

# General Characteristics and Reasons for the Discontinuation of Drug Clinical Trials in Mainland China

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## Research article

**Keywords:** Clinical trials, Discontinuation, Drug Trial Registration and Information Publication Platform, China

**Posted Date:** December 21st, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-131119/v1>

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**Version of Record:** A version of this preprint was published at BMC Medical Research Methodology on November 13th, 2021. See the published version at <https://doi.org/10.1186/s12874-021-01443-2>.

# Abstract

**Background:** Although discontinuation is common in clinical trials, no study has been conducted to analyse the current situation and reasons for the suspension or discontinuation of drug clinical trials in China. This study aims to analyse the general characteristics and reasons for the discontinuation of registered clinical trials in mainland China and to identify the associated factors.

**Methods:** Trials with a status of terminated or stopped in the Drug Trial Registration and Information Publication Platform before March 31, 2020, were classified as discontinued trials and included in the analysis. Information related to researchers, studied drugs, the trials and the reasons for discontinuation were recorded. Fisher's exact and  $\chi^2$  tests were used to examine the associations of trial characteristics with different issues related to trial discontinuation.

**Results:** Three hundred and twelve discontinued trials were included in this study. The studied drugs were mainly chemical drugs [229 (73.4%)]. The indications of the studied drugs were mainly neoplasms [77 (24.7%)]. The study type was mainly bioequivalence studies [97 (31.1%)]. More than half [177 (56.7%)] of the trials were discontinued because of trial issues, among which the main causes were negative results [69 (22.1%)], protocol issues [41 (13.1%)], and poor recruitment [35 (11.2%)]. Ninety-five (30.4%), 15 (4.8%) and 26 (8.3%) trials were discontinued because of sponsor issues, research centre issues and administration issues, respectively. Study design, blinding status, number of centres, planned sample size and whether participants had been enrolled may have been associated with one to three of the issues related to trial discontinuation.

**Conclusions:** Discontinuation of clinical trials was commonly due to trial issues, sponsor issues, research centre issues and administration issues, such as negative results, and protocol issues. Study design, the number of centres, and sample size may be related to the discontinuation of trials. Careful study designs, smart business decisions, sufficient preparation of supplies such as the research drugs, and whether research centres have enough availability and patients are factors that should be considered before conducting trials.

## Background

The supply of drugs in mainland China had been affected by the so-called drug lag that occurred prior to 2013, mainly due to the backlog of applications and delays in the approval process. However, in recent years, particularly since 2015, a series of measures have been taken to promote drug development, speed up the review and approval process, and transform it from strict entry and tolerant exit (i.e., it was difficult to obtain approval for clinical trials but easy to obtain marketing authorization) to tolerant entry and strict exit<sup>[1–3]</sup>. In 2018, the approval of clinical trials changed from the so-called "nodding system" to the "shaking system". If the applicant does not receive any negative or doubtful opinions from the Drug Evaluation Center (CDE) of the National Medical Products Administration (NMPA) within 60 days of application acceptance, the drug clinical trials can be carried out according to the submitted scheme<sup>[4]</sup>.

This will improve the efficiency of clinical trials, but pharmaceutical companies should be more cautious in conducting clinical trials. Stopping the trial halfway due to uncontrollable risks or any subject non-compliance behaviour will have a considerable impact on the companies.

Discontinuation is common in clinical trials, and it is estimated that more than \$240 billion is wasted on discontinued clinical trials in the world every year<sup>[5]</sup>. Recruitment might be a major cause of discontinuation; in Switzerland <sup>[6]</sup>, 26% of randomized controlled trials (RCTs) were discontinued due to slow recruitment. Studies based on the RCTs registered in ClinicalTrials.gov showed that approximately 32% of trial discontinuations were due to patient recruitment issues <sup>[7]</sup>, and recruitment problems were the most common cause of trial discontinuation in paediatric RCTs <sup>[8]</sup>. Trial discontinuation may lead patients to receive unnecessary treatment interventions, cause ethical controversy, and waste financial resources <sup>[6–9]</sup>. Additionally, discontinued trials are more likely to remain unpublished than completed trials<sup>[10, 11]</sup>. Despite these serious concerns, few studies have examined the problem of clinical trial discontinuation, and no study has analysed the current situation and reasons for suspension or discontinuation of drug clinical trials in China. Considering the improvement of drug supervision and management policies in recent years, it is important to analyse the characteristics and reasons for trial discontinuation in China and provide a basis for consideration of related countermeasures and reducing resource waste.

In 2012, the CDE established a Drug Trial Registration and Information Publication Platform, which is a national authoritative database for clinical trials in China. All drug clinical trials being conducted as registration trials including phase I–IV drug trials and bioequivalence studies must be registered on the platform before enrolment of the first patient, and the NMPA is responsible for the validity and integrity of the data<sup>[12]</sup>. Publicly accessible information in the platform includes trial status, sponsor, study design, and study institutions. For clinical trials stopped or terminated due to different reasons, trial status and the corresponding reason is recorded. Thus, we analysed the general characteristics and reasons for all the discontinued clinical trials registered on the platform to provide an up-to-date and comprehensive profile of clinical trial discontinuation in mainland China and to identify the causes and associated factors.

## Methods

### Data source

To strengthen the supervision and management of drug clinical trials, promote the openness and transparency of drug clinical trial information, and protect the rights, interests and safety of subjects, the NMPA in China established the web-based Drug Trial Registration and Information Publication Platform database, and it was officially released in 2013. Industry sponsors approved to conduct clinical trials must complete registration on the platform before the enrolment of the first patient, and the NMPA routinely cross-checks the information on the platform with the related data and summary report

submitted with a given trial to ensure that the information remains accurate and up to date. All clinical trials were identified and classified by trial status with categories listed in the database including "Ongoing", "Completed", "Terminated", and "Stopped". Terminated trials were defined as trials that were halted by the sponsor for different reasons (for example, negative results, security issues, lack of funding) but that may start again, and stopped trials were defined as trials that were halted by the drug administration department. In this study, we classified the terminated trials and stopped studies as discontinued trials.

