

EXPERIENCE AND SCALE AND SCOPE ECONOMIES: TRADE-OFFS AND PERFORMANCE IN DEVELOPMENT

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This paper examines how knowledge created by firm experience (learning economies) and scale and scope economies affect performance in firms' development activities. The empirical results suggest that each factor has a significant effect on development performance. Moreover, knowledge that results from greater experience within a particular technological area, when combined with knowledge spillovers from greater scope in other technological areas, significantly improves development performance. The results suggest that experience shapes and facilitates firms' abilities to absorb knowledge spillovers. Our empirical findings thus provide a more nuanced examination of the drivers of performance and have implications for the management of firms' development activities. Copyright © 2006 John Wiley & Sons, Ltd.

INTRODUCTION

Research in the economics of research and development (R&D) suggests that performance is conditioned in large part by the size and breadth of firms' R&D activities (Cohen, 1995; Patel and Pavitt, 1995). These explanations for differential R&D performance trace their roots back to the Schumpeterian hypothesis of increasing returns in R&D (Schumpeter, 1951), and have spawned a large body of research that explores whether there are advantages to firm size and firm scope in the conduct of R&D activity itself (Galbraith, 1952; Pavitt, 1987). Despite this cumulative research, much of the literature examines scale and scope economies in manufacturing and production—empirical ambiguity remains over exactly how scale and scope affect performance in more

knowledge-based activities such as research and development.

A separate body of research has emerged over the last two decades that documents and attempts to explain the role of knowledge in differentiating firm performance (Conner and Prahalad, 1996; Grant, 1996b; Kogut and Zander, 1996). This approach maintains that through a cumulative activity of exploitation (Levinthal and March, 1993; March, 1991), firms develop competitive advantage from experiential learning (Baum, Li, and Usher, 2000), idiosyncratic routines (Nelson and Winter, 1982), and localized knowledge and expertise (Leonard-Barton, 1992). Superior performance results not from scale and scope per se, but from the informational advantages and reductions in uncertainty from greater experience.

We compare and contrast these two perspectives in an empirical examination of development performance. Our results indicate that experience within particular technological areas and scale economies improves development performance, while scope economies reduce performance. Moreover, we find evidence of a complementary relationship between experiential learning and scope

Keywords: knowledge-based view (KBV); learning economies; scale and scope economies

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economies. Knowledge from greater experience in a particular technological area, when combined with knowledge spillovers that result from working in other technological areas, significantly improves development performance. We argue that greater experience facilitates firms' absorptive capacity related to knowledge spillovers (Cohen and Levinthal, 1990). Our findings thus provide a more nuanced examination of the drivers of performance in firms' development activities.

We utilize a unique dataset from pharmaceutical contract research organizations (CROs) to explore these issues. We examine the speed with which drug development projects are completed, which is an increasingly important performance metric in the pharmaceutical industry. First-mover advantages and intense post-patent generic competition provide firms strong incentives to get new drug products to market. Case study evidence suggests that when virtually identical products are brought to market as little as 3–6 months apart, the first-to-market product achieves the largest market share and maintains this advantage indefinitely (Wiggins, 1981). Even when new drug products do not face initial competition, time to market is strategically important since the majority of new product returns are reaped between regulatory approval and patent expiration (Grabowski and Vernon, 1990).

We make several contributions to literature that examines knowledge development in firms' R&D activities. The availability of detailed project- and firm-level data allows us to more directly assess the effects of learning economies and scale and scope economies, and their relationship to each other, on development performance. Previous research on these topics provides inconclusive and contradictory results, mainly due to aggregated firm-level data. We also make important theoretical linkages between research in the economics of R&D and the knowledge-based view (KBV) of the firm. While our results suggest an important role for scope economies in the production of knowledge within the firm, experience moderates this effect due to the requirements and roles of specialized and common knowledge. Finally, we examine an area of R&D (pharmaceutical drug development) that has received more limited scholarly attention in comparison to research that examines pharmaceutical drug discovery. Nevertheless, drug development costs typically exceed those of drug discovery, and are often cited as a primary rationale for

vertical and horizontal mergers in the pharmaceutical industry.

Our empirical findings also have important implications for firms and managers concerned with knowledge development and management related to R&D in this and other related industries. The development and management of knowledge is, not surprisingly, strategically important as it can differentiate firm performance. We find in particular that the interactive effect of learning economies and scope economies presents both benefits and costs. Superior performance requires that firms not only balance development activities so that they are neither overly broad (too many technological areas) nor overly specific (too few technological areas), but also sequence and prioritize development activities so that new knowledge can more easily be absorbed and applied. Performance penalties exist for those firms who are broad in scope but possess relatively little experience in any one particular technological area. These findings thus have implications for firms pursuing technological area depth vs. breadth strategies in particular and technological area exploitation vs. exploration strategies in general. We discuss these implications in more detail in the discussion section below.

The next section provides a brief review of the relevant strategy and economics literatures. It then develops hypotheses related to scale and scope economies and firm experience in development. The following section sets the empirical context, highlighting the distinction between drug discovery and drug development, the pharmaceutical industry's evolving organization and the increasingly important role of CROs. The next section discusses the data and variables, while the section after that presents and discusses the results, significance, and implications of the econometric analysis. The final section makes concluding comments.

HYPOTHESIS DEVELOPMENT

We conceptualize scale and scope economies as they relate to knowledge development in firms' R&D activities. Scale economies in R&D exist when particular development activities are supported by a larger number of development inputs, while scope economies exist when a particular development activity is supported by knowledge

spillovers from other development activities. In our context of pharmaceutical drug development, scale economies result from a larger number of clinical researchers overall and in particular functional areas, while scope economies result from knowledge spillovers from operating in several therapeutic areas. We develop these concepts in more detail below.

Scale and scope economies

The association of firm size with scale and scope economies, market power, and the ability to aggregate inputs is asserted to confer performance advantages on large firms (Scherer, 1980). This argument has been interpreted by many as a claim that there are increasing returns in research and development, both to R&D establishment size and to firm size. Size may also provide advantages in the conduct of firms' R&D efforts (Cohen, 1995) or their innovative activities (Galbraith, 1952). Large firms may be better able to spread the fixed costs of R&D over a larger sales base in the absence of fully functioning markets for innovation (Cohen and Klepper, 1996). Large firms may also be able to exploit economies of scale in the conduct of the R&D activity itself (Panzar and Willig, 1981). Finally, large firms may have greater access to the complementary technologies and downstream capabilities (i.e., marketing and finance) that are presumed to make R&D more productive (Cohen, 1995).

Despite these persuasive arguments, theoretical counter-arguments have been made for each of the above propositions (Scherer and Ross, 1990). Moreover, empirical findings regarding the influence of scale economies on R&D performance are mixed (Cohen and Levin, 1989; Patel and Pavitt, 1995). Some researchers note that these inconsistent findings result from difficulty in developing good measures of R&D or innovation (Cohen, 1995), while others argue that a lack of sufficiently detailed data make it difficult to distinguish between measures of scale and scope (Henderson and Cockburn, 1996). Finally, much of the extant literature examines scale and scope economies in manufacturing and production. Empirical ambiguity remains over exactly how scale and scope affect performance in more knowledge-based environments, such as research and development.

Development performance in knowledge-based activities such as R&D is most likely impacted positively by scale economies for several reasons.

Greater size permits the undertaking of development on a larger scale. Because development entails significant trial and error, larger firms are able to conduct more experiments in more diverse scientific and/or technological areas that guide problem solving in ways that smaller firms cannot. Finally, critical resource inputs can be spread over a larger base of development activity, allowing for greater variation in problem-solving approaches and potential outcomes. We therefore examine the following hypothesis:

Hypothesis 1: Greater size improves development performance, ceteris paribus.

