JOURNAL OF Economic Behavior & Organization

ISSN 0167-2681

Special Issue: Academic Science and Entrepreneurship: Dual engines of growth

Guest Editors: Adam Jaffe, Josh Lerner, Scott Stern and Marie Thursby

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Academic science and the birth of industrial research laboratories in the U.S. pharmaceutical industry

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Received 16 June 2005; accepted 19 May 2006
Available online 16 January 2007

Abstract

We investigate the rise of industrial research laboratories in the U.S. pharmaceutical industry from 1927 to 1946. Our analysis demonstrates that the growth of industrial pharmaceutical laboratories is positively and significantly correlated with the extent of local university research, after controlling for other observables and correcting for simultaneity bias using instrumental variables. Overall, our analyses suggest that while the presence of industrial facilities helped shape the direction of university research programs in some cases, there was a significant, positive, and causal effect running from university research to the growth of pharmaceutical research laboratories in the first half of the twentieth century in the United States.
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1. Introduction

The establishment and growth of industrial research laboratories is one of the key organizational innovations affecting technological progress in the United States in the 20th century (Mowery, 1990). We investigate in this paper the rise of industrial research laboratories in the U.S. pharmaceutical industry between 1927 and 1946. Our evidence suggests that universities played a significant role in the establishment and diffusion of industrial research laboratories in the U.S. pharmaceutical industry during this period. We demonstrate that the emergence and growth of

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private pharmaceutical research laboratories depends upon the extent and growth of nearby academic science. We are alert in our analysis to the fact that this relationship may not have been unidirectional and we devote particular attention to the possibility that the local industrial base affected the nature of academic science at universities during this period. Our analyses provide suggestive though not dispositive evidence of the impact of local firms on university programs. When we correct for this endogeneity bias, however, the result that laboratory births are positively related to Ph.D. program graduates remains. We interpret this combination of qualitative and quantitative evidence as support for the hypothesis that universities played a significant role in the birth of early American pharmaceutical research laboratories.

Although mutually beneficial relationships between universities and firm laboratories have become commonplace in the life sciences in the past few decades, such collaborations were substantially less common a century ago. Reflecting the U.S. pharmaceutical industry's roots in patent medicines and quackery, academic scientists were skeptical (if not openly scornful) of university ties with industry.[1] Academic disdain for industry abated over the first decades of the 20th century as industrial research laboratories became an increasingly common form of research organization and as collaboration between firms and universities emerged and began to take root in these laboratories. In large part, the increasing relevance of academic science for industrial purposes in the late 19th and early 20th centuries appears to have been a principal underlying force that enabled collaborations between universities and industry to be ultimately fruitful (Mowery and Rosenberg, 1998; Murmann, 2003). In this paper, we argue that the existence of U.S. universities (and their specific form and nature) animated the potential for interaction between academic scientists and pharmaceutical firms in the U.S. interwar period.

Our argument relies in large part on the expectation that the potential benefits of adopting in-house pharmaceutical research laboratories and the costs of doing so vary as a function of geographic proximity to academic research. Consistent with findings from the late 20th century (e.g., Zucker et al., 1998), historical accounts suggest that regular and rich interactions between academic scientists and pharmaceutical firms played an important role in transforming historically manufacturing- and marketing-oriented ventures into research-oriented organizations (Swann, 1988, 1990). Thus, we argue that firms located near research universities were more likely to adopt in-house R&D facilities because local universities provided both part-time faculty consultants with highly specialized knowledge and scientifically trained university graduates who could be employed as full-time research employees. Because long-distance collaboration was more difficult in the first half of the twentieth century than it is today, firms were more likely to focus their search for scientific expertise on nearby institutions.

We assess the relationship between academic science and the establishment of pharmaceutical research laboratories by estimating the impact of academic science research (proxied by the number of Ph.D. graduates in relevant disciplines) on the number of industrial pharmaceutical laboratories established and the number of pharmaceutical R&D workers in geographically proximate areas. The analysis reveals that pharmaceutical labs were more likely to be located in counties that contained research in academic chemistry or science. Specifically, the number of pharmaceutical laboratories in a county in 1938 and 1947 is, across a wide range of specifications, positively and significantly associated with the initial number of research laboratories and the contemporaneous count of local science Ph.D. graduates. To correct for potential simultaneity

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[1] Quoting a 1915 report of the Committee of the Board of Trustees of the American Medical Association, Parascandola (1985) illustrates the contempt held by medical scientists for industry: "It is only from laboratories free from any relations with manufacturers that real advances can be expected."
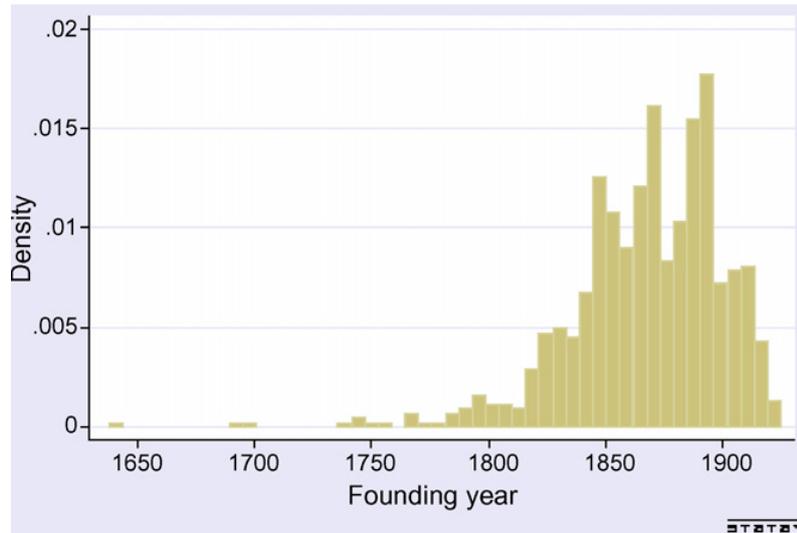
Fig. 1. Founding dates of U.S. universities prior to 1924. *Source*: Biennial of Education, 1924.

bias (i.e., that would arise if both research universities attracted industrial laboratories and the research conducted in these laboratories affected nearby academic departments) we employ an instrumental variables approach. These results demonstrate that, even after correcting for simultaneity, the growth of pharmaceutical research labs in a county is significantly and positively related to the number of local science Ph.D. graduates, implying a causal relationship.