## Trial screening and data extraction

Trials registered on the Drug Trial Registration and Information Publication Platform (chinadrugtrials.Org.cn) through March 31, 2020, were screened for inclusion; terminated trials and stopped trials were included as discontinued trials, ongoing trials and completed trials were excluded, and trials with registration errors were excluded. Two authors reviewed the full information of all the included trials and extracted study characteristics, and any disagreements were resolved through discussion or by consulting the third author. The following trial information was recorded:

1. Information related to researchers: the first affiliation and geographical location of the principal investigator (north, east, south, central, northeast, northwest, or southwest).
2. Information related to the studied drugs: type of drugs (chemical drugs, traditional Chinese drugs, biological drugs and others) and indications; in this study, the indications of the studied drugs were coded according to the International Statistic Classification of Diseases and Related Health Problems, Tenth Revision, International Classification of Diseases (ICD)-10 classification<sup>[13]</sup>.
3. Information related to the trial: study phase, date of first ethical approval, date of discontinuation, study design, randomization status, blinding status, single-centre or multi-centre trial design, control types, planned sample size, whether participants had been enrolled, whether a data monitoring committee (DMC) had been establish, whether insurance had been purchased for participants.
4. Reasons for trial discontinuation: reasons for discontinuation were categorized as trial issues, sponsor issues, research centre issues and administrative issues.

## Statistical analysis

Descriptive analyses were used to summarize the data, and the number (%) was used for qualitative variables. A simple regression model was used to analyse the trends in the number of discontinued trials, The chi-square test was used for proportions and to compare difference among subgroups; if there were  $n < 5$  trials in a category, Fisher's exact test was used. A significant difference between groups was indicated by a p-value of  $< 0.05$ . All statistical analyses were performed on a personal computer with the statistical package SPSS for Windows (version 22.0).

## Results

## General characteristics of discontinued trials in mainland China

A total of 10234 drug clinical trials were registered on the Drug Trial Registration and Information Publication Platform as of March 31, 2020. Among the registered trials, 316 were recorded as terminated, no trials were stopped by the administration department, and 4 terminated trials due were excluded due to registration errors. Thus 312 (3.0%) discontinued trials were selected for inclusion and data analysis (Fig. 1). After data collection, we found that more than half [181(58.0%)] of the trials did not record the date of termination. In this study, we recorded the date of first ethical approval of the trials as the trial year and calculated the annual number. The first ethical approval date of the trials ranged from July 19, 2004 to November 5, 2019. The annual number of discontinued trials increased significantly over time, with an average annual growth rate of 23.6% ( $p = 0.000$ ). A notable increase occurred in 2017 with 64 trials discontinued, corresponding to an increase of 266% relative to the number of trials initiated in 2016 (Fig. 2). The majority of the studied drugs were chemical drugs [229(73.4%)], followed by traditional Chinese drugs [57(18.3%)] and biological drugs [26(8.3%)] (Fig. 2). Regarding the geographical location of the principal investigator, the trials were carried out in 24 different cities and were mostly in north and east China (Fig. 3), as most clinical trials in China are carried out in these regions. The distribution of the indications for the studied drugs is shown in Fig. 4. Bioequivalence studies accounted for the largest proportion [97(31.1%)] of the studies, followed by phase III trials (86[ 27.6%]), phase II trials (52 [16.7%]), phase I trials [48 (15.4%)], and phase IV trials [4 (1.3%)]. The remaining 25 trials were studies on safety/efficacy and pharmacokinetics/pharmacodynamics of new drugs without a definitive phase (Fig. 5). Other general characteristics of the 312 discontinued clinical trials are shown in Table 1. Further retrieval and trial information analysis found that 90 trials restarted and re-registered, and 42 of those trials had enrolled participants.

Table 1  
General characteristics of 312 discontinued clinical trials in China

Characteristic	n, (%)
<b>Research institute</b>	
Tertiary hospital	285 (91.3)
Secondary hospital	5 (1.6)
Scientific research institutions	4 (1.3)
other	18 (5.8)
<b>Study design</b>	
Parallel assignment	169 (54.2)
Crossover assignment	109 (34.9)
Single group assignment	34 (10.9)
<b>Randomization status</b>	
Randomized	282 (90.4)
Non-randomized	30 (9.6)
<b>Blinding status</b>	
Open label	178 (57.1)
Single blind	13 (4.2)
Double blind	121 (38.8)
<b>No. of centers</b>	
Single-center trial	142 (45.5)
Multiple-center trial	170 (54.5)
<b>Control type</b>	
Active drug	154 (49.4)
Placebo control	105 (33.7)
Blank control	2 (0.6)
Uncontrolled	51 (16.3)
<b>Planned sample size</b>	

Abbreviations: DMC, data monitoring committee.

<b>Characteristic</b>	<b>n, (%)</b>
< 100 participants	156 (50.0)
100–499 participants	106 (34.0)
> 500 participants	37 (11.9)
Unclear	13 (4.2)
<b>Has enrolled participants</b>	
Yes	135 (43.3)
No	177 (56.7)
<b>DMC has been establish</b>	
Yes	53 (17.0)
No	259 (83.0)
<b>Insurance has been purchased</b>	
Yes	151 (48.4)
No	161 (51.6)
Abbreviations: DMC, data monitoring committee.	

## Reasons for trial discontinuation

Reasons for discontinuation of the trials are shown in Table 2. In total, we identified 15 different reasons for discontinuation which were classified into four categories: trial issues, sponsor issues, administrative issues and research centre issues. Trial issues were the leading cause of discontinuation, and the most common reason was negative results [69(22.1%)]. Negative results were mostly due to the disappointing interim results for the study drug and results of fasting tests not meeting expectations. Protocol issues were mainly related to an unreasonable clinical trial protocol the need for protocol revisions. The main reasons for poor recruitment were slow enrolment of subjects, strict inclusion and exclusion criteria, and low incidence of subjects. Security issues were mainly drug-related adverse effects or serious adverse event (leading to death) in the subjects. The main reason for quality issues was because the sponsor carried out self-inspection and verification of the trial with reference to the Key Points for On-site Verification of Drug Clinical Trial Data released by NMPA on November 10, 2015 <sup>[14]</sup>, and judged that the trial was unlikely to pass the NMPA's on-site verification and review.

