How Does VC Specialization Backfire in Startup Experimentation?

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July 31, 2024

Abstract

Prior research suggests that specialized VC funds with small portfolios benefit startup performance due to active investor engagement. Using project-level data from the life science sector, we investigate this argument through a novel channel of VC activism: the strategic decision of project prioritization. We document that despite more interactions from smaller and more focused VCs, their biotech startups are *less* likely to exit via IPOs. Consistent with such activism prematurely prioritizing the research pipeline, startups backed by concentrated VCs exhibit slower progress in clinical trials and tend to discontinue projects due to pipeline priority rather than other reasons. For identification, we use limited partners' adoption of ESG objectives as instruments for affected VCs' portfolio size and diversification. Lastly, we highlight conflicting experimentation preferences between general partners and founding teams due to investment horizon and diversification.

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1 Introduction

Most venture capital (VC) funds feature a specialized portfolio with a small number of invested companies. Despite this limited diversification exposing general partners to idiosyncratic risks, researchers argue that a small portfolio size can be theoretically beneficial due to the VC activism (e.g. Kanniainen and Keuschnigg, 2003; Fulghieri and Sevilir, 2009). Various academic and anecdotal evidence suggests that VCs frequently interact with their portfolio companies for financing and operational decisions. Given their limited capacity and human capital, increasing the portfolio size may diminish VCs' attention on each startup, hurting the fund performance. This argument builds upon the prior that such engagement adds real value to the success of portfolio firms. However, a recent survey by Gompers et al. (2020) shows that only 27% of responding VCs list their services as most important for value creation. Even fewer VCs rank the board of directors or their own contribution as most important for a startup's success. Meanwhile, the emergence of the "spray and pray" investment approach (Ewens et al., 2018) suggests that VCs are increasingly constructing large portfolios with minimal engagement. These new findings necessitate further research to revisit the optimality of concentrated portfolios, zooming into whether and how the associated engagement influences startup growth.

We explore this question using granular data from the life science sector and delve into an understudied yet pivotal aspect of VC activism: the strategic decision of project prioritization. We document that while smaller and more focused VCs indeed engage more actively with portfolio firms, their involvement can hinder startups' strategic experimentation by prematurely prioritizing the pipeline and holding back many early-stage innovative projects. This value destruction likely reflects the conflicting preferences between the general partners and the founding team. Our findings do not necessarily contradict previous research on the benefits of VC monitoring; rather, they highlight the heterogeneity in the hard-to-observe involvement processes. The notion of VC activism encompasses many activities, and we acknowledge the value-adding channels such as professionalization (Hell-

mann and Puri, 2002), fundraising (Bottazzi et al., 2008), and recruiting (Amornsiripanitch et al., 2019). We complement these findings by examining how involvement influences R&D decisions, echoing the recent concern of Lerner and Nanda (2020) that the VC structure is optimized only for a narrow slice of technological progress. The net effect of specialization and engagement depends on a startup's demand for these various VC services.

In this paper, we focus on VC investments in drug development startups for several reasons. First, pharmaceutical and biotech startups require substantial scientific expertise for effective research and development activities. Second, VCs are crucial players in the drug development landscape: more than 20% of annual VC funding is allocated to the biotech and healthcare industry, according to a 2023 VC industry report.[1] Lastly, our data allows us to observe the experimentation details at the project level. Indeed, Ewens and Sosyura (2023) recently document that losing a VC director has inconclusive impacts on startup patenting activities, calling for further investigation with more granular measures in the innovation process.

We start with three stylized facts to clarify the institutional settings of entrepreneurship in the life science sector. First, empirical tests of fund size and specialization's impacts on startup performance remain inconclusive (Bernile et al., 2007; Matusik and Fitza, 2012), suggesting large heterogeneity across industries. As a benchmark, we first document that biotech startups held by smaller and more specialized VCs are *less* likely to successfully exit by going public. Second, more concentrated VCs are indeed more likely to interact with portfolio firms, as proxied by board representation (Lerner, 1995). These two facts are at odds with the assumption that activism by smaller VCs adds value to innovative startups.

We propose a channel to reconcile these puzzling facts through the third observation that innovative startups must make a strategic decision to prioritize their research pipeline. Simple summary statistics of 160 biotech IPOs in our sample suggest that these companies

[1]For more details, see the article from Carta on December 19, 2023: https://carta.com/blog/vc-shifts-2023.

initiate more than 12 projects to experiment. However, by the IPO time, more than one-third of the initial projects will be discontinued and the majority remain in the pre-clinical stage. Only 1 project is prioritized to Phase 2, with 1.4 other projects having progressed to Phase 1. While *ex-ante* startups have hedging incentives to explore various diseases with their focal technology, the availability of cash and R&D capital effectively limits the number of prioritized projects. Generalizing our studies from the biotechnology sector, this project prioritization process is inherently embedded in entrepreneurship as a real option problem, where startups decide when and which projects to proceed. Active VC oversight can involve or even interfere in this process due to conflicts of interest. This intervention is underscored in the widely-cited "Entrepreneurship as Experimentation" perspective by Kerr et al. (2014), which argues that investment and continuation of novel ideas are not made in a competitive Darwinian contest, but are instead impacted by "*a myriad of incentive, agency, and coordination problems*" of investors.

To establish direct evidence of specialized VCs holding back scientific experimentation, we use comprehensive project-level development data from Cortellis, tracking the progress of clinical trials across phases in a quarterly panel of approximately 90,000 observations. Our baseline measure is the logarithm of equal-weight portfolio sizes of all VCs investing in a focal startup. Consistent with our hypothesis, a one-standard increase in the size measure is associated with an increased chance of progressing by 0.45%, equivalent to a third of the unconditional quarterly progressing rate. Alternatively, we measure the concentration of each VC's investments using the Herfindahl-Hirschman Index (HHI) based on the allocation weights among portfolio startups. Conversely, the coefficients of HHI-based measures are negative and significant, further suggesting that more VC specialization is associated with worse innovation outcomes.

We acknowledge that the screening and selection in VC deals could confound our interpretation of the previous results. Larger and more diversified VCs may endogenously match with higher-quality biotech startups, creating a natural positive correlation between

VC size and progress rate. To establish causal evidence, we need to obtain exogenous variations of VC portfolio sizes and diversification, while holding the *ex-ante* matched VC-startup pair consistent to alleviate selection, and then study the impacts of such variations on project-level innovation outcomes. Our instrument utilizes the staggered adoption of environmental and sustainable investment principles by an important category of VC limited partners (LPs), the state public pension funds. Life science startups are arguably neither green nor brown companies, suggesting that VC financing activities in the biotech sector are not directly affected by the shock, and the exclusion restriction likely holds. For the relevance condition, previous research suggests that preferences by startup pensions will constrain the general partners' portfolio choices (Andonov et al., 2018) and we argue that previously-concentrated VCs have to increase their portfolio size and diversification after their exposure to the policy changes. This is indeed what we find in the first stage, with the t-statistics of the instrument around 20 and all F-statistics above 10. Consistent with our OLS results, the second-stage coefficients for size-based measures are positive and significant, while the coefficients for HHI-based measures are negative and significant. These results again suggest that after a life-science startup's existing VCs become less specialized, its R&D efficiency significantly improves.

We further support the intervention argument through the subset of sample drug projects that are discontinued with disclosed reasons. The data provider categorizes the reasons for discontinuation into four categories: pipeline priority, lack of efficacy, lack of funding, and other reasons. Consistent with our hypothesis, we find that projects are more likely to be discontinued for prioritization when the company is held by specialized VCs. In contrast, we do not find any significant correlations between VC specialization and funding-related discontinuation. This null result alleviates the concern that larger and more diversified VCs may be more lenient in capital provision for financing more costly experimentation. Additionally, lack of financing sufficiency, as demonstrated by Inderst et al. (2007), does not necessarily imply weaker innovation performance because the threat of "shadow pockets"

improves entrepreneurial incentives through internal competition among portfolio startups.

Lastly, we highlight the conflicting preferences in prioritization decisions between investors and founders. In many disease areas, the sequence of clinical trials can take over twenty years to resolve scientific uncertainty. As a result, VCs may need to liquidate their investments before proof-of-concept evidence is realized, suffering an underpricing discount due to information asymmetry. Consequently, despite societal interests, VCs prefer to avoid projects with high uncertainty or prolonged time frames to generate efficacy signals. This argument echoes Nanda et al. (2014)'s observation of declining interest from VCs in renewable energy startups due to the lengthy and costly experimentation process. The direct implication is that VCs would not hold back projects that have produced publicly observed positive signals. Indeed, we confirm that the negative effects of prioritization only hold significantly in the subsample of early-phase (pre-clinical or Phase 1) projects but remain insignificant in later phases. We also find that specialized VCs value monopoly power protections, such as the orphan drug designation that grants additional market exclusivity conditional on approval. Finally, we split the projects into fast or slow disease groups based on the median expected length of experimentation time to reach Phase 3. The cut-off is roughly 8 years, suggesting that projects in the lengthy group may expose VCs to underpricing risks. Consistently, the negative relation between VC specialization and trial progress only significantly exists in the slow disease groups.

We perform a series of robustness checks on the baseline results. First, we replicate the analysis using each focal startup's lead VC specialization instead of all VC investors, and we document similarly significant results. Besides, our baseline results also incorporate investment-weighted measures to adjust for the heterogeneous control power of each VC. Second, while our baseline results use investment information from PitchBook data, we show that all our findings remain robust when using VentureXpert data. Lastly, we follow the alternative identification strategy by Bernstein et al. (2016), which utilizes

the introduction of direct flights as exogenous variations of VC involvement. We find that increased lead-VC activism likely hinders strategic experimentation progress, particularly in the early stages. However, on-site monitoring has positive impacts on progress in late-stage experimentation, where the strategic commercialization of novel projects becomes the main focus. This result is consistent with Bernstein et al. (2016)'s findings on the positive impacts on patent issuance, which represents critical market protection strategies in the life science sector.

Our paper is closely related to the portfolio size and specialization of VC funds. Early evidence suggests that VCs limit both fundraising frequency and fund size (Gompers and Lerner, 1996), and top-performing VCs voluntarily choose to stay smaller (Kaplan and Schoar, 2005). Various research studies the optimal portfolio size using trade-off theories. Larger portfolios can be beneficial due to diminishing returns of advice per firm (Kanniainen and Keuschnigg, 2003), diversification of idiosyncratic risks (Bernile et al., 2007), and *ex-post* bargaining advantage and resource reallocation (Fulghieri and Sevilir, 2009). However, a trade-off exists because a smaller portfolio allows the VC to spend more effort on each startup.[2] While we agree with the aforementioned value-adding services by VC monitoring, our empirical results highlight the heterogeneity of VC activism and suggest that active engagement may backfire in startup experimentation. As a result, trade-off theories may fail to hold in certain sectors. Our results also echo the inconclusive empirical evidence on how VC specialization impacts startup performance. Gompers et al. (2009) shows that when the individual venture capitalist is a specialist, the performance difference between specialized and general VC firms is minimal. Portfolio diversification also encourages managers to take on riskier projects and facilitates knowledge sharing between portfolio firms (Buchner et al., 2017; Humphery-Jenner, 2013; Matusik and Fitza, 2012). None of these papers focus on the strategic experimentation of innovative ideas as we do.