The remainder of the paper proceeds as follows: Section 2 introduces background research on university-industry interaction and reviews the history of the pharmaceutical industry in the early 20th century and the origins of industrial research laboratories. Section 3 outlines our empirical approach for investigating the relationship between academic science and laboratory formation. Section 4 describes our data. Section 5 presents our core empirical analysis. Section 6 discusses our instrumental variables estimates. Section 7 concludes, discussing the implications of the results and speculating regarding related future research.

2. University-industry interaction and the origin of industrial research laboratories

In this section, we lay the groundwork for our argument that U.S. universities contributed to the establishment and growth of industrial research laboratories. In particular, we review evidence that describes the growth of U.S. universities in the late 1800s and early 1900s, suggests the importance of universities to the United States' emerging industrial leadership, and suggests that proximity and specific institutional arrangements played an important role in university-industry interaction.

2.1. The emergence of U.S. universities and the nature of university-industry interaction

Figs. 1 and 2 display the number of universities and industrial research labs by founding date, beginning in 1830. They reveal that more universities were founded in the late 19th century than in any other period. In large part, the rise of universities was due to the Morrill Act of 1862, which established the land-grant universities, and the Hatch Act of 1887, which provided aid for the study of scientific agriculture.[2] The emergence of industrial research labs came somewhat later,

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[2] Goldin and Katz (1999) refer to the period of 1890–1940 as the "formative years" of U.S. higher education.
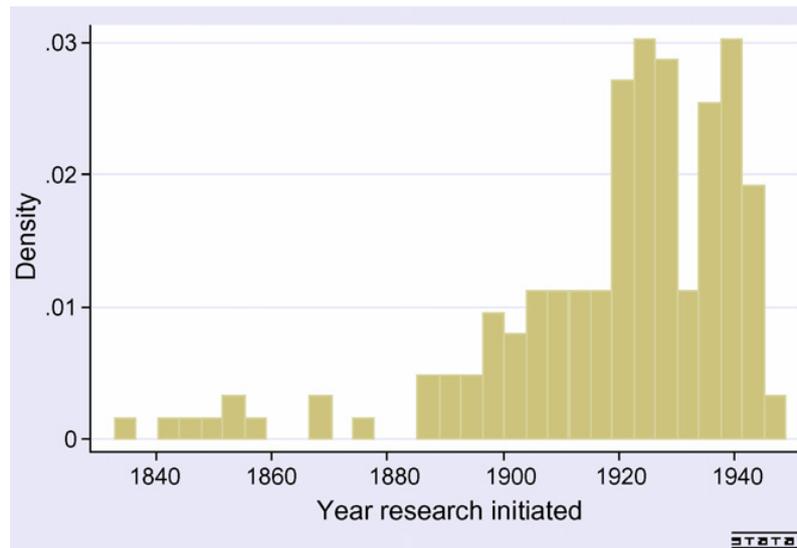
Fig. 2. Founding dates of pharmaceutical research labs. *Source*: Industrial Research Laboratories of United States, 1946.

in the 1920s and 1930s.[3] The boom during this period was quite substantial, so substantial in fact that university-industry interaction reached a high point in the period between World War I and World War II. As Mowery and Rosenberg (1998) note, "university-industry research linkages... were well-established before World War II. Indeed, the share of university research expenditures financed by industry appears to have declined throughout much of the postwar period" (p. 37).[4]

Rosenberg, Mowery, Nelson and a number of co-authors have argued that the research universities that emerged during this period – and, in particular, the aspects of academic science that responded to the needs of industry – became one of the main drivers of American technological leadership in the twentieth century.[5] These authors describe a number of examples of commercially important early inventions that originated in universities.[6]

The role of proximity in facilitating university-industry linkages is central in our investigation of the factors that led to the rise of industrial research laboratories. Existing empirical studies of contemporary university-industry research linkages suggest that research conducted in universities has a significant and geographically focused effect on innovation. Jaffe (1989) provides evidence that corporate patenting in certain industries is positively associated with state-level spending on university research in related academic disciplines. Acs et al. (1992) substitute innovation counts

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[3] It should be taken into account that these graphs are snapshots taken at two different points in time: the university data were compiled in 1924 and the industrial research lab survey was conducted in 1946. As a result, firms that were founded prior to 1946 but did not survive to that date are not counted.

[4] Also, Swann (1988) argues that post-war increases in federal funding for university research in the health sciences reduced collaboration between universities and the pharmaceutical industry.

[5] See Nelson and Wright (1992), Rosenberg and Nelson (1994), Mowery and Rosenberg (1998), Rosenberg (2000) and Mowery et al. (2004).

[6] These include the Babcock test (which improved the way dairy producers tested the butterfat content of milk); Edwin Armstrong's research on vacuum tubes at Columbia University (which influenced the development of radio technology); the development of hybrid corn at agricultural experiment stations. As another example, the University of Akron supplied local rubber producers with skilled employees, and its scientists conducted research in the processing of rubber and, later, polymer chemistry (Mowery et al., 2004, p. 1). Additional examples include the University of Oklahoma's research in the field of petroleum, the University of Kentucky's and the University of North Carolina's focus on the processing of tobacco, and the University of Illinois and Purdue University's work on railroad technologies (Rosenberg and Nelson, 1994).

for patent data and find even stronger evidence for spillovers from university research. Jaffe et al. (1993) find that knowledge spillovers from university research, as measured by patent citations, are geographically concentrated.[7] In a study of the biotechnology industry, Zucker et al. (1998) show that biotechnology firms tend to locate near universities in order to take advantage of the areas' higher levels of "intellectual capital".

2.2. The origins of industrial research

The first organized industrial research laboratories appeared in Germany in the 1870s in firms that sought to commercialize inventions based on recent breakthroughs in organic chemistry (Mowery and Rosenberg, 1998, p. 13.). Murmann (2003) describes the co-evolution of the dye industry and academic research in chemistry in nineteenth-century Germany and argues that spillovers from universities to the dye industry and vice versa enabled Germany to dominate the international dye industry in the 19th century. Mowery and Rosenberg argue that it was not scientific developments alone that led to the growth of in-house research in the United States, but also the strength of U.S. anti-trust policy following the Sherman Act (which triggered a search for alternative sources of market power through industrial innovation) and stronger protection of intellectual property rights through the patent system.[8] It could also be argued that the increasing strength of intellectual property rights in the late 19th and early 20th centuries would seem to promote greater specialization in innovation and vertical *dis*-integration rather than a shift in innovative activity from the realm of the independent inventor to within the boundaries of the corporation. Indeed, Lamoreaux and Sokoloff (1996, 2002) document a well-functioning market for technology in the late nineteenth century United States. In 1870–1871, for example, 72 percent of all patents that were assigned to a party other than the inventor were assigned after issue. By 1910–1911, this number was halved (36.5 percent). Fisk (1998) explains that, prior to the 1890s, courts almost always favored the rights of the inventor in cases where the ownership of an employee's invention was contested by an employer. Starting in the 1890s, Fisk documents the emergence of the "shop right" patent doctrine, which favored the employer in intellectual property disputes. This change in intellectual property doctrine no doubt made it much more attractive for firms to establish in-house research labs.

