countries).

In the next section, I will provide background and motivation for the econometric model of premature mortality, which is developed in Section III. Data sources are discussed in Section IV. Empirical results are presented in Section V. Implications of the results are discussed on Section VI. Section VII concludes.

## II. Background and motivation

Before describing the econometric model I will use to estimate the effect of new drug launches on premature mortality, I will provide some theoretical and empirical background and motivation for the model, which can be summarized by the following figure:




Starting on the right of this figure: longevity increase is a very important part of economic growth, broadly defined. Nordhaus (2005) argued that "improvements in health status have been a major contributor to economic welfare over the twentieth century. To a first

approximation, the economic value of increases in longevity in the last hundred years is about as large as the value of measured growth in non-health goods and services." Murphy and Topel (2006) estimated that cumulative gains in life expectancy after 1900 were worth over $1.2 million to the representative American in 2000, whereas post-1970 gains added about $3.2 trillion per year to national wealth, equal to about half of GDP. The United Nations' Human Development Index, which is used to rank countries into four tiers of human development, is a composite statistic of life expectancy, income per capita, and education (United Nations (2017)).

There is a consensus among macroeconomists that technological progress is the principal source of GDP growth. Romer (1990) argued that "growth…is driven by technological change that arises from intentional investment decisions made by profit-maximizing agents" (S71). Jones argued that "long-run growth is driven by the discovery of new ideas throughout the world."[3] And Chien (2015) said that "it has been shown, both theoretically and empirically, that technological progress is the main driver of long-run growth."

Since technological progress, or the discovery of new ideas, is the fundamental source of one of the major components—GDP growth—of "human development," or economic growth, broadly defined, it is quite plausible that the discovery of new ideas has also played a major role in longevity growth. Some previous authors have suggested that this is the case. Fuchs (2010) said that "since World War II…biomedical innovations (new drugs, devices, and procedures) have been the primary source of increases in longevity," although he did not provide evidence to support this claim. Cutler, Deaton and Lleras-Muney (2006) performed a survey of a large and diverse literature on the determinants of mortality, and "tentatively identif[ied] the application of scientific advance and technical progress (some of which is induced by income and facilitated by education) as the ultimate determinant of health." They concluded that "knowledge, science, and technology are the keys to any coherent explanation" of mortality.

In general, measuring the number of ideas is challenging. One potential measure is the number of patents, but Patterson (2012, p. 8) noted that only 1% of patent applications made by Bell Labs "generated [commercial] value." Fortunately, measuring pharmaceutical "ideas" is

[3] The discovery of new ideas could increase economic output for two different reasons. First, output could simply be positively related to the *quantity* (and variety) of ideas ever discovered. Second, output could be positively related to the (mean or maximum) *quality* of ideas ever discovered, and new ideas may be better (of higher quality), on average, than old ideas. As noted by Jovanovic and Yatsenko (2012), in "the Spence–Dixit–Stiglitz tradition…new goods [are] of higher quality than old goods."

considerably easier than measuring ideas in general. The measure of pharmaceutical ideas I will use is the number of new molecular entities used to treat a disease launched in a country. Since we have precise information about when those ideas reached the market and the diseases to which they apply, we can assess the impact of those ideas on longevity in a triple differences framework.

Technological change may be either disembodied or embodied. Suppose firm X invests in R&D, and that this investment results in a valuable discovery. If the technological advance is disembodied, consumers and other firms could benefit from the discovery without purchasing firm X's goods or services; they could benefit just by reading or hearing about the discovery. However, if the technological advance is embodied, consumers and other firms must purchase firm X's goods or services to benefit from its discovery. Solow (1960) argued that "many if not most innovations need to be embodied in new kinds of durable equipment before they can be made effective. Improvements in technology affect output only to the extent that they are carried into practice either by net capital formation or by the replacement of old-fashioned equipment by the latest models…"[4] Romer (1990) also assumed that technological progress is embodied in new goods: "new knowledge is translated into goods with practical value," and "a firm incurs fixed design or research and development costs when it creates a new good. It recovers those costs by selling the new good for a price that is higher than its constant cost of production." Grossman and Helpman (1993) argued that "innovative goods are better than older products simply because they provide more 'product services' in relation to their cost of production." Bresnahan and Gordon (1996) stated simply that "new goods are at the heart of economic progress," and Bils (2004) said that "much of economic growth occurs through growth in quality as new models of consumer goods replace older, sometimes inferior, models." Hercowitz (1998, p. 223) concluded that "'embodiment' is the main transmission mechanism of technological progress to economic growth."

Most scholars agree with Jones' (1998, pp. 89-90) statement that "technological progress is driven by research and development (R&D) in the advanced world." In 1997, the medical substances and devices sector was the most R&D-intensive[5] major industrial sector: almost twice

[4] We hypothesize that innovations may be embodied in nondurable goods (e.g. drugs) and services as well as in durable equipment.

[5] R&D intensity is the ratio of R&D to sales.

as R&D-intensive as the next-highest sector (information and electronics), and three times as R&D-intensive as the average for all major sectors. (National Science Foundation (2017)). In 2007, 89% of private biomedical research expenditure was funded by pharmaceutical and biotechnology firms; the remaining 11% was funded by medical device firms (Dorsey et al (2010)).

A U.S. government institute (the National Cancer Institute (NCI)) has also played an important role in cancer drug discovery and development.[6] Frequently, NCI's drug development efforts focus on unmet needs that are not being adequately addressed by the private sector. NCI's cancer drug discovery and development activities originated from a congressionally mandated initiative known as the Cancer Chemotherapy National Service Center (CCNSC), which, in 1955, established a national resource to facilitate the evaluation of potential anticancer agents. In 1976, the CCNSC's functions were incorporated into the Developmental Therapeutics Program (DTP) in NCI's Division of Cancer Treatment and Diagnosis (National Cancer Institute (2017)).

## III. Econometric models of premature mortality and medical procedure utilization

To investigate the impact that new drug launches had on the number of years of potential life lost before different ages, I will estimate the following triple-differences model:

$$\ln(YPLL_{ict}) = \beta_k \ln(CUM\_NCE_{ic,t-k}) + \alpha_{ic} + \delta_{it} + \pi_{ct} + \varepsilon_{ict} \quad (1)$$

where

$YPLL_{ict}$ = the number of years of potential life lost due to disease i in country c in year t (y = 2003, 2013)[7]

$CUM\_NCE_{ic,t-k} = \sum_m IND_{mi} LAUNCHED_{mc,t-k}$ = the number of post-1981 drugs (molecular entities) to treat disease i that had been launched in country c by the end of year t-k

$IND_{mi}$ = 1 if drug m is used to treat (indicated for) disease i
= 0 if drug m is not used to treat (indicated for) disease i

[6] Sampat and Lichtenberg (2011) showed that government funding has played an indirect role—for example, by funding basic underlying research that is built on in the drug discovery process—in almost half of the drugs approved and in almost two-thirds of priority-review drugs.

[7] The 8 countries included in the sample are those for which data on drug launches beginning in 1982 and mortality data were available.

$LAUNCHED_{mc,t-k}$ = 1 if drug m had been launched in country c by the end of year t-k
= 0 if drug m had not been launched in country c by the end of year t-k

$\alpha_{ic}$ = a fixed effect for disease i in country c

$\delta_{it}$ = a fixed effect for disease i in year t

$\pi_{ct}$ = a fixed effect for country c in year t

The model will be estimated using data on 39 major diseases comprising the disease classification used in the United Nations Statistics Division's database on Deaths by cause of death, age and sex. Mortality data for these diseases are shown in Appendix Table 1. These diseases accounted for 66% of YPLL before age 70 from natural causes in Colombia in 2013. Deaths from external causes (e.g. accidents, suicide, assault, and war), which accounted for 38% of YPLL before age 70 in Colombia in 2013, are excluded.

My data on drug launches are left-censored: I only have data on drugs launched after 1981. I therefore define $CUM\_NCE_{ic,t-k}$ as the number of *post-1981* new chemical entities (i.e. NCEs first launched anywhere in the world after 1981) used to treat disease i that had been launched in country c by the end of year t-k. Consequently, this measure is subject to error, because $CUM\_NCE_{ic,t-k}$ will not (but should) include pre-1982 NCEs that were first launched in country c after 1981. If this measurement error is random, it is likely to bias estimates of $\beta_k$ towards zero.

