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Kristopher J. Hult
Sonia Jaffe
Tomas J. Philipson

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How Does Technological Change Affect Quality-Adjusted Prices in Health Care? Systematic Evidence from Thousands of Innovations

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ABSTRACT

Medical innovations have improved survival and treatment for many diseases but have simultaneously raised spending on health care. Many health economists believe that technological change is the major factor driving the growth of the heath care sector. Whether quality has increased as much as spending is a central question for both positive and normative analysis of this sector. This is a question of the impact of new innovations on quality-adjusted prices in health care. We perform a systematic analysis of the impact of technological change on quality-adjusted prices, with over six thousand comparisons of innovations to incumbent technologies. For each innovation in our dataset, we observe its price and quality, as well as the price and quality of an incumbent technology treating the same disease. Our main finding is that an innovation's quality-adjusted prices is higher than the incumbent's for about two-thirds (68%) of innovations. Despite this finding, we argue that quality-adjusted prices may fall or rise over time depending on how fast prices decline for a given treatment over time. We calibrate that price declines of 4% between the time when a treatment is a new innovation and the time when it has become the incumbent would be sufficient to offset the observed price difference between innovators and incumbents for a majority of indications. Using standard duopoly models of price competition for differentiated products, we analyze and assess empirically the conditions under which quality-adjusted prices will be higher for innovators than incumbents. We conclude by discussing the conditions particular to the health care industry that may result in less rapid declines, or even increases, in quality-adjusted prices over time.

Kristopher J. Hult
Charles River Associates
1 S Wacker Dr # 3400
Chicago, IL 60606
khult@uchicago.edu

Sonia Jaffe
www.soniajaffe.com
Becker Friedman Institute, Room 213
1126 E 59th St
Chicago, IL 60637
spj@uchicago.edu

Tomas J. Philipson
Irving B. Harris Graduate School
of Public Policy Studies
University of Chicago
1155 E. 60th Street
Chicago, IL 60637
and NBER
t-philipson@uchicago.edu

1 Introduction

Given the rapid expansion of spending on health care in most rich nations, there is an ongoing debate about whether this spending growth is accompanied by greater value and quality of care. Rapid medical innovation that enables us to treat previously untreatable diseases and improve existing treatments is central to both spending growth and improvements in care. A central question of health economics is whether the increased spending is valuable – that is, whether it raises the benefits from health care more than it increases the cost of care. Whether quality-adjusted prices rise or fall with new innovations is central to this debate.

In this paper we provide new systematic evidence on how quality-adjusted prices change with new medical innovations by analyzing thousands of new innovations. We obtain such a large set of technologies by recognizing the economic content of medical "cost-effectiveness" studies, performed over the course of at least half a century. By using an economic lens to reinterpret the cost-effectiveness literature, we can gain more systematic insight into the impact of technological change on quality-adjusted prices. In particular, what this literature calls the "cost-effectiveness ratio" is the price of the technology divided by the quality of the treatment. It is a quality-adjusted price, analogous to the price per square foot of housing. The incremental cost-effectiveness ratio (ICER) compares the price and quality of a new treatment with a "comparator" – usually the incumbent technology representing the standard of care prior to the arrival of the new treatment. The goal of the ICER is to measure the marginal quality-adjusted price of the added quality provided by the new innovation. Therefore, studies reporting ICER levels often offer measures of both the quality and price of innovators and incumbents. We use a database of cost-effectiveness studies from Tufts Medical Center called the Cost-Effectiveness Analysis Registry (CEAR) which contains over four thousand cost-effectiveness studies. This is a comprehensive data set of cost-effectiveness articles published in the peer-reviewed medical literature over the last 40 years.

Using these data, our main finding concerns the cross-sectional relationship between new innovations and incumbent technologies; that is, how the quality-adjusted price between the two compare at a given point in time. We find that, for the median innovation, the entrant has a quality-adjusted price that is four percent higher than that of the incumbent, with 68 percent of new technologies having higher quality-adjusted prices. This comes from a combination of slightly higher quality (median 1%) and moderately higher price (median 8%). We interpret these data in a standard differentiated duopoly model and analyze its implications for differences between innovators and incumbents in quality-adjusted prices. In particular, we analyze how these differences reflect the impact of breakthrough innovations, production costs, and third-party payment policies.

It is often argued that health care differs from other industries in that quality-adjusted prices rise over time instead of falling as they do in other industries, such as telecommunications. At first glance, our findings seem consistent with that pattern. However, this ignores the time series behavior of prices of a given technology due to competition. In particular, new therapeutic competition from related innovations and generic competition due to patent expiration often cause prices of a given treatment to fall overtime. Therefore, the overall price of treating a disease may fall over time, even though new innovations have higher prices in the cross section. In other words, a new innovation can be more expensive than the incumbent after entry and still be cheaper than the incumbent innovation was before entry. We calibrate that if competition caused innovations to cut prices by at least 4.2% before the entry of subsequent new technologies then overall quality-adjusted prices would fall for half of the markets, despite new innovations being more costly in the cross section.

This paper relates to several strands of work. Aggregate growth accounting attributes the residual from health care spending regression to the impact of technological change, but does not measure innovation directly (Newhouse, 1992). Jena and Philipson (2008) used the CEAR data to address topics of a broader nature than the product-specific evaluations for which it was designed by analyzing the relationship between cost-effectiveness thresholds and innovation incentives. The paper also relates to existing case studies that look at quality-adjusted price trends within a given indication, such as Cutler et al. (1998) for heart disease and Frank et al. (1999) for depression.

The paper proceeds as follows. Section 2 discusses the CEAR data on cost-effectiveness studies. Section 3 considers the cross-sectional findings of the relationship between price and quality of new innovations and incumbent technologies. Section 4 interprets the data in the context of a basic duopoly model and analyzes its predictions on causes of differences in quality-adjusted prices. Section 5 discusses time trends of quality-adjusted prices and potential explanations for the discussed findings. Finally, Section 6 summarizes the findings and conclusions.

2 CEAR Data

We use data from the Tufts Medical Center Cost-Effectiveness Analysis Registry (CEAR). CEAR is a dataset of the methods and findings of about 4,800 published cost-utility analysis articles some of which cover multiple treatments. The database is intended to be a comprehensive collection of all such articles published in the peer-reviewed medical literature. The registry uses two trained reviewers to independently review each article and collect a wide variety of variables. Their analyses are compared for accuracy.

Each article compares a newer treatment option to one or more standards of care (SOC).

The registry collects and organizes data on article information, disease classification, methods of the study, and measurement details. The data set covers articles published between 1976 and 2014 with the number of articles increasing from an average of one per year during the first 10 years, to an average of about 475 articles per year during the last five years. As a result, 85% of the data comes from papers published between 2004 and 2014. About half of the articles, all written since 2002 have prices and qualities separately for the innovation and the standard of care. The other articles have only a single measure of the incremental cost efficiency ratio (ICER) – the difference in price divided by the difference in quality.[1]

Table 1: Summary Statistics

	Mean	Min	Max	S.D.	Obs
Year	2010	1976	2014	5	12,560
US dummy	0.39	0	1	0.49	12,560
EU dummy	0.43	0	1	0.49	12,560
Prevention Stage	2.43	1	3	0.76	12,560
Score of Study Reliability	4.69	1	7	1.00	12,557

	Median	5th	95th	S.D.	Obs
Innovator Quality	7.7	0.2	27.3	10.7	6,597
SOC Quality	7.3	0.1	27.0	10.7	6,572
Innovator Price	21,506	263	310,397	303,734	6,886
SOC Price	16,682	84	274,861	282,271	6,854
Innovator Price per QALY	4,532	36	88,345	162,054	6,504
SOC Price per QALY	3,755	20	83,505	196,667	6,391
ICER	17,415	-111,268	419,635	621,768	12,483

Note: This table summarizes the studies in the Cost-Effectiveness Analysis Registry. The US and EU dummies refer to the country in which the study was conducted. The 'Score of Study Reliability' is a rating that the reviewers compiling the database give to each study they read. SOC is the standard of care (incumbent) treatment. Quality is measured in quality-adjusted life years (QALYs). Prices are in 2014 US dollars. The 'ICER' is the incremental cost effectiveness ratio, which is the difference in prices between the innovator and the SOC divided by the difference in qualities.

