Does Public Scientific Research Complement Industry R&D Investment?

The Case of NIH Supported Basic and Clinical Research and Pharmaceutical Industry R&D

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Non-technical Summary

Policymakers in the U.S. and abroad are engaged in an ongoing debate about the proper role of government in the development of scientific and technical knowledge. The debate centers on how much public money should be spent on scientific research and on which areas of research should receive funding. Policymakers who support public funding believe this research creates knowledge that complements private industry R&D investment by providing new ideas for products or processes or by helping firms to solve technical problems with their existing projects. On the other side, those who want to discontinue or reduce public funding believe this research substitutes for private R&D investment by drawing important research inputs out of the private sector or by funding a project that would otherwise have been pursued by industry firms.

This paper sheds light on the relationship between publicly financed biomedical research, which is performed mainly in university and non-profit research labs, and the investment behavior of private pharmaceutical firms. The main question in the paper asks if public basic and clinical research complement private industry R&D. An increase in industry investment in response to public research is strong evidence supporting a complementary relationship.

New micro-level data on public research investment by the U.S. National Institutes of Health allow measures of basic and clinical research in seven medical areas to be included in a distributed lag model explaining pharmaceutical R&D investment. These data are combined with data on pharmaceutical global R&D investment and sales to analyze the relationship between public and private R&D investment within technology areas over time.

The analysis finds strong evidence that both public basic and clinical research are complementary to pharmaceutical R&D and, thereby, stimulate private industry investment. However, differences in the importance and degree of scientific and market uncertainty between basic and clinical public research lead to differences in the magnitude and timing of the pharmaceutical investment response. The results indicate that a dollar increase in public basic research stimulates an additional \$8.38 in pharmaceutical investment after eight years. The industry R&D response to public clinical research is smaller in magnitude and shorter in duration with a dollar increase in public clinical research stimulating an additional \$2.35 in pharmaceutical investment over a three year period.

Does Public Scientific Research Complement Industry R&D Investment? The Case of NIH supported Basic and Clinical Research and Pharmaceutical Industry R&D*

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Abstract

This research investigates the hypothesis that publicly funded scientific research complements private R&D investment in the pharmaceutical industry. New micro-level data on public research investment by the U.S. National Institutes of Health allow measures of basic and clinical research in seven medical areas to be included in a distributed lag model explaining pharmaceutical R&D investment. Using a panel of therapeutic classes observed over eighteen years, the analysis finds strong evidence that public basic and clinical research are complementary to pharmaceutical R&D and, thereby, stimulate private industry investment. However, differences in the relevance and degree of scientific and market uncertainty between basic and clinical public research lead to differences in the magnitude and timing of the pharmaceutical investment response. The results indicate that a dollar increase in public basic research stimulates an additional $8.38 in pharmaceutical investment after eight years. The industry R&D response to public clinical research is smaller in magnitude and shorter in duration with a dollar increase in public clinical research stimulating an additional $2.35 in pharmaceutical investment over a three year period.

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1   Introduction

Policymakers in the U.S. and abroad are engaged in an ongoing debate about the proper role of government in the development of scientific and technical knowledge. The debate centers on how much public money should be spent on scientific research and on which areas of research should receive funding. Policymakers who support public funding believe this research creates knowledge that complements private industry R&D investment. They view this research, which is performed predominantly in universities and non-profit institutions, as providing new ideas for products or processes or as helping firms to solve technical problems with their existing projects. On the other side, those who want to discontinue or reduce funding believe public research substitutes for private R&D investment. They believe this research crowds-out private investment by drawing important research inputs out of the private sector or simply substitutes for private R&D by funding a project that would otherwise have been pursued by industry firms. (David et al. 2000a, 2000b)

Recognizing that complementarity and substitutability may happen concurrently and along dimensions that are not completely observable or measurable, existing research focuses on estimating the "net" effect of publicly funded R&D on private R&D. In a recent survey of the econometric evidence accumulated over the past 35 years, David et al. (2000a) report that most studies find complementarity, however, the overall literature is mixed and inconclusive.[1] The authors point out that the net effect found in many studies depends critically on the nature of the public research under investigation as well as the particular technological opportunity and appropriability conditions facing private firms.

This paper addresses the heterogeneity in publicly funded research and industry response by specifying an empirical model of R&D investment by the pharmaceutical industry across medical technology classes. Focusing on the pharmaceutical industry eliminates variation from inter-industry differences in technological opportunities and

appropriability conditions while distinguishing between medical technology classes addresses heterogeneity in opportunities across scientific areas of research. Similar to previous work (Wiggins 1983, Jaffe 1989, Ward and Dranove 1995) this distinction makes it possible to analyze the relationship between public and private R&D investment within technology areas over time.

The data and econometric improvements used this paper set it apart from the existing research by Ward and Dranove (1995). Unique and comprehensive grant and contract award data covering all of the U.S. National Institutes of Health (NIH) funding allow accurate measurement of public research investments into medical areas. For each medical class, these data allow public biomedical research funding to be separated by character of research into basic "laboratory" research and clinical "human" research. This is a significant advantage because pharmaceutical industry investment responds differently depending on the character of public research in question. Econometrically, the analysis addresses the endogeneity of industry sales in the R&D investment decision using exogenous measures of hospital admissions and mortality as instrumental variables.

Using 2SLS on a panel of seven medical classes over the 1981-1997 period, the estimation results show that both public basic and clinical research complement private pharmaceutical R&D. However, pharmaceutical investment responds differently to each type of public research. For public basic research, which is characterized by a high degree of uncertainty in its scientific "maturity' and its potential market applicability, *changes* in pharmaceutical investment have a "U" shape. Firms respond quickly to new information from public basic research then, after a period of holding the level of investment constant and allowing scientific and market uncertainties to resolve, firms again increase private R&D investment. This finding is consistent with established theory on investment under uncertainty described by Pindyck (1991) and Dixit (1992). The long-run elasticity estimate is

1.69 and suggests a dollar increase in public basic research stimulates an additional $8.38 of industry R&D investment after eight years.

Relative to basic research, public clinical research has very little scientific or market uncertainty and this difference is reflected in the timing of the pharmaceutical investment response. The industry R&D response to public clinical research is shorter in duration and smaller in magnitude. The results suggest that firms increase private R&D investment in response to public clinical research within the first three years with no significant impact thereafter. The long-run elasticity estimate is 0.40 and suggests a dollar increase in public clinical research stimulates an additional $2.35 of industry R&D investment after three years.

The paper begins with a discussion of the interaction between public and private research drawn mainly from case study evidence on pharmaceutical innovation. Section III outlines the empirical model of pharmaceutical investment while section IV discusses the data. Section V presents the estimation results and section VI contains concluding remarks.

2   Interaction between Public Research and Pharmaceutical R&D

How public scientific research influences private R&D depends on the nature of the research problems that industry scientists face in the pharmaceutical innovative process. There are two stages in this process, called drug discovery and drug development, and each stage involves a unique set of research activities. Drug discovery or "pre-clinical" research involves a wide spectrum of laboratory and non-human research activities ranging from identification of new drug concepts through to animal models and compound patenting. Having identified a promising new compound, drug development follows this stage with a full set of human clinical trials to determine compound safety and efficacy before seeking product approval from the U.S. Food and Drug Administration.[2]

Paralleling this division of industry research, public research investment can also be separated by character of research activity.[3] Basic or "fundamental" biomedical research can be broadly defined as bench-level laboratory research directed at the discovery and characterization of physiologically active substances and the definition of metabolic pathways related to normal and disease function. Public clinical biomedical research is patient-oriented research involving human subjects, including epidemiological research but excluding social, behavioral, occupational, and health services research.[4]

In both pharmaceutical research stages, the overall influence of public research will be determined by the degree to which industry scientists draw from and add to public scientific knowledge. Since it is not feasible to observe, measure and aggregate across individual scientists to calculate a "net flow" of knowledge from public research to industry R&D, the interpretation of the direction and magnitude established by statistical methods must rely on insights gained from case studies.[5]

There is a substantial body of case study research that describes a predominantly complementary relationship between private industry R&D investment and public basic research.[6] Most of this research highlights the role that basic research plays in opening up new avenues to therapeutic outcomes. It is useful to think of the new therapies being pursued by industry scientists as "therapeutic jigsaw puzzles" that must be completed before any new drug treatment can be taken to the market. Using this analogy, public basic research is providing either completely new puzzles or it is "resurrecting" puzzles that were previously believed to be unsolvable. In either situation, almost all of the case studies characterize the new puzzles emerging out of public basic research as "embryonic." (Colyvas 2002) These puzzles are in their early stages of scientific development and may only embody the faintest outline of a promising new therapy. A key takeaway from these studies is that public basic

research is characterized by a high degree of uncertainty in both its scientific "maturity" and its potential market applicability.

