

International Good Practice Guidelines and Standards in *Integrative Medicine* Research & Development.

整合医药研发的国际标准与规范.

Dr Qihe Xu's PPT for his keynote speech at *The Fourth Integrative Medicine in Nephrology & Andrology International Forum*, Beijing, China, 26th October 2024.

徐启河博士在肾脏病学与男科学整合医学第四届论坛发表主旨演讲幻灯稿（2024年10月26日 · 中国北京）

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International Good Practice Guidelines and Standards in
Integrative Medicine Research & Development

整合医药研发的国际标准与规范

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PI, The GP-TCM EU-China Collaboration funded by the European Commission

Board Member, The GP-TCM Research Association

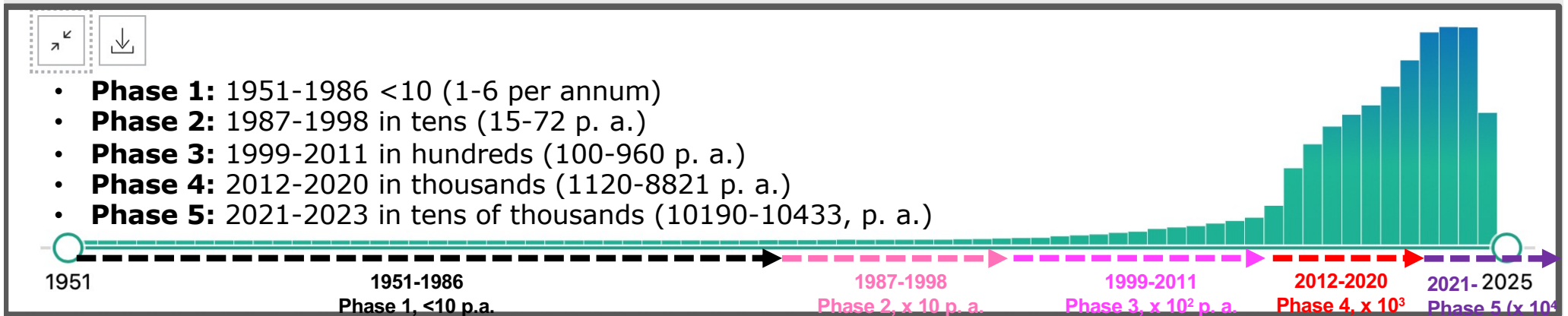
Director, King's Centre for Integrative Chinese Medicine initiative 2.0

King's College London, The University of London

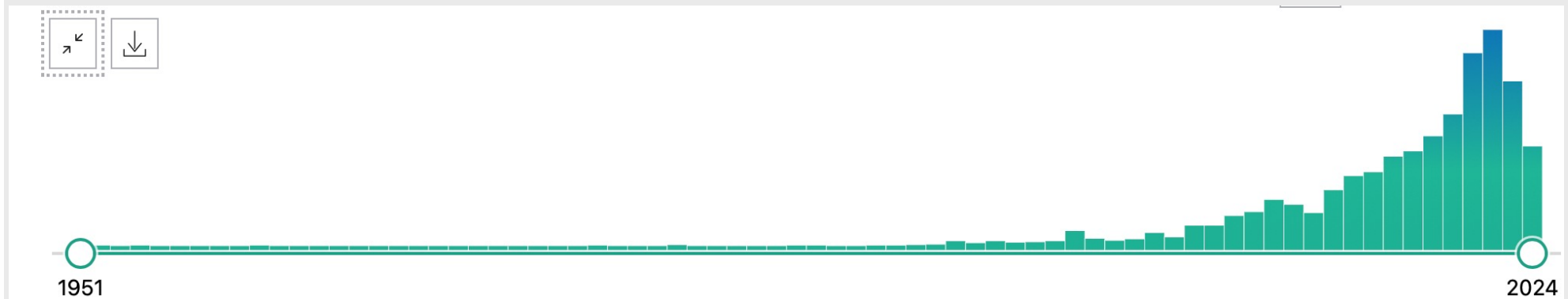
E-mail: qihe.xu@kcl.ac.uk

Integrative Medicine: a term gaining popularity in the past decade

Pubmed search “integrative-medicine”, **79,365** hits up to 18-07-24



Integrated-medicine: similar trend fewer use; **2902** hits by 18-07-24



Is this a new era just begun?

Or is it an unsustainable campaign?

It depends.

It depends on **what to integrate** and **how**



滥竽充数？



琴瑟和鸣！

Integrative Medicine (IM)

The definition by the WHO

The April 2024 Draft WHO traditional medicine strategy (2025-2034) for consultation:

Integrative Medicine is:

- an interdisciplinary and evidence-informed approach
- aimed at achieving whole-person health and well-being
- by using a *respectful* combination or fusion of biomedical and traditional and/or complementary medical knowledge, skills and practices.