Summary statistics for the main variables are provided in Table 1. Each article may provide multiple studies (comparing different subgroups, patient settings or standards of care), so we have a total of 12,560 studies, about 6,500 of which have complete price and quality data. The main variables of interest are the ones related to cost and effectiveness. The price of an intervention (either the innovation or the standard of care) includes all the

[1] ICER is commonly used in the cost-effectiveness literature as a measure of the marginal price for the additional quality gained from the innovation, relative to the standard of care.

costs that the article was able to measure – both direct costs and non-health care costs.[2] Since the total cost is the full price of the treatment, we simply refer to it as the price of the treatment. The price for both the new treatment and the SOC are measured per person treated. We convert them to 2014 US dollars using the medical CPI and yearly exchange rates.[3]

Effectiveness is measured in quality-adjusted life years (QALY), which is a combination of the length of life and quality of life added by the treatment. A year of perfect health is equal to one QALY and a year of death is zero QALY, with different levels of health in between so that a person is indifferent between living x years at a QALY of $1/x$ and one year at perfect health. The effectiveness of a treatment is how many QALYs it adds to a patient, which we refer to as quality. Similar to costs, both the innovation and the SOC have quality measures. We omit observations with quality values greater than 100, since it does not make sense for a treatment to add more than 100 years to someone's life. We also omit studies with negative quality values.

Prices of the innovations range dramatically, from around $282 to $315,324 between the 5th and 95th percentile since a wide variety of treatments are included. The median is around $22,000. Quality also has a large range, roughly between 0.26 and 27 QALY for the 5th and 95th percentile, with a median of 7.8 QALY. The treatments with large prices and qualities include surgeries such as prophylactic oophorectomy, a surgery that reduces risk of breast cancer and ovarian cancer, or treatments that have to be administered with very high frequency over a very long period of time, such as HIV antiretroviral therapies atazanavir-ritonavir or lopinavir-ritonavir.

One potential concern about using CEAR is that there may be great heterogeneity in the quality of studies that are recorded by the registry. An unusual feature of these data is that each study in the registry has been evaluated in terms of its quality through a scoring system. In compiling the dataset, the readers of the registry rate each article on a scale from 1 to 7, based on perceived correctness and comprehensiveness. This is a nice feature because it tells us which observations we should rely on more. We report our findings for the overall sample of studies as well as for the *high-score studies* – studies that have the median score

[2] The data codebook defines: *Direct Medical Costs* as "Health care resource costs related to the intervention and its side effects. These costs include those impacts directly attributable to the intervention and those related to current and future consequences to the intervention (e.g. hospitalization, MD or other provider, long-term care, other health care which includes medications, outpatient procedures and laboratory costs)" and *Non-Health Care Costs* as "Non-health care [costs] resources related to the intervention and its side effects (e.g. travel time to doctor, caregiver time and workplace productivity impacts, transportation costs, patient productivity costs)." Only about a quarter of the studies list direct costs separately and less than 5% list non-health costs separately, so we focus on the total costs.

[3] We omit observations with negative cost for either the innovation or the SOC. We also omit observations where the ICER, price, or price per QALY for the innovation or the SOC is over 10^7.

rating or higher.

In discussing the other study characteristics, we limit the sample to the 6,472 studies for which we have price and quality data for both the innovation and the standard of care. There are studies from 70 countries, but North America and Europe account for 81% of the studies, including 38% from the United States and 17% from the United Kingdom. The dataset includes variables on the primary disease addressed by the treatment, the treatment's type of intervention, and the study sponsor. There are 65 disease categories, with about 50% of the studies coming from the 5 most studied diseases (infectious diseases (12%), cardiovascular diseases (12%), malignant neoplams (12%), musculoskeletal and rheumatologic diseases (8%), neuro-psychiatric/neurological conditions (4%)) Each study covers one or more types of interventions including pharmaceutical (54%), surgical (11%), screening (18%) and medical procedures (11%).[4] The studies include sponsors with the main sponsors being governments (38%), industry pharmaceutical, biotech, and medical device companies (32%), and non-profit organizations (8%). As with interventions, there may be multiple sponsors for a treatment so the sponsor indicators average to greater than one.

There may be selection issues in determining which articles get studied and published, which would bias our attempts to understand how the average new innovation affects quality-adjusted prices. For instance, if only the most cost-effective new treatments get studied or there is a publication bias in favor of findings of high cost-effectiveness, that would bias our estimates. For selection to be an issue it would need to occur independent of the intervention type, disease, country, and sponsor type since we control for these. We do not have data on market share, so we are comparing product level differences in price and quality between the innovation and the standard of care.

[4]The intervention types are *Care Delivery:* Provision of care, development of facility or distribution of personnel (e.g. a policy that changes the nurse-to-patient ratio, patient self-management program). *Health Education or Behavior:* An intervention designed to educate individuals on behaviors that promote, maintain or restore health (e.g. smoking cessation and prevention program). *Pharmaceutical:* Any drug or biotech product used for medical treatment or prevention (e.g. Lovastatin, Herceptin). *Surgical:* Invasive; cutting involved (e.g. transplantation, although bone marrow transplantation would be a medical procedure, appendectomy). *Immunization:* Receipt of vaccination (e.g. flu vaccine, HPV vaccine). *Diagnostic:* A method used to determine if and what type of disease is present (e.g. imaging, biopsy, PET scan, x-rays, in-vitro testing). *Medical Procedure:* Non-surgical, non-diagnostic procedures (e.g. angiogram, blood donation, mole removal, casting). *Medical Device:* May or may not require a surgical or implantation procedure (e.g. pacemaker, insulin pump, leg brace and crutches). *Screening:* Refers to measures that detect disease (or test for risk factors) before it is symptomatic (e.g. breast cancer screening mammogram). *Other:* Any intervention not described above (e.g. injury prevention, food safety, or environmental health).

3 Comparing Innovators and Incumbents in the Cross-section

The measurements provided by the CEAR are highly relevant to economists interested in the value of health care in terms of quality-adjusted prices for health. Figure 1 below depicts a schematic of the variables measured in the CEAR in a traditional quality-price space. The incumbent technology corresponds to the standard of care and has quality and price (q_s, p_s), while the new innovation has quality and price (q, p). The slopes from the origin represent the quality-adjusted prices; the slope between the incumbent and the innovators quality price pairs represents the ICER. The figure illustrates that the average price of quality (quality-adjusted price) of the innovator is larger than that of the incumbent when the marginal price (ICER) is higher than the quality-adjusted price of the incumbent. Put simply, the average rises if and only if the marginal price is higher than the previous average.

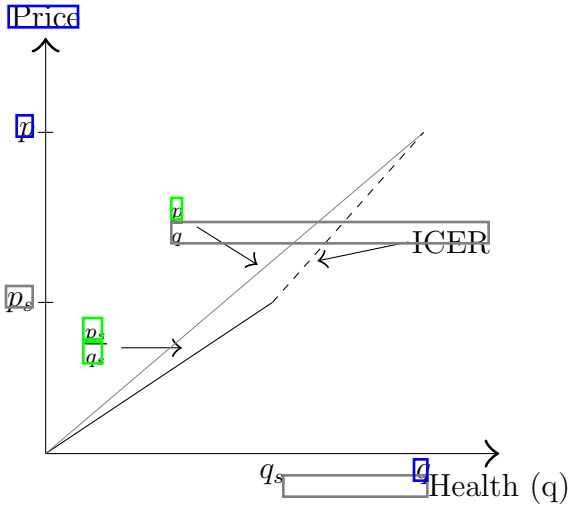


Figure 1: Price-Quality Space

If one imagines centering a graph around the incumbents price and quality, (q_s, p_s), the quadrants represent combinations of price and quality differences that the new innovator can represent. For example in the northwest quadrant the innovator has both higher quality and price; within that quadrant, quality-adjusted prices rise if price differences dominate quality differences. Figure 2 provides the unconditional scatter plot of the joint distribution of price and quality differences between innovations and incumbents. In this figure, the origin represents an incumbent's quality and price and the axes reflect the percentage difference in quality and price between the innovator and the incumbent. The dashed 45° line represents when the innovator has the same quality-adjusted price as the incumbent which corresponds

to when the percentage difference in price equals the percentage difference in quality: $\frac{p}{q} = \frac{p_s}{q_s}$ implies $\frac{p-p_s}{p_s} = \frac{q-q_s}{q_s}$.