Table 2  
Reasons for discontinuation of 312 clinical trials in China

Reasons	n, (%)
<b>Trials' issues</b>	<b>177 (56.7)</b>
Negative results	69 (22.1)
Protocol issues	41 (13.1)
Poor recruitment	35 (11.2)
Security issues	21 (6.7)
Quality issues	9 (2.9)
Poor compliance of volunteers	2 (0.6)
<b>Sponsors' issues</b>	<b>95 (30.4)</b>
Company/business decision	68 (21.8)
Insufficient preparation	11 (3.5)
Inadequate supplies/lack of study drug	9 (2.9)
Lack of funding	7 (2.2)
<b>Research centres' issues</b>	<b>15 (4.8)</b>
Schedule was too full	11 (3.5)
Experimental conditions failed to meet the requirements	2 (0.6)
Poor management ability of the principle investigator	2 (0.6)
<b>Administration issues</b>	<b>26 (8.3)</b>
Update of relevant regulations	23 (7.4)
Trials were exempted	3 (1.0)
<b>No reason given</b>	<b>5 (1.6)</b>
Note that some trials cited multiple reasons for discontinuation and as a result have been coded multiple times.	

Company/business decisions were the main sponsor issues and were mainly due to the company's research and development strategy changing or the market prospects of the studied drug not being wide enough. Insufficient preparation was mainly related to the biological sample testing company being unable to complete the planned sample testing or the partner of the producer or the reference product not qualifying as the national announcement. In terms of research centre issues, the most common reason for trial discontinuation was because the schedule of the centre was too full [11(3.5%)], as the principal



investigators conducted too many trials simultaneously or were unable to conduct bioequivalence trials due to full schedule of the phase I trial ward. Additionally, poor management ability of the principle investigator and the laboratory testing items of the research centre not being certified by external quality assessment were also reasons for discontinuation. For administration issues, updates to some relevant regulations led to discontinuation of 23 clinical trials. In addition, 11 trials were terminated according to the DMC's suggestions, and the main reasons were that the risk to the participants involved in the trial outweighed the benefits and the statistical results showed that the main therapeutic indexes could not be achieved. For the 90 trials that had restarted and re-registered, the most common reason for discontinuation was trial issues [67.8% (61/90)] mainly due to protocol issues [35.6% (32/90)]. For the other 222 trials that had not restarted, the most common reason for discontinuation was trial issues [50.9% (113/222)] mainly due to negative results [24.8% (55/222)].

The number of neoplasm drug trials in mainland China grew remarkably over the years studied herein, and improving outcomes of patients with neoplasms by encouraging biopharmaceutical research and development has become a government priority all over the world, including in China <sup>[15]</sup>. In our study, neoplasm drug trials accounted for the largest number of discontinued trials. Thus, we further explored the reasons for discontinuation in neoplasm clinical trials and found that the majority were trial issues (74.0%) including negative results, poor recruitment, clinical trial protocol issues and security issues (Fig. 6).

### **Influencing factor analysis for trial discontinuation**

Analysis of the association of trial characteristics and the different reasons related to trial discontinuation are shown in Table 3. Compared with parallel trials and single-group trials, crossover design trials showed a significantly higher rate of trial discontinuation associated with research centre issues. The crossover design of clinical trials is thought to have some methodological advantages; however, it may be more prone to problems when the data are incomplete or improper analysis methods are used <sup>[16, 17]</sup>. Thus, researchers should pay special attention when carrying out crossover design trials. In addition, open-label trials also showed a significantly higher rate of trial discontinuation associated with research centre issues, as most of the open-label trials were bioequivalence trials and phase I trials. Research centre issues, such as whether the schedule of the centre is too full, should be considered before starting the trials.

Table 3  
Association of trial characteristics with different issues that related to trial discontinuation

Items	Trials' issues	Sponsor's issues	Research centers' issues	Administrative issues
<b>Study design</b>				
Parallel assignment (n = 169)	100(59.2%)	49(29.0%)	4(2.4%)	13(7.7%)
Crossover assignment (n = 109)	54(49.5%)	32(29.4%)	11(10.1%)	12(11.0%)
Single group assignment (n = 34)	20(58.8%)	11(32.4%)	0(0)	1(2.9%)
<i>p</i>	0.268	0.925	0.006	0.300
<b>Blinding status</b>				
Open label (n = 178)	98(55.1)	50(28.1%)	14(7.9%)	14(7.9%)
Single blind (n = 13)	7(53.8%)	4(30.8%)	0(0)	1(7.7%)
Double blind (n = 121)	69(56.6%)	38(31.1)	1(0.8%)	11(9.0%)
<i>p</i>	0.935	0.822	0.014	0.928
<b>No. of centers</b>				
Single-center trial (n = 142)	70(49.3%)	47(33.1%)	10(7.0%)	14(9.9%)
Multiple-center trial (n = 170)	104(61.2%)	45(26.5%)	5(2.9%)	12(7.1%)
<i>p</i>	0.035	0.201	0.092	0.373
<b>Planned sample size*</b>				
< 100 participants (n = 156)	58(37.2%)	34(21.8)	4(2.6%)	9(5.8%)
100–499 participants (n = 106)	28(26.4%)	6(5.7%)	0(0)	1(0.9%)
> 500 participants (n = 37)	7(18.9%)	5(13.5%)	0(0)	1(2.7%)
<i>p</i>	0.042	0.002	0.256	0.091
<b>Has enrolled participants</b>				
Yes (n = 135)	96(71.1%)	20(14.8%)	1(0.7%)	10(7.4%)
No (n = 177)	78(44.1%)	72(40.7%)	14(7.9%)	16(9.0%)
<i>p</i>	0.000	0.000	0.003	0.605

Items	Trials' issues	Sponsor's issues	Research centers' issues	Administrative issues
<p>* We excluded trials that did not state planned sample size.</p> <p>Note that some trials cited multiple reasons for discontinuation and as a result have been coded multiple times.</p>				

Multicentre trials showed a significantly higher rate of trial discontinuation associated with trial issues. It is known that heterogeneity among subject characteristics, clinical practice and management requirements in different centres can lead to heterogeneous interpretations of research results, which is called the centre effect. When the results show serious centre effects, the evidence regarding effectiveness and safety is unreliable<sup>[18]</sup>. Electronic management systems such as clinical trial management systems and electronic data capture help improve the efficiency and accuracy of management, improve the timeliness of data collection, and make the information exchange and sharing between centres more convenient in the implementation stage<sup>[19]</sup>.

