Does Public Biomedical Research Complement Industry R&D Investment? The Case of Basic and Clinical Public Science and Pharmaceutical R&D

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ABSTRACT

This research examines the relationship between basic and clinical biomedical research and private R&D investment in the pharmaceutical industry. The paper introduces new measures of basic and clinical research into a pharmaceutical R&D investment model and uses disease incidence and severity as instruments for industry sales revenue. Increases in public basic and clinical science are shown to substantially increase pharmaceutical investment. For a dollar increase in public basic science funding, pharmaceutical investment increases $3.15 while a dollar increase in public clinical science stimulates a $1.18 increase in private R&D. The impact of public basic research, however, is spread over a longer time horizon.

Understanding the relationship between public science and private industry R&D is critically important for understanding the process of innovation and the Federal role in research. A central issue is whether public research complements or substitutes for private R&D. Public science may complement industry R&D by providing new ideas for products or processes and by helping firms to solve technical problems with their existing projects. On the other hand, public science may substitute for private R&D by financing a project that would otherwise have been pursued by industry firms or by launching large-scale research programs that alter the competitive environment or draw important research inputs out of the private sector. (David et al. (2000a), (2000b))

Recognizing that complementarity and substitutability may happen concurrently and along dimensions that are not completely observable or measurable, the existing research focuses on estimating the "net" effect of public science 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 science under investigation as well as the particular technological opportunity and appropriability conditions facing private firms. Reporting on a major survey of R&D labs in the manufacturing sector, Cohen et al. (2002) find that the influence of public science on industrial R&D varies enormously across industries with the respondents from the pharmaceutical industry indicating a particularly close linkage between their investment and changes in the public science knowledge base.

This paper addresses the heterogeneity in public science and industry response by specifying an empirical model of R&D investment in 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 minimizes heterogeneity in opportunities across scientific areas of research. The technology classes used in this study are medical therapeutic areas, a distinction that separates research according to the biological system in question. For example, research on the cardiovascular system is grouped separately from research on cancer, which is grouped separately from research on infectious disease, etc. 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.

This paper improves upon the existing research in two ways. First, the analysis uses new microeconomic data on public science funding by the U. S. Department of Health and Human Services, which is the umbrella agency housing the U. S. National Institutes of Health (NIH) and related agencies. For each medical class, these data allow public biomedical science to be separated by character of research into basic "laboratory" research and clinical "human" research. One would expect that different types of publicly supported science have different impacts on industry R&D investment. Second, the analysis addresses the endogeneity of industry sales using measures of disease incidence and severity as instrumental variables. Unlike industry sales, these disease

measures are determined in the patient population and are not under the direct control of pharmaceutical executives involved in the R&D investment decision.

Using 2SLS on a panel of seven medical classes over the 1981-1997 period, the estimation results indicate that both public basic research and public clinical research complement private pharmaceutical R&D investment. The elasticity estimates suggest that a 1% increase in public funding for clinical research stimulates a 0.19% increase in private R&D investment after two years. A 1% increase in public funding for basic science stimulates a 0.64% increase in industry R&D after eight years. In terms of the marginal impacts of public funding, a dollar increase in clinical science produces an additional $1.18 in industry R&D after two years while a $1 increase in basic science stimulates an additional $3.15 in industry investment after eight years. The results also indicate that industry sales are an important determinant of industry R&D with an elasticity estimate of 1.16. For each dollar increase in sales, pharmaceutical R&D investment increases by 18.6 cents. The data and estimation improvements in this research notwithstanding, the paper's empirical findings should be viewed as suggestive rather than definitive. The diverse and interactive nature of public and private research in this industry make it difficult to pinpoint individual effects and attach causal interpretations.

The paper begins with a discussion of the interaction between public and private research drawn from the case study literature 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 provides an interpretive discussion of the empirical results. Concluding remarks appear in section VII.

II. Interaction between public science and pharmaceutical R&D: Background

How public science influences private R&D depends largely on the nature of the problems and solutions that industry scientists face in the pharmaceutical innovative process. As such, the organization of the industry's innovative process into two stages, commonly called drug discovery and drug development, brings with it a broad separation in the character of research problems addressed. 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 science 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 science 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 science 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 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 development and may only embody the faintest outline of a promising new therapy. Needless to say, there is a high degree of uncertainty in the process of "solving" any of these puzzles and significant follow-on private investment is normally required.

Beyond supplying new ideas for therapies, public basic science can contribute to industry solutions by providing "puzzle pieces" or, as is more common, by providing the clues required for discovering new pieces. In the case study research, 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 science are very rarely the "plug and play" variety. Information from public science must be "shaped" to fit the specific puzzle under investigation. Moreover, when public science only provides clues, new pieces must be invented to fit the puzzle. In both cases, industry firms respond by increasing investment to take advantage of complementary information.[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] Generally, one would expect public clinical research to have a higher degree of substitutability for industry R&D than public basic research. 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 also make industry investment more efficient. 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 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. (1994) point out that public sector clinical researchers may have an important role to play in reducing uncertainly 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.

While industry scientists ultimately determine the degree of public-private interaction in the pharmaceutical innovative process, the case study research is clear to point out that these interactions are diverse and bi-directional. The diversity of interactions reflects the myriad of ways that private researchers can access public scientific knowledge. Public scientific knowledge can be accessed through a variety of channels including publications, patents, conferences, personal networks, and consulting. Economists and sociologists are currently trying to gauge the "connectedness" between public and private research by tracking different channels using measures like co-authorships, citations to papers, citations to patents, and network models.[9] Cohen et al. (2002), from their survey of manufacturing R&D labs, find that the pharmaceutical industry relies heavily on nine out of ten possible channels of access to public science. The main channels reported by industry respondents were publications, conferences, consulting, and informal interactions.