Beyond supplying new ideas for therapies, public basic research can contribute to industry solutions by providing "puzzle pieces" or by providing the clues required for discovering new pieces. In the case studies, these pieces and clues take the form of methods for identifying target compounds, validating these targets, scaling-up the quantities for animal and human testing, as well as laboratory models for animal studies. (OTA 1993, Cockburn and Henderson 1997, NIH 2000, Arora and Gambardellla 1994, Gambardella 1995) Because of the complexity and diversity of the puzzles confronting industry scientists, the pieces drawn from public basic research are rarely the "plug and play" variety. Information from this research must be "shaped" to fit the specific puzzle under investigation. Moreover, when public basic research only provides clues, new pieces must be invented to fit the puzzle.[7]

While most observers believe that public clinical research is complementary to industry research, there is relatively little case study evidence shedding light on this interaction.[8] The most specific type of clinical research, the drug trial, is a pure substitute for private industry research. At least with respect to a specific compound, a publicly supported clinical trial allows the industry to use their R&D resources elsewhere. If, for instance, a particular compound is shown to be toxic or ineffective, industry researchers do not need to spend additional funds to duplicate that research. This being said, the knowledge gained about a compound's absorption, toxicity, elimination, side-effect, and efficacy profile may provide valuable information to industry scientists. Using the specific knowledge gained from a publicly supported clinical trial, industry researchers might investigate a modified compound from the same "chemical family" or a modified dosage regime and find a safe and effective drug.

Cockburn and Henderson (1997) and others point out that publicly supported clinical research plays an important role in the process of finding new uses for older drugs. If

promising new indications are revealed from early phase clinical trials performed in the public sector, the industry may choose to pursue the full complement of clinical trials necessary for FDA approval. This type of complementarity may also arise in cases where the expected market value of a new use is low due to a high degree of uncertainty. Gelijns et al. (1998) suggest that public sector clinical researchers may have an important role to play in reducing uncertainty and perhaps facilitating the adoption of new drug candidates by industry firms. Moreover, public epidemiologic studies help the industry gauge demand for new therapies in the patient population. These alternative types of public clinical research are likely to stimulate additional investment by the industry.

The most recent empirical contribution looking directly at the relationship between public and private R&D investment is Ward and Dranove (1995).[9] Their analysis relates pharmaceutical investment to NIH research obligations using a panel of five therapeutic classes observed between 1970 and 1988. The authors' data did not allow them to differentiate between basic and clinical research. Instead, they use total financial obligations by National Institute (such as the National Cancer Institute, the National Heart Lung and Blood Institute, and so on) as a measure of public "basic" research in each therapeutic area. Unfortunately, NIH obligations by institute are a diverse set of financial commitments including basic, clinical, administrative, training, demonstration, construction, and other activities. Their main finding indicates that a 1% increase in NIH research obligations leads to an increase in industry R&D of 0.6% to 0.7 % after a lag of seven years.

3   The Model of Pharmaceutical Investment

The empirical model of pharmaceutical R&D presented below follows the investment framework described in David et al. (2000a). This framework is commonly used in the literature and has been applied to pharmaceutical investment using firm level data by Grabowski et al. (1980, 2000) and industry level data by Giaccotto (2004). The model

postulates that the level of investment is determined by the interaction between the marginal cost of capital (MCC) and the marginal rate of return (MRR). Factors that affect the availability of funds, such as sales revenue and interest rates, determine the shape and position of the MCC schedule. Factors that affect the demand, cost, and probability of success in research, such as health status, FDA regulatory stringency, and public scientific knowledge, determine the shape and position of the MRR schedule. Together, the equilibrium level of investment is determined.

In the empirical model used here, this framework is specified across medical technology classes. The factors affecting the availability of funds include gross revenues from sales and dummy variables to account for differences across classes and shifts over time due to, among other things, changes in the cost of capital. The factors that affect the returns to industry investment include measures of demand, proxies for basic and clinical public scientific knowledge, FDA regulation, and dummy variables to account for differences across classes and shifts over time due to, among other things, changes in drug regulations. The reduced form fixed effects model for an individual therapeutic class, i, in year, t, is:

Equation (1):

$$\ln I_{it} = \beta_0 + \beta_1 \ln S_{it-1} + \sum_{j=1}^{9} \alpha_j \ln B_{it-j} + \sum_{j=1}^{9} \delta_j \ln C_{it-j} + \beta_2 \ln R_{it-1} + \beta_3 \ln D_{it} + a_i + \gamma_t + \varepsilon_{it}$$

I_{it} is industry R&D investment in therapeutic class, i, and year, t and S_{it-1} is sales revenue in class, i, in the previous year, t-1. Gross sales revenue is a measure of the availability of funds for R&D investment and is lagged one year to reflect the pharmaceutical budgeting process (Grabowski 2000).[10] B_{it-j} is a distributed lag of public basic research investment in class, i, and year, t-j. C_{it-j} is a distributed lag of public clinical research investment in class, i, and year, t-j. The data allow these distributed lags to extend back nine years prior to industry investment.

R_{it-1} is a measure of FDA regulatory stringency. D_{it} represents a group of drug demand measures for class, i, and year, t. A sub-group of these measures, the ones that have no effect on industry R&D, are potential instruments for industry sales. The therapeutic class unobserved effect is a_i and the time dummies are γ_t. ε_{it} is an idiosyncratic error with the standard properties.

In order to estimate equation (1), the industry R&D series must be weakly dependent. However, using a standard Dickey-Fuller test, it is not possible to reject the null that industry R&D is a unit root process.[11] High persistence in the pharmaceutical investment series is hardly surprising when one remembers that it takes an average of twelve to fifteen years to develop a new drug.[12] To make the series weakly dependent, the analysis uses the log-difference estimator. Differencing the equation eliminates the therapeutic class fixed effects and specifies the equation in growth rates. The new estimating equation (2) is:

$$\Delta \ln I_{it} = \beta_1 \Delta \ln S_{it-1} + \sum_{j=1}^{8} \alpha_j \Delta \ln B_{it-j} + \sum_{j=1}^{8} \delta_j \Delta \ln C_{it-j} + \beta_2 \Delta \ln R_{it-1} + \beta_3 \Delta \ln D_{it} + \Delta \gamma_t + \Delta \varepsilon_{it}$$

The main hypotheses are that public basic and clinical research complement industry R&D investment in the long-run. To reduce multicollinearity and smooth the private investment response, the finite distributed lags for public basic and clinical research are restricted to lie on a 2nd degree polynomial. These are commonly referred to as Almon lags.[13] Across time, the estimated lag coefficients may be investment stimulating (positive lag coefficient) or investment saving (negative lag coefficient) for the industry depending on the nature and evolution of research projects in each sector. The long-run elasticity is calculated as the sum of the statistically significant lag coefficients. A positive long-run elasticity is interpreted as evidence supporting complementarity where public research stimulates additional private pharmaceutical investment. A negative long-run elasticity, however, is not conclusive evidence for substitution. Substitution has the additional requirement that firms

would have undertaken the research themselves and this cannot be determined from the available data.

In equation (2), growth in sales, $\Delta\ln(\text{Sales})$, should be viewed as endogenous. A common rule-of-thumb for industry executives is to set R&D investment as a fixed proportion of sales. (Grabowski et al. (1980, 2000)) Moreover, in a review of research in this area, Scherer (1996) points out that industry R&D growth may simply reflect an endogenous response to "the actual rise in gross profitability" instead of changes in response to "richer technological opportunities." (Scherer (1996), p. 269) Scherer (2001) explores this relationship further using industry time-series data and finds a positive relationship between gross profitability and R&D spending. Moreover, the causation runs in the opposite direction as well. R&D spending ultimately feeds back to determine sales revenue. This feedback is a violation of the strict exogeneity assumption needed for consistency of estimators.

To correct for endogeneity, I need instruments that do not belong in the industry R&D investment equation (2) but are also highly correlated with industry sales. Valid instruments may come from the group of hospital admissions and mortality demand measures as long as they meet these two conditions. In the empirical section, I use a two-step approach. First I determine the potential set of instruments from the demand variables by finding out which of these variables are appropriately excluded from the investment model. Next, from the set of potential instruments, I determine which of these has a strong partial correlation with pharmaceutical sales. Any demand measures that meet these criteria are valid instruments. It is important to recognize that the instruments are determined exogenously in the patient population and are not under the direct control of the pharmaceutical R&D decision makers. For the empirical model, I assume these measures are strictly exogenous.

While the empirical model used in this paper improves on the current literature, there are two modeling limitations that should be noted and addressed in future research. First, better data would allow one to estimate a structural model that explicitly characterizes the

channels through which public research and private R&D interact. At this point, research efforts intended to explore the channels such as publications, personal networks, and so on, face significant data limitations. The model in this paper treats the channels as an implicit "black box."[14]

Second, the model assumes that public research investment is exogenous to the private R&D decision by pharmaceutical firms. This is reasonable since pharmaceutical R&D decision makers have no direct control over the quantity or allocation of Federal research funding. Based on the lags in the model, public research is clearly a predetermined variable; however, the assumption does rule out feedback from current industry R&D to future public research investment. Failure of this strict exogeneity assumption can lead to inconsistency of the estimators. These limitations should be kept in mind when interpreting the empirical results.

4 Data and Descriptive Statistics

To estimate the impact of public basic and clinical research on industry investment, I use a panel of 7 medical therapeutic classes with observations running from 1981-1997. The therapeutic classes are defined by the U.S Department of Commerce, Bureau of Census. This classification scheme has been used by the industry to group R&D and sales data since the early 1960s. Seven therapeutic classes are considered: endocrine/neoplasm (cancer), central nervous system, cardiovascular, anti-infective, gastro-intestinal/genito-urinary, dermatologic, and respiratory.