Trials with sample sizes of less than 100 participants showed a significantly higher rate of trial discontinuation associated with trial issues and sponsor issues. Unsurprisingly, poor recruitment was the most common reason for trial discontinuation<sup>[20, 21]</sup>. Trials with limited numbers of patients, such as rare disease trials or those with a sample that is too small for meaningful analysis, consume financial and material resources, and the competitiveness of the sponsors should be considered.

Compared with trials that had not enrolled participants, trials that had enrolled participants showed a significantly higher rate of trial discontinuation associated with trial issues and a lower rate of trial discontinuation associated with sponsor issues and research centre issues. Identifying potential problems before starting clinical trials is very important for success of the trials. In this study, we found that 135 trials had enrolled participants before discontinuation, and this may lead to more waste of human and financial resources and related patient safety issues.

## Discussion

Trial registration can be useful to increase transparency of clinical trial results<sup>[22, 23]</sup>. In this study, we provided an up-to-date and comprehensive profile of the discontinued clinical trials in mainland China and identified the reasons and associated factors based on the national authoritative database of registration trials. More than half [177 (56.7%)] of trials were discontinued because of trial issues, and the main reason was negative results [69 (22.1%)]. Carefully considering potential discontinuation related to negative results, poor recruitment, protocol issues, security issues, and inadequate supplies/lack of study drug is important to avoid wasting resources. It is also important to assess the management ability of the principle investigator and the schedule or the ability to take on trials at the study centre.

Previous studies showed that low recruitment is a known barrier to successful completion of clinical trials including oncological clinical trials, while it is also difficult for oncology patients to find an appropriate trial<sup>[24, 25]</sup>. In this study, we found that negative results and poor recruitment were the most common reasons for oncological clinical trial discontinuation. Failure to meet the planned sample size within the initial expected time frame may eventually result in early trial discontinuation, which could trigger feelings of frustration for researchers and participants and the scarce resource of patients being underutilized<sup>[26]</sup>. Improving clinical trial recruitment is an understudied challenge for clinical research.

DMC is an independent expert panel that regularly reviews the data as the trial progresses, serving an important role in safeguarding the interests of research participants and ensuring trial integrity<sup>[27]</sup>. If there are serious safety concerns or poor efficacy during the clinical trial, DMC will assist the sponsor in making decisions, such as whether to terminate the trial early<sup>[28]</sup>. Trials with large sample sizes, multicentre trials, trials including vulnerable participants or complex designs and trials with long observation periods typically require a DMC<sup>[29]</sup>. In this study, we found that only 17.0% of trials established a DMC; among those trials, 20.8% were terminated based on DMC's suggestions. In 2019, CDE of China issued the "Guideline on Clinical Trial Data Monitoring Committees (Draft for Public Review)" to guide the establishment of DMCs and facilitate their full use. In the future, DMCs will play an increasingly important role in clinical trials in China<sup>[30]</sup>.

Maintaining subject safety, ensuring the authenticity, reliability, and integrity of the trial data, and accelerating the process of drug development are the biggest concerns for regulators. On September 21, 2015, the China Food and Drug Administration issued some policies to strengthen the clinical trial data self-inspection and verification. If the sponsors responsible for drug registration found that the clinical trial data was untrue or incomplete after self-inspection, they could withdraw the registration application within an indicated time frame<sup>[4]</sup>. This marks a new change of data verification in a comprehensive way, which is of great significance for improving the quality of clinical trials and standardizing industry standards. In this study, we found that 60.3% (188/312) of the trials were discontinued after 2015, showing that the formulation of relevant policies had promoted further standardization of clinical trials. In 2019, the CDE issued "General Risk Management and Work Procedures of Suspension and Termination in the Process of Drug Clinical Trials (Draft for Comment)", emphasizing the risk management of clinical trials and the criteria, conditions and procedures for suspension of clinical trials. For example, when there is a large safety risk in the clinical trial according to the dynamic risk assessment results, the trial can be suspended immediately by CDE<sup>[31]</sup>. The clinical trial could be placed on hold, and the hold could also be lifted or transferred into inactive status, thus protecting the health and rights of improving review efficiency. Recently, the NMPA issued an updated "Quality Management Standards for Drug Clinical Trials", further emphasizing the management of termination or suspension of clinical trials<sup>[32]</sup>. Although the experience of these policies is relatively new, most potential clinical trial suspensions can be avoided through early communication and discussion between the regulators and the sponsors.

To answer the pre-specified scientific questions, it is important to ensure that the trial will not be prematurely discontinued; however, trials shown to be invalid should obviously be discontinued. According to our analysis, the following aspects should be considered in the planning and implementation stage: 1) the sponsors and researchers should carefully design the study to ensure the feasibility of the clinical trial <sup>[33]</sup>, and pretesting or simulating the trial is often necessary, 2) the sponsors should identify preventive measures and a quality management plan based on the anticipated possible risks, 3) the sponsors should ensure that sufficient material and human resources are available to achieve the proposed goals <sup>[22]</sup> by assessing the production of research drugs and capacity of research centres, 4) the sponsors should ensure that research centres are able to enrol enough subjects according to the trial protocol within the agreed period of time and ensure that there is sufficient time to implement and complete clinical trials, 5) before obtaining informed consent, the researcher should give the subject or guardian sufficient time and opportunity to understand the details of the clinical trial, answer questions raised by the subject or the guardian in detail, and strengthen the communication with the subjects during the trial to ensure the compliance, 6) the sponsor must stop trials in a timely manner when an unsolvable problem is encountered.