This diversity of interactions is further complicated with bi-directional flows of information between private and public researchers. It is certainly not the case that an industry scientist is simply a passive recipient of a unidirectional flow of knowledge from public science. In their study of 21 important drugs, Cockburn and Henderson (1997) characterize public-private interaction as "complex" and "iterative." They suggest that new drugs have offered scientists in the public sector "new tools for understanding human physiology and molecular biology." (Cockburn and Henderson (1997), p. 14)

While the 1990s saw a surge in case study research on public-private interactions in pharmaceutical innovation, the empirical research aimed at exploring the generality of the findings has lagged behind. The most recent empirical contribution looking at public-private complementarity is Ward and Dranove (1995). 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 (i.e. National Cancer Institute, National Heart Lung and Blood Institute, etc.) as a measure of public "basic" science in each therapeutic area. Unfortunately, NIH obligations are far too broad a measure. These obligations represent a diverse set of financial commitments including basic, clinical, administrative, training, demonstration, construction, and other activities. Their model relates the current level of industry R&D to the number of deaths, the number of physicians, real personal health care expenditure, predicted FDA regulatory stringency, and a seven year distributed lag of "direct" as well as "indirect" NIH research obligations. Their main finding suggests

that a 1% increase in NIH research obligations leads to an increase in industry R&D of 0.6 to 0.7 percent after a lag of seven years.[10]

III. A Simple 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). 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. The factors that affect the returns to industry investment include measures of demand, proxies for basic and clinical public science, regulation, and dummy variables to account for differences across classes and shifts over time. The reduced form fixed effects model for an individual therapeutic class, i, in year, t, is:

Equation (1):

$$\ln I_{it} = \beta_0 + \beta_1 \ln S_{it-1} + \sum_{j=1}^{9} \alpha_j \ln B_{it-j} + \sum_{j=1}^{9} \delta_j \ln C_{it-j} + \beta_2 \ln R_{it-2} + \beta_3 \ln D_{it} + a_i + \gamma_t + \varepsilon_{it}$$

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)) 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. Each of these public investment flows is lagged one year prior to current industry investment to allow for some research lag and to avoid any potential simultaneity bias. The data allow these distributed lags to extend back nine years prior to industry investment. R_{it-2} is a measure of FDA regulatory stringency. D_{it} represents a set 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, serve as instruments for industry sales. The therapeutic class unobserved effect is a_i and the time dummies are γ_t. Finally, ε_{it} is an idiosyncratic error with the standard properties.

The primary focus of the analysis is on the effects of public basic and clinical research. As one would expect, collinearity between the public research flows will lead to problems with low precision of the estimates. Thus, the hypotheses that public basic and clinical research complement private pharmaceutical research will be tested using the joint significant of all the public research variables. The magnitude of the impact will be

assessed using the long-run impact propensity calculated as the sum across all the coefficient estimates.

In order to estimate equation (1), the industry R&D series must be weakly dependent. However, using a standard Dickey-Fuller test and an Augmented Dickey-Fuller test, it is not possible to reject the null that industry R&D is a unit root process. 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.[11] 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 is:

Equation (2):

$$\Delta \ln I_{it} = \beta_1 \Delta \ln S_{it-1} + \sum_{j=1}^{8} \alpha_j \Delta \ln B_{it-j} + \sum_{j=1}^{8} \delta_j \Delta \ln C_{it-j} + \beta_2 \Delta \ln R_{it-2} + \beta_3 \Delta \ln D_{it} + \Delta \gamma_t + \Delta \varepsilon_{it}$$

Based on the investment framework, growth in sales, Δln(Sales), should be viewed as endogenous in this equation. 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)

To correct for endogeneity, I use measures of drug demand that have no direct effect on industry investment but are highly correlated with industry sales. The instruments are measures of disease incidence and severity rates by therapeutic class and

year in each of five age groups. 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. The identifying assumption is that these measures of patient demand are correlated with $\Delta \ln SALES_{it-1}$ but uncorrelated with $\Delta \varepsilon_{it}$. Testing the over-identifying restrictions shows that the instruments are exogenous. Further, they are strongly correlated with the lagged sales in the first stage regression. (For the eight available instruments, the value F-statistic for their joint significance in the first stage is 2.66 with a p-value<0.012.)

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 model the channels through which public science and private R&D interact. At this point, research efforts intended to explore the channels such as publications, personal networks, etc., face significant data limitations. The model in this paper treats the channels as an implicit "black box." Further, better data would allow one to model the feedback from industry R&D to public science. Using lags of public science eliminates simultaneity bias, however, the current model still treats public science as exogenous. These limitations should be kept in mind when interpreting the empirical results presented below.

IV. Data

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, central nervous system, cardiovascular, anti-infective, gastro-intestinal/genito-urinary, dermatologic, and respiratory. Table 1 provides summary statistics for each of the variables by therapeutic class.

The empirical analysis uses public investment into basic and clinical science 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 2002 is $23.1 billion, an increase of $2.8 billion over the FY 2001 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 of 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 science flows that happen through conferences, networks or consulting. Third, other indicators of research output are not under the control of policy

makers 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 investment are defined using the CRISP database (Computer Retrieval of Information on Scientific Projects) maintained by the NIH and covering the years 1972-1996.[12] 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 (i.e. basic, clinical, other) and to further allocate grants and contracts to therapeutic classes.[13] (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, 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. PhRMA membership represents well over 90% of the total industry. 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 (FDA). 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 instruments used in the analysis are disease incidence rates (incidence per population) and mortality rates (deaths per population) by therapeutic class and year for 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 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 of the therapeutic classes and age groups, incidence rates are defined as the number of hospital admissions per population and were taken from the National Hospital Discharge survey. Similarly, the mortality rates by therapeutic class and age group are defined as the number of deaths per

population and were taken from the National Vital Statistics System, multiple-cause-of-death file.

V. Estimation Results

Table II shows both OLS and 2SLS estimates of equation (2) in log-differences. In the log-difference specification, all of the parameters are identified using only within-medical class variation over time. Regression diagnostics are listed at the bottom of the table, in particular, the relevant F-statistics for testing the joint significance are reported. When individual explanatory variables are statistically significant, they are shown in boldface. The first model in the analysis, column (1), is an OLS regression starting from a "fully specified" model in which all potential explanatory variables are included. From this initial regression, several point are worth noting. First, the public investment flows into basic research show high joint significance with an F-statistic of 2.80 and a p-value < 0.011. The long-run elasticity estimate is positive and equal to 0.12. Second, the eight year distributed lag of public investment into clinical research is not jointly significant. Notice, however, that public clinical research funded two years prior to industry research is individually significant with a positive coefficient. These initial OLS results support the hypotheses that both public basic and clinical research stimulate private industry R&D. Turing to the other variables, the elasticity estimate for industry sales is positive and marginally significant while FDA regulatory stringency is insignificant. Neither group of demand measures, hospital admissions or mortality, is jointly significant. However, hospital admissions and mortality for individuals age 55-64 are each individually significant and positive.

The second OLS model in column (2) shows the results after sequentially eliminating the insignificant demand variables from the model using F-tests. The results for the distributed lags of public investment in basic and clinical research remain largely unchanged. The magnitude and significance of industry sales increases while the regulatory stringency proxy remains insignificant. The number of hospital admissions for individuals age 55-64 becomes individually insignificant after hospital admission for those over 65 is dropped from the model. To be conservative, I left both of these demand measures in the model. Finally, mortality in age groups 45-54 and 55-64 are both jointly and individually significant. The negative sign on mortality 45-54 may reflect collinearity between these measures.

