The Royal Society of Medicine

Journal of the Royal Society of Medicine; 2025, Vol. 118(8) 258–264
DOI: 10.1177/01410768251347259

The history of controlled clinical trials in China. Part 2: from the advent of large-scale multicentre randomised controlled trials through contemporary self-reflection

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As detailed in Part 1, researchers began to conduct randomised controlled trials (RCTs) in mainland China in the 1960s, followed by more robust expansion beginning in the late 1970s. In Part 2, we examine the advent of large-scale multicentre RCTs and the development of evidence-based medicine in mainland China from the 1990s onward. We then briefly trace the history of the development and evaluation of artemisinin as a case example of the history of clinical investigation in mainland China, before turning to more recent ethical and epistemic self-reflection.

With the development of clinical epidemiology and evidence-based medicine in China, the number and quality of randomised controlled trials (RCTs) have been improved. Yet, we find an enduring tension between aspirations to conduct clinical trials, and self-critique concerning the current standards of trial ethics and methodological rigour. Such tension persists to the present day.

Large-scale multicentre RCTs and the development of evidence-based medicine (1990s onwards)

Amid ongoing discussion in mainland China concerning the size and conduct of clinical trials, large, seemingly well-designed trials *had* emerged by the 1990s. Notably, researchers initiated a large-scale RCT of the angiotensin converting enzyme (ACE)-inhibitor captopril in acute myocardial infarction.[1] This double-blind controlled clinical trial, using a sealed envelope system with strict randomisation, involved over 600 hospitals in 30 provinces, municipalities and autonomous regions, and enrolled 14,962 patients. The pilot study finished by the end of 1989 and the trial officially started on 1 January 1990, and finished in May 1995. Interim reports were published in 1994[2] and 1995,[3,4] and the final results were published in 1997 in the *Chinese Journal of Cardiology*.[5]

Around the same time, demonstrating increasing collaboration between Chinese and international researchers, the Chinese Acute Stroke Trial (CAST) randomised more than 21,000 patients with acute ischaemic stroke to early aspirin or placebo in 413 Chinese hospitals, with recruitment lasting from November 1993 to March 1997.[6] These trials were followed by even larger trials in the early 2000s, including the second Chinese Cardiac Study, which was also called COMMIT (ClOpidogrel and Metoprolol in Myocardial Infarction Trial). This 2×2 factorial randomised trial of adding oral clopidogrel to aspirin and of using intravenous then oral metoprolol recruited nearly 46,000 patients admitted to 1250 hospitals with a suspected acute myocardial infarction between August 1999 and February 2005.[7–9]

However, in the 1990s, other investigators expressed concerns that RCTs conducted in China and with results published in Chinese were not being incorporated into global databases and existing systematic reviews. Ming Liu et al.[10] conducted a systematic search for stroke-related RCTs published in Chinese, manually searching the proceedings of one stroke conference and five leading Chinese medical and neurology journals that may have published relevant RCTs. From 1965 to 1995, they found 178 RCTs related to a wide range of medical specialties, constituting 1.4% of all articles in these journals, and with the majority of the RCTs not identified in MEDLINE.[a] Although the trials were mostly small (i.e. $\leq$200 participants), the world's largest randomised, double-blind and placebo-controlled trial of

blood pressure reduction on the secondary prevention of stroke, involving 5665 patients, was identified in their study and had been published in China in 1995, but was not widely cited.[11]

All of this took place amid the global rise of attention to 'evidence-based medicine', first articulated as a term in 1991.[12] The term 'Evidence Based Medicine' (EBM) was first translated into Chinese as '循证医学(xun zheng yi xue)' in 1996 by Jiyao Wang from Fudan University.[13] At the same time, Chinese scholars began introducing systematic reviews and meta-analyses.[14] In 1999, the Chinese Cochrane Center (now known as the Cochrane China Center) was formally established at the West China Hospital of Sichuan University, receiving support from the Ministry of Health of China.[15] In 2002, the Chinese Cochrane Center extended its reach by establishing a branch in Hong Kong at the Chinese University of Hong Kong SAR.[15] In 2007, the Chinese Clinical Trial Registry (ChiCTR) was officially launched, serving as a national clinical registry for China and a contributor to the World Health Organization's international Clinical Trial Registry Platform. Its primary aim was to enhance the transparency of clinical research and reduce publication bias.[16] Since then, the number of registered clinical trials in China has continued to increase.