[2]Note that Fulghieri and Sevilir (2009) also argues that a small portfolio ensures that VCs will not threaten to divert resources to extract *ex-post* rents.

Our focus on the project prioritization problem aligns with the experimentation view of entrepreneurship (Kerr et al., 2014; Ewens et al., 2018). VC financing is optimally structured into stages for interim signals, creating a real option problem for the continuation and termination of innovative projects (Bergemann and Hege, 2005; Manso, 2011). Existing theoretical literature argues that VCs may hold up startups for rent exploitation by threatening funding discontinuation, thereby hurting experimentation incentives (Fulghieri and Sevilir, 2009; Inderst et al., 2007). Instead, our paper highlights the distortion in the direction of innovations during this experimentation process, as VCs selectively prioritize projects that match their investment preferences. While this distortion has been noted by Kerr et al. (2014) and Lerner and Nanda (2020), to our knowledge, this paper is the first empirical study to test and confirm this hypothesis. Additionally, related literature documents that VCs may pass business cycle risks to the innovative sector (Nanda and Rhodes-Kropf, 2013, 2017). Howell et al. (2020) find that innovation conducted by early-stage VC-backed firms is of lower volume and quality in recessions. Unlike the financing channel, our paper shows that increased VC involvement could impede radical innovation's progress.

Our paper is also related to the strand of literature on financing novel and radical drug innovation. Existing literature documents the distorted direction of innovation towards short-term and less innovative drugs through two channels. First, Budish et al. (2015) argue that drugs taking longer to complete clinical trials will enjoy a shorter intellectual property right after commercialization due to a fixed patent term. Second, Krieger et al. (2022) show that risk aversion prevents pharmaceutical companies from optimally investing in novel drug development. Unlike their findings, we focus on the conflict of interests between investors and developing companies. Lastly, our paper falls into the broad literature on the impacts of external financing conditions on drug innovations, such as mergers and acquisitions (Cunningham et al., 2021; Phillips and Zhdanov, 2013), IPOs (Aghamolla and Thakor, 2021), and licensing (Hermosilla, 2021; Hammoudeh et al., 2022).

2 Institutional background and Data

2.1 The Life Science Industry

Drug development involves a structured regulatory process that firms must navigate before launching the product on the market. In the US, the FDA evaluates candidate molecule structures (labeled by the generic name of drugs) for specific diseases and symptoms (known as indications) based on their safety and efficacy. The drug development process consists of several phases. The initial phase involves the discovery stage and pre-clinical stage, where thousands of molecules are screened, and only a few promising candidates undergo testing in laboratories and on animals. Then, drugs move to get tested on human beings. In Phase 1, the safety and efficacy of a drug are evaluated in a small group of 10 to 50 volunteers. If a drug proves safe in humans, it advances to Phase 2 trials, involving a larger sample of 50 to 200 volunteers to evaluate both safety and efficacy. Drugs with robust Phase 2 evidence move on to Phase 3 trials, where safety and efficacy are rigorously tested in a large sample of 200 to 3,000 volunteers.

Developing novel drugs is of high social value, with the COVID-19 pandemic revealing a lack of progress in developing novel drugs and vaccines. Yet, developing drugs is characterized by high research and development costs, lengthy development timelines, and large scientific uncertainty. The average cost of getting a new drug into the market between 2009 and 2018 was $1.3 billion (Wouters et al., 2020). The journey of clinical development time can take from five to more than twenty years, with the median being over eight years (Brown et al., 2022). As of June 2023, according to Cortellis data, less than 18% of drugs that undergo clinical trials ultimately receive approval from the Food and Drug Administration (FDA) by June 2023.

Startups are active drivers in drug development, and the activeness has been increasing over time. As per Pitchbook and Cortellis data, the percentage of new drugs from VC-backed startups rises steadily from 2000 to 2020. The average is 10.43% from 2010

to 2015 and increases to 15.94% from 2016 to 2020. Related, VC investors play a pivotal role in financing innovation within the pharmaceutical sector. They assist drug development teams in navigating the "valley of death," an intermediary stage where the science has progressed beyond research funded by federal sources but remains too premature for significant involvement from large pharmaceutical companies. According to Pitchbook data, biotech companies raised an impressive $81.76 billion in VC funding rounds in 2021 alone. In the life science sector, VC's impact goes beyond financial contributions; they actively engage in the scientific development process. For example, Atlas Venture adopted a venture creation model that assists startups in designing killer experimentation, exploring potential pivots, attracting talents, and assessing market interest from big pharmaceutical companies and other investors.[3]

2.2 Drug development data

We construct a project-level quarterly panel from the Cortellis Drug Discovery Intelligence Platform following Li et al. (2023), Guenzel and Liu (2023), and Krieger et al. (2022). Cortellis aggregates drug data from various public resources, including clinical trial registries, FDA submissions, patent filings, company press releases, financial filings, and other scientific publications. This comprehensive dataset covers the drug's originator company, indications, and both current and historical development status, among other details. Notably, Cortellis provides updates on when an indication progresses to the next clinical phase or is discontinued in the current phase, enabling us to trace the evolution of each indication's development status over time.

Following the institutional convention, each project is a sequence of trials studying a molecule structure's potential for a given indication, i.e. a drug-indication combination. The rationale is that the FDA will separately approve a given product's commercialization

[3]For more details, see the article from Fortune on August 15, 2019: The Creation Of Biotech Startups: Evolution Not Revolution.

targeting various indications. Logically, different diseases require different endpoints and indicators to prove safety and efficacy. Developing companies have to design different sequences of trials for approval. By extracting project-level development records from the Cortellis database, we create a drug-indication quarterly panel documenting each project's furthest active stage (e.g., Phase 1) in a given quarter. Building on the development status, we introduce a dummy variable *Next Phase* as our focal outcome variable to indicate whether the project will progress to subsequent phases in the following quarter. For example, *PRX-8066* is the generic name of a drug developed for multiple types of lung diseases, such as lung infection and MRSA infection. In our panel data, the *PRX-8066*-pulmonary-fibrosis combination is constructed as a separate project from the *PRX-8066*-pulmonary-hypertension combination. In May 2005, the pulmonary hypertension project progressed to Phase 1 clinical from discovery and further progressed to Phase 2 clinical in June 2006. In this case, we code *Next Phase* for *PRX-8066's* pulmonary hypertension project as one at 2005Q1 and 2006Q1. We consolidate three pre-Phase-1 statuses in Cortellis "discovery," "pre-clinical," and "clinical" into a single pre-clinical stage and ignore progressing between pre-Phase-1 statuses. These pre-clinical status designations are more arbitrary decisions by developing companies and may not represent significant scientific milestones. For each project, our quarterly panel includes the quarters when the drug has active trials and excludes records with terminated or perfected development status.[4]

2.3 VC investment data

We obtain data on VC deals from 2000 to 2020 from Pitchbook, which sources private equity, venture capital, and mergers and acquisitions data from regulatory filings, press releases, company websites, financial statements, and industry professionals. For each transaction, the Pitchbook details the investor company, primary investor type, investee

[4]These statuses include "outlicensed", "no development reported", "discontinued", "withdrawn", "suspended", "pre-registration", "registered" and "launched."

company, deal type, investment amount, investment date, type of stock, etc. We collect data VC data from Pitchbook in view of its granularity and accuracy (Chen and Ewens, 2021; Jang and Kaplan, 2023; Fragkiskos et al., 2022; Haltiwanger et al., 2017). In the online appendix, we show that our baseline regression results are robust using the alternative VentureXpert data.

We focus on VC deals made to US startups and exclude non-VC deals, VC deals made by non-VC investors, and VC deals made to companies headquartered outside the US. Next, we match the Pitchbook investee and Cortellis drug companies in the following steps. First, we utilize official company websites to match Cortellis drug companies with Pitchbook startups. Second, we proceed with exact company name matching when website matching is completed. Third, we implement fuzzy matching for company names and manually review all potential matches for those not matched in the above steps. In so doing, we are able to pin down 1,413 unique US drug companies that have ever received VC funds from 2000Q1 to 2020Q4 and also appear in the initial panel we construct in Section 2.2.

Following the literature, we then develop two variables to measure how diversified and specialized a VC investor is at a given quarter based on its investment activities in the past ten years. The first measure is *Size*, defined as the unique number of startups in which this VC has invested during this window. VCs typically limit the number of startups in their portfolios because they would otherwise devote less time and effort to each company when investing in more firms (Bernile et al., 2007; Fulghieri and Sevilir, 2009). Ewens et al. (2013) argue that the requirement of monitoring efforts restricts the size of the portfolio and the scope of diversification, exposing VC compensations to idiosyncratic risk. We construct the second measure as a Herfindahl-Hirschman Index (*HHI*) index, reflecting the concentration of a VC's allocation weights across portfolio startups. By definition, *Size* (*HHI*) positively (negatively) relates to a VC's diversification level in a given quarter, echoing the fact that portfolio size and specialization are substitutes documented by Hochberg and Westerfield (2010). A VC investor's *HHI* index is the sum of the squares of the percent-

ages of its investments in each drug company over its all investments for drug companies during the 10-year rolling window. Hypothetically, a VC with an HHI of one concentrates all its investment in only one drug company, with smaller HHI suggesting more diversified portfolios.

In our drug project quarterly panel, each startup may have multiple VC investors in a given quarter. Therefore, we need to aggregate the above measures across various investors at the startup level. For each matched drug company in a given quarter, we track all VC investors that have invested in this company over the past three years and average both *Size* and *HHI* either equally or weighted by the total deal amounts. For example, for drug startup i in a given quarter t, we track all VC deals invested in startup i from quarter $t-11$ to quarter t (three years). If startup i is invested by investor j multiple times during that period, we aggregate all the investments made by j for weighting purposes. Next, we aggregate the *Size* and *HHI* measures from the startup-VC-quarter level to the startup-quarter level. *Ln(EW-Size)* is the (logarithm of) equally-weighted VC sizes, and *EW-HHI* is the equally-weighted VC HHI index of a given startup at the focal quarter. *Ln(VW-Size)* and *VW-HHI* are similarly defined, except that the corresponding measures are weighted by the total amount of investments in the past three years by each VC. By integrating these startup-level measures with the drug indication development data, we arrive at a drug-indication-quarter panel containing 99,806 observations on drug indication development status and VC specialization measures from 2000Q1 to 2020Q4.

2.4 Other data

The investor base for a startup company usually becomes significantly diversified post-IPO (Bodnaruk et al., 2008), diluting VC's control over the startup. We collect the IPO dates data from Pitchbook and supplement missing IPO dates with the CRSP header file (which reports the first trading day of listed companies). After excluding post-IPO records for matched drug companies, the number of observations in our panel reduces to 90,632.

To uncover the mechanism by which VC investors may monitor drug companies, we follow Gompers et al. (2023) and Jang and Kaplan (2023) and collect board entrance data for matched drug companies from Pitchbook. Specifically, for a drug company in a given quarter, we check whether there are any new additions to the company's board representing certain VC investors who have previously invested in this company. We then construct a dummy variable *New Board*, which takes the value of one if a drug company gains a new board member from its VC investors in a given quarter and zero otherwise.