Column (3) of Table II shows the regression results after correcting for the endogeneity of industry sales in the pharmaceutical R&D decision. The six eliminated demand measures are used as instruments. The instruments are validated using tests for over-identification. Moreover, these instruments are strongly correlated with industry sales in the first stage regression. As a group, the flows of public investment into basic science remain highly significant while those into clinical science are not jointly significant. Public clinical science funding two years prior to industry investment is individually significant with an elasticity of 0.16. The long-run elasticity of public basic research increases from 0.19 to 0.48. Looking at industry sales, the elasticity estimate increases from 0.38 to 0.79 and remains significant even though the standard error of the estimate is three times larger. The proxy for FDA regulatory stringency is still insignificant. Finally, turning to the demand measures, mortality rates for individuals age 45-64 are jointly and individually significant. Also, the effect of mortality in the 55-64

year old age group increases. On the other hand, the hospital admissions measures of disease incidence are not jointly or individually significant.

Table III presents the final group of 2SLS regressions. Column (1) reproduces the third regression from Table II for ease of comparison. Column (2) shows the 2SLS results after eliminating the insignificant FDA proxy and the hospital admissions measures. The final column of Table III presents the preferred model. In this model, the hospital admissions variables have been added to the instrument list and sequential F-tests have been used to eliminate the insignificant public clinical research variables. Once again, the distributed lag of public basic research is highly significant. The long-run elasticity estimate is 0.637. While an eight year distributed lag of public investment flows may be too short to capture the full impact of basic research, the elasticity estimate suggests that a 1% increase in public basic science stimulates a 0.64% increase in industry R&D investment after eight years. For public clinical research, its effect is only significant an average of two years prior to industry investment. This stands to reason as one would expect the impact of public basic research to extend over a longer time horizon than the impact of public clinical research. The elasticity estimate suggests that a 1% increase in public clinical science stimulates a 0.19% increase in industry investment after two years. Turning to industry sales, a 1% increase in industry sales leads to a 1.16% increase in industry R&D investment in the following year.

VI. Discussion

The estimation results are consistent with the case study research and support the hypotheses that public basic and clinical research are complementary to and stimulate

additional private industry investment. However, it would be useful to know how the elasticity estimates translate into marginal rates of return from public funding. The marginal return is calculated as the product of the elasticity and the ratio of pharmaceutical R&D investment to the variable of interest. The marginal impacts, consequently, depend on the relative magnitude of private to public investment. Estimates of the marginal rate of return for public basic, public clinical and industry sales are presented in Table IV. A $1 increase in public basic research generates at the margin a $3.15 "net" increase in private R&D after eight years. A $1 increase in public clinical research generates at the margin a $1.18 increase in private R&D after two years. With respect to industry sales, each new dollar in revenue increases next year's R&D investment by 18.6 cents.

What does this mean in light of the $2.8 billion increase in the NIH budget for FY 2002? If 40% of this funding is spent on basic research, then public basic science increases by $1.2 billion and private industry R&D will have a net increase $3.5 billion at the end of eight years, assuming the industry has the cash flow to support this increase.[14] If 34% of the funding is spent on clinical research, an increase of $952 million, then pharmaceutical R&D will increase $1.12 billion after two years. Of course, these calculations are only "back-of-the-envelope" estimates.

As discussed earlier in the analysis, one should be cautious about interpreting these numbers too literally. The NIH investment flows are proxies in the analysis for *all* of public science. Clearly, there are contributions to public science funding from other institutions in the U.S. and abroad. Assuming the NIH investment flows provide a good relative picture of basic versus clinical public science, then the log-log functional form

implies the elasticity estimates are still valid even without having total world public science investment figures to use in the study. However, the story is not the same when one tries to calculate marginal rates of return because these rates depend on accurate numbers for total world investment in basic and clinical public science. Under the reasonable but somewhat arbitrary assumption that the NIH represents 50% of the total world investment into public basic and clinical science, a number that probably underestimates the NIH share, the marginal impacts are themselves scaled down by 50%. This would mean that a $1 increase in world public research would stimulate a $1.58 net increase in industry investment after eight years while a $1 increase in world public clinical science would stimulate a $0.60 increase in private pharmaceutical R&D after two years.

With respect to public policy, this research suggests the debate on pharmaceutical pricing is likely to become even more important and heated as time passes. Given the enormous investment required to bring new drugs to the market and the desire of the industry to keep up with emerging opportunities from academic science, industry firms are going to face mounting pressure on cash flows. On the one hand, firms need to continue to invest to stay competitive and bring new therapies to the market; on the other hand, pressure to lower pharmaceutical prices will lower sales revenue and likely result in a cash flow problem for the industry. I suspect that the full significance of this looming situation is not fully appreciated by the parties involved.

VII. Conclusion

This paper uses an investment model specified across medical technology areas to explore the hypotheses that public basic science and public clinical science complement pharmaceutical industry R&D investment. The findings suggest that both public basic and public clinical science stimulate industry R&D. For basic research, a 1% increase in public investment will stimulate an average of 0.637% more industry R&D after eight years. For clinical public science, a 1% increase will lead to an average increase of 0.19% in industry R&D after two years. The marginal impacts of increased public funding are substantial with pharmaceutical investment increasing $3.15 in response to public basic science and $1.18 in response to public clinical science.

The data and estimation improvements introduced in this paper notwithstanding, the empirical findings should be viewed as suggestive rather than definitive. The diverse and interactive nature of public and private research in this industry make it difficult to pinpoint individual effects and attach causal interpretations. Future research should focus on developing empirical models of public-private interaction that allow the channels of information exchange to be identified and allow for feedback from private industry R&D to public science.

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, etc.) For each grant and contact 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 by 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 by 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, etc. 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, etc. Fifth, for those Institutes that are too general to be classified (i.e. the National Institute of General Medicine, etc.), 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). Figure1 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 supports the substitution 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 science 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 science.

6. Maxwell et al. (1990), OTA (1993), Galambos et al. (1995), Cockburn and Henderson (1997), NIH (2000), Public Citizen (2001), 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. Cockburn and Henderson (1997) and (2000) provide a good overview of this type of research as it applies to the pharmaceutical industry.

10. NIH obligations are far too broad a measure of public basic science. NIH Institute obligations represent a diverse set of commitments including basic, clinical, administrative, training, demonstration, construction, and other activities. Refer to the NIH website for further information at: http://www.nih.gov.