In general, price and quality are both higher for the new innovation relative to the incumbent. There is a price increase in 78% of observations and a quality increase in 85%. The distribution is *very* skewed to the right. The average innovation increases price by 139% relative to the incumbent, but the median is an 8% increase; the average quality difference is 26%, but the median is 1%. The percentage change in price has a much wider range than the percentage change in quality. The 31% of innovations below the 45° line (green) in Figure 2 have lower quality-adjusted prices. The innovations with higher quality-adjusted prices than the incumbent are split into the 11% that lower quality (red) and the 56% that improve quality (blue). Even though these innovations have higher quality-adjusted prices, those that improve quality can be better for consumers because they offer more quality than what was available to purchase at the lower quality-adjusted price.

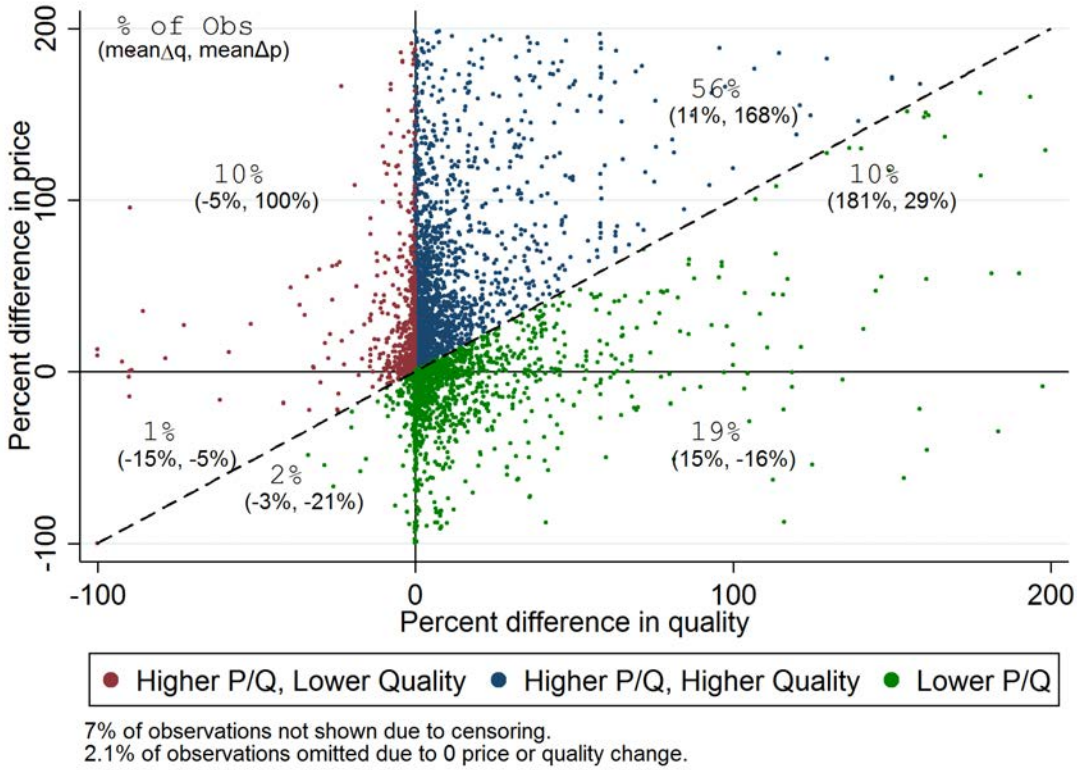


Figure 2: Price and quality differences.

Note: The x-axis is the difference in quality between the innovation and the incumbent as a percent of the incumbent's quality. The y-axis is the same measure for price. The top number in each section is the percent of observations that fall in that quadrant or octant, including the outliers that are censored from the graph. They do not sum to 100% because of the 2% of observations that fall on one of the axes. The numbers in parentheses are the average percent difference in quality and price for observations in that quadrant.

Under extreme substitutability of demand across treatments, off-diagonal elements in Figure 2 (where $(p_2 - p_1) \cdot (q_2 - q_1) < 0$) would not be observed. This is broadly true in the data, as 69% of the innovations lie on the diagonal quadrants where higher quality treatments command higher prices. However, note that there is a non-trivial fraction of innovations with higher quality and lower price (19%), but nevertheless do not destroy the market for the SOC. There are also some innovations with that enter with a higher price and lower quality (10%). This may be due to heterogeneity in treatment effects. Another explanation is that the first type of innovation will eventually replace the SOC after being shown to be of higher value and the latter will exit after it becomes evident they are of lower value.

The median quality-adjusted prices for new innovations and the SOC, measured as the cost per QALY, are \$2,700 and \$2,400 respectively. Figure 3 plots the distribution of the ratio of the quality-adjusted prices of the new innovation and the SOC, $\frac{p}{q} / \frac{p_s}{q_s}$. If this *quality-adjusted price ratio* is above one, it means the new innovation had a higher quality-adjusted price than the SOC. The histogram indicates that a high fraction of new technologies do not change quality-adjusted prices much, but new innovations do tend to have higher quality-adjusted prices than the SOCs. The median ratio is 1.04, meaning the quality-adjusted price of the innovation is 4% higher than the standard of care; the distribution is very right skewed with a standard deviation of 32, so only 2.4% of innovations have cost effectiveness ratios that are statistically larger than one. If we focus on highly scored studies, the median is about the same, but the standard deviation is even higher. Only 0.9% of those studies are statistically different from one.

These are the overall effects for all disease categories and modes of intervention. Table 2 breaks down the change in quality-adjusted-price for the most common disease categories. Infectious disease, malignant neoplasms, and breast cancer have the highest quality-adjusted prices relative to the incumbents. Table 3 does the same for intervention types.[5] Pharmaceuticals are the intervention type with the highest relative price. Educational interventions tend to be less expensive relative to the incumbent and also vary less. The differences across intervention type are not as robust to the exclusion of low-scored studies as the disease categories. These tables indicate that the large variation we see in relative cost effectiveness of an innovation is not due primarily to differences across disease categories or treatment types. There is more variation within categories than across categories.

One reason one may suspect innovators to command high quality-adjusted prices is if they offer "breakthrough" innovations. To investigate this we examine the impact of the

[5] Since studies may have multiple intervention types, the sum of the number of observations is greater than the number of studies.

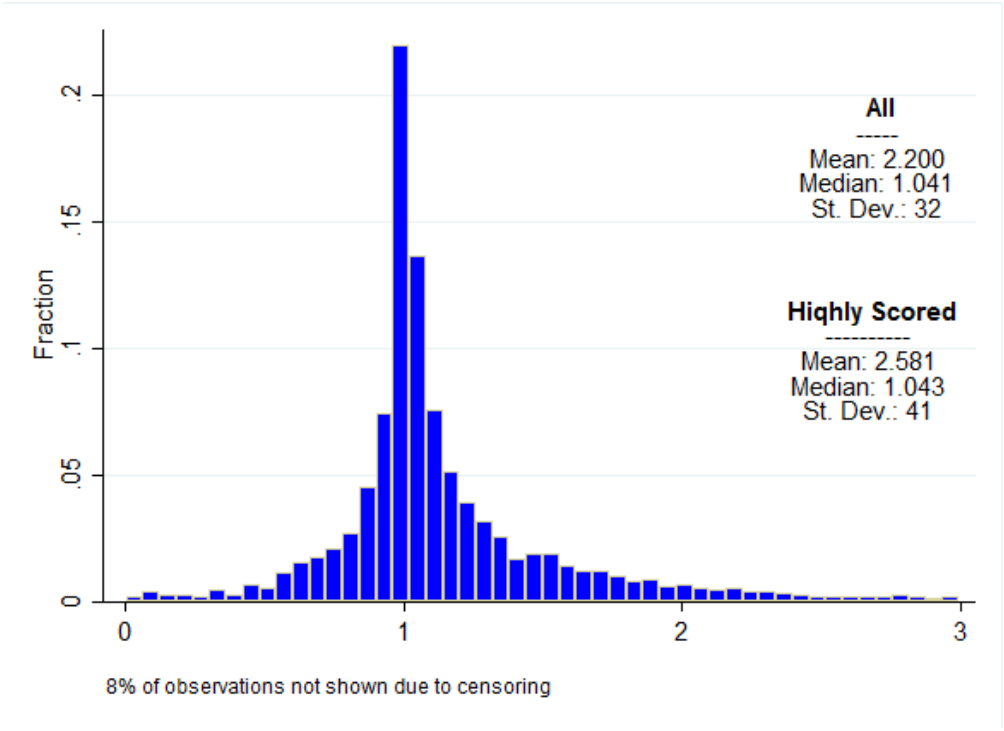


Figure 3: Ratio of quality-adjusted prices.

