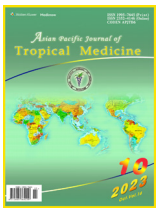

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Impact of H1N1, H7N9, ASFV, dengue virus and COVID-19 on pharmaceutical manufacturing firms´ R&D investments and economic consequences: Evidence from China

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ABSTRACT

Objective: To determine the impact of major disease epidemics on pharmaceutical manufacturing firms' Research & Development (R&D) investments and economic consequences.

Methods: The sample consists of 1 582 firm-year observations from 2009 to 2022 in China, of which, 26.6% of pharmaceutical companies are involved in the diagnosis and treatment of prevalent diseases. Linear models using R&D investments, patent applications, operating performances and stock returns as dependent variables are constructed separately to examine the response of pharmaceutical companies to disease epidemics and the resulting economic consequences.

Results: The prevalence of five major diseases led to a 17.5% increase in the amount of R&D investment and an 87.8% rise in the ratio of R&D investment to total assets by disease-related pharmaceutical companies, compared to unrelated pharmaceutical companies. Further evidence indicated that the patent applications for disease-related firms increased by 44.3% relative to unrelated firms after the epidemics. Though the impacts of the epidemics on firms' operating performances were insignificant in the short term, a major disease epidemic was associated with an increase in stock returns of 67.4% and 44.6%, respectively, as measured by the capital asset pricing model and Fama-French five-factor model. Additional analysis revealed that the impacts of the epidemics on R&D investments and patent applications were more pronounced for non-state-owned enterprises than state-owned enterprises.

Conclusions: This study demonstrates that disease-related pharmaceutical firms respond to the disease epidemics through increasing R&D investment. More patent applications and higher market value are the main gains from the firms' increased investments in R&D following the epidemic, rather than the improvements of short-term operating performances.

KEYWORDS: Exogenous demand shock; Research & Development; Disease epidemic; State-owned enterprise; Pharmaceutical manufacturing

1. Introduction

The National Health Commission of China defines major public health emergencies as "significant infectious disease outbreaks, widespread enigmatic illnesses, extensive foodborne intoxications, and other events precipitously arising that gravely jeopardize public health[1]." In recent years, the recurrent emergence of formidable diseases, such as COVID-19 in 2019, has engendered deleterious ramifications on both human health and economic growth[2-6], culminating in a 6.8% year-on-year contraction in GDP and a 4.9% year-on-year escalation in the Consumer Price Index (CPI) in the first quarter of 2020, as COVID-19 proliferated throughout China.

The emergence of pervasive diseases generates a significant exogenous demand shock for the relevant pharmaceutical manufacturing companies, primarily because such diseases

Significance

This study indicates that disease epidemics promote R&D investments of disease-related pharmaceutical companies and result in more patent applications. Although the short-term operating performance does not improve immediately, the capital markets recognise the long-term competitiveness of companies, which sheds light on the positive role of R&D on firm values.

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increase the need for medical and healthcare services, especially novel therapeutics[7-10]. The People's Bank of China promulgated the "Report on the Implementation of China's Monetary Policy in the First Quarter of 2020", which unequivocally advocated for the amplification of Research & Develop (R&D) investments in pharmaceutical entities and the fortification of the financial sector's backing for the pharmaceutical manufacturing industry[11]. Prevalent diseases severely undermine societal public health, and pharmaceutical commodities constitute a vital instrument in combating these pernicious maladies. The R&D decision-making of disease-related pharmaceutical manufacturers is more susceptible to the influence of major diseases compared to unrelated enterprises. Consequently, it is imperative for policymakers, corporate managements, and market investors to ascertain whether major diseases, as exogenous demand shocks, impinge upon the R&D of pharmaceutical manufacturing firms, and to discern the economic repercussions of intensified R&D investments.

Drawing upon the lens of exogenous demand shocks, this study delves into the repercussions of large-scale disease outbreaks on the R&D investments of pharmaceutical enterprises specializing in the treatment of diseases. Our empirical findings reveal that these firms react to pandemics by augmenting their R&D investments, consequently catalysing an upsurge in patent applications. Moreover, the epidemics enhance the stock performance of disease-related firms compared to unrelated firms. Nevertheless, no discernible ramifications on operational performance are observed. Further analyses denote that the ramifications of exogenous demand shocks on R&D investments and outputs are more salient for non-state-owned enterprises (non-SOEs) compared to their state-owned counterparts (SOEs).

This research constitutes a substantial contribution to the burgeoning body of literature examining the determinants of firms' R&D investments. First, while the existing literature delineates factors influencing corporate innovation activities, encompassing managerial attributes[12], fintech advancements within urban environments[13], and fiscal policies[14], scant attention has been devoted to exploring exogenous demand shocks caused by the epidemics as a catalyst for R&D investment[15]. By scrutinizing the repercussions of large-scale disease outbreaks on corporate innovation, this study enriches the extant literature on firm innovation. Moreover, unlike all prior studies which focus on the impact of the epidemics on the whole pharmaceutical industry, we divide pharmaceutical manufacturing companies into disease-related and disease-unrelated companies based on manually collected data, thus providing a clearer examination of the impact of disease prevalence on firms' R&D investments compared to the existing literature. Although pandemics affect all pharmaceutical companies simultaneously in the form of macro shocks, differences in operating characteristics lead firms to react differently to exogenous shocks. Pharmaceutical companies whose core business is directly related to a pandemic will respond more positively to an increase in external demand, so the impact of exogenous demand shocks can be examined in more details when these pharmaceutical companies were categorized into disease-related and disease-unrelated groups according to whether or not their core business styles suit to the pandemic.

Further, the consequences of the exogenous demand shock caused by the epidemics in an economic sense remain understudied. We originally examine the impact of disease epidemics on the stock price performance and operating performance of disease-related companies, which indicates that market investors react positively, thus boosting the market value of the companies, but that the short-term operating performance is not significantly improved. For the first time, our results suggest that the main driver for increased R&D investment in the aftermath of a pandemic is to improve the company's long-term competitiveness rather than to enhance short-term operating performance, while the capital markets recognize the positive role of the innovative activities. Finally, although Yuan and Wen[16] underscore significant disparities between SOEs and non-SOEs concerning innovation, the extent and manner in which these entities divergently respond to pandemics through R&D investment and output enhancement remain inadequately explored. Addressing this lacuna, we furnish empirical evidence elucidating the moderating effect of state ownership on corporate innovation.