Artemisinin (Qinghaosu) trials as a telling case example

In 2015, the Nobel Prize in Physiology or Medicine was awarded to Youyou Tu for her role in the discovery and study of artemisinin as an antimalarial. The progression of clinical studies of artemisinin echoes most – but not all – of the trends outlined in Part 1 and above. As indicated in Part 1, most scientific research, including clinical trials, was halted during the Cultural Revolution. However, artemisinin research officially commenced during this period. Qinghao (*Artemisia annua* L.) had a millennium-long history in treating malaria, dating back to the 4th century.[17] Since the late 1950s, clinical trials utilising Qinghao for malaria treatment gradually emerged. For instance, in 1959, Rushao Huang et al. published a study in the *Journal of Traditional Chinese Medicine*, reporting the treatment of 27 patients with symplocos chinensis (Lour.) and 18 patients with artemisia apiacea hance in the Tibetan Autonomous Region of Guangxi, observing that symplocos chinensis had inferior antipyretic effects compared with artemisia, although it apparently exhibited stronger control over other unspecified symptoms.[18] In 1967, the Chinese government initiated a nationwide research project named the '523 Project', which was aimed at discovering novel therapies for malaria, leading to the discovery of artemisinin (Qinghaosu) as a new antimalarial drug.[19,20] As Youyou Tu has described this history, after an arduous investigation of more than 2000 Chinese herbal preparations, and insights from ancient works on the preparation of *A. annua* L. extract, they had derived the active principle from Qinghao and were ready by 1972 for clinical investigation. Yet, as she has related:

> *During the Cultural Revolution, there were no practical ways to perform clinical trials of new drugs. So, in order to help patients with malaria, my colleagues and I bravely volunteered to be the first people to take the extract. After ascertaining that the extract was safe for human consumption, we went to the Hainan province to test its clinical efficacy.*[21]

These would be uncontrolled – but very promising – trials on patients with malaria. In December 1972, the drug was officially named 'Qinghaosu'.[22]

Large-scale clinical trials involving Qinghaosu began to be published in the late 1970s. In 1979, the Qinghaosu Antimalaria Coordinating Research Group – representing seven institutes, academies and bureaus – published an article in the *Chinese Medical Journal* describing the chemical structure of Qinghaosu, pharmacological studies and uncontrolled clinical trials, having treated 2099 cases of malaria with various preparations of Qinghaosu.[23] That same year, one of the earliest RCTs involving Qinghaosu was published in the *Chinese Journal of Medicine*, with the researchers having randomly allocated 80 patients to either the Qinghaosu group (50 patients) or to the chloroquine control group (30 patients), with both groups achieving a cure rate of 100%, indicating that Qinghaosu oil solution could be used for severe malaria.[24] By 1984, Guoqiao Li et al. from the Malaria Research Unit at Guangzhou College of Traditional Chinese Medicine – along with the Roche Far East Research Foundation, Hong Kong – published in the *Lancet* an RCT, conducted between 1982 and 1984, aiming to assess the efficacy and side effects of combinations of mefloquine, fansidar and Qinghaosu.[25] Artemisinin would thus bridge ancient and modern approaches to drug production, application and evaluation alike.

Ethical and enduring epistemic critiques and reform

As with trial methodology, formal attention to clinical trial research ethics has had a relatively

concentrated history in mainland China compared with the West. The term 'Ethics Committee' was first proposed in China in the late 1980s, leading to the establishment of such committees in various hospitals over the next decade.[26] However, during this period, the ethical review of scientific research was not widely practised, with such committees focusing primarily on medical ethics education and the development of professional conduct.[27] Towards the end of the 1990s, there was a notable increase in the number of Ethics Committees focusing on ethical review of biomedical research involving human subjects. These committees were not only established in hospitals but also in the majority of medical schools, large pharmaceutical research institutions and biomedical technology companies.