2.5 Summary statistics

Table 1 reports the summary statistics for our drug development variables and VC specialization measures from 2000Q1 to 2020Q4. Consistent with the scientific difficulty, around 1.4% of the drug indications unconditionally make it to the next phase in a given quarter. The typical drug company in our sample has an average investor size of around 40. If these investors equally invest in all portfolio startups, then the hypothetical average HHI would be around 0.03 ($40 \times (1/40)^2$). Instead, the average weighted HHI is about 0.22, suggesting that VCs rationally allocate additional funding towards certain startups and hold back others in the continuation decisions. Experimentation in the life science sector is costly, with a typical company receiving about $30 million in a three-year rolling window. In the appendix Table IA.1, we split the sample into early-stage (pre-clinical and Phase 1) and late-stage (Phase 2 and Phase 3). The success rate of clinical trials not surprisingly reduces (to 0.9%) in the later phases. Late-stage clinical trials appear to be more expensive, receiving about $32 million every three years.

3 Stylized Facts

In this section, we document three descriptive observations in the life science entrepreneurial sector to motivate and guide our empirical studies. These facts do not necessarily imply

causal relations, and we defer more rigorous analyses in later sections. They provide unique institutional knowledge to help us understand the empirical setting.

Fact 1: Life science startups invested by more specialized VCs are *less* likely to exit through IPO.

We start with a simple cross-sectional correlation study for all startups in our sample. For each startup, we indicate whether it successfully exits by 2020Q4 via the variable *IPO*. Then for both the *Size* and *HHI* measures, we take a simple time-series average to quantify the general degree of VC specialization over a startup's life cycle. Figure 1 best visualizes Fact 1 using a simple mean comparison, where we sort all startups into 20 equal-sized buckets. Within each bucket, we calculate the fraction of IPO exits among all startups in it. Panel A exhibits an obvious increasing relation: startups invested by larger funds are more likely to go public. The group of startups held by the smallest VCs exit via IPO by a chance 1.4%, which is ten times smaller than those held by the largest investors (15.7%). Consistently, the relation is starkly reversed in panels C and D, suggesting that more concentrated VCs see fewer IPOs in their portfolio companies.

There exist many potential non-exclusive explanations for this observation. Larger and more diversified VCs may have sufficient funding and provide additional capital for startups. In Table 2, we explicitly control for the average quarterly investment amounts received by the startup. Indeed, larger capital inflows significantly increase the chance of IPOs. However, the previous relationship remains robust, even controlling for financing amounts. Alternatively, less specialized VCs may receive better deal flows and match with high-quality startups. In Table 2, we include additional fixed effects such as the initial therapeutic areas, founding times, and locations to absorb the unobserved heterogeneity across startups. Note that Kerr et al. (2014) suggests that even conditional on initial VC investments, it is hard to predict the final success of startups. Moreover, there exists a counterargument to this explanation suggested by Kaplan and Schoar (2005). It is possible that good deals are scarce, and VCs face diseconomies due to decreasing qualities

when growing in size. Fund manager human capital is also not easily scalable, and more specialized VCs will arguably spend more time and effort in the screening process. It is ex-ante unclear whether more diversified or specialized VCs will match startups with better qualities.

Fact 2: More specialized VCs are indeed more engaged in monitoring startups in the life science sector.

The literature argues that one benefit of venture specialization is to ensure the monitoring efforts of general partners given limited human capital (e.g. Bernile et al., 2007; Fulghieri and Sevilir, 2009). We test this hypothesis in our sample using a simple measure of engagement in the following regression: whether the startups observe VC investors join their company board.

$$New\ Board_{k,t} = \alpha + \beta VC\ Spec_{k,t} + \Phi X_{k,t} + \gamma_k + \delta_t + \epsilon_{i,j,k,t}, \tag{1}$$

We perform the analysis of Equation (1) at the startup quarterly sample. $New\ Board_{k,t}$ is one if drug company k has any new board members from its VC investors at time t. $VC\ Spec_{k,t}$ indicates the four VC specialization measures. Besides company and time fixed effects, we further control for VC investment amounts and a company's active portfolio size in $X_{k,t}$. Table 3 reports the results for estimating Equation (1). The coefficient estimates of *Ln(EW-Size)* and *Ln(VW-Size)* in Columns (1) and (2) are both negative and statistically significant at 5%, suggesting that larger VCs are significantly less likely to take the board seats of their portfolio startups. Consistently, the positive and significant coefficient estimates of *EW-HHI* and *VW-HHI* in Columns (3) and (4) also suggest that VCs with more diversified portfolio companies are less likely to sit on their investing drug company's board.

The findings in Table 3 align with recent evidence by Fu (2024), which uses cell phone signals to show that larger VCs monitor less per deal across all industries. The fact that

more specialized VCs engage more actively further puzzles the interpretation of Fact 1, suggesting that increased monitoring does not necessarily lead to better exit outcomes. To reconcile these puzzling facts, we need to introduce a third observation in the growth of innovative startups.

Fact 3: Life science startups need to prioritize drug projects before the IPO.

In Table 4, we present the characteristics of drug projects for the 160 startups in our sample that successfully exited by going public. A typical startup actively experiments with ideas, initiating more than 12 projects throughout its pre-IPO life cycle. There are two explanations for this high degree of experimentation. Scientifically, many indications share common pathways, allowing one molecular structure to be effective for multiple diseases. Additionally, startups explore various projects from a hedging perspective, given the substantial risk of failure in this process. Indeed, about one-third of the projects are suspended by the time of the IPO, resulting in an average active pipeline size of 7.8.

The existence of project prioritization becomes evident when we examine the stages of the active pipeline. The majority of projects (68.8%) do not progress and remain in the pre-clinical phase. On average, a typical IPO startup will have just over one Phase 2 project and 1.4 Phase 1 projects. Progressing a project to Phase 3 is almost impossible for startups. These summary statistics highlight two key aspects of prioritization. First, drug experimentation requires substantial investments in both cash and time, effectively limiting the number of projects that can feasibly progress. Given the significant risk of failure, startups are incentivized to focus resources on the most promising projects based on early evidence from pre-clinical trials. Second, life science IPOs substantially increased following the Jumpstart Our Business Startups (JOBS) Act in 2012. The preference of primary market investors shifted toward biotech companies with products earlier in the FDA approval process (Dambra et al., 2015; Lewis and White, 2023). Most investors value startups based on the leading pipeline's proof-of-concept clinical trials in Phase 1 or dose-ranging Phase 2. Therefore, it is sufficient for life science startups to enter the IPO market,

with only a small number of projects moving beyond pre-clinical stages. While project prioritization is a necessary task for life science startups, the optimal timing of prioritization and the choice of prioritized projects are complicated decisions requiring careful consideration.

Summary: Project prioritization is a fundamental decision in the strategic experimentation of entrepreneurship. It is not surprising that specialized VCs actively engage in this process through monitoring. However, the founding team and investors may have conflicts of interest. For example, VCs may be interested in a narrow band of drugs that are easy to commercialize in the short term. Due to a limited investment horizon, they may intentionally hold back more radical but also more time-consuming, risky, and innovative projects. As a result, many promising projects are unnecessarily delayed or even terminated at a very early stage. Therefore, the engagement of specialized VCs interferes with the performance of startups and hurts their chances of successful exits.

This conflict is evident in the story of Acerta Pharma, a startup that originated the later-approved blockbuster Bruton's tyrosine kinase (BTK) inhibitor drug acalabrutinib (commercialized as Calquence). Acalabrutinib was initially investigated for multiple blood cancer indications, including mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL). In 2014, the company was considering moving these trials toward Phase 2. The founding CEO wanted to continue the trials of CLL, the most common type of leukemia in adults. However, acalabrutinib's competing drug ibrutinib (Imbruvica) had already been fully approved by the FDA for CLL, and acalabrutinib had to demonstrate significant improvement against ibrutinib in a head-to-head Phase 3 trial for approval. Although the founding CEO was confident in the projected results based on scientific knowledge, this trial would require tracking patient survival for many years. Instead, the lead investor, which was a small fund specializing in blood cancers, wanted to prioritize MCL, a rare disease eligible for accelerated approvals and not requiring comparison with ibrutinib. The founding CEO was ultimately replaced due to the disagreement. In fact, the investors had

already forced the CEO to prioritize acalabrutinib in the blood cancer space and move away from autoimmune diseases such as rheumatoid arthritis. This internal turnover held back the overall progress of the startup, leading it to be acquired by the pharmaceutical company AstraZeneca PLC in 2015. Following the prioritization strategy, the FDA granted Calquence accelerated approval for use in MCL in October 2017. However, the initial sales were below $100 million due to the small market of MCL as a rare disease. Consistent with the founding CEO's prediction, acalabrutinib successfully completed the head-to-head Phase 3 trial and received full approval for CLL in November 2019. Sales skyrocketed afterward, with Calquence recording annual sales of $2.5 billion in 2023.

4 Empirical analysis

4.1 Evidence of Project Prioritization

We hypothesize that more specialized VCs will hold back drug project progress during strategic experimentation. A direct implication is that a drug company's projects will become less likely to progress when its VCs are more focused and engaged. These projects may be held back prematurely even with promising pre-clinical evidence since they do not align with the VCs' preference. We make use of the quarterly project panel from the Cortellis to test this implication. In particular, we focus on the clinical trial progression of drug-indications developed by VC-backed companies and estimate the following baseline regression:

$$Next\,Phase_{i,j,k,p,t} = \alpha + \beta VC\,Spec_{k,t} + \Phi X_{k,t} + \gamma_{i,j} + \delta_p + \zeta_t + \epsilon_{i,j,k,p,t} \tag{2}$$

where $Next\,Phase_{i,j,k,p,t}$ is a dummy variable equal to one if indication i of drug j at phase p from company k enters next phase at time $t+1$. $VC\,Spec_{k,t}$ represents one of the four VC specialization measures: $Ln(EW\text{-}Size)_{k,t}$, the logarithmic number of the simple mean

of company k's investing VC portfolio sizes at quarter t; $Ln(VW\text{-}Size)_{k,t}$, the logarithmic number of the weighted mean (by investment amount) of company k's investing VC portfolio sizes at quarter t; $EW\text{-}HHI_{k,t}$, the simple average of the HHI index for company k's investing VCs at quarter t; and $VW\text{-}HHI_{k,t}$, the investment-amount-weighted HHI index for company k's investing VCs at quarter t. We control for additional startup-level characteristics that potentially affect project progress in $X_{k,t}$. $Ln(VC\ Amount_{k,t})$ is the logarithmic aggregated investment amount for company k's VC investors at time t, controlling for funding sufficiency. $\#\ Developing\ Drugs_{k,t}$ denotes the number of drugs under active development from company k at time t, controlling for the pipeline size. Besides, we include granular fixed effects to absorb unobserved heterogeneity at the project level. $\gamma_{i,j}$ is the drug-indication fixed effect, absorbing the scientific potential of each molecule targeting a given therapeutic field. δ_p is the phase fixed effect, reflecting the fact that progressing becomes increasingly difficult in later stages. Lastly, ζ_t is the year-quarter fixed effect, which accounts for time-varying scientific changes.