2. Material and methods

2.1. Research hypothesis

It is well documented in literatures that demand shocks caused by government policies stimulate innovation in the pharmaceutical industry. The government's policy guidance and support create a favourable market environment for the pharmaceutical industry, stimulating more innovation and technological progress[17-19]. The adoption of health policies aimed at stimulating the use of drugs and vaccines will stimulate research into innovative drugs and clinical trials of new vaccines[20]. Meanwhile, the model developed by Dubois *et al*.[21] demonstrates a significantly positive elasticity of innovation to expected market size, with an additional $200 million in revenue incentivizing the invention of a new chemical entity. In addition, emerging epidemics create a surge in demand for vaccines because getting the majority of people vaccinated with effective and safe vaccines to create herd immunity is an important way to stop the spread of epidemics[22-25]. Furthermore, the complications of epidemics lead to a shortage of related medical supplies[26]. Major

epidemics trigger a surge in public demand for medical products. As the epidemic spreads, hospitals and healthcare facilities often face shortages of medical supplies[25]. To meet this urgent demand, pharmaceutical companies must not only increase the production and supply of existing products, but also step up their research and development efforts to develop more effective, safer and innovative medical products[27,28]. A major disease is therefore an external demand shock for the pharmaceutical industry, leading to an expansion of the market size and demand for pharmaceutical products, and thus prompting pharmaceutical companies to increase their innovation efforts[29]. Based on the theoretical and empirical evidence, we expect a positive relationship between major diseases and R&D investments by disease-related firms.

Hypothesis 1: The epidemic of a major disease will result in significantly higher R&D investment by disease-related firms than by unrelated firms.

The management of companies are highly interested in determining whether R&D investment generates sufficient returns to offset the significant costs associated with the R&D process. The number of patent applications is a critical metric for measuring a company's innovation capabilities and gauging the outcomes of R&D investment[30]. Literatures suggest that adequate R&D investment is an essential prerequisite for achieving innovative outcomes[14,31,32]. Consequently, we posit that the growth of R&D investment prompted by disease epidemics can increase a company's R&D output, leading to an increase in the number of patent applications. Moreover, the growth of R&D investment serves as a mediating variable for the increase in the number of patent applications. Based on this fact, we put forth Hypotheses 2a and 2b.

Hypothesis 2a: The epidemic of a major disease will result in significant more patent applications for disease-related firms than for unrelated firms.

Hypothesis 2b: The increased R&D investments play a mediating role in the impact of disease epidemics on increasing the number of patent applications for disease-related firms.

The literature show evidence that an increase in R&D investment leads to an improvement in operating performance[33,34]. Higher R&D intensity can improve firms' competitiveness and increase the quantity and quality of operating revenue[35]. In addition, Pandit *et al*.[31] reported that high quality patents with a large number of citations are positively associated with future operating performance and can reduce the instability of operating performance. Therefore, we infer that the increased R&D following exogenous demand shocks caused by the epidemic of major diseases will lead to improved operating performance of disease-related firms.

Hypothesis 3: The epidemic of a major disease will result in significant better operating performance for the disease-related firms than for the unrelated firms.

Theoretically, an increase in a firm's intangible assets will be reflected in its market value, which will manifest itself in an increase in the share price. The existing literature highlights the essential role of R&D investment in asset pricing. For example, Eberhart *et al*.[33] show that firms have significant higher stock returns in the five years following an increase in R&D. Hou *et al*.[34] confirm the role of R&D investment in the asset pricing of international stock markets, indicating that R&D-intensive firms tend to have significantly higher stock returns and that the relationship is driven by the risk premium of investors. Since the value of intangible assets created by R&D investment following exogenous demand shocks will be reflected in the stock price and stock returns will be enhanced, we propose Hypothesis 4.

Hypothesis 4: The epidemic of a major disease will result in significant higher stock returns for disease-related firms than for unrelated firms.

The research model is presented in Figure 1 and is based on the demand shock, innovation, and asset pricing literature. We aim to examine the effect of the epidemic of major diseases on corporate R&D investment. We are also interested in the economic effects (*i.e.*, patent application, operating performance and stock return) following the epidemic.

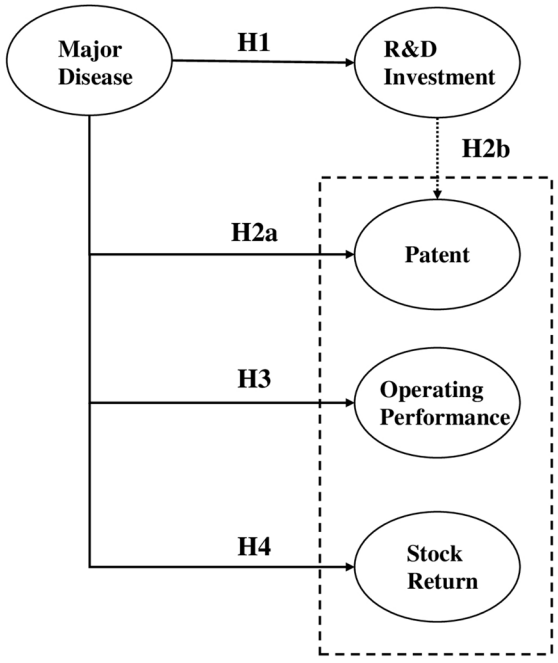

Figure 1. The hypothetical model. H1: Hypothesis 1; H2a: Hypothesis 2a; H2b: Hypothesis 2b; H3: Hypothesis 3; H4: Hypothesis 4.

2.2. Data and variable construction

Our sample consists of the pharmaceutical manufacturing firms

in China from 2009 to 2022. The data sources include: (1) China Stock Market & Accounting Research Database (CSMAR), which provides financial data, stock return and major diseases in China; (2) China Research Data Service Platform (CNRDS), which provides data on firms' patent applications. We exclude the ST (Special Treatment) stocks for their trading rules are significantly different from other stocks. The filtered sample contains 241 pharmaceutical manufacturing firms with a total of 1 582 firm-year observations.