Mowery and Rosenberg also emphasize the importance to industrial innovation of science conducted in universities. In this paper, we argue that the unique form taken by American universities in the late nineteenth and early twentieth centuries helped promote the adoption of industrial research laboratories within the boundaries of firms. Whereas during the nineteenth century, "most industrialists believed the manufacturer's job was to manufacture; new ideas to improve manufacturing could be purchased or otherwise appropriated ... managers offered little support for research until they had evidence that a worker's results indicated likely commercial application," (Swann, 1988, p. 13) the institutionalization of scientific research in universities facilitated the adoption of scientific research in industry. The scientific research undertaken in

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[7] Patent citations are references in the patent document to other patented technologies that bear a similarity to the invention or that influenced the inventor. Note that Adams (2002) also finds evidence of geographically mediated university spillovers and that Furman et al. (in press) find evidence of a relationship between local academic science and pharmaceutical research productivity in the 1980s and 1990s.

[8] However, as Mowery points out, "a weak antitrust climate in other nations, such as Germany, was associated with growth in industrial research, making it difficult to assert a direct cause-and-effect relationship between anti-trust policy and the growth of intrafirm R&D" (Mowery, 1990, p. 346).

universities reduced the cost to firms of acquiring scientific knowledge and this led firms located near universities to access and, in many cases, engage in research.[9] Furthermore, the trend towards specialization and professionalization in science increased the supply of qualified workers with easily identifiable skills. Once firms could access a pool of potential research workers whose academic credentials reduced the uncertainty associated with hiring them, firms could establish labs to engage in long-term research projects.

Several interrelated historical forces combined to favor the organization of invention within the firm. Changes in the nature of technology, in the extent to which firms could claim intellectual property rights over their employees' inventions, and in the enforcement of anti-trust rules contributed to firms seeking to adopt in-house industrial research facilities. In order for firms to respond to these forces to organize invention within firm boundaries, they needed skilled R&D workers and scientific expertise. Universities provided these inputs to production of new technology through consulting relationships and by providing certification for the skills of potential R&D employees.

2.3. Research in the U.S. pharmaceutical industry in the early 20th century

Although a select number of pharmaceutical firms employed in-house researchers in the early years of the 20th century, the period between 1920 and World War II witnessed a substantial change in the organization and function of U.S. drug makers (Swann, 1988). Over this period, the industry changed from consisting of nearly entirely manufacturing-oriented firms to being largely comprised of firms dedicated to the systematic discovery and introduction of efficacious medicines. Some of the changes in the industry were preceded or accompanied by legislative changes, such as the Biologics Control Act of 1902 and Pure Food and Drug Act of 1906 (and the 1912 Shirley Amendment), each of which pushed the industry towards more rationalized practices and away from 'patent' medicines, nostrums of dubious medicinal value, often containing blends of narcotics and caffeine, and marketed under fanciful names and with fanciful claims. One of the key implications of the 1906 Food and Drug Act arose from its ascribing dominion over labeling to the federal government. Government-mandated labeling helped physicians and the general public to discern patent medicines from 'ethical' pharmaceutical products (Rasmussen, 2005). Evolving medical norms also played a significant role in increasing the value of university-based research to ethical pharmaceutical firms. In 1905 the American Medical Association created a Council on Pharmacy and Chemistry (CPC), whose membership was comprised of qualified chemists and other academically accredited scientists and mandated that no pharmaceutical products could be advertised in the *Journal of the American Medical Association* (JAMA) or any other cooperating journals without the Council's approval; as JAMA and other medical journals constituted a significant source of advertising for drug-makers, the incentives to gain CPC approval were high (Rasmussen, 2005). Meeting these standards required providing increasing evidence of safety, which in turn increased firms' needs to and benefits of working with qualified scientists and academic physicians.

The development of research capabilities in U.S. pharmaceutical firms was further accelerated by World War I. The loss of access to European medicines increased the need for national medicine-making capabilities, and the ability to develop medicines was enhanced both by Euro-

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[9] For related historical examples, see Hounshell and Smith (1988), Mann and Plummer (1991), Galambos et al. (1995), and Furman (2003).

pean immigration and by the seizure and auction of German intellectual property by the Office of the Alien Property Custodian.

Government intervention in the late 1930s further increased incentives for pharmaceutical firms to collaborate with researchers or engage in-house research. Responding both to scientific opportunity and to the increasingly salient dangers of unregulated medications, the U.S. Congress passed the Federal Food, Drug, and Cosmetic Act in 1938.[10] One of the key aspects of this act was to require that all new drugs receive approval by the Food and Drug Administration (FDA) as a condition for market introduction. Other aspects of this Act led to a distinction between prescription and over-the-counter medications, which had the impact of increasing the fraction of drugs marketed through and to physicians (Temin, 1979).

Finally, the loss, once again, of medicines from Europe and the exigencies of war prompted significantly increased investment in research during World War II. Prior to the war, the U.S. federal government offered limited support for university science (Mowery and Sampat, 2001). During the war, however, the U.S. government became actively involved in promoting drug development and manufacturing. Two major projects in which the government played a large role were the production of penicillin and dried plasma.[11] These projects were mainly dedicated towards large-scale manufacturing, but significant R&D capabilities were a pre-requisite for achieving the knowledge to produce the products effectively, and those firms that had already achieved some level of in-house research expertise were at considerable advantage.