Eq. (1) includes a large number of parameters, mainly due to 312 (39 diseases * 8 countries) disease/country fixed effects ($\alpha_{ic}$'s). A (simpler) "difference-in-differences" model can be derived from the triple-difference model (eq. (1)). Setting t equal to 2003 and 2013 yields eqs. (2) and (3), respectively:

$$\ln(YPLL_{ic,2003}) = \beta_k \ln(CUM\_NCE_{ic,2003-k}) + \alpha_{ic} + \delta_{i,2003} + \pi_{c,2003} + \varepsilon_{ic,2003} \quad (2)$$

$$\ln(YPLL_{ic,2013}) = \beta_k \ln(CUM\_NCE_{ic,2013-k}) + \alpha_{ic} + \delta_{i,2013} + \pi_{c,2013} + \varepsilon_{ic,2013} \quad (3)$$

Subtracting (2) from (3) yields:

$$\Delta\ln(YPLL_{ic}) = \beta_k \Delta\ln(CUM\_NCE\_k_{ic}) + \delta'_i + \pi'_c + \varepsilon'_{ic} \quad (4)$$

where

$\Delta\ln(YPLL_{ic})$ = $\ln(YPLL_{ic,2013}) - \ln(YPLL_{ic,2003})$ = the log change from 2003 to 2013 in the number of years of potential life lost due to disease i in country c

$\Delta\ln(CUM\_NCE\_k_{ic})$ = $\ln(CUM\_NCE_{ic,2012-k}) - \ln(CUM\_NCE_{ic,2002-k})$ = the log change from 2003 - k to 2013 - k in the number of drugs for disease i that had ever been launched in country c

$\delta'_i$ = $\delta_{i,2013} - \delta_{i,2003}$ = the difference between the 2003 and 2013 fixed effects for disease i

$\pi'_c$ = $\pi_{c,2013} - \pi_{c,2003}$ = the difference between the 2003 and 2013 fixed effects for country c

I will analyze the effect of new drug launches on the number of years of potential life lost before four different ages: 70, 65, 60, and 55. Eq. (4) will be estimated by weighted least squares, weighting by the mean number of years of potential life lost due to disease i in country c. The disturbances of eq. (4) will be clustered within diseases.

Eq. (4) will be estimated for different values of k: k = 0, 1,…,5. A separate model is estimated for each value of k, rather than including multiple values ($CUM\_NCE_{i,t}$, $CUM\_NCE_{i,t-1}$, $CUM\_NCE_{i,t-2}$,…) in a single model because CUM_NCE is highly serially correlated (by construction), which would result in extremely high multicollinearity if multiple values were included. One would expect there to be a lag because new drugs diffuse gradually—they aren't used widely until years after launch.

The effect of a drug's launch on mortality is likely to depend on both the *quality* and the *quantity* of the drug. Indeed, it is likely to depend on the *interaction* between quality and quantity: a quality improvement will have a greater impact on mortality if drug utilization (quantity) is high. Although newer drugs tend to be of higher quality than older drugs (see Lichtenberg (2014)), the relative quantity of very new drugs is quite low, so I expect the impact on mortality of very new drugs to be lower than the impact of older drugs.

As noted earlier, I will also provide estimates of the effect that new drug launches had on utilization of medical procedures in Colombia. Data on the number of inpatient and outpatient procedures performed, by associated disease and year, are not available for countries other than Colombia, so these estimates will be based on the following difference-in-differences model, estimated from Colombia data only:

$$\ln(N\_PROC_{it}) = \beta_k \ln(CUM\_NCE_{i,t-k}) + \gamma \ln(N\_VISITS_{it}) + \alpha_i + \delta_t + \varepsilon_{it} \quad (5)$$

where

$N\_PROC_{it}$ = the number of inpatient and outpatient procedures associated with disease i performed in Colombia in year t (t = 2009, 2015)

$CUM\_NCE_{i,t-k}$ = the number of post-1981 drugs (molecular entities) to treat disease i that had been launched in Colombia by the end of year t-k

$N\_VISITS_{it}$ = the number of doctor visits associated with disease i in Colombia in year t

The variable $N\_VISITS_{it}$ may serve as a measure of disease prevalence. I will estimate eq. (5) both excluding and including $\ln(N\_VISITS_{it})$.

## IV. Data sources

*Mortality data.* Data on the number of years of potential life lost before ages 70, 65, 60, and 55, by disease (coded by ICD-10), country, and year, were constructed from data obtained from the WHO Mortality database. That source provides data on the number of deaths by 5-year age group, disease, country, and year. I assume that all deaths in an age group occur at the midpoint of the age group, e.g. deaths in age-group 65-69 occur at age 67.5.

*Population data.* Data on population by country, age group, and year (needed to compute premature mortality *rates*), were obtained from United Nations World Population Prospects 2017.

*Drug launch data.* Data on new chemical entity launches, by country and year (1982-2015), were obtained from the IMS Health *New Product Focus database* (now known as QuintilesIMS Ark New Product Intelligence).

*Drug indications data.* Data on drug indications (coded by ICD-10) were obtained from Theriaque, a database produced by the French Centre National Hospitalier d'Information sur le Médicament (2017).

*Drug expenditure data.* Data on drug expenditure in Colombia in 2013, by ATC code, were obtained from SISMED (Sistema de información de precios de medicamentos).

*Drug utilization data.* Annual data on the number of standard units of drugs sold, by molecule, country, and year (1999-2010) were obtained from the IMS Health MIDAS database.

*Medical procedure data.* Data on the number of inpatient and outpatient medical procedures performed in Columbia in 2009 and 2015, by associated disease, were obtained from SISPRO (Sistema Integral de Información de la Protección Social).

*Disease classification.* The disease classification used for the main analysis of premature mortality is the one used in the Tabulation list for ICD-9 and ICD-10 data for presentation in the United Nations Demographic Yearbook.[8] The disease classification used for the analysis of premature cancer mortality is the one used in the WHO Cancer Mortality Database. The disease classification used for the analysis of medical procedure utilization is the WHO ICD-10 block classification.

## V. Empirical results

*Premature mortality from all diseases.*

Estimates of $\beta_k$ parameters from eq. (4) based on data for all diseases are presented in Table 1 and plotted (on an inverted scale) in Figure 4. Each estimate is from a separate model. All models include disease fixed effects and country fixed effects. In rows 1-6, the dependent variable is the 2003-2013 log change in the number of years of potential life lost before age 70. In row 1, the lag (k) equals zero: the regressor is the 2003-2013 log change in the number of drugs ever launched. The estimate of $\beta_0$ is negative and significant (p-value = .049). The point estimate indicates that a 10% increase in the number of drugs ever launched resulted in a 2.5% contemporaneous reduction in the number of years of potential life lost before age 70. In lines 2-6, the lag length is 1, 2,…,5 years, respectively. Four of the six estimates are statistically significant (p-value < .05). The largest and most significant estimate (in row 4) corresponds to a lag of 3 years; the regressor in this model is the 2000-2010 log change in the number of drugs ever launched. The effect after 3 years is 18% larger than the contemporaneous effect.

In rows 7-12, the dependent variable is the 2003-2013 log change in the number of years of potential life lost before age 65. The YPLL65 estimates are fairly similar to the YPLL70 estimates, but the YPLL65 estimates are slightly (7-20%) larger than the YPLL70 estimates, and in this case 5 of the 6 estimates are statistically significant.

In rows 13-18, the dependent variable is the 2003-2013 log change in the number of years of potential life lost before age 60, and in rows 19-24, the dependent variable is the 2003-2013

[8] This disease classification is also used in the United Nations Statistics Division's Deaths by cause of death, age and sex website.

log change in the number of years of potential life lost before age 55. Ten of the twelve estimates are statistically significant. The largest estimates again correspond to a 3-year lag. The estimate in row 22 indicates that a 10% increase in the number of drugs ever launched resulted in a 3.9% reduction in the number of years of potential life lost before age 55 three years later.

Overall, the estimates are highly consistent with the hypothesis that the greater the relative number of drugs for a disease launched in a country, the greater the subsequent relative decline in premature mortality from that disease. The fact that the estimates tend to be somewhat larger and more significant when a lower age threshold is used for measuring premature mortality suggests that pharmaceutical innovation reduced mortality more at lower ages than it did at higher ages.

*Premature cancer mortality.*

Estimates of $\beta_k$ parameters from eq. (4) based on data for 26 cancer sites are presented in Table 2 and plotted (on an inverted scale) in Figure 5. When premature mortality is measured before age 70 (rows 25-30 of Table 2), none of the estimates are statistically significant. However, when premature mortality is measured before ages 65, 60, and 55, the estimates of $\beta_3$ and $\beta_4$ are negative and significant. This indicates that the number of years of potential life lost from cancer before these ages is inversely related to the number of drugs for treating cancer that had been launched 3-4 years earlier.

*Medical procedure utilization.*

Estimates of $\beta_k$ parameters from the model of medical procedure utilization in Colombia (eq. (5)) are presented in Table 3. The left side of the table shows estimates of $\beta_k$ parameters when $\ln(N\_VISITS_{it})$ is excluded from the model. The estimates of $\beta_2$ and $\beta_3$ are negative and statistically significant when $\ln(N\_VISITS_{it})$ is excluded from the model. This indicates that the growth in the number of medical procedures performed in Colombia is inversely correlated across diseases with the growth in the number of drugs that had ever been launched 2-3 years earlier. A 10% increase in the number of drugs ever launched is associated with a 9% reduction

in the number of medical procedures performed 2-3 years later. Figure 6 shows the mean 2009-2015 increase in the number of procedures performed, by extent of pharmaceutical innovation during 2006-2012. Diseases with high rates of pharmaceutical innovation (those with a mean 2006-2012 CUM_NCE increase of 37%) had smaller 2009-2015 increases in the number of procedures performed than diseases with low rates of pharmaceutical innovation (those with a mean 2006-2012 CUM_NCE increase of 0%).

The right side of the table shows estimates of $\beta_k$ parameters when $\ln(N\_VISITS_{it})$ is included in the model.[9] All of the estimates are negative and highly significant when $k \geq 1$.