2.2.1. Dependent variables: R&D investments and economic consequences

Following Ren *et al*.[32] and Chi *et al*.[36], we adopt the natural logarithm of the total amount of R&D investment (*RD_amount*) and the ratio of R&D investment to total assets (*RD_asset*) to measure the intensity of R&D investment. In the robustness test, we also take the ratio of R&D investment to operating revenue (*RD_revenue*) as a measure of R&D investment.

To examine the economic consequence of the increased R&D investment caused by the exogenous demand shock, we take three aspects into consideration, including patent applications, operating performances, and stock returns. First, following Cumming *et al*.[37], we use the logarithm of 1 plus the total number of patent applications to measure the patent creation (*Patent*). We use the logarithm of 1 plus the number of invention patent applications to measure the patent creation (*PatentInv*) for the robustness test. Besides, we use patent applications instead of patent granted because Griliches *et al*.[30] suggest the patent application is more representative of the innovation and therefore significantly more informative. Second, following Chang *et al*.[38], we use the return on assets (*Roa*) and the operating revenue (*OR*) to measure the firm's operating performance. Finally, we measure the firm's stock performance using the cumulative abnormal return adjusted by Capital Asset Pricing Model (*CAR_CAPM*) and the cumulative abnormal return adjusted by Fama-French five-factor model (*CAR_FF5F*), following Fama and French[39].

2.2.2. Explanatory variables: major diseases and disease-related firms

We manually collect information related to 5 major diseases from the official website of the National Health Commission of the People's Republic of China, which were widespread and had significantly adverse impact on public health in China. Table 1 presents the detailed information on the 5 major diseases prevalent in China during the period between 2009 and 2022, including the disease name, the virus name, the city where the first case is detected, the date when the first case is detected, and the epidemic duration. The dummy variable *Epid* equals 1 if there is an epidemic of major diseases during the year, and equals 0 otherwise.

Importantly, we construct an indicator to measure whether an enterprise is related to the major disease based on whether its core business is involved in the prevalent disease (*Related*). Specifically, we manually collect and read the annual reports to determine the correlation between a pharmaceutical manufacturing company and the prevalent disease of the year. An enterprise is defined as a disease-related firm (*Related*=1) if its core business involves the research, production and marketing of drugs and vaccines for related diseases.

2.2.3. Control variables

Following previous studies[13,37], the market value (*Size*), Tobin's Q value (*TobinQ*), market-to-book ratio (*Mtb*), leverage ratio (*Lev*), analyst attention (*Anaattention*), equity concentration (*H*10), return on equity (*Roe*) and the proportion of tangible assets (*Tangible*) are adopted as control variables. The detailed definitions of all of the variables used in the paper are presented in the notes of Table 2.

2.3. Empirical model

To investigate the effect of a major disease on disease-related firms' R&D investment, we adopt the ordinary least squares (OLS) regression model as specified in Model (1):

$$RD_{i,t} = \beta_0 + \beta_1 Epid_t + \beta_2 Related_{i,t} + \beta_3 Epid_t * Related_{i,t} + \sum \beta_c Controls_{i,t} + YearFE + \varepsilon_{i,t} \quad (1)$$

Where $RD_{i,t}$ is the R&D investment intensity of firm i in year t. $Epid_t$ is a dummy variable indicating whether there is an epidemic of major diseases in year t. $Related_{i,t}$ is a dummy variable indicating whether firm i is related to the major diseases in year t. $Controls_{i,t}$ is a set of control variables. *YearFE* are year fixed effects. $\varepsilon_{i,t}$ is the error term.

Moreover, we investigate the economic consequence of the prevalence of major disease from three respects: patent applications, operating performances and stock returns. First, we establish the OLS regression Model (2) to examine the impact of the major disease epidemics on the patent applications.

Table 1. Major diseases prevalent in China from 2009 to 2022.

Disease name	Virus name	Origin city	Origin time	Epidemic duration
Influenza A (H1N1)	H1N1	Chengdu, Sichuan	May 11, 2009	15 months
H7N9 avian influenza	H7N9	Shanghai	March 31, 2013	3 months
African swine fever	ASFV	Shenyang, Liaoning	August 3, 2018	28 months
Dengue fever	Dengue virus	Chongqing	September 7, 2019	3 months
Corona virus disease 2019	COVID-19	Wuhan, Hubei	December 8, 2019	37 months

$$Patent_{i,t+1}=\beta_0+\beta_1 Epid_t+\beta_2 Related_{i,t}+\beta_3 Epid_t*Related_{i,t}+\sum\beta_c Controls_{i,t}+YearFE+\varepsilon_{i,t} \quad (2)$$

Where $Patent_{i,t+1}$ is the patent applications of firm i in year t+1. $Epid_t$ is a dummy variable indicating whether there is an epidemic of major diseases in year t. $Related_{i,t}$ is a dummy variable indicating whether firm i is related to the major diseases in year t. $Controls_{i,t}$ is a set of control variables. *YearFE* are year fixed effects. $\varepsilon_{i,t}$ is the error term.

Further, following Baron and Kenny[40], we construct Model (3) to test the mediating role that increased R&D investment plays in the number of patent applications boosted by the prevalence of major diseases.

$$Patent_{i,t+1}=\beta_0+\beta_1 Epid_t+\beta_2 Related_{i,t}+\beta_3 Epid_t*Related_{i,t}+\beta_4 RD_{i,t}+\sum\beta_c Controls_{i,t}+YearFE+\varepsilon_{i,t} \quad (3)$$

Where $Patent_{i,t+1}$ is the patent applications of firm i in year t+1. $Epid_t$ is a dummy variable indicating whether there is an epidemic of major diseases in year t. $Related_{i,t}$ is a dummy variable indicating whether firm i is related to the major diseases in year t. $RD_{i,t}$ is the R&D investment intensity of firm i in year t, which is the mediating variable of interest to us. $Controls_{i,t}$ is a set of control variables. *YearFE* are year fixed effects. $\varepsilon_{i,t}$ is the error term.