3. Empirical approach and data on universities and pharmaceutical research laboratories, 1920–1946

3.1. Empirical approach

We now turn to our empirical analysis of the role of academic science in the establishment of industrial research labs during the first half of the 20th century. Although there are clear benefits to investigating the adoption of an organizational innovation around the time of its inception are clear, there are many challenges associated with the analysis of historical data. Free of all data constraints, an ideal research design would observe a panel dataset including the universe of pharmaceutical manufacturers and marketers, with which we could investigate firm-level adoption of in-house research to the characteristics of geographically proximate academic science. The data at our disposal differ from the ideal dataset in a number of ways. First, we are unable to observe a universe of potential adopters over the sample period; instead, we are able to observe (with some noise) firms that self-identify as having adopted industrial research laboratories, using data from the publication *Industrial Research Laboratories of the United States*, a survey based record published by the National Research Council. As a consequence of our inability to track the panel of firms that do not adopt laboratories (and, hence, to perform firm-level analysis), we conduct

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[10] The case of sulfanilamide illustrates both the best and the worst of the pharmaceutical industry at the time. Sulfanilamide played an important role in reducing military deaths during World War II. In 1937, only a few years before the war, a Tennessee-based drugmaker sold an untested product, which it called Elixir Sulfanilamide, that was marketed for children and whose active ingredients included "a highly toxic chemical analogue of antifreeze" that ultimately killed more than 100 people (Swann, 1998). The outrage generated by this tragedy helped the Food, Drug, and Cosmetic Act, which had been proposed to Congress more than five years earlier, ultimately pass into law in 1938.

[11] In the period leading following the discovery of antibiotics, Lee (2003) notes a significant divergence between those firms that invested heavily in R&D and those that did not.

our analysis at the level of geographic regions, examining whether the extent of academic science in a county is associated with the emergence of pharmaceutical research laboratories and the employment of pharmaceutical researchers within that geographic unit.

A second limitation imposed by historical data regards our ability to measure the extent of relevant academic science proximate to pharmaceutical firms. Counts of academic publications (potentially weighted by journal quality or citations) could be used to construct precise and nuanced measures of the extent and quality of relevant academic science in a geographic region. Major large scale datasets do not, however, include data prior to World War II (e.g., Medline's coverage begins in the mid-1960s, while Thomson-ISI's Science Citation Index's earliest systematic records begin in 1946). Counts of faculty members by university and department would also provide suggestive indicators of the level of commitment to academic science by institution and geographic region. We were not, however, able to identify a source for these data in the early 1900s. Data do exist, though, that enable us to identify the counts of Ph.D. graduates by institution for a number of academic fields (from the *Bulletin of the Office of Higher Education (Biennial of Education)* and the American Council on Education's serial publication *American Universities and Colleges)*.[12] As institutions that devote greater faculty resources to conducting academic research are more likely to have doctoral programs, we believe that university-specific counts of Ph.D. graduates in science are likely to be useful indicators of university scientific output.[13]

Our empirical approach evaluates the impact of academic science (the flow of Ph.D. graduates) on the extent of pharmaceutical research laboratories in a geographic region. The basic empirical model takes the following form:

$$R\&D_{it} = \alpha + \gamma_t + \beta_1 R\&D_{i0} + \beta_2 Sci_{it} + \beta_3 Sci_{i0} + b_4 Pop_{it} + \beta_5 Mfg_{it} + \varepsilon_{it} \tag{1}$$

where $R\&D_{it}$ is either the number or the employment of R&D laboratories in county i in year t, Sci_{it} is our proxy for academic science, and Pop_{it} and Mfg_{it} are the population of the county and the number of manufacturing establishments located within its boundaries. The 0 subscript refers to the initial period (in this case, 1927). In addition to estimating models that control for the characteristics of focal regions, we examine the robustness of our results to spatial correlation.

Because our dependent variables are non-negative integers truncated at zero (i.e., count variables), we employ Negative Binomial regressions designed to account for these characteristics of the data. To facilitate the interpretation of the coefficients on the covariates as elasticities, each of these enters in logs.[14] In our analysis, we also estimate a fixed-effects model to account for county heterogeneity and also pursue an instrumental variables approach to address the possibility that panel estimates of the relationship between university and industrial research are characterized by simultaneity bias.

3.2. Data sources and descriptive statistics

We draw our data on the number of research labs by city from the publication Industrial Research Laboratories of the United States, collected by the National Research Council. In 1920, the National Research Council began to circulate surveys inquiring about firms' industrial research

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[12] We thank Claudia Goldin for making the *Biennial* data available.

[13] We also obtained data on the universities' research expenditures for certain years. While this variable comes closer to the effect we are trying to estimate, it is not available for a sufficient number of universities and years during our sample period.

[14] In each case, we add 1 to the variable before taking logs.

Table 1
Descriptive statistics

	Obs.	Mean	S.D.	Min	Max
County-level data					
Pharma laboratories	9318	0.11	1.19	0.00	41.00
R&D personnel	9318	3.29	37.06	0.00	936.00
Ph.D.s granted in biomedical science in county[a]	9318	0.43	3.88	0.00	75.09
Ph.D.s granted in biomedical science in county (continuous distance measure)	9318	1.32	6.49	0.00	127.33
Ph.D.s granted in chemistry in county[a]	9318	0.30	2.77	0.00	47.18
Ph.D.s granted in chemistry in county (continuous distance measure)	9318	0.95	4.86	0.00	96.22
County population (in millions)	9318	0.04	0.15	0.00	4.29
County manufacturing establishments (in hundreds)	9318	0.72	5.12	0.00	263.28
University-level data					
Total Ph.D.s granted	342	16.97	29.23	0.00	171.55
Ph.D.s granted in science	342	12.58	19.92	0.00	105.91
Ph.D.s granted in chemistry	342	4.60	7.32	0.00	43.45

[a] The Ph.D. counts by discipline for 1946 are obtained by taking the yearly average of the total count for 1939–1950, obtained from "American Universities and Colleges" (sixth edition, 1952) published by the American Council on Education. This explains why the maximum in these fields is not an integer.

activities. While the term "industrial research" was interpreted broadly to include development and product improvement, the term "laboratory" was restricted to apply only to those departments of companies that had "separate and permanently established research staff and equipment," excluding "firms that indicated they only occasionally carry out research, using teams temporarily recruited for the purpose or assembled from their operating staffs" (National Research Council, "Industrial Research Laboratories of the United States," 1956, Introduction, p. 2). We include all firms classified in the pharmaceutical/chemical sectors. Government and university laboratories were excluded, as were labs that conducted testing and analysis but no research.

These publications contain information on the characteristics of industrial research labs in nineteen years between 1920 and 1985; we use data from the editions published in 1927, 1938, and 1946.[15] In the earliest years in which the series was published, these characteristics include the firm's address, the number of its research employees, and a brief description of its activities. In later years, the surveys list the labs' founding dates, number of scientific and other personnel by type (i.e.: biologists, chemists, etc.), the names of important researchers, research publications issued by the company, and their partners in collaborative research.[16] We report descriptive statistics for our data in Table 1. The number of laboratories per county is skewed; the modal number of laboratories is zero, however, counties can have up to 41 laboratories over the course of the sample. The number of employees per county is similarly skewed; while the mean number of reported R&D personnel is 3.3, the standard deviation is 37.1.

