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ORIGINAL RESEARCH

Factors Affecting Success of New Drug Clinical Trials

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Abstract
Clinical trials are an essential process in the development of new drugs. In spite of time-consuming processes and high costs, the overall success rate of clinical trials is only 7.9%, which is a high risk for biopharmaceutical companies. However, despite these huge risks, research on finding factors affecting clinical trials to overcome and manage to risks has been insufficient. Considering these characteristics of the pharmaceutical industry, this study investigated the factors affecting the success of sponsor-initiated clinical trials. The success factors investigated were categorized into four factors: quality of clinical trials, speed of clinical trials, relationship type, and communication. Logistic regression was performed to measure each factor by analyzing 24,295 cases of Phase 1 to 4 trials from ClinicalTrials.gov. Because of the analysis, the factors affecting the success of the clinical trials were varied according to each clinical phase and the drug types: New Molecular Entity (NME)/Biologics, and the success ratio in the quality variable affected the overall clinical trial phases. Additionally, the experience, speed, relationship type, and communication variables were also found to be statistically significant for the success of each phase and drug type.

Keywords Clinical trials · Success factor · New drug development · New Molecular Entity · Biological drugs

Introduction

The R&D process of new drug development is a time-consuming and expensive process. The new drug development process consists of a series of steps to evaluate the safety and efficacy of new drug candidates, and the most time-consuming and costly stage is the clinical trial stage. It takes more than 10 years to develop the technology for an overall biopharmaceutical [1] and the cost of a successful clinical trial is about $2.6 billion [2]. For most time-consuming process of R&D is clinical trials. Although there are differences among studies related to the development period of a new drug, an average of 7.6 years was found for a Phase 1 clinical trial by a Korean pharmaceutical company [3] and 6.8 years for a foreign pharmaceutical company [2].

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Clinical trials are long-term projects and, at the same time, are expensive. In a 2015 study on the cost of new drug development, DiMasi found that the total cost of clinical trials conducted from 2000 to mid-2010 was $14.6 billion, exceeding the total cost of clinical trials from 1970 to 2000 ($8.2 billion) [2]. However, despite the investment of large amounts of time and money, the success rate of new drug development from conception to new drug registration is 7.9%, which shows low investment efficiency [4]. Although new drug development requires a large amount of investment in terms of time and cost, the reason pharmaceutical companies strive to develop new drugs is that the rewards they receive from successful new drug development are large. When a new drug is developed successfully, pharmaceutical companies can not only recover their investment costs for new drug development but also create huge added value and secure a long-term monopoly and professional market position [5].

As we have seen so far, the clinical trial process in new drug development is an essential process to prove the efficacy and safety of a drug, and it is also a challenge that pharmaceutical companies must solve for new drug development. Analyzing these challenges effectively and finding strategic solutions can be a way to raise therapeutic innovation through inspiring R&D productivity in the pharmaceutical industry and to successfully develop new drugs. Therefore, this study aimed to conduct research that can help the success of clinical trials by reviewing studies related to the success of clinical trials. The previous studies are survey studies conducted by experts in the pharmaceutical industry, the studies using small-scale data related to specific diseases, factor analysis studies through literature reviews, and studies on the success of clinical trials as the next stage of entry or regulatory approval. These studies were qualitative studies that did not use actual clinical data, or used only small-scale data focusing on specific diseases even if data were used. To differentiate it from the existing studies, in this study, the success factors of clinical trials were revealed through survey research by experts in the pharmaceutical industry, and various success factors extracted through a literature review were synthesized and categorized into four factors: quality of clinical trials, speed of clinical trials, relationship type, and communication. Furthermore, the factors were analyzed by drug type and clinical stage using the actual clinical trial data provided by ClinicalTrials.gov which is a database operated by the US. National Library of Medicine and the US. National Institute of Health. This database includes clinical trial information related to disease and condition for researchers, patients, and various stakeholders related with healthcare industry.

To briefly introduce this study, in "Theoretical Background and Modelling" section, through a literature review, the importance of clinical trials, which account for a large part of new drug development, and the theoretical background of the definitions and factors of clinical trials' success are reviewed. Additionally, a research model and hypothesis are presented, using the definitions and factors for the success of the clinical trial used in this study. "Materials and Methods" section describes the data collection and purification process, the analysis method, and variables for performing this study. In "Results and Discussion"section, the results of the statistical analysis of the success factors of the clinical trials discussed above are presented, and in "Conclusion" section, the significance and l imitations of this study are presented.

Theoretical Background and Modeling

The Importance of Clinical Trials in the New Drug Development Process

When designing a clinical trial, a new drug developer starts the new drug research process by considering the goals to be achieved at each clinical trial stage. The goal of new drug development is to bring a new compound with a proven therapeutic effect to the market, and approval from clinical trials attracts investors and increases the company's value. However, there is not only an optimistic future for clinical trials. Most compounds fail before being brought to the market, which means a cumulative consumption of resources devoted to conducting clinical trials. In particular, the impact of the failure of Phase 3 clinical trials poses a risk to the survival of small biotech companies (and investors), and large companies find themselves in a situation of mergers [6].

Therefore, pharmaceutical companies must plan clinical trials through thorough clinical trial planning and pre-preparation before starting clinical trials and establish strategies to increase the likelihood of a clinical trial's success through multi-faceted analysis according to the drug and clinical trial type. Based on the need for research on the success of clinical trials, in this study, the success factors were analyzed by reviewing the literature related to the success of clinical trials, and the success factors revealed through this review were analyzed by empirical data. Research and clinical trial data registered on ClinicalTrials.gov was used to investigate the drug types and success factors in the clinical phase.