Note: This graph shows the distribution across innovations of the ratio of innovator's and incumbent's quality-adjusted prices. For readability, the graph omits studies with a cost effectiveness ratio above 3, thereby censoring 8% of observations. 'Highly Scored' refers to studies with at least the median rating given by the readers.

Table 2: Percent difference in quality-adjusted-price by disease type

	All				High Score			
	Obs	Median	Mean	St. Dev.	Obs	Median	Mean	St. Dev.
Maternal/Child	65	-0.17	-7.60	37.73	23	-0.17	-9.60	39.74
Genito-Urinary	277	0.25	17.44	75.21	148	0.55	14.56	53.85
Neuro-Psychiatric/ Neurological	490	1.57	21.05	104.59	311	1.55	13.33	74.61
Endocrine Disorders	413	1.71	22.14	118.30	234	3.11	22.09	98.59
Cardiovascular	1176	2.87	28.48	98.04	796	2.76	21.57	72.67
Musculoskeletal/ Rheumatologic	633	3.00	31.25	124.46	356	3.55	36.95	135.27
Digestive	300	6.37	44.25	116.14	136	0.99	31.81	93.37
Respiratory	158	7.41	42.86	159.29	120	7.47	42.12	152.17
Malignant Neoplasms	1064	7.58	42.37	122.31	637	7.49	47.70	137.01
Sense Organ	108	8.19	57.50	125.11	62	11.59	72.02	127.88
Infectious	973	8.91	42.26	126.71	626	9.87	47.03	134.39

Note: This table shows the percent difference in quality-adjusted prices, $100 \cdot \left(\frac{\frac{p}{q}}{\frac{p_1}{q_s}} - 1\right)$, across innovations by disease category. It omits the top 1% of quality-adjusted price ratios. The right panel shows only studies with at least the median score – the rating of the study given by the readers.

Table 3: Percent difference in quality-adjusted-price by intervention type

	All				High Score			
	Obs	Median	Mean	St. Dev.	Obs	Median	Mean	St. Dev.
Education	319	0.78	13.70	79.69	217	2.14	16.15	59.30
Diagnostic	528	1.35	19.16	88.48	297	1.55	27.89	106.68
Care Delivery	498	1.49	28.18	99.09	255	1.71	20.03	70.00
Screening	1109	2.59	31.57	122.83	676	3.17	43.72	149.00
Surgical	697	3.43	25.54	93.79	294	9.77	37.09	100.33
Immunization	193	3.99	64.37	163.49	128	2.25	41.05	138.41
Device	491	5.23	29.22	94.56	250	7.76	26.80	57.56
Pharmaceutical	3448	5.67	40.36	128.43	2220	4.93	37.80	120.62
Procedure	696	6.38	34.24	100.19	351	7.49	38.82	102.23

Note: This table shows the percent difference in quality-adjusted prices, $100 \cdot \left(\frac{\frac{p}{q}}{\frac{p_1}{q_s}} - 1\right)$, across innovations by intervention type. Studies may have multiple intervention types so the sum of the number of observations is greater than the number of studies. The table omits the top 1% of quality-adjusted price ratios. The right panel shows only studies with at least the median score – the rating of the study given by the readers.

quality difference $q - q_s$ on the relative price. As shown in Table 4, for highly-scored studies, innovations in the top quartile of quality improvement tend to have higher quality-adjusted price ratios. The mean is about 0.15 higher and the median is 0.034-0.06 higher, meaning the percent difference in quality-adjusted price is 3-6 percentage points higher. The difference is much smaller and statistically insignificant if we look at all studies instead of just the highly-scored ones, so it is not clear how robust this relationship is. Note that the last column of Table 4 controls for the type of intervention, disease and sponsor, but one may not want to control for these; if certain intervention types or disease tend to have higher quality improvements, that may be why they have higher quality-adjusted-price ratios, so we may want to include that effect in the estimate of the effect of large quality improvements.

Table 4: Quality-adjusted price ratio by size of quality difference

	Quantile Regression			
	(1)	(2)	(3)	(4)
50th-75th Percentile Quality Change	0.0320	0.116*	0.00749	0.000666
	(0.0515)	(0.0548)	(0.0107)	(0.0142)
$>$ 75th Percentile Quality Change	0.159**	0.187**	0.0613***	0.0341*
	(0.0515)	(0.0571)	(0.0107)	(0.0147)
Controls:				
Year Dummies	X	X	X	X
Intervention, Disease & Sponsor Type		X		X
Observations	3783	3783	3821	3821
Adjusted R^2	.01114	.04431	.0013	.01038

Standard errors in parentheses. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Note: This table shows coefficients from regressions of the quality-adjusted price ratio, $\frac{p}{q}/\frac{p_s}{q_s}$, on dummies for the top two quartiles of quality change, $\frac{q-q_s}{q_s}$. The first two columns are linear regressions and omit the top 1% of quality-adjusted price ratios; the last two columns are median regressions. All regressions include only highly-scored studies – those which received at least the median ranking from the readers.

Another factor that one may think drive differences in prices may be the price controls more frequently imposed in Europe than in the United States. As shown in Table 5, there is no systematic difference in the ratio of quality-adjusted price between studies done in the United States and those done in Europe, including the United Kingdom. However, these countries do have substantially lower quality-adjusted price ratios than studies done in the rest of the world, including Japan. On average the quality-adjusted-price ratio is about 0.2 higher in non-EU/US countries; the median is 0.05 higher. These results are qualitatively unchanged if we look at all studies instead of just highly rated ones.

Table 5: Quality-adjusted price ratio by geography

			Quantile Regression	
US dummy	-0.353***	-0.304***	-0.0881***	-0.0661***
	(0.0622)	(0.0654)	(0.0128)	(0.0170)
EU dummy	-0.383***	-0.240***	-0.0994***	-0.0601***
	(0.0639)	(0.0684)	(0.0132)	(0.0178)
UK dummy	0.0453	0.0659	0.0262*	0.0167
	(0.0632)	(0.0668)	(0.0131)	(0.0174)
Japan	-0.399**	-0.407*	-0.0525	0.00999
	(0.155)	(0.158)	(0.0321)	(0.0414)
Controls:				
Year Dummies	X	X	X	X
Intervention, Disease, & Sponsor Type		X		X
Observations	3783	3783	3821	3821
Adjusted R^2	.01936	.04721	.00161	.01078

Standard errors in parentheses. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Note: This table shows coefficients from regressions of the quality-adjusted price ratio, $\frac{p}{q} / \frac{p_s}{q_s}$, on dummies for the country or region in which the study took place. The first two columns are linear regressions and omit the top 1% of quality-adjusted price ratios; the last two columns are median regressions. All regressions include only highly-scored studies – those which received at least the median ranking from the readers. Studies in the UK are also included in the EU category, so the coefficient on the UK dummy is relative to the level in the EU.

Pharmaceuticals make up about half of our sample and the high prices of new drugs have received a lot of media coverage. Table 6 looks at how the quality-adjusted price ratios for pharmaceutical innovations in highly-rated studies differ in different time blocks. Pharmaceutical innovations have somewhat higher prices than others, with the effect being driven by studies from 2012-2014 having a median (mean) quality-adjusted price ratio that is 0.058 (0.145) higher than other innovations. If we look at all studies, instead of just highly rated ones, the coefficient for 2012-2014 is slightly larger and the median in quality-adjusted price ratio for pharmaceuticals is also somewhat larger than other innovations in 2007–2010.