Finally, Models (4) and (5) are constructed to investigate the impact of a major epidemic on firms' operating performances and stock returns.

$$OP_{i,t}=\beta_0+\beta_1 Epid_t+\beta_2 Related_{i,t}+\beta_3 Epid_t*Related_{i,t}+\sum\beta_c Controls_{i,t}+YearFE+\varepsilon_{i,t} \quad (4)$$

$$Return_{i,t}=\beta_0+\beta_1 Epid_t+\beta_2 Related_{i,t}+\beta_3 Epid_t*Related_{i,t}+\sum\beta_c Controls_{i,t}+YearFE+\varepsilon_{i,t} \quad (5)$$

Where $OP_{i,t}$ is the operating performance of firm i in year t, including the return on assets (*Roa*) and the operating revenue (*OR*). $Return_{i,t}$ is the stock return of firm i in year t, including the cumulative abnormal return adjusted by Capital Asset Pricing Model (*CAR_CAPM*) and the cumulative abnormal return adjusted by Fama-French five-factor model (*CAR_FF5F*). $Epid_t$ is a dummy variable indicating whether there is an epidemic of major diseases in year t. $Related_{i,t}$ is a dummy variable indicating whether firm i is related to the major diseases in year t. $Controls_{i,t}$ is a set of control variables. *YearFE* are year fixed effects. $\varepsilon_{i,t}$ is the error term.

3. Results

3.1. Descriptive statistics

All continuous variables used in the paper are winsorized at the 1% and 99% percentiles. Table 2 reports descriptive statistics for the key variables. During the sample period, 32.0% of the firm-year observations have witnessed an epidemic of a certain disease. Moreover, the mean value of the ratio of R&D investment to total asset (*RD_asset*) is 2.532% which is consistent with previous reports.

Table 2. Summary statistics for all the variables.

Variable	Observations	Mean±SD	Range
Related	1.582	0.266±0.442	0, 1
Epid	1.582	0.320±0.467	0, 1
RD_amount	1.582	17.928±1.228	14.618, 20.824
RD_asset	1.582	2.532±2.087	0.110, 13.205
RD_revenue	1.582	5.479±5.417	0.181, 39.694
Patent	1.402	1.126±1.221	0.000, 4.466
Patent_Invention	1.402	0.923±1.061	0.000, 3.829
Roa	1.582	0.072±0.073	-0.847, 0.470
OR	1.582	21.188±1.148	12.701, 24.897
CAR_CAPM	1.582	-0.342±1.910	-4.305, 3.819
CAR_FF5F	1.582	-0.275±0.971	-4.986, 0.797
Size	1.582	22.741±0.963	20.874, 25.223
TobinQ	1.582	2.680±1.712	1.002, 9.890
Mtb	1.582	0.486±0.213	0.101, 0.998
Lev	1.582	0.300±0.176	0.034, 0.782
Anaattention	1.582	8.358±9.197	0.000, 39.000
H10	1.582	59.916±14.305	26.390, 90.750
Roe	1.582	0.099±0.089	-0.345, 0.310
Tangible	1.582	0.909±0.091	0.229, 1.000

Related: A dummy variable, which equals 1 when the firm is a major disease-related firm, and equals 0 otherwise; Epid: A dummy variable, which equals 1 if there is an epidemic of major diseases during the year, and equals 0 otherwise; RD_amount: The natural logarithm of the total amount of R&D investment; RD_asset: The ratio of firm's R&D investment to total assets; RD_revenue: The ratio of firm's R&D investment to operating revenue; Patent: The logarithm of 1 plus the total number of patent applications; Patent_Invention: The logarithm of 1 plus the number of invent patent applications; Roa: The return on assets; OR: The logarithm of firm's operating revenue; CAR_CAPM: The cumulative abnormal return adjusted by Capital Asset Pricing Model; CAR_FF5F: The cumulative abnormal return adjusted by Fama-French five-factor model; Size: he logarithm of the market value of equity; TobinQ: The ratio of market-to-book value of firm assets; Mtb: The market-to-book ratio; Lev: The ratio of the value of debt to total assets; Anaattention: The number of analysts following; H10: The shareholding percentage of the top 10 largest shareholders of the firm; Roe: The return on equity; Tangible: The tangible asset divided by the total asset.

3.2. R&D investment and economic consequence

3.2.1. R&D investment

Epidemic-driven demand shocks expand the market size of pharmaceutical products and thus promoting pharmaceutical companies' innovation activities. We examine whether disease-related firms tend to increase R&D investment when faced with major diseases using Model (1). Columns (1) and (2) of Table 3 presents the regression results, which shows that the coefficients of the interaction term (*Epid * Related*) are significantly positive, indicating that the prevalence of major diseases leads to a 17.5% increase in the amount of R&D investment and a 87.8% rise in the ratio of R&D investment to total assets by disease-related pharmaceutical companies, compared to unrelated pharmaceutical companies.

Table 3. The impact of the epidemic on R&D investment and patent application.

Variables	(1) RD_amount	(2) RD_asset	(3) Patent	(4) Patent	(5) Patent
Epid*Related	0.175***	0.878***	0.443***	0.445***	0.424***
	(0.065)	(0.180)	(0.144)	(0.143)	(0.145)
RD_amount				0.198***	
				(0.061)	
RD_asset					0.052*
					(0.028)
Epid	1.273***	1.842***	-0.520**	-0.770***	-0.614**
	(0.250)	(0.475)	(0.243)	(0.237)	(0.242)
Related	-0.057	-0.188**	-0.057	-0.046	-0.047
	(0.036)	(0.076)	(0.068)	(0.067)	(0.067)
Size	0.740***	-0.520***	-0.076	-0.229***	-0.057
	(0.055)	(0.139)	(0.069)	(0.086)	(0.069)
TobinQ	-0.087***	0.135**	0.007	0.024	-0.001
	(0.025)	(0.065)	(0.033)	(0.031)	(0.032)
Mtb	0.895***	-1.521***	-0.045	-0.250	0.007
	(0.188)	(0.455)	(0.270)	(0.269)	(0.270)
Lev	0.157	0.464	-0.022	-0.047	-0.044
	(0.171)	(0.390)	(0.245)	(0.243)	(0.243)
Anaattention	0.009***	0.020***	0.006	0.004	0.005
	(0.003)	(0.007)	(0.004)	(0.004)	(0.004)
H10	0.008***	0.019***	0.009**	0.007*	0.008**
	(0.003)	(0.006)	(0.004)	(0.004)	(0.004)
Roe	-0.311	-1.541**	0.561	0.570	0.579
	(0.266)	(0.638)	(0.385)	(0.393)	(0.391)
Tangible	0.492	0.070	-0.063	-0.173	-0.090
	(0.342)	(0.642)	(0.463)	(0.478)	(0.466)
Constant	-0.109	12.527***	2.239	2.410	1.764
	(1.206)	(2.865)	(1.504)	(1.545)	(1.537)
Observations	1.582	1.582	1.402	1.402	1.402
R-squared	0.739	0.231	0.121	0.127	0.122
Year FE	Yes	Yes	Yes	Yes	Yes

***, **, and * indicate significant at the statistical level of 1%, 5%, and 10%, respectively. Year FE indicates year fixed effects. Robust standard errors are indicated in parentheses, which provide a more reliable and robust estimate of standard errors by taking into account the potential heteroscedasticity and correlation of errors in the data.