Economies of scope are present if cost savings or performance benefits are realized when two or more activities are conducted jointly in comparison to when these activities are conducted separately (Panzar and Willig, 1981). In the standard analysis of production, scope economies result when activities can share productive inputs at little or no additional cost. Henderson and Cockburn (1996) identify internal spillovers of knowledge as a second source of returns that results from greater diversity in R&D. Knowledge developed and accumulated in one R&D activity can be transferred to other R&D activities at little cost, but with potentially significant performance benefits.

Scope economies in development likely arise from the knowledge spillovers that Henderson and Cockburn (1996) illuminate. Knowledge generated in a given technological area is not only informative, but also potentially beneficial to the development of other technological areas. If this knowledge can be articulated and codified within the firm (Zollo and Winter, 2002), it can then be utilized by other technological areas to improve current development efforts. We therefore hypothesize that knowledge spillovers resulting from greater technological area diversity improve development performance:

Hypothesis 2: Greater technological area diversity improves development performance, ceteris paribus.

Experience

The KBV of the firm documents and attempts to explain the role of knowledge in differentiating performance (Conner and Prahalad, 1996; Grant, 1996b; Kogut and Zander, 1996). Firms are

described as routine-based and history-dependent systems that adapt incrementally to past experiences (March and Simon, 1958). Capabilities grow as experiential learning accumulates from established routines (Nelson and Winter, 1982) and localized knowledge and expertise (Leonard-Barton, 1992), but also importantly depends on the integration of knowledge (Grant, 1996a). Deeply embedded organizational routines both enable and constrain what firms can do (Baum *et al.*, 2000). Because experiential learning is based on highly tacit knowledge it is not only largely immobile and difficult for other firms to easily acquire or imitate (Teece, 1982), but also highly specific to product, technological, or functional areas.

These characteristics suggest that firm knowledge can be an important source of sustainable competitive advantage. If experiential learning provides informational advantages or gains via the perceived legitimacy or past success of repetition (Baum *et al.*, 2000), or the accompanying reduction in uncertainty from learning by doing (Argote, 1999), it should be reflected in superior performance. By contrast, firms relatively new to specific areas are unlikely to have detailed information filters or developed heuristics in place for effective problem solving and decision making. Research that examines firm experience has been largely supportive of these claims, including studies in populations of commercial banks (Pennings and Harianto, 1992), investment banks (Podolny, 1994), and acquiring firms (Haleblian and Finklestein, 1999); technological choices among firms (Christensen and Bower, 1996; Stuart and Podolny, 1996); and foreign market entry (Henisz and Macher, 2004; Mitchell, Shaver, and Yeung, 1992), among others.

Performance in development likely improves from knowledge accumulation via learning economies. Greater experience not only deepens knowledge related to particular technological areas, but also facilitates the creation of common knowledge within the firm (Grant, 1996b). The development of detailed information filters, improvements in shared understanding and more focused problem-solving strategies brought on by greater experience will improve development performance. We therefore examine the following hypothesis:

Hypothesis 3: Greater technological area experience improves development performance, ceteris paribus.

Experience and scope: Trade-offs and contingencies

Per the discussion above, firms improve development performance from their own experience within particular technological areas and from knowledge spillovers that result from working in other technological areas. Two important and relatively unexamined questions are whether these information sources are distinct or compound and interact with each other; and, if related, whether they act as substitutes or complements in improving development performance. On the one hand, knowledge gained from greater experience might not have any relevance to the information provided from knowledge spillovers. Such a scenario is more likely in diversified conglomerates that sell products to distinct markets under different regulatory regimes. But this scenario is less likely in firms whose products, markets, or regulatory environments have some commonality. In this latter case, information gained from experiential learning may either substitute for or complement the information gained from knowledge spillovers.

New knowledge is created as firms expand the number of technological areas that they operate in. While this knowledge is likely to be novel, it might not be relevant to the development efforts of other technological areas that the firm is active in, especially when it possesses significant experience in those technological areas. Firms may therefore discount knowledge spillovers as information sources as their experience grows within a particular technological area, indicating experiential knowledge and knowledge spillovers are substitutes. Experiential learning, however, is likely to have diminishing returns associated with improved development performance (Argote, 1999). As knowledge builds and firms move down the learning curve, subsequent improvement becomes increasingly more difficult.

Knowledge based on other technological areas may present firms with different approaches or problem-solving strategies to consider, however. As knowledge develops through experience in any one particular technological area, moreover, it is more likely that this knowledge is novel, relevant, and useful to other technological areas. Greater experience in a technological area also facilitates common knowledge (Grant, 1996b), which likely improves firms' absorptive capacity related

to knowledge spillovers by improving the understanding and potential application of this information (Cohen and Levinthal, 1990). Current, new, and potential development projects can learn from the mistakes made and successes had (Mitchell, Shaver, and Yeung, 1994), and alter their problem-solving strategies and approaches if necessary and where warranted. Experiential learning and knowledge spillovers are thus more likely to be complements to improving development performance than substitutes. We therefore hypothesize that experience within a technological area improves development performance as the number of technological areas increases.

Hypothesis 4: The positive effect of technological area experience on development performance is increasing in technological area diversity, ceteris paribus.

INDUSTRY CONTEXT

There are two main activities required to bring a new drug product to market in the pharmaceuticals industry. The first set of activities—commonly referred to as drug discovery—involves the initial screening and extraction of a molecule or compound with certain desired therapeutic properties. Once a new substance has been ‘discovered,’ a second set of development-oriented activities involving extensive laboratory, animal and human testing, and considerable regulatory oversight begins. Although the four main phases of drug development are applied to virtually every new drug product, the specific activities undertaken in each vary considerably by product. The preclinical phase includes the development of basic drug profiles, pharmacologic tests to define mechanism of action and dose response, and toxicological tests to determine harmful effects of dosage levels, typically conducted in animals. Phase 1 clinical activities include the cautious administration of the drug to a small number of healthy human patients to determine the metabolism and pharmacologic action of the drug and to demonstrate and assess clinical safety. Phase 2 clinical activities include the administration of the drug to a small sample of human patients actually suffering from the disease or ailment that the drug is meant to address to determine appropriate dosage and regimen, and evaluate effectiveness with respect to key clinical endpoints. Phase 3

clinical activities include evaluations of the overall benefits and risks on a larger and representative human patient population in several testing centers in multiple countries to identify adverse reactions, determine appropriate dosage levels, and further demonstrate product safety and efficacy. The most important concerns to Food and Drug Administration (FDA) regulators are ensuring that sponsor firms develop accurate drug profiles (i.e., basic activity, dose response, mechanism of action, etc.); prove drug safety and effectiveness; and demonstrate safe manufacture that preserves drug composition and stability.

Over the last 25 years, scientific advances in the fields of physiology, pharmacology, enzymology, and cell biology have provided a better understanding of the ‘mechanisms of action’ of many drug compounds, and have facilitated the drug discovery process itself by allowing researchers to more carefully screen, select, and test a wider range of drug compounds. Over the same time period, the rise of biotechnology has created new opportunities for pharmaceutical and biomedical research (Malerba and Orsenigo, 2001). The combined effect of these advances has given rise to what is commonly known as ‘rational drug design,’ or the application of biomedical knowledge to the design of new compounds, as well as to the ways in which new compounds are tested (Cockburn, Henderson, and Stern, 1999; Malerba and Orsenigo, 2001). These advances have reduced the degree of uncertainty involved with drug research and have allowed scientists to better design target compounds through more established scientific theory (Arora and Gambardella, 1994), thereby decreasing the centrality of subsequent *in vitro* and *in vivo* testing to the discovery process.

