DOES FOCUS IMPROVE OPERATIONAL PERFORMANCE? LESSONS FROM THE MANAGEMENT OF CLINICAL TRIALS

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ABSTRACT

For over three decades, the benefits of focus have been touted under the guiding principle that dedicated attention to a small set of linked tasks improves operating performance. Numerous studies have suggested that the performance of a division, plant, or business unit is improved to the extent that it remains focused on a narrow range of activities. Others have found similar benefits associated with focus at the level of the entire firm. A question that has received less attention, however, is whether focus at the divisional level is complementary with, or a substitute for, focus at the firm level. We explore this question by considering the performance of investigative sites in biopharmaceutical clinical trials. First, we establish that firms focusing on a particular task—at *either* a divisional or firm level—experience higher output and productivity with respect to that task than unfocused firms. After controlling for selection, scale, and learning effects, we find that sites that focus on conducting clinical trials significantly outperform those that mix trial activity with the provision of traditional patient care. Second, we find evidence that focus at the divisional level and firm level are substitutes. That is, organizations characterized by divisional focus alone achieve statistically similar performance to sites that are characterized by both divisional and firm focus.

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There is little debate about the benefits associated with having an individual worker focus on a limited range of tasks. This concept—initially illustrated by Smith's (1776) pin factory and later discussed by others including Taylor (1911) and Fayol (1916)—serves as the basis of the commonly accepted division of labor among individuals. Of somewhat more debate, however, is whether focus at the level of a larger organization improves performance.[1] For example, does a plant dedicated to manufacturing a single car model have higher productivity than one that manufactures several models using different body types and engine platforms? Or does an airline that specializes in short-haul, domestic routes perform better than one that offers both domestic and international routes through a hub-and-spoke system? As one takes the level of focus from the individual worker to a larger organization, the benefits of focus become less obvious from a theoretical perspective. March and Simon (1958) note: "…there is a problem of specialization among individual employees, and a problem of specialization among organizational units. There is no reason to suppose that both sets of problems have the same answers or that the same general principles apply to both (p. 179)."

The empirical literature on focus at the organizational level emerges from two broad streams. The first considers the effects of *divisional* focus (i.e., focus at the level of an organizational subunit such as an individual plant or business unit). Skinner's (1974) discussion of the benefits of the "focused factory" serves as the foundation for much of this work. Subsequent studies have built upon this work by considering the impact of focused operations in manufacturing (Hayes and Wheelwright, 1984; Hill, 1989; Brush and Karnani, 1996; Suarez,

[1] Numerous organizational theorists (e.g., March and Simon, 1958; Lawrence and Lorsch, 1967; Blau, 1970; Galbraith, 1977) note that organizational growth is associated with the subdivision, or differentiation, of activities across organizational subunits. A key concern surrounding this differentiation is how to balance the apparent benefits of this segmentation with the need for integration among subunits either to support the performance of a single segment or to achieve larger organizational objectives. To the extent that organizations become too fragmented, the performance of either individual subunits or the organization as a whole may be reduced.

Cusumano, and Fine, 1996). The second stream considers the impact of *firm* focus (i.e., focus at the level of the entire firm) and emerges from the strategy and finance literature on corporate diversification.[2] These studies examine the impact of firm focus on either total corporate performance (Montgomery and Wernerfelt, 1988; Wernerfelt and Montgomery, 1988; Lang and Stulz, 1994; Berger and Ofek, 1995; Schoar, 2002; Villalonga, 2004) or division performance (Lichtenberg, 1992; Maksimovic and Phillips, 2002; Schoar, 2002; Siggelkow, 2003). The body of empirical evidence from these two streams offers mixed findings concerning the benefits of focus.[3]

Additionally, most prior studies consider the impact of focus at a *single* level of the organizational hierarchy—at the level of *either* the division or the firm. A question that has received less attention in the literature is the impact of focus at *multiple* levels of an organization.[4] That is, to what extent is the performance of a focused business unit improved by placing it within a focused firm? For example, would the performance of GE Aviation be improved if it were owned by a parent company focused in the aviation industry (e.g., Boeing) or the design of aircraft engines (e.g., Pratt & Whitney), rather than by the diversified conglomerate that is General Electric?

This paper seeks to address this issue through empirical analysis of a setting where focus can be observed separately at the divisional and firm levels. Specifically, we consider the effects of focus with respect to investigative sites in clinical drug trials. This setting is well suited for this analysis for three reasons. First, within a given clinical trial, multiple investigative sites

[2] See Montgomery (1994) and Siggelkow (2003) for reviews of this literature.
[3] In their recent study, Ketokivi and Jokinen (2006) note the absence of "compelling empirical evidence on the effectiveness of the focused factory approach" (p. 250).
[4] Gompers *et al*. (2006) consider the complementarity between focus at the level of the *individual worker* and the firm in their analysis of venture capital firms. They find that the marginal benefit of focus at the firm level is reduced to the extent that individual investment professionals within the firm are focused on particular industries.

enroll similar patient populations and perform a uniform set of procedures as outlined in the trial's protocol, which is dictated by the pharmaceutical firm sponsoring the trial. Thus, we can observe the efforts of multiple "factories" which produce a common product to identical quality standards.

Second, the clinical trial setting is also characterized by a straightforward measure of performance: the level of patient enrollment in a trial. The uniformity of the protocol within a given trial explicitly controls for selection effects and eliminates the need to worry about unobserved variation in production activities across investigative sites involved in that trial.

Third, these sites are characterized by differing levels of focus on the performance of a specific task—the execution of clinical trial protocols. Some sites correspond to Skinner's vision of a focused factory, as they exclusively treat volunteers who are enrolled as subjects in clinical trials. They are thus characterized by focus on clinical trials at *both* the divisional and firm level.[5] Others, however, mix the performance of clinical trials with the provision of traditional patient care (i.e., care that is provided solely for the benefit of the patient rather than as part of a clinical trial). As a result, they are not focused at *either* the divisional or firm level. A final group of sites corresponds to Skinner's concept of "plant within a plant" (PWP). They are involved with both clinical trials and traditional patient care, but have developed structures—either distinct operational units or the outsourcing of their clinical trial management—that separate the two branches of their business. These sites thus exhibit divisional focus but lack firm focus.

[5] Given that most of the firms in our sample have a single physical location, we use the term "focused factory" interchangeably with "corporate focus" and use the term "plant within a plant" interchangeably with "divisional focus". One could also imagine more generally using the terms "focused firm" and "firm within a firm" to capture the concepts of corporate and divisional focus, respectively, for larger, multi-site organizations.

Using data on the enrollment of 113 investigative sites participating in 72 trials (for a total of 320 trial-site observations), we find evidence that divisional focus on clinical trials (as opposed to traditional patient care) is associated with better operational performance in clinical trials as measured by both output and productivity. This result holds even after we control for several factors—namely economies of scale, learning, and favorable risk selection—which are correlated with, but distinct from, focus. Nevertheless, we also find that sites characterized by *both* divisional and firm focus on clinical trials do not statistically outperform those sites with only divisional focus. That is, there do not appear to be additional benefits to firm focus once adequate divisional focus has been achieved.

This paper proceeds as follows. Section II describes the clinical trial industry and outlines how investigative sites differ in their levels of focus. Section III reviews the literature on focus and motivates our hypotheses. Section IV presents an overview of the data and variables employed in our empirical analysis. Section V presents and discusses our results, Section VI presents several extensions and robustness checks, and Section VII concludes.

II. BACKGROUND ON THE CLINICAL TRIALS INDUSTRY

Before bringing a new medical therapy to market in the United States, a biopharmaceutical firm must establish its safety and efficacy through at least three, and often four, phases of clinical trials. Each phase of trials tests the safety and efficacy of the study medication on an increasingly targeted population. Following the third phase of clinical trials for a given drug, the sponsoring biopharmaceutical firm may seek final approval from the Food and Drug Administration (FDA).

Each of these studies is governed by a detailed trial protocol. Developed by the sponsoring firm, this protocol dictates patient eligibility for the trial through specific inclusion criteria. It stipulates the clinical procedures that must be done, tests that must be performed, and precise data that must be gathered. Depending on the size and phase of a given trial, a sponsor may contract with as many as several hundred investigative sites, each consisting of a team of researchers including a principal investigator (i.e., a physician), a study coordinator, and, potentially, other sub-investigators, sub-coordinators, or administrators. A contract between the sponsor and each principal investigator identifies the target number of study subjects to be enrolled, the amount of money per patient to be paid to the site, the length of the enrollment period, and the details on how the protocol will be implemented and monitored. Fees are paid to the site on a piece-rate basis per subject enrolled.

We consider each of these investigative sites as a "factory", where the end-product is a fully-evaluated study subject. The contract between the sponsor and the site specifies the product quantity (enrollment goal) and price (budget per completed subject), as well as the expected date of delivery (duration of enrollment period). The protocol dictates the specifications of the product, which are identical across all sites in a given trial. Each site, however, makes operational and management decisions concerning access to raw materials (finding potential study subjects), allocation of activities (between the investigator, study coordinator, and other administrative or clinical personnel), and operational execution (enrolling and processing subjects).