Overall, the results support our Hypothesis 1 that when faced with the epidemic of major diseases, related firms tend to increase R&D investments to respond to the following demand shock, which is in line with Finkelstein[17] and Blume-Kohout and Sood[20] that the increases in market size introduced by public health policies will stimulate firms' R&D investments.

3.2.2. Patent application

The extant literature[14,32] posit that sufficient investment in R&D is a critical prerequisite for achieving innovative outputs. We employ Model (2) to examine the impact of disease epidemics on the number of patent applications for disease-related pharmaceutical companies. Column (3) of Table 3 reports the estimation results, which shows that the coefficient of the interaction term (*Epid * Related*) is positively significant at the 1% level. The results indicate that the patent applications (*Patent*) for disease-related firms increase by 44.3% relative to unrelated firms after the epidemics, which is consistent with the findings of Griliches *et al*.[30], providing supporting evidence for Hypothesis 2a.

To further investigate the mechanism underlying the relationship between major diseases and patent applications, we examine the mediation effect of R&D investments following Baron and Kenny[40]. Specifically, we estimate the magnitude of the mediation effect by multiplying the coefficient on the impact of disease epidemics on R&D investment with the coefficient on the impact of R&D investment on patent applications. Columns (4) and (5) of Table 3 present the regression results of Model (3), demonstrating the mediating effect of R&D investments, measured by R&D expenditure (*RD_amount*) and the ratio of R&D investment to total asset (*RD_asset*), on innovation output, with the estimated mediation effects of 3.5% (0.175*0.198) and 4.6% (0.878*0.052), respectively. The results indicate that the firms' investment in R&D pays off in terms of more innovative outputs, thus confirming Hypothesis 2b.

3.2.3. Operating performance

The literature provides evidence that increasing R&D investment can enhance a company's operating performance, such as Eberhart *et al*.[33] and Hou *et al*.[34] reported. We construct Model (4) to examine the impact of the epidemics on disease-related firms' operating performances in the short term and the empirical results are presents in Table 4. Columns (1) and (2) of Table 4 show that the coefficient of interaction term (*Epid * Related*) are statistically insignificant, thereby implying that exogenous demand shocks resulting from disease epidemics exert no significant effect on firms' operating performances measured by the return on assets (*Roa*) and the operating revenue (*OR*) in the short term. Consequently, our findings fail to lend support to Hypothesis 3, which could be attributed to the fact that heightened investments in R&D triggered by major disease epidemics can potentially enhance firms' long-term market competitiveness without commensurately ameliorating short-term operational performance. Our results challenge the findings of previous literature[33] that increased R&D investment can improve operational performance in the short term, but are congruent with other literature that argues that the beneficial effect of R&D investment on operational performance exhibits a lag of 2-3 years[41], while innovation enhances long-term competitiveness and elicits an immediate response in market valuation[42].

3.2.4. Stock return

We examine Hypothesis 4 by testing the effect of major diseases on stock returns with Model (5). Columns (3) and (4) of Table 4 demonstrate significant differences in stock returns between disease-related and unrelated firms following a major disease. The coefficients of interaction term (*Epid * Related*) are all positive and

significant at the 1% level. Specifically, on average, a major disease epidemic is associated with 67.4% and 44.6% higher stock returns for related firms relative to unrelated firms, measured by the capital asset pricing model (CAPM) and Fama-French five-factor model (FF5F), which consistent with results of previous literatures that R&D investments increase market values[33,34]. In comparison, Hou *et al*.[34] point out that the difference in stock returns between the highest and lowest quartile of R&D investment in listed companies amounted to approximately 7%. For these disease-related firms, high R&D investments caused by disease-driven demand shocks enable them to exploit growth opportunities and to possess intangible assets, thus leading to higher stock returns. The Hypothesis 4 is therefore verified. These results suggest that the main economic motivations for companies to increase their R&D investments following the demand shock caused by the epidemics is to improve the long-term competitiveness rather than to enhance short-term operating performance, while the financial market investors are willing to give higher stock valuations and recognize the company's efforts in innovation.

Table 4. The impact of the epidemic on operating performance and stock return.

Variables	(1)	(2)	(3)	(4)
	Operating performance		Stock return	
	Roa	OR	CAR_CAPM	CAR_FF5F
Epid*Related	-0.001	0.049	0.674***	0.446***
	(0.005)	(0.038)	(0.202)	(0.139)
Epid	-0.012	-0.069	-1.920***	-1.288***
	(0.010)	(0.103)	(0.474)	(0.167)
Related	0.001	-0.026	-0.105	-0.753***
	(0.002)	(0.018)	(0.146)	(0.096)
Size	0.002	0.878***	-0.109*	0.331***
	(0.001)	(0.035)	(0.058)	(0.044)
TobinQ	0.003***	-0.100***	-0.026	0.041**
	(0.001)	(0.012)	(0.053)	(0.019)
Mtb	0.023**	1.145***	0.277	0.052
	(0.010)	(0.088)	(0.447)	(0.180)
Lev	-0.102***	0.502***	-0.137	0.363*
	(0.012)	(0.106)	(0.307)	(0.193)
Anaattention	-0.000	0.002	0.001	-0.009***
	(0.000)	(0.002)	(0.007)	(0.003)
H10	-0.000	-0.004***	0.000	-0.018***
	(0.000)	(0.001)	(0.003)	(0.003)
Roe	0.678***	1.240***	0.363	0.070
	(0.046)	(0.167)	(0.743)	(0.340)
Tangible	0.014	0.568***	-0.156	-1.227***
	(0.014)	(0.202)	(0.503)	(0.297)
Constant	-0.032	0.358	3.651**	-4.374***
	(0.029)	(0.830)	(1.464)	(0.893)
Observations	1582	1582	1582	1582
R-squared	0.800	0.823	0.101	0.346
Year FE	Yes	Yes	Yes	Yes

***, **, and * indicate significant at the statistical level of 1%, 5%, and 10%, respectively. Year FE indicates year fixed effects. Robust standard errors are indicated in parentheses, which provide a more reliable and robust estimate of standard errors by taking into account the potential heteroscedasticity and correlation of errors in the data.