Table 5 presents the regression results of Equation (2). Consistent with our predictions, we find that the coefficients of average VC sizes in columns (1) and (2) are positive and significant, suggesting that drug projects backed by larger VCs are more likely to pass clinical trials. Economically, a one-standard-deviation increase in the *Ln(EW-Size)* (i.e., 1.13 units increases in the sample) increases the chance of progressing to the next phase for drug projects developed by VC-backed drug companies by 0.45% ($= 0.004 \times 1.13 \times 100\%$), equivalent to a third of the unconditional average probability of progressing to next phase. Conversely, the coefficients of average *HHI* in columns (3) and (4) are negative and significant, further suggesting that less VC concentration is associated with better innovation outcomes. Overall, these results support the interpretations that specialized VCs interfere with their portfolio company's project progressing.

Other confounding characteristics of VCs could have driven the above results. For example, larger and more diversified VCs may be more reputable and have high-quality

human capital. As a result, they observe better deal flows and match with better startups. Alternatively, they may have deeper pockets and support more expensive and advanced research designs. The ideal experiment is to hold the VC-startup matched pair consistent to alleviate the ex-ante sorting concerns and then exogenously let the VC investors become more diversified and study the downstream effects on innovation progress. To implement this research design, we make use of an instrument variable (IV) analysis. Our instrument utilizes the state-level variation in incorporating environmental and sustainable principles into their public pension funds' investment process. Public pension funds have been active in socially responsible investments for a long time for various reasons (Hong and Kacperczyk, 2009; Dimson et al., 2015). Sixteen states explicitly started to include sustainability in their investment goals in a staggered fashion from 2013 to 2020. This emerging trend in investment practices has incurred a significant impact, ultimately leading to a 2023 March Senate bill trying to prevent pension fund managers from including factors such as climate change in their investment decisions. President Biden later rejected this bill as the first veto of his presidency.

Below, we explain how we construct the instrumental variable based on the variation in adopting sustainability as an investment goal by VC's LPs. First, we hold each focal drug company's VC investors constant as those having invested in the past three years. For each VC, we investigate whether at least one of its LPs has adopted the sustainability goal. Second, we (reversely) weigh the treatment status of each VC by its size, i.e., the number of previous deals, and denote the outcome as treatment intensity. Logically, a VC with large portfolios before the shock is more likely to have diversified portfolios, satisfying the ESG investment principle and less constrained by the shock. Last, we aggregate the VC-level treatment intensity to the focal drug company and use it as our instrumental variable. In particular, our instrumental variable, $Weighted\,Exposure$, is defined as the natural logarithm of one plus the aggregation of a drug company's all VC-level treatment intensity.

Table 6 reports the 2SLS regression results using instrumented VC specialization measures. Columns (1), (3), (5), and (7) present the first-stage results. We argue that our IV is relevant given the fact that state public pension funds are among the most important LPs in the venture capital industry due to the adoption of prudent investor rules (González-Uribe, 2020). Political agendas by state pensions have a direct impact on investment decisions by general partners (Andonov et al., 2018). In line with our expectation, all four columns report significant coefficients with predicted signs, suggesting that the exposure to the pension funds' ESG investment requirements has a positive impact on VC specialization, both in terms of the number of firms and the portfolio concentration measures. The t-statistic for our IV is between 19 and 22 across the four first stages, with F-statistics all above 10. These tests provide strong support for the relevance condition. The exclusion restriction condition requires that after a VC firm's state pension adopts sustainable investment, this adoption affects the drug progression of the VC firm's portfolio biotech only through VC specialization and reduced activism. Our instrument is similar to the shareholder "distraction" measure in Kempf et al. (2017). They define investor distraction for each firm as its shareholders' portfolio holdings *in other industries* have substantial shocks and document that distraction temporarily reduces monitoring for the focal firm. Similarly, we utilize the fact that a biotech startup's VC investors will shift their attention towards investing in clean technology if those affected VCs have pressures from state pension LPs that have adopted "green-investing" plans. One concern is that this shift in investment interest will crowd out VC investments in life sciences in general and therefore, hurt the drug development progress in portfolio companies. Note that this channel holds against our results, as we document positive effects on innovation after diversification. To address this concern, we further test whether VC specialization affects drug project discontinuation through lack of funding and find it is not the case, as shown in Table IA.4.

Columns (2), (4), (6), and (8) present the second-stage results for drug development status with instrumented VC specialization measures. Consistent with our baseline results

in Table 5, the coefficients for size-based measures are positive and significant while the coefficients for *HHI*-based measures are negative and significant. For comparison, their magnitudes are around four times greater than the corresponding OLS estimates. Jiang (2017) shows that it is common for IV estimates to be much larger than their OLS counterparts. This magnitude change in our paper is likely due to differences between local average treatment effects (LATE) captured by the state pension shocks in the 2SLS framework and average treatment effects (ATE) captured in the OLS regressions. We argue that our IV compilers are the VCs that have to respond to the sustainable investment requirement by diversification. Previously, these VCs tended to be more specialized in limited areas without green technology holdings. Echoing the busy board literature (Ferris et al., 2003; Fich and Shivdasani, 2006), these treated VCs would reduce their engagement due to increased portfolio size, resulting in substantial drops in the intervention of project prioritization. Therefore, we expect to observe a larger LATE among the compilers.

We interpret the above findings as specialized VCs holding back innovative projects prematurely in the priority prioritization process. To further support this interpretation, we examine the disclosed reasons when startups discontinue an innovative drug project. To be specific, the Cortellis database collects the reasons for drug indications that have ever experienced discontinuation and categorizes them into pipeline priority, lack of funding, and lack of efficacy, if possible. Note that VC-induced project prioritization does not necessarily lead to the actual suspension of projects. Many projects, as in the CLL case in the BTK inhibitor example, are temporarily shelved and progress slower (when they are resumed later). However, we could not track the exact timing and the rationales of these temporary holds. Instead, we perform a cross-sectional regression in the subsample of projects ending up being discontinued. In our project sample, there are 376 initial projects being discontinued from 2000Q1 to 2020Q4. Lack of funding is the most common reason accounting for 25% of all discontinuations, with lack of efficacy and pipeline priority contributing 15% and 17% respectively. In total, around 57% of all the projects have explicit

reasons, and we group the remaining projects into the "unknown reason" category.[5] We perform the following regression:

$$Reason_{i,j,k,t} = \alpha + \beta VC\ Spec_{k,t} + \Phi X_{k,t} + FEs + \epsilon_{i,j,k,l} \tag{3}$$

Conditional on a project of drug j in indication i terminated by company k at quarter t, $Reason$ indicates whether it is suspended for a particular reason. The focal regressors are defined similarly in Equation (2). Since each project only has one observation upon discontinuation, we are no longer working on a panel sample constraining us from including the same set of fixed effects. Instead, we include the ICD-9 fixed effects to absorb the heterogeneity of research difficulty across different therapeutic categories. The International Classification of Diseases 9th Revision (ICD-9) is a code set used to classify diseases, symptoms, and other factors. We also include the startup founder year and location fixed effects to absorb the impacts from startup seniority and R&D clusters. In the control variables, we include VC financing amounts and the number of indications targeted the drug. The later captures the degree of experimentation at the molecule level.

Table 7 reports the regression results for drugs discontinued due to pipeline priority. The outcome variable is one if the project is discontinued because the developing company wants to prioritize the development of other projects, and zero otherwise. We find the coefficient estimates of size-based measures are negative and significant at the 1% level, suggesting that less specialized VCs are associated with fewer projects discontinued due to pipeline priority. Further, the coefficient estimates of HHI-based measures are positive and significant. The broad implication is that less specialized VCs, while being less engaged, have a lower chance to intervene in the prioritization of the pipeline.

Table IA.4 presents the regression results for drugs discontinued due to lack of funding or efficacy. Figure 2 summarizes the results by plotting the coefficients and confidence

[5]In the regression sample, a few observations are dropped due to being singleton observations with the fixed effects. The distribution is similar: lack of funding (23%), pipeline priority (16%), and lack of efficacy (17%).

intervals of the four VC specialization measures for all three categories. First, we do not find any significant relation between specialization and lack of funding. In Panels (a) and (b), larger VCs seem to be associated with more financing-induced discontinuations, although the estimates are highly insignificant and the magnitudes substantially reduce in Panels (c) and (d). This suggests that there exists no evidence that startups invested by smaller funds are financially constrained. Secondly, VC specialization does not correlate with the lack of efficacy at all, suggesting that even professional investors have difficulty distinguishing project qualities. These null results help rule out the alternative interpretation that larger VCs contribute to drug project success by providing funding and they are better at screening projects. Overall, these results suggest that specialized VCs intervene in the drug development process mainly through project prioritization.

4.2 Economics of the Conflicts

We argue that VC specialization and engagement lead to premature project prioritization due to conflicts of interest between investors and founders. What are the economics behind these conflicts? First, while the founding team aims to maximize the startup's value over their careers, VCs operate with a much shorter investment horizon due to the 10-year contractual structure. Without information asymmetry, this mismatch in horizon would not matter: even if VCs exit earlier, they would be compensated based on the fairly discounted value of the startup. However, investments in innovative startups, particularly in the life science sector, feature substantial uncertainty and a high degree of information asymmetry. As outsider investors cannot distinguish between good and bad startups, they will impose an underpricing discount for high-quality projects in the pooling equilibrium (Akerlof, 1978). Consistent with this argument, Barrot (2017) shows that VC funds with a longer remaining horizon select younger companies at an earlier stage of their development. Thus, we hypothesize that VCs prefer projects that can generate publicly observable signals as soon as possible within a limited time horizon. A direct implication is that

VCs would not hold back projects when their uncertainty has been substantially reduced. The most straightforward public signals about project quality are the progressions across phases. Therefore, we first divide the sample into two subsamples based on whether a drug project has progressed to a certain stage: (1) an early-stage subsample that consists of pre-clinical stage and Phase 1 clinical trial records, and (2) a late-stage subsample that consists of Phase 2 and Phase 3 clinical trial records. The rationale is that having passed Phase 1, most projects would have completed proof-of-concept trials, demonstrating the efficacy of treatments to the public. Furthermore, it takes more time and involves more risk for drug indications in the early-stage subsample to successfully pass all trials compared to those in the late-stage subsample. As a result, we expect the project prioritization effects to hold more strongly among early-stage drug projects.

Table 8 confirms this prediction by reporting the regression results for these two subsamples. We document that significant effects only exist in early-stage drug project samples, as shown in Panel A. In comparison, the estimated coefficients in Panel B are all insignificant. Indeed, we have lower statistical power in Panel B due to fewer late-stage project observations. However, the economic magnitudes are also significantly different. For example, the coefficients of HHI-based measures in Panel A are at least twice as large as those in Panel B.