The biomedical advances that have been made have thus helped to decouple organizational capabilities that underlie drug discovery from those required in drug development (Arora and Gambardella, 1994). The effective separation of the skills required in drug discovery and drug development has led to an increase in the number of small, specialized drug development firms. CROs have subsequently come to represent an important part of pharmaceutical drug development. Since the early 1980s, an estimated one-third of industry R&D spending on clinical trials is now conducted by such independent organizations (CMR International, 1999).

Several aspects of pharmaceutical drug development make it an appropriate setting in which to examine the direct and interactive effects of scale, scope, and learning economies on development performance. Drug development is fundamentally a planning exercise whereby information obtained in one stage must be reviewed and analyzed to determine how best to proceed in terms of allocating resources in subsequent stages over several years and multiple organizations (Spilker, 1989). Because development approaches vary significantly according to the therapeutic area of the drug product, experience in specific technological areas matters. The difficulties associated with development of new drug protocols suggest that localized experience and established knowledge bases within specific technological areas may offer performance benefits. FDA requirements for and auditing of clinical trials have also increased in recent decades,¹ requiring CROs to manage significant amounts of information associated with networks of patients and clinicians. The need to collect, make accessible, and exchange information across space and time entails significant investment to ensure data accuracy and provides some rationale for the importance of scale in the drug development process.

ECONOMETRIC ANALYSIS

Data

Data for this paper were obtained from three sources. A proprietary dataset of drug development projects by CROs was obtained from DataEdge (purchased by Fast Track Systems), a provider of enterprise software and service solutions to pharmaceutical and biotechnology companies engaged in clinical drug development. This dataset contains detailed firm-level information on U.S. and European CROs, including firm age, size and geographic presence; employees' functional backgrounds; and ownership structures (e.g., private,

public, university affiliated, government affiliated). The dataset also contains detailed project-level information, including the type of drug developed (e.g., therapeutic area), the specific tasks undertaken by the focal CRO, the phases of development covered, start and end dates, and the number of subjects and test centers involved, etc.

Our unit of observation is the drug development project, defined as activity directed toward the testing of a drug compound in one of the three phases of a clinical trial. DataEdge provides data in a standardized format and at the same level of aggregation across CROs. To ensure data integrity and empirical validity, however, we conducted a detailed review of industry publications and promotional material for each of the CROs included in the dataset. This information provided greater detail on the histories of individual CROs, as well as the specific types of information and technology services provided. We also conducted a series of telephone and in-person interviews with a number of CROs in the dataset and with other pharmaceutical firms to reduce ambiguity and provide greater detail around the factors that drive drug development performance. Although the firms in the dataset represent a subset of all CROs in existence, our analysis indicates that they are representative of the overall CRO industry in terms of size, technical capability, and financial performance.

Variables

A central critique of empirical work within the economics of R&D has been the frequent use of aggregated data to proxy for the variables of interest. To address this criticism, we construct detailed firm- and project-level data using the DataEdge database.

Performance measures

There are a number of important dimensions of drug development performance in the pharmaceutical industry. Arguably the two most important are the profit achieved and cost incurred for drug development. For CROs, these measures translate into the profit and cost for each drug development project completed for sponsoring pharmaceutical firms. Such data would provide an indication of performance at the project level, as well as overall when aggregated, but are

¹ Since the early 1970s, the number of clinical trials per new drug application (NDA) has increased from 30 to over 70 today. These trials involve increasingly larger numbers of patients, increasing from 500 in 1970 to roughly 4000 today (PhRMA, 1999). On average, each of these patients undergoes nearly 150 clinical tests, with the results of these tests eventually submitted to regulators as part of the formal request for marketing approval for an NDA. The average NDA consists of roughly 30 volumes and more than 100,000 pages of data.

unfortunately neither reliably tracked nor available from DataEdge. Another potentially important performance dimension is the level or rate of innovativeness, as captured by patents or some other intellectual property (IP) measure. As all of the drug compounds in the dataset are patented, an examination of this performance measure is relatively uninformative and uninteresting.

Similar to Cockburn and Henderson (2001) and Danzon, Nicholson, and Pereira (2005), we focus on performance in drug development. Whereas the above authors examine technological success—defined as regulatory approval of a compound in clinical stage(s) of drug development—the nature of our data allows us to examine technological performance—defined as the speed with which CROs complete drug development projects for sponsoring pharmaceutical firms. Our main dependent variable corresponds to the fractional number of months from the date a given drug development project was initiated by a CRO to its completion date. Time to complete is considered one of the most important performance measures for CROs, especially in consideration of the substantial competitive and financial costs associated with delay. We also modify this performance measure by dividing it by the number of clinical employees of the focal CRO and present these results in our econometric analysis. This latter performance measure is intended to provide a test of robustness by examining whether differences in drug development project completion time result from either increasing or decreasing development input factors.

Scale and scope variables

Scale economies. Prior research that examines the effects of scale on R&D performance in the pharmaceutical industry is inconclusive. Early work by Comanor (1965) and Vernon and Gusen (1974) find evidence of decreasing returns to scale in pharmaceutical R&D, but this research is based on highly aggregate data. More recent research confirms the lack of scale advantages with respect to drug research (Henderson and Cockburn, 1996) and drug development (Cockburn and Henderson, 2001) at the drug program level, while other research finds evidence of scale economies in both drug research (DiMasi, Grabowski, and Vernon, 1995; Schwartzman and Cognato, 1996) and drug development (Danzon *et al.*, 2005).

Scale economies likely affect drug development performance in several ways. Drug development requires substantial fixed cost investment. To the extent that human resources, laboratories and testing facilities, and computer resources and data analysis technologies are able to be (re)deployed to multiple projects, firms may reap economies by spreading these fixed costs over a larger development base. Large firms may also obtain scale economies through their superior abilities to attract and support specialized scientific and clinical personnel, or through investments in specialized knowledge and technologies related to given therapeutic areas (e.g., specialized patient and investigator databases in particular areas; researchers and clinicians with relevant expertise; specialized testing equipment and facilities).

The effective design and execution of the battery of clinical and non-clinical tests that are required to successfully complete drug development projects also suggests the importance of scale. Successful drug development efforts, not surprisingly, require CROs to bring together and effectively plan, coordinate, and control a broad range of business functions. Representation (or at least some minimum efficient scale) in several functional disciplines is thought to be required to effectively manage the clinical trial process (Spilker, 1989). CROs' abilities to transfer information across these functional areas, or to impart medical knowledge from operating in more functional areas, are also scale-related and tied to performance (Cockburn and Henderson, 2001). Larger and more functionally diverse CROs may be able to utilize development resources more cost-effectively in comparison to other CROs that are less functionally diverse. We therefore examine two scale-related measures in our econometric analysis. The variable *Employees* represents the logged number of full-time employees within the focal CRO at the time the focal drug development project was undertaken. The variable *Functional Areas* represents the number of functional areas in which the focal CRO has at least 20 full-time employees (FTEs), and measures whether development performance advantages exist from a more functionally related size measure.²

² Two other measures of size—R&D spending and revenue—were rejected because of accuracy questions and anomalies in reporting. The numbers of employees per functional area are provided to DataEdge by CROs through questionnaires. The

Scope economies. The most likely effect of scope economies on drug development performance arises from knowledge spillovers, where the information generated in a given technological area influences the costs and/or timing associated with other technological areas. Firms that are active in several therapeutic areas may develop knowledge that is transferable to other therapeutic areas with little cost but with potentially significant performance benefits. A more diverse drug development project portfolio may allow firms to decrease the time associated with developing new drugs in a particular technological area from spillovers of knowledge. The variable *TA Scope* therefore represents a count of the number of technological areas (therapeutic areas discussed below) in which the focal CRO is active.