Despite the similarity across sites with respect to the terms and requirements of any given trial, the organizational structure of these sites differs dramatically. Investigators can be employed in academic medical centers, community hospitals, solo or group medical practices, or

dedicated research centers (i.e., sites that only see patients as part of clinical trials). The composition of the clinical trials marketplace is in flux and has changed substantially over the last 15 years. Between 1991 and 2004, the share of all industry-sponsored trials conducted in non-hospital settings more than doubled from 30% to 62% (Zisson, 2002). Much of this change is due to physicians who increasingly see industry-sponsored trials as a lucrative way to augment their income from traditional practice. This paper focuses on these non-hospital investigative sites, many of which seek to balance the requirements of clinical trials with their traditional business of patient care.

Though related, the provision of traditional patient care and the performance of clinical trials require different operational routines, which we schematically present in three stages—preparation, evaluation, and treatment—in Figure 1. For the most part, traditional patient care is a reactive process: a patient initiates an appointment, care is delivered, and follow-up visits are scheduled accordingly. In contrast, successfully running clinical trials demands a significant amount of preparation before any study subjects are enrolled. While many physician practices can draw study volunteers from their roster of patients, these efforts are often insufficient to reach enrollment targets. Additional effort is thus required to identify, screen, and recruit study subjects into a trial.

Differences also exist in the treatment routines for traditional patients and trial subjects. Traditional patient care is characterized by multiple cycles of diagnosis and treatment (at follow-up visits). With each cycle, care plans may be modified as uncertainty is resolved along certain dimensions and, potentially, created along others. In contrast, the care provided as part of a clinical trial protocol is more certain and linear.

We divide the non-hospital sites in our study into three categories based on their degree and type of focus on clinical trials. Figure 2 provides a mapping of divisional and firm focus onto the categories of sites in our setting. At one extreme of our categorization are *focused firms* (or *focused factories*), which, in this setting, are referred to as dedicated research centers (DRCs). As their name suggests, these organizations only conduct clinical trials. As such, they are characterized by firm—and, by definition, divisional—focus on clinical trials. The physician-investigators are employees, and often owners, of the DRC. DRCs have grown considerably in number and market share, expanding from only 6% of industry-sponsored trials to nearly in 1991 to almost 30% just ten years later (Zisson, 2002).

At the other extreme, are *unfocused firms*—investigative sites at which physicians both participate in clinical trials and provide traditional patient care. As such, they lack both firm and divisional focus. These sites include private physicians in community-based practices who participate in clinical trials either as a second source of revenue or simply as a side interest.

In between these extremes is the multi-divisional firm characterized by divisional focus alone. Given the single-site structure of the firms in our sample, an alternate description of these sites can be found in Skinner's (1974) concept of a "plant within a plant" (PWP). Similar to their unfocused peers, these firms simultaneously conduct both patient care and clinical trials. However, these community-based sites have set up organizational (and sometimes legal) partitions between the two activities, creating distinct business units for each function.[6] Thus, while each division is focused, the firm is diversified across multiple businesses or functions.

[6] For example, the Alaska Clinical Research Center, LLC is the educational and research affiliate of Alaska Urological Associates, APC, and is located one floor above the patient care practice within the same medical complex (example from www.centerwatch.com). While both centers are owned and operated by the same partnership of physicians, each business is a distinct legal corporation. Dedicated support and administrative personnel are employed by the patient care and clinical trial units (i.e., nursing staff and study coordinators, respectively)

III. LITERATURE REVIEW AND HYPOTHESES

Defining the concept of focus represents one of the first challenges in studying its effects. Prior studies offer myriad dimensions along which organizations can chose to focus. For example, Hayes *et al*. (2005) note that companies can focus around product lines, process technologies, geographies, or customer groups and, as a result, it is difficult for a firm to focus along multiple dimensions simultaneously. In certain settings—including that of this study—several of these dimensions may overlap substantially. Ketokivi and Jokinen (2006) observe that specific products may map directly onto specific processes, such that product focus and process focus become indistinguishable from each other.

In this study, we adopt a definition of focus that considers the breadth of a firm's operational activities and is consistent with Skinner's (1974) view of the "focused factory" in manufacturing. He observed:

> The focused factory does a better job because repetition and concentration in one area allow its work force and managers to become effective and experienced in the task required for success. The focused factory is manageable and controllable. Its problems are demanding but limited in scope (Skinner, 1974, p. 115)

Following Skinner, we claim that an organization is more focused to the extent that it limits the set of conflicting or competing operational activities in which its workers and managers are engaged. This definition emphasizes the importance of maintaining a small number of organizational routines (Nelson and Winter, 1982; Mukherjee, Mitchell, and Talbott, 2000) as a determinant of performance.

The empirical literature on focus finds its roots in studies of manufacturing. In support of focus, Hayes and Wheelwright (1984) provide cross-sectional evidence from 11 manufacturing plants showing a negative relationship between operating margin and the number of product

lines manufactured in a given facility. Vokurka and Davis (2000) use survey data from the managers of roughly 300 plants in multi-plant firms and find evidence of higher performance at focused relative to unfocused plants. Similarly, Bozarth and Edwards (1997) find evidence that a lack of focus in either the market requirements or manufacturing characteristics of a given plant is associated with poorer plant performance. Finally, Anderson (2001) finds that managers—recognizing that complexity and task heterogeneity hinder performance—compensate though strategic plant scheduling and capacity management. Her results suggest that the negative relationship between operating performance and product mix may be understated in some studies.

Other authors, however, suggest that the implications of focus for manufacturing performance are not as clear and some even suggest that its implications for a plant's overall financial performance may be negative.[7] Using plant-level data from the Census of Manufacturers, Brush and Karnani (1996) find that *process* focus – as measured by the absence of vertical integration – is negatively associated with labor productivity. In their analysis of 31 plants in the printed circuit board industry, Suarez, Cusumano, and Fine (1996) find that a broader product mix is not associated with decreased performance in terms of either cost or quality. Kekre and Srinivasan's (2000) examination of over 1,400 business units yields similar results. Specifically, they find that business units with broader product lines are characterized by larger market shares and higher profitability than more focused units. Further, they find that these benefits in overall performance do not come at the expense of higher production costs.

A smaller set of studies considers the role of focus outside of traditional manufacturing environments. Consistent with our study, much of this empirical work occurs in health care

[7] Upton (1997) highlights the importance of flexibility in product and process range as an operational objective in certain competitive environments.

settings. Heskett (1983) and Herzlinger (1997) describe focused operating strategies among health care providers. A large-sample survey by McLaughlin, Yang, and van Dierdonck (1995) finds that freestanding outpatient-surgery centers perform better than hospital-based outpatient-surgery units. Henderson and Cockburn (1996) examine focus in the research and development activity of pharmaceutical firms, a setting related to that studied in this paper. They note that pharmaceutical firms experience positive returns to scope (i.e., negative returns to focus) in their research productivity. They also find positive returns to scope in the development productivity of pharmaceutical firms, but the association disappears when firm-level fixed effects are introduced (Cockburn and Henderson, 2001).

One of the biggest challenges in the empirical study of focus is that it is correlated with other factors that are distinct from focus but that might affect performance and result in misleading inferences. These correlated characteristics are best illustrated by reference to the prototypical example of a focused factory in a service setting—the Shouldice Hernia Centre. By performing only hernia operations, Shouldice has streamlined its internal processes to concentrate on a single procedure and the finite set of repeated tasks that it requires (Heskett, 1983). As a result, Shouldice is able to perform these surgeries cheaper, faster, and with improved clinical outcomes.

Though focus may help improve Shouldice's performance, there may be several reasons—correlated with, but distinct from focus—that explain its success. First on this list is pure *returns to scale*; Shouldice's higher volume of procedures may enable it to invest in product-specific technologies, such as specially-designed facilities, or hire dedicated nursing staff with expertise in the rehabilitation of hernia patients. Second, Shouldice's high cumulative volume of procedures may lead to enhanced *learning*; its surgical processes have been refined

over the course of thousands of cases, thereby improving clinical outcomes and reducing recovery time for patients. A third and final explanation is favorable *risk selection*; critics argue that because most patients have to travel significant distances to get to Shouldice, they are likely to be healthier and more mobile than the average hernia patient at other hospitals. In essence, Shouldice may be selecting its inputs to be more homogenous, thereby helping it achieve superior outcomes. Though all three of these explanations are correlated with focus, none of them *requires* focus. For example, large academic medical centers could, in theory, achieve all of these benefits with respect to hernia patients, but these large hospitals are more akin to diversified firms than focused factories.

At a minimum, one must be sure to compare firms doing similar work, thus controlling for potential selection effects. The finance literature's continuing debate on whether focused firms trade at a premium relative to their diversified peers provides a useful example of how selection bias may affect the empirical study of focus. Several authors document a "diversification discount" in public markets and conclude that diversification destroys value (Lang and Stulz, 1994; Berger and Ofek, 1995). In response, others have shown that these firms and their acquisitions tend to trade lower even before diversifying (Campa and Kedia, 2002) and that the acquisition of new subsidiaries by a diversified firm tends to be discounted prior to its purchase (Graham, Lemmon, and Wolf, 2002), negating any effect of focus. Recently, Villalonga (2004) has even documented a diversification *premium* using a new census dataset representing more industry segments. It, therefore, is critical that an investigation of operating focus strive to compare plants or firms performing comparable activities.