## Conclusions

Due to trial issues, sponsor issues, research centre issues and administration issues such as negative results and protocol issues, discontinuation of clinical trials was common. The study design, number of centres, and sample size may be related to trial discontinuation. Careful study design and business decisions, sufficient preparation of supplies such as the research drugs, and the capabilities and availability of research centres should be considered before conducting the trials. Efficiently answering clinical questions with limited resources requires further effort; ensuring effective policies and effective communication between the sponsors and the regulators and between the sponsors and research centres are definitely important.

## Abbreviations

CDE: Center for Drug Evaluation; NMPA: National Medical Products Administration; RCTs: Randomized Controlled Trials; DMC: Data Monitoring Committee.

## Declarations

### Acknowledgements

The authors are indebted to the Wei Zhao from Shan Dong University for his helpful advice on manuscript writing and to the information center engineers for their help in creating the figure of the manuscript. Also, we would like to thank all our participants for participating in the study and sharing their experiences.

## Authors' contributions

LS, BNH and MLA conceived and designed the study. BNH, MLA and NGY performed searches and extracted the relevant data. YL and YTJ verified the data. LS, YTJ and BNH analysed the data and wrote the paper. All authors contributed to the interpretation of study data, revised the paper critically for content and approved the final version.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Availability of data and materials

The data of drug clinical trial discontinuation from the Drug Trial Registration and Information Publication Platform are publicly available.

The datasets analysed during the current study are available in the Drug Trial Registration and Information Publication Platform under:

<http://www.chinadrugtrials.org.cn/index.html>: Click "Advanced Query" and select "Terminated" and "Stopped" in the "Experiment Status" drop-down box.

## Ethics approval and consent to participate

Not Applicable.

## Consent for publication

Not Applicable.

## Competing interests

None.

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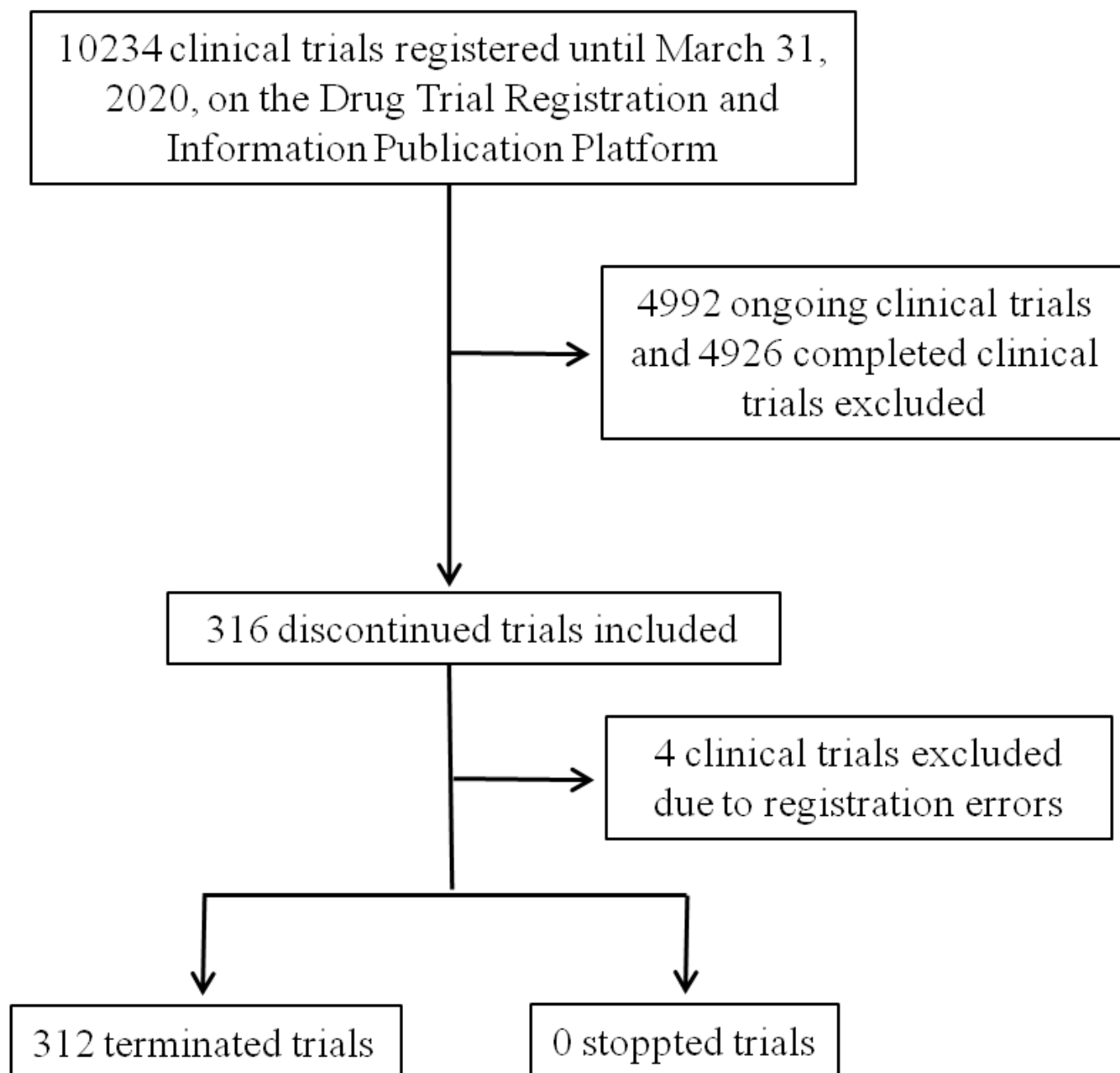
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## Figures



**Figure 1**

Flow chart of trial inclusion.