Besides the obvious signals of scientific progression, there are other indicators of commercialization potential through the FDA designation system. The most established program is the orphan drug designation, which rewards the novel development of treatments for rare diseases through extended market exclusivity after approval. These designations thus become good indicators of projected monopoly power and FDA's endorsement of technology potential. In Table 9, we perform a subsample test based on whether a drug indication has obtained the orphan drug designation.[6] Similarly, we document that coefficient estimates are statistically significant only in drug indications without any regulatory desig-

[6]Due to data limitations for project regulatory designations, our sample period for orphan drug designation analysis ends in 2018Q2.

nations, as shown in Columns (5)-(8). Not only are the coefficients not statistically significant in the first four columns, but the signs are also completely the opposite, suggesting potential preferences of specialized VCs for these designated programs.

While it is straightforward for specialized VCs to reduce *ex-post* prioritization once the uncertainty has been resolved, we argue that they would also rationally hold back projects with *ex-ante* longer periods to progress. The logic is that VCs expect that the public progression signals are likely to arrive beyond the contractual window, exposing them to underpricing risks. So, we sorted the sample into two subsamples based on the average trial length of each drug indication (at the ICD-9 level). In particular, we leverage all drug development information from the Cortellis database and calculate the average quarters that it takes for all projects in each ICD-9 clustering 2 level from the commencement of the early phase to the completion of the Phase 3 clinical trial. We then code indications from ICD-9 classifications that have developing lengths below (above) the median as "fast (slow) ICD-9" indications.

Table 10 reports the regression results for these two subsamples. We indeed find that coefficient estimates on the VC specialization measures are only statistically significant among the slow ICD-9 drugs. As shown in Columns (5) and (6), the coefficients of the size-based measures are twice as large as those in the fast ICD-9 subsample (Columns 1 and 2). Meanwhile, the coefficients in the first four columns are all insignificant, even with a more balanced subsample split compared to the previous two tables.

The second conflict arises because founders and VCs have different scopes of diversification. From each startup's perspective, it hedges the technology failure risks by exploring multiple indications using the same molecule. In contrast, VCs diversify across startups through their portfolio management (Brown et al., 2023). Li et al. (2023) show that VCs tend to invest in multiple early-stage life science startups targeting the same indication with competing technologies. In other words, specialized VCs hedge uncertainty by exploring multiple technologies for the same disease. In the previous Acerta Pharma exam-

ple, the lead investor was also investing in other BTK inhibitor startups in the blood cancer space. Indeed, he was also the initial financier of the competing drug ibrutinib. Consequently, while the startup values the continuation of additional projects, VCs may view them as diverting resources from the primary indication and undermining portfolio-level diversification.

4.3 Robustness checks

We perform a battery set of robustness checks. We validate the findings by focusing only on the lead VC investor, using an alternative VC investment data database, and using an alternative measure of VC monitoring.

First, in the previous results, we focus on the specialization of all VC investors of the focal startup. The alternative empirical design is to focus on the lead VC investors, as they arguably have the most significant control power to navigate the experimentation process. We benchmark our results using all the VCs as the Pitchbook data itself has substantial missing observations in the lead VC indicator and we have to infer the lead status by cumulative investment amounts. Consistent with this strategy, our value-weighted measures utilize a three-year rolling window investment amounts to capture the relative importance across active investors. One may argue that the three-year window is too short or the investment weights do not proportionally capture the control power. Instead, Table IA.2 repeats the analyses focusing solely on the specialization of the lead VC investor. For any given quarter, the lead VC investor is defined as the one who has made the most investment in the startup over the past five years. Consistent with the results in Table 5, the positive coefficient of *Ln(Lead VC Size)* and negative coefficient of *Lead VC HHI* suggest that a more specialized lead VC impedes the progress of clinical trials.

Second, we test whether our results are robust to use alternative data sources. We recollect VC investment data from VentureXpert data, re-construct VC specialization measures with VentureXpert deals, match Cortellis drug companies with VentureXpert investees, and

replicate our baseline results. Table IA.3 reports the results for Equation (2) with VentureXpert data. We have slightly more observations when using VentureXpert data since VentureXpert might misclassify PE deals as VC deals. Nevertheless, all columns (1)-(4) are consistent with those in Table 5. Hence, our baseline findings are robust to the alternative VC data source (or, in other words, our baseline results are not driven by different coverage of VC deals).

Third, we interpret our main results through the channel that the VC activism associated with the specialization interferes with the strategic experimentation process. Our identification strategy utilizes the exogenous variations of VC diversification due to LPs' investment policy. A related strategy is to follow Bernstein et al. (2016) and leverage the introduction of direct flights between the headquarters of drug companies and their lead VC investors as an exogenous shock for conducting on-site engagement. To do so, we identify nearby airports for each drug company and its lead VC investors by those located within 50 miles of driving distance from headquarters city centers. We then collect monthly airline route data from the T-100 Domestic Segment Database from 2000 to 2020, maintained by the Bureau of Transportation Statistics (BTS), and construct a dummy variable to indicate the availability of direct flights between drug company k and its lead VC investors at quarter t. $Direct\,Flight_{k,t}$ equals one if there is at least one flight per week with at least 100 seats available between any pairs of company k's nearby airports and its lead VC's nearby airports by quarter t, and zero otherwise. Among the 1,397 unique drug companies in our baseline sample, 257 experienced the introduction of new direct airlines originating from their lead VC investors from 2000 to 2020.

To evaluate the effects of VC engagement intensity on drug development progress, we employ the difference-in-difference (DiD) approach with the following regressions:

$$Next\,Phase_{i,j,k,p,t} = \alpha + \beta Direct\,Flight_{k,t} + \Phi X_{k,t} + \gamma_{i,j} + \delta_p + \zeta_t + \epsilon_{i,j,k,p,t}. \quad (4)$$

Equation (4) is almost the same as Equation (2), except that we replace the focal regressors with $Direct\,Flight_{k,t}$. Given that $Direct\,Flight_{k,t}$ is time-variant and only turns on after a lead VC investor gets treated, β should be viewed as the DiD coefficient. Since OLS regressions with two-way fixed effects (TWFE method) similar to Equation (4) are the workhorse models for staggered adoption research designs, we first report our results using the TWFE method in Columns (1), (3), and (5) of Table 11. Nevertheless, recent literature has shown that the estimates of such equations are consistent only with strong assumptions about homogeneity in treatment effects (Sun and Abraham, 2021; Baker et al., 2022). So we re-estimate the dynamic treatment effects with the interaction weighted (IW method) estimator proposed by Sun and Abraham (2021) and report the average treatment effects from IW estimators in Columns (2), (4), and (6).

Columns (1) and (2) of Table 11 report the results based on Equation (4) in the full sample. The coefficient estimates of β are negative in both columns and statistically significant at a 5% significance level in Column (2). These results suggest that when increased lead-VC activism likely hurts the strategic experimentation process, following the direct flight introduction. Inspired by Table 8, we split the full sample into early-stage and late-stage projects. We document conclusive negative effects in the early-stage subsample as shown by the negative and significant coefficients of β in both Columns (3) and (4). On the other hand, the effect of VC monitoring on late-stage clinical trial progress, if anything, is mixed.

Figure IA.1 plots the coefficient dynamics in the early-stage and late-stage subsamples, respectively. Both panels exhibit the absence of any pre-trends, and we document significant negative effects after the treatment using the IW method for pre-clinical and Phase 1 projects. Our results do not necessarily contradict with Bernstein et al. (2016), as only 5.6% of their sample companies are in the life science sector. Besides, drug companies frequently adopt an "evergreening" strategy, in which they patent small modifications of existing molecules to extend the potential market power of existing products (Hemphill

and Sampat, 2012; Li et al., 2021). So patents also reflect strategic marketing decisions in late-stage trials. Indeed, we do find positive and significant effects after the treatment among Phase 2 and 3 projects in Figure IA.1. Overall, the analyses suggest the heterogeneous roles of VC activism in R&D. Excessive engagement may lead to premature withholding of early-stage projects. However, more monitoring might be beneficial to the commercialization of late-stage projects.

5 Conclusion

This paper revisits the optimality of specialized VC portfolios and investigates the real effects of associated VC activism. By utilizing granular data from the life science sector, we explore an understudied aspect of VC engagement in startups' strategic experimentation processes: project prioritization. Contrary to the common wisdom that VC oversight inherently leads to superior innovation outcomes, we document that startups backed by smaller and more concentrated VCs exhibit slower progress in clinical trials. We observe that specialized VCs tend to prematurely hold back early-stage innovative projects, focusing instead on a narrow range of novel technologies.

Our results underscore the conflicts of interest between investors and founders during the strategic experimentation process. The limited-horizon investment structure of VCs may force them to focus on projects that are easier to commercialize in the short term, despite the societal impacts of other long-term projects. This preference of VCs could potentially stifle high-risk, novel projects with radical innovations. Our findings highlight the heterogeneity in the VC engagement process and provide a more balanced view of its influences alongside the documented benefits from prior literature. Lastly, this paper provides new insights into the impact of VC financing on the direction of technological progress. The limitations of VC financing call for a more nuanced approach to fostering radical innovation in industries where scientific progress is more pervasive.

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Table 1: Summary statistics

This table reports the summary statistics of project quarterly data in our sample from 2000Q1 to 2020Q4. The unit of observation is a drug-indication×year-quarter combination. The number of observations, mean, standard deviation, 25th percentile, median, and the 75th percentile of the following variables are displayed: *Next Phase* is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter, and zero otherwise; *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *VC Amount* is the aggregated investment amount for a drug company's VC investors in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The project development status data is sourced from Cortellis. The VC investment data to construct VC specialization measures is collected from Pitchbook.

	Obs.	Mean	STD	p25	Median	p75
Next Phase	90,632	0.014	0.116	0.000	0.000	0.000
EW-Size	90,632	39.510	40.808	29.500	13.400	51.400
Ln(EW-Size)	90,632	3.176	1.135	3.384	2.595	3.940
VW-Size	90,632	40.631	42.959	30.000	13.300	52.976
Ln(VW-Size)	90,632	3.189	1.148	3.401	2.588	3.970
EW-HHI	90,632	0.220	0.218	0.140	0.068	0.288
VW-HHI	90,632	0.216	0.218	0.133	0.067	0.284
VC Amount (in millions)	90,632	29.814	40.626	18.000	6.576	39.000
Ln(VC Amount)	90,632	16.442	1.483	16.706	15.699	17.479
# Developing Drugs	90,632	7.155	6.151	5.000	3.000	9.000

Table 2: VC specialization and life science startup IPO exits

This table shows the relation between investor specialization and life science startup IPOs from 2000Q1 to 2020Q4. As a cross-sectional analysis, the unit of observation is a drug company. The dependent variable is *IPO*, which is a dummy variable equal to one if the drug company exits via IPOs within the sample period. For both the simple mean and weighted mean (by investment amount) of a drug company's investing VC portfolio sizes (*EW-Size* and *VW-Size*), we first take the time-series average across the sample period of a focal company. We then take the logarithm to generate *Ln(EW-Size)* and *Ln(VW-Size)*. The equal-weighted and the investment-amount-weighted HHI indexes, *EW-HHI* and *VW-HHI*, are also averaged across the sample period of a focal company. *Ln(Avg VC Amount)* is the logarithm of the average investment amount for a drug company over the sample period. The VC investment data to construct VC specialization measures is collected from Pitchbook; the IPO dates for drug companies are sourced from CRSP. All columns include ICD-9, drug company founded year, and startup headquarter fixed effects. Standard errors clustered at ICD-9 and drug company headquarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	IPO			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.022**			
	(2.33)			
Ln(VW-Size)		0.023**		
		(2.34)		
EW-HHI			-0.088*	
			(-1.88)	
VW-HHI				-0.098**
				(-2.06)
Ln(Avg VC Amount)	0.058***	0.058***	0.061***	0.061***
	(6.20)	(6.19)	(6.45)	(6.39)
ICD-9 FE	Yes	Yes	Yes	Yes
Startup HQ FE	Yes	Yes	Yes	Yes
Founded Year FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.0383	0.0388	0.0368	0.0374
Number of observations	1,155	1,155	1,155	1,155