In our study, the nature of the work required may differ significantly across trials (i.e., protocols). The ability of a site to enroll volunteers into a trial depends on several external

factors, including the prevalence of the targeted condition (e.g., influenza vs. prostate cancer), the intended patient population (e.g., children under 16 years old vs. women aged 65 and over), and the type and intensity of treatment (e.g., monthly check-ups vs. weekly injections). While the nature of work may differ *across* trials, *within*-trial activities are, as mentioned above, uniform and dictated by the sponsor's protocol. We thus are able to explicitly control for trial difficulty in our empirical work through the use of protocol-specific fixed effects. Though this approach does not test for the direction of any selection, it does reduce concerns about selection biasing our estimates of focus' effect on performance.

Beyond controlling for the difficulty of a given trial, we account for two other factors that are correlated with focus: scale and learning. Simple returns to scale permit firms to allocate the costs of fixed investments across more units of output. Pesch and Schroeder (1996) observe that processes requiring large investments in dedicated equipment tend to promote operational focus due to the high costs associated with set-ups and production changeovers. This suggests that focused factories are likely to be seen in settings marked by potential scale economies.[8] To the extent that focus and scale are correlated, one must control for the latter in precisely identifying the effects of the former on performance.

In our setting, an organization that can run more trials simultaneously may be able to reduce per-patient costs associated with activities such as patient recruitment (i.e., advertising) or trial administration. Alternatively, scale may allow a site to justify investments in fixed assets

[8] At first glance, this statement may appear to be at odds with Schmenner's (1983) observation that focused factories tend to be smaller than their unfocused counterparts. These statements may be reconciled, however, once one accounts for the important distinction between a plant's *overall* scale and its *activity*- or *product-specific* scale. For example, it is quite likely that a factory that produces only product A will be smaller (in terms of total production capacity) than a factory that produces products A and B. The first factory, however, may produce more of product A than the second plant. In our study, we compare sites based on the scale of their clinical trial business only, regardless of their scale with respect to traditional patient care.

that are specific to the conduct of trials, such as an administrative staff or information systems for the electronic capture of trial data. This leads us to the following hypothesis:

HYPOTHESIS 1a: The operational performance of an investigative site will be positively related to scale, as measured by the number of trials that can be simultaneously conducted at that site.

Another factor that may be mistaken for focus is learning (i.e., returns to experience). The positive correlation between experience and productivity or performance (Wright, 1936; Arrow, 1962) is now regarded as an empirical regularity. This relationship has been found to exist at the level of individuals (Newell and Rosenbloom, 1981; Delaney *et al*., 1998), teams (Weick and Roberts, 1993; Pisano, Bohmer, and Edmondson, 2001), and organizations (Argote and Epple, 1990; Adler and Clark, 1991). The proposed benefits of learning (e.g., lower cost or improved quality) stem from the repetition of certain routines. We argue that the benefits of focus, however, are attributable not simply to *repeating* routines, but to *limiting* the number of different routines pursued within a given site or organization. We thus need to control for the former effect in attempting to identify the latter.

The most common proxy for learning in these studies is cumulative production volume. In the clinical trials industry, the cumulative experience of the principal investigator (i.e., physician) is widely believed by sponsors to be a significant predictor of enrollment. Given the range of activities that must be performed by the site coordinator and other non-physician personnel, one might also believe that higher levels of cumulative experience for the site coordinator and for the site as a whole would lead to higher levels of subject enrollment and retention. We are thus led to the following hypothesis:

HYPOTHESIS 1b: The operational performance of an investigative site will be positively related to the level of learning, as measured by the cumulative number of trials performed by the principal investigator, the site coordinator, and the organization as a whole.

After controlling for the effects of selection, scale, and learning, we are able to isolate whether focus has an impact on performance. We begin by comparing sites with some degree of focus (i.e., either divisional or firm focus) to those that are unfocused. We test the following hypothesis:

HYPOTHESIS 2: Operational performance will be positively related to the presence of either divisional or firm focus at an investigative site.

As mentioned earlier, the benefits of focus have been identified by several studies at *either* the divisional or firm level. Nonetheless, a question that has received little empirical attention is whether divisional focus and firm focus are complements or substitutes in terms of their effects on operational performance. That is, are the effects of divisional and firm focus on performance additive?

The heterogeneity in the types of focused sites in our sample allows us to distinguish the performance of sites with *both* divisional and firm focus from that of sites with only divisional focus. We note that the focused factories (i.e., dedicated research centers) in our sample represent the former group, while the PWP structures (i.e., community sites with a separate business unit for trials) represent the latter. Based on the support for independent and beneficial effects of both divisional and firm focus, we arrive at the following:

HYPOTHESIS 3: The operational performance of investigative sites that are characterized by both divisional and firm focus will be superior to that of sites characterized by divisional focus alone.

IV. DATA AND METHODS

Study Data

The main source of data for this analysis is the Rapidtrials™ research network, a registry of more than 600 investigative sites assembled by Physician Clinical Research Services, Inc. The Rapidtrials™ database collects detailed data at the level of a principal investigator working on a given clinical trial (i.e., protocol). These data include: per-patient budget for the trial, enrollment performance, site structure and staffing, and previous trial experience at the level of the principal investigator, study coordinator, and site as a whole. The Rapidtrials™ network does not include all of the sites participating in any given trial. Given our need to control for risk selection using protocol fixed effects, we limit our sample to protocols that were contracted to at least two investigators in the network. Our final sample includes data from 72 unique protocols (ranging from Phase II to Phase IV) initiated between 1999 and 2003 and completed by July 2004. These trials were sponsored by 50 separate biopharmaceutical companies and involved 113 unique investigative sites. Our 320 observations provide an average of 4.4 investigative sites per protocol.

To develop one of our performance measures, we supplement the Rapidtrials™ data with information from the Food and Drug Administration (FDA)'s Bioresearch Monitoring Information System File. Each time a site participates in a trial, the principal investigator must register with the FDA. By counting the number of filings for a given site over a certain time frame (e.g., within one year of signing a contract to participate in a given trial), we are able to obtain an estimate of that site's overall level of concurrent trial activity during the same period as the studied protocol.

While the Rapidtrials™ database includes observations from several hospital-based sites, we exclude these observations from our base regressions for several reasons. First, the Rapidtrials™ data under represent hospitals—especially academic medical centers—involved in clinical trials. Nationally, approximately 30% of the sites involved in clinical trials are based at academic medical centers (Centerwatch, 2002); in our sample this figure is only 5%. Second, academic physicians have teaching and research responsibilities that compete for their attention, and it is not possible for us to observe the extent of these activities in our data. Excluding these sites from our base regressions thus helps reduce the impact of unobserved heterogeneity in site activities on our identification of focus' effects.

Though we exclude hospital-based sites from our base regressions, we do examine the robustness of our results to including these data in our sample. We do this because hospitals can be viewed as large, multi-divisional firms in which the administration of industry-sponsored clinical trials is only one of hundreds of activities. In many hospitals, trial activities are not organizationally separated from the other portions of the hospital's business. They are, therefore, analogous to the unfocused sites in our community-based sample. In others, trial-related activities are part of a separate research unit, creating a hospital-based analogue to the PWP model in our office-based sample. These trial units, however, tend not to focus on the execution of trial activities, as is the case with the community-based PWP models. Rather, they assist the principal investigator at a higher level in terms of contracting with sponsors and recruiting subjects. Combined, these two groups of hospital-based sites account for 57 observations, which we separate into two categories—PWP and unfocused—depending on whether the hospital maintains a clinical research unit.

Table 1 presents descriptive statistics for our main sample, which excludes observations from hospital-based sites. Nearly three-quarters of the data from the 72 protocols in this study come from Phase III trials that are designed to show safety and efficacy for regulatory approval by the Food and Drug Administration. These trials cover a wide variety of conditions and therapeutic areas.

The 113 unique investigative sites in our sample range from large, group practices to solo practitioners. The number of clinical study coordinators ranges from one-quarter of a full-time equivalent (FTE) to over 15 dedicated FTEs. As part of the Rapidtrials™ network, these sites are actively seeking clinical trial work. Thus, they are likely to be more experienced than the general population of sites involved in trials. This does not pose a substantial problem for our analysis, however, as we control for variation in experience across principal investigators, study coordinators, and sites. As seen in Table 1, this variation is substantial.

The budget-per-patient and the goal enrollment are rough indications of a protocol's complexity. The sponsors in our sample set recruitment targets between four and 50 subjects per site and pay from $225 to more than $15,000 per completely-evaluated subject. In general, enrollment into these protocols is lower than the target goal. The median site achieves only 35% of its target, while the average is raised by a few extremely-high performers.

Table 2 compares many of these variables between sites with some level of focus (i.e., focused factories and PWPs) and those that are unfocused. The sites with some level of focus are significantly larger than unfocused sites, with more employed physicians and study coordinators. Furthermore, they have significantly more experience at all levels of the organization—investigator, coordinator, and site as a whole. On the other hand, focused firms

do not have as much access to a local volume of patients. Finally, Table 3 presents the correlations between key variables.

Dependent Variables

We measure the operational performance of trial sites using two different dependent variables. The first, **Percent to Enrollment Goal**, is a measure of a site's production output during a given trial. It is defined as the number of patients enrolled in a study divided by the enrollment goal for that trial.[9] For each protocol, the sponsoring firm sets a common enrollment goal across all sites. Normalizing by the enrollment goal, allows us to compare across trials of varying sizes.[10] For the purposes of this study, this is a meaningful outcome measure, as it directly captures a site's performance with respect to the activity (i.e., clinical trial execution) on which sites have focused to varying degrees. Reaching (or even surpassing) the enrollment target is important to the overall financial performance of the research site and biopharmaceutical sponsor. For the site, enrollment drives revenue since payment is based on a piece-rate contract. In addition, a site's reputation and ability to secure future trial business is based, in large part, on past enrollment performance. For the sponsor, final enrollment is critical to the successful completion of the project and determines the cost and speed with which successful compounds can enter the market.