3.3. State ownership

We further investigate the difference of the impact of the epidemics on the R&D investment between state-owned enterprises (SOEs) and non-state-owned enterprises (non-SOEs). The literature suggests that SOEs may be committed to social and political goals rather than economical goals, and therefore SOEs are less efficient than non-SOEs in innovation activities[16]. As a result, we expect that disease-related SOEs respond more positively to the exogenous demand shock than disease-related non-SOEs in terms of both R&D investments and patent applications. The empirical results shown in Table 5 indicate that the coefficients of interaction term (*Epid * Related*) are more significant in the subsample of non-SOEs, demonstrating that the epidemic of major diseases results in increasing innovations of the disease-related non-SOEs, while has insignificant effect on SOEs. The results are consistent with the report of Yuan and Wen[16], supporting the argument that SOEs are less motivated to innovate than non-SOEs.

3.4. Robustness test

To confirm the robustness of the empirical results, we adopt an alternative measure of R&D investment intensity, which is taken as the ratio of a firm's R&D investment to the operating revenue (*RD_revenue*). Columns (1) and (2) of Table 6 report the estimation results of Model (1), which indicates that major diseases have a positive and significant relationship with the R&D investment of disease-related firms, confirming that our baseline results are robust for different measures of the R&D intensity.

Furthermore, patents in China are divided into three categories: invention patents, utility model patents, and design patents. Invention patents mainly involve the proposal of new products or processes, which have the highest technological content and novelty among the three types of patents. In order to take into account the quality of the patents obtained by firms, we use the logarithm of 1 plus the number of invention patent applications (*Patent_Invention*) as an alternative measure of R&D output to confirm the robustness of our results. The estimation results of Model (2) are reported in Columns (3) and (4) of Table 6, suggesting that there is a strong positive correlation between major epidemics and patent creation by disease-related firms, supporting the robustness of our baseline results.

4. Discussion

This paper examines the effect of exogenous demand shocks caused by the epidemic of major diseases on the R&D investments and outputs of pharmaceutical manufacturing firms in China. We

Table 5. The moderating effect of the state ownership on R&D investment and patent application.

Variables	(1)	(2)	(3)	(4)	(5)	(6)
	Non-state-owned enterprises			State-owned enterprises		
	RD_amount	RD_asset	Patent	RD_amount	RD_asset	Patent
Epid*Related	0.216***	0.906***	0.406***	-0.453	0.214	-0.202
	(0.061)	(0.187)	(0.147)	(0.590)	(0.663)	(0.303)
Epid	1.025***	1.864***	-0.807***	1.599**	1.902**	0.142
	(0.321)	(0.613)	(0.269)	(0.656)	(0.749)	(0.606)
Related	-0.070*	-0.203**	-0.046	0.085	0.013	-0.042
	(0.037)	(0.081)	(0.071)	(0.156)	(0.157)	(0.217)
Size	0.723***	-0.571***	-0.050	0.992***	-0.126	-0.237
	(0.059)	(0.150)	(0.074)	(0.101)	(0.118)	(0.177)
TobinQ	-0.095***	0.122**	-0.011	0.207	1.085**	0.455**
	(0.024)	(0.059)	(0.033)	(0.233)	(0.492)	(0.182)
Mtb	0.844***	-1.753***	-0.062	2.240**	2.997*	1.812**
	(0.189)	(0.482)	(0.289)	(1.050)	(1.582)	(0.911)
Lev	0.140	0.363	-0.032	-0.816	-0.147	0.741
	(0.176)	(0.403)	(0.241)	(0.548)	(0.695)	(0.946)
Anaattention	0.009***	0.021***	0.007*	0.009	0.004	0.034**
	(0.003)	(0.007)	(0.004)	(0.011)	(0.013)	(0.017)
H10	0.007***	0.017***	0.008**	-0.007	0.008	-0.012
	(0.003)	(0.006)	(0.004)	(0.009)	(0.010)	(0.014)
Roe	-0.262	-1.664**	0.748*	0.179	0.320	-1.704
	(0.258)	(0.650)	(0.385)	(1.182)	(1.430)	(1.754)
Tangible	0.463	0.041	-0.064	-0.875	-0.685	-2.853
	(0.345)	(0.680)	(0.469)	(1.049)	(1.468)	(1.902)
Constant	0.661	13.966***	2.029	-7.183***	-1.102	3.790
	(1.285)	(3.054)	(1.613)	(2.220)	(2.952)	(3.920)
Observations	1470	1470	1294	112	112	108
R-squared	0.739	0.240	0.132	0.770	0.285	0.263
Year FE	Yes	Yes	Yes	Yes	Yes	Yes

***, **, and * indicate significant at the statistical level of 1%, 5%, and 10%, respectively. Year FE indicates year fixed effects. Robust standard errors are indicated in parentheses, which provide a more reliable and robust estimate of standard errors by taking into account the potential heteroscedasticity and correlation of errors in the data.

find evidence that the epidemic of major diseases promotes R&D investment, hence leading to significantly more patent applications. Moreover, the epidemics enhance the stock performance of disease-related firms compared to unrelated firms. However, there is no significant difference between their operating performances in the short term. Further, we find that the R&D investments and outputs of non-state-owned enterprises are more significantly promoted by exogenous demand shocks. This study makes valuable contributions to the literature by demonstrating whether and how firms, especially disease-related firms, respond to exogenous demand shocks through R&D investment. The mediation effect test shows that major diseases boost the number of patents produced by firms by increasing their R&D investments, which proves the effectiveness of firms' efforts on innovation. Even though the enhanced R&D investments cannot promote their operating performance immediately, stock prices respond significantly positive to the higher R&D investments, offering the policy insight that increasing R&D investments will have a powerful positive effects on firm values. These results show that stronger long-term market competitiveness and higher market value are the main gains from the firms' increased investments in R&D following the epidemic, rather than short-term operating performances.