Table 3: VC specialization and board representation

This table shows the results of Equation (1) with Cortellis drug companies from 2000Q1 to 2020Q4. The unit of observation is a drug company $\times$ year-quarter combination. The dependent variable is *New board*, which is a dummy variable equal to one if the drug company has any new board members from its VC investors in a given quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC specialization measures and board entrance indicators is collected from Pitchbook. All columns include company and year-quarter fixed effects. Standard errors clustered at company and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	New Board			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	-0.007***			
	(-2.65)			
Ln(VW-Size)		-0.006**		
		(-2.21)		
EW-HHI			0.042***	
			(3.33)	
VW-HHI				0.037***
				(2.93)
Ln(VC Amount)	0.011***	0.011***	0.010***	0.010***
	(4.63)	(4.59)	(4.34)	(4.36)
# Developing Drugs	-0.001	-0.001	-0.001	-0.001
	(-1.12)	(-1.09)	(-1.12)	(-1.12)
Company FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.0314	0.0313	0.0316	0.0314
Number of observations	20,553	20,553	20,553	20,553

Table 4: Pipeline summary statistics of life science IPOs

This table reports the pipeline summary statistics of drug companies exiting via IPOs from 2000Q1 to 2020Q4. The unit of observation is each drug company. The number of observations, mean, standard deviation, 25th percentile, median, and the 75th percentile of the following variables are displayed: *# Projects Ever* is the number of projects that a drug company has ever initiated over the sample period; *# Projects Active Upon IPO* is the number of active projects from a drug company upon its IPO; *# Preclinical Projects Upon IPO* is the number of projects in the pre-clinical stage from a drug company upon its IPO; *# Phase-1 Projects Upon IPO* is the number of projects in Phase 1 from a drug company upon its IPO; *# Phase-2 Projects Upon IPO* is the number of projects in Phase 2 from a drug company upon its IPO; *# Phase-3 Projects Upon IPO* is the number of projects in Phase 3 from a drug company upon its IPO; *% Projects Suspended before IPO* is the percentage of projects suspended by a drug company before its IPO; *% Preclinical Projects Upon IPO* is the percentage of active projects in the pre-clinical stage from a drug company upon its IPO; *% Phase-1 Projects Upon IPO* is the percentage of active projects in Phase 1 from a drug company upon its IPO; *% Phase-2 Projects Upon IPO* is the percentage of active projects in Phase 2 from a drug company upon its IPO; *% Phase-3 Projects Upon IPO* is the percentage of active projects in Phase 3 from a drug company upon its IPO. The project development status data is sourced from Cortellis. The VC investment data to construct VC specialization measures is collected from Pitchbook. The IPO dates for drug startups are provided by Pitchbook and supplemented by CRSP header files.

	Obs.	Mean	STD	p25	Median	p75
# Projects Ever	160	12.400	10.624	6.000	9.000	16.000
# Projects Active Upon IPO	160	7.750	6.642	3.000	6.000	10.000
# Preclinical Projects Upon IPO	160	5.138	4.331	2.000	4.000	7.000
# Phase-1 Projects Upon IPO	160	1.431	3.465	0.000	0.000	1.000
# Phase-2 Projects Upon IPO	160	1.050	2.268	0.000	0.000	1.000
# Phase-3 Projects Upon IPO	160	0.131	0.436	0.000	0.000	0.000
% Projects Suspended before IPO	160	32.884	25.799	5.903	33.333	50.000
% Preclinical Projects Upon IPO	160	68.812	33.316	49.000	77.778	100.000
% Phase-1 Projects Upon IPO	160	13.310	21.332	0.000	0.000	22.650
% Phase-2 Projects Upon IPO	160	14.254	25.563	0.000	0.000	20.000
% Phase-3 Projects Upon IPO	160	3.624	14.977	0.000	0.000	0.000

Table 5: VC specialization and innovation progress

This table shows the results of Equation (2) using Cortellis drug development data from 2000Q1 to 2020Q4. The unit of observation is a drug-indication×year-quarter combination. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI*, the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC specialization measures is collected from Pitchbook. All columns include phase, drug-indication and year-quarter fixed effects. Standard errors clustered at company and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.004**			
	(2.51)			
Ln(VW-Size)		0.005**		
		(2.57)		
EW-HHI			-0.027***	
			(-3.13)	
VW-HHI				-0.027***
				(-2.92)
Ln(VC Amount)	0.002*	0.002*	0.002**	0.002**
	(1.84)	(1.73)	(2.39)	(2.29)
# Developing Drugs	-0.001	-0.000	-0.000	-0.000
	(-1.04)	(-1.01)	(-1.00)	(-0.95)
Phase FE	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1268	0.1268	0.1270	0.1269
Number of observations	89,953	89,953	89,953	89,953

Table 6: Instrumented VC specialization and innovation progress

This table shows the 2SLS results of Equation (2) using an instrument based on LPs' ESG investment preference. The unit of observation is a drug-indication×year-quarter combination. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. $Weighted\,Exposure$ is the logarithm of one plus the aggregation of a drug company's all investing VCs' treatment intensity. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC specialization measures is collected from Pitchbook. All columns include phase, drug-indication and year-quarter fixed effects; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase							
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
$Weighted\,Exposure$	0.092***		0.096***		-0.019***		-0.019***	
	(21.16)		(22.26)		(-19.28)		(-19.00)	
$\widehat{Ln(EW\text{-}Size)}$		0.026*						
		(1.80)						
$\widehat{Ln(VW\text{-}Size)}$				0.025*				
				(1.80)				
$\widehat{EW\text{-}HHI}$						-0.122*		
						(-1.80)		
$\widehat{VW\text{-}HHI}$								-0.126*
								(-1.80)
Ln(VC Amount)	0.059***	0.000	0.075***	-0.000	0.010***	0.003***	0.007***	0.003***
	(24.27)	(0.28)	(31.51)	(-0.01)	(18.34)	(3.28)	(11.94)	(3.29)
# Developing Drugs	-0.013***	-0.000	-0.015***	-0.000	0.003***	-0.000	0.004***	-0.000
	(-13.31)	(-0.58)	(-15.29)	(-0.48)	(12.73)	(-0.52)	(17.48)	(-0.12)
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Cragg-Donald F-test	447.89		495.51		371.76		360.89	
Adjusted R^2		0.127		0.127		0.127		0.127
Number of observations	89,953	89,953	89,953	89,953	89,953	89,953	89,953	89,953

Table 7: VC specialization and project discontinuation due to pipeline priority

This table shows the results of Equation (3) with a sub-sample of discontinued projects from 2000Q1 to 2020Q4. The unit of observation is the drug indication. The dependent variable is *Pipeline Priority*, which is a dummy variable equal to one if the drug indication is discontinued due to pipeline priority. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VCAmount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *Ln(# Indications)* is the logarithmic one plus the number of indications under active development from a focal drug. The VC investment data to construct VC specialization measures is collected from Pitchbook. All columns include ICD-9, startup-founded year, and headquarters fixed effects. Standard errors clustered at ICD-9 and drug company headquarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Pipeline Priority			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	-0.099***			
	(-3.03)			
Ln(VW-Size)		-0.100***		
		(-3.27)		
EW-HHI			0.743**	
			(2.53)	
VW-HHI				0.760**
				(2.47)
Ln(VC Amount)	-0.019	-0.018	-0.035	-0.032
	(-0.60)	(-0.54)	(-1.22)	(-1.09)
Ln(# Indications)	-0.186**	-0.183**	-0.174*	-0.171*
	(-2.41)	(-2.38)	(-2.01)	(-1.98)
ICD-9 FE	Yes	Yes	Yes	Yes
Founded Year FE	Yes	Yes	Yes	Yes
Startup HQ FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.4765	0.4782	0.4822	0.4828
Number of observations	253	253	253	253

Table 8: VC specialization and innovation progress: heterogeneity due to R&D stages

This table shows the results of Equation (2) in subsamples split by R&D stages. The unit of observation is a drug-indication×year-quarter combination. Columns (1)-(4) report the results with pre-clinical phase and Phase 1 records and column (5)-(8) report the results with Phase 2 and Phase 3 records. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC specialization measures is collected from Pitchbook. All columns include phase, drug-indication and year-quarter fixed effects. Standard errors clustered at company and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase							
	Preclinical Phase & Phase 1				*Phase 2 & Phase 3*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Ln(EW-Size)	0.003*				0.002			
	(1.89)				(0.91)			
Ln(VW-Size)		0.003*				0.002		
		(1.89)				(0.80)		
EW-HHI			-0.019***				-0.008	
			(-2.90)				(-0.80)	
VW-HHI				-0.019**				-0.006
				(-2.63)				(-0.62)
Ln(VC Amount)	0.001	0.001	0.002*	0.002	0.003	0.003	0.004	0.004
	(1.35)	(1.27)	(1.72)	(1.64)	(1.04)	(1.04)	(1.06)	(1.05)
# Developing Drugs	-0.000	-0.000	-0.000	-0.000	-0.003***	-0.003***	-0.003***	-0.003***
	(-0.32)	(-0.31)	(-0.31)	(-0.29)	(-3.21)	(-3.17)	(-3.05)	(-3.02)
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Number of observations	0.1334	0.1334	0.1335	0.1334	0.0884	0.0884	0.0884	0.0884
Adjusted R^2	76,449	76,449	76,449	76,449	13,363	13,363	13,363	13363

Table 9: VC specialization and innovation progress: heterogeneity due to regulatory designations

This table shows the results of Equation (2) in subsamples split by orphan drug designations. The unit of observation is a drug-indication×year-quarter combination. Columns (1) - (4) report the results with drug indications that ever have obtained orphan drug designations; columns (5) - (8) report the results with drug indications that never have obtained orphan drug designations. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC specialization measures is collected from Pitchbook. All columns include phase, drug-indication and year-quarter fixed effects; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase							
	Focal-orphan Drug Indications				*Non-orphan Drug Indications*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Ln(EW-Size)	-0.010				0.005**			
	(-0.91)				(2.19)			
Ln(VW-Size)		-0.010				0.005**		
		(-0.92)				(2.21)		
EW-HHI			0.012				-0.034***	
			(0.18)				(-2.93)	
VW-HHI				0.021				-0.033***
				(0.29)				(-2.73)
Ln(VC Amount)	0.002	0.002	0.002	0.002	0.002*	0.002*	0.003**	0.003**
	(0.43)	(0.42)	(0.35)	(0.34)	(1.81)	(1.70)	(2.50)	(2.39)
# Developing Drugs	-0.004	-0.004	-0.004	-0.004	-0.001	-0.001	-0.001	-0.001
	(-1.22)	(-1.22)	(-1.18)	(-1.18)	(-1.18)	(-1.14)	(-1.15)	(-1.08)
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.0925	0.0925	0.0922	0.0922	0.1026	0.1026	0.1030	0.1030
Number of observations	3,001	3,001	3,001	3,001	66,922	66,922	66,922	66,922