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[15] The years in which volumes were published are: 1920, 1927, 1931, 1933, 1938, 1940, 1946, 1948, 1950, 1956, 1960, 1965, 1970, 1975, 1977, 1979, 1982, 1983, and 1985.

[16] Starting in 1950, the volumes also contain indices of universities that participate in collaborative research, indicating whether or not the university possesses "facilities for research in practically all fields of science", its facilities are limited to specific fields, or it has particular capabilities in certain areas.

We combine data on industrial research labs with (a) information on American universities drawn from the *Bulletin of the Office of Higher Education* (*Biennial of Education*) and the American Council on Education's serial publication *American Universities and Colleges* in the years 1927, 1938, and 1946 and (b) data on county-level population and manufacturing establishments drawn from the US censuses of population and US censuses of manufacturing, respectively, for the years 1920–1950.[17] Population and manufacturing data allow us to control for the extent to which the size and level of economic activity affect the extent of industrial pharmaceutical research in U.S. counties. There are, indeed, numerous indicators of region-specific social, economic, and demographic characteristics that we could include in our analysis and that may yield nuanced implications. Nonetheless, we limit our consideration to these two principal measures as they have the most direct interpretation as indicators of local economic activity that might drive the adoption of industrial research laboratories. In order to control for all time invariant influences on the foundation of industrial pharmaceutical labs, we also estimate models that include region- or county-specific fixed effects.

4. Evaluating the role of universities as a determinant of pharmaceutical laboratory growth

Table 2 contains results from negative binomial panel regressions in which the dependent variable is either the number of pharmaceutical industrial research labs by county and year or the number of R&D personnel identified by biochemical firms in the NRC data. Each regression includes (logged) county population and the number of manufacturing establishments in the county to control for factors associated with county size and economic activity. Throughout the Table, we address county-specific heterogeneity by controlling for the impact of initial conditions (conditions in the county in 1927) on the number of laboratories in subsequent years of the data. In Table 3, we include county fixed effects to further control for heterogeneity.

In the first four columns of Table 2, we model the number of pharmaceutical labs in a county as a function of county population, county manufacturing establishments, the initial number of pharmaceutical labs in the county in 1927, and, depending on the column, both the 1927 count and contemporaneous count of Chemistry or Biomedical Ph.D.s granted by universities in the county.[18] The initial number of pharmaceutical labs is relevant for adjudicating competing hypotheses regarding the birth of industrial research labs. Specifically, the significance and direction of the coefficient on initial labs helps evaluate whether their growth is random or follows a pattern consistent with convergence or divergence. This variable enters positively and significantly in each of the models, implying that counties with disproportionately more labs in 1927 tended to have disproportionately more labs in later years. The finding is consistent with the pattern of path dependent growth evident in Feldman and Schreuder's (1996) study of the early pharmaceutical industry in the Mid-Atlantic region.

The specifications in Columns 1–4 relate measures of the growth of academic science to the count of country-level laboratories in 1938 and 1946; each Column includes both a contemporaneous measure of academic science (a count of either Chemistry or Biomedical Ph.D.s) and a

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[17] In matching the county-level manufacturing and population data to the county-level lab data, we were careful to account for changes over time in county boundaries.

[18] Biomedical Ph.D.s include degrees in anatomy, bacteriology and microbiology, biochemistry, chemistry, genetics, pharmacology, physiology, and public health.

Table 2
Location of pharmaceutical research, 1938–1946 negative binomial regressions, controlling for initial conditions

	(1) Laboratories in county	(2) Laboratories in county	(3) Laboratories in county	(4) Laboratories in county	(5) County-level sum of R&D workers	(6) County-level sum of R&D workers
Chemistry Ph.D.s in county[a]	0.660 (0.201)***					
1927 chemistry Ph.D.s in county[a]	−0.471 (0.231)*					
Biomedical Ph.D.s in county[a]		0.529 (0.198)***				
1927 biomedical Ph.D.s in county[a]		−0.343 (0.204)				
Distance-weighted chemistry Ph.D.s in county[a]			0.552 (0.193)***		1.462 (0.865)*	
1927 distance-weighted chemistry Ph.D.s in county[a]			−0.282 (0.271)		−0.912 (1.145)	
Distance-weighted biomedical Ph.D.s[a]				0.574 (0.218)**		2.248 (1.123)**
1927 distance-weighted biomedical Ph.D.s in county[a]				−0.223 (0.215)		−1.390 (1.181)
1927 pharma labs in county[a]	2.095 (0.328)***	2.066 (0.361)***	1.944 (0.355)***	1.927 (0.383)***	1.410 (0.218)***	
1927 R&D workers in county[a]						1.443 (0.208)***
Population[a]	−2.772 (0.636)***	−2.783 (0.634)***	−2.355 (0.603)***	−2.366 (0.628)***	−1.684 (2.178)	−1.815 (2.194)
Manufacturing[a]	0.959 (0.103)***	0.965 (0.107)***	0.817 (0.115)***	0.845 (0.117)***	1.000 (0.225)***	1.024 (0.224)***
Year = 1938	−0.611 (0.234)***	−0.612 (0.236)***	−0.603 (0.237)**	−0.569 (0.248)**	−0.892 (0.544)*	−0.775 (0.498)*
Constant	−6.621 (0.428)***	−6.645 (0.429)***	−6.422 (0.426)***	−6.443 (0.422)***	−4.762 (0.877)***	−5.629 (0.798)***
Observations	6184	6184	6184	6184	6184	6201

Standard errors, corrected for spatial correlation, are reported in parentheses.

[a] In logs.

* Significant at 10 percent.

** Significant at 5 percent.

*** Significant at 1 percent.

Table 3
Conditional fixed effects negative binomial regressions, 1927, 1938 and 1946

	(1) Laboratories in county	(2) Laboratories in county	(3) Laboratories in county	(4) R&D workers in county	(5) R&D workers in county
Chemistry PhDs in county[a]	0.201 (0.218)				
Distance-weighted Chemistry PhDs in county[a]		0.469 (0.228)**		0.045 (0.119)	
Biomedical PhDs in county[a]					
Distance-weighted Biomedical PhDs in county[a]			0.579 (0.268)**		0.141 (0.135)
Population[a]	−1.439 (1.970)	−1.643 (1.930)	−1.738 (1.856)	0.833 (0.541)	0.748 (0.549)
Manufacturing[a]	0.247 (0.257)	0.274 (0.238)	0.287 (0.251)	0.306 (0.126)***	0.270 (0.127)**
Year = 1938	0.233 (0.089)	0.033 (0.139)	0.073 (0.123)	0.333 (0.243)	0.302 (0.245)
Year = 1946	0.705 (0.114)	0.478 (0.183)***	0.444 (0.181)**	1.384 (0.219)***	1.345 (0.227)***
Constant	15.452 (1.914)	15.154 (1.860)***	14.784 (1.858)***	−4.152 (0.579)***	−4.037 (0.581)***
Observations	584	584	584	545	545
Number of groups (county state)	186	186	186	173	173

Dependent variable is either the number of laboratories in county i in year t or the total employment of laboratories in the county, Robust standard errors, corrected for spatial correlation, are reported in parentheses.

