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·临床研究·

# 基于ClinicalTrials. gov和ChiCTR数据库对牙体牙髓病的临床试验注册特点分析

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**【摘要】　目的**　汇总注册于美国ClinicalTrials.gov和中国临床研究注册中心（Chinese Clinical Trial Registry，ChiCTR）的牙体牙髓病临床注册资料，分析牙体牙髓病临床试验的注册特征。**方法**　通过检索2000年1月1日至2023年8月20日期间在两个数据库中注册的牙体牙髓病临床研究，提取并分析牙体牙髓病相关临床研究的信息，提取的内容包括注册地区、注册年度、试验题目、研究方向、样本量、试验进展、研究类型、试验设计、盲法、临床试验分期和参与机构名称等信息。**结果**　两个数据库中临床研究的总注册数为536 191项，其中牙体牙髓病的临床研究共634项；涉及到43个国家，排名前三的分别是埃及（188项）、中国（130项）和美国（46项）；2015年开始牙体牙髓病临床研究注册数量显著增加；研究方向以牙髓病（434项）、龋病（106项），根尖周病（77项）为主，内容主要涉及到病因学、药物干预、外科干预、新技术、新材料等方面；临床试验样本量＜100例的临床研究有430项（67.82%），样本量为100～999例的有185项（29.18%）；注册时的研究进展状态为已完成试验的项目数最多，有286项（45.11%），其次是未知项（125项）、招募中（110项）、尚未招募（81项）；研究类型主要是干预性研究546项，占86.12%，以随机平行对照设计方式为主要设计模式（473项，74.61%）；研究设计类型中使用盲法的有423项（66.72%），其中以双盲为主（195项），其次是其他/未注明情况（123项，19.40%），开放性研究（88项，13.88%）；临床分期中标记为其他/未标记的项目数量最多（388项），其次是Ⅱ期研究（69项）和初步研究（62项）。临床研究参与机构数量＜3的有611项（96.37%），参与机构数量≥3的有23项（3.63%）。**结论**　牙体牙髓病的临床试验注册数量总体呈上升趋势，但仍旧偏少，研究设计的质量有待加强，临床分期的注册信息的完整性有待提高，且多中心临床研究数量较少。今后应充分开展高质量、多中心的临床研究，实现成果的转化。

**【关键词】**　ClinicalTrials.gov；　中国临床研究注册中心；　牙体牙髓病；　龋病；　牙髓病；　根尖周病；　临床研究；　注册
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**Characteristics analysis of clinical trial registration for endodontic diseases based on the ClinicalTrials.gov and ChiCTR databases**

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**【Abstract】　Objective**　To summarize the clinical registration data of endodontic diseases registered in ClinicalTrials.gov in the United States and Chinese Clinical Trial Registry (ChiCTR), and analyze the registration characteristics at home and abroad. **Methods**　We searched the clinical studies related to endodontic disease registered in the two databases from January 1, 2000, to August 20, 2023. We extracted and analyzed the information from clinical studies related to endodontic diseases. The extracted content included information on the registration region, registration year, trial

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title, research direction, sample size, trial progress, study type, trial design, blinding method, clinical trial phase, and participating institutions. **Results**　The two databases contained a total of 536 191 registered items, of which 634 were endodontic diseases. Clinical trials in the registry of endodontic diseases involved 43 countries, of which the top three were Egypt (188 items), China (130 items), and the America (46 items). In addition, the number of registrations of clinical trials on endodontic diseases has significantly increased since 2015. The research directions were mainly pulposis (434 items), caries (106 items), and periapical diseases (77 items), which mostly involved etiology, drug intervention, surgical intervention, new technology, and new materials. Moreover, there were 430 clinical trials (67.82%) with a sample size < 100 and 185 (29.18%) with a sample size of 100-999. The progress status at the time of registration showed the largest number of completed trials, accounting for 286 items (45.11%), followed by unknown (125 items), recruiting (110 items), and not yet recruiting (81 items). The main research types were intervention studies (546 items, 86.12%), and the main design model was randomized parallel controlled trials (473 items, 74.61%). Additionally, 423 items (66.72%) were marked using the blind method, mainly double-blind trials (195 items), followed by other/unmarked (123 items, 19.40%) and open study (88 items, 13.88%). Furthermore, the largest number of items in the study phase were marked other/unlabeled (388 items), followed by phase Ⅱ study (69 items) and preliminary study (62 items). Additionally, 611 items (96.37%) were clinical trials with a number of participating institutions < 3, and 23 items (3.63%) had a number of participating institutions ⩾ 3. **Conclusion**　The number of clinical trials registered for endodontic diseases is generally on the rise, but it is still relatively small. The quality of the study design needs to be enhanced, and the registration information in the study phase needs to be improved. Moreover, the number of multicenter trials is small. In the future, we should fully mobilize the talent advantages of well-known stomatology majors in China, take the lead in conducting high-quality, multi-center clinical research, and realize the transformation of results.