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

12. Starting in January 1997, the NIH stopped reporting the financial award amounts associated with its individual grant and contract awards. This field in the CRISP database was replaced and the public no longer has access to systematic and comprehensive information about individual financial awards given by the U.S. Department of Health and Human Services.

13. The "other" category includes awards from agencies like the National Library of Medicine, the National Institute of Nursing Research, the Centers for Disease Control, etc. This group of awards also includes monies for administrative activities, construction, demonstration, occupational research, environmental research, training, and fellowships.

14. Forty percent is the fraction of the NIH awards invested in basic science in 1996 as defined in this study. Similarly, thirty-four percent of the total NIH awards went to clinical research.

References

American Association for the Advancement of Science (AAAS). (2001). Report XXVI Research and Development FY 2002, May 2001, (www.aasa.org/spp/dspp/rd/).

Arora, Ashish, Alfonso Gambardella. (1994). "Evaluating Technological Information and Utilizing It," Journal of Economic Behavior and Organization, Vol. 24, No. 1, pp. 91-114.

Cockburn, Iain, M., Rebecca Henderson. (1997). "Public-private Interaction and the Productivity of Pharmaceutical Research," NBER Working Paper No. 6018, Cambridge, MA, April 1997.

Cockburn, Iain M., Rebecca M. Henderson. (2000). "Publicly Funded Science and the Productivity of the Pharmaceutical Industry," in Innovation Policy and the Economy, Volume 1, Adam B. Jaffe, Josh Lerner, and Scott Stern (editors), Cambridge: The MIT Press.

Cohen, Wesley M., D.A. Levinthal. (1989). "Innovation and Learning: The Two Faces of R&D," Economic Journal, Vol. 99, pp. 569-596.

Cohen, Wesley M., Richard R. Nelson and John P. Walsh. (2002). "Links and Impacts: The Influence of Public Research on Industrial R&D," Management Science, Vol. 48, No. 1, January 2002, pp. 1-23.

Colyvas, Jeannette, Michael Crow, Annetine Gelijns, Roberto Mazzoleni, Richard R. Nelson, Nathan Rosenberg, Bhaven N. Sampat. (2002). "How do university inventions get into practice?" Management Science, Vol. 48, No. 1, January 2002, pp. 61-72.

David, Paul A., Bronwyn H. Hall, Andrew A. Toole. (2000a). "Is public R&D a complement or substitute for private R&D? A review of the econometric evidence," Research Policy, Volume 29, No. 4-5, pp. 497-529.

David, Paul A., Bronwyn H. Hall. (2000b). "Heart of Darkness: modeling public-private funding interactions inside the R&D black box," Research Policy, Vol. 29, No. 9, December 2000.

Flowers, Christopher R., Kenneth L. Melmon. (1997). "Clinical investigators as critical determinants in pharmaceutical innovation, Commentary, Nature Medicine, Vol. 3, No. 2, February 1997.

Gambardella, Alfonso. (1995). Science and Innovation: the US Pharmaceutical Industry in the 1980s, Cambridge: Cambridge University Press.

Galambos, Louis, Jane Eliot Sewell. (1995). Networks of Innovation, Cambridge: Cambridge University Press.

Gelijns, Annetine C., Nathan Rosenberg, Alan J. Moskowitz. (1998). "Capturing the Unexpected Benefits of Medical Research," The New England Journal of Medicine, Volume 339, No. 10, September, 1998, pp. 693-698.

Gelijns, Annetine, Nathan Rosenberg. (1994). "The Dynamics of Technological Change in Medicine," Health Affairs, Health Affairs, Summer 1994, pp. 28-56.

Grabowski, Henry G., John Vernon. (1980). "The Determinants of Research and Development Expenditures in the Pharmaceutical Industry," in Drugs and Health, R. B. Helms (editor), Washington: AEI Press, 1980.

Grabowski, Henry, G., John Vernon. (2000). "The Determinants of Pharmaceutical Research and Development Expenditures," Journal of Evolutionary Economics, Vol 10, Issue 1/ 2, pp. 201-215.

Guellec, Dominique, Bruno van Ottelsberghe. (2000). "The Impact of Public R&D Expenditure on Business R&D," Working paper, OECD, 2000.

Hall, Bronwyn H., Zvi Griliches, Jerry A. Hausman. (1986). "Patents and R&D: Is there a lag?" International Economic Review, Vol. 27, No. 2, June 1986, pp. 265-283.

Henderson, Rebecca, Iain M. Cockburn. (1996). "The Determinants of Research Productivity in Ethical Drug Discovery," in Competitive Strategies in the Pharmaceutical Industry, Robert B. Helms (editor), Washington: The AEI Press, 1996, pp. 167-193.

Jaffe, Adam B. (1989). "The Real Effects of Academic Research," American Economic Review, Volume 79, pp. 957-970.

Koenig, Michael E.D. (1983). "A bibliometric analysis of pharmaceutical research, Research Policy, Vol. 12, pp. 15-36.

Maxwell, Robert, A., Shohreh Eckhardt. (1990). Drug Discovery: A Case Book and Analysis, Clifton, NJ: Humana Press.

Narin, F., K. Hamilton, D. Olivastro. (1997). "The increasing linkage between US technology and public science, Research Policy, vol. 26, pp. 317-330.

NIH Office of Director. (1997). Executive Summary: Director's Panel on Clinical Research Report, http://www.nih.gov/news/crp/97report/execsum.htm.

NIH Office of Science Policy. (2000). "NIH Contributions to Pharmaceutical Development: Case Study Analysis of the Top-Selling Drugs," in Rx R&D Myths: The Case Against Drug Industry's R&D "Scare Card," Public Citizen, Congress Watch, July 2000.

OECD. (2002). Benchmarking Industry-Science Relationships, Organization for Economic Co-operation and Development.

Pharmaceutical Research and Manufacturers Association, "Annual Survey Report," Washington D.C.: PhRMA, various years.

Reichert, Janice M., Christopher-Paul Milne. (2002). Public and Private Sector Contributions to the Discovery and Development of 'Impact' Drugs, Tufts Center for the Study of Drug Development White Paper, May 2002.

Scherer, Frederic, M. (1996). "Commentary on Part Three," in Competitive Strategies in the Pharmaceutical Industry, Robert B. Helms (editor), Washington: The AEI Press, 1996, pp. 269-273.

Scolnick, Edward M. (1990). "Basic research and its impact on industrial R&D," The IRI Medalist's Address, Industrial Research Institute, May 1990.