Though a meaningful measure of output and performance, **Percent to Enrollment Goal** is not a measure of productivity—output per unit input. To determine the impact of focus on productivity, we repeat our basic analysis using **Enrollment Per Study Coordinator FTE** as the dependent variable. This measure represents an estimate of the enrollment output achieved per

[9] To ensure normality, we use the log of the dependent variable in all multivariate regressions.
[10] We note that the value of this dependent variable may exceed 100 percent; since most sites do not reach their target, sponsors routinely allow sites to exceed their enrollment goal.

unit of labor, measured as the number of FTE study coordinators dedicated to the trial.[11] The numerator for this measure (i.e., enrollment) is directly available in the Rapidtrials™ data. We calculate the denominator (i.e., study coordinator FTEs per trial) as follows. First, we estimate the number of concurrent trials conducted at the site by counting the number of FDA-registrations submitted by *all* physician-investigators at that site within one year before or after the month in which the site signed a contract to participate in the trial of interest.[12] Next, we divide the number of study coordinator FTEs at the site (from the Rapidtrials™ data) by the number of concurrent trials to obtain an average value of FTE study coordinators per trial. Though the *actual* number of study coordinators dedicated to any given trial may differ from this site average, this measure represents our best estimate of the administrative resources dedicated to a trial. We then use average FTE study coordinators per trial as the denominator of our **Enrollment Per Study Coordinator FTE** measure.

Independent Variables

Our main independent variables are indicators for each site's level of focus: firm focus, divisional focus only, and unfocused (the excluded category in our regressions). We also include variables to control for factors that are correlated with focus: scale, learning, and selection. **Scale** is defined as the number of full-time equivalent study coordinators at each site. The larger the number of study coordinators employed, the greater the number of simultaneous protocols the site can perform. **Learning** is measured at three levels based on the cumulative number of

[11] Ideally, we would like to have measures of either total factor productivity or financial performance at the site-trial level. Unfortunately, neither of these measures is available in our data sources.

[12] This two year window corresponds to the approximate length of most clinical trials. By using this rolling window around the date of a site's enrollment in a given trial, we are able to identify changes in a site's overall level of trial activity over time. Adjusting this window to include only trials initiated within six months before and after the trial of interest did not substantially change the results of the analysis.

trials completed by the investigator, study coordinator, and the site as a whole. These data are self-reported in the pre-trial site qualification survey conducted by Rapidtrials™. To control for potential risk **selection**, we include fixed effects for each protocol, which captures unobserved heterogeneity in the difficulty of implementing a given trial. Performance is thus measured relative to the average percent enrollment achieved by other sites within the same trial.[13]

We also control for other potential determinants of patient enrollment. For example, enrollment is likely easier for sites that have a larger, local volume of patients from which subjects can be naturally recruited. The variable, **Local Volume**, represents the average number of indication-specific patient visits seen by each physician at the site in a given year. It is matched to the target condition in the trial protocol (e.g., depression, congestive heart failure). For dedicated research centers, this value represents the number of patients with the specific condition within their contact database of potential study volunteers. Finally, we also control for any variation in the **Budget per Patient** across sites. Only 10.3 percent of the observations in the sample involve sites that were able to negotiate a budget higher than the median for their trial, with the average increase for these sites being 11.1 percent. This small, additional incentive, however, may be associated with higher enrollment.

[13] Though this approach addresses most selection concerns, it is still possible that, to the extent that the most difficult trials are systematically being performed by a particular type of site, our results may reflect the impact of these unobserved differences in trial difficulty. In response to this remaining concern, we note that key measures of trial complexity (i.e., budget per patient and percent of trials in Phase III) are close in magnitude and do not show statistically significant differences across the types of sites (Table 2). Because we only observe sites that choose to participate in these trials, we cannot rule out the possibility that more sophisticated, focused sites disproportionately select out of difficult-to-perform trials. However, we believe that any such bias favoring focused over unfocused sites would be small for two reasons. First, we measure performance relative to the other sites within a given trial, and any site experienced enough to decline a complicated protocol based on its pre-screening process would likely have achieved *relatively* high performance compared to less sophisticated peers. Second, unfocused sites that do clinical trial work less frequently may be more likely to participate only in those protocols that best match their interests and abilities. If true, either of these factors would actually bias our analysis *against* finding benefits from operational focus.

Addressing Missing Data

With records for every contract and descriptions of the structure of each investigative site in our sample, all of our dependent and key independent (i.e., level of focus) variables are fully populated. Due to the nature of pre-trial, site-qualification surveys, however, some of the control variables are missing individual observations. For example, some sites did not fully answer all of the questions on the qualification surveys (e.g., Q: "How many patients do you see with this condition each year?", A: "Many" or left blank). Similarly, some investigators and study coordinators did not state their full clinical trial experience. The final model contains eight independent variables across 320 observations and the values in 77.0% of the resulting cells are known from the original data. Sensitivity analyses demonstrate no substantive differences between the responders and non-responders across other, observed variables.

We assign missing values using the multiple imputation (MI) method (Rubin and Schenker, 1991; King *et al*., 2001). In this process, incomplete items are regressed on all other variables to generate an imputation that most closely resembles the missing data item. Simply substituting this imputed value for the missing observation, however, could deflate standard errors, causing spurious correlations to be interpreted as precise relationships. MI addresses this problem, as suggested by Faris *et al*. (2002):

> Multiple imputation methods randomly draw observations from a fitted distribution for the covariates and the outcome variable…For each imputed data set, the missing data are filled in with values drawn randomly from this distribution. Analyses are performed on each data set as though the data had been completely observed. The results of these analyses are then pooled to provide point and variance estimates for the effects of interest. (p. 186)

We use the *Amelia* program (Honaker *et al*., 2000) to perform MI and create five parallel datasets, modeling each independently. The final estimates presented below represent the average values across all five models, with the standard errors adjusted to reflect the variance

within and between the datasets. In essence, the benefit of MI is that it not only generates an estimate of every missing data point but also uses a more conservative measure of the precision of those estimates in determining the final standard errors.

V. RESULTS AND DISCUSSION

Table 4 presents our base results concerning the impact of focus on output performance. Column 1 shows that, without protocol fixed effects and controls for any other covariates, focused firms (i.e., those with at least divisional focus) perform better, but not significantly better, than unfocused firms. Here, and in all models presented, statistical significance is determined using robust standard errors clustered by investigative site. Column 2 adds our secondary controls. As expected, the coefficient on local patient volume is positive and highly significant, showing that there is a benefit from accessing a local population of potential study volunteers. Also as expected, the coefficient on budget per patient is negative and significant. Because we have not yet incorporated protocol fixed effects, the budget-per-patient variable captures the effect of trial complexity – trials with a higher budget are likely to be more complex and, therefore, associated with lower enrollment.

The inclusion of protocol-specific fixed effects (Column 3) allows us to measure a site's performance relative to other sites *within* the same clinical trial. Here, budget per patient represents the marginal economic incentive for sites with higher trial-specific budgets to recruit more patients. It is now positive, as expected, but not significant. More importantly, the addition of protocol fixed effects allows us to estimate the impact of focus after controlling for trial complexity. We now find that focused sites have significantly higher enrollment than their unfocused counterparts.

Columns 4 and 5 add in the scale and learning variables, respectively. Scale is positively, though not significantly, associated with productivity suggesting that Hypothesis 1a is not supported by the data. Nevertheless, after controlling for a site's scale in clinical trials, focused sites still outperform their unfocused counterparts. Similar results are seen when learning measures are introduced in Column 5. Only study coordinator experience predicted higher enrollment ($p=0.04$), indicating some support for Hypothesis 1b. Again, however, we are most interested in the fact that, even after controlling for all of the key correlates, the effect of focus on output performance remains positive and significant.

Table 5 repeats the regressions in Table 4 using **Enrollment Per Study Coordinator FTE**, our measure of productivity, as the dependent variable. We again find a positive and significant relationship between focus and performance in models that include the focus variable on its own (Column 1) as well as those including both partial and full sets of controls (Columns 2 through 5). Together, the results in Tables 4 and 5 provide strong support for Hypothesis 2 regardless of how performance is measured.[14]

Relative to Table 4, there are a few differences in terms of the results for certain control variables. First, the estimate for study coordinator experience is no longer significant at conventional levels, suggesting that the limited support for Hypothesis 1b using the output measure is further weakened by using productivity. In addition, the significance of the

[14] One alternate explanation for our findings is that investigators at unfocused sites simply do not have the same motivation or incentive as investigators at focused sites to achieve their enrollment targets. For example, the former may see trial activity as a very small part of their overall workload or may find traditional patient care to be more lucrative than sporadic trial activity. While we cannot rule out this possibility, there are several reasons to believe that this bias, if present, would be muted in this setting. First, all of the sites in this analysis have shown substantial interest in growing their clinical trial business by joining the Rapidtrials™ network and actively seeking out new protocols. Second, the finances of clinical trials are characterized by high set-up costs for both the overall trial business itself (e.g., hiring a dedicated study coordinator) and each individual trial (e.g., the up-front costs associated with evaluating a protocol and searching for volunteers), while the payment is based on each additional subject enrolled. The marginal profitability associated with enrolling incremental subjects is thus quite high.

coefficient for patient volume per physician falls below significant levels. Finally, the coefficient on scale, which was positive but insignificant in Table 4, is negative and significant in Columns 4 and 5 of Table 5. This result suggests the presence of diseconomies of scale *after controlling for the type of site* (i.e., at least divisional focus vs. unfocused).[15] Based on the reasonably large correlation between focus and scale (Table 3), one might wonder if this negative relationship between scale and productivity remains if we drop the indicator for focused sites. Column 6 illustrates that doing so causes the coefficient on scale to return to being insignificantly different from zero (as in Table 4).

