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THE IMPACT OF MEDICARE PART D ON PHARMACEUTICAL R&D

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ABSTRACT

Recent evidence suggests that Medicare Part D has increased prescription drug use among the elderly, and earlier studies have indicated that increasing market size induces pharmaceutical innovation. This paper assesses the impact of Medicare Part D on pharmaceutical research and development (R&D), using time-series data on (a) the number of drugs in clinical development by therapeutic class, and (b) R&D expenditures by firm. We demonstrate that the passage of Medicare Part D was associated with significantly higher pharmaceutical R&D for drug classes with higher Medicare market share, and for firms specializing in higher-Medicare-share drugs.

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1. INTRODUCTION

Medicare Part D is a voluntary federal prescription drug program that provides subsidized outpatient prescription drug coverage for the elderly and disabled. This program was enacted as part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), and coverage began in January 2006.

Prior to the implementation of Medicare Part D in 2006, with only a few exceptions[1] Medicare covered only prescription medicines "incident to" physician services, i.e., drugs provided in physician offices and hospitals. Recent evidence indicates that Medicare Part D has expanded drug coverage and increased prescription drug use by the elderly (Lichtenberg and Sun 2007; Duggan and Scott Morton 2008; Ketcham and Simon 2008; Yin et al. 2008). Prices received by the pharmaceutical companies for many drugs may also have increased, in part due to dual eligibles' loss of lower Medicaid-negotiated prices (Frank and Newhouse 2008).[2] Before Part D, dual eligibles (i.e., those receiving both Medicare and Medicaid) had prescription drug coverage under Medicaid, and Medicaid programs were legally entitled to receive the best price offered by pharmaceutical manufacturers to any private payer. In 2006, dual eligibles were automatically enrolled in private Part D plans, comprising some 29% of total enrollees. Because the MMA forbade federal price negotiation for Part D, pharmaceutical manufacturers could expect higher revenues for drugs used by the dual-eligible population, as well as increased utilization by newly-covered elderly individuals. This expectation of higher revenues most likely contributed to the pharmaceutical industry's switch from opposition towards advocacy for the Part D legislation in 1999 (Oliver et al. 2004).

Previous studies have shown that such increases in market size are significant drivers of pharmaceutical innovation (Kremer 2002; Acemoglu and Linn 2004). In addition, (Finkelstein

2004) found that increasing government payment (e.g., the 1993 decision for Medicare to cover influenza vaccination) induced greater investment in pharmaceutical R&D for vaccines. Finally, the pharmaceutical industry trade group PhRMA itself drew a connection between passage of a Medicare prescription drug benefit and increased R&D:

> "Successfully expanding prescription drug coverage for seniors and disabled persons will ensure that breakthroughs in basic scientific knowledge become safe and effective medicines for patients. If we fail, pharmaceutical innovation—especially with respect to medicines designed to treat the illnesses of aging—may suffer, thereby reducing hope for Medicare beneficiaries and their families. Modernizing Medicare is our best hope that today's and tomorrow's beneficiaries will reap the rewards of innovation: longer, happier, healthier, and more fulfilling lives." (Holmer, 1999)

Taken together, this evidence naturally raises the question: will expansion in the market for prescription drugs due to Medicare Part D induce increased pharmaceutical R&D? In this paper, we employ time-series data on (a) the number of drugs in clinical development by therapeutic class, and (b) R&D expenditures by firm to assess the impact of Medicare Part D on pharmaceutical R&D. We find that the passage of Medicare Part D was associated with significant increases, as compared with expected trends, in the number of drugs entering clinical development for drug classes most likely to be affected by Medicare Part D. Furthermore, although growth in R&D expenditures appears to have slowed overall since 2003, we find a significant positive correlation between the Medicare share of firms' R&D portfolios and firms' R&D expenditures since passage of Medicare Part D.

2. DATA AND METHODS

Data on Pharmaceutical R&D. Time-series data on the number of drugs by therapeutic class at each stage of the pharmaceutical research and development (R&D) pipeline were derived from the Pharmaprojects trend data "snapshot" published each May from 1998 through 2007. Pharmaprojects data are collected from a variety of public sources including press releases, patent filings, conference proceedings, regulatory agencies, and the medical literature, as well as through direct contacts with pharmaceutical companies and researchers. As noted by (Adams and Brantner 2006), this collection process may miss some drugs in early stage development. For this reason, we exclude preclinical R&D data from our analysis. However, commercial databases like Pharmaprojects are generally considered fairly complete for Phase II & III clinical trials—existence of a recruiting clinical trial is more difficult to hide than proprietary work in a firm laboratory. Even if some underreporting remains, we are less concerned about potential omissions for two reasons: (1) because our analyses estimate percent changes in R&D, rather than quantity or level changes after the introduction of Part D; and (2) because we have no reason to expect systematic bias in reporting across therapeutic classes that both (a) coincides with the introduction of Part D and (b) is correlated with Medicare market share. Unless both conditions (a) and (b) are met, underreporting will not bias our estimates.