Definition of Clinical Trial Success

With respect to the success of clinical trials, there is a universal perception that patient registration is a key factor in determining the success of clinical trials, and an analysis of clinical trials registered as closed in 2011 showed that 19% of clinical trials were terminated due to insufficient numbers

of participants [7]. Johnson noted that approximately 80% of clinical trials do not meet the initial enrollment goals and timelines, and these delays result in a loss of $8 million in revenue per day for drug discovery companies [8]. In the data investigated in this study, among the clinical trials that were terminated, many cases were found that were terminated due to failure in patient registration. Additionally, in the case of Phase 2 and 3 clinical trials, the number of patients required to prove the safety and efficacy of a drug increase from 100 to 1000, and thus, patient registration in clinical trials could be considered a key success factor.

As mentioned above, many studies have revealed the importance of patient registration, but studies conducted by defining successful patient registration as the measure of success in clinical trials have not been investigated. Additionally, the only data collected from ClinicalTrials.gov that can be considered a success factor for clinical trials are those on the patient registration status. Therefore, in this study, successful patient registration is defined as clinical trial success, and the success factors of the clinical trial are identified using a new definition that has not been used in previous studies. Table 1 shows the definition of clinical trial success in previous studies.

Success Factors of Clinical Trials

To investigate the success factors of clinical trials, the literature was searched by combining keywords such as "clinical trial", "success factor", "success rate", "clinical trial phase", "experience", and "duration".

First, in light of the existing research on the quality of clinical trials, the research was subdivided into studies on the success ratio and experience of clinical trials. In relation to studies related to the success rate of clinical trials, it is essential to prove drug efficacy and safety, which increase the clinical success rate. Additionally, high-level clinical research quality, understanding and compliance with the related regulations (GCP, etc.), research design and planning, etc., were investigated as factors of successful clinical trials [13–15]. In research related to clinical trial experience, Lo revealed the most important features for predicting success through drug approval prediction research using machine learning techniques. These factors are trial outcomes, trial status, trial accrual rates, duration, prior approval for another indication, and the sponsor's track record. Lo also said that expertise in drug development and candidate substances sponsored by a company that has experienced successful clinical trials in the past increases the likelihood of success in clinical trials [9]. Similar to Lo's research, Thunecke investigated the experience before clinical trials in the field as the factor with the highest predictive value for clinical trial success [6].

Second, the duration of a clinical trial relates to the speed of a clinical trial and is directly related to the investment cost, and the shorter the clinical trial period, the lower the clinical trial cost, thereby reducing the financial burden on the company. The speed of clinical trials is important when companies select clinical trial partners for rapid clinical trial progress [14, 15]. In addition, it has been found that rapid patient recruitment for clinical trials affects the speed of clinical trial completion [16]. A study by Big Pharma companies, such as TTC Inc., Merck, and Quintiles, found that trial sites that randomized the first patients tended to perform better overall [17]. Taken together, rapid clinical trial execution shortens the clinical trial period, which is an important factor in clinical trial success.

Third, in research related to relationship types, Lin conducted multinomial regression analysis with data from 4494 organizations and 18,040 clinical trials. The analysis built temporal networks of clinical trial collaborations among large and small pharmaceutical companies, academic institutions, nonprofit organizations, hospital systems, and government agencies to determine the relationships of clinical trial success and the collaborative network structure of each actor, organizational behavior, and partnership characteristics. Especially in the context of clinical trials not explored in previous studies, cooperation between organizations was characterized and the trends of successful organizations were investigated. As a result, it was found that the diversity of collaboration was associated with better research results and high efficiency, and the analysis found that collaboration networks tended to select other actors with proven success records as the preferred negotiators. Historically, successful large pharmaceutical companies benefit when attracting actors with diverse therapeutic expertise and experience, which explains the correlation between success and collaborative diversity [18].

Forth, in terms of communication, Getz discovered that research sites with sufficient infrastructure for clinical trials are 41% better than sites dedicated to clinical trials in terms

Table 1 Definition of clinical trial success

	Definition	Previous studies
Clinical trial success	A successful clinical trial is one that passes on to the next stage after the regulatory body has approved the use of the drug or the clinical trial has been completed	[2, 9]
	Patient registration is recognized as an important factor for the success of clinical trials	[10–12]

of patient enrollment based on data provided across 10 therapeutic areas by 50 pharmaceutical and biotech companies [17]. Jung and Kim et al. investigated the need for close collaboration and communication between the sponsor and the researcher when conducting clinical trials [13, 14]. Jung also investigated the need for a coordinating center that shares information and controls the entire clinical trial process for multi-institutional collaboration in clinical trials [13].

In addition, Smietana et al. analyzed the probability of the clinical trial success of pharmaceutical companies through an external analysis from 1996 to 2014. He used Informa's Pharma project database for an industry-wide evaluation to track the clinical and regulatory progress of more than 9200 new compounds. The subjects of this analysis were synthetic and biological drugs, and natural substances with possible biological origin were excluded. The success rate of each development stage was determined based on the ratio of successful drugs among all compounds that escaped the stage during a given period, and major trends related to clinical trials were analyzed. The recent increase in the success rate of clinical trials was related to the tendency of pharmaceutical companies to focus on pipelines such as orphan drugs, immuno-oncology drugs, and antiviral drugs, which have a relatively high probability of success and to increase the success rate of clinical trials through partnerships [19]. In a study on the importance of clinical trial partners, it was found that the higher the clinical trial success rate, the higher the number of affiliated drugs, large companies, and partners [20].