I also estimated models similar to eq. (5) (but excluding $\ln(N\_VISITS_{it})$ as a regressor), with three alternative dependent variables: the number of hospital discharges, the number of emergency department visits, and the number of physician visits (i.e. $\ln(N\_VISITS_{it})$ as a dependent rather than an independent variable). Estimates of $\beta_k$ parameters from these models were generally insignificant. The only significant estimates were $\beta_0$ in the model of emergency department visits ($\beta_0 = -1.77$; Z= -1.98; p-value = .0477), and $\beta_5$ in the model of physician visits ($\beta_5 = 0.58$; Z= 2.54; p-value = .011). The latter finding may indicate that the launch of new drugs increases the number of physician visits 5 or more years later because these visits are required to obtain prescriptions.

## VI. Discussion

Now I will use the estimates of the $\beta_k$ parameters from eq. (4) presented in Table 1 to estimate the number of life-years gained in 2013 from drugs previously launched in Colombia. Then I will estimate expenditure on these drugs in 2013, and combine these two estimates to calculate the overall cost-effectiveness of (or cost per life-year gained from) pharmaceutical innovation in Colombia.

Table 4 shows the calculation of the 2003-2013 log change in YPLL attributable to new drug launches. Rows 55-60 show the calculation for YPLL before age 70. Column 1 shows the lag length, k (k = 0, 1,…,5). Column 2 shows the estimates of $\beta_k$ from Table 1. Column 3

[9] Estimates of $\gamma$ (the coefficient on $\ln(N\_VISITS_{it})$) are positive and highly significant. For example, when k = 3, the estimate of $\gamma$ is 1.22 (std. err. = 0.193; Z = 6.31; p-value < .0001).

shows the weighted mean value of Δln(CUM_NCE_k) for Colombia, weighted by average YPLL in Colombia.[10] Column 4 shows the product of column 2 and column 3, which is the estimated 2003-2013 log change in YPLL attributable to the increase in the number of drugs ever launched k years earlier. Column 5 shows the average of the estimates in column 4; column 6 shows the maximum of the estimates in column 4. The average estimate indicates that new drug launches reduced YPLL70 by 8.0% (= exp(-.083) – 1) during the period 2003-2013; the maximum estimate (based on a 3-year lag) indicates that new drug launches reduced YPLL70 by 10.6%, i.e. at an average annual rate of 1.06%. Column 7 shows the actual 2003-2013 log change in YPLL per 100,000 population.[11] YPLL70 declined by 26% during this period. The average of the estimated declines attributable to new drug launches (column 5) implies that pharmaceutical innovation accounted for 27% (= -.083 / -0.307) of the decline in YPLL70; the maximum of the estimated declines (column 6) implies that pharmaceutical innovation accounted for 36% (= -.112 / -.307) of the decline in YPLL70.

Rows 62-78 of Table 4 shows similar calculations for YPLL before ages 65, 60, and 55. The results are slightly larger, but qualitatively similar. In the case of YPLL55, the average estimate in column 5 implies that new drug launches reduced premature mortality by 9.8% (26% of the observed decline), and the maximum estimate in column 6 implies that new drug launches reduced premature mortality by 12.5% (33% of the observed decline).

Let $YPLL_{actual}$ represent actual YPLL in 2013; $YPLL_{no\_innov}$ represent predicted YPLL in 2013 in the absence of a decade of innovation; and r represent the percentage reduction in YPLL due to pharmaceutical innovation. Then $YPLL_{no\_innov} = YPLL_{actual} / (1 – r)$, and the absolute reduction in YPLL due to pharmaceutical innovation is

$$YPLL_{no\_innov} - YPLL_{actual} = YPLL_{actual} * (r / (1 – r)) \quad (6)$$

As shown above, the average estimate indicates that new drug launches reduced YPLL70 by 8.0% during the period 2003-2013. In the absence of a decade of pharmaceutical innovation, YPLL70 would have been 8.7% (= 1 / (1 - .08)) higher in 2013 than it actually was. Actual YPLL70 from all natural causes in 2013 was 1.64 million.[12] This implies that a decade of

[10] The weighted mean 2003-2013 increase in the number of drugs ever launched was 33% (= exp(.285) – 1); the weighted mean 1998-2008 increase in the number of drugs ever launched was 74% (= exp(.554) – 1).
[11] Since eq. (4) includes country fixed effects, it controls for the country's population growth.
[12] I will assume that pharmaceutical innovation had no effect on premature mortality from external causes. This assumption is likely to make my estimates conservative.

pharmaceutical innovation reduced YPLL70 from all natural causes in 2013 by 142,318 (= 1.64 million * (.08 / (1 - .08))).

To estimate expenditure in 2013 on new drugs (e.g. drugs launched during 2004-2013) by people below age 70 (NEW_DRUG_EXPEND_AGE<70), I will use the following formula:

$$NEW\_DRUG\_EXPEND\_AGE<70 = AGGREGATE\_DRUG\_EXPEND * NEW\_DRUG\_EXPEND\_\% * DRUG\_EXPEND\_AGE<70\_\% \quad (7)$$

where

AGGREGATE_DRUG_EXPEND = aggregate prescription drug expenditure in Colombia in 2013

NEW_DRUG_EXPEND_% = the fraction of drug expenditure that was on new drugs (e.g. drugs launched during 2004-2013)

DRUG_EXPEND_AGE<70_% = the fraction of drug expenditure that was for people below age 70

According to two sources (Manufacturing Chemist.com (2014), Ribbink K (2014)), aggregate prescription drug expenditure in Colombia in 2013 was $US 4.35 billion. Data from SISMED (*Sistema de información de precios de medicamentos*) indicate that the fraction of 2013 expenditure on new drugs was 17%.[13] This is quite consistent with data from the IMS Health MIDAS database, which indicates that 16% of 2010 retail drug expenditure ($US 1.81 billion) in Colombia was on products containing molecules that had zero sales in 1999.[14] Data on drug expenditure by age group for Colombia are not available, but data for the U.S. indicate that, in the U.S., people 70 years of age and older accounted for 10% of the population and 22% of

[13]

| period | % of 2013 drug expend that was on drugs launched during period |
|---|---|
| 1999-2008 | 22% |
| 2000-2009 | 21% |
| 2001-2010 | 18% |
| 2002-2011 | 14% |
| 2003-2012 | 14% |
| 2004-2013 | 11% |
| average | 17% |

[14] More recent IMS data are not available.

outpatient drug expenditure, i.e. that their share of outpatient drug expenditure was 2.2 times their population share.[15] In Colombia in 2013, people 70 years of age and older accounted for 4.04% of the population, so I will assume that they accounted for 8.9% (= 2.2 * 4.04%) of drug expenditure. Hence, I estimate that people below age 70 accounted for 91.1% of drug expenditure.

Substituting these estimates into eq. (7) implies that expenditure in 2013 on new drugs by people below age 70 was $US 674 million (= 4.35 billion USD * 17% * 91%). Combining this estimate with my estimate of the reduction in YPLL70 from all natural causes in 2013 from previous new drug launches (142,318), the estimated expenditure on new drugs per life-year below age 70 gained from the drugs was $US 4734 (= $US 674 million / 142,318 life-years).

As noted by Bertram et al (2016), authors writing on behalf of the WHO's *Choosing Interventions that are Cost–Effective* project (WHO-CHOICE) suggested in 2005 that "interventions that avert one DALY [disability-adjusted life-year] for less than average per capita income for a given country or region are considered very cost–effective; interventions that cost less than three times average per capita income per DALY averted are still considered cost–effective."[16] Per capita income in Colombia in 2013 was $US 8031, so my estimates indicate that the new drugs launched there were very cost–effective overall, even if they did not reduce other medical costs or increase productivity.

But the evidence strongly suggests that new drugs launched in Colombia *did* reduce other medical costs and increase productivity. The estimates in Table 4 indicated that the growth in the number of medical procedures performed in Colombia is inversely correlated across diseases with the growth in the number of drugs that had ever been launched 2-3 years earlier. The estimate in row 52 of Table 4 implies that new drugs launched during 2006-2012 reduced the number of medical procedures in 2015 by 13.9%.[17] Also, Lichtenberg (2014) showed that in the U.S., new drugs tend to "crowd out" old drugs, and that about 25% of new drug cost is offset by reduced expenditure on old drugs. If that also applies to Colombia, the *net* increase in

[15] The share of the elderly in total (outpatient + provider-administered) drug expenditure may be higher than their share in outpatient drug expenditure alone. A substantial fraction of provider-administered drug expenditure is on cancer chemotherapy, and cancer is predominantly a disease of the elderly.

[16] Lichtenberg (2009) showed that the number of DALYs gained could be either less than or greater than the number of life-years gained.

[17] Since I don't have a reliable estimate of the total cost of all medical procedures performed in Colombia in 2015, I am unable to calculate the (absolute) reduction in medical procedure cost attributable to 2006-2012 drug launches.

pharmaceutical expenditure per life-year before age 70 gained was $US 3550 (= 75% * $US 4734). Lichtenberg (2014) also showed that, in the U.S., pharmaceutical innovation resulted in substantial reductions in work-loss and school-loss days.