**【Key words】** ClinicalTrials.gov; ChiCTR; endodontic diseases; caries; pulposis; periapical disease; clinical research; registration

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世界卫生组织(WHO)在《全球口腔卫生状况报告》最新的数据显示,全球有35亿人有口腔疾病,约占全球总人数的45%。未治疗的龋齿是最常见的口腔疾病[1],全球约25亿人有龋齿。因此牙体牙髓病已成为口腔疾病预防和治疗的关键问题。临床试验是为发展新的治疗技术的手段之一,因此全世界各国都陆续展开各项临床试验研究[2-4]。临床试验注册可以促进试验方案的设计与实施的公开与透明化,减少潜在的偏倚风险[5],同时可以保障开展临床试验的质量以及结果的可靠性[6],避免不必要的重复研究,还可以加强不同地区学科之间的科研合作[7]。

目前国际上临床试验注册平台有很多,其中美国ClinicalTrials.gov是美国国立医学图书馆(National Library of Medicine,NML)与美国食品与药物管理局(Food and Drug Administration,FDA)在2000年共同创办的用于确保临床试验透明度的数据库[8],是全球临床试验注册数量最多、涉及范围最广的临床试验注册网站[9],同时还可以提供免费的检索服务[10]。中国临床试验注册中心(Chinese Clinical Trial Register,ChiCTR)是于2005年建立,2007年代表中国参加世界卫生组织(World Health Organization,WHO)国际临床试验注册平台的国家临床试验注册中心,被认证为WHO国际临床试验注册平台的一级注册机构,也是国内唯一被WHO认证的一级注册机构。本研究通过检索美国ClinicalTrials.gov和中国ChiCTR数据库,对牙体牙髓疾病的临床注册情况进行全面的特征分析,为牙体牙髓相关疾病研究的开展及管理提供依据。

## 1　资料和方法

### 1.1　检索策略

在ClinicalTrials.gov与ChiCTR数据库中进行全面检索,期限为2000年1月1日至2023年8月20日。在ClinicalTrials.gov数据库中,通过检索功能栏目“Condition or disease”,以关键词“Endodontic

disease”进行检索；在ChiCTR数据库中，通过检索功能栏目“研究疾病名称”，以关键词“牙体牙髓病”“龋病”“根尖周病”“牙本质过敏”“牙髓病”“牙髓炎”“牙髓坏死”“非龋性牙体组织缺损”等进行检索。

1.2　纳入与排除标准

纳入标准：所有与牙体牙髓病相关的临床研究。排除标准：重复注册的临床研究。

1.3　研究筛选和数据提取

本研究由2名人员分别按照纳入和排除标准对已注册的牙体牙髓病临床试验进行信息提取。提取的内容包括注册地区、注册年度、试验题目、研究方向、样本量、试验进展、研究类型、试验设计、盲法、临床试验分期和参与机构名等信息。