Our findings have rich policy implications regarding the enhancement of innovation dynamics in the pharmaceutical industry. Firstly, companies should be fully aware of the positive role of innovation in improving patent outputs and market values, and increase their R&D intensity when faced with exogenous demand shocks to seize growth opportunities. Moreover, the positive feedback from the financial markets on pharmaceutical companies' R&D investments can be leveraged to guide the financial markets to better serve the real economy. In addition, the government may formulate industrial policies to increase the willingness of pharmaceutical manufacturing companies to participate in innovation, for example by providing subsidies and tax breaks to reduce the cost of innovation. In fact, the Chinese government has introduced a number of policies to support R&D in pharmaceutical companies in recent years. For example, in 2020, the Chinese government has reduced the tax burden on enterprises by providing full refunds of incremental VAT credits to manufacturers of key materials for epidemic prevention and control. In 2023, the Chinese government expects to provide RMB 1.8 billion in financial resources to support enterprises in research and development for monitoring key infectious diseases and health hazards. Finally, given the shortcomings of the incentive mechanism of state-owned

enterprises, the government is supposed to improve the management efficiency of state-owned enterprises to increase the enthusiasm of state-owned enterprises in R&D activities.

We acknowledge that there are several limitations that need to be addressed in future studies. Firstly, we confirm the impact of major diseases on the quantity of R&D inputs and outputs of firms, while the efficiency or quality of innovation have not been taken into consideration and need to be further explored in future studies. Secondly, we find that increased R&D investment driven by exogenous demand cannot significantly improve firm operating performance, and future research needs to further examine the mechanism by which the increased R&D investments increase firm value. Finally, future research could utilize global cases to provide more comprehensive findings.

Table 6. Robustness test-alternative measure of R&D investment and patent application.

Variables	(1) RD_revenue	(2) RD_revenue	(3) Patent_Invention	(4) Patent_Invention
Epid*Related	2.470***	2.046***	0.293**	0.313**
	(0.555)	(0.491)	(0.128)	(0.130)
Epid	1.982**	3.637***	-0.381*	-0.311
	(0.878)	(0.933)	(0.223)	(0.229)
Related	-0.384*	-0.325*	-0.013	-0.054
	(0.227)	(0.187)	(0.063)	(0.066)
Size		-0.670**		-0.068
		(0.333)		(0.057)
TobinQ		0.116		-0.008
		(0.146)		(0.032)
Mtb		-4.013***		-0.108
		(1.333)		(0.253)
Lev		-0.007		0.065
		(1.039)		(0.226)
Anaattention		0.036*		0.009**
		(0.019)		(0.004)
H10		0.049***		0.007**
		(0.014)		(0.003)
Roe		-13.960***		0.344
		(2.666)		(0.366)
Tangible		-0.702		-0.034
		(2.082)		(0.402)
Constant	5.147***	19.531**	0.889***	1.967
	(0.933)	(8.155)	(0.220)	(1.359)
Observations	1582	1582	1402	1402
R-squared	0.130	0.206	0.094	0.100
Year FE	Yes	Yes	Yes	Yes

***, **, and * indicate significant at the statistical level of 1%, 5%, and 10%, respectively. Year FE indicates year fixed effects. Robust standard errors are indicated in parentheses, which provide a more reliable and robust estimate of standard errors by taking into account the potential heteroscedasticity and correlation of errors in the data.

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Data availability statement

The data that support the findings of this study are available from China Stock Market & Accounting Research Database (CSMAR) and China Research Data Service Platform (CNRDS), but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of CSMAR and CNRDS.

Authors' contributions

Conceptualization by JL and WQZ; Formal analysis by WQZ and ZL; Methodology by JL; Supervision by JL, ZL and XJJ; Writing-original draft by JL and WQZ; Writing-review & editing by JL, ZL and XJJ.

References

[1] National Health Commission of the People's Republic of China (NHC). *Regulations on emergency response to public health emergencies.* [Online]. Available from: http://www.nhc.gov.cn/yjb/s3580/200804/b41369aac27847dba3e6aebccc72e2f8.shtml. [Accessed on 9 May 2003].

[2] Dawood FS, Iuliano AD, Reed C, Meltzer MI, Shay DK, Cheng PY, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: A modelling study. *Lancet Infect Dis* 2012; **12**(9): 687-695.

[3] Zhang J, Litvinova M, Wang W, Wang Y, Deng X, Chen X, et al. Evolving epidemiology and transmission dynamics of coronavirus disease 2019 outside Hubei province, China: A descriptive and modelling study. *Lancet Infect Dis* 2020; **20**(7): 793-802.

[4] Ayittey FK, Ayittey MK, Chiwero NB, Kamasah JS, Dzuvor C. Economic impacts of Wuhan 2019-nCoV on China and the world. *J Med Virol* 2020; **92**(5): 473-475.

[5] Ceylan RF, Ozkan B, Mulazimogullari E. Historical evidence for economic effects of COVID-19. *Eur J Health Econ* 2020; **21**(6): 817-823.

[6] Fan VY, Jamison DT, Summers LH. Pandemic risk: How large are the expected losses? *B World Health Organ* 2018; **96**(2): 129-134.

[7] Tran XH, Le TTP, Nguyen QH, Do TT, Nguyen VD, Gay CG, et al. African swine fever virus vaccine candidate ASFV-G- I177L efficiently protects European and native pig breeds against circulating Vietnamese field strain. *Transbound Emerg Dis* 2022; **69**(4): e497-e504.

[8] Graham BS. Rapid COVID-19 vaccine development. *Science* 2020; **368**(6494): 945-946.

[9] Ayati N, Saiyarsarai P, Nikfar S. Short and long term impacts of COVID-19 on the pharmaceutical sector. *Daru* 2020; **28**(2): 799-805.

[10]Emanuel EJ, Buchanan A, Chan SY, Fabre C, Halliday D, Heath J, et al. What are the obligations of pharmaceutical companies in a global health emergency? *Lancet* 2021; **398**(10304): 1015-1020.