Experience variable

As CROs become more experienced in conducting drug development projects, they develop storehouses of knowledge that can be drawn upon for subsequent projects. To the extent that this knowledge becomes organizationally embedded, localized expertise may lead to performance advantages and come to represent sources of lasting competitive advantage. Because clinical development approaches vary significantly by the therapeutic characteristics of the drug, prior experience is particularly important in determining subsequent performance in new drug development in the same therapeutic area. As firms become more experienced in a particular therapeutic area, they acquire localized expertise and develop problem-solving strategies that can be drawn on in subsequent and similar efforts. Greater experience might also improve relationships with important constituents, such as clinicians, patient populations, and regulators (Danzon *et al.*, 2005). The existence of an established knowledge base in a given technological area, as well as established routines for handling similar types of problems (Nelson and Winter, 1982), partially explains why some firms have acquired strong reputations for developing drugs in particular therapeutic areas.

classification scheme creates the following functional areas: (1) clinical; (2) data management; (3) laboratory; (4) medical; (5) quality assurance; and (6) regulatory.

Pharmaceutical drug development employs a fairly standard taxonomy into which drug products can be assigned through major therapeutic areas (e.g., cardiovascular, oncology, central nervous system). The variable *Therapeutic Area Experience* utilizes this taxonomy and is determined by

$$TA_EXP_{i,j,t} = \delta \cdot TA_EXP_{i,j,t-1} + TA_{i,j,t} \quad (1)$$

where $TA_EXP_{i,j,t}$ represents the summation of prior drug development projects completed by CRO i in therapeutic category j at time t , and $TA_{i,j,t}$ represents a count of completed drug development projects for CRO i in therapeutic category j at time t . The depreciation factor (δ) allows recent experience to be weighted more heavily than past experience, which is consistent with the notion of organizational forgetting (Argote, 1999; Benkard, 2000). We depreciate *Therapeutic Area Experience* by 20 percent per period in the econometric analysis, but varied this factor from 10 to 40 percent per period to test its robustness and confirm no significant changes in the econometric results obtain.

Interaction variable

Because we examine the compounding effect of scope economies and experience, we create an interaction term of these two variables. We mean-center the constituent variables in this interaction term to minimize multicollinearity concerns and facilitate interpretation of the results by linking individual coefficient estimates to specific hypotheses (Aiken and West, 1991).

Other variables

Drug characteristics. The size of a drug development project likely affects development time. We employ two variables to control for project size considerations, which respectively represent the number of clinical study *Centers* and *Subjects* (patients) involved in a drug development project. The number of clinical study centers should decrease development project completion time due to scale economies, while the number of subjects should have the opposite effect due to the managerial burdens presented.

Drug novelty should also influence the time required to complete drug development projects.

With less preexisting knowledge regarding the therapeutic characteristics of more novel drugs, CROs likely expend extra effort profiling and exploring clinical effects, *ceteris paribus*. At the same time, drug development projects for conditions where existing standards of care are high require more stringent clinical endpoints, which subsequently take CROs more time to complete. The variable *Drug Novelty* measures the number of marketed drug products within the therapeutic area of the focal drug development project. Along with the therapeutic area indicator variables described below, drug novelty helps control for the effects of differences in drug type and the nature of the disease on development time.

Firm (CRO) characteristics. We include several general and development-specific firm-level factors that may influence the speed with which CROs complete drug development projects. *Public Firm* is an indicator variable that controls for whether the focal CRO is publicly or privately held. *Country* is a count of the number of countries that the focal CRO operates in, and is intended to capture geographic presence. *Firm Age* represents CRO age since its founding to the start of the focal drug development project. *Customer Percent Business* represents the percentage of business that the sponsoring pharmaceutical firm represents to the focal CRO. More established customer relationships may facilitate communication, improve understanding, and improve upon work structures, which might be reflected in productivity benefits.

Project characteristics. As CROs become more experienced in particular development phases, they acquire stocks of generalized expertise related to either the early-stage testing and profiling of new drug products or the later-stage management of clinical trials. These firms may also become more familiar with the general regulatory and administrative issues associated with clinical development and dealing with the FDA within a specific development phase. *Phase Experience* measures the number of development projects completed by a CRO in a particular clinical phase and is determined by

$$\begin{aligned}
 PHASE_EXP_{i,j,t} = & \delta \cdot PHASE_EXP_{i,j,t-1} \\
 & + PHASE_{i,j,t} \quad (2)
 \end{aligned}$$

where $PHASE_EXP_{i,j,t}$ represents the summation of prior drug development projects completed for CRO i in clinical phase j at time t , and $PHASE_{i,j,t}$ represents a count of completed drug development projects for CRO i in clinical phase j at time t . Similar to technological area experience, we use a 20 percent depreciation factor per period. *Own Firm Projects* represents the number of other drug development projects currently ongoing by the CRO separate from the focal drug development project. This variable is time-varying and is intended to separate the effects of therapeutic area scope from the managerial difficulties associated with CROs being spread too thin.

Competitive environment. The variable *Other Firm TA Experience* represents a count of the number of other CROs with experience in the same therapeutic area as the focal drug development project. On the one hand, therapeutic areas with fewer active CROs likely have weaker competitive environments, which reduce firm incentives to complete drug development projects as quickly as possible. On the other hand, therapeutic areas with fewer CROs might represent scarcity conditions in particular skill sets necessary to completing drug development projects in a timely manner. This variable represents an improvement over using just therapeutic area indicator variables (discussed below), as it varies over time.³

Indicator variables. We control for any unmeasured variation that might exist from differences in technological opportunity or development phase using up to 13 therapeutic area and three clinical phase indicator variables, respectively. These indicator variables have been identified in the pharmacoeconomics literature as having a significant effect on drug development time (DiMasi *et al.*, 1991). We also control for unobserved time-varying factors that influence firms' development performance by introducing a yearly time trend. Finally, in some econometric models we control

³ We tested two other competitive environment variables that measure other firm experience. The first represents the number of completed projects for all CROs in the dataset (the depth of other firm experience) in a given therapeutic area. The second represents the number of ongoing projects for all CROs in the dataset in a given therapeutic area. Both variables were highly correlated with our preferred variable. The replacement of our preferred variable with each produced no significant changes to our results. We therefore did not include either in our econometric analysis.

for unobserved heterogeneity among the population of CROs in the dataset by introducing firm-level indicator variables.

EMPIRICAL ANALYSIS

Summary statistics

Table 1 summarizes the dependent and independent variables for the econometric model below. Table 2 provides sample and correlation statistics for the dependent, independent, and control variables. The dataset includes 252 unique drug development projects from 26 different CROs between 1993 and 1999 that cover the four major phases of development. Drug development projects take on average slightly more than 29 months to complete, with minimum and maximum completion times from 0.3 months to 72 months, respectively. CROs participate in an average of slightly more

than eight drug development projects at the same time, with a range between 1 and 13.⁴ CROs have experience in slightly more than six therapeutic areas, on average, with a range between 1 and 14. Finally, drug development projects are spread fairly evenly across the therapeutic areas in our dataset, with an average of slightly more than 18 projects per therapeutic area and a range between 6 and 38.

Some of the variables have high pair-wise correlations, which present multicollinearity concerns and require consideration for identification purposes in the econometric analysis. Our two measures of scale are highly correlated with each other and with the number of countries a given CRO operates in. A variation inflation factor (VIF) test confirms harmful multicollinearity between the scale measures and moderate collinearity between

⁴ CROs with only single projects in the dataset are dropped when firm fixed effects are utilized.