Since 2000, China has accelerated efforts to institutionalise research ethics. That year, the Ministry of Health established the first session of the Expert Committee on Medical Ethics, tasked with researching ethical issues in medical research and providing recommendations for ethics education. In 2003, the State Food and Drug Administration issued 'Norms on Quality Management of Drug Clinical Trials', which mandated certification for all medical institutions conducting clinical trials and the establishment of independent research ethics committees registered with the administration. The aim was to safeguard the rights and interests of all participants and applicants involved in clinical trials.[28] In 2010, ChiCTR established the Chinese Ethics Committee of Registering Clinical Trials (ChiECRCT). ChiECRCT proposed the establishment of an ethical review system while simultaneously integrating the registration of clinical trials with ethical review. This initiative aimed to facilitate the registration of clinical trials in China and improve the overall quality of clinical trials.[28]

Although there has been an increasing emphasis on the importance of ethics and informed consent starting in the 21st century, this transformation remains incomplete and continues to be scrutinised. After analysing clinical research articles published in 1998 across 14 biomedical journals in China regarding the disclosure of informed consent, Mouyue Wang found that only 1% of the clinical studies reported obtaining informed consent.[29] Nearly two decades later, Hongjie Zhao et al. found that, among 395 clinical RCTs published in the top 20 medical journals with high impact factors and indexed by the China Science Citation Database during 2016–2017, only 46.8% of the trials reported having undergone ethical review and 64.1% of the trials obtained informed consent. While the quantity of ethical reviews had substantially increased compared with a decade prior, the authors suggested that the ethical review platform was still not robust, emphasising the need to improve awareness and accessibility of ethical review processes.[30]

With the increasing number of clinical trials conducted in China, it has also faced ongoing criticism concerning the validity of such trial results. In 2007, an article published in the *Lancet* titled 'Reforming research in China' pointed out that, in 2006, there were several allegations[b] of scientific misconduct in China, though there appeared to be a positive shift in 2007.[31] In response to such criticism, the Chinese Ministry of Science and Technology issued its *Measures for Handling Scientific Research Misconduct in the Implementation of National Science and Technology Programs (Trial)* to address misconduct in nationally funded programmes.[32] Additionally, the Chinese Academy of Sciences published a *Declaration of Scientific Ideology*.[33] In 2007, China officially established the 'Joint Meeting System for Research Integrity Construction' (in Chinese as '科研诚信建设联席会议制度'), involving six departments and units, including the Ministry of Science and Technology, the Ministry of Education, the Chinese Academy of Sciences, the Chinese Academy of Engineering, the National Natural Science Foundation of China and the China Association for Science and Technology.[34] As the *Lancet* article concluded:

> *Ethical principles can guide all stages of research. If grant awards are transparent, institutional review boards invite debate, participant autonomy is respected, and analysis and presentation of findings is accountable, then China has the opportunity to lead the world not only in research quantity, but also in quality*.[31]

And yet, critiques persisted. In the early 21st century, Western countries had already begun adopting *The Consolidated Standards of Reporting Trials* (CONSORT) statement, aimed at improving the quality of RCTs. This statement was officially introduced in China in 2001 and formally translated into Chinese in 2007.[35] In 2008, Dalu Zhang et al. from the University of Birmingham published a paper in *Trials* with the intention of assessing the quality of Chinese RCTs published in English in 2004.[36] The authors noted that 'this is the first systematic study to evaluate the quality of trial conduct and reporting in a sample likely to be more representative of

Chinese RCTs in general'. Among the 307 RCTs included in the study, 199 (64.8%) failed to report their randomisation methods, and 254 (82.4%) did not mention blinding of either participants or investigators. Fewer than 11% of RCTs mentioned ethical approval, and only 18.0% were reported to have adequately discussed informed consent. Notably, nearly 44% of trials reported a zero dropout rate. Simultaneously, research indicated that until 2011, only eight Chinese-language journals had officially listed the requirements of the CONSORT Statement in the 'Introductions to authors'.[35,37] In contrast, 458 major international peer-reviewed medical journals on PubMed had endorsed the CONSORT statement before 2011.[35]