## 2　结　果

2.1　牙体牙髓病临床注册区域分布情况

2.1.1　基于ClinicalTrials.gov数据库注册的牙体牙髓病临床试验注册区域分布情况　已注册的临床试验项目共462 813项，其中牙体牙髓病相关研究514项（0.11%），43个国家注册了该疾病的临床试验，埃及牙体牙髓病研究188项（36.58%），排名第一；美国46项（8.95%），排名第二；土耳其45项（8.75%），排名第三，见表1。

2.1.2　基于ChiCTR数据库注册的牙体牙髓病临床试验注册区域分布情况　已注册的临床试验共73 378项，其中牙体牙髓病相关临床试验120项（0.16%），注册区域均为中国，涉及15个省及直辖市，其中北京32项（26.67%）；四川15项（12.50%）；上海14项（11.67%）。其余地区数量分别是广东13项，湖北13项、陕西9项、天津6项、浙江6项、福建3项、江西和江苏各2项，甘肃、云南、新疆、山东、吉林各1项。其中实施组长单位大部分为国内知名大学附属医院，北京大学口腔医院、武汉大学口腔医院、四川大学华西口腔医院、空军军医大学第三附属医院是分列前四，占总数的43.33%。

2.2　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床注册量与时间变化趋势

在两个数据库中未发现重复注册的临床试验，其中ClinicalTrials.gov数据库中注册的中国牙体牙髓病研究有10项。自2015年开始牙体牙髓病临床试验注册量逐渐增长。我国牙体牙髓病的临床试验注册始于2007年，2020年开始注册量明显增多，见图1。

**表1**　基于ClinicalTrials.gov数据库中各国牙体牙髓病的临床试验注册项目的分布情况

Table 1　Distribution of clinical trial registrations for endodontic diseases based on the ClinicalTrials.gov database

| Registered country | Registration number | Proportion (%) | Registered country | Registration number | Proportion (%) |
|---|---|---|---|---|---|
| Egypt | 188 | 36.58 | Syria | 2 | 0.39 |
| America | 46 | 8.95 | Serbia | 2 | 0.39 |
| Turkey | 45 | 8.75 | Norway | 2 | 0.39 |
| Brazil | 36 | 7.00 | Malaysia | 2 | 0.39 |
| India | 33 | 6.42 | Lithuania | 2 | 0.39 |
| Pakistan | 25 | 4.86 | Croatia | 2 | 0.39 |
| Iran | 24 | 4.67 | Finland | 2 | 0.39 |
| France | 11 | 2.14 | Poland | 2 | 0.39 |
| China | 10 | 1.95 | Vietnam | 1 | 0.19 |
| Britain | 10 | 1.95 | Hungary | 1 | 0.19 |
| Jordan | 7 | 1.36 | New Zealand | 1 | 0.19 |
| Italy | 7 | 1.36 | Greece | 1 | 0.19 |
| Spain | 7 | 1.36 | Venezuela | 1 | 0.19 |
| Mexico | 7 | 1.36 | Thailand | 1 | 0.19 |
| Saudi Arabia | 6 | 1.17 | Sudan | 1 | 0.19 |
| Chile | 4 | 0.78 | Slovenia | 1 | 0.19 |
| Singapore | 4 | 0.78 | Rumania | 1 | 0.19 |
| Belgium | 4 | 0.78 | Lebanon | 1 | 0.19 |
| Sweden | 3 | 0.58 | Canada | 1 | 0.19 |
| Germany | 3 | 0.58 | Colombia | 1 | 0.19 |
| Denmark | 3 | 0.58 | Australia | 1 | 0.19 |
| Israel | 2 | 0.39 | | | |