The Pfizer Journal, "Clinical Trials: A cornerstone of biomedical research and innovation," Impact Communications, Global Edition, Vol. 3, No. 1, 2002.

Toole, Andrew A. (1999). "Public Research, Public Regulation, and Expected Profitability: The Determinants of Pharmaceutical Research and Development Investment," mimeo, Stanford University, 1999.

U.S. Congress, Office of Technology Assessment. (1993). Pharmaceutical R&D: Costs, Risks, and Rewards, OTA-H-522, (www.wws.princeton.edu/~ota/)

Ward, Michael R., David Dranove. (1995). "The Vertical Chain of Research and Development in the Pharmaceutical Industry," Economic Inquiry, Volume 33, January 1995, pp. 70-87.

Wiggins, Steven, N. (1983). "The Impact of Regulation on Pharmaceutical Research Expenditures: A Dynamic Approach," Economic Inquiry, Volume 21, January 1983, pp. 115-128.

Wooldridge, Jeffrey, M. (1995). "Score Diagnostics for Linear Models Estimated by Two Stage Least Squares," in Advances in Econometrics and Quantitative Economics, G. S. Maddala, Peter C. B. Phillips, T. N. Srinivasan (editors), Cambridge: Blackwell Publishers Inc., 1995, pp. 66-87.

Wooldridge, Jeffrey, M. (2002) Econometric Analysis of Cross Section and Panel Data, Cambridge: The MIT Press.