Figure 1 shows the trends over time in the number of drugs entering each phase of clinical development for our panel of therapeutic classes. We observe the following notable features in our data. The number of drugs entering Phase I was steady, on average, through 2002, but increased markedly in 2003, and continued at that higher rate until another major increase in 2007. With the exception of an anomalous increase in 2001, the number of drugs entering Phase II clinical trials was steady through 2003, increased markedly in 2004, and then

like Phase I continued at a higher rate until another major increase in 2007. Finally, the number of drugs entering Phase III trials trended slightly downwards through 2003, then like Phase II increased markedly in 2004 and continued at that higher rate until another increase in 2007.

<FIGURE 1>

Data on Medicare share by therapeutic class. We estimated the share of total prescriptions filled by Medicare-covered individuals in each therapeutic class, using data from the 2004 Medical Expenditure Panel Survey (MEPS), a nationally representative survey of the US civilian non-institutionalized population. Because MEPS explicitly excludes drugs received while in hospital, it is particularly well-suited to estimating the Medicare-eligibles' share of outpatient prescription drugs newly covered under Part D. Approximately 42% of outpatient prescriptions were filled by Medicare-covered individuals. Therapeutic classes from Pharmaprojects were matched to therapeutic subclasses from the MEPS 2004 Prescribed Medicines file. Therapeutic classes were then grouped into a panel of 27 therapeutic categories based on common indications or biological system, and on similar elderly market share. Over 96% of the weighted total prescriptions in MEPS were assigned to one of these therapeutic categories. Figure 2 shows the resulting categories, ranked by Medicare market share.

<FIGURE 2>

Data on R&D expenditures and Medicare shares by firm. Pharmaceutical firms were identified in Compustat by SIC codes 2830-2836, and NAICS codes 325412-325414.[3] Firms were then hand-matched by name with originator firms in Pharmaprojects. Due to our focus on R&D decisions, we only included firms with non-zero, non-missing R&D expenditure data for all years 1997-2006, and for which at least one drug was reported in clinical development (Phase I trials through FDA registration) during our five-year baseline period, 1998-2002. We then

calculated for each firm the weighted average Medicare share of the firm's baseline clinical portfolio, as the sum of the MEPS-estimated Medicare share for each drug in the firm's portfolio divided by the total number of drugs in the portfolio.[4] This process resulted in a panel of 108 publicly-traded pharmaceutical firms, with an average baseline portfolio Medicare share of 41.4% (standard deviation 9.8%). For the US, at least, this panel appears to be fairly complete: for example, in 2006 the US-incorporated firms in our panel reported spending $56.2 billion on R&D; Burrill and Company estimated total US pharmaceutical industry R&D expenditures at $56.1 billion that year, for a difference within 1% (Pharmaceutical Research and Manufacturers of America 2007). Finally, firms' R&D expenditures were inflated using the Biomedical Research and Development Price Index (BRDPI)[5] to constant 2006 dollars. Figure 3 shows that, for our panel of 108 firms, real R&D expenditure growth overall slowed after 2003, then increased again in 2006.

<FIGURE 3>

Estimating the impact of Part D on R&D. We use two outcome variables for our analysis: (1) the number of drugs entering a given R&D stage, in a given therapeutic class and year; and (2) R&D expenditures by firm and year. If pharmaceutical companies respond to the increased market size as predicted, then all else equal we would expect to see an increase in the flow of drugs entering clinical development. We would also expect to see an increase in R&D expenditures at firms specializing in drugs for the Medicare market.

For each stage of R&D, we estimated difference-in-difference Poisson regression models. All our models include year fixed effects and therapeutic category fixed effects. These fixed effects provide a completely non-parametric approach to control both for underlying year-on-year differences in total R&D and time-invariant differences in the levels of R&D across drug

classes. In addition to these fixed effects, in each model we also include separate linear time trends for each therapeutic class.[6] These allow us to accommodate differences across classes in year-on-year R&D growth not only due to predictable changes in market size (e.g., due to demographics), but also differences in relative market saturation, existing marketed drugs' remaining patent life, and scientific understanding and technological advances for each disease category. Identification of the Part D effect, then, relies on changes in R&D versus expected trends, controlling for year-on-year variation, across therapeutic classes with different Medicare market shares. We estimate this effect via interaction of Medicare market share with a Part D dummy variable (Year > 2003). Intuitively, since the *absolute* change in the number of drugs entering clinical development following Part D should be proportional to the *size* of the Medicare market, the *percent* change in the number of drugs entering clinical development following Part D should be proportional to the Medicare *share* for the market.