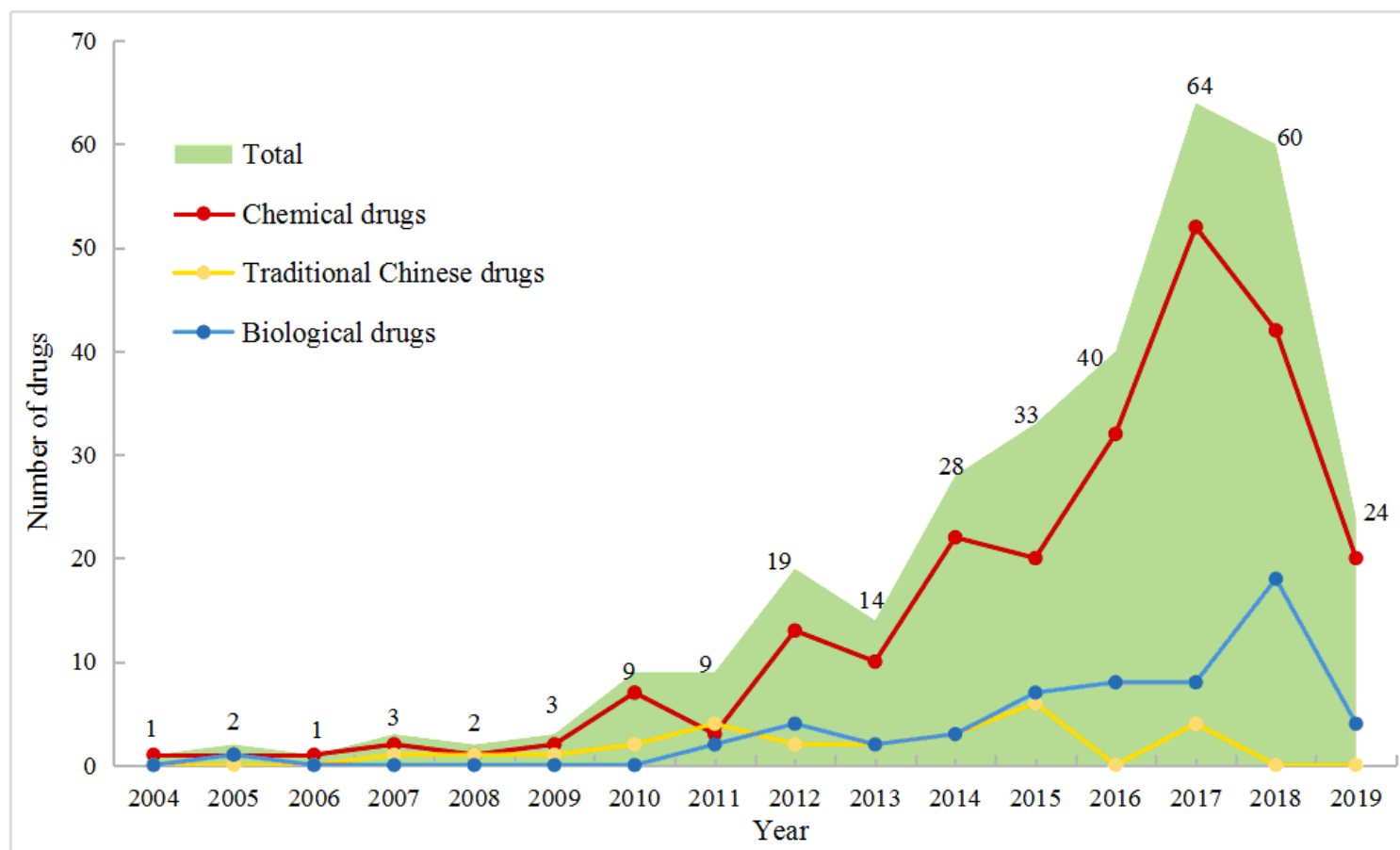


Figure 2

Annual number of discontinued trials registered on the Drug Trial Registration and Information Publication Platform in mainland China.