The logarithmic transformation of many independent variables makes it difficult to interpret the magnitude of the focus effects directly from the estimated coefficients. Figure 3 thus presents the average performance of focused and unfocused sites, assuming mean values for all control variables. The average enrollment achieved by focused firms is 11.7 percentage points higher than that of unfocused sites (40.0% vs. 28.3%, respectively). The second panel of Figure 3 shows that focused firms achieve this elevated output using fewer resources than their unfocused peers (13.43 vs. 6.75 enrolled subjects per study coordinator FTE). In other words, after controlling for relative scale, experience, selection, local volume, and economic incentives, focused firms achieve 41% greater output and are almost twice as productive as unfocused firms.

[15] To the extent that the results in Columns 4 and 5 of Table 5 suggest diseconomies of scale, they run counter to Hypothesis 1a. We can imagine several potential explanations for this result. First, it may be that, as sites become larger, they move into trials that are less suited to their particular skills or area of expertise. For example, a site may begin by accepting only cardiovascular trials but may move into trials for other medical conditions, such as diabetes, as its scale increases. Alternatively, it may be easy for a site to obtain a "first scoop" of trial subjects from its active patient roster. Nevertheless, efforts to expand the number of patients in trials may require significantly higher levels of resources, thereby leading to a negative relationship between scale and productivity. Given that patients can typically participate in only one trial at a time, this problem is likely to be non-trivial. Finally, larger sites may suffer from a "free-rider" problem—having more coordinators (and potentially more physicians) may provide weaker incentives for efficient levels of effort by individuals. See Zenger (1994) and references therein for additional discussion of the association between firm size and induced effort.

The magnitude of these differences is striking when compared to changes in other variables that significantly affect performance. For example, the experience of study coordinators is positively correlated with output. Yet an unfocused site employing a relatively experienced coordinator (40 trials representing the 75th percentile in the dataset) would generate only a 5.5 percentage-point increase in output relative to an otherwise-similar site with a novice coordinator (9 trials, 25th percentile). Similarly, a site at the 75th percentile of local patient volume (90 patient visits per MD per year) is predicted to experience output that is 8.9 percentage points greater than that for a site at the 25th percentile of local volume (5 patient visits per MD per year).

Table 6 presents estimates from regression models in which we distinguish between the types of sites in our sample with some degree of focus: firm focus (i.e., focused factories) and divisional focus (i.e., community sites with dedicated business units akin to the PWP model). We find that each of the types of focused sites achieves significantly higher (at the 5-10% level) output than unfocused sites (Column 1), and these results also hold when we use productivity as the dependent variable (Column 2). As shown in the first panel of Figure 4, the percent of enrollment goal achieved (evaluated at the mean of all other variables) is 29.6% for the unfocused sites compared to 41.1% and 45.0% for the various types of focused sites. Between the two types of focused sites, however, we do not find significant differences in enrollment.

Despite the support we find for Hypothesis 2 concerning the benefits of divisional focus, we do not find similar evidence in favor of Hypothesis 3. Specifically, the focused factories in our sample do not achieve significantly higher output or productivity than the PWPs. Consequently, we do not find evidence that firm focus provides benefits beyond those offered by divisional focus in this setting.

This lack of support for Hypothesis 3 has important implications. Specifically, it suggests that, in settings similar to ours, companies or factories that aim to benefit from focus may not need to jump to the "pure" models of firm focus or the focused factory. Rather, they may obtain similar operational performance by pursuing a hybrid model in which focused, but distinct, divisions are combined under the umbrella of a more diversified organization, whether a firm or factory. To make such a hybrid model successful, however, firms must manage a delicate tension. Specifically, they must balance the desire to leverage economies across divisions with the need to maintain adequate separation between divisions so as to prevent divisional focus from lapsing into a lack of focus.

Our finding about the statistical equivalence of divisional and firm focus is consistent with the substantial literature in strategy and operations suggesting that the benefits of diversification are "non-linear" (Palich, Cardinal, and Miller, 2000). On the one hand, the absence of diversification (i.e., pure focus) may reduce a firm's ability or willingness to react to market changes, increase financial risk through the loss of diversification opportunities, and slow the pace of innovation in products or services (e.g., Hayes and Wheelwright, 1984; Henderson and Clark, 1990; Kekre and Srinivasan, 1990; Sigglekow, 2003; Guedj and Scharfstein 2004; O'Reilly and Tushman, 2004). On the other hand, broad diversification may be problematic to the extent that it causes firms to lose the productive benefits of focus or otherwise stray from those areas or activities in which they possess meaningful competitive advantage (Porter, 1985; Montgomery and Wernerfelt, 1988; Prahalad and Hamel, 1990).

VI. EXTENSIONS AND ROBUSTNESS

Types of Divisional Focus

A key concern for managers pursuing an organizational model with divisional, but not firm, focus is to make sure that divisions remain clearly delineated. Our definition of divisional focus emphasizes the importance of restricting the scope of any business unit to a small number of organizational routines (Nelson and Winter, 1982; Mukherjee, Mitchell, and Talbott, 2000).

In theory, it is possible for performance to be affected by focus at the level of either front-line workers or managers (Simon, 1947; Ocasio, 1997). We are fortunate that our data can distinguish between divisionally-focused firms that concentrate attention at each of these levels. Among the PWP models, two types of organizations exist. The first is the community-based physician group that establishes a separate, parallel business unit for clinical trials. Both businesses are managed by the same physician (or group of physicians), although each has a separate budget and distinct, front-line production workers. That is, one group of clinical support employees (e.g., nurses or technicians) performs procedures required for volunteers in clinical trials while another group provides clinical services associated with traditional office visits. As such, this model is characterized by shared management and focused production (i.e., *production focus*).

The second PWP model is the trial management organization (TMO). TMOs are for-profit firms that provide trial-related administrative services on a contract basis to physician practices.[16] As such, TMOs consist of professional managers who perform all of the activities associated with managing and running a trial except those that require medical care and thus must be delivered by a physician or licensed practitioner. TMO responsibilities include: identifying the trial opportunity, contracting with the trial sponsor, recruiting study volunteers,

[16] We note that TMOs are distinct from contract research organizations (CROs), which provide outsourced management of certain operational activities that would otherwise be performed by the biopharmaceutical firm sponsoring the trial. Azoulay (2005) discusses the circumstances under which CROs are likely to be used by biopharmaceutical firms.

managing trial paperwork, shipping laboratory specimens, and communicating with the trial sponsor on behalf of the investigative site. TMOs share the revenue from clinical trials with the investigative site as part of a pre-negotiated contract. Most TMOs employ a cadre of experienced study coordinators who travel to sites and review internal medical records to identify potential trial enrollees. Unlike community sites with parallel business units, TMO sites have the same group of front-line production workers treating both clinical trial and traditional patients. This model is thus characterized by focused management and shared production (i.e., *management focus*).

Table 7 presents estimates from regression models in which we sub-divide divisional focus into these two categories. Sites with either production or management focus achieve significantly higher (at the 5-10% level) output than unfocused sites (Column 1). Using productivity as the dependent variable (Column 2), we find that sites with production focus only are not significantly more productive than unfocused sites at conventional levels ($p=0.12$), although they also are not statistically distinguishable from focused firms ($p=0.11$). The consistently high performance of the PWP with management focus suggests that the benefits of focus are not simply found in limiting the activities of front-line workers. As suggested by Rotemberg (1999), focusing the supervisory span of managers may allow them to build relevant expertise and improve the instruction they provide to front-line employees.

Divisional Focus in Large Firms

As a second extension, we consider whether the findings from our base sample extend to larger, multi-divisional organizations—in this case, hospitals that participate in clinical trials. We reiterate that the number of hospital-based sites in our data is small in absolute terms (n=57)

and under represents the proportion of clinical-trial activity that actually occurs in hospital-based sites in the United States. Nevertheless, Column 3 of Table 7 examines the robustness of our results to including these hospital-based trial sites in our sample. We find that the hospital-based PWP model (i.e., with a separate clinical trials unit) performed better—though not significantly better—than unfocused, community-based sites but worse than each of the three types of focused community-based sites. Unfocused hospital-based sites had the worst performance in the entire sample, though their performance was not significantly worse than that of unfocused, community-based sites. We do not know whether the coefficients on the two types of hospital-based sites would become significant with a larger sample of observations for each category. Nonetheless, we find some evidence that our results for community-based sites are robust to adding hospital-based sites to the sample.