Figure 1: Public Biomedical Science by Type: Basic, Clinical, Other

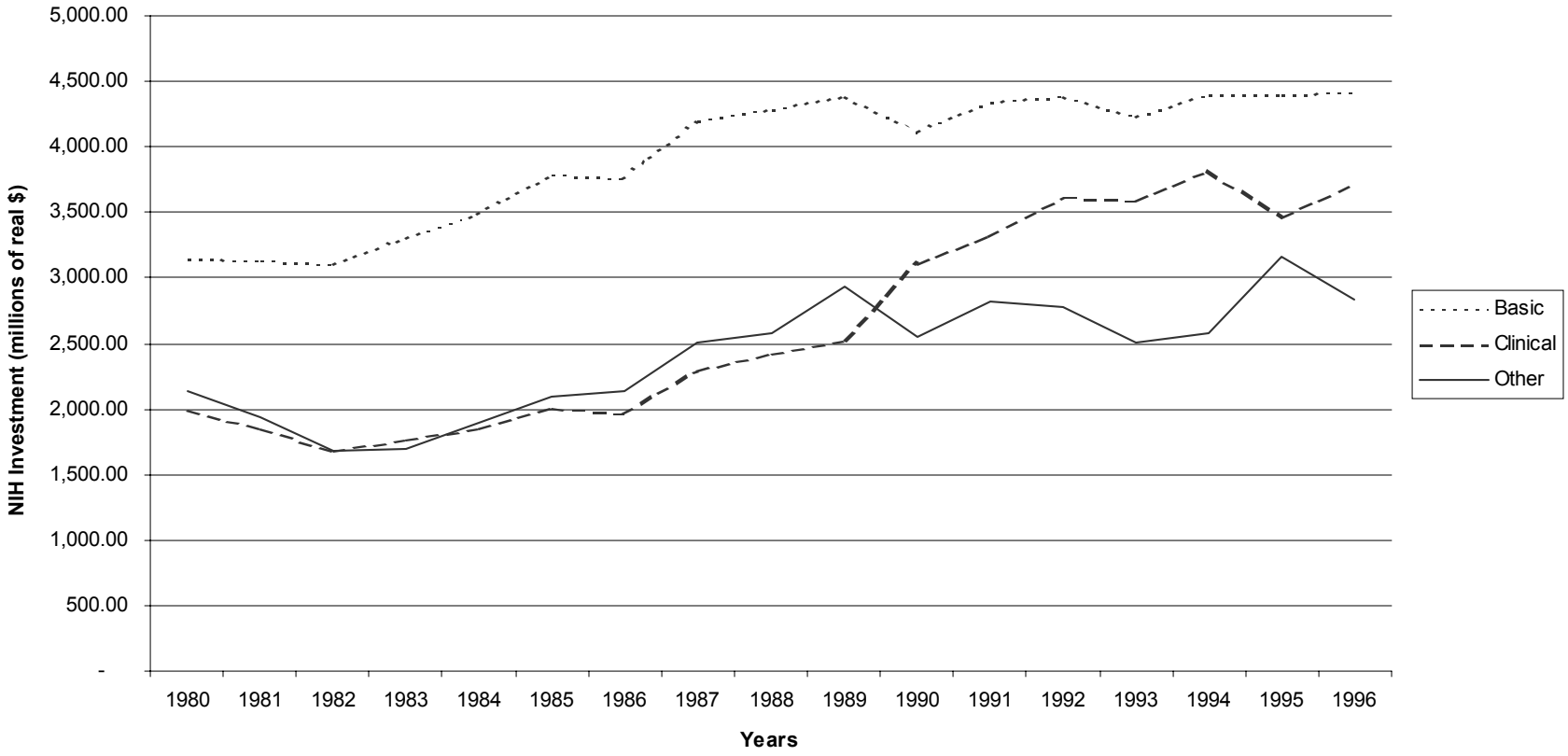

Figure 2: Anti-infective Therapeutic Class

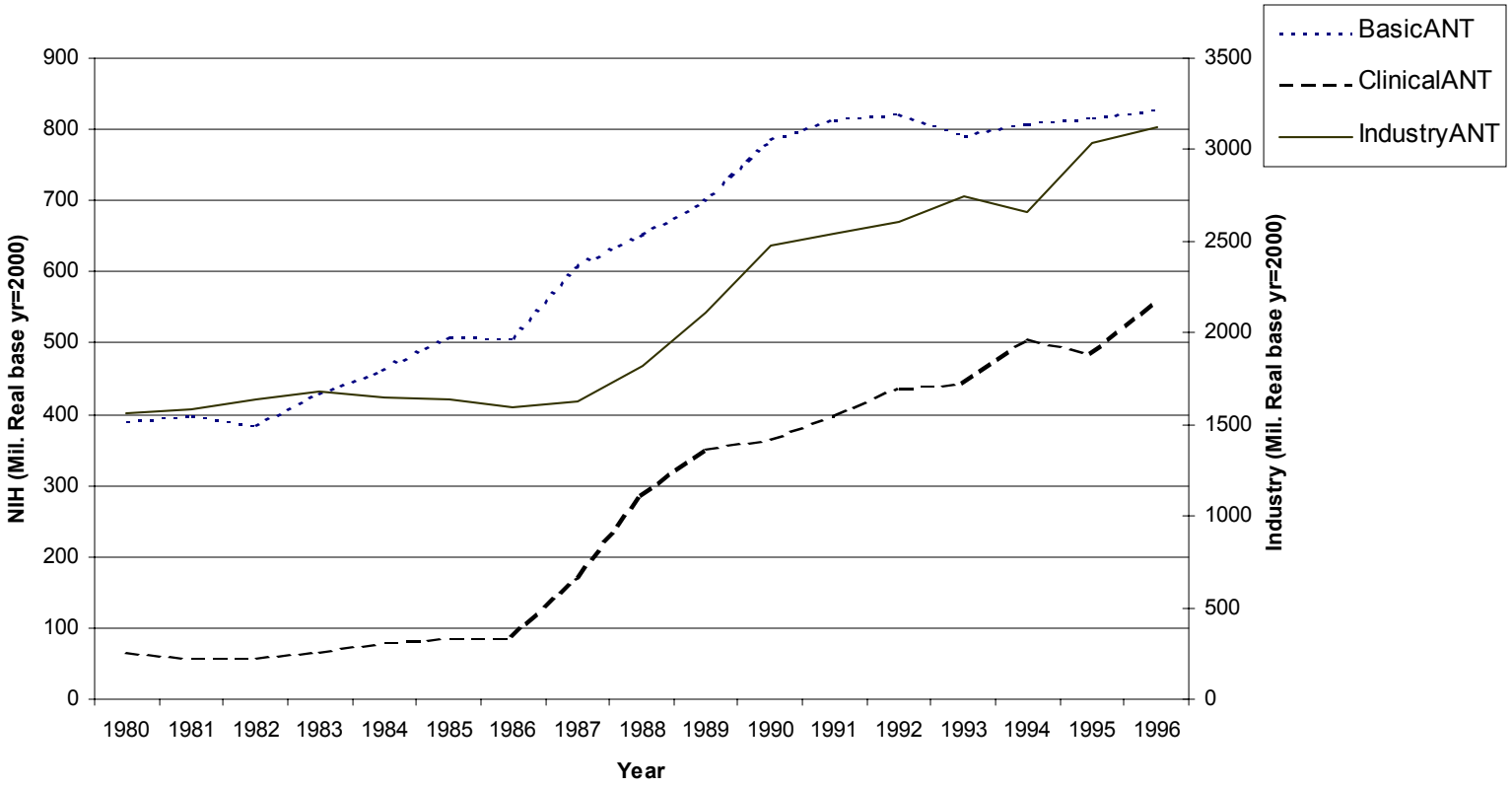

Figure 3. Gastro-intestinal/Genito-urinary Therapeutic Class

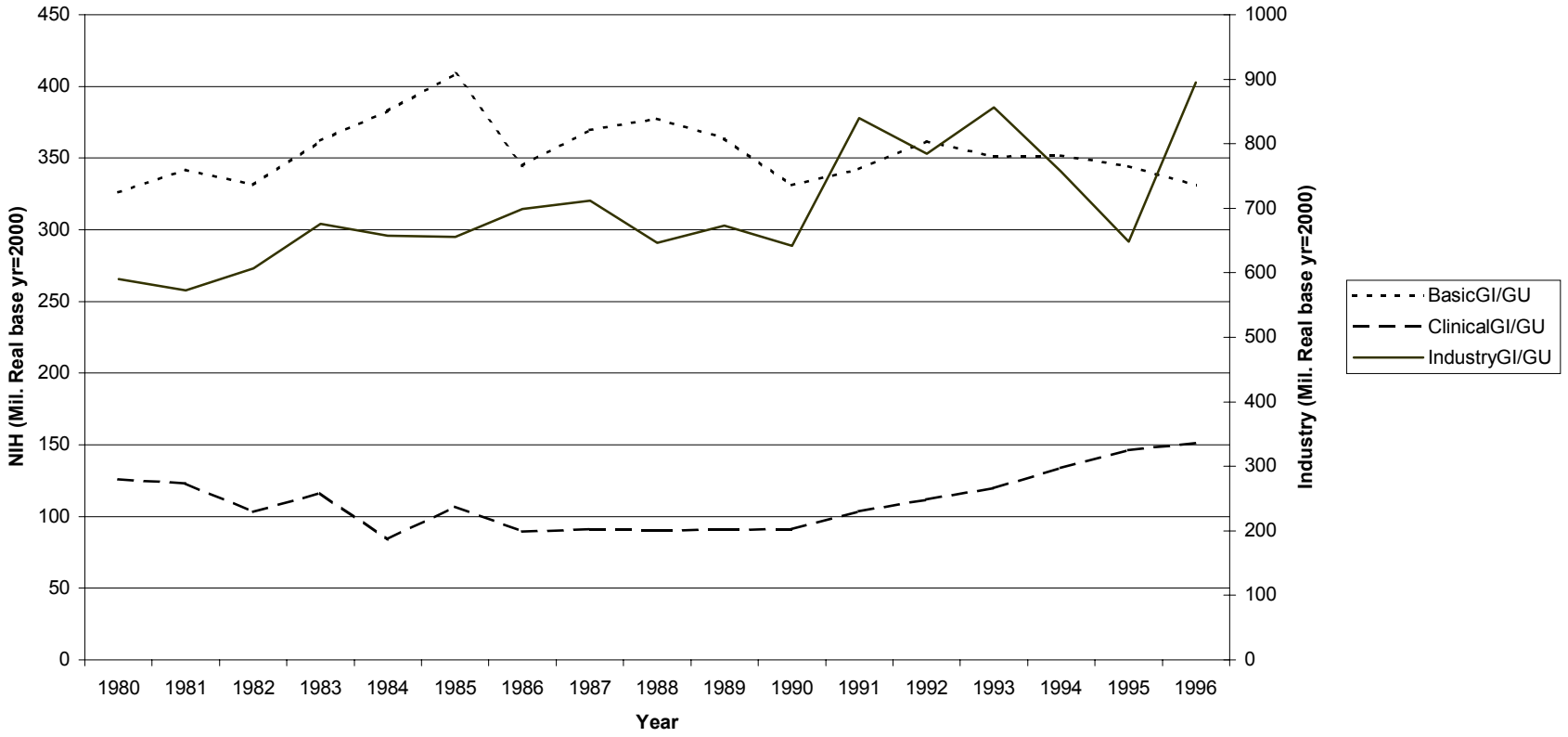

Figure 4. Endocrine/neoplasm Therapeutic Class

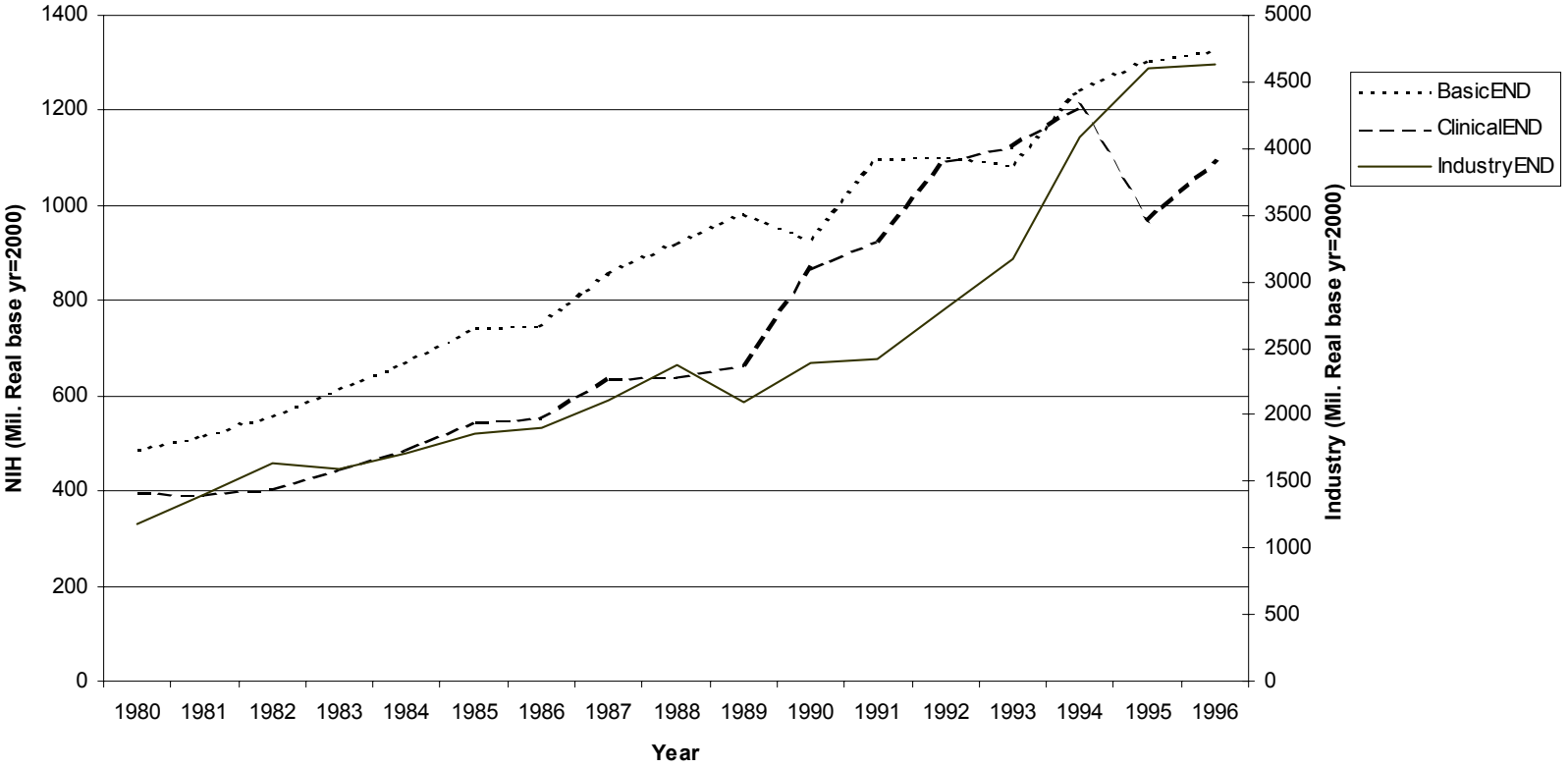

TABLE I. Summary Statistics

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 Science on Pharmaceutical Investment

	(1) - OLS		(2) - OLS		(3) - 2SLS	
Dependent Variable:	Δ ln Research(t)		Δ ln Research(t)		Δ ln Research(t)	
Δ ln Sales(t-1)	**0.315**	**(0.177)***	**0.381**	**(0.165)****	**0.790**	**(0.455)***
Δ ln PubBasic(t-1)	**0.423**	**(0.162)*****	**0.439**	**(0.161)*****	**0.391**	**(0.172)****
Δ ln PubBasic(t-2)	0.082	(0.186)	0.078	(0.171)	0.221	(0.230)
Δ ln PubBasic(t-3)	**-0.298**	**(0.172)***	**-0.287**	**(0.160)***	**-0.344**	**(0.174)***
Δ ln PubBasic(t-4)	0.039	(0.186)	0.113	(0.175)	0.205	(0.203)
Δ ln PubBasic(t-5)	**-0.457**	**(0.163)*****	**-0.506**	**(0.156)*****	**-0.556**	**(0.169)*****
Δ ln PubBasic(t-6)	-0.097	(0.168)	-0.066	(0.164)	0.048	(0.205)
Δ ln PubBasic(t-7)	0.171	(0.126)	0.148	(0.119)	0.177	(0.126)
Δ ln PubBasic(t-8)	**0.255**	**(0.172)****	**0.268**	**(0.118)****	**0.336**	**(0.140)****
Δ ln PubClinic(t-1)	0.079	(0.068)	0.076	(0.066)	0.071	(0.068)
Δ ln PubClinic(t-2)	**0.117**	**(0.064)***	**0.124**	**(0.062)****	**0.161**	**(0.074)****
Δ ln PubClinic(t-3)	0.007	(0.065)	0.009	(0.062)	-0.016	(0.069)