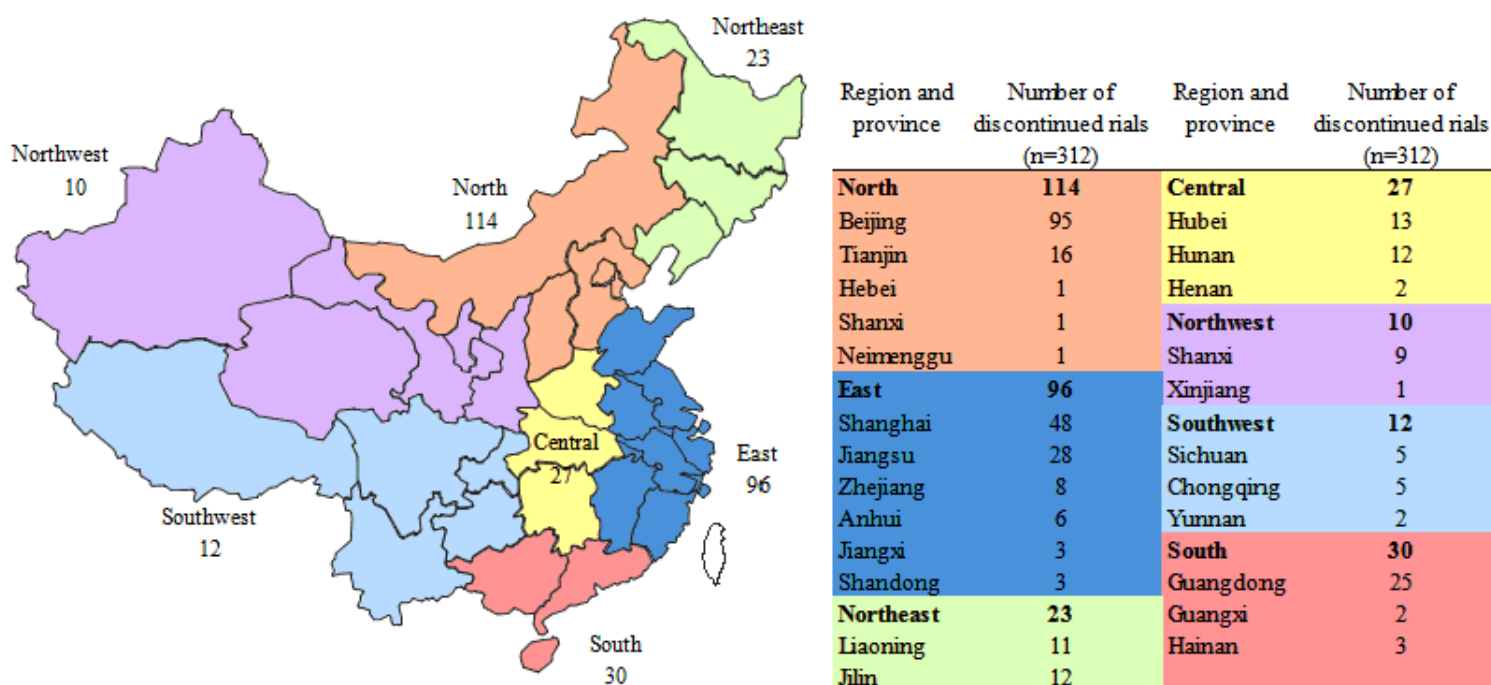


Figure 3

Geographical distribution of discontinued trials registered on the Drug Trial Registration and Information Publication Platform in mainland China. (the map depicted in figure 3 was created by our engineers from information center) Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

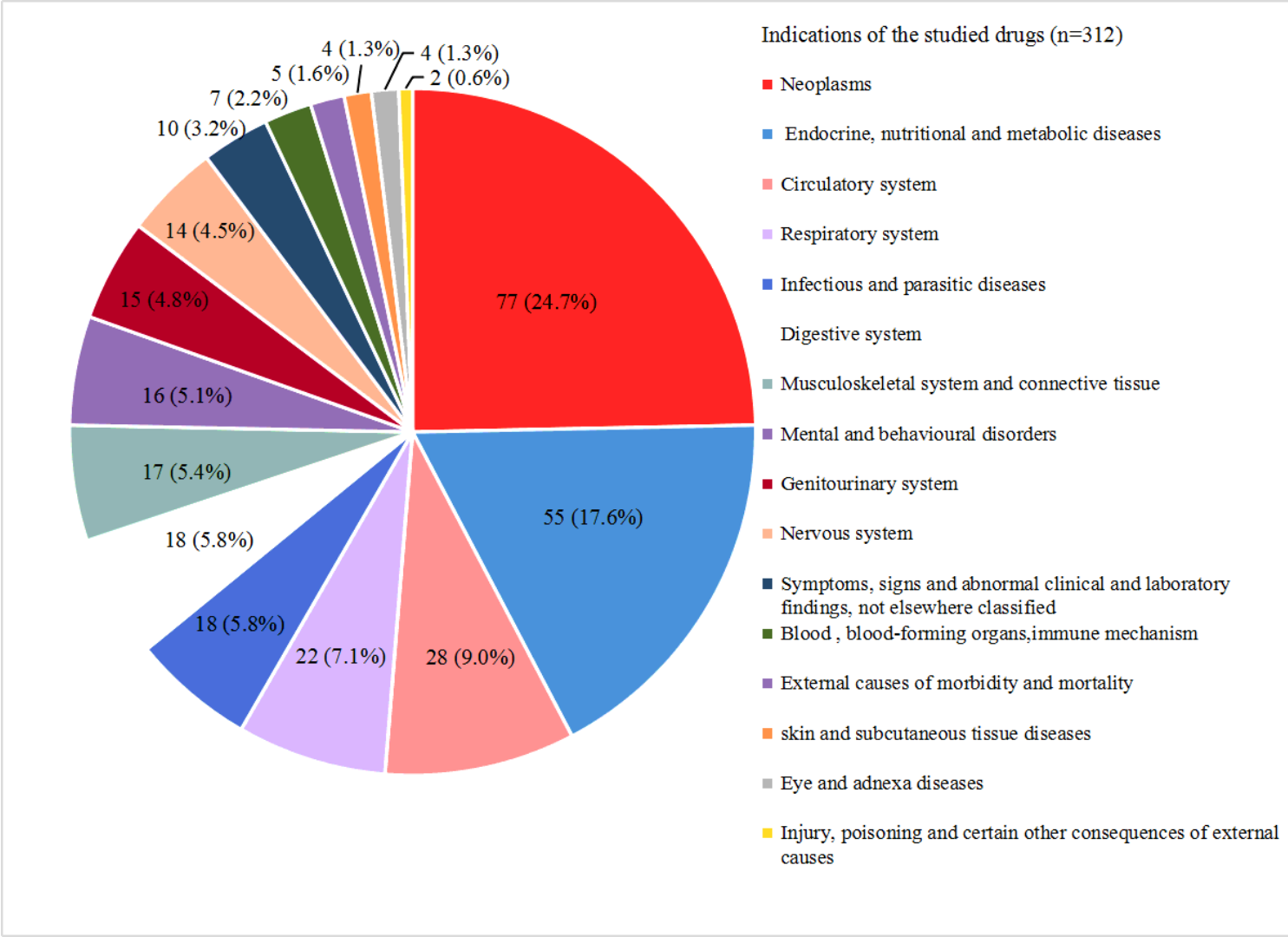
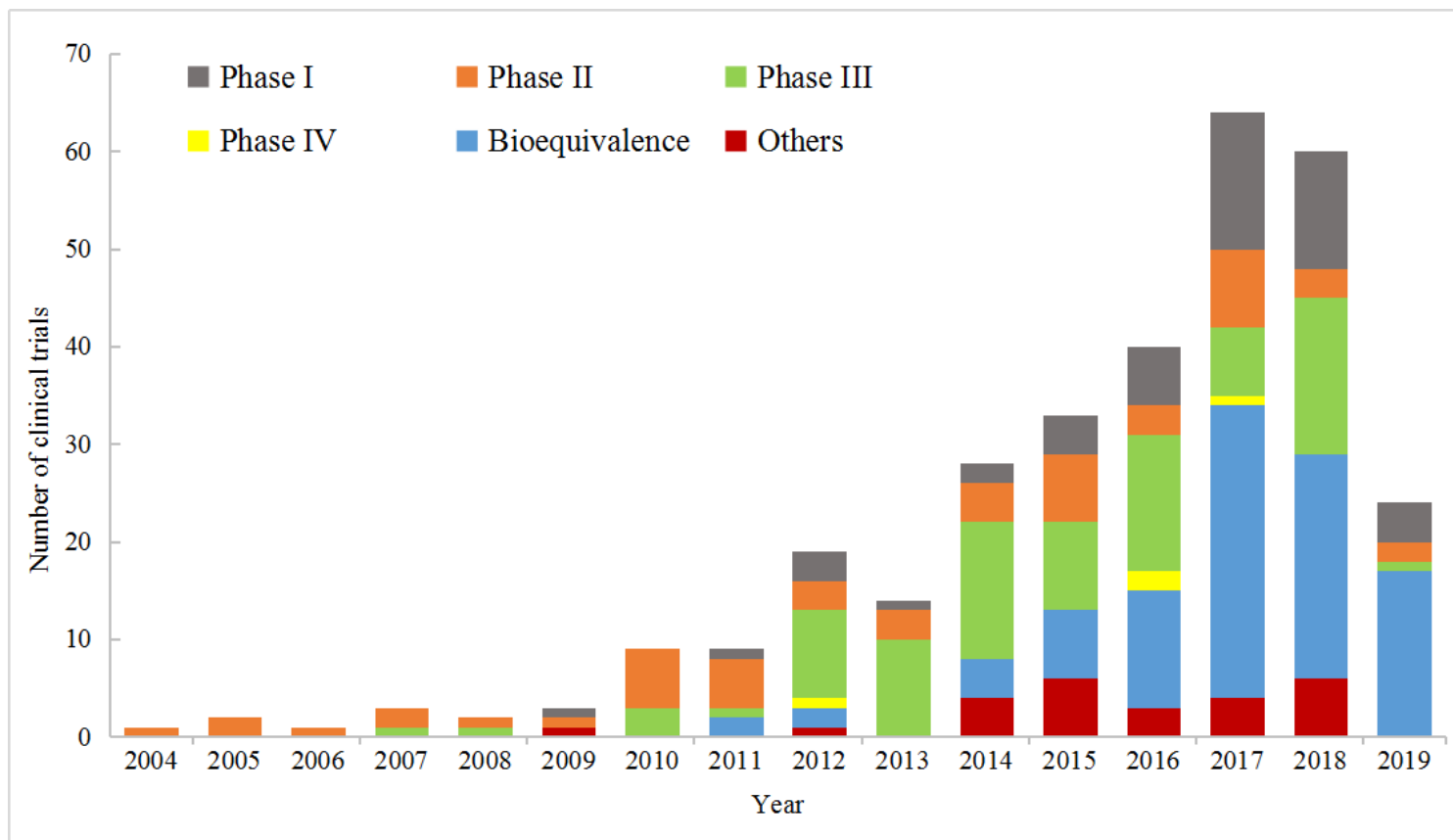