Next, we investigated whether therapeutic classes which were previously heavily covered under Medicare Part B had lower R&D growth than one might otherwise expect, given their Medicare market share, by interacting those individual drug classes with the Medicare market share * Part D variable. We then considered possible dynamic effects of Part D over three time periods: (1) anticipatory effects in 2003, while the legislation was under debate in Congress; (2) transitional effects in 2004-2005, after passage but before Part D was implemented;[7] and (3) post-implementation effects in 2006-2007.

Finally, we investigated whether firms with higher average Medicare market share in their baseline R&D portfolios also had relatively greater investment in R&D after passage of Part D. For each firm we estimated the Medicare market share of their R&D portfolio, based on the average Medicare share of the drugs in their R&D pipeline (Phase I through FDA registration)

during a 5-year base period prior to Part D, 1998-2002. We then used these data to estimate ordinary least squares difference-in-difference models, for which the dependent variable was log(R&D expenditures). These models include time fixed effects to account for secular year-on-year variation in R&D that might be unrelated to Medicare Part D, firm fixed effects to account for time invariant differences in R&D levels across firms, and a firm-year operating income covariate to improve model fit. The key independent variables are the interaction of each firm's baseline Medicare share with one or more dummy variables for the passage of Part D.

Although the Poisson regression used with our first outcome variable is relatively robust to misspecification, over-dispersion in the data can create problems for estimating effect size. One measure of dispersion is the ratio of the deviance to the degrees of freedom, which for a good-fitting model should approach 1. Some of our models evidenced modest over-dispersion (dispersion is reported for each model in Tables 1-3), so we repeated our analyses using both zero-inflated Poisson and negative binomial regression (a generalization of Poisson), and obtained very similar results for our coefficients of interest.[8] Finally, we report confidence intervals and p-values for the coefficients using robust standard errors, clustered on therapeutic class to allow for serial correlation in the errors over time.

3. STUDY FINDINGS

First, we evaluated whether Part D differentially affected drug classes with higher Medicare market share. We find significant positive correlation after passage of Part D between the number of drugs entering Phase I ($p<.10$), Phase II ($p<.10$), and all clinical trials ($p<.05$), and therapeutic class Medicare share. That is, drug classes with higher Medicare share experienced significantly greater percentage growth in R&D post-2003 than classes with lower Medicare

share, versus the classes' expected trends. For the average Medicare share class (Medicare share = 42%), these results translate to an estimated 31% increase in Phase I trials, a 44% increase in Phase II trials, a 60% increase in Phase III trials, and a 40% increase in all clinical trials versus expected trends.

<TABLE 1>

Prior to the passage of Medicare Part D, certain drugs (e.g., IV cancer drugs, insulin for patients using pumps, COPD medications for patients using nebulizers, etc.) were already covered under Medicare Part B. For example, 12 of the top 20 medications covered by Part B, representing over 40% of Part B expenditures in 2001, were for cancer treatment, and 2 of the top 5 medications, representing over 12% of expenditures in 2001, were for COPD (Medicare Payment Advisory Commission 2003). Because a significant fraction of cancer and COPD drugs did not experience a change in insurance coverage with Part D, we would expect relatively lower effects of Part D on R&D for these classes. We tested this hypothesis by interacting the Medicare share*Part D variable with indicator variables for cancer and COPD, and as expected, nearly all of the coefficient estimates are significant ($p<.001$) and negative (see Table 2).

Finally, we looked for differential effects of Part D, over three different time periods: (1) anticipatory effects in 2003; (2) transitional effects in 2004-2005, after passage but before Part D was implemented; and (3) post-implementation effects in 2006-2007. We expected some ambiguity in 2003, due to two competing effects. On the one hand, the pharmaceutical industry was well aware of the progress of the MMA through Congress, and could have anticipated its passage by ramping up R&D. On the other hand, uncertainty about the bill's passage, provisions, or implementation might have deterred investment. For Phase I, we see no significant relationship between Medicare share and the percentage change in clinical trials in

2003. Thus, we cannot exclude the possibility that this year's marked increase in Phase I trials (per Figure 1) was due either to secular changes in R&D or to improvement in the Pharmaprojects data collection process. However, despite our observation that *overall* the number of drugs entering Phase III trials decreased in 2003, we do find strong positive correlation in 2003 between the percentage change in number of Phase III trials by class and Medicare market share. Thus, in the uncertain political climate of 2003, the pharmaceutical industry appears to have cut back the most expensive, late-stage trials, but predominantly for classes with lower Medicare share.