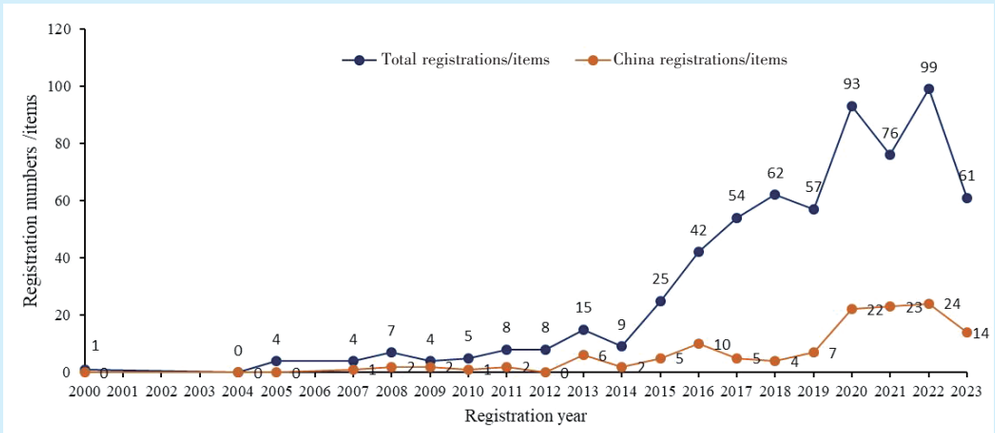
Note: international multicenter studies are included in organizational unit countries

2.3　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验的研究方向

两个数据库数据库共注册的634项牙体牙髓病研究中，研究龋病的有106项，牙髓病434项，根尖周病77项，牙外伤9项，牙慢性损伤3项，牙发育异常3项，牙本质敏感症2项，见图2。

2.4　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床注册的样本量和进展情况

在两个数据中总注册的牙体牙髓病临床试验中，样本量＜100例的临床研究有430项（67.82%），样本量为100～999例的有185项（29.18%），样本量为1 000～10 000例的有11项（1.74%），样本量≥10 000例的有3项（0.47%），样本量未知有5项（0.79%）。在130项中国牙体牙髓病临床试验中，样本量＜100例的有51项（39.23%），样本量为100～999例的有65项（50.00%），样本量为1 000～10 000例的有7项（5.38%），样本量≥10 000例的有3项




The number of registrations of clinical trials on endodontic diseases has significantly increased since 2015. The total registrations were sourced from the ClinicalTrials.gov database and the ChiCTR database on endodontic diseases, and China registrations were obtained from two databases registered by Chinese researchers. The search period was from January 1, 2000, to August 20, 2023

Figure 1　Annual trends in the number of clinical trial registrations for endodontic diseases based on the ClinicalTrials.gov and ChiCTR databases

**图1**　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验注册量与时间变化趋势

(2.31%)，样本量未知的临床研究有4项(3.08%)，见表2。所有牙体牙髓病临床试验注册中，注册时的状态为已完成试验的项目数最多，有286项(45.11%)；其次是未知项125项、招募中(110项)、尚未招募(81项)等。在中国的临床试验注册中，招募中的项目数最多，有60项(46.15%)，其次是未注册(39项)、已完成(25项)，见图3。

2.5　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验研究类型与设计情况

在牙体牙髓病的所有临床注册试验中，干预性研究546项，占86.12%，其中以随机平行对照设计方式为主，占74.61%；观察性研究63项，其他研究25项。中国的注册试验中，干预性研究79项，占60.77%，也以随机平行对照试验设计方式为主，占46.15%；观察性研究26项，以析因、连续入组和队列研究设计为主，见表3。在所有临床试验中，研究设计类型中使用盲法的有423项(66.72%)，其中以双盲为主(195项)；其次是其他/未注明情况(123项，19.40%)，开放性研究(88项，13.88%)。中国的临床试验注册中设计类型主要以其他/未注明为主(85项，65.38%)，其次盲法研究(28项，21.54%)，开放性研究(17项，13.08%)，见表4。