Additionally, factors such as drug characteristics, patient recruitment, organizational structure, researchers' interest, and finances were found to affect the clinical trial success by various studies. However, in this study, four success factors, namely quality, speed, relationship type, and communication, were analyzed due to the limitations of data gathering. The quality factor of clinical trials was analyzed in terms of the success rate and experience of clinical trials, and the speed factor of clinical trials was analyzed by the duration of the clinical trial. For the relationship type factor, the diversity of collaborators was found to have a positive effect on the results of clinical trials. In this study, the presence or absence of collaborators was investigated to find whether

Table 2 Success factors of clinical trials

Factors	Details	Descriptions	Related studies
Quality	Clinical trial experience	The strength of the Phase 2 data The sponsor's previous experience in the field	[6]
		As predictors of clinical trial success, test results, test status, increase in the patient recruitment rate, trial period, sponsor's prior approval for other drugs, and sponsor's past success were revealed	[9]
	Clinical trial success ratio	Proof of drug efficacy and safety is essential and increases the clinical success rate	[21, 22]
		Understanding and compliance with GCP	[3, 13]
Speed	Clinical trial duration	An increase in the patient recruitment speed increases the speed of clinical completion	[16]
		Time taken to conduct clinical trials	[15]
		Investigators who can recruit enough patients	[14, 15]
		Rapid clinical trial progress	[14]
Relationship	Collaboration	Research networks (collaboration) in various subject areas influence the success of clinical trials	[18]
		Use of licensed compounds through cross-organizational collaboration	[19]
		The clinical trial success rate is improved by the number of partners, the number of alliance medicines, and company size	[20]
Communication	Regional coherence	Close communication and cooperation between the sponsor and the investigator	[14]
		Close cooperation between companies and government departments	[13]
Other	Drug properties	Orphan drugs, immunotherapeutic drug development, and use of biomarkers have a high success rate	[23]
		Selection of good drug candidates	[24]
	Patient registration	Patient burden (patients' abandonment of the clinical trial)	[25]
		Lack of eligible patients	[26, 27]
	Organization	Sufficient auxiliary personnel needed to conduct research	[15]
		A system that enables researchers to conduct systematic research	[13]
	Finance	Importance of financial support in Phase 3 clinical trials	[21]

they affect the success of clinical trials. Lastly, in the communication factor, close cooperation between sponsors and collaborators in clinical trials was found to affect the success of clinical trials. In this study, the regional coherence of the institutions was investigated by dividing the institutions by country and continent. The variables of the previous studies summarized above are arranged in Table 2 into five factors: Quality, Speed, Relationship, Communication and the Others.

Hypothesis Development

Quality of Clinical Trial and Clinical Trial Success

The quality of clinical trials is an important indicator for moving clinical trials to the next stage. Regarding the quality of clinical trials, it was found that the adequacy of clinical trial planning and operation was the main characteristic, and it could be linked to the success of clinical trials [13, 28]. Quality in clinical trials also means the quality of GCP compliance. Therefore, successful clinical trial means that a well-planned clinical trial protocol and compliance with related regulations were thoroughly followed. In this context, experiences and success ratio of the former clinical trials can be treated as factors leading the future successful clinical trials. This study measured the quality of clinical research as a factor influencing a clinical trial's success by analyzing the clinical trial experience and the clinical trial success rate based on the sponsor's past clinical trial data, and established Hypotheses H1 and H2.

H1 The sponsor's clinical trial experience will have a positive impact on the clinical trial's success.

H2 The sponsor's clinical trial success rate will have a positive impact on the clinical trial's success.

Speed of Clinical Trials and Clinical Trial Success

The duration of clinical trials is a key factor in determining the financial risks and rewards of drug development projects [23]. The duration of clinical trials is 2.7 years, 3.2 years, and 3.8 years, respectively, for Phase 1, 2, and 3 trials [2], and the success rate from clinical trial success to new drug approval is less than 7.9% [4]. Therefore, as the clinical trial's duration becomes longer, it creates a financial risk, along with an increase in research expenses from the company's perspective. In addition, as a result of analyzing the difference between terminated and successful clinical trials, it was found that Phase 2 trials of drugs that did not proceed to Phase 3 trials tended to end 8.1 months earlier [23]. As such, the speed of clinical trials is focused on whether clinical investigators can quickly recruit patients and conduct research as well-planned clinical trials [14, 28, 29]. Therefore, in this study, as stated in Hypothesis H3, the number of days from the actual clinical trial data to the success of the clinical trial were measured and analyzed as a success factor.

H3 The duration of the clinical trial will have a negative impact on the clinical trial's success.