We expected to see increased impact of Medicare Part D in 2006-2007 versus 2004-2005 for two reasons. First, over time there was less uncertainty and more information available about the implementation and probable impact of Part D for the pharmaceutical industry. Second, the generally linear progression of drugs through the R&D phases seemed likely to yield lagged effects, especially for later-stage clinical trials. That is, while the number of drugs in preclinical development might respond rapidly, it would take time for those new drugs to proceed through the R&D pipeline. In Table 3, we observe evidence of one or both of these effects. First, we observe a significant positive relationship ($p<.10$) between Medicare share and the number of clinical trials, for all phases of R&D in both 2004-2005 and 2006-2007. Furthermore, this relationship becomes more pronounced over time: for all models except Phase II, the coefficient on Medicare Share * Part D is significantly larger ($p<.02$) in 2006-2007 versus 2004-2005. Thus, after controlling for anticipatory changes in 2003, we find that for the average drug class (with Medicare share 42%), Medicare Part D is associated with 37% more drugs entering Phase I trials in 2004-2005 ($p=.02$), and 52% more entering in 2006-2007 ($p=.01$) than would have been expected based on prior trends. Phase II clinical trials for the average drug class also appear to

have increased versus expectation, by 44% in 2004-2005 (p=.09) and 60% in 2006-2007 (p=.03), though as noted above this apparent increase over time is not significant (p>.10). Finally, compared with expected trends, Medicare Part D is associated with doubling the number of Phase III clinical trials for drug classes with average Medicare share in 2004-2005 (p=.04), and nearly tripling the number of Phase III trials (p<.001) in 2006-2007. These apparently dramatic effects in Phase III can be explained, in part, by the following observation: the median number of drugs entering Phase III trials in any given class and year is 3, with range 0 to 20 (i.e., these large percentage increases are occurring over a small denominator). In addition, because the confidence intervals for our point estimates are fairly wide, the Phase III results are not statistically different from those for Phase I and Phase II. Finally, due to inclusion of year fixed effects in our models, these coefficients should not be interpreted to indicate that all classes experienced positive R&D growth after 2003. In particular, in a separate analysis we found that after 2003, Phase III clinical trials significantly decreased versus prior year trends for drug classes with Medicare share of 20% and lower.

Given our results above, we expected that firms with more exposure to the Medicare market would have greater percentage increases in R&D expenditures after the passage of Part D. To test this, we investigated whether firms that had higher (weighted average) Medicare market share R&D portfolios prior to Medicare Part D also had greater percentage change in investment in R&D after passage of the Part D legislation. As shown in Table 4, consistent with our results above, even after controlling for year-to-year variations in overall R&D expenditures (e.g., there was essentially no growth in real R&D expenditures from 2003-2005, but growth resumed in 2006), we find that percentage change in R&D expenditures was not only positively correlated with Medicare share (p<.10) after passage of Part D, but that Medicare share became

significantly more important ($p<.05$) as a determinant of R&D expenditures over time. Interestingly, we also looked for anticipatory effects in 2003, but found no significant relationship between Medicare share and R&D expenditures prior to the legislation's passage.

4. DISCUSSION

Our results indicate that the increased outpatient prescription drug coverage provided through Medicare Part D has had substantial short-run impact on pharmaceutical R&D. We observe clear evidence of a break in established R&D trends beginning in 2004, just months after the Medicare Part D legislation was enacted, with greater percentage increases in R&D versus prior trends for drug classes that are most used by Medicare beneficiaries, and were not previously covered under Medicare Part B. Although we cannot completely rule out exogenous changes in R&D trends both coincident with Medicare Part D and correlated with Medicare share, this evidence does seem to suggest a causal relationship. As Finkelstein (2004) suggests, the relatively rapid response we observe may be due to "a substantial reservoir of technologically feasible products on the shelf for whom the decision to begin clinical trials is responsive, on the margin, to increases in the expected economic return to the clinical trial." These changes not only persist for the three years following the change in policy, but in fact become more pronounced over time. However, given that the *total* number of drugs entering clinical trials post-2003 did not significantly increase versus prior trends, this pronounced post-2003 shift towards clinical trials for drugs with higher Medicare market share may have come at the expense of new drugs for diseases which predominantly affect younger people. So, while Medicare Part D is associated with dramatic increases in R&D for high-Medicare-share classes,

this effect is being tempered either by contemporaneous decreases in overall R&D, or by targeted substitution away from low-Medicare-share classes.