2.6　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验的临床分期

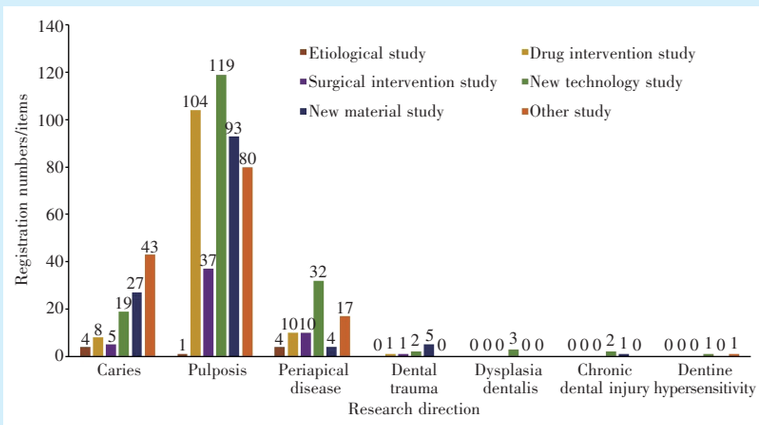
在注册的牙体牙髓病临床试验中，标记为其他/未注明的项目数有388项；标记研究阶段的有246项，其中以Ⅱ期(69项)和初步研究(62项)为主。中国注册的临床研究中，以其他/未注明的为主(67项)，其次是初步研究(48项)，Ⅳ期研究(7项)，见图4。

2.7　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验参与机构情况

在所有牙体牙髓病注册临床研究中，参与机构数量＜3的临床研究有611项(96.37%)，参与机构数量≥3的临床研究有23项(3.63%)，参与机构数量＞20的临床研究1项(0.16%)，其中国际多中心试验只有1项。由中国注册的130项试验中，参与的机构数量＜3家的临床研究有119项(91.54%)，参与机构数量为≥3的临床研究有11项(8.46%)，其中参与机构数量均未超过10个，也无中国牵头的国际多中心试验。

## 3　讨　论

通过对ClinicalTrials. gov数据库中牙体牙髓病临床试验注册分布情况发现，埃及的注册量是明显高于其他国家的，而中国注册的数量很少。ChiCTR数据库中注册临床试验全部来自中国，无其他国家的注册临床试验，其原因可能是ChiCTR数据库为中国的一级临床注册平台，主要针对的是中国地区临床试验注册，其他国家的临床试验更趋向于首选ClinicalTrials. gov数据库以及当地的临床注册试验平台。从两个数据库中可以看出




The numbers in the picture represent the registrations of clinical trials on different study topics for different endodontic diseases. ①Among 106 studies on caries, 4 were etiological studies, mainly investigating the relationship between saliva microorganisms, mental stress, and the occurrence and progression. Eight were drug intervention studies, including the efficacy and safety evaluation of local anesthetics and probiotics in caries treatment. Five were surgical intervention studies, mainly the clinical studies of cariogenic living pulp preservation, root canal therapy, and endodontomy. Nineteen were new technology studies, including near infrared imaging technology, artificial intelligence, and iTero mouth scan in the diagnosis of caries application, and dynamic and static navigation-assisted micro-apical surgery, Hall and modified Hall technique, laser, quantitative light-induced fluorescence (QLF), and transitional filling repair technique in the preservation of living pulp and early remineralization of caries. Twenty-seven were new material studies, mainly including the clinical efficacy comparison of new biological dentin replacement materials (Biodentine), bioceramic materials (iRoot SP, MTA, iRoot BP Plus), photocured tricalcium silicate substrates [TheraCal (LC)], and bioactive glass resin composites. The other 43 studies mainly focused on the prevention, risk assessment, and trend prediction of caries. ②Among 434 studies on pulposis, one was etiological, and 104 were drug intervention studies, which mainly focused on the anesthetic effect of common anesthetics in therapy, the analgesic effect of non-steroidal anti-inflammatory drugs after surgery, and the application of glucocorticoids after therapy. Thirty-seven were surgical intervention studies, focusing on the analysis of therapeutic effects such as root canal treatment and pulp cutting surgery. A total of 119 were new technology studies, including unidirectional membrane, pulp revasoplasty, microinvasive vital pulp therapy under a microscope, erbium laser washing minimally invasive therapy, pulp stem cell transplantation, hypothermia therapy, real-time dynamic navigation, 3D printing, photodynamic therapy, and other clinical applications in pulp diseases. Ninety-three were new material studies, including the clinical application of bioceramics, resin root fillers (AH Plus), and Bulk filling flow resins (Filtek Bulk fill and SonicFill Bulk fill). There were 80 other studies that mainly involved endodontic microbiology research, postoperative pain management, and endodontic teaching. ③Among the 77 studies on periapical diseases, four were etiological studies, including analyses of the correlation with diabetes, cardiovascular disease, and smoking. Ten were drug intervention studies, mainly involving the application of anesthetics and antibiotics in periapical inflammation. Ten were surgical interventions, mainly root canal therapy. Thirty-two were new technology and four were new material studies, and they were roughly the same in number as pulp disease. The other 17 studies mainly included microbiological studies and a database of periapical diseases. The data in the figure were sourced from the ClinicalTrials.gov database and the ChiCTR database on endodontic diseases from January 1, 2000, to August 20, 2023