During this same period, Taixiang Wu et al. reported that among 3137 RCTs (1452 in conventional medicine and 1685 in Traditional Chinese Medicine (TCM)) published in Chinese and conducted from 1994 to 2005, only 6.8% of these trials could be considered 'authentic', adhering 'to accepted methodology for randomization', as ascertained through interviews with the authors of the reports.[38,c] Likewise, Jia He et al. proposed in the *Lancet* that the most common design errors in Chinese biomedical research pertained to sample size estimation and randomisation, such as the absence of formal estimation or the use of an incorrect formula for sample size calculation, as well as the failure to describe the randomisation procedure or casually mentioning it.[39]

In this context, in 2010, Jiyao Wang discussed in the *Lancet* that the growth of evidence-based medicine in China presented both challenges and opportunities.[40] Notably, between 1999 and 2008, only 0.21% of clinical research articles published in the *New England Journal of Medicine,* the *Lancet* or *JAMA* originated from mainland China.[41] Consequently, Wang proposed recommendations for improving research quality and transparency, covering clinical trial registration, management platforms, ethics and reporting standards. She concluded by referencing the *Lancet*'s 2007 statement concerning 'reforming research in China'[31]: 'There is a long way to go before the words of a *Lancet* Editorial—"China has the opportunity to lead the world not only in research quantity, but also in quality"—are fulfilled'.[40] A year later, Yonghua Hu et al., in their 2011 the *Lancet* analysis of the current status of clinical research in China, echoed such concerns about China's global presence. They noted that while the number of published RCTs in China reported in PubMed had increased from 85 in the year 2000 to 743 in 2009, these RCTs accounted for only 1.7% of RCTs published globally.[42]

As of 2013, China was therefore still considered to have remained a country that primarily imported medical evidence rather than exporting it, owing to the inadequacy of 'robust clinical research and data'.[43] To enhance clinical research, in 2013, the Chinese government officially launched 13 national-level clinical research centres among six key areas.[44] This number increased to 20 common diseases and frequently occurring conditions by 2022, with the establishment of 50 national-level clinical research centres.[45] Chen Wang and Qian Liu pointed out in the *Lancet* in 2013 that China's substantial disease burden can actually serve as a valuable clinical resource for physicians to design clinical research and gather clinical data.[43] Yet, many trials, it appeared, would turn out to be 'redundant', yielding results that had already been established (e.g. the utility of statins in patients with coronary artery disease) and therefore violating notions of clinical equipoise.[46]

In recent years, in addition to those concerning Western medicine, clinical trials involving TCM and acupuncture have also garnered significant attention to increasing the quality of evidence. In 2017, researchers from Hong Kong SAR, mainland China, UK and Canada published the CONSORT extensions for Chinese Herbal Medicine (CHM) formulas, hoping it could improve the reporting quality of CHM formulas.[47] In 2022, the *BMJ* released a collection of articles titled 'Acupuncture: How to Improve the Evidence Base'.[48] This series analysed the progress of high-quality research in acupuncture, summarised the current status, and provided evidence-based guidelines for designing high-quality acupuncture trials.[49] In 2023, the China Academy of Chinese Medical Sciences and the China Center for Evidence Based Traditional Chinese Medicine operated the International Traditional Medicine Clinical Trial Registry (ITMCTR), which became a member of the primary registry network of the International Clinical Trials Registry Platform (ICTRP) and added to the ICTRP database. It is the first formal registration platform for traditional medicine, and through 14 February 2024, a total of 4246 trials have been registered.[50]

Thus, in recent decades, Chinese researchers have taken a self-reflective stance on the conduct of clinical research in mainland China. They have generally described an incomplete transition to this point, against the backdrop of similar developments outside of China, and the unique relationship between conventional medicine and TCM. We see an enduring tension between enthusiasm for the opportunities for clinical trial expansion, and concerns regarding the limits of existing efforts.