The empirical analysis uses public investment into basic and clinical research as proxies for the generation of scientific knowledge. The proxies are defined using detailed data on grant and contract awards by the U.S. Department of Health and Human Services, particularly the NIH. The NIH is the largest public agency supporting biomedical research in the world. Their total budget for FY 2003 is $27.3 billion, an increase of $4.2 billion over the

FY 2002 budget. Further, the American Association for the Advancement of Science reports that the NIH is the second largest public agency supporting R&D in the U.S. after the Department of Defense and the largest agency supporting undirected or "basic" research. (AAAS 2001)

While the limitations of using investment flows to proxy for knowledge generation are well known, investment flows have at least three advantages over other measures of knowledge creation. First, other indicators such as patent and publication counts, perhaps weighted by citations, capture only one form of codified knowledge. At least in principle, investment proxies are general enough to capture all forms of knowledge creation, either codified or tacit. Second, investment flows are not restricted to any particular channel of dissemination. Only looking at published papers, on the other hand, misses public research flows that happen through conferences, networks or consulting. Third, other indicators of research output are not under the control of policymakers whereas the allocation of public funds for research is one of the most important policy tools available.

The investment proxies for public basic and clinical research knowledge are defined using the CRISP database (Computer Retrieval of Information on Scientific Projects) maintained by the NIH and covering the years 1972-1996. These data contain specific information about each biomedical grant and contract awarded by the NIH and other agencies in the DHHS. A multistage procedure was used to separate these data by character of research (basic, clinical, other) and further allocate grants and contracts to therapeutic classes. (Refer to Appendix A for a detailed description of the procedure.) This process results in seven public basic research flows and seven clinical research flows for every year in the CRISP database for 1972-1996. These flows are deflated using the NIH Biomedical Research and Development Price Index (BRDPI) maintained by the Bureau of Labor Statistics (base year is 2000). Figure 1 shows the broad level breakout of the complete CRISP database into basic, clinical, and other research types in real dollars. Figures 2, 3, and

4 plot the real flows of industry R&D and the real flows of public basic and clinical research for three of the seven therapeutic classes over the 1980 to 1996 period.

Pharmaceutical industry investment and sales by therapeutic class were gathered from various years of the Annual Survey report published by Pharmaceutical Research and Manufacturers Association (PhRMA). The R&D data correspond to PhRMA member R&D investment in the U.S. and abroad. The sales figures correspond to total industry sales, including non-PhRMA members, in the U.S. and sales of U.S. companies abroad. The nominal flows were deflated using the BLS Producer Price Index for Pharmaceutical Preparations (base year is 2000).

Regulatory stringency proxies by therapeutic class and year are constructed using data from the U.S. Food and Drug Administration. Following Wiggins (1983), the proxy is defined to be the average delay in months between the date of submission of a New Drug Application and the date of FDA marketing approval. If more than one compound is approved in a particular therapeutic class, then the regulatory delay variable is an arithmetic average of the observed review periods. For instance, if a therapeutic class has two approved drugs in a particular year, one with a ten-month delay and another with a fourteen month delay, then the delay period used in the analysis would be twelve months. This averaging methodology is intended to capture how pharmaceutical firms adjust their expectations of FDA regulatory review.

The demand variables and potential instruments are hospital admissions and mortality rates by therapeutic class and year in five age groups. These data were gathered from the National Center for Health Statistics and grouped into therapeutic classes using the ICD-9-CM (International Classification of Diseases Ninth Edition, Clinical Modification). Classification was performed at the 3-digit diagnosis level for each of the five age groups: less than 35 years old, 35-44 years old, 45-54 years old, 55-64 years old, and 65 and older. For each therapeutic class and age group, the hospital admission rates come from the

National Hospital Discharge survey and are defined per 1000 population. Similarly, the mortality rates come from the National Vital Statistics System, multiple-cause-of-death file, and are defined per 1000 population.

5   Estimation Results and Discussion

The empirical analysis takes place in two steps. The first step consists of three pooled OLS regressions that are used to determine which variables belong in the model. This is a necessary first step since it is unknown which of the hospital admissions and mortality demand variables are potential instruments for pharmaceutical sales. If these variables have a significant effect on pharmaceutical R&D, then they should not be excluded from the model and are not valid IV candidates. Having determined the IV candidates and verified their partial correlation with pharmaceutical sales, the second step in the analysis consists of three pooled 2SLS regressions.

Before turning to the actual estimates, it is also important to recall that the lag distributions for public basic and clinical research are specified as 2nd degree polynomials.[15] The coefficient estimates for the quadratic polynomial terms are reported in the tables. The implied lag coefficient estimates and their statistical significance will be reported and discussed for the final specification of the 2SLS model. In Tables II and III, the explanatory variables that are statistically significant are shown in boldface. The bottom of each table lists various regression diagnostics.

Columns (1)-(3) of Table II report the OLS regression results. Column (1) contains the "fully specified" model that includes all of the available explanatory variables including year time dummies. Since the year time dummies are not jointly or individually significant, the model in column (2) replaces these with a time trend. Model (3) cleans up the specification by dropping the other insignificant regressors.

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Looking across the regressions in Table II, it is evident that both public basic and clinical research significantly impact the growth of pharmaceutical R&D investment. The quadratic specification works well for public basic research, however, both the linear and quadratic terms are insignificant for public clinical research. This will be addressed in the 2SLS regressions in Table III. Growth in pharmaceutical sales is significant in models (2) and (3) when the time dummies are dropped and replaced with a linear time trend. The insignificance of industry sales in model (1) is probably due to multicollinearity between industry sales and the time dummies. The effect of FDA regulatory delay, which is a proxy for regulatory stringency, is not economically or statistically significant in either model (1) or (2) and is dropped in model (3).

As for the patient demand variables, four of the ten are significant. The results indicate that pharmaceutical R&D investment increases strongly in response to the health conditions of people in the 55-64 year old age group. These are the conditions driving increases in hospital admissions and mortality. However, growth in pharmaceutical R&D falls in response to greater hospital admissions for people over sixty-four. It is difficult to know exactly why this occurs but it could reflect that fact that hospital admissions for the oldest people are for conditions that are not amenable to drug therapy. Also, growth in pharmaceutical investment decreases with higher mortality rates in those individuals between 35 and 44 years old. This probably reflects the fall in expected returns to investment as these potential customers are lost.

While the OLS regressions are the proper place to start, Scherer and others note that the volume of pharmaceutical sales is an endogenous variable in a pharmaceutical investment model. On the one hand, increases in sales lead to greater R&D investment, either by providing internal funds for investment or by capturing expected demand; on the other hand, current R&D leads to future sales. Of the six potential IV candidates identified in the first step of this analysis, hospital admissions for people less than 35 years old is the only valid

IV. This variable has strong partial correlation with pharmaceutical sales in a first stage regression with a t-statistic of -2.19 and a p-value < 0.03 while the other variables have no significant partial correlation with sales. Consequently, one valid instrument is available and the 2SLS regressions presented in Table III are just-identified.

Columns (1)-(3) of Table III report the 2SLS regression results. Column (1) uses the same specification as model (3) of Table II. As is typical in an instrumental variables regression, the standard errors are larger than the OLS regressions and, consequently, hospital admissions for people over sixty-four years of age are insignificant. The time trend also becomes insignificant. The model in column (2) drops these variables. The final model, which is given in column (3), tightens up the specification on public clinical research. High multicollinearity between the polynomial terms for public clinical research is the likely culprit for the insignificance of the linear and quadratic terms; however, these terms are not jointly significant using a standard F-test. Dropping the quadratic term dramatically reduces the standard errors for public clinical research and the linear term is now significant. This confirms the presence of multicollinearity. While model (3) is used for the subsequent discussion, one could easily use model (2) as well. The only difference between the models is that model (3) gives slightly larger magnitudes for the effects of public basic and clinical research while model (2) provides a more intuitive shape for the lag distribution for public clinical research (quadratic versus linear).

The empirical analysis finds strong evidence that public basic research is complementary to private pharmaceutical R&D investment and, thereby, stimulates additional private investment. Using the estimated polynomial parameters in model (3) of Table III, Figure 5 graphs and reports the estimates of the underlying lag coefficients for public basic research. Each of these lag coefficients is an elasticity and measures the percentage change in the growth of pharmaceutical R&D in response to a one percent increase in the growth of public investment into basic research. Only four of the eight

elasticities reported at the bottom of Figure 5 are significantly different from zero. These are the first two lags and the final two lags of public basic research. Using a two-sided test, the p-values of each of these coefficients are, respectively: p-value < 0.006, p-value < 0.034, p-value < 0.026 and p-value < 0.002. The long-run elasticity, which is the sum of the statistically significant lag coefficients across time, is 1.69. This is over twice as large as the elasticity found by Ward and Dranove (1995); however, the estimates are not directly comparable since their analysis used a very different model and data.

What about the "U" shape of the industry response over time to public investment in basic research? Recall that public investment is a proxy for scientific knowledge generated by research institutions outside the pharmaceutical industry, primarily universities. Scientific knowledge generated by basic research is characterized by a high degree of uncertainty with respect to both its scientific "maturity" or "completeness" and its potential market application. The newest ideas emerging from public basic research are the most uncertain and will appear in the first lag. With each successive year, these ideas are further developed by researchers in public research institutions. As the idea "ages" and moves through the lag distribution many of the scientific and market uncertainties will be resolved. The latter part of the lag distribution, lags seven and eight, represent knowledge from public basic research that has evolved through seven or eight years of further development.