Table 1. Dependent and independent variables

Name	Units	Description
<i>Dependent variables</i>		
Development Time	#	Fractional number of months from the start to completion of a given drug development project
Development Time/Employee	#	Fractional number of months from the start to completion of a given drug development project divided by the number of clinical employees of the focal CRO
<i>Experience variables</i>		
TA Experience	#	Discounted therapeutic area experience of focal CRO
Phase Experience	#	Discounted clinical phase experience of focal CRO
<i>Economies variables</i>		
Employees	#	Total number of CRO employees of focal CRO
Functional Areas	0...6	Number of functional areas focal CRO has at least twenty employees
TA Scope	#	Number of therapeutic areas in which focal CRO has project experience
<i>Other variables</i>		
Subjects	#	Number of subjects involved in focal drug development project
Centers	#	Number of centers involved in focal drug development project
Drug Novelty	#	Number of marketed products in given therapeutic area
Public Firm	0/1	Ownership structure of focal CRO (1 = public)
Countries	#	Number of countries focal CRO operates in
Age	#	Age of focal CRO since founding
Customer Percent Business	0..1	Percentage of overall business pharmaceutical firm represents to focal CRO
Own Firm Projects	#	Number of ongoing drug development projects within the focal CRO
Other Firm TA Experience	#	Number of other CROs with experience in the same therapeutic area as focal drug development project.
<i>Indicator variables</i>		
TA		Therapeutic area fixed effect
Phase		Development phase fixed effect
Firm		Firm fixed effect
Year		Time trend or year fixed effect

Table 2. Descriptive and correlation statistics

	(1) Development Time	(2) Development Time/Clinical Emp.	(3) Subjects	(4) Centers	(5) Drug Novelty	(6) Public Firm	(7) Countries	(8) Firm Age	(9) Customer Percent Business	(10) Phase Experience	(11) CRO Ongoing Projects	(12) Other Firm TA Experience	(13) LN(Total Employees)	(14) Functional Areas	(15) TA Scope	(16) TA Experience
Mean	29.243	2.737	789.086	98.399	8.630	0.399	4.299	9.375	58.596	12.808	8.296	11.003	4.557	1.565	6.825	3.938
S.D.	13.817	4.803	2006.746	391.613	8.796	0.490	5.912	6.395	27.553	17.043	3.399	10.722	1.516	1.554	3.378	2.430
Min.	0.300	0.000	0.000	0.000	1.000	0.000	1.000	-0.085	0.000	0.000	1.000	0.000	2.639	0.000	1.000	0.000
Max.	72.000	16.750	16 000	3 000	30.000	1.000	20.000	33.307	100.000	90.000	13.000	33.000	8.189	6.000	14.000	24.000
(1)	1.000															
(2)	0.548	1.000														
(3)	0.082	-0.004	1.000													
(4)	-0.018	-0.090	0.919	1.000												
(5)	0.034	-0.181	0.210	0.262	1.000											
(6)	0.190	0.527	0.203	0.220	0.034	1.000										
(7)	0.057	-0.255	0.024	-0.067	0.097	-0.265	1.000									
(8)	-0.353	-0.246	0.221	0.316	0.030	0.145	-0.100	1.000								
(9)	0.145	-0.027	0.108	0.198	0.275	0.001	-0.277	-0.002	1.000							
(10)	0.227	0.508	0.016	0.032	0.110	0.226	-0.083	-0.013	0.159	1.000						
(11)	-0.060	0.329	-0.008	-0.062	-0.130	0.027	0.013	-0.009	0.181	0.209	1.000					
(12)	-0.115	-0.039	-0.037	-0.053	-0.068	-0.088	-0.018	-0.073	-0.232	-0.198	0.151	1.000				
(13)	-0.256	-0.605	0.085	0.055	0.106	-0.326	0.726	0.359	-0.284	-0.280	-0.030	0.070	1.000			
(14)	-0.250	-0.504	0.131	0.087	0.095	-0.355	0.771	0.319	-0.275	-0.224	0.142	0.048	0.944	1.000		
(15)	0.138	-0.099	0.026	-0.066	0.156	-0.008	0.743	-0.111	-0.122	-0.009	0.131	-0.075	0.581	0.621	1.000	
(16)	-0.319	-0.175	-0.079	-0.061	0.068	-0.172	0.311	0.070	-0.143	-0.140	0.195	0.290	0.350	0.419	0.315	1.000

Bold indicates pair-wise correlation significance at 0.05 level.

the number of countries and each scale measure. We therefore utilize a single measure of scale economies in separate models of the baseline analysis and eliminate the number of countries from the econometric specification but test for its effects in the robustness analysis. High pair-wise correlation also obtains for the number of clinical study centers and human subjects control variables. A VIF test again confirms harmful multicollinearity, so we accordingly utilize the number of clinical study centers in the econometric specification but test for the effects of patient population in the robustness analysis.

Econometric model

Because we examine the completion of drug development projects by CROs over time, we use event history analysis. Each drug development project is considered to be at risk until it is completed. We model this as a stochastic process, and define the transition rate $r(t)$ of development completion for CRO i at time t as

$$r_i(t) = \frac{\lim_{t' \rightarrow t} \Pr(t \leq t' | T \geq t')}{t' - t}$$

We estimate models that specify the transition rate as a function of time t and a vector of covariates Z that measure experience, scale economies, scope economies, and our control variables. This estimation approach takes the general form $r_i(t) = f(t, Z_{it})$. Our specific approach is a piecewise constant rate model that takes the form $\ln r_i(t) = m_p + \beta Z_{it}$, $t \geq 0$, $t \in I_p$, where Z_{it} represents the covariates and m_p denotes a set of duration-specific effects defined by specific breakpoints $0 \leq \tau_1 \leq \tau_2 \leq \dots \leq \tau_p$ under the assumption that $\tau_{p+1} = \infty$. This specification produces P distinct periods: $I_p = \{t | \tau_p \leq t \leq \tau_{p+1}\}$ and a set of ordered constant terms m_p that indicates whether duration dependence follows any particular pattern. This specification utilizes maximum likelihood estimation that adjusts standard errors for within-firm clustering (by CRO), and is implemented via a user-defined routine in STATA (Sorensen, 1999).

The piecewise exponential specification preserves flexibility without imposing any parametric assumptions or restrictions on the dataset. Constant hazard rates are defined over P periods, in contrast to the Gompertz and Weibull distributions,

which assume a single exponentially increasing (or decreasing) hazard rate, and the exponential distribution, which assumes a single constant hazard rate.⁵ As our measures represent the hazard of a drug development project being completed, variables that lead to shorter (longer) drug development times have positive (negative) coefficients.

As DataEdge does not monitor and track internal drug development by pharmaceutical firms, our dataset includes only outsourced clinical development projects managed by CROs. We also do not possess data on development projects that either did not complete or were unsuccessful in gaining regulatory approval, but do have the exact start and end calendar dates for all drug development projects undertaken by CROs in the sample. While the former condition presents conditional interpretations for our results, the latter two conditions ease left and right censoring concerns.

Econometric results

The econometric results are presented in Tables 3 and 4. Table 3 presents the results for our primary event history analysis, incrementally adding the independent variables of theoretical interest. Table 4 presents several robustness tests using different independent variables and alternative empirical specifications. Each model in Tables 3 and 4 easily rejects likelihood ratio null hypothesis tests for the inclusion of fixed effects and the control and independent variables, at least at the 0.001 level.

Model 1 of Table 3 includes the therapeutic area and development phase fixed effects, as well as a yearly trend variable. Model 2 adds the drug project-level control measures of novelty and centers; the firm-level control measures of firm type, age, customer percent business and phase experience; and the competitive environment control measure of other CROs' therapeutic area experience. Models 3 and 4 add the firm-level independent measures for experience and scope economies and, respectively, our measures of scale economies. Models 5 and 6 add the interaction between experience and scope economies to Models 3 and 4, respectively. As each of the models improves the fit on its predecessor, we focus our attention on Models 5 and 6.