Table 6: Quality-adjusted price ratio of pharmaceuticals

			Quantile Regression		
	(1)	(2)	(3)	(4)	(5)
Pharmaceutical	0.0428		0.0167*		
	(0.0427)		(0.00715)		
Pharma and 2002-2006		0.128		-0.0326	0.000199
		(0.131)		(0.0237)	(0.0345)
Pharma and 2007-2010		-0.160		-0.0473**	-0.00868
		(0.0861)		(0.0156)	(0.0230)
Pharma and 2011-2014		0.108*		0.0383***	0.0603***
		(0.0532)		(0.00969)	(0.0139)
2006-2011		0.226		0.0104	0.00631
		(0.123)		(0.0223)	(0.0329)
2012-2014		0.0348		-0.0482*	-0.0424
		(0.112)		(0.0203)	(0.0311)
Controls:					
Disease & Sponsor Type					X
Observations	3783	3783	3821	3821	3821
Adjusted R^2	0	.00111	.00011	.00058	.00897

Standard errors in parentheses. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Note: This table shows coefficients from regressions with the quality-adjusted price ratio, $\frac{p}{q}/\frac{p_s}{q_s}$, as the dependent variable. It uses only highly-scored studies – those which received at least the median ranking from the readers. Columns (1) and (3) look at the difference between pharmaceutical and non-pharmaceutical innovations; Columns (2), (4), and (5) interact the pharmaceutical dummy with three time periods. The first two columns are linear regressions and omit the top 1% of quality-adjusted price ratios; the last three columns are median regressions.

4 Economic Interpretation of Price Changes

Having described the general patterns in the data, we now use standard duopoly pricing models to analyze the conditions under which the innovator's quality-adjusted price is expected to be higher than the incumbent's.

Consider the incumbent and innovator having costs c_s and c and qualities q_s and q, and setting prices p_s and p. Denote two Nash best responses functions $p(p_s; q, q_s)$ and $p_s(p; q, q_s)$ leading to equilibrium prices $p(q, q_s)$ and $p_s(q, q_s)$.

The difference in quality-adjusted prices and the marginal price of health (ICER) between innovators and incumbents are given by

$$\Delta \equiv \frac{p(q, q_s)}{q} - \frac{p_s(q, q_s)}{q_s}$$
$$ICER \equiv \frac{p(q, q_s) - p_s(q, q_s)}{q - q_s}$$

We are interested in how these are affected by different characteristics of the incumbent or innovator.

4.1 Quality and Cost Effects

Figure 4 illustrates two typical increasing best response functions $p(p_s)$ and $p_s(p)$, where the intersection is the equilibrium. Consider now the effects of costs and quality levels on the equilibrium difference in quality-adjusted prices between the innovator and the incumbent. For the effects of costs, note that the best response function of one party does not depend on the costs of the other party. Therefore, an increase in cost of the innovator simply raises its price for each price of the incumbent and corresponds to an upward shift in its best response function in Figure 4. The effect on the difference in quality-adjusted prices is

$$\frac{d\Delta}{dc} = \frac{\frac{dp}{dc}}{q} - \frac{\frac{dp_s}{dc}}{q_s}$$

Though stability of the equilibrium requires that $\frac{\partial p_s}{\partial p} < 1$, so the incumbent's price changes less than the innovator's, the incumbent may have lower quality so the sign of $\frac{d\Delta}{dc}$ is indeterminate. This has the non-intuitive implication that cost-reducing innovations may raise the difference in quality-adjusted prices.

The effects of the quality of the innovator on the price difference is given by

$$\frac{d\Delta}{dq} = -\frac{p}{q^2} + \frac{\frac{dp}{dq}}{q} - \frac{\frac{dp_s}{dq}}{q_s}$$

This is simply the direct effect of higher quality lowering quality-adjusted prices together

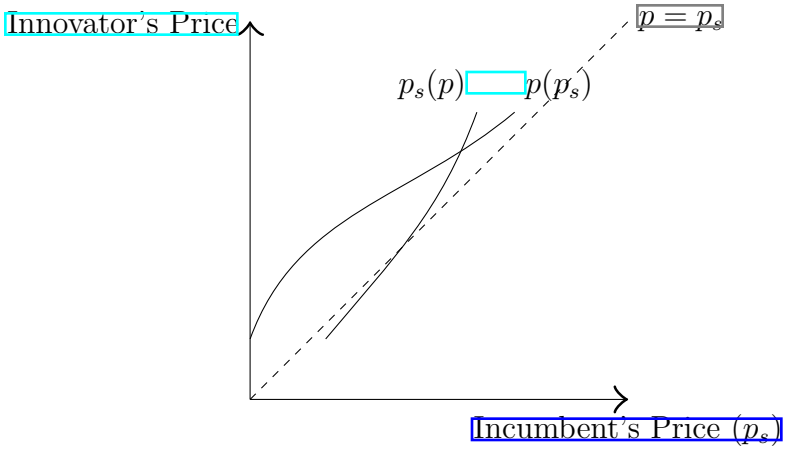


Figure 4: Typical best response functions

with the indirect effects via prices. If a higher quality of the innovator raises its price and lowers the price of the incumbent the indirect effect is always positive but the total effect on the price difference indeterminate. A similar argument applies to the quality of the incumbent.

4.2 The Impact of Breakthrough Innovations

One argument that is often made is that breakthrough innovations are responsible for increases in quality-adjusted prices. In our framework, innovations with high innovator quality relative to incumbents, $\frac{q}{q_s}$, can be thought of as breakthrough innovations. The effect of the large quality difference on Δ operates both directly through quality but also indirectly through the effect on price. These effects will tend to be offsetting, so the size of the quality difference has an indeterminate effect on the difference in quality-adjusted prices; breakthrough innovations may lower quality-adjusted prices.

More precisely, quality-adjusted prices are larger for the innovator whenever the ratio of prices is larger than the ratio of qualities,

$$\Delta > 0 \iff \frac{p}{p_s} > \frac{q}{q_s} \iff \frac{m}{m_s}\frac{c}{c_s} > \frac{q}{q_s}. \tag{1}$$

Where m and m_c are equilibrium markup factors. In order for breakthrough innovations to raise quality-adjusted prices, the price difference must dominate the quality difference. The price ratio is made up of markup differences and cost differences. An increase in quality-adjusted prices is therefore more likely if there is a large markup difference (e.g., when the incumbent standard of care has gone generic) or large cost differences (e.g, injected large molecule biologics replacing oral small molecule pills).

4.3 The Impact of Price Controls

It is often argued that in countries with price controls on medical innovations such as in the United Kingdom, changes in quality-adjusted prices will be lower than for countries with market based pricing such as the United States. However, this is not necessarily implied by standard duopoly models. First consider when there is cost-based pricing of the incumbent technology due to competition. With "cost-effectiveness threshold" policies, price controls are imposed in terms of reservation prices above which the single-payer system does not reimburse for new technologies. Such policies restrict the marginal price of quality (ICER) charged for new innovations to be below a given threshold level T. The resulting upper bound on the monopoly price depends on the price of the incumbent and the qualities of the incumbent and the innovator

$$\frac{p - p_s}{q - q_s} \leq T \Longleftrightarrow p \leq p_s + T(q - q_s).$$

Such thresholds imply that the innovator cannot price higher than the incumbent's price after it is adjusted for any difference in the quality. However, the innovation may still have a higher quality-adjusted price. If the innovator prices at the price ceiling, then quality-adjusted prices are higher whenever

$$\frac{p_s + T(q - q_s)}{p_s} \geq \frac{q}{q_s} \Longleftrightarrow T \geq \frac{p_s}{q_s}.$$

Quality-adjusted prices may increase under price controls if the allowed price-adjustment for quality (the threshold) is larger than the quality-adjusted price of the incumbent (i.e. the incumbent has not priced up to the threshold). Put simply, the average new price, p/q, is above the incumbent price, p_s/q_s, only if the marginal price, T, is above the incumbent price.

Differences in quality-adjusted prices may be larger under price controls than under free-market pricing if the allowed markup on quality, T, allows for higher pricing than the optimal price given the elasticity of demand in a private market. If the public sector sets 'too generous' a reservation price (threshold), the resulting demand curve (which is a step-function) may lead to a higher price than the monopoly price in a market with multiple buyers. Public price controls per se do not mean smaller changes in quality-adjusted prices, because their ceilings apply to a market with only one buyer as opposed to the unregulated price that occurs under several buyers. The imposition of a single payer price ceiling does not hold market structure constant.

When innovators price at the price ceiling, this determines not only the price of the new innovation, but also the reference point for price of future care. If the price has not decreased over time and the next generation innovation prices up to the limit, a monopolist setting the

ICER equal to the threshold T means

$$p_{t+1} = p_t + T(q_{t+1} - q_t),$$

which implies

$$p_t = p_0 + T(q_t - q_0)$$

The marginal prices of quality for each subsequent innovation are equal over time; therefore the average price of quality is equal to this constant marginal price. In this extreme case, under price controls both the marginal and average price do not change due to innovation.