Relationship Type and Clinical Trial Success

Regarding the type of relationship between the sponsor and the collaborator, as in Lin's study, for examining the association between cohesion and diversity in the cooperative network of clinical trials according to the relationship type, it was suggested that the diversification of the network affects the success [18]. In addition, Smietana analyzed recent trends in the success rate of clinical trials and found that the success rate of clinical trials with partnerships was high [19]. Recently, as the pharmaceutical industry has shifted to an open innovation framework due to the high risk of the development process, the role of the sponsor's collaborator in clinical trials has become important [30]. In particular, Pammolli et al. calculated the success rate of a new drug development project based on the number of non-industrial partners, not the pharmaceutical industry, and confirmed that the success rate of clinical trials increased by 11.3 percentage points when non-industrial partners participated [31]. These results highlight the benefits of collaboration between the pharmaceutical industry and organizations outside the industry in terms of the success of clinical trials. In light of the research investigated above, in this study, the effect of the sponsor's collaborator on the success of the clinical trial was analyzed, as described by Hypothesis H4.

H4 The presence of a clinical trial collaborator will have a positive effect on the clinical trial's success.

Communication and clinical trial success

In many existing studies related to communication, it was found that close communication between the sponsor and the collaborator affects the success of clinical trials [13, 14, 18]. To analyze the impact of communication, formal and informal communication methods and data collection are required during the specific processes of the clinical trial. Reus & Lamont found that when there is a regional distance difference between the two parties to a collaboration, the

cultural differences are exacerbated, making communication more difficult [32]. Therefore, within the scope of data collection for this study, the influence of communication was analyzed by exploring whether the sponsor and collaborator were from the same region (Hypothesis H5).

H5 The regional coherence of sponsors and collaborators will have a positive impact on the clinical trial's success.

Materials and Methods

Data

To analyze the four factors (quality, speed, relationship type, and communication), data on successful and unsuccessful clinical trials from 2010 to June 2020 and from Phases 1 to 4 were collected from ClinicalTrials.gov. The ClinicalTrials.gov database is the world's largest clinical trial information database, providing more than 430,000 clinical trial information in 221 countries. This database which includes different regional attributes is needed to analyze regional factor effect to the success of clinical trials. And also, the database should provide sponsor and collaborator information by each phase. Therefore, we only focused on the most adequate and enormous open-source database for this research. In the data purification process, data that did not specify the geographic location of the sponsors and collaborators were excluded, and all data in which errors were found after data collection in ClinicalTrials.gov were also excluded. Additionally, the search was limited to industry-led research, but all data in which individual researchers were entered in the sponsor column were also excluded. In addition to the clinical trial data, necessary data were collected through Bloomberg, the companies' websites, and Google and linked with the data matching the sponsor's name. Details of the data collection and cleaning methods are shown in Table 3.

Estimation Procedure

In this study, logistic regression was used to analyze the factors affecting the success of clinical trials. The reason for using logistic regression analysis is that the data expressing the success or failure of the clinical trial were classified as 0 and 1 as the dependent variable. The statistical significance of the independent variables affecting the success of clinical trials was investigated through the odds ratio, and all statistical analyses were performed with p-values of <0.01, <0.05, and <0.1. The collected data were analyzed using the STATA 16.1 program.

$$\log \frac{P}{1-P} = \beta_0 + \beta_1 X_1.$$

Table 3 Data cleaning process

Stage	Process	# of Rows
Stage 1	Clinical trial data gathering:	28,512
	Source: clinicaltrials.gov	
	Retrieval condition	
	Phase 1–4	
	Study type: intervention	
	Status: terminated, completed	
	Funder type: industry	
	Duration: 2010.01–2020.06	
Stage 2	Completion/start date omitted (− 1016)	27,496
Stage 3	Restructuring the data (− 3201):	24,295
	Inadequate sponsor type	
	Including omitted column	
	Wrong company name	
	Separating sponsors and collaborators	
	The first organization name in the sponsor column: sponsor	
	Others: collaborators	
	Gathering address and continent data for each company	

Table 4 Definition and measurement of variables

Variables	Factors	Variables	Definition	Measurement	Related Studies
Dependent Variable	Status	Status	Success of clinical trials	If terminated = 0, Otherwise = 1	[10–12]
Independent Variables	Quality	Experience	Cumulative number of total clinical trials of sponsor	Total number of terminated and completed clinical trials of sponsor	[6]
		Success Ratio	Cumulative success ratio of clinical trials of sponsors	Number of successful clinical trials before the trial / total number of clinical trials before the trial	[6, 13, 21, 22]
	Speed	Duration	Days taken to complete clinical trials	Number of days from the beginning to complete of clinical trials	[14–16]
	Relation Type	Relation Type	Presence of clinical trial partners	If absence of partners = 0, existence of partners = 1	[18–20]
	Communication	Nation	Whether the address-based region of the sponsor and collaborator is the same	If different = 0, same = 1	[13, 14]
		Continent		If different = 0, same = 1	

Variables

Dependent Variables

This study used clinical trial data from ClinicalTrials.gov to analyze the factors influencing clinical trials' success. According to ClinicalTrials.gov, a successful clinical trial is a clinical trial in which patient registration has been completed, and a failed clinical trial is defined as a clinical trial in which patient registration has been completed during or before the completion of the clinical plan. The data were coded as 1 for successful clinical trials and 0 for failed clinical trials.

Independent Variables

In this study, factors affecting clinical trial success were analyzed by dividing them into four factors: quality, speed, relationship, and communication. The quality of clinical trials was investigated by the total number of clinical trials across the duration of the investigation and the success rate of previous clinical trials, and the speed of clinical trials was defined as how many days it took for the trials to succeed. Regarding the presence of collaborators in the clinicaltrials.gov data, the relationship type was classified as 1 if there was a collaborator and 0 if the company conducted an independent study. Communication was based on the address of the sponsor and collaborator to reveal whether the nations or continents were the same, scored as 0 if they were not identical and 1 if they were the same. Table 4 shows how to define and measure all independent and dependent variables used in this study.