⁵ Our results are robust to these other distributions.

Table 3. Baseline results

	(1)	(2)	(3)	(4)	(5)	(6)
Variable	β (S.E.)	β (S.E.)	β (S.E.)	β (S.E.)	β (S.E.)	β (S.E.)
Time since last event: $0 < \mu \leq 1$	-1.4552 (1.2000)	-4.7333 (1.6643)	-5.1043 (1.8705)	-4.6316 (1.7985)	-5.2826 (1.8324)	-4.7844 (1.7831)
Time since last event: $1 < \mu \leq 2$	0.3074 (0.8138)	-2.2995 (0.9277)	-2.6417 (1.2119)	-2.1348 (1.1406)	-2.7198 (1.2211)	-2.2022 (1.1637)
Time since last event: $\mu > 2$	0.7047 (0.8226)	-1.7582 (0.9869)	-1.9096 (1.2976)	-1.4052 (1.2246)	-1.9890 (1.3073)	-1.4749 (1.2469)
Time Trend	0.1289 (0.1341)	0.2604 (0.1483)	0.2419 (0.1569)	0.2532 (0.1587)	0.2540 (0.1676)	0.2617 (0.1686)
Centers	0.0004 (0.0002)	0.040 (0.0002)	0.0003 (0.0002)	0.0002 (0.0002)	0.0002 (0.0002)	0.0002 (0.0002)
Drug Novelty	-0.0091 (0.0253)	0.718 (0.0111)	-0.0111 (0.0202)	-0.0104 (0.0200)	-0.0171 (0.0212)	-0.0157 (0.0208)
Public Firm	-0.1350 (0.2830)	0.633 (0.2503)	0.2503 (0.1944)	0.3616 (0.2122)	0.2034 (0.2187)	0.2877 (0.2350)
Firm Age	0.0349 (0.0116)	0.003 (0.0206)	0.0114 (0.0114)	0.0169 (0.0136)	0.0150 (0.0135)	0.0140 (0.0163)
Customer Percent	-0.0051 (0.0061)	0.405 (-0.0049)	0.0057 (0.0057)	-0.0031 (0.0055)	-0.0022 (0.0050)	-0.0011 (0.0051)
Business						
Phase Experience		0.0510 (0.0443)	-0.0827 (0.0934)	-0.0477 (0.0949)	-0.0519 (0.1038)	-0.0256 (0.1035)
Ongoing Own Firm Projects		0.250 (0.0447)	0.300 (0.0431)	0.300 (0.0427)	0.570 (0.0472)	0.286 (0.0477)
Other Firm TA Experience		-0.0249 (0.0201)	0.215 (-0.0033)	0.788 (0.0122)	0.980 (0.0140)	0.472 (-0.0073)
TA Experience			0.6000 (0.1915)	0.002 (0.1982)	0.005 (0.1407)	0.001 (0.1510)
TA Scope			-0.1236 (0.0665)	0.063 (-0.1349)	0.042 (0.0663)	0.056 (-0.1412)
LN(Employees)			0.2283 (0.0808)	0.005 (0.0892)	0.001 (0.0802)	0.008 (0.0917)
Functional Areas				0.3000 (0.0892)		0.2551 (0.0917)
TA Experience \times TA Scope					0.1144 (0.0488)	0.1015 (0.0488)
TA Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Phase Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	No	No	No	No	No	No
Number of subjects	252	252	252	252	252	252
Number of observations	1008	1008	1008	1008	1008	1008
Log likelihood	-185.68	-177.34	-160.08	-158.86	-155.48	-155.28

Table 4. Robustness results

	(1)	(2)	(3)	(4)	(5)
Variable	β (S.E.)	β (S.E.)	β (S.E.)	β (S.E.)	β (S.E.)
Time since last event: $0 < \mu \leq 1$	-5.2826 (1.8324)	-5.2536 (1.8363)	-5.8361 (1.9994)	-5.7742 (1.6296)	1.3604 (0.6097)
Time since last event: $1 < \mu \leq 2$	-2.7198 (1.2211)	-2.7098 (1.2275)	-3.2101 (1.3186)	-2.9185 (0.9953)	2.4384 (0.6937)
Time since last event: $\mu > 2$	-1.9890 (1.3073)	-1.9743 (1.3135)	-2.4714 (1.3926)	-1.9605 (1.1017)	3.6586 (0.8283)
Time Trend	0.2540 (0.1676)	0.2473 (0.1702)	0.2597 (0.1666)	0.2726 (0.1826)	-0.1043 (0.0442)
Subjects	0.0002 (0.0002)	0.0000 (0.0000)	0.0002 (0.0002)	0.0001 (0.0002)	0.0001 (0.0001)
Centers	-0.0171 (0.0212)	-0.0157 (0.0213)	-0.0063 (0.0265)	0.0222 (0.0123)	0.0031 (0.0170)
Drug Novelty	0.2034 (0.2187)	0.2135 (0.2189)	0.2751 (0.1954)	0.159	-0.2199 (0.1939)
Public Firm	0.0150 (0.0135)	0.0174 (0.0130)	0.0206 (0.0149)	0.166	0.0189 (0.0093)
Firm Age	-0.0022 (0.0050)	-0.0016 (0.0049)	-0.0006 (0.0047)	0.902	-0.0030 (0.0032)
Customer Percent					0.344
Business					
Countries			0.0642 (0.0515)		
Phase Experience	-0.0519 (0.1038)	-0.0485 (0.1032)	-0.0204 (0.0971)	-0.1033 (0.1470)	-0.0400 (0.0512)
Ongoing Own Firm	0.0503 (0.0472)	0.0481 (0.0467)	0.0510 (0.0439)		-0.0391 (0.0345)
Projects					
Other Firm TA	-0.0094 (0.0130)	-0.0106 (0.0133)	-0.0087 (0.0139)	0.0227 (0.0364)	0.0963 (0.0200)
Experience					
TA Experience	0.4699 (0.1407)	0.4729 (0.1366)	0.4955 (0.1416)	0.4208 (0.1700)	0.2907 (0.0718)
TA Scope	-0.1372 (0.0719)	-0.1386 (0.0729)	-0.1905 (0.1035)	0.1862 (0.1067)	-0.0631 (0.0442)
LN(Employees)	0.2126 (0.0802)	0.2102 (0.0805)	0.1273 (0.0872)	0.0704 (0.1181)	0.2673 (0.0597)
TA Experience \times TA Scope	0.1144 (0.0488)	0.1159 (0.0495)	0.0992 (0.0413)	0.1578 (0.0478)	0.0110 (0.0364)
TA Fixed Effects	Yes	Yes	Yes	No	Yes
Phase Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	No	No	No	Yes	No
Number of subjects	252	252	252	249	252
Number of observations	1008	1008	1008	1002	364
Log likelihood	-155.28	-155.77	-153.96	-124.08	-281.83

A comparison of the constant piecewise hazards coefficients indicates that drug development project completion time increases monotonically with time elapsed since the last event. These results indicate that the likelihood of completion is moderated in part by drug development project age. Drug development projects that involve more clinical study centers decrease development time, while drug novelty increases development time. Although neither coefficient achieves statistical significance, they are in directional agreement with the pharmacoeconomics literature (Kaitin and Manocchia, 1997).

For the general firm-level indicator variables, older and public CROs have shorter drug development project completion times in comparison to their younger and privately held peers. The percentage of business that the sponsoring pharmaceutical firm represents to the focal CRO has no significant effect on development performance. For the drug development specific firm-level variables, the number of ongoing drug development projects improves performance, while the phase experience of the focal CRO decreases performance, although neither achieves statistical significance.