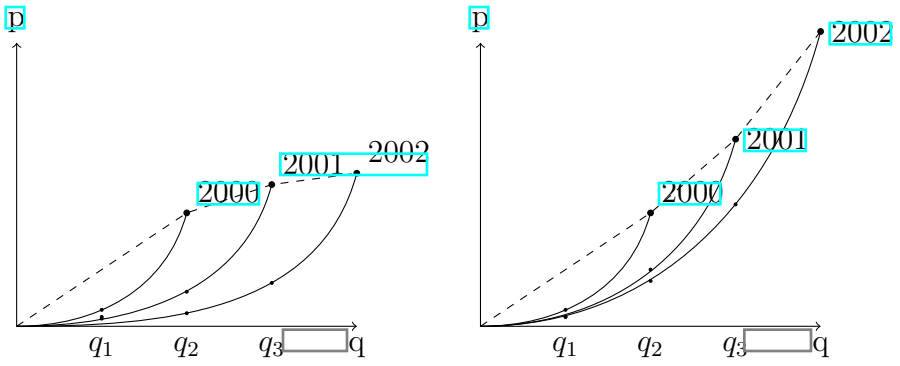
If the incumbent has market power, rather than setting price exogenously equal to cost, it sets p_s according to a best response function, as depicted earlier in Figure 4. If the innovator has a higher quality the best response function $p(p_s)$ of the innovator will generally start above the origin and never cross over the 45 degree line. The restriction ICER$\leq T$ is equivalent to $p \leq p_s + T(q - q_s)$, so the price cannot be more than $T \cdot (q - q_s)$ above the 45 degree line. The logic is the same as when the incumbent technology is competitively supplied. If the ICER constraint is binding, the regulated difference in quality-adjusted prices between the innovator and incumbent is smaller than the unregulated one $p = p_s + T(q - q_s)$. If the constraint would not be binding in a competitive market, the regulated price may be higher because the innovator can price up to the constraint, without facing the loss in demand that they would have in a competitive market.

This implies that differences in quality-adjusted prices between innovators and incumbents may not differ between places such as the United States and European Union, though differences in price levels may exist. For example, if the United States has market-based pricing and the United Kingdom has a cost-effectiveness threshold of $50,000, quality-adjusted prices may be lower in the United Kingdom, but differences in quality-adjusted prices between innovators may be smaller in the United States (if the competitive market causes the entrant to price below $p_s + \$50,000(q - q_s)$). Table 5 suggests that the price controls used in the United Kingdom and other parts of the European Union do not lead innovations to have systematically lower quality-adjusted prices, relative to incumbents.

5 Implications for the Time Series of Prices

Empirically, the quality-adjusted price of an innovation is often higher than the incumbent standard of care once the new innovation has entered the market. However, the overall time trend in prices does not depend only on the cross-sectional difference between innovators and incumbents, but also on the difference in price over time within products.

Figure 5 shows two hypothetical cross sections of price and quality relationships over time where each subsequent entry raises quality, as in a quality ladder model. Each year, a new



(a) Decreasing $\frac{p}{q}$ (b) Increasing $\frac{p}{q}$

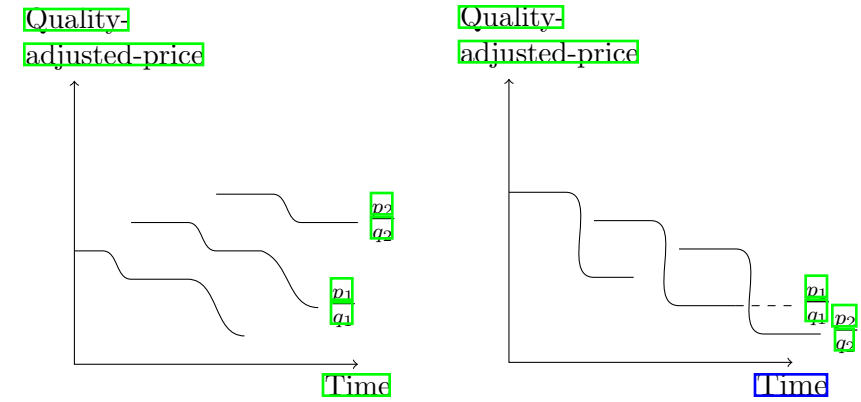
Figure 5: Different possible price trends.

product enters with a higher quality and the prices of the incumbents fall. In both cases, the price-quality relationship is convex within a year; the entrant has a higher quality-adjusted-price than existing products, so quality-adjusted-price is increasing in quality. However, the overall trend in quality-adjusted-price can be increasing or decreasing. The fact that new innovations may have higher quality-adjusted prices in the cross section does not restrict the path of quality-adjusted prices of new innovations over time – the top point on each line. Figure 6 demonstrates this same idea by considering the quality-adjusted-price of each product over time. Figure 6a shows a market where the price of each product falls over time, particularly when a new entry occurs, but the higher prices of new products cause an overall upward trend in quality-adjusted prices. Figure 6b shows a market where the fall in prices upon entry is large relative to the cross-sectional difference between the incumbent and the entrant, so there is an overall downward trend. Innovators having a higher price at a given point in time is consistent with both, for example, Cutler et al. (1998) who found falling quality-adjusted prices over time for heart attack treatments, and Howard et al. (2015), who found rising quality-adjusted prices over time for oncology drugs.

To formalize these intuitions, let $p_1, \ldots p_{k-1}$, $q_1, \ldots q_{k-1}$ and $s_1 \ldots s_{k-1}$ be the prices, qualities and marketshares of the products in the market at time zero, before the innovation enters. The innovation enters with quality q'_k and the new prices, and marketshares are $p'_1 \ldots p'_k$ and $s'_1, \ldots, s'_k$. The change in the market's average quality-adjusted-price (QAP) depends on changes in quality-adjusted prices and changes in market shares:

$$QAP' - QAP = s'_k \frac{p'_k}{q'_k} + \sum_{j=1,\ldots,k-1} \left(s'_j \left(\frac{p'_j}{q'_j} - \frac{p_j}{q_j} \right) + \frac{p_j}{q_j} (s'_j - s_j) \right).$$

Quality-adjusted prices may fall over time even if the quality-adjusted price of the new



(a) Pre-entry Trends Leading to Overall Downward Trend in Prices.

(b) Pre-entry Trends Leading to Overall Upward Trend in Prices.

Figure 6: Different possible pre-entry trends in the price for the standard of care.

innovation is higher than the other prices in the market, $\frac{p'_k}{q'_k} > \frac{p'_j}{q'_j}$.

If we think of the standard of care as a composite of all the other goods in the market, then

$$QAP' - QAP = s'_2 \frac{p'_2}{q_2} + s'_1 \left(\frac{p'_1 - p_1}{q_1} \right) + \frac{p_1}{q_1}(s_1 - 1) = s'_2 \left(\frac{p'_2}{q_2} - \frac{p'_1}{q_1} \right) - \frac{\Delta p_1}{q_1},$$

where $\Delta = \frac{p_1 - p'_1}{p_1}$ is how much higher the incumbent's price was prior to entry, as a fraction of the pre-entry price. Whether overall quality-adjusted prices are going up or down depends on

$$\Delta \gtrless s'_2 \frac{\left(p'_2 \frac{q_1}{q_2} - p'_1 \right)}{p_1}.$$

If the incumbent's price is relatively unchanged between when it entered and when the innovation enters, then even a small difference in the quality-adjusted prices between the innovator and the incumbent could indicate an overall upward trend in prices. Conversely, if the incumbent's price has dropped dramatically since initial entry (for example, if the incumbent is a drug that is available in a generic form), it is likely that even with a substantial price difference between innovator and incumbent, there may be an overall downward price trend in the market. Even if the incumbent is a relatively recent innovation, the entrance of the innovator may itself generate competition that causes the incumbent to drop its price. Medical innovation may reduce prices even though quality-adjusted prices of new entrants are higher than those of the incumbents in the cross section.