Table 10: VC specialization and innovation progress: heterogeneity due to experimentation length

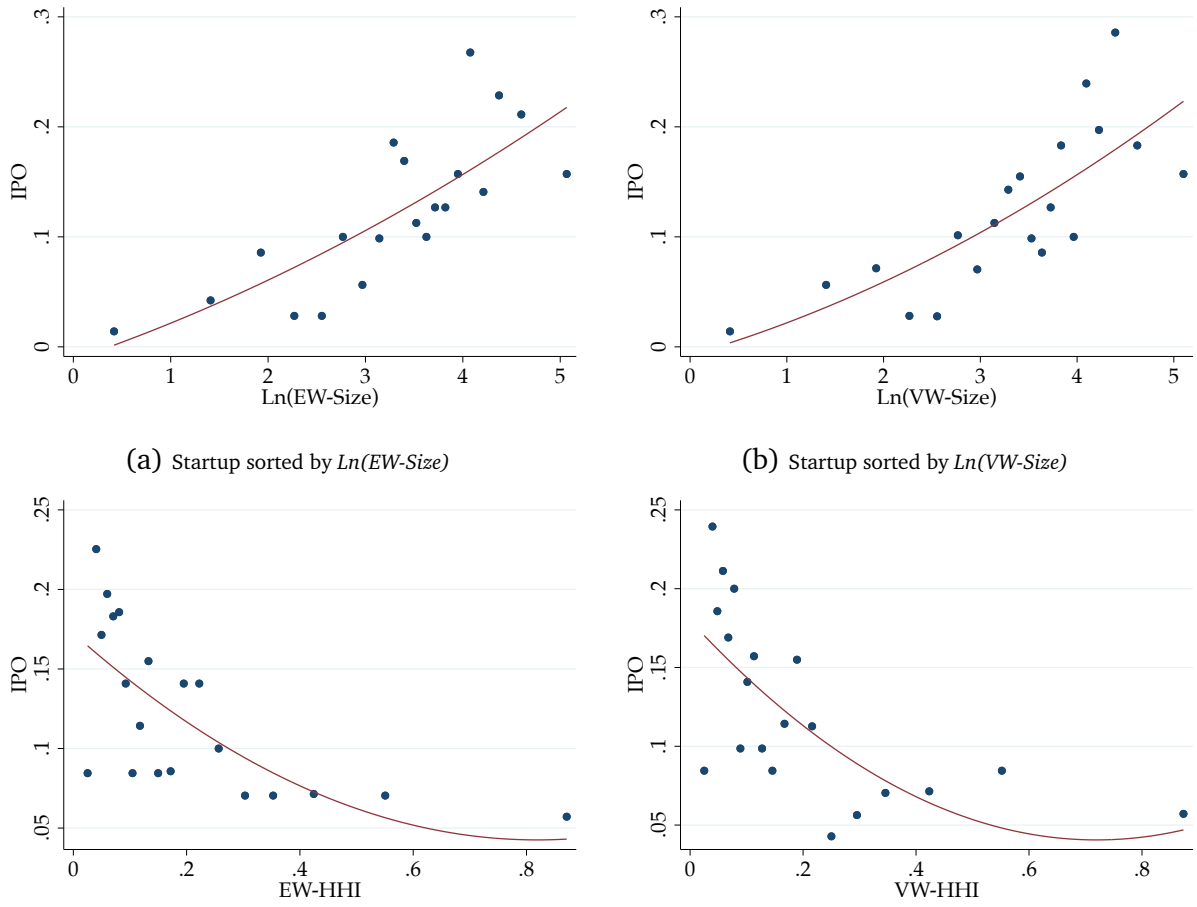
This table shows the results of Equation (2) in subsamples split by experimentation length. The unit of observation is a drug-indication×year-quarter combination. Columns (1) - (4) report the results with drug indications from ICD-9 classifications that have below-median developing lengths; columns (5) - (8) report the results with drug indications from ICD-9 classifications that have above-median developing lengths. The unit of observation is the drug-indication×year-quarter. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC specialization measures is collected from Pitchbook. All columns include phase, drug-indication and year-quarter fixed effects; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase							
	Fast ICD-9 Drug Indications				*Slow ICD-9 Drug Indications*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Ln(EW-Size)	0.002				0.006***			
	(0.68)				(2.89)			
Ln(VW-Size)		0.002				0.006***		
		(0.80)				(2.90)		
EW-HHI			-0.021				-0.031***	
			(-1.53)				(-3.36)	
VW-HHI				-0.022				-0.029***
				(-1.55)				(-2.99)
Ln(VC Amount)	0.000	0.000	0.000	0.000	0.003**	0.003**	0.004***	0.003***
	(0.15)	(0.11)	(0.30)	(0.28)	(2.28)	(2.20)	(2.83)	(2.70)
# Developing Drugs	0.000	0.000	0.000	0.000	-0.001*	-0.001*	-0.001	-0.001
	(0.28)	(0.30)	(0.29)	(0.32)	(-1.70)	(-1.68)	(-1.62)	(-1.58)
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.1281	0.1281	0.1282	0.1282	0.1259	0.1259	0.1261	0.1260
Number of observations	34,997	34,997	34,997	34,997	54,956	54,956	54,956	54,956

Table 11: Flight-induced VC engagement and innovation progress

This table shows the results of Equation (4) using Cortellis drug development data from 2000Q1 to 2020Q4. The unit of observation is a drug-indication×year-quarter combination. Columns (1)-(2) report the full sample results; columns (3)-(4) report the results with pre-clinical and Phase 1 projects; columns (5)-(6) report the results with Phase 2 and Phase 3 projects. Columns (1), (3), (5) use the OLS estimator; Columns (2), (4), (6) report the post-treatment average IW estimators proposed by Sun and Abraham (2021). The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Lead VC-treated* is a dummy variable equal to one if direct flights between a drug company's headquarters and its lead VC's headquarters have become available by quarter t; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* is the number of drugs under active development from the drug company in a given quarter; *# Quarters since first inv* is the number of quarters since first investment from a drug startup's lead investor. The US airline route data to construct *Lead VC-treated* is collected from T-100 Domestic Segments data maintained by the Bureau of Transportation Statistics. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors clustered at company and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase					
	All Phases		*Preclinical & Phase 1*		*Phase 2 & Phase 3*	
	(1)	(2)	(3)	(4)	(5)	(6)
Lead VC-treated	-0.004	-0.006**	-0.007*	-0.015***	0.006	0.014***
	(-1.21)	(-2.48)	(-1.82)	(-4.51)	(0.61)	(3.11)
Ln(VC amount)	0.002**	-	0.002*	-	0.005	-
	(2.47)	-	(1.86)	-	(1.44)	-
# Developing Drugs	-0.001	-	-0.000	-	-0.003***	-
	(-1.12)	-	(-0.38)	-	(-3.40)	-
# Quarters since first inv	0.000	-	0.000	-	0.001**	-
	(1.48)	-	(1.10)	-	(2.04)	-
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.1267	0.1163	0.1334	0.1226	0.0892	0.0557
Number of observations	89,953	89,953	76,449	76,449	13,363	13,363



(a) Startup sorted by *Ln(EW-Size)*

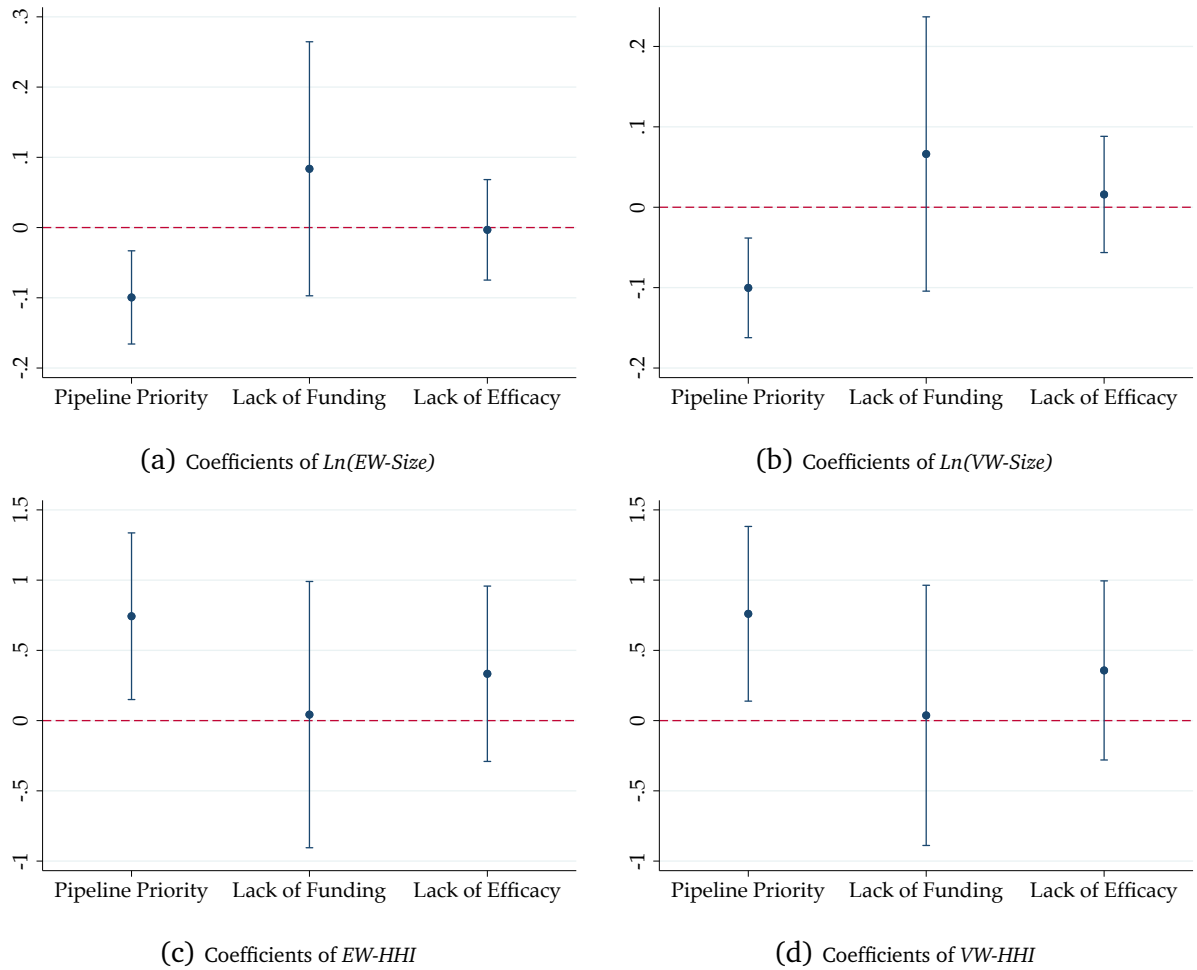
(b) Startup sorted by *Ln(VW-Size)*

(c) Startup sorted by *EW-HHI*

(d) Startup sorted by *VW-HHI*

Figure 1: **VC specialization and life science startup IPO outcomes**

Figure 1 shows the relation between VC specialization and life-science startup IPO probability from 2000Q1 to 2020Q4. In each figure, all startups are sorted into 20 equal-size bins with similar levels of VC specialization over the sample period. Figures 1a to 1d measure VC specialization with *Ln(EW-Size)*, *Ln(VW-Size)*, *EW-HHI*, and *VW-HHI*, respectively. The y-axis indicates the fraction of IPO startups within each bin. Each red curve plots the fitted quadratic regression for VC specialization and IPOs. The project development status data is sourced from Cortellis. The VC investment data to construct VC specialization measures is collected from Pitchbook. The IPO dates for drug startups are provided by Pitchbook and supplemented by CRSP header files.