Conclusion

In 2022, it was estimated that nearly 28% of all clinical trials, globally, were conducted in China.[51] And yet persisting attention has focused on the limitations – ethical and methodological – to such trial activity.[52] As this overview has shown, such a dynamic between growth, self-reflection and critique is not new, but has characterised China's RCT landscape for over seven decades.

Some of these enduring growing pains may be ascribed to the relatively rapid evolution of RCTs in China. And yet, this is an older and richer history than has been conventionally described. This history – serving as the backdrop to current trial expansion – illustrates the co-development of methodology, medicine(s), the state and the larger global contexts in which Chinese medicine has developed.

We have provided a prelude to additional and more nuanced and contextualised examinations. Scholars examining the evolution of RCTs in the West have the benefit of a robust historiography, and rich databases like the James Lind Library. There is no equivalent Ben Cao Tu Jing Library of the history of 'fair tests of treatment in healthcare' in China. At least not yet. We hope to have made a useful start, and invite others to join in this work and further enrich our understanding of the history of clinical trials in China.

Declarations

Competing Interests: None declared.

Funding: The National Social Sciences Foundation of China: 'Research on the Theoretical System, International Experience and Chinese Path of Evidence-based Social Science' (Project No. 19ZDA142).

Ethics approval: Not applicable.

Guarantor: XY, SHP, and YC.

Contributorship: Conceptualisation: XY, SHP, and YC. Translating Chinese documents into English: XY. Writing – original draft: XY and SHP. Writing – review and editing: XY, SHP, and YC.

Acknowledgements: The authors would like to express their deepest gratitude to Iain Chalmers, Jinling Tang, Ted Kaptchuk, Ming Liu, Mike Clarke and Karen Robinson for their insights and feedback on the manuscript.

Provenance: Invited article from the James Lind Library.

Notes

a. The authors mentioned in the results section that they found two RCTs from 1965 to 1983; unfortunately, the authors did not specify which two papers they were referring to.

b. The article did not specify exact allegations. Through searches on Baidu and Google, it was found that a serious scientific research fraud case occurred in China in 2006 – the Hanxin Project: https://www.nytimes.com/2006/05/15/technology/in-a-scientists-fall-china-feels-robbed-of-glory.html. Moreover, *Nature Medicine*[53] published an article in 2006 titled 'Frequent cases force China to face up to scientific fraud', mentioning six high-profile cases of scientific misconduct over eight months: 'for China's biomedical research, still struggling for global credibility, the frequent accusations of plagiarism, falsified data and fabricated resumes spell out a serious warning—one that the government is finally preparing to heed'.

c. 'A randomisation sequence generated from a random number table, calculator or computerised random-number generator was considered authentic. Coin-tossing or drawing straws in the presence of the participant to decide which group he or she would be assigned to were considered ineligible randomisation techniques. Allocation of participants according to date of birth, or their hospital record number, or the date on which they were invited to participate (for example, an odd or even day) was not considered adequate'.[38]

References

1. Wang W, Liu L, Tao S, Gong L and Wu N. A retrospective drug study of large-scale clinical trials on cardiovascular disease in China. *Chin J Cardiol* 2000; 28: 335–338. [王文,刘力生,陶寿淇,等 (2000). 我国大样本心血管药物临床试验的回顾与展望. 中华心血管病杂志 28(5): 335–338.]
2. Chinese CEI-AMI Trial Collaborative Group. Early Intervention with ACE inhibitor captopril in acute myocardial infarction – Chinese multicenter, large-scale, randomized, double-blind, placebo-controlled clinical trial (preliminary analysis of 11345 cases). *Chin J Hypertens* 1994; 2: 67–72. [全国CEI-AMI临床试验协作组(1994). 血管紧张素转换酶抑制剂卡托普利早期治疗急性心肌梗塞随机临床试验全国多中心大规模随机双盲安慰剂对照临床试验11345例阶段小结. 中国高血压杂志 2(2): 67–72.]
3. Chinese Cardiac Study Collaborative Group. Oral captopril versus placebo among 13,634 patients with suspected acute myocardial infarction: interim report from the Chinese Cardiac Study (CCS-1). *Lancet* 1995; 345: 686–687.
4. Chinese CEI-AMI Clinical Research Collaboration, Wang W, Liu L and Tao S. Clinical trial on the differential effects of captopril in anterior and inferior myocardial infarctions. *Chin J Cardiol* 1995; 23: 165–170. [中国CEI-AMI临床研究协作组,王文,刘力生,等(1995). 卡托普利对前壁与下壁心肌梗塞作用差异的临床试验. 中华心血管病杂志 23(3): 165–170.]
5. Chinese Cardiac Study-I (CCS-I) Collaboration Group, Liu L, Wang W and Tao S. Chinese Cardiac Study-I (CCS-I): effects of captopril on the early mortality and complications in 14,962 patients with acute myocardial infarction – a multicenter, large-scale,