[11]The People's Bank of China (PBC). *Report on the implementation of China´s monetary policy in the first quarter of 2020.* [Online]. Available from: http://www.pbc.gov.cn/zhengcehuobisi/. [Accessed on 10 May 2020].

[12]Bernile G, Bhagwat V, Yonker S. Board diversity, firm risk, and corporate policies. *J Financ Econ* 2018; **127**(3): 588-612.

[13]Ding N, Gu L, Peng Y. Fintech, financial constraints and innovation: Evidence from China. *J Corp Financ* 2022; **73**: 102194.

[14]Zheng G, Wang S, Xu Y. Monetary stimulation, bank relationship and innovation: Evidence from China. *J Bank Financ* 2018; **89**: 237-248.

[15]Agarwal R, Gaule P. What drives innovation? Lessons from COVID-19 R&D. *J Health Econ* 2022; **82**: 102591.

[16]Yuan R, Wen W. Managerial foreign experience and corporate innovation. *J Corp Financ* 2018; **48**: 752-770.

[17]Finkelstein A. Static and dynamic effects of health policy: Evidence from the vaccine industry. *Q J Econ* 2004; **119**(2): 527-564.

[18]Saville M, Cramer JP, Downham M, Hacker A, Lurie N, Van der Veken L, et al. Delivering pandemic vaccines in 100 days-What will it take? *N Engl J Med* 2022; **387**(2): e3.

[19]Trouiller P, Olliaro P, Torreele E, Orbinski J, Laing R, Ford N. Drug development for neglected diseases: A deficient market and a public-health policy failure. *Lancet* 2002; **359**(9324): 2188-2194.

[20]Blume-Kohout ME, Sood N. Market size and innovation: Effects of medicare part D on pharmaceutical research and development. *J Public Econ* 2013; **97**: 327-336.

[21]Dubois P, De Mouzon O, Scott-Morton F, Seabright P. Market size and pharmaceutical innovation. *Rand J Econ* 2015; **46**(4): 844-871.

[22]Ferguson NM, Cummings DAT, Fraser C, Cajka JC, Cooley PC, Burke DS. Strategies for mitigating an influenza pandemic. *Nature* 2006; **442**(7101): 448-452.

[23]Bahl K, Senn JJ, Yuzhakov O, Bulychev A, Brito LA, Hassett KJ, et al. Preclinical and clinical demonstration of immunogenicity by mRNA vaccines against H10N8 and H7N9 influenza viruses. *Mol Ther* 2017; **25**(6): 1316-1327.

[24]Krammer F, Palese P. Advances in the development of influenza virus vaccines. *Nat Rev Drug Discov* 2015; **14**(3): 167-182.

[25]Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y, et al. Challenges in ensuring global access to COVID-19 vaccines: Production, affordability, allocation, and deployment. *Lancet* 2021; **397**(10278): 1023-1034.

[26]Lee J, Lee MK, Jeong S, Lee B, Park M. Responding to epidemic-driven demand: The role of supply channels. *Int J Prod Res* 2022. doi: 10.1080/00207543.2022.2118890.

[27]Meissner HC. Understanding vaccine safety and the roles of the FDA and the CDC. *N Engl J Med* 2022; **386**(17): 1638-1645.

[28]Lurie N, Keusch GT, Dzau VJ. Urgent lessons from COVID 19: Why the world needs a standing, coordinated system and sustainable financing for global research and development. *Lancet* 2021; **397**(10280): 1229-1236.

[29]Kickbusch I, Leung GM, Shattock RJ. Learning from crisis: Building resilient systems to combat future pandemics. *Lancet* 2021; **398**(10294): e2-e6.

[30]Griliches Z, Pakes A, Hall BH. The value of patents as indicators of inventive activity. In: Dasgupta P, Stoneman P, eds. *Economic policy and technical performance*. Cambridge: Cambridge University Press; 1987, p. 97-124.

[31]Pandit S, Wasley CE, Zach T. The effect of research and development (R&D) inputs and outputs on the relation between the uncertainty of future operating performance and R&D expenditures. *J Account Audit Fina* 2011; **26**(1): 121-144.

[32]Ren S, Cheng Y, Hu Y, Yin C. Feeling right at home: Hometown CEOs and firm innovation. *J Corp Financ* 2021; **66**: 101815.

[33]Eberhart AC, Maxwell WF, Siddique AR. An examination of long-term abnormal stock returns and operating performance following R&D increases. *J Finance* 2004; **59**(2): 623-650.

[34]Hou K, Hsu PH, Wang S, Watanabe A, Xu Y. Corporate R&D and stock returns: International evidence. *J Financ Quant Anal* 2021; **57**(4): 1377-1408.

[35]Ciftci M, Cready WM. Scale effects of R&D as reflected in earnings and returns. *J Account & Econ* 2011; **52**(1): 62-80.

[36]Chi JD, Su X, Tang Y, Xu B. Is language an economic institution? Evidence from R&D investment. *J Corp Financ* 2020; **62**: 101578.

[37]Cumming D, Ji S, Peter R, Tarsalewska M. Market manipulation and innovation. *J Bank Financ* 2020; **120**: 105957.

[38]Chang EC, Lin TC, Ma X. Governance through trading on acquisitions of public firms. *J Corp Financ* 2020; **65**: 101764.

[39]Fama EF, French KR. A five-factor asset pricing model. *J Financ Econ* 2015; **116**(1): 1-22.

[40]Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986; **51**(6): 1173-1182.

[41]Ernst H. Patent applications and subsequent changes of performance: Evidence from time-series cross-section analyses on the firm level. *Res Policy* 2001; **30**(1): 143-157.

[42]Lee M, Su HN. Technology portfolio, patent litigation probability and firm performance. In: Dundar F. Kocaoglu, Timothy R. Anderson, Tugrul U. Daim, Dilek Cetindamar Kozanoglu, Kiyoshi Niwa, Gary Perman. (eds.) Infrastructure and Service Integration: Proceedings of PICMET'14 Conference: *Portland International Center for Management of Engineering and Technology* (July 27-31, 2014 Kanazawa, Japan). Portland: Portland State University, 2014; p. 870-878.

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