To understand the time profile of the private pharmaceutical investment response one must look to the theory of investment under uncertainty described by Pindyck (1991) and Dixit (1992). A fundamental insight of this work is that a firm's optimal investment response can involve waiting or delaying investment until uncertainties have been sufficiently resolved. Further, the theory points out that the value of waiting depends on the degree of uncertainty and the degree of inter-firm competition. Greater uncertainty increases the value of waiting while competition reduces the value of waiting.

The results shown in Figure 5 illustrate both a competitive effect and a waiting effect. The newest ideas emerging from public basic research elicit an initial burst of investment by pharmaceutical firms as they try to evaluate this new information, build absorptive capacity and compete with rival firms. This is a competitive "buy-in" effect. After this initial burst, firms maintain their research programs and monitor research progress at universities and other research institutions. It is in this period that firms exercise their option to wait and do not significantly increase investment. When scientific and market uncertainties are sufficiently resolved, an average of seven years following the emergence of the original idea, pharmaceutical firms again significantly increase their investment in response to public basic research.[16] It is important to note that the level of private investment does not fall over this period. Figure 6 shows how the level of private pharmaceutical investment responds over time to changes in public basic research.

The empirical analysis also finds strong evidence that public clinical research is complementary to private pharmaceutical R&D investment and, thereby, stimulates additional private investment. However, relative to public basic research, public clinical research has very little scientific or market uncertainty. Accordingly, the value of waiting is much smaller and one should see firms responding quickly to new and valuable information, particularly when competitive pressures are strong. This is exactly the pattern that emerges from the analysis. Figure 7 shows that pharmaceutical R&D investment increases in the first three years following public investment in clinical research. After this, there is no significant change in private investment as public clinical research "ages." Using a two-sided test, the p-values of each of the first three lags of public clinical research are, respectively: $p < 0.018$, $p < 0.02$ and $p < 0.032$. Summing the coefficient estimates of these three lags gives a long-run elasticity for public clinical research of 0.40. Figure 8 shows how the level of private pharmaceutical investment responds over time to changes in public clinical research.

The results from model (3) in Table III also show that changes in pharmaceutical sales and patient demand influence the growth in pharmaceutical R&D investment. With the impact of expected demand on pharmaceutical investment is held constant, the partial effect of pharmaceutical sales measures how changes in the availability of internal funds affects pharmaceutical R&D investment.[17] A 10% increase in internal funds leads to a 5% increase in R&D investment and this is strongly significant with a p-value < 0.05. In previous work, Giaccotto (2004) find a slightly larger elasticity of 0.58; however, their estimate includes both a cash flow and an expected demand effect. The demand variables, which were discussed above in the context of the OLS specification, have larger magnitudes in the 2SLS regressions.

It is informative for policy purposes to calculate the marginal impacts of the key explanatory variables on pharmaceutical R&D investment. The marginal impact is calculated as the product of the long-run elasticity and the ratio of mean pharmaceutical R&D investment to the mean of the variable of interest. The marginal effects, consequently, depend on the relative magnitude of the measured variables. Table IV reports these data for public basic research funding, public clinical research funding and industry sales. A \$1 increase in public basic research generates an \$8.38 increase in private pharmaceutical R&D after eight years. A \$1 increase in public clinical research generates a \$2.35 increase in private R&D after three years. With respect to industry sales, each new dollar of revenue increases next year's R&D investment by 8 cents.

6 Conclusion

This paper sheds light on the relationship between publicly financed biomedical research, which is performed mainly in university and non-profit research labs, and the investment behavior of private pharmaceutical firms. The main question in the paper asks if public basic and clinical research complement private industry R&D. An increase in industry

investment in response to public research, reflecting the genesis of new projects or the further development of "embryonic" ideas, is strong evidence supporting a complementary relationship. The analysis finds that both public basic research and clinical research investment stimulate additional private pharmaceutical R&D.

There are three other notable conclusions stemming from this research. First, to evaluate how private investment responds to public research investment it is critically important to take into account the character of the public research under investigation. Depending on the information content and the degree of uncertainty characterizing the public research, the investment behavior of firms will be different in both magnitude and timing. Second, the pharmaceutical investment response to public basic research is over 3.5 times larger than it is for public clinical research. This suggests that public basic research is more important to the pharmaceutical innovative process than public clinical research. However, looking back at Figure 1, it is clear that the NIH has dramatically increased clinical research investment relative to basic research investment since the early 1990s. This trend will probably reduce the future opportunities for new drug innovation stemming from public research. Third, this analysis finds that internal cash flow is an important determinant of pharmaceutical R&D. If price controls on pharmaceutical products are put in place, as many policymakers favor, pharmaceutical R&D investment will fall.

While this paper improves both the data and econometric method used in previous research, the empirical findings should be viewed as suggestive rather than definitive. The diverse and interactive nature of public and private research in the pharmaceutical industry makes it difficult to pinpoint individual effects and attach causal interpretations. Future research should focus on developing empirical models of public-private interaction that explicitly identify the channels of information exchange and relax the strict exogeneity assumption on public research investment.

Further, one should be cautious about interpreting the marginal impacts too literally. The NIH investment flows are proxies in the analysis for *all* of public research investment. Clearly, there are contributions to investment from other public institutions in the U.S. and abroad. Assuming the NIH funding flows provide a good relative picture of basic versus clinical investment, the log-log functional form implies the elasticity estimates are valid even without having total world public research investment figures in the study. However, the story is not the same when one tries to calculate marginal impacts because these estimates depend on accurate figures for total world investment in basic and clinical public research. For instance, if the NIH represents 50% of the total world investment into public basic and clinical research, a number that probably underestimates the NIH share, then the marginal impacts are themselves scaled down by 50%.

It is also important to keep in mind that universities are the primary performers of basic and clinical public research analyzed in this paper. In addition to the creation of new knowledge, public support of university research helps to train both undergraduate and graduate students. These students may become employed in the pharmaceutical industry and carry with them the research knowledge and experience made possible through public support of their training. So, it is not possible to separately identify complementarity due to disembodied knowledge spillovers and complementarity due to the transfer of knowledge in people. Both mechanisms are probably important and, given improvements in data, future research should try to decompose the impact of public research into its labor and pure knowledge spillover components.

Appendix A: Data Construction

Proxies for public basic and clinical research investment are created using the CRISP database (Computer Retrieval of Information on Scientific Projects) maintained by the NIH and covering the years 1972-1996. This database contains information on extramural and intramural biomedical research grant and contract awards by the NIH and other governmental agencies under the authority of the U.S. Public Health Service. (These other agencies include the FDA, the Center for Disease Control, the Agency for Health Care Policy and Research, and so on.) For each grant and contract the database contains: record ID, investigator name, title of project, narrative description of project, organization receiving the award, address, administrative organization of the NIH or other agency, award amount, type of award, fiscal year of award, city, and state. Using a second administrative NIH database, called IMPAC, CRISP records were supplemented to include the scientific review group that recommended approval. A scientific review group is a committee of peers within a scientific field that review grant applications and recommend applications for approval to the National Advisory Councils.

Identifying relevant research took place in two stages. This first stage separates all awards into three groups (mixed, clinical, and other) using the "type of award code" field. (These are codes like R01 for traditional research award or K08 for clinical investigator award.) A second step in this stage requires taking the mixed group and separating out any remaining clinical and other awards using keyword searches over the grant and contract titles. This finalizes the breakout into basic, clinical, and other. The second stage takes the basic and clinical groups and separates them into the seven therapeutic classes and a general category. This is done is five steps. First, eliminate agencies that do not fund basic or clinical research relevant to the pharmaceutical industry. This eliminates organizations like the CDC, the National Library of Medicine, the National Institute of Nursing Research, and so on. Second, match scientific review groups to their respective therapeutic areas. Third, use keyword filters to further sort those grants and contracts not matched by scientific review group. Fourth, allocate the remaining uncategorized grants and contracts to therapeutic classes using the Institute codes. For instance, the remaining National Cancer Institute grants go to the endocrine/neoplasm class; the remaining National Eye Institute goes to the central nervous system class, and so on. Fifth, for those Institutes which are too general to be classified (such as the National Institute of General Medicine), allocate these grants and contracts across the seven classes in proportion to those successfully categorized.

The process results in seven public basic research flows and seven clinical research flows for every year in the CRISP database, 1972-1996. These flows are deflated using the NIH Biomedical Research and Development Price Index (BRDPI) maintained by the Bureau of Labor Statistics (base year is 2000). Figure 1 shows the broad level breakout of the complete CRISP database into basic, clinical, and other research types in real dollars.

Notes

1.   Most of this literature is focused on the impact of publicly funded research that is performed directly by the private firms receiving the money. The current paper considers the impact of public financing of research that is performed mostly by non-profit research scientists in universities and asks how this research affects private R&D investment. Guellec et al. (2000), in a recent contribution to this literature, find that government funded research performed directly by firms stimulates additional firm R&D while government funded research performed by universities reduces industry R&D investment. While this finding does not support the complementarity hypothesis, the authors point out that they are only able to allow a four year lag in the relationship between university and industry research.