Results and Discussion

All descriptive statistics and multicollinearity of the variables used in this study are shown in Table 5.

In order to analyze the relative influence of variables that affect the success of a clinical trial, Pearson's correlation analysis was performed to investigate the correlations between variables. As a result, the correlation between nation and continent of sponsors and collaborators showed the most positive relationship ($r = 0.861$, $p < 0.01$), and the clinical trial success rate and clinical trial duration had the

Table 5 Descriptive statistics

Variables	Obs	Mean	Std. Dev	Min	Max	VIF
Experience	24,295	235.651	320.016	1	1026	1.02
Success ratio	24,295	0.881	0.193	0	1	1.18
Duration	24,295	573.997	531.174	0	3555	1.1
Relationship type	24,295	0.764	0.424	0	1	1.74
Nation	24,295	0.886	0.317	0	1	4.62
Continent	24,295	0.912	0.284	0	1	3.91

Table 6 Correlation analysis of variables ($N = 24,295$)

	Intervention	Phase	Experience	Success ratio	Duration	Relationship type	Nation	Continent
Intervention	1							
Phase	0.068 0.000	1						
Experience	− 0.015 0.019	− 0.018 0.004	1					
Success ratio	− 0.003 0.578	− 0.028 0.000	− 0.033 0.000	1				
Duration	0.089 0.000	0.258 0.000	0.0102 0.113	− 0.118 0.000	1			
Relationship type	− 0.051 0.000	− 0.056 0.000	0.017 0.005	0.061 0.000	− 0.098 0.000	1		
Nation	− 0.028 0.000	− 0.028 0.000	0.098 0.000	0.013 0.038	− 0.043 0.000	0.644 0.000	1	
Continent	0.018 0.003	− 0.006 0.340	0.069 0.000	0.024 0.000	− 0.041 0.000	0.560 0.000	0.861 0.000	1

Table 7 Result of success factors of new drug clinical trials

Variables	Model 1	Model 2	Model 3	Model 4
Experience	1.000*** (0.000)	1.000*** (0.000)	1.000*** (0.000)	1.000*** (0.000)
Success ratio	42.522*** (3.598)	42.774*** (3.620)	42.583*** (3.588)	42.568*** (3.588)
Duration	1.000*** (0.000)	1.000*** (0.000)	1.000*** (0.000)	1.000*** (0.000)
Relationship type	1.009 (0.067)	0.934 (0.049)		
Nation	0.803 (0.134)		0.845** (0.063)	
Continent	1.055 (0.182)			0.861* (0.070)
N	24,295	24,295	24,295	24,295
Pseudo-R^2	0.1360	0.1358	0.1360	0.1359
Prob > chi^2	0.000	0.000	0.000	0.000
Log-likelihood	− 7152.497	− 7154.334	− 7152.556	− 7153.442

***$p < 0.01$, **$p < 0.05$, *$p < 0.1$

most negative correlation ($r = -0.118$, $p < 0.01$). Table 6 presents the correlations between the variables.

Although there is no significant associated multicollinearity among independent variables using VIF analysis (Table 5), nation and continent variables should be treated carefully for a more appropriate model. As the result of Pearson's correlation analysis, there are three relatively high correlation pairs in the lower right corner of Table 6. Therefore, we made four regression models with pseudo-R^2 close to zero by backward selection method. Model 1 concerns every factor of quality, speed, relation type and communication. Model 2 doesn't consider the factor of communication. Model 3 and Model 4 discard relation type factor but each model includes different variables of communication factor.

Table 7 shows the results of the logistic regression analysis of the effects of clinical trial experience and success rate, clinical trial duration, relation type, and the regional coherence of sponsors and collaborators on overall clinical trial success. The p-value of the log-likelihood ratio, excluding the presence of sponsors (relationship type) and the regional coherence of sponsors and collaborators (nation, continent), was also under 0.01. This result shows that the quality and speed variables are related to a clinical trial's success. According to the odds ratio of each independent variable, the variables with statistically significant results are the experience, success ratio. However, the results were derived that the duration variable also had a positive effect on the success of the clinical trial, so Hypothesis 3 was not supported.

Table 8 Result of success factors of new drug clinical trials (Phase 1—NME vs. Biologicals)

Variables	NME (Phase 1)				Biologicals (Phase 1)			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
Experience	1.000*** (0.000)	1.000*** (0.000)	1.000*** (0.000)	1.000*** (0.000)	0.999*** (0.000)	0.999*** (0.000)	0.999*** (0.000)	0.999*** (0.000)
Success ratio	43.488*** (7.307)	43.363*** (7.281)	42.232*** (7.031)	42.369*** (7.058)	194.739*** (106.905)	208.407*** (112.914)	202.980*** (109.648)	197.228*** (107.177)
Duration	0.999*** (0.000)	0.999*** (0.000)	0.999*** (0.000)	0.999*** (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)
Relationship type	0.808 (0.121)	0.815* (0.092)			1.073 (0.526)	0.955 (0.415)		
Nation	1.231 (0.442)		0.850 (0.128)		1.013 (1.280)		0.704 (0.541)	
Continent	0.798 (0.290)			0.816 (0.134)	0.497 (0.782)			0.533 (0.565)
N	8829	8829	8829	8829	812	812	812	812
Pseudo-R^2	0.1319	0.1318	0.1313	0.1314	0.3312	0.330	0.3307	0.3312
Prob > χ^2	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Log-likelihood	− 1912.316	− 1912.508	− 1913.569	− 1913.379	− 132.769	− 132.983	− 132.878	− 132.781