Figure 2　Research direction of clinical trial registrations for endodontic diseases based on ClinicalTrials.gov and ChiCTR database registration

**图2**　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验的研究方向

牙体牙髓病的试验注册数最多的是埃及与中国，这可能口腔疾病发病情况相关，报告显示在低收入以及中等收入国家中口腔疾病的发生率更高，更容易进行临床试验[11]。

牙体牙髓病临床试验注册量增长一直比较平缓，与所有口腔类疾病临床试验注册量增长保持相对一致[12]。ClinicalTrials. gov数据库注册的第一个牙体牙髓病临床试验是2000年，ChiCTR数据库注册的第一个临床试验是2007年。根据2015年第四次全国口腔健康流行病学调查结果显示，与第三次调查相比，居民口腔保健意识逐渐提高，牙痛患者就诊意识增强，医生的临床研究关注度也随之提升。本研究显示全球牙体牙髓病的注册量从2015年开始显著增长，中国地区的注册量从2020年开始急剧上升，说明中国的牙体牙髓科医生越来越重视临床试验的注册。但搜索PubMed从2000年1月1日至2023年8月20日有关于牙体牙髓病发表的临床研究论文（5 628篇）而言，注册的临床研究总数量（634项）依旧偏少。根据研究显示，目前国内总体的临床试验注册率仅15%[13]。目前我国应重视并大力倡导临床试验注册，提高临床试验的注册率和注册质量，进一步保证课题研究的公开性、透明性以及发表论文数据的真实性，以获取高质量的循证医学证据。

**表2**　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验注册的样本量情况

Table 2　Sample size of clinical trial registrations for endodontic diseases based on ClinicalTrials.gov and ChiCTR databases　*n* (%)

| Sample size (numbers) | Total registrations /items | China registrations /items |
|---|---|---|
| < 20 | 46(7.26) | 5(3.85) |
| 20 ~ 49 | 185(29.18) | 17(13.08) |
| 50 ~ 99 | 199(31.38) | 29(22.31) |
| 100 ~ 199 | 121(19.08) | 37(28.46) |
| 200 ~ 299 | 32(5.05) | 9(6.93) |
| 300 ~ 399 | 17(2.68) | 8(6.15) |
| 400 ~ 499 | 6(0.95) | 4(3.08) |
| 500 ~ 999 | 9(1.42) | 7(5.38) |
| 1 000 ~ 4 999 | 10(1.58) | 6(4.62) |
| 5 000 ~ 9 999 | 1(0.16) | 1(0.77) |
| ≥10 000 | 3(0.47) | 3(2.31) |
| Unknown* | 5(0.79) | 4(3.08) |
| Total | 634(100) | 130(100) |

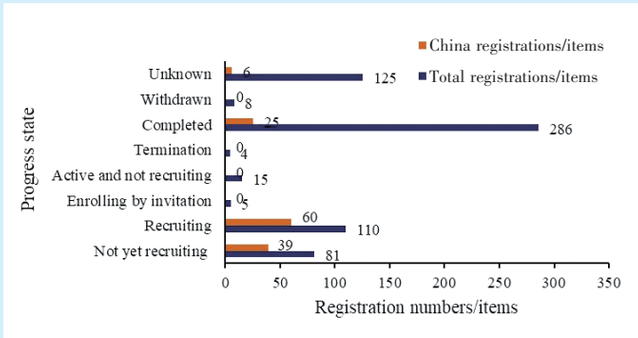
*Replacing a small number of experiments with unknown items without specifying the expected sample size