## VII. Summary and conclusions

This study has provided econometric evidence about the impact of new drug launches on premature mortality, medical procedure utilization, and medical expenditure in Colombia during the period 2003-2015. A "triple-differences" research design—an analysis of premature mortality from 39 diseases in 8 Latin American countries during the period 2003-2013—was used, enabling me to control for all determinants of mortality decline that were invariant across diseases within a country, and for all determinants that were invariant across countries within a disease.

Overall, the estimates were highly consistent with the hypothesis that the greater the relative number of drugs for a disease launched in a country, the greater the subsequent relative decline in premature mortality from that disease. The estimates were somewhat larger and more significant when a lower age threshold was used for measuring premature mortality; this suggests that pharmaceutical innovation reduced mortality more at lower ages than it did at higher ages. One estimate indicated that a 10% increase in the number of drugs ever launched resulted in a 3.9% reduction in the number of years of potential life lost before age 55 three years later. A specific analysis of cancer mortality indicated that the number of years of potential life lost from cancer before ages 65, 60, and 55 is inversely related to the number of drugs for treating cancer that had been launched 3-4 years earlier.

The estimates indicated that a decade of pharmaceutical innovation reduced the number of years of potential life lost before age 70 from all natural causes in 2013 by 142,318. Estimated expenditure on new drugs per life-year below age 70 gained from the drugs was $US 4734. According to the standards of the WHO's *Choosing Interventions that are Cost–Effective* project, new drugs launched in Colombia were very cost–effective overall, even if they hadn't reduced other medical costs or increased productivity.

But the evidence strongly suggested that new drugs launched in Colombia *did* reduce other medical costs and increase productivity. The growth in the number of medical procedures

performed in Colombia was inversely correlated across diseases with the growth in the number of drugs that had ever been launched 2-3 years earlier. The estimates indicated that new drugs launched in Colombia during 2006-2012 reduced the number of medical procedures in 2015 by 13.9%. Also, a previous study based on U.S. data showed that about 25% of new drug cost is offset by reduced expenditure on old drugs, so the *net* increase in pharmaceutical expenditure per life-year before age 70 gained may have been $US 3550, and that pharmaceutical innovation resulted in substantial reductions in work-loss and school-loss days.

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Figure 1
Life expectancy and GDP per capita in Colombia, 1990-2015

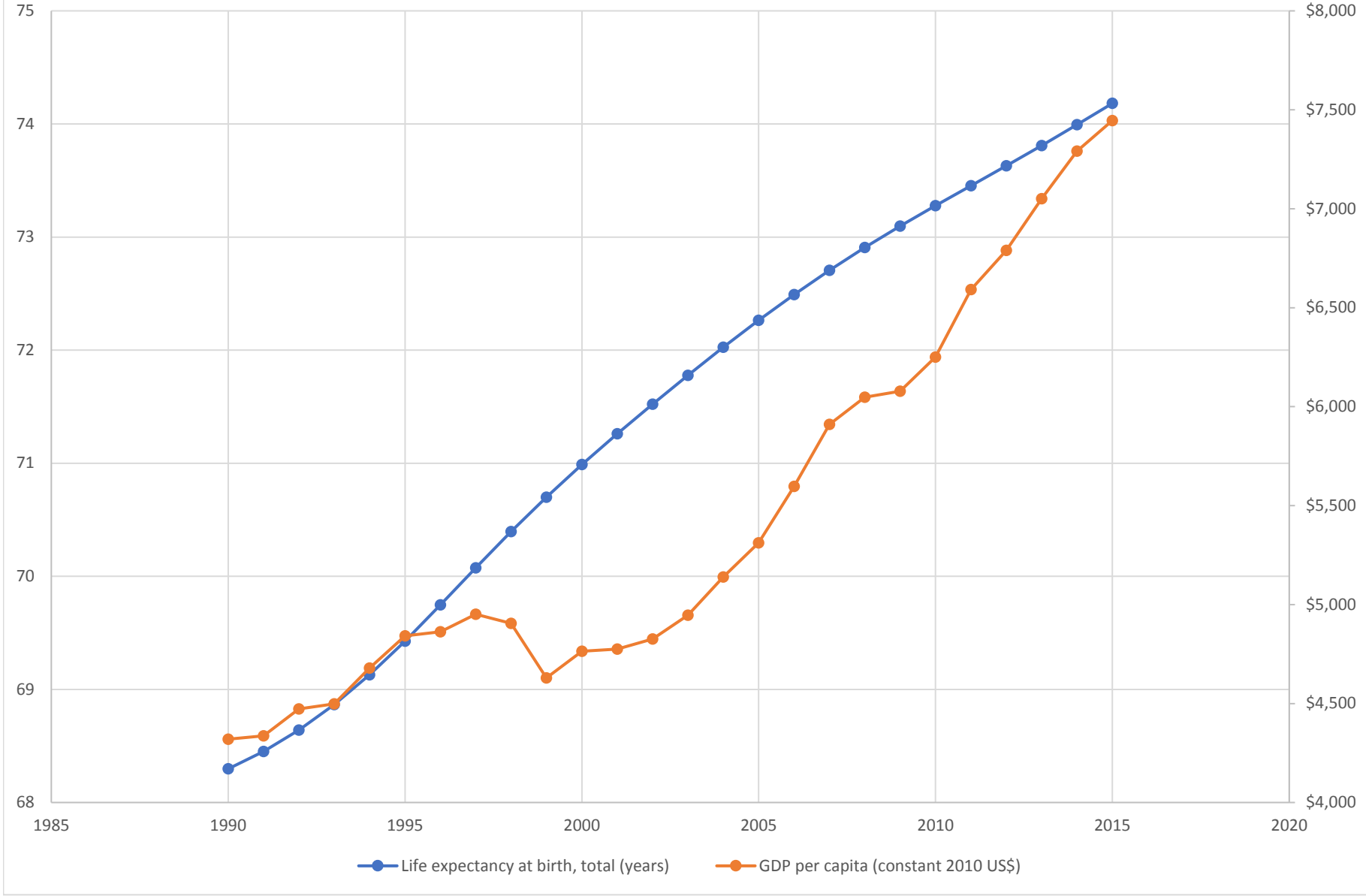
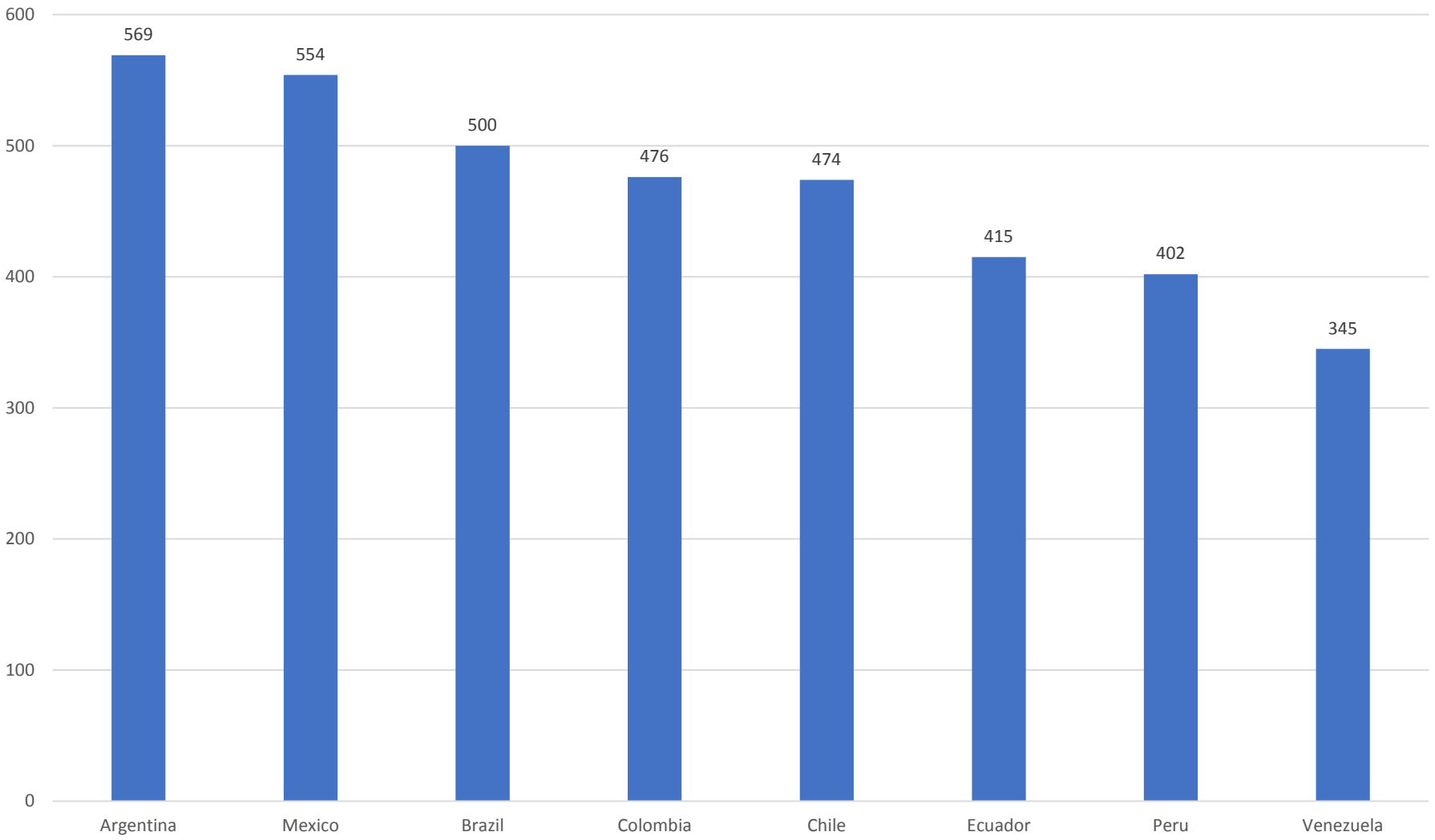
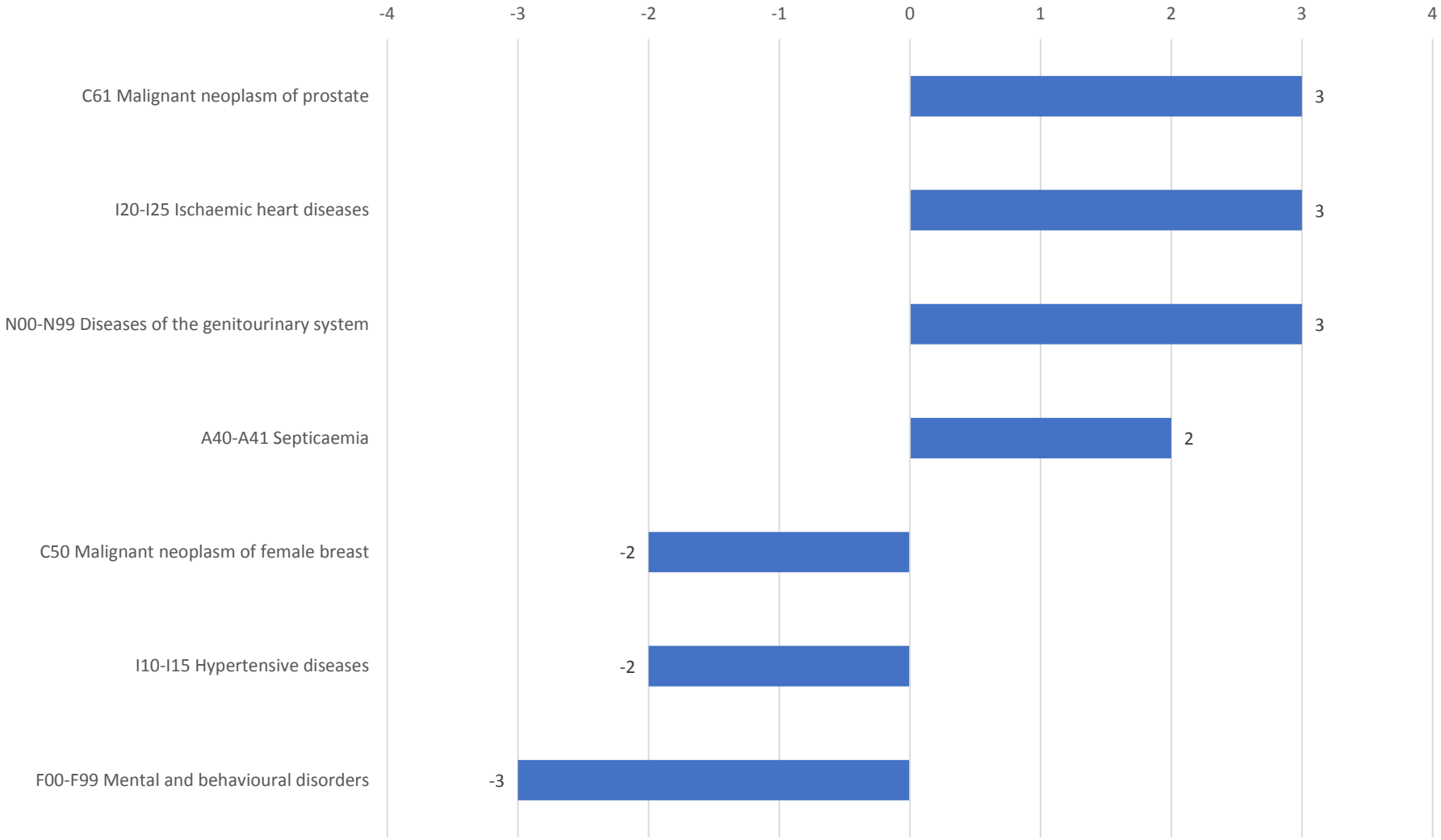