***$p < 0.01$, **$p < 0.05$, *$p < 0.1$

Table 9 Result of success factors of new drug clinical trials (Phase 2 – NME vs. Biologicals)

Variable	NME (Phase 2)				Biologicals (Phase 2)			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
Experience	0.999*** (0.000)	0.999*** (0.000)	0.999*** (0.000)	0.999*** (0.000)	0.999* (0.000)	1.000* (0.000)	0.999* (0.000)	0.999* (0.000)
Success ratio	31.877*** (4.443)	32.023*** (4.462)	32.067*** (4.456)	32.019*** (4.450)	36.144*** (11.381)	36.145*** (11.483)	35.735*** (11.230)	35.984*** (11.302)
Duration	1.000*** (0.000)	1.000*** (0.000)	1.000*** (0.000)	1.000*** (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)
Relationship type	1.041 (0.112)	1.001 (0.087)			1.206 (0.348)	1.086 (0.270)		
Nation	0.671 (0.209)		0.941 (0.118)		0.635 (0.442)		0.851 (0.339)	
Continent	1.445 (0.464)			1.012 (0.136)	1.235 (0.966)			0.933 (0.442)
N	5981	5981	5981	5981	961	961	961	961
Pseudo-R^2	0.1366	0.1363	0.1363	0.1363	0.1955	0.1948	0.1948	0.1947
Prob > χ^2	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Log-likelihood	− 2314.360	− 2315.237	− 2315.119	− 2315.233	− 312.307	− 312.584	− 312.553	− 312.627

***$p < 0.01$, **$p < 0.05$, *$p < 0.1$

Table 8, 9, 10, 11 show the differences in effects by clinical trial stage and by NME and Biologics. The analysis of all variables including the overall model, drug type, and clinical stage was defined as Model 1 in the Tables. However, in the correlation analysis of the variables, the relationship type and the national and continental consistency variables showed a high correlation. Therefore, Models 2 to 4 are defined in the Tables.

Table 8 presents the logistic regression results of phase 1 clinical trials of NME and biological drugs. In the phase 1 clinical trials, there were differences in the factors affecting the success of clinical trials of NME and biologics. According to the odds ratios of the two drug preparations, it can be seen that the experience and success ratio variables are related to the success of clinical trials ($p < 0.01$). In addition, for NME, the duration had a strong effect on clinical trial

Table 10 Result of success factors of new drug clinical trials (Phase 3—NME vs. Biologicals)

Variable	NME (Phase 3)				Biologicals (Phase 3)			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
Experience	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.001 (0.000)	1.000 (0.000)	1.000 (0.000)
Success ratio	52.783*** (11.632)	54.019*** (11.882)	51.986*** (11.316)	51.461*** (11.211)	120.289*** (64.640)	112.953*** (59.042)	115.227*** (60.599)	116.815*** (60.748)
Duration	0.999 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)
Relationship type	0.898 (0.132)	0.796** (0.091)			0.737 (0.305)	0.787 (0.270)		
Nation	0.933 (0.391)		0.704** (0.113)		1.496 (1.065)		0.941 (0.457)	
Continent	0.804 (0.344)			0.685** (0.118)	0.631 (0.569)			0.738 (0.504)
N	5119	5119	5119	5119	863	863	863	863
Pseudo-R^2	0.1063	0.1057	0.1060	0.1061	0.2602	0.2595	0.2584	0.2588
Prob > χ^2	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Log-likelihood	− 1629.515	− 1630.431	− 1629.916	− 1629.876	− 164.954	− 165.128	− 165.369	− 165.272

***$p < 0.01$, **$p < 0.05$, *$p < 0.1$

Table 11 Result of success factors of new drug clinical trials (Phase 4—NME vs. Biologicals)

Variable	NME (Phase 4)				Biologicals (Phase 4)			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
Experience	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.001)	1.000 (0.001)	1.000 (0.001)	1.000 (0.001)
Success ratio	47.776*** (16.638)	45.963*** (15.862)	46.676*** (15.834)	47.128*** (15.968)	53.885 (99.519)	38.034 (55.944)	41.296 (60.675)	31.627 (46.973)
Duration	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	1.000 (0.000)	0.999 (0.000)	0.999 (0.000)	0.999 (0.000)	0.999 (0.001)
Relationship type	0.928 (0.234)	1.118 (0.220)			0.427 (0.613)	0.971 (0.767)		
Nation	1.372 (0.679)		1.423 (0.364)		2.300 (4.030)		1.720 (1.447)	
Continent	1.146 (0.589)			1.461 (0.429)	2.081 (2.902)			2.497 (2.442)
N	1511	1511	1511	1511	219	219	219	219
Pseudo-R^2	0.1448	0.1432	0.1446		0.177	0.1129	0.1188	0.1241
Prob > χ^2	0.000	0.000	0.000		0.1302	0.101	0.086	0.074
Log-likelihood	− 452.757	− 453.581	− 452.838		− 29.861	− 30.453	− 30.252	− 30.070

***$p < 0.01$, **$p < 0.05$, *$p < 0.1$

success ($p < 0.01$), and relationship type had a statistically significant effect ($p < 0.1$).