**表3**　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验注册的研究类型分布情况

Table 3　Distribution of study types in clinical trial registrations for endodontic diseases based on the ClinicalTrials.gov and ChiCTR databases　*n* (%)

| Study type and design | Total registrations /items | China registrations /items |
|---|---|---|
| Intervention study | 546 (86.12) | 79 (60.77) |
| Randomized parallel control | 473 (74.61) | 60 (46.15) |
| Signal group | 32 (5.05) | 3 (2.31) |
| Non-randomized controlled | 17 (2.68) | 7 (5.38) |
| Factorial | 10 (1.58) | 3 (2.31) |
| Crossover | 7 (1.10) | 0 (0.00) |
| Sequential | 1 (0.16) | 0 (0.00) |
| Other/unknown | 6 (0.95) | 6 (4.62) |
| Observational study | 63 (9.94) | 26 (20.00) |
| Signal group | 7 (1.10) | 1 (0.77) |
| Cohort | 6 (0.95) | 5 (3.85) |
| Continuous enrollment | 5 (0.79) | 6 (4.62) |
| Cross-sectional | 3 (0.47) | 3 (2.31) |
| Non-randomized controlled | 2 (0.32) | 2 (1.54) |
| Factorial | 1 (0.16) | 7 (5.38) |
| Other/unknown | 39 (6.15) | 2 (1.54) |
| Etiology/related factor study | 5 (0.79) | 5 (3.85) |
| Treatment study | 2 (0.32) | 2 (1.54) |
| Diagnostic test | 6 (0.95) | 6 (4.62) |
| Preventive study | 6 (0.95) | 6 (4.62) |
| Epidemiologic study | 3 (0.47) | 3 (2.31) |
| Basic scientific study | 3 (0.47) | 3 (2.31) |
| Total | 634 (100) | 130 (100) |

全球牙体牙髓病的临床研究样本量主要集中在200例以下，样本量差异较大。研究类型主要以干预性研究为主，其次是观察性研究，而干预模式以随机平行对照试验为主，由中国的临床人员注册的情况大致相同。随机平行对照试验（randomized parallel controlled，RCT）从根本上改变了医学实践，通常被认为是等级较高的临床医学证据[14]，遵循随机、对照、双盲等基本原则；以RCT为基础进行系统性评价，可以得出科学的结论，从而为指导临床实践提供依据。本研究的临床试验设计以RCT为主，说明牙体牙髓病的医师在临床研究上具备一定的质量管理规范与循证医学证据。完备的临床研究公开制度是为了实现及时、完整和准确地报告所有试验的伦理和科学目标[15]。而盲法




Among the total registrations, the progress status at the time of registration showed the largest number of completed trials, accounting for 45.11% (286 items), followed by unknown (125 items), recruiting (110 items), and not yet recruiting (81 items). Among China registrations, the progress status at the time of registration showed the largest number of recruiting trials, accounting for 46.15% (60 items), followed by not yet recruiting (39 items), and completed (25 items). The total registrations were sourced from the ClinicalTrials.gov database and the ChiCTR database on endodontic diseases, and China registrations were obtained from two databases registered by Chinese researchers. The search period was from January 1, 2000, to August 20, 2023

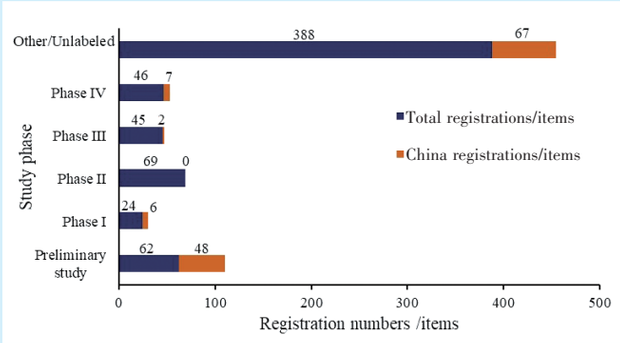
Figure 3　Progress status of clinical trial registrations for endodontic diseases at the time of registration based on the ClinicalTrials.gov and ChiCTR databases