It is beyond the scope of this paper to estimate Δ and s'_k, but for each innovation in our

data, we can calculate how big the price drop would have to have been for overall prices not to have increased. The hypothetical pre-price so the average quality-adjusted price remains unchanged is

$$p_1^* = s_2 \frac{p_2}{q_2} q_1 + (1 - s_2) p_1$$

We calculate $\frac{p_1^* - p_1}{p_1^*} \cdot 100$, which is what the percent drop in prices would have been for overall prices to have remained constant. Figure 7 shows the cumulative distributions for the minimum price drops for different s_2. Since 32% of innovations have lower quality-adjusted prices than the incumbent, they do not require a price drop. For the other 68% of innovations, the median price drop required is 15%; if prices dropped 75% then 95% of innovations would have prices lower than the incumbent's pre-entry price. If the new innovation only gets 60% marketshare, then the median of those requiring a price drop is 10%; a price drop of only 64% is needed for 95% of all innovations to have prices lower than the incumbent's pre-entry price.

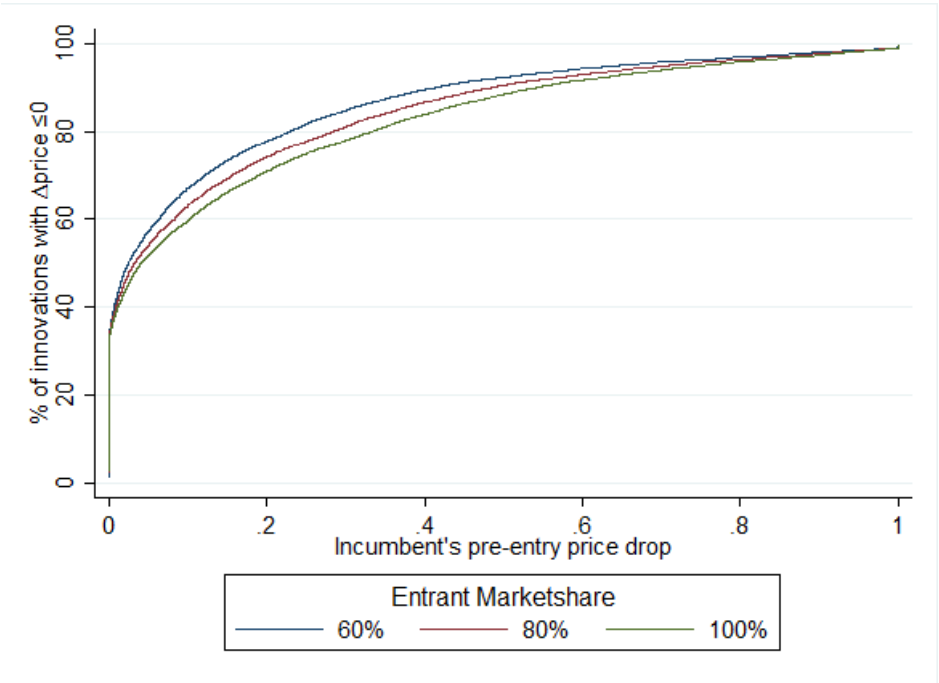


Figure 7: CDF of offsetting price drop

Note: This graph shows the cumulative distribution across innovations of incumbent's pre-entry percentage price drop necessary to generate no change in overall price-levels, for different entrant marketshares. For each innovation and marketshare, we calculate average quality-adjusted price in the market and then the incumbent price p_1^* that would give that average prior to the innovation's entry. The graph shows the CDF of $\frac{p_1^* - p_1}{p_1^*} \cdot 100$.

5.1 Illustration for two important case studies

Much of the policy discussion of pharmaceutical pricing in the last few years has been centered on new 'specialty drugs' and whether their incremental benefits justify their larger prices, i.e. whether they have higher or lower quality-adjusted prices. We use two salient specialty drug classes: treatments for the hepatitis C virus (HCV) and multiple sclerosis (MS) to illustrate potential differences in time series and cross sectional pricing patterns. These two drug classes have received much policy attention, the former for providing truly new innovations through cures and the latter because of rapidly rising prices of the same product over time. This analysis is the empirical analogue to Figure 6, which illustrated the theoretical possibility of prices falling or rising over time, depending on whether or not changes in incumbent prices over time offset the higher price of innovators in the cross-section.

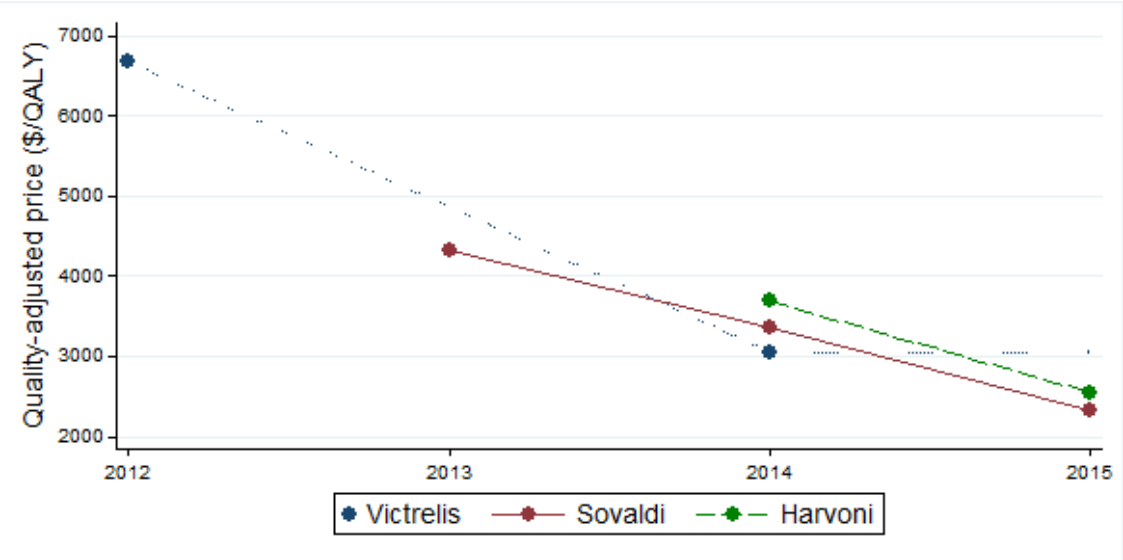


Figure 8: Hepatitis C drugs

Note: This graph shows the quality-adjusted prices for three Hepatitis C drugs over time. For Victrelis, the data are from two studies in the CEAR. For Sovaldi the prices come from Beasley (2015) and the the QALY is from a 2013 CEAR study. For Harvoni, the QALY and initial price are from Zhang et al. (2015) and the 2014 and 2015 price discounts are from Beasley (2015).

In the case of hepatitis C, Figure 8 shows the price patterns for the different products over time, with the entry date defined as the start of the series. Because the HCV drugs are fairly new, there are relatively few observations in the CEAR data, so we supplement from other sources. For Victrelis, CEAR has price and QALY estimates in 2012 and 2014, from which we calculate quality-adjusted prices. For Sovaldi we use the company's prices and announced discounts for 2014 and 2015 (Beasley, 2015), combined with the QALY estimate

from a 2013 CEAR study. We get the QALY and initial price for Harvoni from Zhang et al. (2015), which is the same type of study as the articles in CEAR, just published more recently. We again use the announced discounts to adjust the price over time.[6]

Sovaldi was the first innovation which offered a major increase in quality through essentially curing HCV through a 3 month treatment. As the graph indicates, the incumbent Victrelis dropped its price dramatically around Solvaldi's entry. Thus even though comparing their quality-adjusted prices in 2014, just after this entry occurred, would show the new innovation was more expensive, there was a substantial decrease in quality-adjusted prices. The HCV case is illustrative of the more general idea that when therapeutic price competition occurs through innovation, cross sectional and time series differences can be offsetting.