randomized, double-blind, placebo-controlled clinical trial. *Chin J Cardiol* 1997; 25: 245–249. [中国心脏研究协作组,刘力生,王文,等(1997). 中国心脏研究:卡托普利对急性心肌梗塞患者早期病死率和并发症影响的多中心临床试验——全国大规模随机双盲安慰剂对照临床试验14962例资料总结. 中华心血管病杂志 25: 245–249.]
6. CAST (Chinese Acute Stroke Trial) Collaborative Group. CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. *Lancet* 1997; 349: 1641–1649.
7. Chen Z and Jiang L. Changing strategies in the management of acute myocardial infarction in modern China. *CVD Prevent Control* 2009; 4: 9–18.
8. COMMIT (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet* 2005; 366: 1607–1621.
9. COMMIT (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet* 2005; 366: 1622–1632.
10. Liu M, Counsell C and Sandercock P. Report of randomized controlled trials identified in the Chinese literature vs MEDLINE. *JAMA* 1998; 280: 1308–1309.
11. PATS Collaborating Group. Post-stroke antihypertensive treatment study: a preliminary result. *Chin Med J* 1995; 108: 710–717.
12. Guyatt GH. Evidence-based medicine. American College of Physicians Journal Club 1991; 114(2): A16.
13. Li B, Yan Y, Lv M, Zhao G, Li Z and Feng S. Clinical epidemiology in China series. Paper 1: evidence-based medicine in China: an oral history study. *J Clin Epidemiol* 2021; 140: 165–171.
14. Liu M. New methods in clinical stroke research: an introduction to meta-analysis. *Int J Cerebrovasc Dis* 1996; 4: 352–356. [刘鸣 (1996). 脑卒中临床研究的新方法——Meta-分析介绍. 国外医学(脑血管疾病分册) 4(6): 352–356.]
15. Li Y, Sun X and Wang L. Evidence-based medicine in China. *Value Health* 2008; 11: S156–S158.
16. Wu T, Li Y, Liu G, Li J, Wang L and Du L. Chinese clinical trial registry: mission, responsibility and operation. *J Evidence-Based Med* 2011; 4: 165–167.
17. Hsu E. The history of qing hao in the Chinese materia medica. *Trans R Soc Trop Med Hyg* 2006; 100: 505–508.
18. Huang R, Wei Y and Zhou D. Clinical observation on the treatment of malaria using Guangxi Symplocos Chinensis and Artemisia. *J Trad Chin Med* 1959; 4: 33–35. [黄汝绍,韦用宽,周典谟 (1959). 用广西土常山和青蒿两药试治疟疾的临床观察. 中医杂志 4: 33–35.]
19. Tu Y. The discovery of artemisinin (qinghaosu) and gifts from Chinese medicine. *Nat Med* 2011; 17: 1217–1220.
20. World Health Organization. From 30 million cases to zero: China is certified malaria-free by WHO. 2021. See www.who.int/news/item/30-06-2021-from-30-million-cases-to-zero-china-is-certified-malaria-free-by-who (last checked 16 May 2025).