Figure 2
New Chemical Entities launched, 1982-2015




Source: Author's calculations based on IMS Health *New Product Focus* database.
Note: 2015 data are incomplete.

Figure 3
Difference between the number of New Chemical Entities launched in Colombia and Chile for 7 diseases, 1982-2013

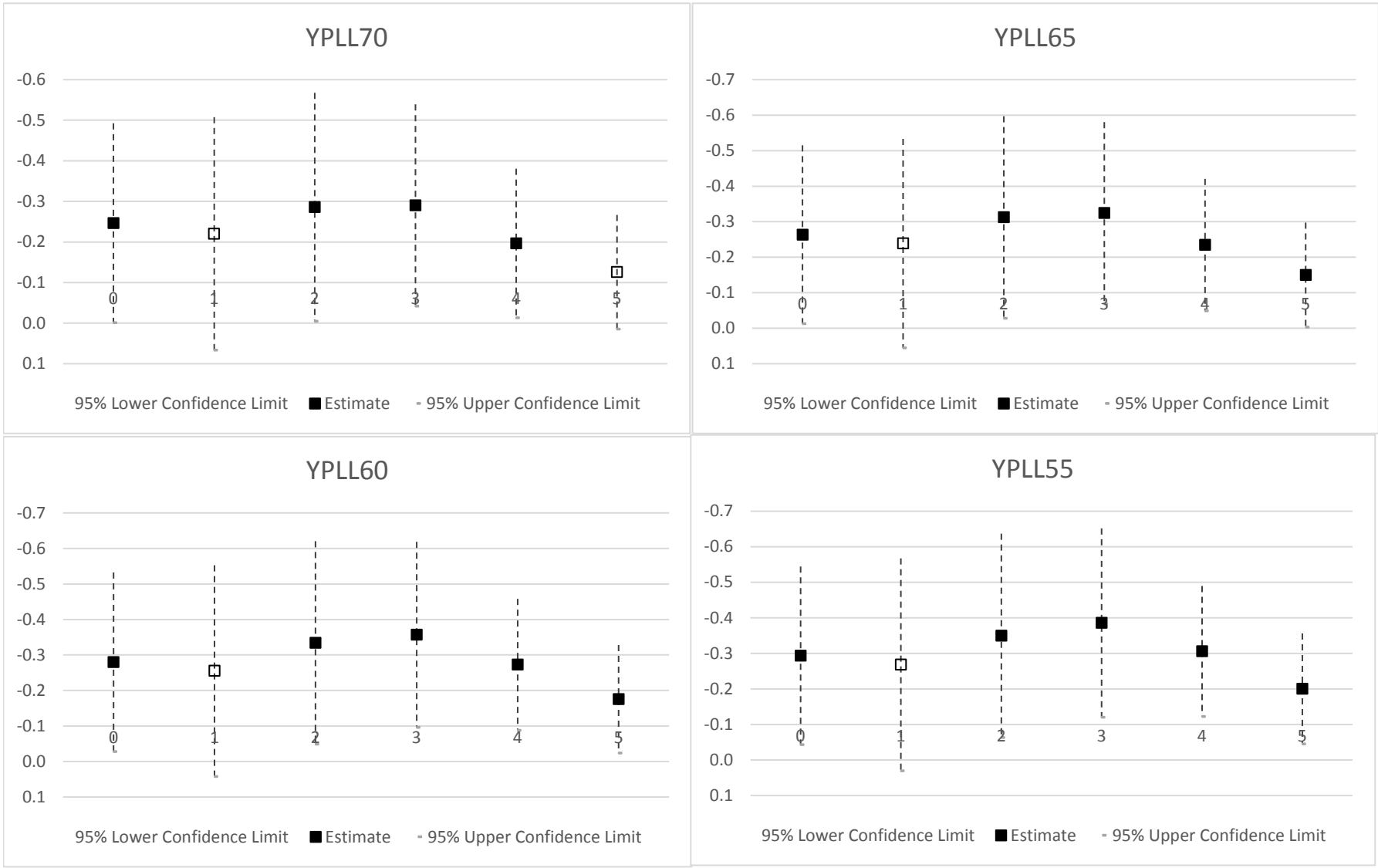



Source: Author's calculations based on IMS Health *New Product Focus* database and Theriaque database.