(a) Coefficients of *Ln(EW-Size)*

(b) Coefficients of *Ln(VW-Size)*

(c) Coefficients of *EW-HHI*

(d) Coefficients of *VW-HHI*

Figure 2: **VC specialization and drug project discontinuation**

Figure 2 shows the relation between VC specialization and drug project discontinuation from 2000Q1 to 2020Q4. Each figure plots the coefficients of *VC Spec* (i.e., β) by estimating the following regression for discontinuation reasons of *pipeline priority* , *lack of funding* and *lack of efficacy*:

$$Reason_{i,j,k,t} = \alpha + \beta VC\ Spec_{k,t} + \Phi X_{k,t} + FEs + \epsilon_{i,j,k,l}.$$

Figures 2a to 2d measure VC specialization with *Ln(EW-Size)*, *Ln(VW-Size)*, *EW-HHI*, and *VW-HHI*, respectively. The error bars denote 95% confidence intervals. The project development status and discontinuation data is sourced from Cortellis. The VC investment data to construct VC specialization measures is collected from Pitchbook.

Internet Appendix to "The Downside of Venture Capital Monitoring: Evidence from Novel Drug Development"

Table IA.1: Summary statistics by R&D stages

This table replicates the summary statistics of Table 1 by splitting the sample into early and late stages. Panel A reports the statistics for projects in the pre-clinical phase or Phase 1, and Panel B reports the statistics for projects in Phase 2 or Phase 3. The other details are the same as Table 1.

	Obs.	Mean	STD	p25	Median	p75
Panel A: Preclinical Phase & Phase 1						
Next Phase	77,132	0.014	0.119	0.000	0.000	0.000
EW-Size	77,132	39.908	40.380	14.000	29.909	52.143
Ln(EW-Size)	77,132	3.197	1.121	2.639	3.398	3.954
VW-Size	77,132	41.046	42.407	14.000	30.500	53.500
Ln(VW-Size)	77,132	3.212	1.134	2.639	3.418	3.980
EW-HHI	77,132	0.216	0.214	0.068	0.138	0.283
VW-HHI	77,132	0.212	0.214	0.066	0.132	0.278
VC Amount (in millions)	77,132	29.412	40.425	6.000	17.000	39.000
Ln(VC Amount)	77,132	16.400	1.514	15.607	16.649	17.479
# Developing Drugs	77,132	7.182	6.162	3.000	5.000	9.000
Panel B: Phase 2 & Phase 3						
Next Phase	13,500	0.009	0.096	0.000	0.000	0.000
EW-Size	13,500	37.240	43.102	10.464	27.293	48.000
Ln(EW-Size)	13,500	3.053	1.200	2.348	3.307	3.871
VW-Size	13,500	38.256	45.911	10.500	27.333	48.697
Ln(VW-Size)	13,500	3.056	1.218	2.351	3.308	3.886
EW-HHI	13,500	0.243	0.236	0.073	0.152	0.325
VW-HHI	13,500	0.241	0.239	0.072	0.144	0.323
VC Amount (in millions)	13,500	32.111	41.680	8.200	22.500	39.300
Ln(VC Amount)	13,500	16.682	1.259	15.920	16.929	17.487
# Developing Drugs	13,500	7.000	6.086	3.000	5.000	9.000

Table IA.2: Lead VC specialization and innovation progress

This table shows the results of Equation (2) with lead VC specialization. The unit of observation is a drug-indication×year-quarter combination. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(Lead VC Size)* is the logarithmic number of a drug company's lead VC's portfolio sizes; *Lead VC HHI* is the the HHI index for a drug company's lead VC's portfolio; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. A drug company's lead VC in a given quarter is defined as the VC investor who has made the most investment in the company over the past five years. The VC investment data to construct VC specialization measures is collected from Pitchbook. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors clustered at company and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05$,** $p < 0.01$,*** $p < 0.001$.

	Next Phase	
	(1)	(2)
Ln(Lead VC Size)	0.005***	
	(2.84)	
Lead VC HHI		-0.021**
		(-2.18)
Ln(VC Amount)	0.002*	0.002**
	(1.98)	(2.01)
# Developing Drugs	-0.000	-0.000
	(-1.02)	(-0.99)
Phase FE	Yes	Yes
Drug Indication FE	Yes	Yes
Year-Quarter FE	Yes	Yes
Adjusted R^2	0.1268	0.1268
Number of observations	89,953	89,953

Table IA.3: Robustness VC specialization and innovation progress using VentureXpert data

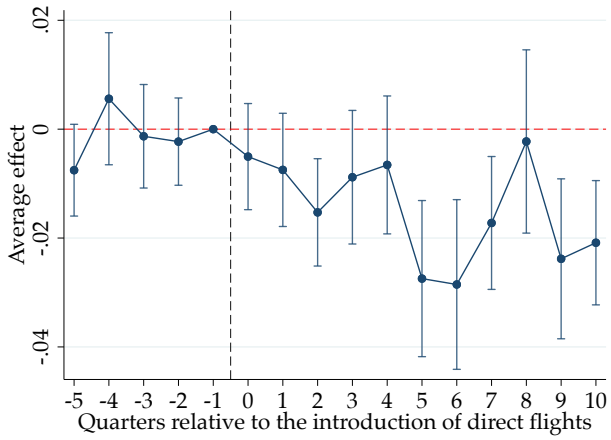
This table shows the results of Equation (2) using the VentureXpert data. The details are the same as Table 5, except that the VC investment data to construct VC specialization measures is collected from VentureXpert. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors clustered at company and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05$,$^{**}p < 0.01$,$^{***}p < 0.001$.

	Next Phase			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.003***			
	(2.70)			
Ln(VW-Size)		0.004***		
		(3.20)		
EW-HHI			-0.015**	
			(-2.45)	
VW-HHI				-0.016**
				(-2.50)
Ln(VC Amount)	0.002***	0.002***	0.002***	0.002***
	(2.77)	(2.70)	(3.00)	(2.97)
# Developing Drugs	-0.001***	-0.001***	-0.001***	-0.001***
	(-6.12)	(-6.18)	(-6.00)	(-6.03)
Phase FE	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1184	0.1185	0.1184	0.1184
Number of observations	97,226	97,226	97,226	97,226

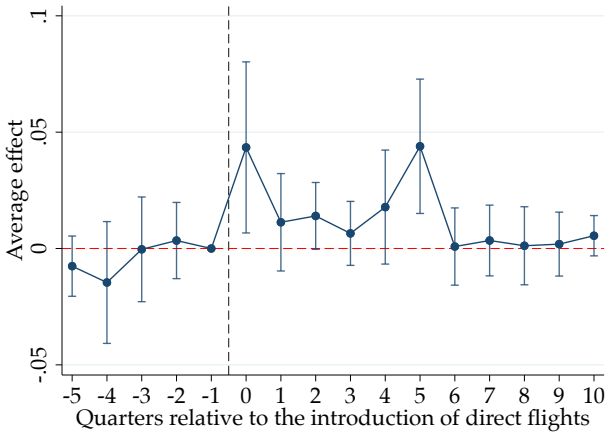
Table IA.4: VC specialization and project discontinuation due to other reasons

This table shows the results of Equation (3) for other discontinuation reasons. The unit of observation is the drug indication. The dependent variable in columns (1) - (4) is *Lack of Funding*, which is a dummy variable equal to one if the drug indication is discontinued due to lack of funding; the dependent variable in columns (5) - (8) is *Lack of Efficacy*, which is a dummy variable equal to one if the drug indication is discontinued due to lack of efficacy. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VCAmount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *Ln(# Indications)* is the logarithmic one plus the number of indications under active development from a drug. The VC investment data to construct VC specialization measures is collected from Pitchbook. All columns include the 9th International Classification of Diseases (ICD-9), startup-founded year, and headquarters fixed effects. Standard errors clustered at ICD-9 level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Discontinuation Reason							
	Lack of Funding				*Lack of Efficacy*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Ln(EW-Size)	0.084				-0.003			
	(0.94)				(-0.09)			
Ln(VW-Size)		0.066				0.016		
		(0.78)				(0.44)		
EW-HHI			0.043				0.333	
			(0.09)				(1.08)	
VW-HHI				0.037				0.357
				(0.08)				(1.13)
Ln(VC Amount)	-0.011	-0.005	0.025	0.025	0.035	0.027	0.045	0.047
	(-0.24)	(-0.10)	(0.57)	(0.56)	(0.82)	(0.63)	(1.29)	(1.34)
Ln(# Indications)	-0.076	-0.084	-0.106	-0.106	0.197*	0.203**	0.187*	0.188*
	(-0.90)	(-1.03)	(-1.28)	(-1.30)	(2.00)	(2.05)	(1.81)	(1.83)
ICD-9 FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Found Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Startup HQ FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.3610	0.3566	0.3481	0.3480	0.2382	0.2388	0.2440	0.2447
Number of observations	253	253	253	253	253	253	253	253



(a) Pre-clinical & Phase 1



(b) Phase 2 & Phase 3

Figure IA.1: **Impacts of direct flights on drug development progress**

Figure IA.1 shows the event-study plots of the following equation using IW estimators proposed by Sun and Abraham (2021):

$$Next\,Phase_{i,j,k,p,t} = \alpha + \sum_{s=-5}^{10} \beta_s D_{s(k,t)} + \Phi X_{k,t} + \gamma_{i,j} + \delta_p + \zeta_t + \epsilon_{i,j,k,p,t}$$

Panel (a) estimates the results using early-stage projects and Panel (b) uses late-stage projects. The dependent variable is $Next\,Phase_{i,j,k,p,t}$, which is a dummy variable equal to one if indication i of drug j at phase p from company k enters next phase at time $t+1$. The key independent variable $D_{s(kt)}$ is a collection of indicator variables equal to one if for drug company k at time t, the introduction of a direct flight between k and its lead investor is s quarters away. The drug development progress data is collected from Cortellis. The US domestic direct flight data to construct treatment dummies is collected from T-100. Both figures include phase, drug-indication and year-quarter fixed effects. The bars represent 95 percent confidence intervals. Standard errors are clustered at drug company and year-quarter level.