Table 9 presents the logistic regression results for phase 2 clinical trials of NME and biologicals. In phase 2 clinical trials, the factors affecting the clinical trial success of synthetic new drugs and biological agents were different. There was also a difference in the degree of influence on clinical trials. In the case of NME, clinical trial experience, success ratio and duration had a strong influence ($p < 0.01$, respectively) on the success of clinical trials, whereas for biologicals, only experience and success ratio had a statistically significant effect ($p < 0.1$; $p < 0.01$).

Table 10 shows the logistic regression results for phase 3 clinical trials NME and biologicals. In the phase 3 clinical trials, the factors affecting the success of the clinical trials of NME and biologicals were different. It can be seen that the success ratio is commonly related to clinical trial success ($p < 0.01$) according to the odds ratio. Unlike

Table 12 Summary of the results

Phase	NME	Biologicals
Phase 1	Experience, success ratio, duration, relationship type	Experience, success ratio
Phase 2	Experience, success ratio, duration	Experience, success ratio
Phase 3	Success ratio, relationship type, nation, continent	Success ratio
Phase 4	Success ratio	N/A

phase 1 and 2 clinical trials, in Phase 3 clinical trials of a synthetic new drug, the presence of a sponsor and a collaborator (relationship type) ($p < 0.05$) and the regional identity of the sponsor and collaborator (nation, continent) had a statistically significant effect ($p < 0.05$, respectively).

Table 11 shows the logistic regression results of phase 4 clinical trials of NME and biologicals. For biological agents, the alternative hypothesis related with clinical trial success ratio was rejected, as the p-value of the likelihood ratio was greater than 0.1. As a result of measuring the odds ratio of NME, it was found that only the clinical trial success rate was related to clinical trial success ($p < 0.01$).

In summary, the factors affecting clinical trials are revealed differently by interventions and phases. Especially, success ratio is strongly related with clinical trials of every intervention and phase except phase 4 of biologicals. In addition, experience affects the success of phase 1 and 2 clinical trials for both NME and biologicals. These results complement Lo's study [9], which showed that the sponsor's prior clinical trial success record is useful factor for predicting a clinical trial's success. It provides statistical background to support Getz's study [17] showing that a site that performed well previously has a 70% chance of yielding a better research outcome.

On the other hand, relationship type, and nation and continent, which are variables related to communication, were not significant in the overall model (Model 1 in Table 7, 8, 9, 10, 11, 12), but significant effects were found in the detailed model. Factors related with relation type only affect NME in Model 2 of phase 1, 3 ($p < 0.1$; $p < 0.05$). And nation and continent variables, which are proxies of communication, positively and significantly affected the success in Model 3, 4 of phase 3 of the clinical trial ($p < 0.05$, respectively). Being inferred as representing the characteristics of phase 3 trials. The purpose of a phase 3 clinical trial is to confirm the efficacy of the drug in a large patient group, and research into racial diversity in responses to new drugs is being conducted in many hospitals including various ethnic groups in various regions [29]. Reflecting these characteristics of phase 3 trials, the presence of a collaborator (relationship type) and the geographical coherence of the sponsor and collaborator (nation, continent) were statistically significantly related to the success of the phase 3 clinical trials.

Further results of this study are summarized in the Table 12.

Conclusion

In previous studies related to the success of clinical trials, there have been many studies with complete information on several characteristics based on drug types and indications in general, and these have mostly been based on a small number of examples [9]. To overcome this limitation, factors affecting clinical trial success were analyzed with the data of 24,695 cases of actual successful and unsuccessful clinical trials registered at ClinicalTrials.gov. In this study, the characteristics of successful clinical trials are investigated leveraging vast amount of actual clinical trial data relative to previous studies through four categorized factors by drug types. Our study found that the experience and success rate of clinical trials, which are qualitative factors of clinical trials, can have a positive effect on the success of clinical trials in phase 1–4, excluding biologics in phase 3. Furthermore, this study emphasizes that the factors affecting clinical trial success differ by interventions and phases. In particular, this study found out the roles of relationship type and communication in phase 3.

With the above findings, this study draws following three practical implications. First, since many products in biopharmaceutical industry, with high risk due to regulatory nature, are approved with more robust post-licensing requirements, the result of this study would be useful for it. License contract consist of the upfront payment which guarantees 5–20% of entire payment and milestone which is a contingent fee for each phase, loyalty based on sales volume after approval [33]. In particular, probability of success in the phase of clinical trials is an important factor in deciding whether or not to license, the size of it, and the timing of it. Therefore, considering the factors that affect the success of clinical trials is important for biotechnology companies, which are technology providers. For this reason, biotechnology firms face decision-making problem of at what stage the contract with big pharmaceutical companies or competent pharmaceutical companies for late-stage technology commercialization, can maximize profits. Decisions for technology transfer

can determine the profits that biotechnology companies can earn in tens or hundreds of billions of units in the future, and sometimes affect survival of biotechnology firms, which has a weak financial structure. Therefore, this study will help biotechnology firm to decision making and licensing process for more robust post-licensing requirements.