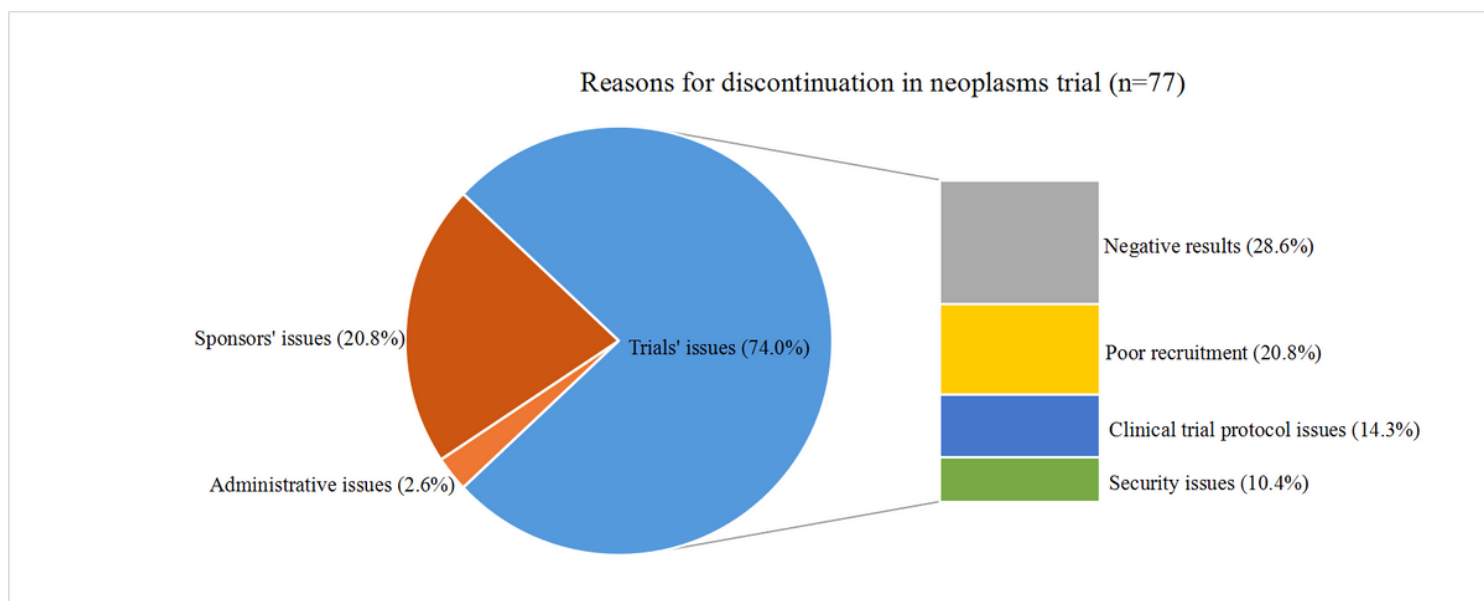
Figure 4

Distribution of indications of the studied drug registered on the Drug Trial Registration and Information Publication Platform in mainland China.



**Figure 5**

Annual numbers of discontinued trials by study phase registered on the Drug Trial Registration and Information Publication Platform in mainland China.



**Figure 6**

Reasons for discontinuation in neoplasm trials.