Δ ln PubClinic(t-4)	0.031	(0.065)	0.020	(0.061)	0.014	(0.063)
Δ ln PubClinic(t-5)	0.052	(0.060)	0.061	(0.059)	0.048	(0.062)
Δ ln PubClinic(t-6)	0.010	(0.053)	0.013	(0.050)	-0.006	(0.055)
Δ ln PubClinic(t-7)	-0.003	(0.052)	-0.020	(0.049)	-0.044	(0.056)
Δ ln PubClinic(t-8)	0.047	(0.047)	0.045	(0.045)	0.028	(0.050)
Δ ln FDA Delay(t-2)	-0.018	(0.016)	-0.020	(0.016)	-0.022	(0.017)
Δ ln Hosp Admis. (age<35)	-0.135	(0.915)				
Δ ln Hosp Admis. (age 35-44)	-0.074	(0.159)				
Δ ln Hosp Admis. (age 45-54)	0.009	(0.134)				
Δ ln Hosp Admis. (age 55-64)	**0.437**	**(0.211)****	**0.347**	**(0.180)***	0.230	(0.220)
Δ ln Hosp Admis. (age>64)	-0.368	(0.238)	-0.361	(0.234)	-0.235	(0.273)
Δ ln Mortality (age<35)	0.084	(0.111)				
Δ ln Mortality (age 35-44)	-0.190	(0.124)				
Δ ln Mortality (age 45-54)	-0.040	(0.172)	**-0.187**	**(0.083)****	**-0.187**	**(0.085)****
Δ ln Mortality (age 55-64)	**0.620**	**(0.335)***	**0.649**	**(0.288)****	**0.790**	**(0.329)****
Δ ln Mortality (age>64)	-0.040	(0.299)				
Class dummies	None		None		None	
Time dummies	Not Sig.		Not Sig.		Not Sig,	
R-squared	.4447		.4376		.4195	
Adjusted R-squared	.1145		.1705		.1438	
Number of Observations	119		119		119	
F-statistic for Pub Clinical	F=0.78, p-value< .6257		F=0.98, p-value< .4601		F=1.05, p-value< .4094	
F-statistic for Pub Basic	F=2.80, p-value< .0110		F=3.52, p-value< .0016		F=3.38, p-value< .0022	
F-statistic for Hosp Visit	F=1.09, p-value< .3753		F=2.07, p-value< .1329		F=0.58, p-value< .5621	
F-statistic for Mortality	F=1.41, p-value< .2294		F=3.81, p-value< .0263		F=4.08, p-value< .0205	