Second, organizations conducting and supporting clinical trials must, above all, make efforts to strengthen and accumulate qualitative capabilities. And, if necessary, a regulatory device to enhance the project management capabilities of clinical trial organizations is also needed. This study implies the importance of capacity building through accumulation in clinical trials. Clinical trials require various project management skills such as design of clinical trials, human resources management, budget management, process management, risk management, data management, and portfolio management [34]. Competitive advantage of these things does not appear easily, but happen through the accumulation of experience and trials. Even if a clinical trial project ends in failure, it should also be acceptable as an enhancement of the organization's clinical trial management capability for the other success. Therefore, this study explains us that competency management for enhance quality of clinical trial through experiences is important for the success of a clinical trial, and to conduct a clinical trial through a sponsor and collaborator who has done it well.

Third, the result of study suggests that in order to increase successes of clinical trials in phase 3, to cooperate with various organizations; sponsors and collaborators, and to consider national and continental consistency for communications, are required. Since phase 3 clinical trials aim to secure effective evidence on a large scale, financing or collaborating is inevitably requested in many cases, and it can be said that the capacity to manage them is required. In addition, in order to succeed in such a huge clinical trial, coordination capabilities at the project level are considered to be important than anything else. Meanwhile, the results of this study emphasize the national and continental homogeneity of cooperation in terms of communication for the success of the phase 3 clinical trials. This leads to the interpretation that the effectiveness of communication will be enhanced due to cultural, cognitive, and racial similarities at the regional level, which can increase the probability of clinical trial success.

Nevertheless, caution is needed in interpreting the results of national and continental consistency for communications in phase 3 clinical trial, as they can be linked to the issue of health equity in clinical trials. Cooperation in clinical trials should proceed in the direction of securing evidences a high-level quality. Evidence with a high level of quality guarantees the universality of the subjects of clinical trials. Therefore, efforts in the aspect of communication are needed to proceed with phase 3 clinical trials to secure ethnic and social diversity. Health equity in clinical trials to increase the diversity of the population enrolled in clinical trials for new drugs, is one of the latest issues related to the success of clinical trials. For example, clinical trials for Alzheimer's disease (aducanumab) of which only 0.6 percent of participant were black people and the recent controversy over the lack of diversity in COVID-19 vaccines highlighted the ongoing gap in clinical trials across disease domains [35]. There is a risk that potential negative aspects of health and economics outcomes may emerge from the lack of phase 3 clinical trials with diversity.

This study has a several limitations and suggests future studies. First, this study did not conduct qualitative analysis and consider structural model. Although this study was conducted from a quantitative point of view to overcome the limitations of previous qualitative case studies, ultimately a qualitative analysis needs to be added. Field studies from a microscopic point of view will be able to supplement the results derived from statistical analysis in detail. Furthermore, structural model including latent variables in addition to the explanatory variables in this study can be considered. The structural relationship between these factors makes it possible to distinguish between direct and indirect factors, which can lead to richer interpretations.

Second, a more meaningful analysis of success factors may be possible by analyzing the characteristics of each organization type through additive study, such as survey, of clinical trial success factors that were not covered in this study. The value chain of the biopharmaceutical industry has recently been fragmented. In past, organizations related to biopharmaceutical industry tried to integrate more functions on the value chain but they are concentrating on core capacity nowadays. Active collaboration network through open innovation catalyze this phenomenon. In particular, at a time when the importance of contract research organization (CRO) is highlighted due to the decline in R&D productivity in the global biopharmaceutical industry [36], an additional analysis of the relationship between cooperation between pharmaceutical companies and CRO and the success of clinical trials can be analyzed.

Third, since the data in this study are from controlled clinical trials, they do not accurately provide implications for clinical research in the real world. Recently, efforts have been made to derive clinical evidence using real world data (RWD), and it is expected that various problems such as securing subjects in clinical trials and lack of control groups, post-approval follow-up will be resolved [37, 38]. For example, if more data related to clinical trials to use artificial intelligence (AI) such as machine learning can be used, a clinical trial execution strategy suitable for each organization's situation could be developed. AI can select proper patients for disease-related clinical trials, and AI can also design future clinical trial plan [39]. If it is

hard to set a control group, it can be set in an externally controlled or matched manner with RWD. It has the potential to fill the evidence gap that randomized control trials (RCT) in clinical trials has not solved [40].

Fourth, since the outcome indicators of clinical trials are expanding not only to health effectiveness but also to the quality of life aspects, and clinical trials using smart devices are also increasing starting with digital transformation revolution and COVID-19, it should be considered to discover additional explanatory variables in these circumstances. Indicators related with quality of life in clinical trial, should be about patient-centeredness and take into account the patient's habits, environments, and social determinants (e.g., income, occupation, housing, education, welfare, safety) [41]. In addition, on only objective metrics, but also awareness of changes from the past to the present about health in terms of subjective perception of patients, and expectations for the future are used as indicators of clinical trials.

On the other hand, the trend of clinical trials is moving from testing institution leading, face-to-face, on-site monitoring and passive patients to on-line process based, un-tact, remote-monitoring and active patients [33]. COVID-19 had also catapulted digital transformation of clinical trials, and this change brought the born of decentralized clinical trials (DCT). Inconvenience of mobility to clinical trial institute makes 40% of patient terminate clinical trials [42]. DCT minimize visit of patient, so retention rate can be improved. The role of patients on DCT process may be certainly differed from the traditional clinical trials [43, 44]. Therefore, the discovery of indicators considering these new trends in clinical trials should be added in future studies.

Author Contributions

All authors contributed to the design of this study and participated to the interpretation of the results. EK and KS prepared the datasets for analysis. SP and JY performed the analyses. EK, JY and KS drafted the manuscript.

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Declarations

Conflict of interest

The authors declare no conflict of interest.

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