Figure 4

Estimates of $\beta_k$ parameters from eq. (4), $\Delta\ln(YPLL_{ic}) = \beta_k \Delta\ln(CUM\_NCE\_k_{ic}) + \delta'_i + \pi'_c + \varepsilon'_{ic}$

**Estimates based on data for all diseases**

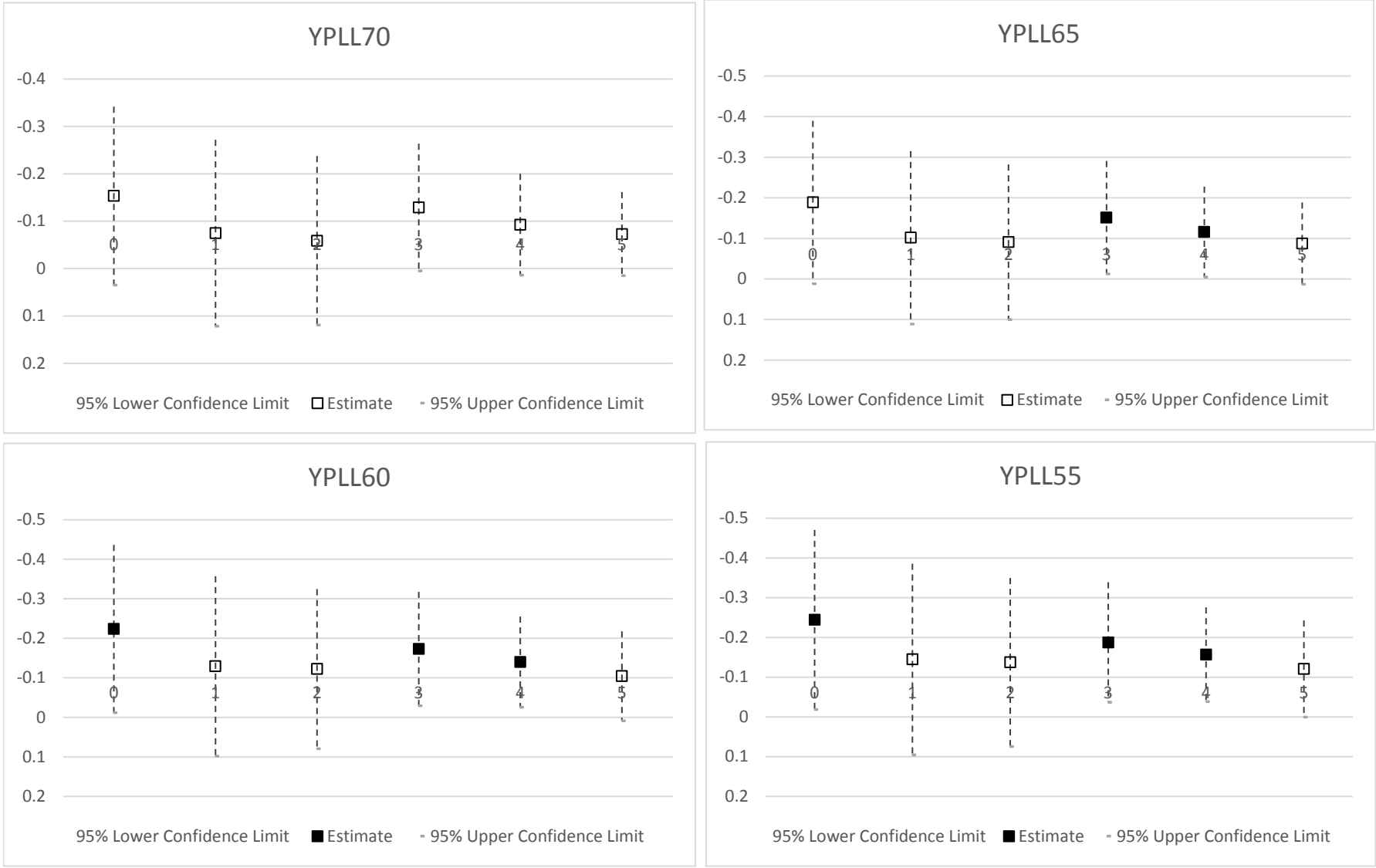



Note: solid squares represent significant (p-value < .05) estimates; hollow squares represent insignificant estimates.

**Figure 5**

Estimates of $\beta_k$ parameters from eq. (4), $\Delta\ln(YPLL_{ic}) = \beta_k \Delta\ln(CUM\_NCE\_k_{ic}) + \delta'_i + \pi'_c + \varepsilon'_{ic}$

**Estimates based on data on 26 cancer sites**




Note: solid squares represent significant (p-value < .05) estimates; hollow squares represent insignificant estimates.

Figure 6
Mean 2009-2015 increase in number of procedures performed,
by extent of pharmaceutical innovation during 2006-2012

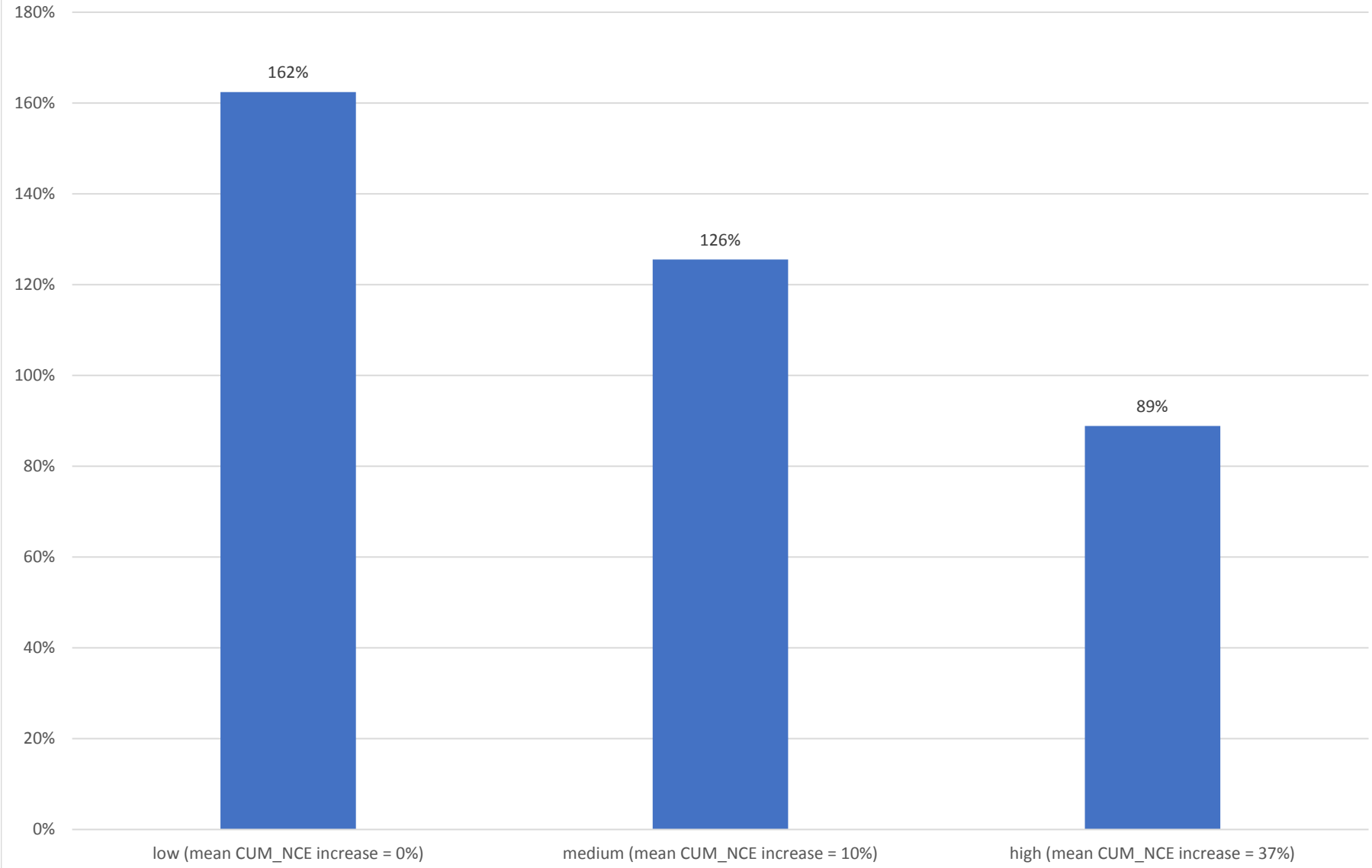


**Table 1: Estimates based on data on all diseases**

Estimates of $\beta_k$ parameters from eq. (4), $\Delta\ln(YPLL_{ic}) = \beta_k \Delta\ln(CUM\_NCE\_k_{ic}) + \delta'_i + \pi'_c + \varepsilon'_{ic}$