The magnitude of our estimates appears reasonable, given the prior literature. Acemoglu and Linn (2004) found that the elasticity of innovation with respect to market size ranged from 3.5 for new molecular entities to 6 for all drug approvals. Duggan and Scott Morton (2008) predict that Medicare Part D increased pharmaceutical revenues by roughly 33% for drugs with Medicare market share of 100%. For a drug class with the average Medicare market share in our sample (42%), Duggan and Scott Morton's result translates to a 14% change in pharmaceutical revenues following Medicare Part D. Combining these results, we would expect an increase of between 49% and 83% in new drug development for the average drug class. Nearly all of our estimates are well within this range, and in many cases they are on the more conservative end. One surprising finding is the relatively rapid increase in number of Phase III clinical trails following Part D. Given the relatively short time elapsed since passage of Part D, we suspect that much of the observed increase in Phase III trials may be for drugs that were 'on the shelf', already marketed, and/or combination therapies that had already been tested in humans. These drugs could simply bypass Phases I & II. Anecdotally, this phenomenon is exactly what we're seeing in the market for cholesterol drugs—a significant increase in the number of Phase III trials mainly driven by new trials for combinations of drugs already on market[9].

These results should be viewed in light of our study's limitations. First, analysis of the overall effect of Part D on innovation is limited both by the relatively short time-series available post-2003, and by the fact that R&D is an imperfect predictor of the number and quality of new drugs ultimately developed. Given the long lag between drug discovery and development and new drug approvals, we cannot yet determine whether Medicare Part D will result in more (or

better) drugs entering the market. For example, the drugs added to the pipeline in response to Part D could be riskier investments, with potentially lower expected benefits. Finally, these relatively short-run effects on R&D may not result in increased innovation if the government implements aggressive price negotiations.

Medicare Part D not only reduces financial risk for elderly individuals today, but also has the potential to benefit the future elderly through increased flows of new drugs. If the flow of new and more expensive brand-name drugs increases, the federal cost of the Medicare Part D program may be higher than anticipated. On the other hand, these relatively short-run effects on R&D may not result in increased innovation if federal price negotiation is introduced, curtailing the expected market. Future research will be needed to determine whether these observed increases in R&D have any effect on new drug introductions and ultimately on health outcomes.