2.   The separation of research into medical therapeutic classes is a similar delineation of research problems and solutions by broad character.

3.   Public research is scientific research that is financially supported with public funds and performed almost exclusively in hospitals, not-for-profit research institutes and universities.

4.   This definition is more restrictive than the definition of clinical research put forth by the NIH Director's Panel on Clinical Research. (NIH 1997) However, the NIH definition of clinical research has been criticized as being too broad. (Reichert et al. 2002)

5.   To assess complementarity versus substitutability using investment it is also necessary to track how private R&D funding decisions respond to information from public research.

6.   Maxwell et al. (1990), OTA (1993), Cockburn and Henderson (1997), NIH (2000), Reichert et al. (2002), Colyvas (2002).

7.   The discussion here encompasses the idea of "absorptive capacity" which posits that private firms must be actively investing in research in order to access, evaluate, and use public scientific knowledge. (Cohen and Levinthal 1989, Arora and Gambardella 1994)

8.   Maxwell and Eckhardt (1990) find that clinical research played an important role in the initiation of 23% of the 30 lines of research in their study. (page xxiii) However, they define the term clinical to mean "…the research was carried out in humans or *human material* [emphasis added]." In the current paper, clinical research is defined to include only research involving actual patients. Consequently, research using "human material" is included in the basic research category to the extent that it did not involve direct contact with patients.

9.   There is an active empirical literature that attempts to measure the connectedness between public and private research and relate this to productivity in the pharmaceutical industry. Cockburn and Henderson (2000) provide a good overview. This literature, however, is not directly relevant to this analysis. This analysis explores the relationship between R&D inputs and not between public research and industry productivity.

10. Scherer (2001) examines the relationship between gross profitability and pharmaceutical R&D. Vernon (2004) points out that industry sales serve two roles: an indicator of expected profitability and internal funds for investment. Since the model used here already includes controls for demand that affect expected profitability, the partial effect of gross sales is interpreted as measuring the impact of internal financing. The availability of internal funds

for financing investment is important when capital markets are imperfect. See Hubbard (1998) for a discussion.

11. A Dickey-Fuller test with trend and an augmented Dickey-Fuller test were also performed. The null hypothesis of a unit root for industry R&D could not be rejected in either test. Also, the augmented DF test did not indicate any dynamic misspecification.

12. Henderson and Cockburn (1996) also found high persistence in the R&D process in their analysis using proprietary firm data.

13. I would like to thank the editor for suggesting this formulation. An earlier draft of this research left the lag coefficients completely unrestricted. Imposing the polynomial restrictions leads to slightly larger coefficient estimates but does not change the research findings. These restrictions do facilitate interpretation, however, by eliminating fluctuations in the lag estimates that resulted from multicollinearity between the public research flows.

14. See Cohen et al. (2002) to learn about the many channels that link public and private R&D. Also, see Cockburn and Henderson (2000) for a review of recent empirical work using measures that focus on specific channels like publication co-authorships.

15. Higher order polynomial terms are not significant for either public basic research or public clinical research.

16. An anonymous referee suggested the possibility that the industry response to the newest public research ideas, as captured in lags 1 and 2, could be spurious and simply represent a simultaneous public and private investment response to some scientific breakthrough. If this is true, public and private investment should be contemporaneously correlated as both groups of decision makers respond to the breakthrough. To explore this possibility, contemporaneous public investment was included in the model but was always insignificant with a coefficient near zero. While pharmaceutical decision makers are clearly responding to the most promising research findings emerging from publicly funded research, there does not appear to be any omitted source of scientific breakthroughs that induces a simultaneous reaction by both public and private investors.

17. As noted by an anonymous referee, the pharmaceutical sales data used in the analysis include sales by non-PhRMA members in addition to PhRMA members. Theoretically, the sales data should only represent PhRMA member firms. However, since aggregate totals show that the non-PhRMA members make up a small share of total sales; this is unlikely to significantly influence the results.

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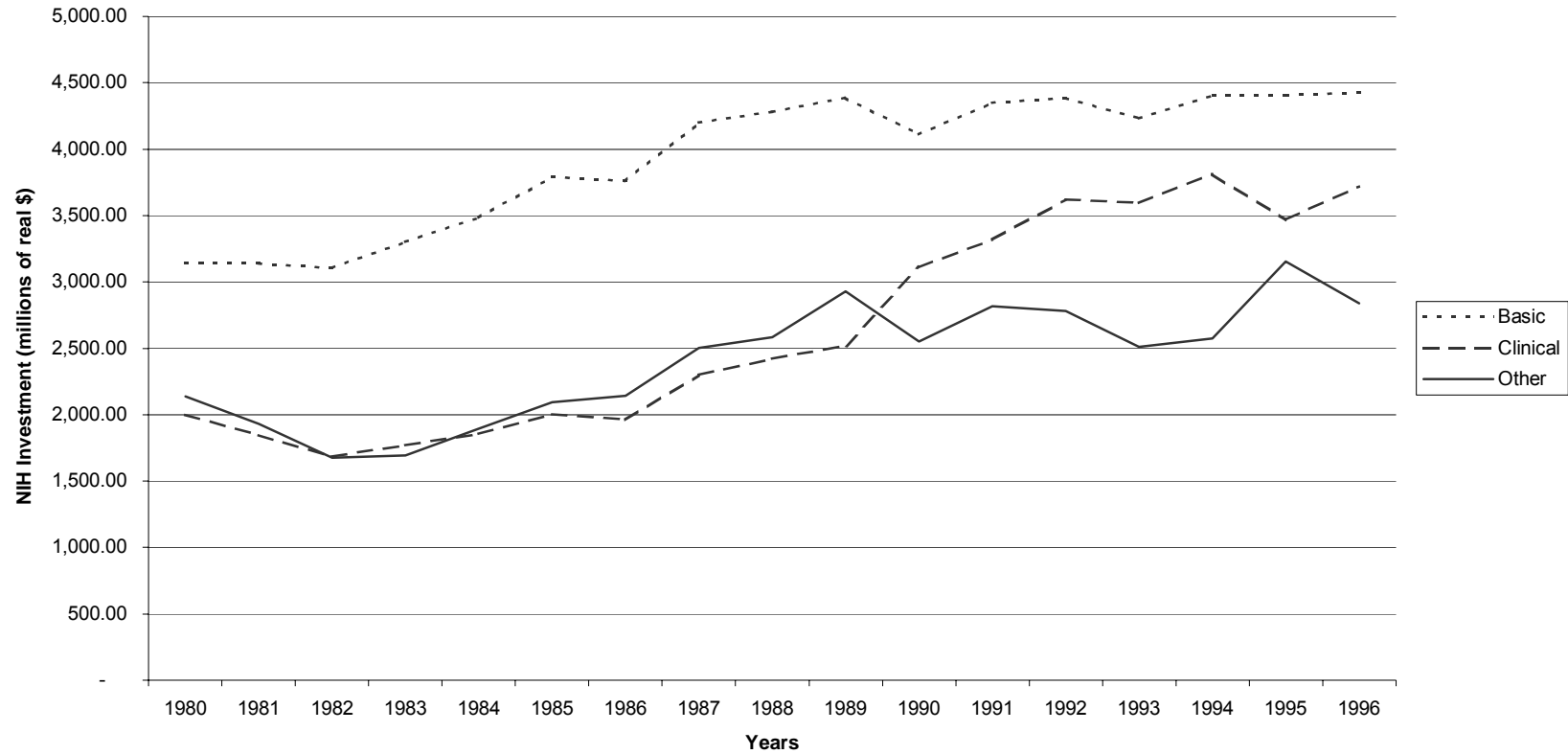**Figure 1: Public Biomedical Research by Type: Basic, Clinical, Other**