21. Tu Y, Luo Z, Li G, Zhang J, Wu Z, Shi L, et al. *Interviews on 523 Project and the Discovery of Artemisinin*. Changsha: Hunan Education Publishing House, 2015. [屠呦呦,罗泽渊,李国桥,等 (2015). '523'任务与青蒿素研发访谈录. 湖南教育出版社.]
22. Su X and Miller L. The discovery of artemisinin and the Nobel Prize in physiology or medicine. *Sci China Life Sci* 2015; 58: 1175–1179.
23. Qinghaosu Antimalaria Coordinating Research Group. Antimalaria studies on Qinghaosu. *Chin Med J* 1979; 92: 811–816.
24. Hubei Academy of Medical Sciences Institute of Parasitic Diseases, Hubei Infectious Disease Hospital of Shashi City and Hubei Health and Epidemic Prevention Station of Shashi City. Observation of the efficacy of Qinghaosu oil solution in the treatment of malaria. *Chin J Med* 1979; 8: 1–2. [湖北省医学科学院寄生虫病研究所,湖北省沙市市传染病医院,湖北省沙市市卫生防疫站(1979). 青蒿素油剂治疗间日疟效果观察. 中级医刊 8: 1–2.]
25. Li GQ, Arnold K, Guo XB, Jian HX and Fu LC. Randomised comparative study of mefloquine, qinghaosu, and pyrimethamine-sulfadoxine in patients with falciparum malaria. *Lancet* 1984; 324: 1360–1361.
26. Tian D. *The Establishment and Mechanism of Chinese Ethics Review Committees' System*. Tianjin: Tianjin Medical University, 2006. [田冬霞 (2006). 中国伦理审查委员会的建构与机制. 天津医科大学.]
27. Zhang X, Zhang W and Zhao Y. The Chinese Ethical Reviews System and its Compliance Mechanisms. 2016. See https://trust-project.eu/wp-content/uploads/2016/03/Chinese-Ethics-Review-System.pdf (last checked 16 May 2025).
28. Wu T, Li Y, Liu G, Li J, Deng S and Du L. The strategies of improving the quality of clinical studies in China. *Chin J Evidence-Based Med* 2010; 10: 1243–1248. [吴泰相,李幼平,刘关键,等 (2010). 中国临床试验注册中心及中国循证医学中心提高我国临床试验质量的策略和措施. 中国循证医学杂志 10(11): 1243–1248.]
29. Wang M. Biomedical journals in China should emphasize informed consent from participants. *Chin J Scient Techn Period* 2000; 11: 293–295. [汪谋岳 (2000). 我国生物医学期刊应重视受试者的知情同意. 中国科技期刊研究 11: 293–295.]
30. Zhao H, Zhang J, Guo L, Yang F, Zhang M, Li Y, et al. The status of registrations, ethical reviews and informed consent forms in RCTs of high impact factor Chinese medical journals. *Chin J Evidence-Based Med* 2018; 18: 735–739. [赵宏杰,张俊华,郭利平,等 (2018). 我国高影响因子中文医学期刊发表随机对照试验注册、伦理、知情同意报告现状及质量评价分析. 中国循证医学杂志 18(7): 735–739.]
31. Anon. Reforming research in China. *Lancet* 2007; 369: 880.