In terms of hypothesis testing, we first argue that scale positively influences development performance (Hypothesis 1). We find strong support for this hypothesis ($p < 0.01$) in both models, using either the natural log of the number of CRO employees or the number of functional areas in which the focal CRO has at least 20 employees. These results suggest that larger size permits the adoption of more effective development problem solving strategies or techniques or allows for development on a larger scale, which subsequently improves performance. We also argue that technological area diversity, our measure of scope economies, improves development performance (Hypothesis 2). Our results indicate instead that therapeutic area scope increases drug development project completion time, which indicates scope diseconomies and suggests that knowledge spillovers are limited or nonexistent between therapeutic areas. Although in agreement with other empirical research on drug development (Danzon *et al.*, 2005), we discuss this somewhat surprising finding in more detail immediately below. We also argue that there are returns to greater experience within a particular therapeutic area (Hypothesis 3), and find strong support for this hypothesis

($p < 0.01$). We thus surmise that greater therapeutic area experience provides useful specialized and common knowledge via experiential learning by doing.

We finally argue that the positive effect of greater therapeutic area experience on drug development project completion time performance is increasing in greater technological area diversity (Hypothesis 4). We find strong support for this hypothesis ($p < 0.05$), which in part helps to explain the counterintuitive scope economies finding above. CROs that have a depth of experience within a particular technological area, as well as breadth of experience in other technological areas, outperform CROs with more limited technological area experience and narrow focus. The knowledge imparted via experiential learning and the knowledge accessible from spillovers among technological areas are therefore complements as opposed to substitutes in improving development performance.

An examination of the economic significance of these results demonstrates that particular threshold levels of experience and scope are required to improve development performance. Figure 1 shows how therapeutic area experience impacts development performance for low (mean - SD), average (mean), and high (mean + SD) levels of therapeutic area scope. This figure normalizes all variables by their mean levels, so all values in the figure indicate the multiplicative effect of changes from this baseline. For low technological area diversity firms, greater therapeutic area experience has a positive but relatively modest impact on development performance. The effects of experience are more profound, however, for CROs with greater levels of technological area diversity. Average diversity CROs improve development performance more than four times from the minimum to maximum level of experience, while highly diverse CROs improve performance more than seven times from the minimum to maximum level of experience. Figure 1 also indicates that average-diversity CROs outperform low-diversity CROs at the mean level of therapeutic area experience, while highly diverse CROs outperform other CROs at experience levels in excess of the mean level.

Table 4 provides several robustness tests for some of our independent variables and alternative empirical specifications. Owing to space constraints we provide only the results for one measure of scale economies (employees), although these

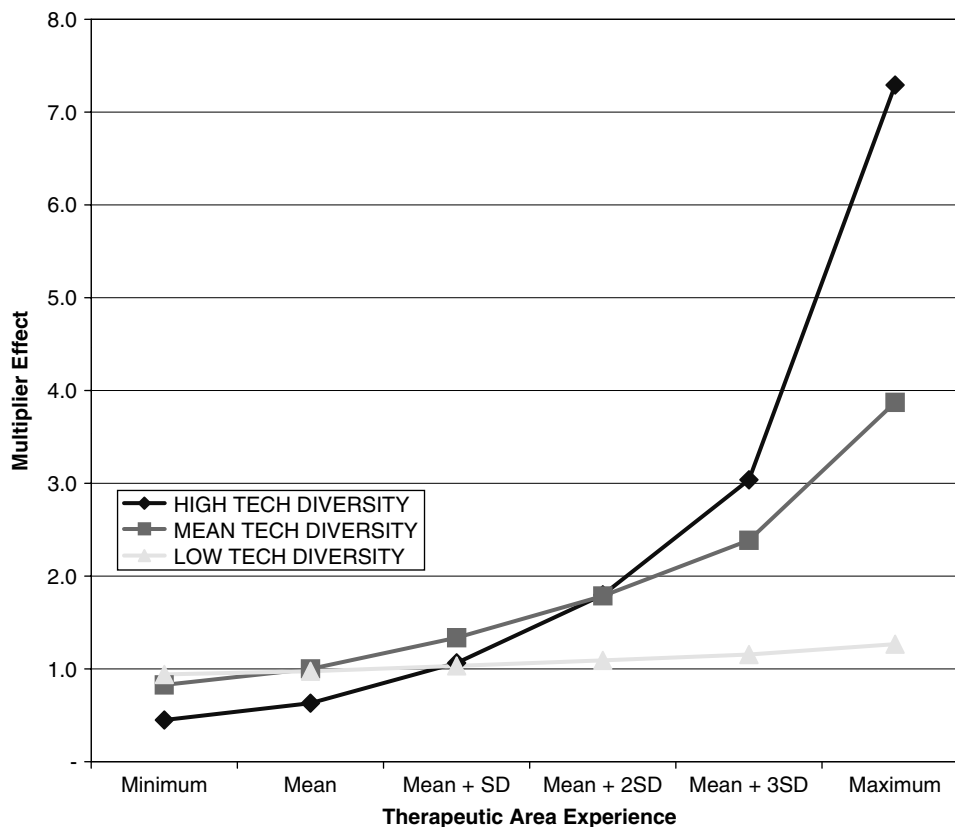


Figure 1. Interaction of experience and scope on development performance

results are qualitatively identical using the other scale measure (functional areas). Model 1 repeats the Model 5 results of Table 3 for comparison purposes. Models 2 and 3 examine the multicollinearity concerns associated with some of our independent variables. Model 2 replaces the number of clinical study centers in Model 1 with the number of human subjects, while Model 3 adds the number of countries the focal CRO operates in to Model 1. Coefficient estimates and standard errors are nearly identical in comparing Model 1 and Model 2, and the same result is true from comparing Model 3 to Model 1, although our measure of scale economies loses statistical significance but is still positive in sign. A likelihood ratio test between Models 1 and 3 indicates that the addition of *Countries* does not improve the explanatory power of the specification ($p > 0.10$).

Model 4 of Table 4 addresses concerns of unobserved firm-level heterogeneity by adding firm-level indicator variables to Model 1. This alternative specification requires us to limit our analysis

to a reduced sample of CROs that undertake multiple drug development projects, and we drop the therapeutic area fixed effects to preserve degrees of freedom. The results are qualitatively similar to Model 1, although one change of note is the loss of statistical significance in our scale measure.

Model 5 addresses concerns that our dependent variable does not control for differences in development performance brought on by increasing or decreasing input factors. This model alters the dependent variable—time to project completion—by dividing it by the number of clinical employees of the focal CRO, which subsequently changes the number of spells for each development project. Some of the Model 4 results are notably different in comparison to Model 1. In particular, the constant piecewise hazards coefficients change sign but still indicate that drug development project completion time increases monotonically with time elapsed since the last event, which again suggests that the likelihood of completion is moderated by project age. Firm age

remains positive and becomes statistically significant, which indicates that older CROs achieve superior development performance in comparison to their younger peers. Finally, most of our main theoretical variables of interest maintain their signs and statistical significance, although the interaction term does not.

DISCUSSION

Our empirical results confirm the role of size in differentiating development performance. In particular, we find that both the number of employees and the size of functional representation within the firm improve performance. Interviews with pharmaceutical firms and CROs confirm that there are important performance differences between small and large CROs, particularly related to large-scale and data-intensive development. Larger and more functionally diverse CROs appear to more effectively utilize development resources or implement problem-solving strategies related to development in comparison to smaller or less functionally diverse CROs. Our results also suggest that technological area experience yields development performance advantages. CROs with more experience in a particular therapeutic area appear to develop both specialized technological knowledge and general common knowledge, such as problem-solving and decision-making approaches, that can be drawn on in subsequent and similar development efforts. The knowledge gained from working within a particular technological area thus represents an important and lasting source of competitive advantage.