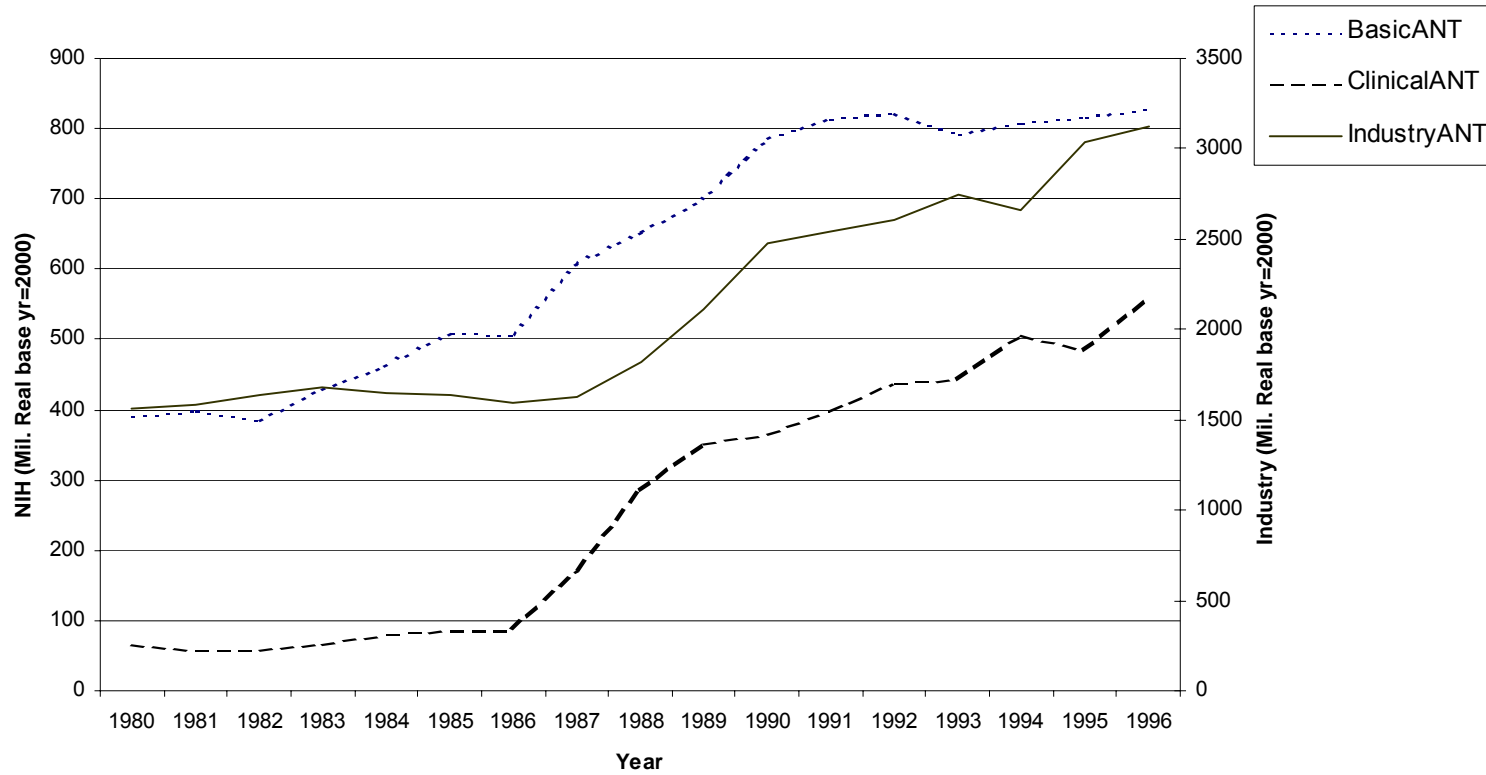**Figure 2: Anti-infective Therapeutic Class**

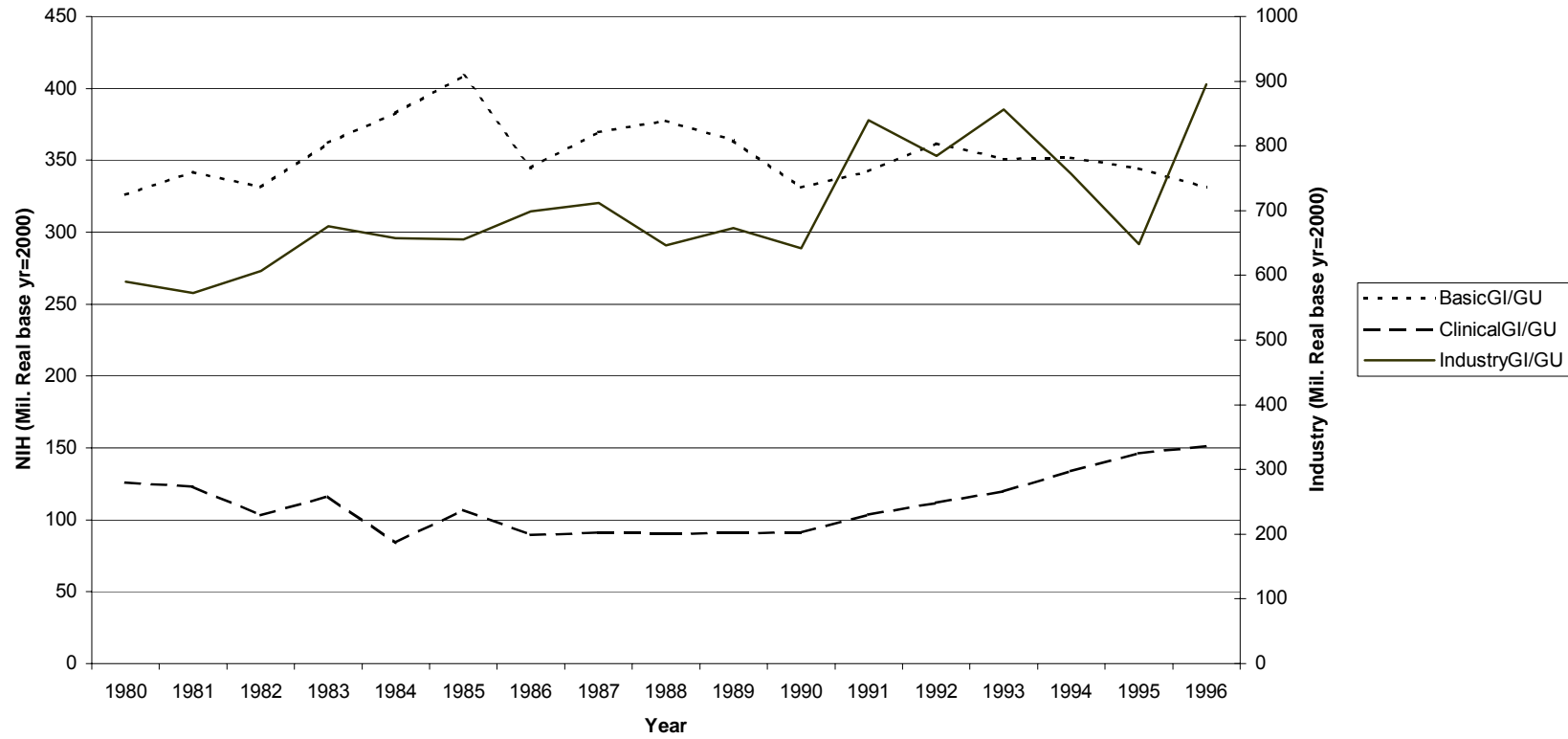28

Figure 3. Gastro-intestinal/Genito-urinary Therapeutic Class
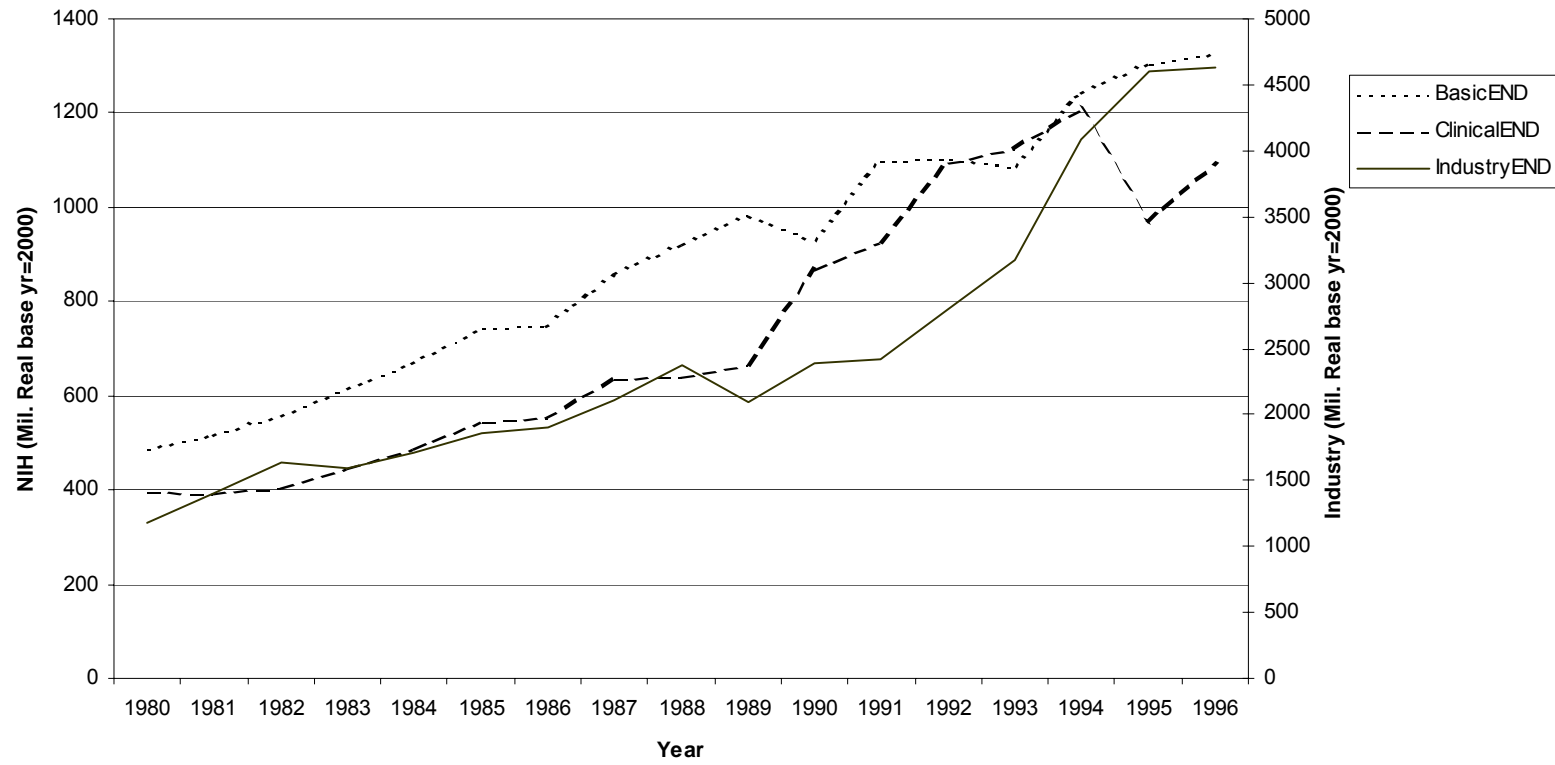
Figure 4. Endocrine/neoplasm(cancer) Therapeutic Class