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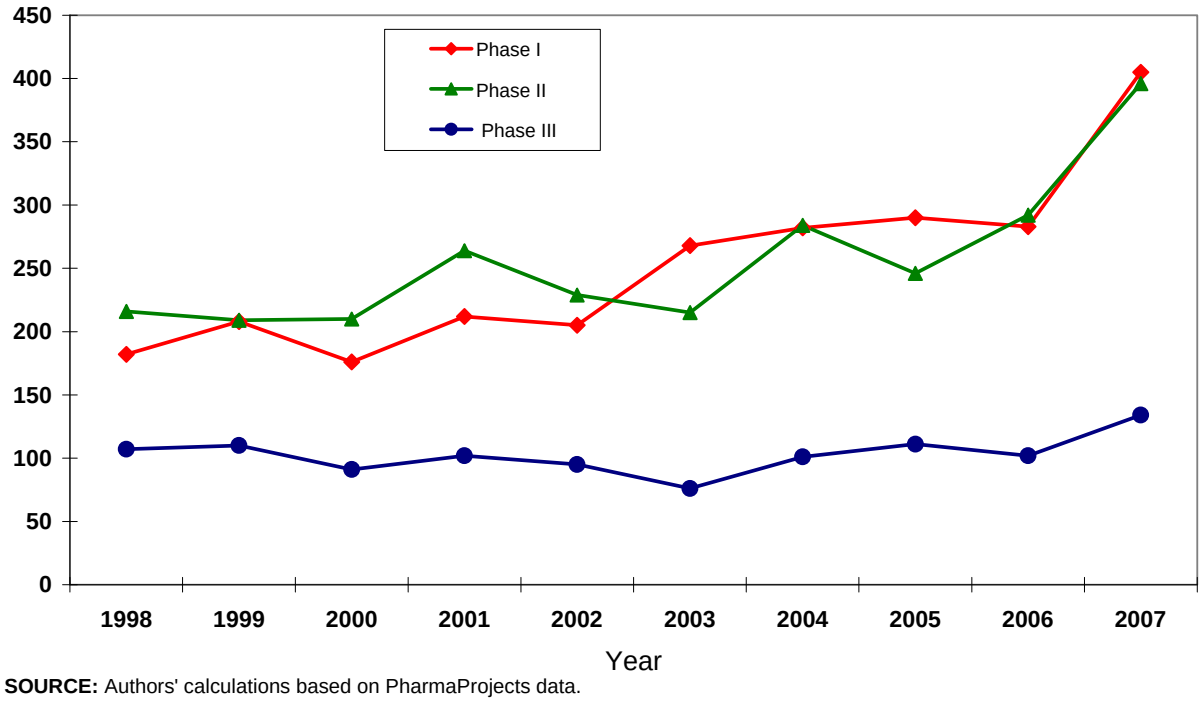
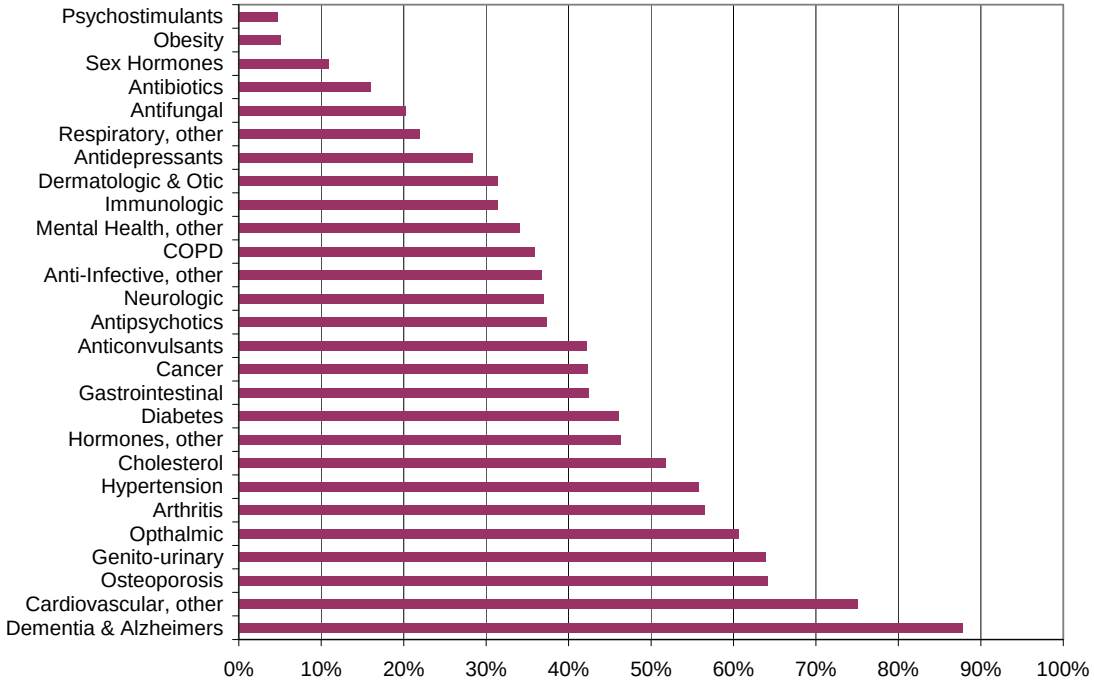
Figure 1.
Number of Drugs Entering Clinical Trials by Phase and Year, Selected Classes, 1998-2007



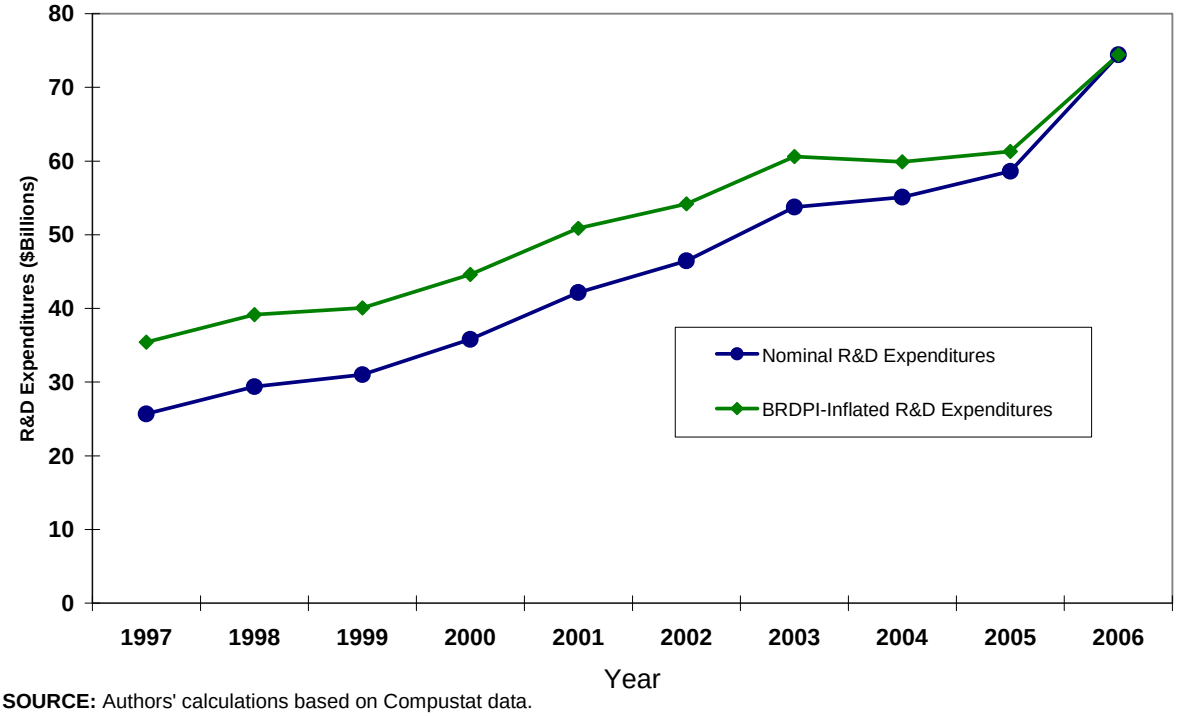
SOURCE: Authors' calculations based on PharmaProjects data.
NOTES: Includes only MEPS-matched therapeutic classes.