Our results suggest that technological area diversity by itself results in scope diseconomies. In particular, CROs who participate in many (possibly unrelated) therapeutic areas achieve worse performance in comparison to those in fewer therapeutic areas. Technological area diversity may overextend or limit CROs—not in their abilities to develop new knowledge, but in their abilities to usefully apply this knowledge to other technological areas. Our results suggest, however, that technological area experience plays an important moderating role in the relationship between scope economies and development performance. CROs with limited technological area scope achieve modest development performance through additional

experience, while CROs with significant technological area scope achieve superior development performance from additional experience.⁶

Our results therefore extend the work of Henderson and Cockburn (1996) and others (Chandler, 1992; Teece, 1980), who suggest that one of the most important determinants of scope in R&D-intensive industries is the opportunity to take advantage of intra-firm spillovers of knowledge within closely related technological areas. We find evidence that development performance is determined in part by the relationship between experience in a particular technological area and diversity across technological areas, perhaps because experience shapes and influences firms' absorptive capacities (Cohen and Levinthal, 1990). Experience increases firms' understanding of the shape and dimensions of the technological area landscape (Levinthal, 1997), and develops the problem-solving strategies that are effective in improving performance. Firms also better understand idiosyncrasies, have likely made efforts in codifying tacit information, and have solved more and more varied problems as experience grows within a technological area. The knowledge gained from operating in other technological areas is also better understood in terms of its relevance to particular technological areas. This storehouse of information and problem-solving approaches can also be used to inform and improve upon the development efforts in other technological areas. Efforts to capitalize on the cost and productivity advantages associated with scope and learning economies may help to explain many of the noticeable changes taking place in the pharmaceutical industry. Both the pharmaceutical and contract research industries have witnessed an intense wave of consolidation in recent years. In the CRO industry in particular, consolidation has led to the emergence of large, functionally and therapeutically diversified firms. Our findings suggest that there is some quantitative justification for this industrial reorganization.

Our results have important implications for managers and firms engaged in the production of knowledge related to development within the firm.

⁶ An alternative hypothesis is that the most difficult development projects are outsourced to the best CROs, as measured by their experience operating in multiple therapeutic areas. If this is the case, then development performance would be worse for those CROs with greater technological area diversity. We cannot rule out the possibility of such an alternative, but doubt that this is the case based upon our analysis and interviews with CROs.

We find that development performance is conditioned in part by a give and take between scope economies and learning economies. This finding suggests that firms lacking experience in a particular technological area are better off first developing knowledge and problem-solving approaches in this area through experience than expanding into other technological areas where they have no experience. Firms with limited technological area experience and broad technological area scope face development performance disadvantages because knowledge spillovers are more difficult to absorb and make use of if they do not possess intimate knowledge on the landscape and the requisite problem-solving approaches first. Our results also suggest an important role for knowledge management in firms' R&D activities. Firms that seek to improve development performance must not only manage their development efforts such that their technological areas are neither overly broad nor overly specific, but also sequence these activities such that new knowledge can be more easily absorbed and usefully applied across these technological areas. The performance penalties associated with broad scope and limited experience in comparison to broad scope and significant experience suggest that experiential learning is a necessary condition for improving development performance. What appears to matter in improving development performance is the order that these activities are conducted. Because technological area depth is a significant determinant of development performance by itself and when interacted with technological area breadth, firms are better off developing experience within a particular technological area first and then leveraging this experience into other (related) technological areas.

The above arguments have some corollary to the exploration–exploitation framework of organizational learning (Levinthal and March, 1993; March, 1991), which has been applied to empirical examinations of patenting (Rosenkopf and Nerkar, 2001) and new product development and commercialization (Rothaermel and Deeds, 2004), among others. Exploitation represents the continual refinement and extension of existing, proximate and more predictable opportunities, whereas exploration represents the search for new, distant and more uncertain opportunities. Although exploration is a necessary precursor to exploitation, firms typically exploit current opportunities

(e.g., current technological areas) while simultaneously exploring for new opportunities (e.g., new technological areas). Our findings complement this research stream by suggesting that the success of exploration can be enhanced and improved upon from greater experience through exploitation. If firms in R&D-intensive industries pursue both exploration and exploitation strategies, we argue that the order with which these activities take place matters for development performance.

We do not believe that our findings are specific to CROs or to the pharmaceutical industry. The same learning and scale and scope economies that exist in the 'market' for drug development (e.g., through CROs) are likely to be found inside pharmaceutical firms. We also believe that our findings are applicable to other settings in which firms make different, but related products; where experience increases knowledge and improves performance; and where intra-firm knowledge spillovers can be applied to other technological areas. Other relevant industry examples are likely to include, but not be limited to chemicals, consumer electronics, semiconductor products, and software. In each of these industries, experience and knowledge within a particular technological area are likely to translate into improving performance in other technological areas.

While the CRO industry provides an appropriate setting to isolate and examine the factors important for drug development independent of those for drug discovery, some limitations and caveats must be noted in our econometric analysis and results. We examine development in a single industry—pharmaceuticals—and by a single organizational form—contract research organizations (CROs). Our results are thus at the mercy of any selection biases that may exist by pharmaceutical firms' drug development outsourcing decisions. In a separate empirical examination (Macher and Boerner, 2005), however, we examine drug development performance by pharmaceutical manufacturers and CROs using a dataset of Investigational New Drug (IND) submission and New Drug Application (NDA) submission and approval times for FDA-approved drug products from 1981 to 1995. This dataset is a random sample of drug products approved by the FDA over this time period. A difference of means test of drug development completion times indicates no statistical performance difference between pharmaceutical manufacturers who internalize drug development vs.

those who outsource drug development to CROs. Furthermore, our interviews with CROs and pharmaceutical firms do not suggest any systematic differences in the selection of drug development projects by pharmaceutical firms for outsourcing. Another potential limitation is that we examine a set of clinical-related activities—therapeutic area experience and scale and scope economies—that we are able to generate good proxies for. Although a narrow focus potentially limits the generalizability of our results, it nevertheless allows for greater precision in our measures and a more direct link between the presence of these factors and differences in firm performance. We also do not control for the inter-firm spillovers that may be present and have been found to be important drivers of innovative performance in prior research. Finally, all of our results are subject to the qualification that drug development project complete time is but one measure of performance in the pharmaceutical industry.

CONCLUSION

This paper provides a detailed examination of the importance of firm experience (learning economies) and scale and scope economies on development performance in an important and highly innovative setting. The analysis presented provides a number of insights into the importance and interaction of experience and scope economies in the development process. In doing so, the paper adds to the literature that examines knowledge development and management and its implications on performance in R&D-intensive settings. Theoretical linkages are made between research in the economics of R&D and the knowledge-based view (KBV) of the firm. Prior literature in the economics of R&D literature has hinted at the importance of scale and scope in development without exploring how knowledge generated through experience in particular technological areas may condition the magnitude of these effects. One central reason for these problems is that many of the factors that are central to firm performance are not observable in publicly available, aggregate data (Rouse and Dallenbach, 1999). This paper overcomes this limitation by utilizing a proprietary dataset containing detailed project- and firm-level information to more accurately measure the factors that condition the time required to perform development.

Our empirical results underscore the importance of learning economies and scale and scope economies in differentiating development performance. These findings importantly denote that both experiential and scale and scope economies help to explain performance differences in research and development. Moreover, our results suggest that experience within particular technological areas shapes and facilitates firms' abilities to absorb knowledge spillovers from other technological areas. To date, few researchers have explored how the size and shape of firms' research portfolios, along with their experience in particular technological areas, affects development performance. Our results extend this approach by finding that an important determinant within innovative intensive industries is taking advantage of intra-firm spillovers of knowledge within closely related areas of technological knowledge.

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