Pooled OLS and Pooled 2SLS Regressions, Years 1981-1997, Seven Therapeutic Classes

Standard Errors in Parentheses

*** 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 Science on Pharmaceutical Investment

	(3) - 2SLS		(4) - 2SLS		(5) - 2SLS	
Dependent Variable:	Δ ln Research(t)		Δ ln Research(t)		Δ ln Research(t)	
Δ ln Sales(t-1)	**0.790**	**(0.455)***	**.772**	**(0.452)***	**1.16**	**(0.387)*****
Δ ln PubBasic(t-1)	**0.391**	**(0.172)****	**0.336**	**(0.171)****	**0.301**	**(0.180)***
Δ ln PubBasic(t-2)	0.221	(0.230)	0.241	(0.220)	**0.323**	**(0.189)***
Δ ln PubBasic(t-3)	**-0.344**	**(0.174)***	**-0.399**	**(0.158)****	**-0.410**	**(0.161)****
Δ ln PubBasic(t-4)	0.205	(0.203)	**0.307**	**(0.173)***	**0.386**	**(0.165)****
Δ ln PubBasic(t-5)	**-0.556**	**(0.169)*****	**-0.586**	**(0.164)*****	**-0.661**	**(0.168)*****
Δ ln PubBasic(t-6)	0.048	(0.205)	0.031	(0.201)	0.081	(0.169)
Δ ln PubBasic(t-7)	0.177	(0.126)	0.174	(0.127)	0.194	(0.120)
Δ ln PubBasic(t-8)	**0.336**	**(0.140)****	**0.315**	**(0.143)****	**0.423**	**(0.137)*****
Δ ln PubClinic(t-1)	0.071	(0.068)	0.062	(0.067)		
Δ ln PubClinic(t-2)	**0.161**	**(0.074)****	**0.145**	**(0.076)***	**0.191**	**(0.076)****
Δ ln PubClinic(t-3)	-0.016	(0.069)	-0.001	(0.070)		
Δ ln PubClinic(t-4)	0.014	(0.063)	-0.001	(0.063)		
Δ ln PubClinic(t-5)	0.048	(0.062)	0.036	(0.059)		
Δ ln PubClinic(t-6)	-0.006	(0.055)	-0.000	(0.055)		
Δ ln PubClinic(t-7)	-0.044	(0.056)	-0.049	(0.054)		
Δ ln PubClinic(t-8)	0.028	(0.050)	0.019	(0.047)		
Δ ln FDA Delay(t-2)	-0.022	(0.017)				
Δ ln Hosp Admis. (age<35)						
Δ ln Hosp Admis. (age 35-44)						
Δ ln Hosp Admis. (age 45-54)						
Δ ln Hosp Admis. (age 55-64)	0.230	(0.220)				
Δ ln Hosp Admis. (age>64)	-0.235	(0.273)				
Δ ln Mortality (age<35)						
Δ ln Mortality (age 35-44)						
Δ ln Mortality (age 45-54)	**-0.187**	**(0.085)****	**-0.179**	**(0.086)****	**-0.165**	**(0.085)***
Δ ln Mortality (age 55-64)	**0.790**	**(0.329)****	**0.830**	**(0.330)****	**0.936**	**(0.321)*****
Δ ln Mortality (age>64)						
Class dummies	None		None		None	
Time dummies	Not Sig,		Not Sig.		Sig,	
R-squared	.4195		.3806		.3612	
Adjusted R-squared	.1438		.1194		.1625	
Number of Observations	119		119		119	
F-statistic for Pub Clinical	F=1.05, p-value< .4094		F=0.82, p-value< .5833			
F-statistic for Pub Basic	F=3.38, p-value< .0022		F=3.93, p-value< .0006		F=4.45, p-value< .0001	
F-statistic for Hosp Visit	F=0.58, p-value< .5621					
F-statistic for Mortality	F=4.08, p-value< .0205		F=4.03, p-value< .0214		F=4.82, p-value< .0103	

Pooled OLS and Pooled 2SLS Regressions, Years 1981-1997, Seven Therapeutic Classes

Standard Errors in Parentheses

*** indicates significance at a 1% level

** indicates significance at a 5% level

* indicates significance at a 10% level

Table IV. Average Marginal Effects of a $1 Increase

Variable	Public Basic Science	Public Clinical Science	Industry Sales
Long-run elasticities	0.637	0.191	1.16
Ratio (Industry R&D / variable)	4.95	6.2	0.16
Marginal effect ($)	3.153	1.184	0.186

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 science for 1995 (Pub clinical average = 495.264 million); average industry sales in 1996 (industry sales average = 19227.81 million); and, the average for public basic research is over the eight year period 1989-1996 and across all classes (Pub basic average = 619.607 million).