Figure 2.
Share of Total Prescriptions Filled by Medicare-Covered Individuals, by Therapeutic Category



SOURCE: Authors' calculations based on Medical Expenditure Panel Survey (MEPS) 2004 data.

Figure 3.
R&D Expenditures by Year, Panel of 108 Pharmaceutical Firms, 1997-2006



SOURCE: Authors' calculations based on Compustat data.
NOTES: Includes only Pharmaprojects-matched firms.

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Table 1.

Changes in the Number of Drugs Entering Clinical-Stage R&D After Passage of Medicare Part D, Associated with Medicare Market Share

	Phase I	Phase II	Phase III	All Clinical Trials
Medicare Share * Part D (Year > 2003)	0.729*	1.035*	1.424	0.947**
	[-0.044 - 1.502]	[-0.128 - 2.199]	[-0.519 - 3.368]	[0.063 - 1.832]
Observations	270	270	270	270
Dispersion	1.043	1.145	1.152	1.078
AIC	5.046	5.093	4.147	6.007

* significant at 10%; ** significant at 5%; *** significant at 1%

Notes: Authors' calculations based on Medical Expenditure Panel Survey (MEPS) 2004 and Pharmaprojects 1998-2007 trend data. All models are Poisson difference-in-difference, and include separate linear time trends and fixed effects for each therapeutic class, as well as time fixed effects. Robust 95% confidence intervals for the Z-statistics are presented in square brackets below each coefficient estimate. Standard errors are clustered on therapeutic class.

Table 2.

Changes in the Number of Drugs Entering Clinical-Stage R&D After Passage of Medicare Part D, for Classes Previously Covered Under Part B

	Phase I	Phase II	Phase III	All Trials
Medicare Share * Part D (Year > 2003)	0.655*	1.006*	1.447	0.906**
	[-0.114 - 1.425]	[-0.138 - 2.150]	[-0.517 - 3.412]	[0.028 - 1.784]
Cancer * Medicare Share * Part D (Year > 2003)	0.058	-0.483***	-0.987***	-0.340***
	[-0.069 - 0.185]	[-0.671 - -0.295]	[-1.318 - -0.656]	[-0.454 - -0.226]
COPD * Medicare Share * Part D (Year > 2003)	-1.769***	-0.533***	0.840***	-0.905***
	[-1.938 - -1.599]	[-0.718 - -0.347]	[0.496 - 1.184]	[-1.005 - -0.805]
Observations	270	270	270	270
Dispersion	1.005	1.145	1.150	1.051
AIC	5.024	5.099	4.152	5.993

* significant at 10%; ** significant at 5%; *** significant at 1%

Notes: Authors' calculations based on Medical Expenditure Panel Survey (MEPS) 2004 and Pharmaprojects 1998-2007 trend data. All models are Poisson difference-in-difference, and include separate linear time trends and fixed effects for each therapeutic class, as well as time fixed effects. Robust 95% confidence intervals for the Z-statistics are presented in square brackets below each coefficient estimate. Standard errors are clustered on therapeutic class.

Table 3.