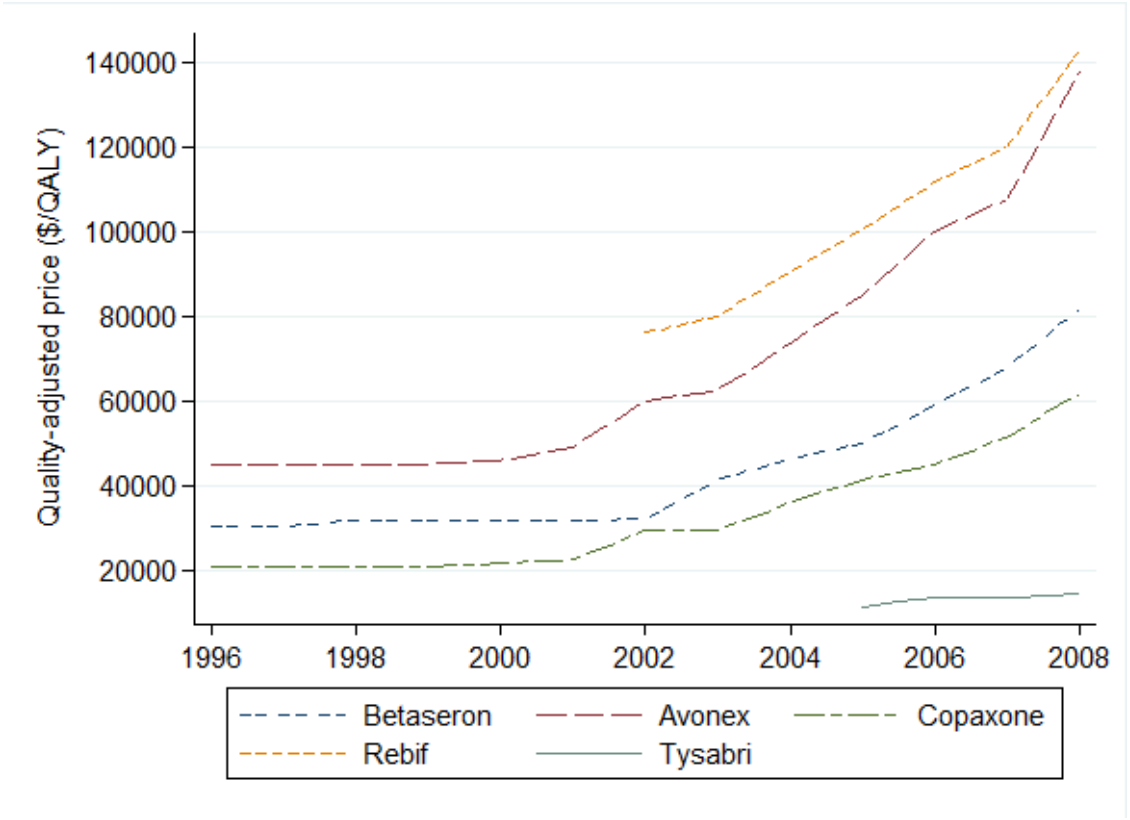


Figure 9: Multiple sclerosis drugs

Note: This graph shows the quality-adjusted prices for five multiple sclerosis drugs over time. The QALY estimates are the average from the CEAR studies and yearly prices are from Hartung et al. (2015).

The price patterns for multiple sclerosis drugs show a very different story. Figure 9 shows

[6] For example, the 2,552 $/QALY number for Harvoni in 2015 is the $94,500 that Zhang et al. (2015) say a course of treatment costs, divided by their estimated quality of 20 QALYs times .54 to account for the 46% discount reported by Beasley (2015).

quality-adjusted prices for MS drugs over time. These drugs have been around longer, so there are more observations in CEAR, but none of the drugs appear yearly. We use the (average) QALY estimate from the CEAR and yearly prices from Hartung et al. (2015) to get yearly quality-adjusted prices. If anything, the entry of Rebif in 2002 coincides with the incumbents raising prices and the prices for all drugs are increasing overtime. Therefore, the difference in quality-adjusted price between the new innovation Rebif and the incumbent one Avonex in 2004 understates the upward trend in prices in the market.

There are three reasonas that MS treatments are less substitutable than treatments for some other diseases. First, there is enormous heterogeneity in the MS population and treatment response, so chemically-similar drugs may have very different outcomes for the same patient (Lucchinetti et al., 2000). Second, MS is managed and not cured by treatments, so patients often need take a range of MS drugs over their course of therapy. Third, there are significant differences across MS drugs in their efficacy, tolerability, and mode of administration. For example, Avonex is an injection treatment that is often used a first line treatment because it has mild side effects though low efficacy. Tysabri, which is administered through infusion, is often used as a later line treatment because it has high efficacy and potentially serious side effects (Smith et al., 2010). Since the drugs are less good substitutes, they do not compete as much, so new drugs are less likely to cause incumbents to lower their prices. The MS case is illustrative of the more general idea that absent therapeutic price competition, prices for a given product may increase over time, so the cross sectional and time series differences may be mutually reinforcing.

6 Conclusion

Using the medical cost effectiveness literature to compare quality-adjusted prices of innovators and incumbents, we found that two-thirds of innovators had a higher quality-adjusted price than that of the incumbent; the median difference in quality-adjusted price was 4%. There are not systematic differences by disease type, though pharmaceuticals have somewhat larger differences, especially in recent years. There is some evidence that an innovator's quality-adjusted price is particularly likely to be high relative to that of the incumbent when there is a large difference in quality between the two. Studies done in the European Union and the United States have somewhat smaller quality-adjusted price ratios than studies done elsewhere, but innovations still tend to be more expensive than the incumbent technologies. We showed how prices may still fall over time, depending on the price trends of the incumbents: a price decline of 4% between a product's entry and the entry of the subsequent innovation would be sufficient to generate a net decrease in quality-adjusted prices over time in the majority of products.

We end by discussing some reasons why innovation may affect quality-adjusted prices differently in health care than in other industries, such as telecommunications, where next generation technologies often reduce quality-adjusted prices. Health care innovations may have fewer substitutes than those in other industries: a "first in class" designation can give a firm substantial market power, which may persist longer than in other industries because of the delay of new entrants due to the FDA approval process. Even average levels of market power may enable innovators to capture increased consumer value for treatments with an increased price; in this case, unmeasured cost offsets and complementarity between a treatment and income or the prevailing level of health can lead to price increases over time.

If a new innovation is only one component of the full set of costs associated with a diagnosis, then its impact on the other episode costs – 'cost offsets' – may be an important part of the value of the innovation. Drugs are usually a small fraction of the total episode cost but may generate cost offsets by preventing future doctor or hospital visits. If monopoly power allows the entrant to capture these cost offsets in a higher price for the innovation, then the quality-adjusted price may seem higher if the cost savings are not measured (though true total costs per quality may be lower). This explanation for larger quality-adjusted prices of innovators could be tested empirically if total costs and treatment costs could be separated, in which case cost offsets should have a positive effect on the innovator's premium.[7]

Two forms of health-related complementarities may raise quality-adjusted prices over time. One is the complementarity between health and more health care: a greater level of health over time raises the value of additional health going forward. For example, the value of treating a life-threatening disease is larger the longer you live in absence of the disease. As discussed by Dow et al. (1999), such complementarities are implied by competing risks models of mortality, which essentially involve a Leontief production function of overall length of lifetime from competing cause-specific lifetimes. If a healthier population values health improvements from a given disease more and this can be priced out by new innovators, quality-adjusted prices may rise with the baseline health level.

The second health related complementarity is between health and consumption (Hall and Jones, 2007). The willingness to pay for increased longevity rises with economic growth because the wealthier one is, the lower is the utility loss from foregoing consumption to extend life. Patent-protected monopolies may be able to extract this increased value of health and raise prices more and more for the same gains in health as incomes rise.

Another proposed explanation for increasing quality-adjusted prices in health care is the fact that a large portion of care is paid for by third-party payers – either public or pri-

[7] The price variable that we use is the most inclusive one available, but non-health costs were recorded for only a fraction of the studies; they may not have captured all indirect costs.

vate – so demand is not sensitive to price. However, this is more of an explanation for why markups in health care may be high than for why they would be increasing (without an increase in health insurance coverage). Others have argued that third-party payers decrease the incentive for cost-reducing innovations (Weisbrod, 1991). However, patients ultimately have to demand and pay the resulting higher premiums. Moreover, third-party payers seem almost "hyper-rational" in their purchasing decisions in that they use the very same cost-effectiveness studies analyzed here. In very few other industries do buyers use explicit quantitative metrics like these to quantify the costs and quality of products before purchasing. Though reimbursement by payers based on cost effectiveness is less institutionalized in the more privately financed US market than in Europe, the majority of cost effectiveness studies are actually done for the US market and funded by US manufacturers that would be unlikely to fund them unless they influenced US payers.

In summary, we believe that more systematic inquiry is needed on the impact of technological change on quality-adjusted prices in health care. The central debate is around whether increased spending is justified by larger health benefits. We have argued that the cost-effectiveness literature has implicitly analyzed such quality-adjusted prices over the last half century, but the analysis of quality adjusted prices by economists has not incorporated this useful, systematic evidence.

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