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TABLE I. Summary Statistics

Variable	Therapeutic Classes						
	Endocrine/ Neoplasm	Central Nervous System	Cardiovascular	Anti-infective	Gastro-Intestinal/ Genito-urinary	Dermatologic	Respiratory
Industry R&D (real mil. $)							
Mean	2,645.36	2,290.40	2,692.80	2,918.47	729.75	837.79	268.97
Standard deviation	1,457.95	771.51	1,179.88	534.89	128.57	298.77	87.11
Avg. growth 1981-97	9.7%	6.4%	8.0%	4.6%	4.0%	7.1%	0.9%
Industry Sales (real mil. $)							
Mean	20,891.1	18,268.0	14,594.5	19,555.0	11,578.9	6,408.2	2,726.9
Standard deviation	2,976.9	1,797.4	4,467.0	4,682.5	3,801.1	1,621.4	636.1
Avg. growth 1981-97	2.1%	1.4%	4.5%	4.4%	5.4%	4.0%	3.4%
NIH Public Basic (real mil. $)							
Mean	1,393.99	818.52	593.71	644.62	355.97	23.62	154.65
Standard deviation	109.63	149.96	58.10	171.83	21.29	4.47	26.07
Avg. growth 1981-96	1.5%	3.5%	1.4%	4.9%	-0.2%	1.6%	3.1%
NIH Public Clinical (real mil. $)							
Mean	1,123.26	769.87	337.20	277.71	109.57	4.90	65.47
Standard deviation	199.47	358.15	65.34	186.55	20.92	3.13	13.52
Avg. growth 1981-96	2.0%	7.6%	3.1%	15.0%	1.4%	14.6%	3.1%
Hosp. Admission Rates (all ages)							
Mean	102.14	122.43	199.20	54.04	122.35	7.54	54.64
Standard deviation	18.89	31.61	10.22	5.62	23.05	3.44	6.34
Avg. growth 1981-97	-3.2%	-3.7%	-0.4%	1.9%	-3.4%	-8.0%	-1.2%
Mortality Rates (all ages)							
Mean	19.29	2.25	33.00	3.68	3.68	0.09	3.68
Standard deviation	0.50	0.57	3.07	0.66	0.11	0.01	0.41
Avg. growth 1981-97	0.4%	5.1%	-1.7%	2.7%	-0.3%	-1.8%	2.4%
FDA Reg. Delay (months)							
Mean	31.41	36.90	38.27	24.11	25.91	22.49	51.13
Standard deviation	22.60	12.53	9.78	8.50	12.68	7.57	23.78
Avg. growth 1981-96	-5.9%	-4.5%	1.7%	0.4%	-1.5%	-0.1%	-7.0%

TABLE II

Estimates of the Elasticity of Publicly Funded Research on Pharmaceutical Investment

Dependent Variable:	(1) - OLS Δ ln Research(t)		(2) - OLS Δ ln Research(t)		(3) - OLS Δ ln Research(t)	
Δ ln Sales(t-1)	0.198	(0.158)	**0.059**	**(0.030)****	**0.073**	**(0.030)*****
PubBasic Poly term 1	**0.341**	**(0.134)*****	**0.343**	**(0.115)*****	**0.347**	**(0.112)*****
PubBasic Poly term 2	**-0.320**	**(0.081)*****	**-0.276**	**(0.073)*****	**-0.271**	**(0.075)*****
PubBasic Poly term 3	**0.045**	**(0.011)*****	**0.039**	**(0.010)*****	**0.038**	**(0.010)*****
PubClinic Poly term 1	**0.109**	**(0.049)****	**0.077**	**(0.047)***	**0.093**	**(0.046)****
PubClinic Poly term 2	-0.042	(0.029)	-0.031	(0.026)	-0.036	(0.026)
PubClinic Poly term 3	0.005	(0.004)	0.003	(0.003)	0.003	(0.003)
Δ ln FDA Delay(t-1)	0.018	(0.017)	0.008	(0.017)		
Δ ln Hosp Admis. (age<35)	-0.254	(0.193)	-0.280	(0.179)		
Δ ln Hosp Admis. (age 35-44)	-0.032	(0.149)	-0.071	(0.141)		
Δ ln Hosp Admis. (age 45-54)	0.081	(0.129)	0.138	(0.125)		
Δ ln Hosp Admis. (age 55-64)	**0.558**	**(0.176)*****	**0.586**	**(0.173)*****	**0.571**	**(0.153)*****
Δ ln Hosp Admis. (age>64)	**-0.589**	**(0.207)*****	**-0.319**	**(0.186)***	**-0.410**	**(0.182)****
Δ ln Mortality (age<35)	0.132	(0.102)	0.124	(0.103)		
Δ ln Mortality (age 35-44)	**-0.212**	**(0.114)***	**-0.220**	**(0.111)****	**-0.216**	**(0.080)*****
Δ ln Mortality (age 45-54)	-0.061	(0.148)	-0.032	(0.132)		
Δ ln Mortality (age 55-64)	**0.632**	**(0.296)****	**0.669**	**(0.283)****	**0.692**	**(0.237)*****
Δ ln Mortality (age>64)	-0.107	(0.299)	-0.285	(0.276)		
Time Trend			**0.063**	**(0.021)*****	**0.060**	**(0.019)*****
Yearly Time dummies	Yes. None Sig.		No		No	
R-squared	.4066		.3134		.2619	
Adjusted R-squared	.1664		.1898		.1860	
Number of Observations	119		119		119	
Durbin-Waston Statistic	DW = 1.96		DW = 1.87		DW = 1.94	

Pooled OLS Regressions, Years 1981-1997, Seven Therapeutic Classes

Standard Errors are in Parentheses. All tests are two-sided.

*** indicates significance at a 1% level

** indicates significance at a 5% level

* indicates significance at a 10% level

TABLE III

Estimates of the Elasticity of Publicly Funded Research on Pharmaceutical Investment

	(1) - 2SLS	(2) - 2SLS	(3) - 2SLS
Dependent Variable:	Δ ln Research(t)	Δ ln Research(t)	Δ ln Research(t)
Δ ln Sales(t-1)	0.344 (0.203)*	0.481 (0.215)**	0.498 (0.223)**
PubBasic Poly term 1	0.494 (0.181)***	0.582 (0.210)***	0.607 (0.218)***
PubBasic Poly term 2	-0.327 (0.105)***	-0.339 (0.131)***	-0.372 (0.134)***
PubBasic Poly term 3	0.045 (0.014)***	0.047 (0.017)***	0.052 (0.018)***
PubClinic Poly term 1	0.163 (0.079)**	0.211 (0.088)**	0.172 (0.072)**
PubClinic Poly term 2	-0.064 (0.040)	-0.075 (0.047)	-0.038 (0.018)**
PubClinic Poly term 3	0.005 (0.004)	0.005 (0.005)	
Δ ln Hosp Admis. (age 55-64)	0.637 (0.204)***	0.579 (0.253)**	0.546 (0.251)**
Δ ln Hosp Admis. (age>64)	-0.202 (0.281)		
Δ ln Mortality (age 35-44)	-0.333 (0.135)**	-0.391 (0.157)**	-0.380 (0.158)**
Δ ln Mortality (age 55-64)	0.856 (0.330)***	0.867 (0.412)**	0.872 (0.424)**
Time Trend	0.042 (0.027)		
R-squared	.1714	.1727	.1648
Adjusted R-squared	.0862	.0968	.0965
Number of Observations	119	119	119
Durbin-Waston Statistic	DW = 1.93	DW = 1.90	DW = 1.96