These findings corroborate our previous results that separating tasks into clearly delineated divisions improves the performance of each of those tasks. Nonetheless, we caution that, in the multi-divisional firm, strong *divisional* performance does not guarantee similar *firm* performance. This problem is particularly acute to the extent that the activities of separate divisions must be coordinated either to leverage shared corporate resources (e.g., management talent or equipment) or reduce intrafirm political conflict (March, 1962; Perrow, 1986). Effectively balancing the need for focus within divisions with the need for coordination across them requires managers to weigh the relative value of focus (in terms of increased productivity or profit) against its potential cost (in terms of duplicative capacity investments or inter-divisional tension).

VII. CONCLUSION

Over thirty years ago, Skinner (1974) emphasized the benefits of focus in a manufacturing setting. Subsequent authors have refined that theory and offered numerous dimensions along which not only factories, but entire organizations, can chose to focus: markets served, mix and volume of products, process type, degree of product customization, or nature of the underlying technology (e.g., Hayes and Wheelwright, 1984). The findings presented here suggest that many of these dimensions are linked by a general underlying mechanism – the separation of unique sets of linked tasks. Our study helps refine the concept of focus and illuminate how focus at the divisional and firm level affects operational performance.

We note several factors that may limit the generalizability of these results beyond the setting we consider. First, we explore only two aspects of operational performance: production output and productivity. Due to the nature of our setting, we cannot test whether focused firms benefit along other dimensions of performance, such as profit, product quality, or lead time. Second, we explore the effect of dividing attention across only two business units and can provide only limited evidence as to how our findings translate to larger, multi-divisional organizations. In some of these settings, the need for coordination among different divisions may outweigh the productive benefits of focus within each division. Though we have no reason to suspect this necessarily to be the case with larger firms, we cannot dismiss this possibility. Third, our study examines a static measure of operating performance. As such, we are not able to address the long-term strategic and financial consequences of focus using these data.

Even with these caveats, however, this paper makes several contributions to the literature on focus. Most directly, it documents that, even after accounting for differences in scale, learning, and selection, focus has a positive effect on operational performance measured in terms of both output and productivity. Our setting is well-suited for isolating the effects of focus, as it

enables us to compare the performance of the same task across varied organizational structures. Beyond establishing the benefits of focus, our study investigates the returns to focus at multiple levels of the organizational hierarchy. Specifically, we find that the benefits associated with focus at the divisional level are statistically equivalent to the benefits of focus at the firm level. This result supports the potential benefits of related diversification at the firm level assuming that there exists adequate delineation among focused divisions. Finally, we find evidence that supports the original theory that focus works by limiting the set of conflicting activities faced by an organization. We show that these constraints work at both the management and, to a lesser extent, the production levels of the organization. Further research is necessary to help define the boundaries of these management and production activities and subsequently test the limits of focus' impact on performance.

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FIGURE 1: Typical Activities Involved in Patient Care and Clinical Trials