32. Central People's Government of the People's Republic of China. Order of the Ministry of Science and Technology of the People's Republic of China. 2006.11.10. 2006. See www.gov.cn/ziliao/flfg/2006-11/10/content_438430.htm (last checked 16 May 2025). [中华人民共和国中央人民政府 (2006). 中华人民共和国科学技术部令. 2006.11.10.]
33. Central People's Government of the People's Republic of China. The Chinese Academy of Sciences Officially Releases 'Opinions' to Further Regulate Research Practices. 2007.2.26. 2007. See www.gov.cn/jrzg/2007-02/26/content_534745.htm (last checked 16 May 2025). [中华人民共和国中央人民政府 (2007). 中科院正式发布《意见》进一步规范科研行为. 2007.2.26.]
34. Lu M and Jiang M. Study on the supervision mechanism of misconduct in scientific research in China. *Sci Technol Progr Policy* 2011; 28: 100–114. [卢明纯,蒋美仕 (2011). 我国应对科研不端行为的监管机制研究. 科技进步与对策 28(4): 100–104.]
35. Song T, Leng H, Zhong L, Wu T-X and Bian Z-X. CONSORT in China: past development and future direction. *Trials* 2015; 16: 243.
36. Zhang D, Yin P, Freemantle N, Jordan R, Zhong N and Cheng KK. An assessment of the quality of randomised controlled trials conducted in China. *Trials* 2008; 9: 1–8.
37. Li X, Tao K, Zhou Q, Moher D, Chen H-Y, Wang F-Z, et al. Endorsement of the CONSORT statement by high-impact medical journals in China: a survey of instructions for authors and published papers. *PLoS One* 2012; 7: e30683.
38. Wu T, Li Y, Bian Z, Liu G and Moher D. Randomized trials published in some Chinese journals: how many are randomized? *Trials* 2009; 10: 46.
39. He J, Jin Z and Yu D. Statistical reporting in Chinese biomedical journals. *Lancet* 2009; 373: 2091–2093.
40. Wang J. Evidence-based medicine in China. *Lancet* 2010; 375: 532–533.
41. Wang J. Follow international reporting guidelines to raise the quality of articles about clinical research in China. *Chin J Digest* 2010; 30: 1–2. [王吉耀 (2010). 遵循国际标准提高国内临床论文质量. 中华消化杂志 30(1): 1–2.]
42. Hu Y, Huang Y, Ding J, et al. Status of clinical research in China. *Lancet* 2011; 377: 124–125.
43. Wang C and Liu Q. A turning point for clinical research in China? *Lancet* 2013; 382: 835–836.
44. Ministry of Science and Technology of the People's Republic of China. The National Clinical Medicine Research Centers Officially Launched. 2013.9.4. 2013. See www.most.gov.cn/kjbgz/201309/t20130903_109083.html (last checked 16 May 2025). [中华人民共和国科学技术部 (2013). 国家临床医学研究中心正式启动. 2013.9.4.]
45. Central People's Government of the People's Republic of China. Significant Advances in Medical Technology Innovation and Medical Education Provide Strong Support for the Development of Health and Wellness in China. 2022.8.26. 2022. See www.gov.cn/xinwen/2022-08/26/content_5706894.htm (last checked 16 May 2025). [中华人民共和国中央人民政府 (2022). 医学科技创新与医学教育进步显著 为我国卫生健康事业发展提供有力保障. 2022.8.26.]
46. Jia Y, Wen J, Qureshi R, Ehrhardt S, Celentano DD, et al. Effect of redundant clinical trials from mainland China evaluating statins in patients with coronary artery disease: cross-sectional study. *BMJ* 2021; 372: n48.
47. Cheng C, Wu T, Shang H, Li Y-P, Altman DG, Moher D, et al. CONSORT extension for Chinese herbal medicine formulas 2017: recommendations, explanation, and elaboration. *Ann Intern Med* 2017; 167: 112–121.
48. *The BMJ*. Acupuncture: How to improve the evidence base. 2022. See https://www.bmj.com/acupuncture (last checked 16 May 2025).
49. Zhang Y, Jiao R, Witt C, Lao L, Liu J-P, Thabane L, et al. How to design high quality acupuncture trials – a consensus informed by evidence. *BMJ* 2022; 376; e067476.
50. International Traditional Medicine Clinical Trial Registry. Terms of References for ITMCTR. Terms of Reference of the ITMCTR Advisory Group. 2022. See http://itmctr.ccebtcm.org.cn/en-US/Home/InformationCode/one (last checked 16 May 2025).
51. Clinical Trials Arena. China accounts for 27.7% share of global clinical trial activity in 2022. 2023. See www.clinicaltrialsarena.com/marketdata/china-accounts-for-27-7-share-of-global-clinical-trial-activity-in-2022/ (last checked 16 May 2025).
52. Fan J, Liu X, Li Y, Xia H, Yang R, Li J, et al. Quality problems of clinical trials in China: evidence from quality related studies. *Trials* 2022; 23: 343.
53. Jia H. Frequent cases force China to face up to scientific fraud. *Nat Med* 2006; 12: 867–868.