[a] In logs.
* Significant at 10 percent.
** Significant at 5 percent.
*** Significant at 1 percent.

control for the initial flow of Ph.D.s in 1927. In each case, the contemporaneous count of Ph.D.s enters positively and with statistical significance at the 5 percent or 1 percent level.

Because neighboring counties are economically linked, shocks are likely to be correlated across counties belonging to the same local economy. We allow for correlation across geographically proximate counties, using standard errors adjusted for spatial correlation in a manner based on Conley (1999) and Rappaport and Sachs (2003). We account for spatial correlation by applying a weighting function g_{ij} to the estimated variance–covariance matrix of the parameters. In the case of the maximum likelihood estimates (i.e. the Negative Binomial and logit models), the estimator solves $\Sigma_t \Sigma_i S_{it}(\hat{\theta}) = 0$, where $S_{it}(\theta) = \partial \log L_{it}(y_{it}, \theta)/\partial \theta$, the vector of derivatives of the log-likelihood for observation *it*. The standard error formula takes the form $\text{Var}(\hat{\theta}) \approx (\text{H})^{-1} [\Sigma_i \Sigma_t \Sigma_j \Sigma_k S_{it}(\hat{\theta}) \, S_{jk}{}'(\hat{\theta}) g_{ij}](\text{H})^{-1}$, where H is the matrix of second derivatives of the likelihood function, $H = \partial S_{it}{}'(\theta)/\partial \theta$, and $g_{ij} = (1 - (\text{distance}_{ij}/200)^2)$ if $\text{distance}_{ij} \leq 200$ km, and 0 if $\text{distance}_{ij} > 200$ km.[19]

In column 1, we include the number of Chemistry Ph.D.s awarded in 1927 separately from the number of Ph.D.s awarded contemporaneously. The coefficients in this column imply that, holding observable county characteristics constant, an increase of 10 percent in the number of contemporaneous Chemistry Ph.D.s is associated with a 6.6 percent increase in the number of labs in the county, respectively. The coefficient in Column 2 implies that a 10 percent increase in the number of contemporaneous Biomedical Ph.D.s is associated with a 5.3 percent increase in the number of county labs. The negative (though insignificant) coefficient on the lagged number of Ph.D.s confirms the importance of the *growth* of science—for a given level of contemporaneous research, counties that had relatively more research in 1927 saw relatively less growth in pharmaceutical R&D.

Because the county-level count of Ph.D.s ignores the potential influence of academic science on labs that are in different counties but geographically proximate, columns 3 and 4 present estimates that use a distance-weighted count of Ph.D.s within a 200 km radius of the county in which the lab is located.[20] We calculate distance-weighted counts by summing up Ph.D.s granted by all universities within 200 km, weighted by the distance between the county and the lab. That is, we calculate:

$$\text{Ph.D.\_wt}_{it} = \sum_j \frac{\text{Ph.D.s}_{jt}}{1 + d_{ij}},$$

where Ph.D._wt for firm *i* is the number of Ph.D.s nearby, weighted by the distance between firm *i* and university *j*. Nearby Ph.D.s would get a high weight (low inverse weight), whereas Ph.D. 200 km away make a smaller contribution to the count. We calculate these variables and estimate the relationship between them and the R&D variables because of concerns about the arbitrary nature of county boundaries. The results using distance-weighted counts of Ph.D.s suggest an association between laboratories and Ph.D. graduates similar to those based on county-level Ph.D. counts.

We also model the growth of pharmaceutical *employment* in addition to the number of labs over this period, although we recognize that the NRC data on lab employment are less reliable. For example, employment data may reflect total firm employment rather than lab-level

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[19] In another robustness check, we clustered the standard errors by BEA economic area. This led to a comparable change in the standard errors.

[20] We thank Toby Stuart for suggesting a distance-weighted measure. We modeled our Ph.D. count on the "IPO concentration" measure found in Stuart and Sorensen (2003).

employment, and, for about 10 percent of the observations, no employment data are listed. Although these data are very noisy, we estimate the correlates of county-level R&D workers in Columns 5 and 6. Consistent with the findings in Columns 1–4, these results also evidence an impact of initial conditions on growth. Counties with disproportionately higher private R&D employment in 1927 also had disproportionately higher private R&D employment in 1927. The relationship between distance-weighted Ph.D. graduates and private R&D workers remains positive and statistically significant (although it is only significant at the 10 percent level using distance-weighted Chemistry Ph.D.s in Column 5, it is significant at the 5 percent level using distance-weighted Biomedical Ph.D.s in Column 6).

It is worth noting that these results are not driven by those counties in which the largest firms (e.g., such as Abbott, Lilly, and Merck) reside. The key results in Table 2 are robust to the exclusion of counties that include firms whose R&D employment falls into the top 10 percent of the distribution. The results are also robust to the exclusion of all counties in states in New England and the Mid-Atlantic area (i.e., MD, DE, PA, NJ, NY, CT, RI, MA, VT, NH, and ME). We have also checked that our results are not an artifact of the way the data was collected. The 1927 NRC volume states that members of the main scientific and engineering associations were consulted in order to establish a list of firms known to have in-house research labs, and the published information is based on surveys were sent to these firms. To guard against the possibility that these societies tend to be located near universities and thus that our results are biased, we ran regressions that include a dummy variable equal to 1 if there was a branch of the American Chemical Society (ACS) located in county i in year t.[21] We found that the presence of an ACS branch is positively but insignificantly correlated with the number of laboratories in a county and that including the ACS dummy did not induce a significant change in the coefficients of interest.