| Row | Parameter | Estimate | Std. Error | Z | Pr > \|Z\| |
|---|---|---|---|---|---|
| | | **YPLL before age 70** | | | |
| 1 | $\beta_0$ | **-0.247** | **0.126** | **-1.97** | **0.0494** |
| 2 | $\beta_1$ | -0.220 | 0.147 | -1.50 | 0.1326 |
| 3 | $\beta_2$ | **-0.286** | **0.144** | **-1.99** | **0.0465** |
| 4 | $\beta_3$ | **-0.291** | **0.127** | **-2.29** | **0.0221** |
| 5 | $\beta_4$ | **-0.197** | **0.094** | **-2.10** | **0.0358** |
| 6 | $\beta_5$ | -0.126 | 0.072 | -1.75 | 0.0796 |
| | | | | | |
| | | **YPLL before age 65** | | | |
| 7 | $\beta_0$ | **-0.264** | **0.128** | **-2.06** | **0.0397** |
| 8 | $\beta_1$ | -0.239 | 0.150 | -1.59 | 0.1117 |
| 9 | $\beta_2$ | **-0.313** | **0.145** | **-2.15** | **0.0313** |
| 10 | $\beta_3$ | **-0.324** | **0.131** | **-2.48** | **0.0130** |
| 11 | $\beta_4$ | **-0.235** | **0.095** | **-2.47** | **0.0134** |
| 12 | $\beta_5$ | **-0.150** | **0.075** | **-2.00** | **0.0457** |
| | | | | | |
| | | **YPLL before age 60** | | | |
| 13 | $\beta_0$ | **-0.280** | **0.129** | **-2.17** | **0.0297** |
| 14 | $\beta_1$ | -0.255 | 0.152 | -1.68 | 0.0927 |
| 15 | $\beta_2$ | **-0.334** | **0.146** | **-2.29** | **0.0220** |
| 16 | $\beta_3$ | **-0.357** | **0.133** | **-2.68** | **0.0074** |
| 17 | $\beta_4$ | **-0.273** | **0.095** | **-2.89** | **0.0039** |
| 18 | $\beta_5$ | **-0.176** | **0.078** | **-2.27** | **0.0234** |
| | | | | | |
| | | **YPLL before age 55** | | | |
| 19 | $\beta_0$ | **-0.294** | **0.128** | **-2.29** | **0.0218** |
| 20 | $\beta_1$ | -0.268 | 0.153 | -1.76 | 0.0788 |
| 21 | $\beta_2$ | **-0.350** | **0.146** | **-2.39** | **0.0169** |
| 22 | $\beta_3$ | **-0.386** | **0.136** | **-2.84** | **0.0045** |
| 23 | $\beta_4$ | **-0.306** | **0.094** | **-3.26** | **0.0011** |
| 24 | $\beta_5$ | **-0.201** | **0.080** | **-2.53** | **0.0116** |

Note: Each estimate is from a separate model. Models were estimated by weighted least squares, weighting by the mean number of years of potential life lost due to disease i in country c. The disturbances were clustered within diseases. Estimates in bold are statistically significant (p-value < .05.)

**Table 2: Estimates based on data on 26 cancer sites**

Estimates of $\beta_k$ parameters from eq. (4), $\Delta\ln(YPLL_{ic}) = \beta_k \Delta\ln(CUM\_NCE\_k_{ic}) + \delta'_i + \pi'_c + \varepsilon'_{ic}$

| Row | Parameter | Estimate | Std. Error | Z | Pr > \|Z\| |
|---|---|---|---|---|---|
| | | **YPLL before age 70** | | | |
| 25 | $\beta_0$ | -0.153 | 0.096 | -1.60 | 0.1103 |
| 26 | $\beta_1$ | -0.075 | 0.100 | -0.75 | 0.4555 |
| 27 | $\beta_2$ | -0.059 | 0.091 | -0.65 | 0.5168 |
| 28 | $\beta_3$ | -0.129 | 0.069 | -1.89 | 0.0594 |
| 29 | $\beta_4$ | -0.093 | 0.055 | -1.70 | 0.0896 |
| 30 | $\beta_5$ | -0.073 | 0.045 | -1.62 | 0.1053 |
| | | | | | |
| | | **YPLL before age 65** | | | |
| 31 | $\beta_0$ | -0.189 | 0.103 | -1.84 | 0.0652 |
| 32 | $\beta_1$ | -0.102 | 0.109 | -0.94 | 0.3487 |
| 33 | $\beta_2$ | -0.091 | 0.098 | -0.93 | 0.3509 |
| 34 | $\beta_3$ | **-0.151** | **0.071** | **-2.13** | **0.0333** |
| 35 | $\beta_4$ | **-0.116** | **0.057** | **-2.04** | **0.0417** |
| 36 | $\beta_5$ | -0.088 | 0.052 | -1.70 | 0.0899 |
| | | | | | |
| | | **YPLL before age 60** | | | |
| 37 | $\beta_0$ | **-0.224** | **0.109** | **-2.06** | **0.0390** |
| 38 | $\beta_1$ | -0.130 | 0.116 | -1.11 | 0.2649 |
| 39 | $\beta_2$ | -0.122 | 0.103 | -1.19 | 0.2348 |
| 40 | $\beta_3$ | **-0.173** | **0.074** | **-2.36** | **0.0185** |
| 41 | $\beta_4$ | **-0.140** | **0.059** | **-2.39** | **0.0169** |
| 42 | $\beta_5$ | -0.104 | 0.058 | -1.80 | 0.0716 |
| | | | | | |
| | | **YPLL before age 55** | | | |
| 43 | $\beta_0$ | **-0.245** | **0.115** | **-2.12** | **0.0337** |
| 44 | $\beta_1$ | -0.145 | 0.123 | -1.18 | 0.2370 |
| 45 | $\beta_2$ | -0.137 | 0.108 | -1.27 | 0.2047 |
| 46 | $\beta_3$ | **-0.188** | **0.077** | **-2.43** | **0.0150** |
| 47 | $\beta_4$ | **-0.157** | **0.061** | **-2.60** | **0.0094** |
| 48 | $\beta_5$ | -0.121 | 0.062 | -1.95 | 0.0516 |

Note: Each estimate is from a separate model. Models were estimated by weighted least squares, weighting by the mean number of years of potential life lost due to disease i in country c. The disturbances were clustered within diseases. Estimates in bold are statistically significant (p-value < .05.)

## Table 3

Estimates of $\beta_k$ parameters from model of medical procedure utilization (eq. (5)),

$$\ln(N\_PROC_{it}) = \beta_k \ln(CUM\_NCE_{i,t-k}) + \gamma \ln(N\_VISITS_{it}) + \alpha_i + \delta_t + \varepsilon_{it}$$

| Row | Parameter | Estimate | Std. Error | Z | Pr > \|Z\| | | Estimate | Std. Error | Z | Pr > \|Z\| |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **ln(N_VISITS$_{it}$)** excluded | | | | | **ln(N_VISITS$_{it}$)** included | | | |
| 49 | $\beta_0$ | -1.414 | 1.068 | -1.32 | 0.1857 | | -0.883 | 0.848 | -1.04 | 0.2977 |
| 50 | $\beta_1$ | -0.716 | 0.459 | -1.56 | 0.1189 | | **-0.864** | **0.308** | **-2.81** | **0.0050** |
| 51 | $\beta_2$ | **-0.916** | **0.447** | **-2.05** | **0.0403** | | **-1.065** | **0.275** | **-3.87** | **0.0001** |
| 52 | $\beta_3$ | **-0.929** | **0.414** | **-2.25** | **0.0247** | | **-1.239** | **0.286** | **-4.34** | **<.0001** |
| 53 | $\beta_4$ | -0.598 | 0.360 | -1.66 | 0.0967 | | **-0.989** | **0.315** | **-3.14** | **0.0017** |
| 54 | $\beta_5$ | -0.414 | 0.329 | -1.26 | 0.2094 | | **-1.020** | **0.354** | **-2.88** | **0.0040** |

Note: Each estimate is from a separate model. Models were estimated by weighted least squares, weighting by the mean number of medical procedures associated with disease i in Colombia. The disturbances were clustered within diseases. Estimates in bold are statistically significant (p-value < .05.)

Table 4

Calculation of 2003-2013 log change in YPLL attributable to new drug launches

| Col. | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Row | k | $\beta_k$ | mean(Δln(CUM_NCE_k)) | $\beta_k$* mean(Δln(CUM_NCE_k)) | average | maximum | Δln(YPLL/ POP) |
| | | **YPLL before age 70** | | | | | |
| 55 | 0 | -0.247 | 0.285 | -0.070 | -0.083 | -0.112 | -0.307 |
| 56 | 1 | -0.220 | 0.287 | -0.063 | | | |
| 57 | 2 | -0.286 | 0.305 | -0.087 | | | |
| 58 | 3 | -0.291 | 0.384 | -0.112 | | | |
| 59 | 4 | -0.197 | 0.492 | -0.097 | | | |
| 60 | 5 | -0.126 | 0.554 | -0.070 | | | |
| | | | | | | | |
| | | **YPLL before age 65** | | | | | |
| 61 | 0 | -0.264 | 0.280 | -0.074 | -0.091 | -0.121 | -0.342 |
| 62 | 1 | -0.239 | 0.282 | -0.067 | | | |
| 63 | 2 | -0.313 | 0.301 | -0.094 | | | |
| 64 | 3 | -0.324 | 0.373 | -0.121 | | | |
| 65 | 4 | -0.235 | 0.476 | -0.112 | | | |
| 66 | 5 | -0.150 | 0.533 | -0.080 | | | |
| | | | | | | | |
| | | **YPLL before age 60** | | | | | |
| 67 | 0 | -0.280 | 0.275 | -0.077 | -0.098 | -0.129 | -0.374 |
| 68 | 1 | -0.255 | 0.277 | -0.071 | | | |
| 69 | 2 | -0.334 | 0.296 | -0.099 | | | |
| 70 | 3 | -0.357 | 0.360 | -0.129 | | | |
| 71 | 4 | -0.273 | 0.457 | -0.125 | | | |
| 72 | 5 | -0.176 | 0.510 | -0.090 | | | |
| | | | | | | | |
| | | **YPLL before age 55** | | | | | |
| 73 | 0 | -0.294 | 0.270 | -0.079 | -0.103 | -0.133 | -0.399 |
| 74 | 1 | -0.268 | 0.271 | -0.073 | | | |
| 75 | 2 | -0.350 | 0.290 | -0.101 | | | |
| 76 | 3 | -0.386 | 0.346 | -0.133 | | | |
| 77 | 4 | -0.306 | 0.436 | -0.133 | | | |
| 78 | 5 | -0.201 | 0.484 | -0.097 | | | |