Dynamic Changes in the Number of Drugs Entering Clinical-Stage R&D After Passage of Medicare Part D

	Phase I	Phase II	Phase III	All Clinical Trials
Medicare Share * Pre-Part D 2003	0.161	-0.012	1.647**	0.383
	[-1.238 - 1.559]	[-0.990 - 0.966]	[0.356 - 2.938]	[-0.310 - 1.076]
Medicare Share * Part D 2004-2005	0.877**	1.044*	2.383**	1.236***
	[0.113 - 1.641]	[-0.166 - 2.253]	[0.157 - 4.610]	[0.394 - 2.078]
Medicare Share * Part D 2006-2007	1.248**	1.421**	4.345***	1.863***
	[0.296 - 2.200]	[0.117 - 2.726]	[1.963 - 6.726]	[0.976 - 2.750]
Observations	270	270	270	270
Dispersion	1.048	1.151	1.111	1.057
AIC	5.057	5.104	4.122	5.998

* significant at 10%; ** significant at 5%; *** significant at 1%

Notes: Authors' calculations based on Medical Expenditure Panel Survey (MEPS) 2004 and Pharmaprojects 1998-2007 trend data. All models are Poisson difference-in-difference, and include separate linear time trends and fixed effects for each therapeutic class, as well as time fixed effects. Robust 95% confidence intervals for the Z-statistics are presented in square brackets below each coefficient estimate. Standard errors are clustered on therapeutic class.

Table 4.

Changes in the R&D Expenditures After Passage of Medicare Part D, by Firm Portfolio Medicare Market Share

	Model 1	Model 2
Medicare Share * Part D (Year > 2003)	1.791* [-0.092 - 3.674]	
Medicare Share * Pre-Part D 2003		0.283 [-1.418 - 1.985]
Medicare Share * Part D 2004-2005		1.742 [-0.912 - 4.395]
Medicare Share * Part D 2006		3.129* [-0.171 - 6.428]
Observations	1080	1080
Adjusted R^2	0.952	0.952

* significant at 10%; ** significant at 5%; *** significant at 1%

Notes: Authors' calculations based on BRDPI-inflated Compustat R&D expenditure data, 1997-2006, and Pharmaprojects 1998-2002 firm pipeline data. Both models are ordinary least squares, with outcome variable log(R&D expenditures), and include separate linear time trends and fixed effects for each firm, as well as time fixed effects. Robust 95% confidence intervals for the coefficient t-statistics are presented in square brackets below each coefficient estimate. Standard errors are clustered by firm.

NOTES

[1] Some exceptions to this rule included oral cancer drugs with IV equivalents, oral anti-emetics used within 48 hours of chemotherapy, immunosuppressants for recipients of Medicare-covered organ transplants, erythropoietin (EPO) for end-stage renal failure, and drugs administered via covered durable medical equipment, such as albuterol sulfate or ipratropium bromide used with a nebulizer or insulin used with an insulin pump.

[2] See also M. Freudenheim, "A Windfall from Shifts to Medicare," *New York Times*, July 18 2006, and A. Berenson, "Big Drug Makers Post Profits That Beat Forecasts," *New York Times*, July 25 2006.

[3] NAICS codes 325412-325414 include manufacturing of pharmaceutical preparations, diagnostic substances, and non-diagnostic biological products. Standard Industrial Classification (SIC) codes 283X include manufacturers of medicinal chemicals and botanical products, pharmaceutical preparations, diagnostic substances, and other non-diagnostic biological substances under the header category “Drugs”.

[4] We exclude from this calculation any drugs not in one of the 27 therapeutic categories matched in MEPS and Pharmaprojects.

[5] The BRDPI is generated by the Bureau of Economic Analysis, Department of Commerce, and was downloaded from: http://officeofbudget.od.nih.gov/UI/GDP_FromGenBudget.htm

[6] We also tested quadratic therapeutic-class time trends, but found little qualitative difference in the coefficient estimates, and model fit was not sufficiently improved by addition of these parameters to justify their inclusion.

[7] Beginning in June 2004, discount cards were issued to Medicare beneficiaries, providing a 15-20% discount on out-of-pocket costs for prescription drugs.

[8] Zero-inflated Poisson regression results available upon request to the authors. Negative binomial results were identical to those reported here, because when the overdispersion parameter in a negative binomial regression is not statistically different from zero, the negative binomial distribution is equivalent to a Poisson distribution.

[9] For example, in 2007, a record six cholesterol drugs entered Phase III trials compared to an average of 2 to 3 drugs in prior years. Several of these drugs were combinations of already marketed drugs: fenofibrate + simvastatin combination (both components already on the market); a new micronized formulation of fenofibrate; niacin + simvastatin (both on the market); niacin alone (again already on the market); ezetimibe + atorvastatin (both on the market); and finally JTT-705, the only novel compound entering Phase III that year. Thus, the total number of cholesterol drugs entering Phase III trials saw a two- or three-fold increase in 2007 versus prior years, and this growth was led mainly by new combination drugs.