Pooled 2SLS Regressions, Years 1981-1997, Seven Therapeutic Classes
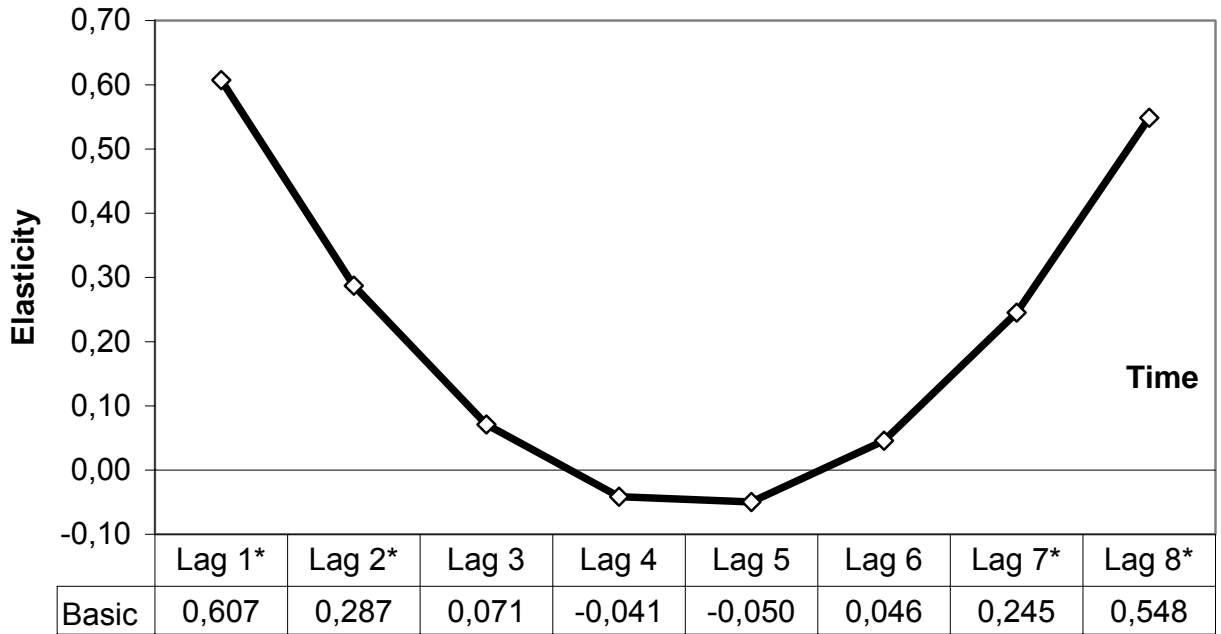
Standard Errors are in Parentheses. All tests are two-sided.
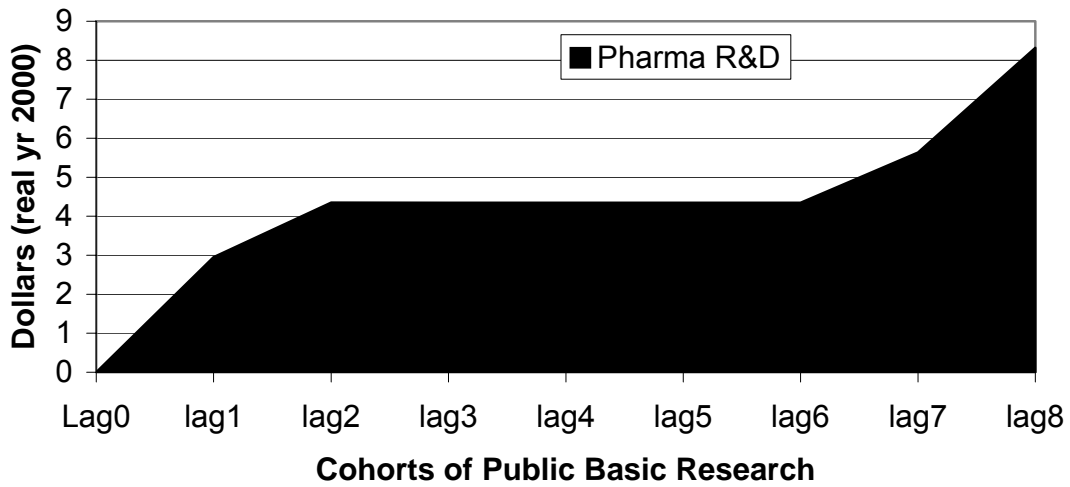
*** indicates significance at a 1% level

** indicates significance at a 5% level
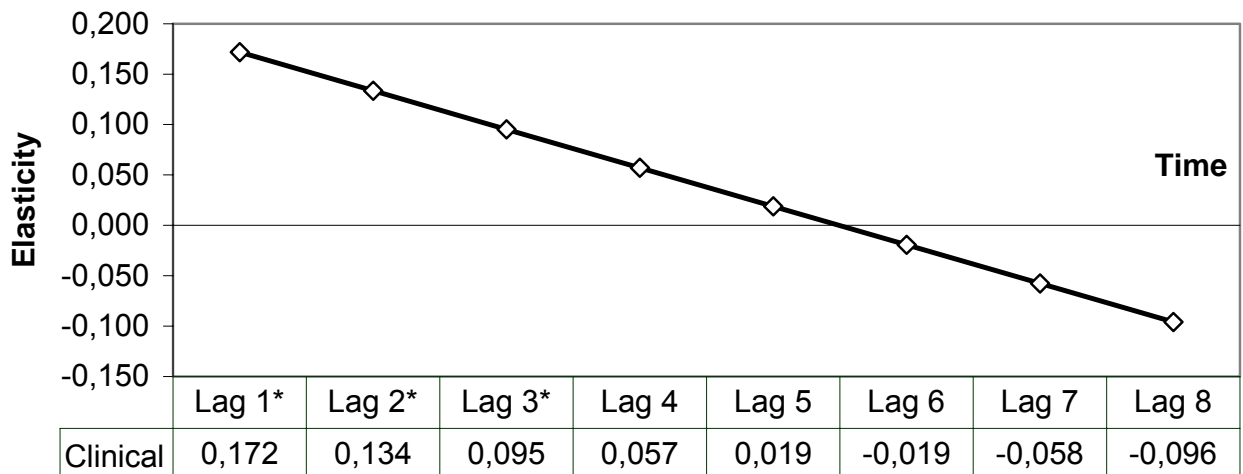
* indicates significance at a 10% level

Figure 5: Changes in Private Investment Response to Age Cohorts of Public Basic Research

	Lag 1*	Lag 2*	Lag 3	Lag 4	Lag 5	Lag 6	Lag 7*	Lag 8*
Basic	0,607	0,287	0,071	-0,041	-0,050	0,046	0,245	0,548

Figure 6: Levels of Private Investment Response to Age Cohorts of Public Basic Research

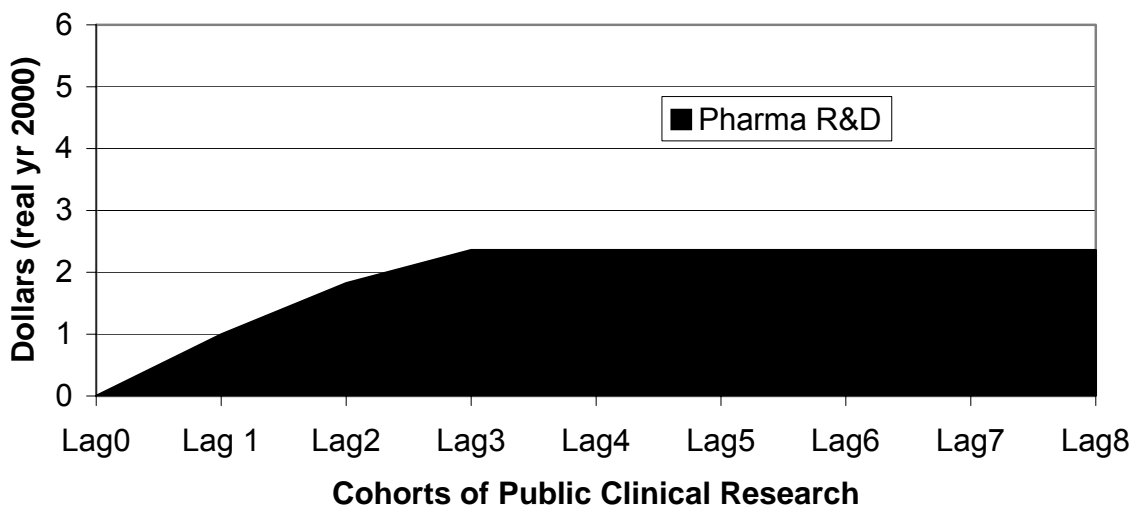**Figure 7: Changes in Private Investment Response to Age Cohorts of Public Clinical Research**

	Lag 1*	Lag 2*	Lag 3*	Lag 4	Lag 5	Lag 6	Lag 7	Lag 8
Clinical	0,172	0,134	0,095	0,057	0,019	-0,019	-0,058	-0,096

Y-axis: Elasticity
Label: Time

Figure 8: Levels of Private Investment Response to Age Cohorts of Public Clinical Research

Y-axis: Dollars (real yr 2000)
X-axis: Cohorts of Public Clinical Research (Lag0, Lag 1, Lag2, Lag3, Lag4, Lag5, Lag6, Lag7, Lag8)
Legend: Pharma R&D

Table IV: Marginal Impacts on Private R&D Investment at the Mean

Variable	Public Basic	Public Clinical	Industry Sales
Long-run elasticities	1.69	0.40	0.50
Ratio (Industry R&D / variable)	4.96	5.86	0.16
Marginal effect (real $)	8.38	2.35	0.08

Representing the individual explanatory variable as X, the estimated elasticities, ε, are equivalent to: $\varepsilon=(\partial I/\partial X)*(X/I)$. The marginal effects are calculated as: $(\partial I/\partial X)= \varepsilon*(I/X)$. The calculation uses average industry R&D investment across all therapeutic classes in 1997 (I = $3069.954 million); average public clinical research for 1996, 1995 and 1994 (Pub clinical average = $523.976 million); average industry sales in 1996 (industry sales average = 19227.81 million); and, the average for public basic research in 1996, 1995, 1990, 1989 across all classes (Pub basic average = 618.934 million).