Table 3 contains the results of conditional fixed-effects Negative Binomial regressions run on all years (1927, 1938, and 1946) and including a county-level fixed effect to control for time-invariant characteristics of the county that may be associated with both the location of R&D and academic science. [22] The coefficients in Table 3 are thus identified by changes over time in the number of Ph.D.s granted and the extent of R&D located in a county. The distance-weighted Ph.D. counts continue to exhibit a positive and significant association between academic research in Chemistry and in Biomedical science more broadly and laboratories, after controlling for unobserved heterogeneity across counties. However, the coefficients on these variables lose their significance in the specifications explaining county-level pharmaceutical R&D workers. This is consistent with our concern that the data reflecting the sum of county-level pharmaceutical R&D workers are noisy. It is worth noting, however, that these variables are significant in the initial conditions regressions in Table 2 and in the instrumental variables estimates presented in Table 5.

5. Statistical evidence on the influence of private industry on university programs

Our qualitative evidence suggests that the research needs of large firms played a role in the evolution of at least a few universities. Our quantitative analysis offers mixed support for this proposition. Table 4 reports the results of logit regressions at the level of the university that examine the determinants of the adoption of a chemical engineering program for the first time between

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[21] These data were obtained from the *Directory of Members* of the American Chemical Society. Directories from 1924, 1930, and 1947 listed the locations of branch headquarters and the year in which they were chartered.

[22] The number of observations falls because the nature of the log-likelihood function makes it impossible to include counties in which no laboratories ever locate.

Table 4
New chemical engineering programs, 1937–1947

	(1)	(2)	(3)	(4)
Pharma labs in 1938	0.475 (0.087)***	0.463 (0.081)***		
Pharma R&D employment in 1938			0.012 (0.003)**	0.011 (0.002)**
Manufacturing in 1939	0.018 (0.168)	−0.009 (0.217)	−0.006 (0.167)	−0.031 (0.224)
Population in 1940	−1.003 (0.263)***	−0.859 (0.289)***	−0.823**** (0.250.)	0.731*** (0.290)
Growth of population, 1940–1950		−0.984 (0.879)		−1.168** (0.920)
Growth of manufacturing, 1939–1947		−0.380 (0.306)		−0.408 (0.307)
Growth of pharma labs, 1938–1946		−0.260*** (0.079)		
Growth in R&D employment, 1938–1946				0.0002 (0.0011.)
Constant	8.201 (2.279)***	7.054*** (2.406)	6.455*** (2.167)	5.826*** (2.390)
Observations	954	954	954	954

Dependent variable = 1 if the university began offering degrees in chemical engineering between 1937 and 1947, Robust standard errors, corrected for spatial correlation, are reported in parentheses.

* Significant at 10 percent.
** Significant at 5 percent.
*** Significant at 1 percent.

1937 and 1947. We use the full sample of universities and colleges drawn from the publication *American Colleges and Universities,* excluding religious seminaries, teacher's colleges, and junior colleges. Data on engineering programs in American universities are drawn from the United States Office of Education's *Bulletins*.[23] The dependent variable takes on the value 1 if the university established a department of chemical engineering for the first time between 1937 and 1947, and 0 if not. Universities that had already established programs by 1937 are omitted from the analysis. This variable is regressed on a measure of pharmaceutical research in industry in the county in 1938, the population and number of manufacturing establishments in the county in 1940 and 1939 respectively, and the growth of population, manufacturing, and industrial research in pharmaceuticals during the period.[24] The results show that universities located in counties that were centers of research in the pharmaceutical industries in 1938 were significantly more likely to establish a department of chemical engineering between that year and 1947, even after controlling for the growth of the industry during that period. This appears to be evidence of a feedback effect in which the presence of nearby firms influenced the programs offered by universities. Such effects were not evident, however, when we looked at universities that began granting Ph.D.s in Chemistry during this period. We were also unable to find evidence of "anchor" effects in the data (Agrawal and Cockburn, 2003; Feldman, 2003), in which especially large firms had a particularly large impact on the growth of local university programs in sciences or chemistry.

6. Instrumental variables estimates

The preceding sections of this paper document a statistically significant, positive relationship between the number of pharmaceutical industrial research laboratories in a county and university research in a county, after controlling for other variables likely to influence the location decision of R&D labs and including a county-specific fixed effect. These results imply that growth over time in the amount of university research (as measured by the number of Ph.D.s granted) in a county was associated with growth over time in pharmaceutical R&D in a county. However, panel estimates of the relationship between university and industrial research are likely to be characterized by simultaneity – research universities attracted industrial laboratories, and the research conducted in these laboratories affected nearby academic departments. In this section, we use instrumental variables to correct for this simultaneity bias. The instruments include the amount of money obtained as the proceeds of the sale of land and scrip granted to the state under the Morrill Act of 1862, a dummy variable equal to 1 if a university in the county was founded before 1800, and the number of non-science Ph.D.s awarded in the county (data on sale prices land grants are from the U.S. Bureau of Education, 1930).

The Morrill Act established the "land-grant" colleges by giving the states public lands that could be sold to finance the colleges. A state received 30,000 acres for each member of its congressional delegation, and since the smallest states had at least two senators and one representative, the minimum land grant consisted of 90,000 acres. The Hatch Act of 1887 provided funding for agricultural experiment stations, and a second Morrill Act in 1890 extended the land grant provisions to southern states.

While the amount of land granted under the Morrill Act was proportional to the size of the state, the sale price per acre obtained by states varied considerably and for somewhat aleatory reasons. Nevins (1962) writes that:

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[23] The Bulletins, part of the series "Accredited Higher Institutions" were published in 1938 and 1948.

[24] For universities in cities that fall in multiple counties, we use the average of these variables.

"A great deal of obscurity yet surrounds the precise disposition made by some states of their share of the Morrill grant... Many university historians tend to pass over the disposition of the grants hastily... partly because the story has occasional elements of folly and rascality that make it embarrassing. A number of states let the land scrip slip through their fingers; fingers loosed by negligent officers, pried apart by speculators, or even greased by corruptionists" (p. 29).

Rhode Island was granted 120,000 acres and asked Rev. Horace T. Love (president of Brown University) to select the land for sale. He went west in the summer of 1863 and came back "to report that the task was impossibly heavy, for it involved choosing lands, paying taxes, negotiating sales, and defending titles" and a committee of five was appointed by Love to take charge. The committee then sold the land to Love in 1865 for $50,000 (the lowest amount received by any state, and the third lowest per acre), accepting payment over five years with no interest. Nevins is "not astonished to learn that the sale aroused much criticism." In Pennsylvania, "Heavy pressure had come from an unholy partnership of land speculators, anxious to obtain a bargain, and officers of the state college, anxious to get funds for a new start." Other states in which the sale of Morrill lands was bungled include New Jersey, New Hampshire, and Connecticut (all quotes from Nevins, 1962, pp. 29–31)

In contrast, states like New York managed to turn the grants into more significant endowments. Faced with a glut of land scrip and depressed land prices following the Act, Ezra Cornell purchased New York's scrip and held it until prices rose. When Cornell returned the land and profits to the university in 1905, the value had risen almost seven-fold, to $5,460,038. California, Illinois, Iowa, Michigan, Minnesota, and Nebraska also obtained higher prices per acre for their scrip.[25]

The price per acre obtained for Morrill Act land grants had a long-run impact on university finances. The states that obtained the most for their scrip are the ones that are even today home to the better-funded public universities. However, because the price per acre obtained by the states varied substantially for reasons unrelated to the state's attractiveness to industrial research labs seventy years hence, it constitutes a valid instrument.[26] We compute the real value of the sale price obtained for Morrill Act land grants (in 1863 dollars) using a CPI-based conversion factor (Williamson, 2005).