**图3**　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验注册时的进展状态

表4　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验使用盲法情况

Table 4　Blinding of clinical trial registrations for endodontic diseases based on the ClinicalTrials.gov and ChiCTR databases

| Study/blind method | Total registrations/items | | | | | | China registrations/items | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Open | Signal | Double | Triple | Quadruple | Other/unknown | Open | Signal | Double | Triple | Quadruple | Other/unknown |
| Intervention study | 83 | 130 | 189 | 58 | 35 | 51 | 12 | 12 | 4 | 1 | 0 | 50 |
| Observational study | 3 | 1 | 1 | 0 | 0 | 58 | 3 | 1 | 1 | 0 | 0 | 21 |
| Other type study | 2 | 2 | 5 | 2 | 0 | 14 | 2 | 2 | 5 | 2 | 0 | 14 |




In the total registrations, the number of items marked as other/unlabeled (388 items) was the highest, followed by phase Ⅱ study (69 items) and preliminary study (62 items). In the China registrations, the other/unlabeled study was the main study phase (67 items), followed by the preliminary study (48 items) and phase Ⅳ study (7 items). The total registrations were sourced from the ClinicalTrials.gov database and the ChiCTR database on endodontic diseases, and China registrations were obtained from two databases registered by Chinese researchers. The search period was from January 1, 2000, to August 20, 2023

Figure 4　Study phase of clinical trial registrations for endodontic diseases based on the ClinicalTrials.gov and ChiCTR databases

图4　基于ClinicalTrials.gov和ChiCTR数据库注册的牙体牙髓病临床试验的研究阶段

是RCT研究中的主要设计方案，通常在临床试验中使用盲法可以避免出现实施偏倚和测量偏倚，且不同类型的盲法影响RCT研究的质量[16-17]。在所有牙体牙髓病的临床试验注册中使用盲法的有423项，而中国临床研究注册中仅有28项标注了使用盲法，这说明国际的注册临床试验中对研究设计更为严谨和规范。

近年来多中心的临床研究已逐渐成为趋势，在我国开展的药品和器械注册临床试验大多采用多中心设计。与单中心临床试验相比，多中心临床试验更易招募受试者，可更快达到试验要求的大样本量；不同地区不同背景的研究者共同参与，能提高临床试验的设计水平；且在不同的中心共同完成试验，其试验结果更加科学、真实、可靠，其结论外推性更好[18-19]。根据本研究的数据显示，全球的牙体牙髓病注册临床试验以单中心试验为主，参与机构大于≥3家的仅占3.63%，且国际多中心试验仅有1项，以Ⅱ、Ⅲ、Ⅳ期临床分期为主要研究方向；而中国注册的也以单中心试验为主，参与机构数量≥3的临床研究占8.46%，以初步研究为主要研究方向。这提示目前牙体牙髓病研究主要还是注册者单一的研究，临床研究的质量和结论推广性存在一定的地理局限性，其中原因可能是与单中心试验相比，不同中心的样本量分配计划、研究方案与实施等仍存在不一致性[20]，导致多中心试验会存在中心异质性及中心效应产生的质量控制困难[21]。此外，李清照等[22]的研究表明多中心药物临床试验启动前会导致多个环节的申请时间延长，这些都可能影响临床研究者注册时的决策。另外我国的口腔疾病医疗负担正在增加，口腔疾病整体行业的发展落后于我国医疗行业的平均发展水平[23]，从而导致临床研究存在一定的困难。因此我国应建立口腔综合防控体系，大力倡导开展多中心临床研究。

**【Author contributions】** Li S collected, analyzed the data, and wrote the article. Guo JC designed the study and reviewed the article. All authors read and approved the final manuscript as submitted.

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