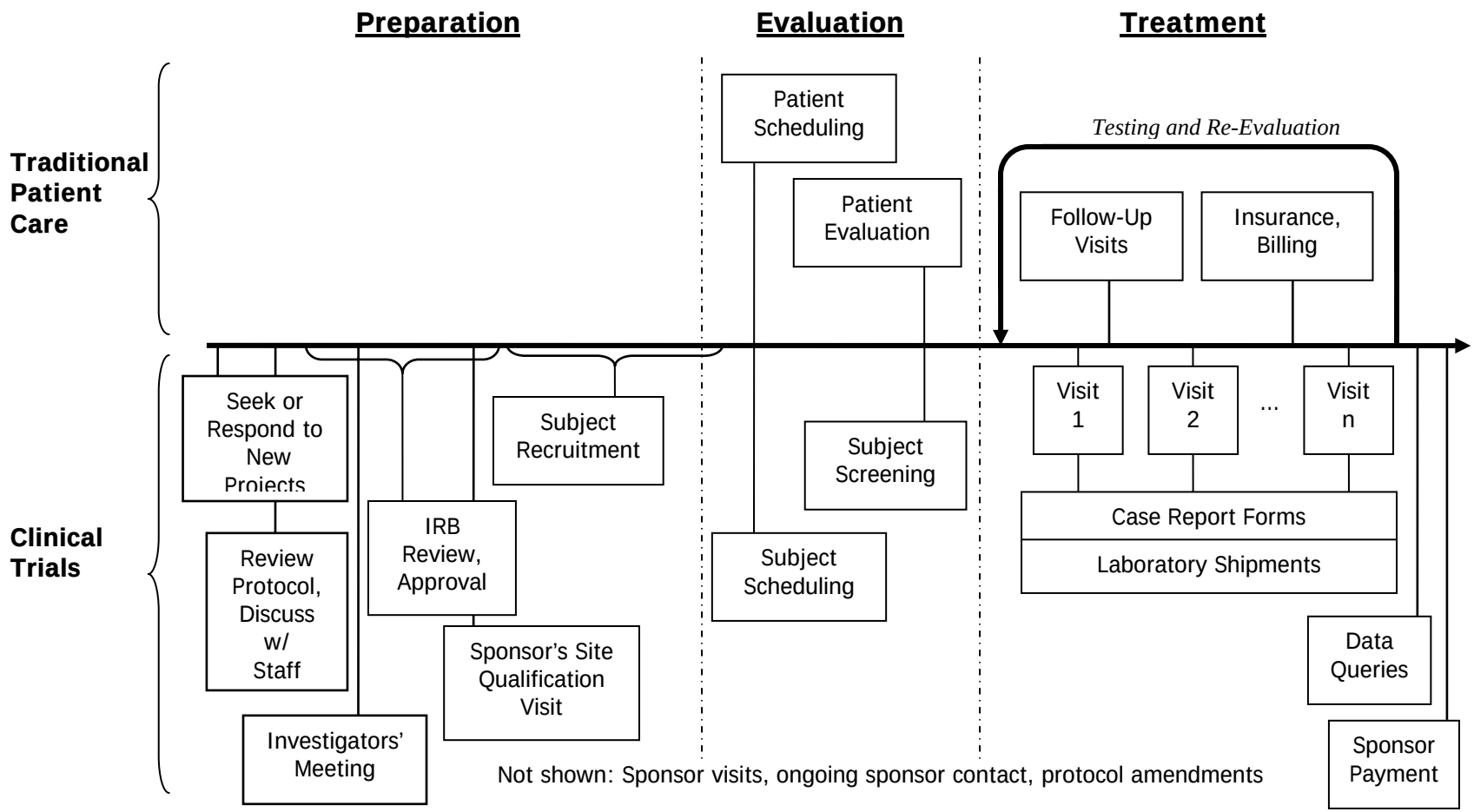


FIGURE 2: Mapping of Divisional and Firm Focus to the Setting of Clinical Trials

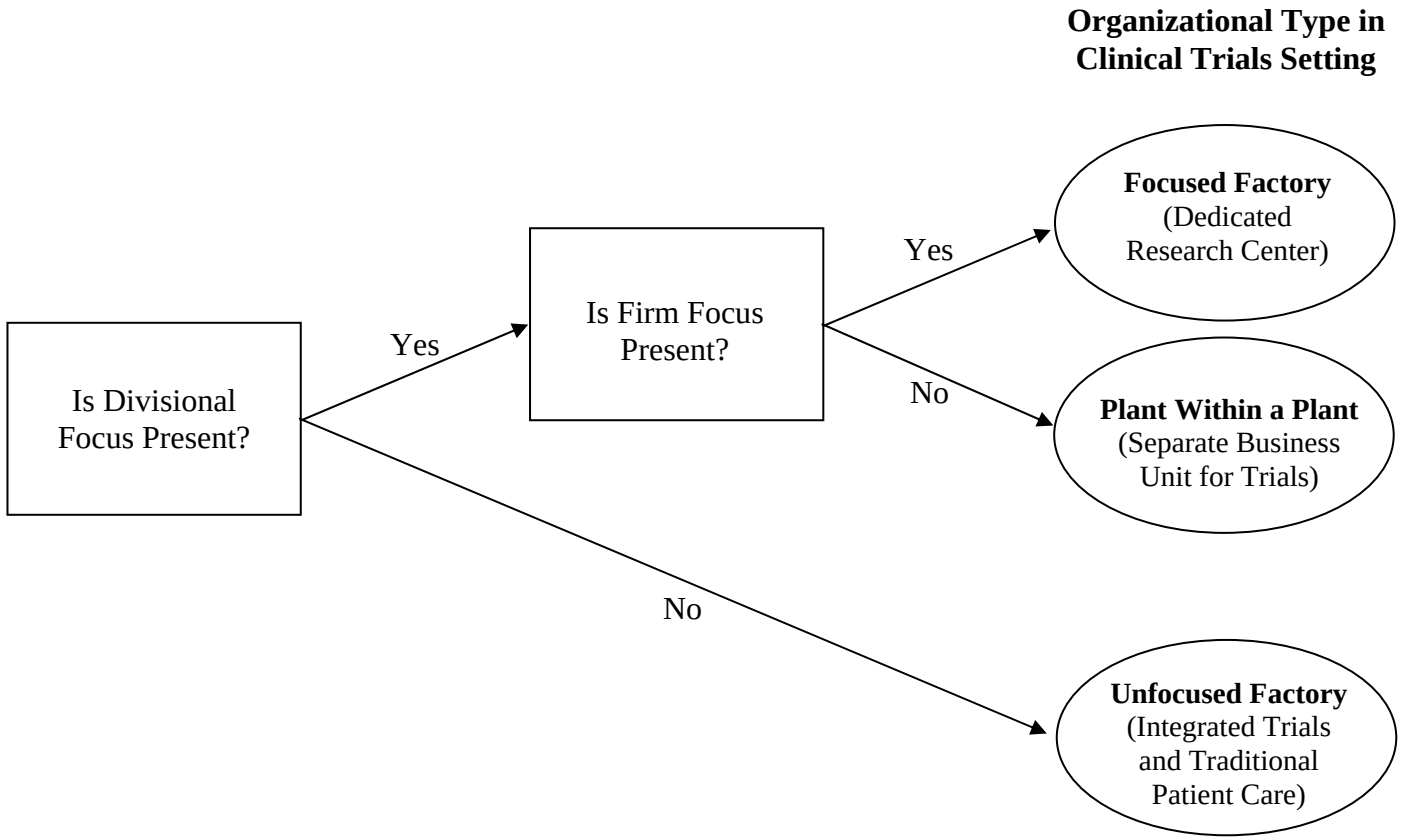
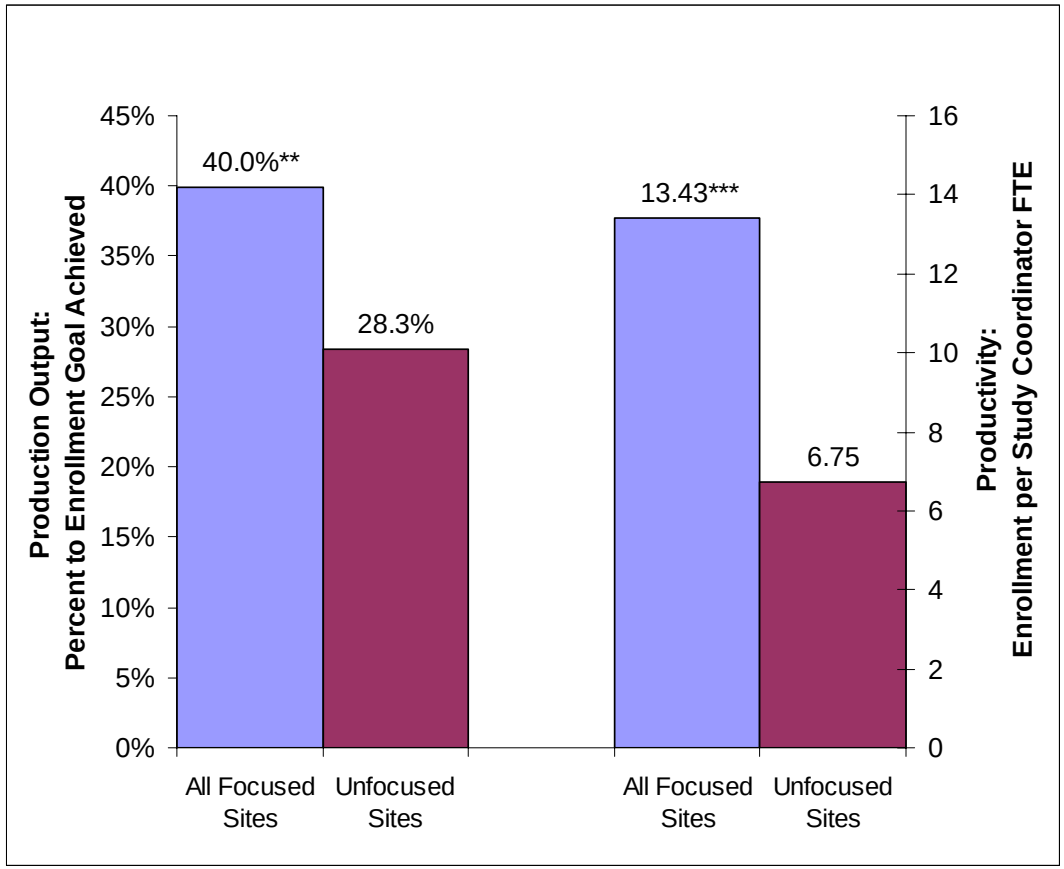
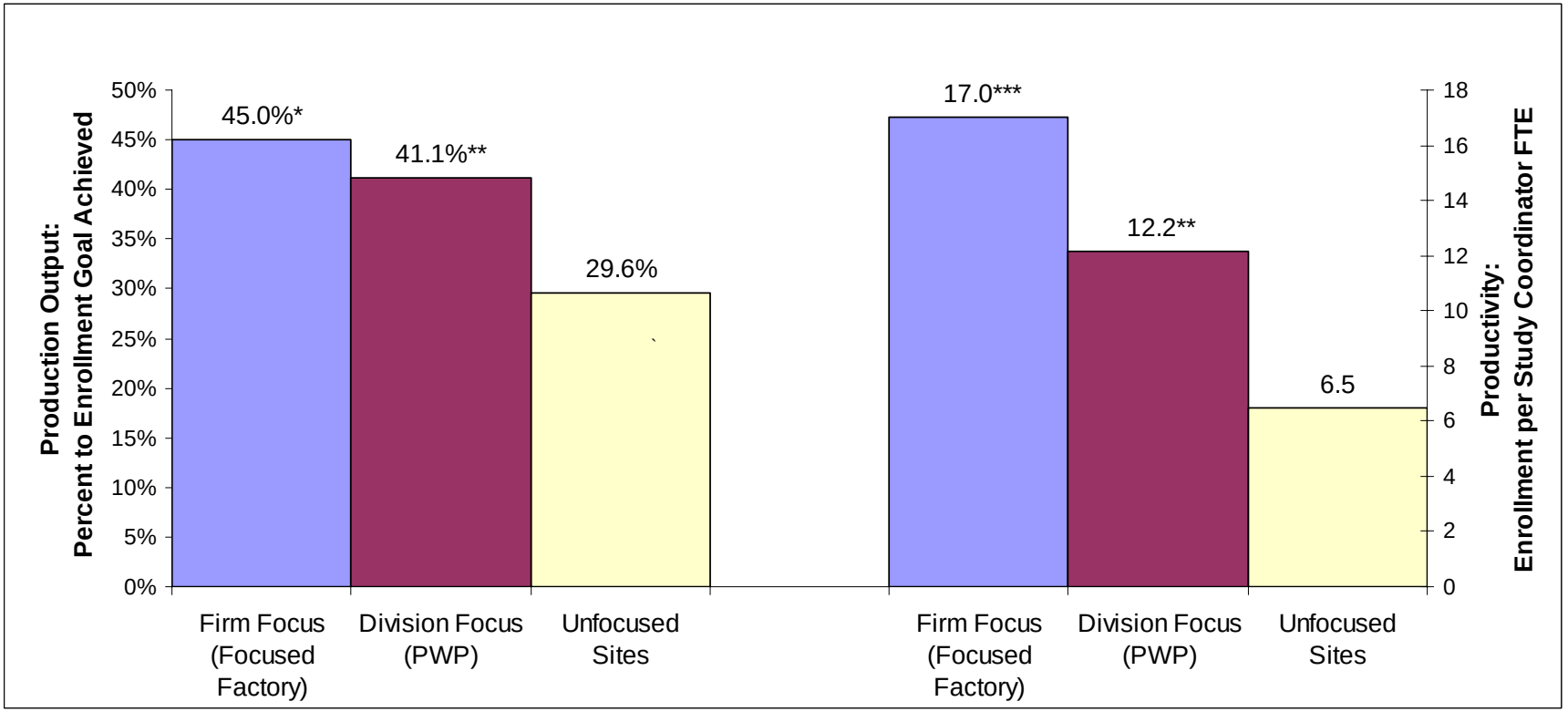


FIGURE 3: Average Effect of any Focus, Controlling for Scale, Learning, and Selection Effects



*Note: *,**, and *** represent significant differences relative to unfocused sites at the 10%, 5%, and 1% levels respectively. Values are determined with all variables (other than level of focus) set to their sample averages. Estimates derived from regressions with robust standard errors clustered by site.*

FIGURE 4: Average Effect of Categories of Focus, Controlling for Scale, Learning, and Selection Effects



*Note: *,**, and *** represent significant differences relative to unfocused sites at the 10%, 5%, and 1% levels respectively. Values are determined with all variables (other than level of focus) set to their sample averages. Estimates derived from regressions with robust standard errors clustered by site.*

TABLE 1: Descriptive Statistics of Protocols, Investigative Sites, and Trial Performance

Protocol Characteristics (n=72)	Number of Protocols	Number of Data Points	Percent of All Data
Phase II	11	30	9.4%
Phase III	51	234	73.1%
Phase IV	10	56	17.5%
Cardiology/Vascular Disease	14	56	17.5%
Gastroenterology	8	44	13.8%
Dermatology	7	28	8.8%
Immunology/Infectious Disease	8	27	8.4%
All Other Therapeutic Categories (n=14)	35	165	51.6%