The other instruments we include are a dummy variable equal to one if the county contains a university founded before 1800 and the number of non-science or engineering Ph.D.s granted in each county in each year of the data. The oldest private universities, with the largest endowments, graduated many more science doctorates during this period than the typical private university. We argue that the establishment of universities in the 18th century is exogenous to the location of pharmaceutical R&D in the early 20th century. The latter instrument changes over time to capture the *growth* of universities during this period. However, the growth in humanities and the social sciences is presumably uncorrelated with the growth in pharmaceutical R&D relative to the level of economic activity in the county.

Table 5 presents non-linear two-stage least squares estimates in which the endogenous variable is log of the number of Ph.D.s granted in a county, and the instruments are the original sale price

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[25] These data come from the U.S. Office of Education's Biennial of Higher Education, 1930 (no. 9, vol. 1 *Survey of Land-grant Colleges and Universities*, pp. 10 and 11).

[26] There may be some concern that states placed universities in counties with heavy manufacturing concentration and that for this reason the land grant instrument is correlated with the errors. While it is true that states had a mandate to serve agricultural and manufacturing interests through public universities, we feel that this concern is misplaced because any influence the location of manufacturing in the mid- to late-19th century may have had on the location of public universities is controlled for through the inclusion in the regression of the number of manufacturing establishments in the county.

Table 5
GMM (non-linear 2SLS) instrumental variables estimates

	Dependent variable = # of labs in county				Dependent variable = R&D employees in county			
	Ph.D.s treated as exogenous		Ph.D.s treated as endogenous		Ph.D.s treated as exogenous		Ph.D.s treated as endogenous	
Constant	−6.385 (0.519)***	−6.573 (0.512)***	−6.338 (0.519)***	−6.510 (0.517)***	−4.498 (0.749)***	−4.548 (0.759)***	−4.592 (0.815)***	−4.620 (0.808)***
Manufacturing[a]	0.904 (0.098)***	0.945 (0.101)***	0.907 (0.093)***	0.941 (0.097)***	0.979 (0.116)***	0.989 (0.118)***	0.989 (0.119)***	0.994 (0.118)***
Population[a]	−1.173 (0.525)**	−1.372 (0.586)**	−1.099 (0.499)**	−1.289 (0.584)**	−1.126 (0.602)**	−1.075 (0.581)**	−0.929 (0.508)**	−0.890 (0.529.)
Biomedical PhDs[a]	0.628 (0.117)***		0.577 (0.121)***		0.390 (0.131)***		0.302 (0.138)**	
Chemistry PhDs[a]		0.709 (0.117)***		0.670 (0.129)***		0.401 (0.123)***		0.318 (0.142)***
1938	0.123 (0.092)	0.225 (0.123)*	0.150 (0.089)*	0.225 (0.115)**	1.869 (0.275)***	1.896 (0.299)***	1.912 (0.328)***	1.927 (0.326)***
1946	0.366 (0.139)**	0.442 (0.099)***	0.406 (0.127)***	0.457 (0.097)***	2.319 (0.181)***	2.364 (0.177)***	2.376 (0.204)***	2.401 (0.198)***
Observations	9307	9307	9307	9307	9307	9307	9307	9307
Over-ID test			0.8340	0.0279			0.8314	0.8753
p-Value			0.659	0.986			0.660	0.646

Year and region dummies included Robust standard errors, corrected for spatial correlation, are reported in parentheses.

[a] In logs.
* Significant at 10 percent.
** Significant at 5 percent.
*** Significant at 1 percent.

received by states for land and scrip obtained through the Morrill Act, the dummy for universities founded before 1800, and number of non-science Ph.D. granted in the county. We use a Generalized Method of Moments (GMM) model for count data with endogenous regressors similar to the additive model described by Windmeijer and Santos Silva (1998). Two sets of regression results are included, one with the number of labs on the left hand side, and another with R&D employment. We control for manufacturing, population, and year and region fixed effects (county or state fixed effects could not be included due to collinearity with the instruments).

The GMM estimates are positive and significant at the 1 percent level in each of our specifications).[27] The coefficient estimates are slightly reduced in magnitude but remain positive and significant at the 5 percent level when the Ph.D. counts are treated as endogenous and instrumented using the variables described above.

7. Discussion

The 1920s, 1930s, and 1940s saw the diffusion of an organizational innovation in the form of the in-house R&D laboratory in the United States. Also during this period, the modern American research university developed and collaborative linkages emerged between industrial and academic researchers. We argue that universities played an important role in the emergence of industrial research situated within the boundaries of the firm, and we present evidence that R&D labs located near universities benefited from increased access to academic scientists and graduates. The results described in this paper characterize the relationship between universities and the pharmaceutical industry between 1927 and 1946. They demonstrate that industrial and academic research were co-located and that proximity to university research was associated with a greater likelihood that firms adopt industrial research facilities and collaborate with academic scientists.

We provide evidence consistent with the possibility of feedback effects, according to which university programs were affected by the presence of pharmaceutical industry activity. Specifically, our empirical results suggest that universities located near larger numbers of industrial research labs in chemistry and pharmaceuticals as of 1938 were more likely to establish new programs of chemical engineering by 1946.

In an attempt to identify the causal effect of academic science on the growth of industrial research, we employ an instrumental variables approach to correct for simultaneity bias in our estimates of the impact of university research on the birth of industrial research laboratories. In sum, our analyses suggest that while the presence of industrial facilities helped shape the direction of university research programs, there was a significant, positive, and causal effect running from university research to the growth of industrial research laboratories in the first half of the twentieth century in the United States.

Acknowledgements

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[27] We obtained similar results using the multiplicative model proposed by Mullahy (1997). We again account for spatial correlation in the standard errors by applying the distance-based weighting function g_{ij}.

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