Appendix Table 1

Number of deaths and years of potential life lost before ages 55, 60, 65, and 70, by disease, Colombia, 2003 and 2013

| **Disease** | **Deaths** | | **YPLL55** | | **YPLL60** | | **YPLL65** | | **YPLL70** | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Year** | **2003** | **2013** | **2003** | **2013** | **2003** | **2013** | **2003** | **2013** | **2003** | **2013** |
| A00-A09 Intestinal infectious diseases | 1,520 | 573 | 52,379 | 9,672 | 57,672 | 10,835 | 63,112 | 12,095 | 68,737 | 13,460 |
| A15-A19 Tuberculosis | 1,201 | 896 | 9,529 | 6,274 | 12,392 | 8,204 | 15,692 | 10,512 | 19,494 | 13,209 |
| A33-A35 Tetanus | 29 | 14 | 387 | 55 | 457 | 78 | 534 | 110 | 614 | 153 |
| A36 Diphtheria | 3 | | 150 | | 165 | | 180 | | 195 | |
| A37 Whooping cough | 9 | 30 | 490 | 1,634 | 535 | 1,784 | 580 | 1,934 | 625 | 2,084 |
| A39 Meningococcal infection | 23 | 14 | 707 | 507 | 804 | 570 | 907 | 635 | 1,012 | 700 |
| A40-A41 Septicaemia | 1,089 | 1,202 | 15,924 | 9,407 | 18,241 | 11,165 | 20,811 | 13,282 | 23,716 | 15,795 |
| A80 Acute poliomyelitis | 3 | | 127 | | 142 | | 157 | | 172 | |
| B15-B19 Viral hepatitis | 60 | 122 | 518 | 550 | 670 | 758 | 853 | 1,048 | 1,065 | 1,405 |
| B20-B24 Human immunodeficiency virus [HIV] disease | 1,825 | 1,832 | 33,839 | 27,232 | 42,409 | 35,155 | 51,229 | 43,587 | 60,204 | 52,360 |
| B50-B54 Malaria | 108 | 14 | 2,783 | 343 | 3,248 | 400 | 3,730 | 463 | 4,230 | 528 |
| C00-C14 Malignant neoplasm of lip, oral cavity and pharynx | 515 | 556 | 1,218 | 1,230 | 1,828 | 1,862 | 2,710 | 2,762 | 3,895 | 3,985 |
| C15 Malignant neoplasm of oesophagus | 682 | 650 | 518 | 450 | 940 | 898 | 1,653 | 1,680 | 2,773 | 2,873 |
| C16 Malignant neoplasm of stomach | 4,375 | 4,817 | 9,315 | 9,853 | 14,410 | 15,855 | 21,368 | 24,243 | 30,903 | 35,350 |
| C18-C21 Malignant neoplasm of colon, rectosigmoid junction, rectum, anus and anal canal | 1,948 | 3,003 | 4,895 | 6,683 | 7,335 | 10,455 | 10,650 | 15,665 | 15,093 | 22,578 |
| C22 Malignant neoplasm of liver and intrahepatic bile ducts | 1,579 | 1,791 | 3,647 | 2,769 | 5,464 | 4,414 | 8,149 | 6,882 | 11,859 | 10,432 |
| C25 Malignant neoplasm of pancreas | 985 | 1,463 | 1,601 | 1,680 | 2,643 | 3,018 | 4,223 | 5,133 | 6,501 | 8,223 |
| C33-C34 Malignant neoplasm of trachea, bronchus and lung | 3,310 | 4,195 | 4,458 | 3,866 | 7,495 | 6,963 | 12,260 | 12,216 | 19,335 | 20,198 |
| C50 Malignant neoplasm of female breast | 1,856 | 2,621 | 7,333 | 8,700 | 11,803 | 14,270 | 17,418 | 21,435 | 24,048 | 29,975 |
| C53 Malignant neoplasm of cervix uteri | 1,724 | 1,503 | 8,623 | 7,020 | 13,023 | 10,673 | 18,303 | 15,100 | 24,433 | 20,250 |
| C61 Malignant neoplasm of prostate | 2,202 | 2,649 | 535 | 308 | 1,005 | 735 | 1,985 | 1,760 | 3,878 | 3,898 |
| C81-C96 Malignant neoplasm of lymphoid, haematopoietic and related tissue | 2,718 | 3,537 | 34,733 | 34,297 | 41,993 | 41,939 | 50,273 | 51,122 | 59,658 | 61,907 |
| D50-D89 Disorders of the blood and blood-forming organs and certain disorders involving the immune mechanism | 795 | 867 | 12,252 | 9,382 | 14,262 | 11,254 | 16,467 | 13,379 | 18,872 | 15,792 |

Appendix Table 1

Number of deaths and years of potential life lost before ages 55, 60, 65, and 70, by disease, Colombia, 2003 and 2013

| **Disease** | **Deaths** | | **YPLL55** | | **YPLL60** | | **YPLL65** | | **YPLL70** | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Year** | **2003** | **2013** | **2003** | **2013** | **2003** | **2013** | **2003** | **2013** | **2003** | **2013** |
| E00-E90 Endocrine, nutritional and metabolic diseases | 8,957 | 8,649 | 26,207 | 23,656 | 34,690 | 31,374 | 46,857 | 42,486 | 64,067 | 57,624 |
| F00-F99 Mental and behavioural disorders | 105 | 233 | 455 | 235 | 578 | 348 | 725 | 495 | 915 | 698 |
| G00-G99 Diseases of the nervous system | 2,212 | 2,417 | 40,607 | 25,069 | 47,155 | 30,319 | 54,207 | 36,299 | 61,870 | 42,991 |
| I00-I09 Acute rheumatic fever and chronic rheumatic heart diseases | 243 | 172 | 2,180 | 777 | 2,860 | 1,054 | 3,637 | 1,414 | 4,502 | 1,869 |
| I10-I15 Hypertensive diseases | 5,571 | 7,053 | 4,254 | 3,123 | 6,646 | 5,540 | 10,424 | 9,503 | 16,261 | 15,520 |
| I20-I25 Ischaemic heart diseases | 23,446 | 32,343 | 24,505 | 23,065 | 40,958 | 40,173 | 65,468 | 67,405 | 101,015 | 107,348 |
| I60-I69 Cerebrovascular diseases | 13,900 | 14,086 | 25,726 | 19,827 | 37,154 | 29,444 | 52,896 | 43,417 | 74,469 | 62,697 |
| I70-I79 Diseases of arteries, arterioles and capillaries | 1,714 | 1,547 | 2,506 | 1,798 | 3,659 | 2,788 | 5,356 | 4,270 | 7,836 | 6,385 |
| J09-J11 Influenza | 17 | 28 | 108 | 418 | 118 | 518 | 128 | 625 | 138 | 738 |
| J12-J18 Pneumonia | 5,354 | 7,065 | 72,779 | 43,482 | 82,194 | 51,694 | 92,507 | 61,482 | 104,159 | 73,172 |
| J40-J47 Chronic lower respiratory diseases | 10,045 | 11,817 | 8,690 | 4,490 | 12,242 | 6,983 | 18,152 | 11,475 | 28,132 | 19,090 |
| K00-K93 Diseases of the digestive system | 6,361 | 7,419 | 27,816 | 22,100 | 36,099 | 29,990 | 46,759 | 40,693 | 60,466 | 54,598 |
| M00-M99 Diseases of the musculoskeletal system and connective tissue | 1,245 | 2,112 | 8,885 | 11,850 | 11,080 | 14,952 | 13,540 | 18,495 | 16,320 | 22,512 |
| N00-N99 Diseases of the genitourinary system | 3,316 | 5,239 | 13,919 | 9,343 | 17,869 | 12,938 | 22,804 | 18,003 | 28,996 | 24,828 |
| P00-P96 Certain conditions originating in the perinatal period | 3,150 | 1,973 | 171,674 | 107,352 | 187,424 | 117,217 | 203,174 | 127,082 | 218,924 | 136,947 |
| Q00-Q99 Congenital malformations, deformations and chromosomal abnormalities | 1,844 | 1,735 | 95,128 | 87,466 | 104,276 | 95,954 | 113,446 | 104,476 | 122,631 | 113,046 |
| TOTAL | 118,042 | 138,250 | 733,392 | 527,968 | 885,930 | 664,575 | 1,075,317 | 844,668 | 1,314,007 | 1,077,220 |

| | | | **Below age 55** | | **Below age 60** | | **Below age 65** | | **Below age 70** | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Year** | | | **2003** | **2013** | **2003** | **2013** | **2003** | **2013** | **2003** | **2013** |
| Population (thousands) | | | 37,731 | 40,455 | 39,076 | 42,591 | 40,048 | 44,263 | 40,799 | 45,428 |