Investigative Site Characteristics (n=113)	Mean	Median	Std. Dev.	Min	Max
Number of Physicians	27.51	12	36.75	1	160
Number of Study Coordinators	4.25	3	3.28	0.25	15
Investigator Experience (trials)	44.46	19	54.34	1	400
Study Coordinator Experience (trials)	31.99	16	35.82	1	157
Site Experience (trials)	53.66	35	59.95	2	300
Patient Volume per MD	84.87	25	167.92	5	1,333.33
Budget per Patient	$3,592	$3,058	$2367	$225	$15,261
Negotiated a higher budget than protocol median (percent)	10.31%	0	0.30	0	1
Trial Performance Characteristics (n=320)	**Mean**	**Median**	**Std. Dev.**	**Min**	**Max**
Patients Enrolled	9.03	4.24	12.14	0	67
Goal Enrollment	15.32	12	10.90	4	50
Percent to Enrollment Goal	72.01%	34.90%	0.92	0%	676.9%
Enrollment Per Study Coordinator FTE Per Trial	44.42	16.15	92.72	0.05	1176.13

TABLE 2: Descriptive Statistics by Type of Investigative Site

	Number of Observations[1]	Unfocused Sites (n=86)	All Focused Sites (n=234)
Budget Per Patient	320	$3,761.36	$3,529.33
Clinical Phase (Percent Phase III)	320	67.4%	75.2%
Number of Physicians	313	15.4	32.0***
Number of Study Coordinators (full time equivalents)	256	1.3	5.2***
Investigator Experience (Cumulative Trials)	217	20.0	52.8***
Study Coordinator Experience (Cumulative Trials)	181	21.3	35.8***
Site Experience (Cumulative Trials)	182	16.5	64.1***
Local Patient Volume (Indication-specific Annual Patient-visits per MD)	174	153.7	60.1**
Negotiated a higher budget than protocol median (Percent)	320	9.3%	10.7%

[1] *Number of observations available from raw data; the multiple imputation method used to handle missing data in regression models is discussed in the text.*

*Note: *,**, and *** represent significant differences (unpaired t-test, unequal variance) relative to unfocused sites at the 10%, 5%, and 1% levels respectively.*

TABLE 3: Pairwise Correlations for Selected Variables

		1	2	3	4	5	6	7
Focus	**1. Any Focus (Divisional and/or Firm)**	1						
Scale	**2. Number of Study Coordinators**	0.47	1					
Learning	**3. Investigator Experience**	0.26	0.14	1				
	4. Study Coordinator Experience	0.19	0.10	0.25	1			
	5. Site Experience	0.36	0.09	0.35	0.55	1		
Other Variables	**6. Patient Volume per MD**	-0.23	-0.14	-0.06	-0.09	-0.03	1	
	7. Budget per Patient	-0.04	-0.06	0.04	-0.04	0.03	0.04	1

TABLE 4: Effects of Operational Focus, Controlling for Selection, Scale, and Learning Effects

Dependent Variable: Output = (log) Percent to Enrollment Goal

Variable	Description	(1)	(2)	(3)	(4)	(5)
Any Focus	Dedicated or Separate Trial Business (vs. Integrated w/ Patient Care)	0.1950 (0.186)	0.2512 (0.153)	0.3898*** (0.120)	0.3351** (0.144)	0.3439** (0.135)
Scale	Number of Study Coordinators				0.0167 (0.024)	0.0140 (0.023)
Learning	Investigator Experience					0.0356 (0.055)
	Study Coordinator Experience					0.1365** (0.065)
	Organizational Experience					-0.0818 (0.060)
Selection	Protocol Fixed Effects (n=72)			Incl.***	Incl.***	Incl.***
Local Volume	Patient Volume per MD (log)		0.1181** (0.044)	0.1081*** (0.030)	0.1102*** (0.031)	0.1095*** (0.029)
Economic	Budget per Patient (log)		-0.6314*** (0.109)	0.6008 (0.665)	0.4939 (0.679)	0.4560 (0.695)
Constant		-1.1525*** (0.138)	3.4988*** (0.905)	-6.4444 (5.349)	-5.6218 (5.458)	-5.5541 (5.589)
N		320	320	320	320	320
R2		0.0049	0.1281	0.6102	.6114	.6256
Adj-R2				0.6065	0.6065	.6157

*Note: *,**, and *** represent significant differences relative to unfocused sites at the 10%, 5%, and 1% levels respectively. Standard errors are robust and clustered by site.*

TABLE 5: Effects of Operational Focus, Controlling for Selection, Scale, and Learning Effects

Dependent Variable: Productivity = (log) Enrollment per Study Coordinator FTE per Trial

Variable	Description	(1)	(2)	(3)	(4)	(5)	(6)
Any Focus	Dedicated or Separate Trial Business (vs. Integrated w/ Patient Care)	0.5239** (0.249)	0.5757** (0.255)	0.4776** (0.219)	0.7719*** (0.237)	0.6883*** (0.240)	
Scale	Number of Study Coordinators				-0.0894** (0.037)	-0.0979*** (0.037)	-0.0529 (0.037)
Learning	Investigator Experience					0.0764 (0.064)	0.0973 (0.065)
	Study Coordinator Experience					0.1223 (0.088)	0.1163 (0.094)
	Organizational Experience					0.0151 (0.091)	0.0611 (0.086)
Selection	Protocol Fixed Effects (n=72)			Incl.***	Incl.***	Incl.***	Incl.***
Local Volume	Patient Volume per MD (log)		0.1163* (0.063)	0.1077* (0.057)	0.0984* (0.058)	0.0960* (0.057)	0.0757 (0.058)
Economic	Budget per Patient (log)		-0.6600*** (0.137)	-1.0180 (1.416)	-0.5869 (1.255)	-0.7827 (1.285)	-1.1018 (1.311)
Constant		2.4212*** (0.218)	7.3109*** (1.100)	10.278 (11.355)	7.0002 (10.060)	7.6378 (10.288)	10.7764 (10.495)
N		320	320	320	320	320	320
R2		0.0257	.1202	0.4690	.4889	.5051	.4815
Adj-R2				.4640	.4824	.4940	.4716

*Note: *,**, and *** represent significant differences relative to unfocused sites at the 10%, 5%, and 1% levels respectively. Standard errors are robust and clustered by site.*

TABLE 6: Comparison of Firm Focus, Divisional Focus, and Unfocused Models

Dep Vars: Output = (log) Percent to Enrollment Goal; Productivity = (log) Enrollment per Study Coordinator FTE per Trial

Variable	Description	DV: Output (1)	DV: Productivity (2)
Firm Focus	Dedicated Research Sites	0.4168*	1.0144***
		(0.236)	(0.322)
Divisional Focus/ PWP	Community Sites with Separate Trial Business	0.3283**	0.6284**
		(0.133)	(0.244)
	(vs. Unfocused Sites)		
Scale	Number of Study Coordinators	0.0129	-0.1156***
		(0.025)	(0.037)
Learning	Investigator Experience	0.0254	0.0434
		(0.056)	(0.067)
	Study Coordinator Experience	0.1447**	0.1705*
		(0.068)	(0.091)
	Organizational Experience	-0.0851	-0.0112
		(0.061)	(0.093)
Selection	Protocol Fixed Effects (n=72)	Incl.***	Incl.***
Local Volume	Patient Volume per MD (log)	0.1059***	0.0821
		(0.029)	(0.056)
Economic	Budget per Patient (log)	0.4993	-0.7806
		(0.732)	(1.237)
Constant		-5.8712	8.1212
		(5.873)	(9.886)
N		320	320
R2		.6261	.5128
Adj-R2		.6153	.4987

*Note: *,**, and *** represent significant differences relative to unfocused sites at the 10%, 5%, and 1% levels respectively. Standard errors are robust and clustered by site*

TABLE 7: Robustness and Extensions Using Divisional Focus Sub-Models and Hospital Observations

Dep Vars: Output = (log) Percent to Enrollment Goal; Productivity = (log) Enrollment per Study Coordinator FTE per Trial

Variable	Description	DV: Output (1)	DV: Productivity (2)	DV: Output (5)
Firm Focus	Dedicated Research Sites	0.4168*	1.0144***	.3585*
		(0.236)	(0.322)	(.214)
Divisional Focus/ PWP	Management Focus: Trial Management Organizations	0.3251*	0.7695***	.3450**
		(0.167)	(0.280)	(.151)
	Production Focus: Community Sites with Parallel Business Units	0.3318**	0.4708	.3026**
		(0.148)	(0.300)	(.144)
	Hospitals with Separate Clinical Trials Units			.2224
				(.221)
Unfocused Sites	Hospitals without Separate Clinical Trials Units			-.2299
				(.262)
	(vs. Unfocused Community Sites)			
Scale	Number of Study Coordinators	0.0129	-0.1156***	0.0261
		(0.025)	(0.037)	(.026)
Learning	Investigator Experience	0.0254	0.0434	0.0298
		(0.056)	(0.067)	(.072)
	Study Coordinator Experience	0.1447**	0.1705*	0.1182*
		(0.068)	(0.091)	(.071)
	Organizational Experience	-0.0851	-0.0112	-.0932
		(0.061)	(0.093)	(.057)
Selection	Protocol Fixed Effects (n=72)	Incl.***	Incl.***	Incl.***
Local Volume	Patient Volume per MD (log)	0.1059***	0.0821	0.1164***
		(0.029)	(0.056)	(0.030)
Economic	Budget per Patient (log)	0.4993	-0.7806	0.1138
		(0.732)	(1.237)	(.574)
Constant		-5.8712	8.1212	-2.8907
		(5.873)	(9.886)	(4.602)
N		320	320	377
R2		.6261	.5128	.6169
Adj-R2		.6153	.4987	.6064

*Note: *,**, and *** represent significant differences relative to unfocused sites at the 10%, 5%, and 1% levels respectively. Standard errors are robust and clustered by site.*