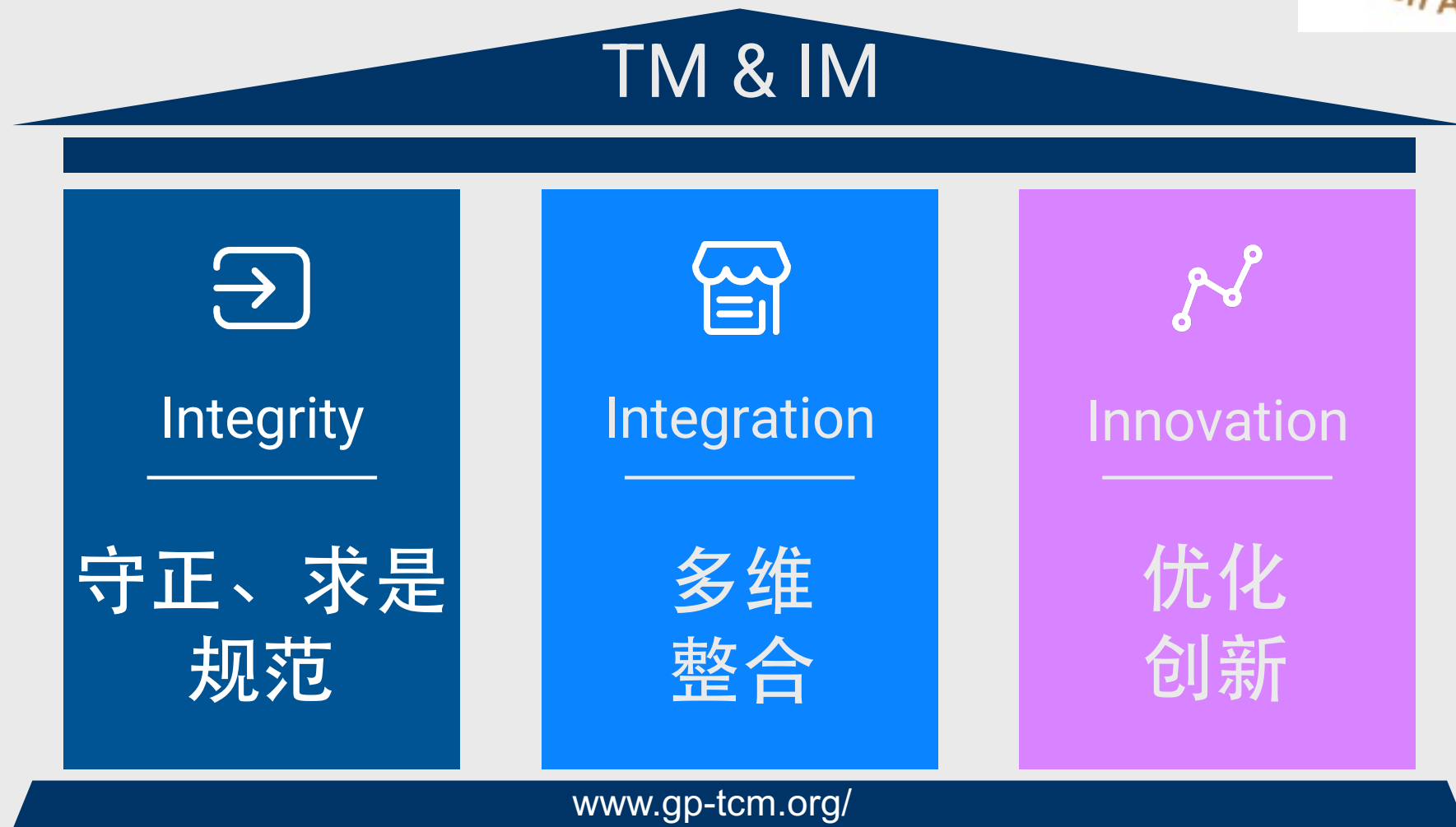
❑ “*respectful*” was removed in the **Sept. 2024 version** submitted for approval by the WHO Executive Board.

Respectful could be subjective.

However, for a sustainable future, it is essential for IM to be *respectful*.

This essentially means that TM R&D and practice must safeguard scientific integrity & rigor, by following **objective good practice standards and guidelines.**

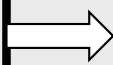
GP-TCM RA regards **integration** a central strategy for **innovation** and emphasizes that integration must be built on **integrity**, esp. [good practice](#).



The quest for modernisation of traditional Chinese medicine.
Xu Q, et al. BMC Complement Altern Med 2013;13:132 (>230 citations)

GP-TCM defines good practice as striving for consensus while respecting differences

- It is compliance with commonly accepted guidelines in biomedical R&D and health sciences, including general **guidelines for scientists** (**EQUATOR**), **journals** (**COPE**) and **regulators** (**ICH**)

- 
- GCCP2.0 (cell study)
 - PREPARE, & ARRIVE2.0 (animal study)
 - CONSORT (RCT)
 - PRISMA (systemic review)
 - MIQE (PCR)
 - SAGER (Sex and Gender); and
 - GATHER (Accurate and Transparent Health Estimates Reporting)
 -

- It also means good practice guidelines & standards of specific fields, e.g. TCM, often covered **by EQUATOR extensions**



Main topic of this talk...

- Uzuner H, et al. Traditional Chinese medicine research in the post-genomic era: **Good practice**, priorities, challenges and opportunities. J Ethnopharmacol. 2012;140:458-68 (>100 citations)
- **EQUATOR**: Enhancing QUALity and Transparency Of health Research. <https://www.equator-network.org>
- **COPE**: The Committee on Publication Ethics guidelines: <https://publicationethics.org>
- **ICH**: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: <https://www.ich.org>

Grey et al. *Nature* 2024;632:26-28.

The Committee on Publication Ethics (COPE) guidelines:
<https://publicationethics.org>

- **They include 15 sets of guidelines, 49 flowcharts and 788 case studies.**
- Although COPE is not a regulatory body, this global, publisher-funded organization holds much sway with journals and publishers. It provides a range of guidance on publication integrity, covering issues such as how to participate in peer review, how to respond to data fabrication and when to retract a paper.
- **Endorsed by >14,000 journals;** they agree to adhere to its 'principles of transparency and best practice in scholarly publishing'. Publishers routinely advertise their membership as evidence of their commitment to publication integrity.
- Endorsement is easy. Implementation takes much more efforts.

TM-specific good practice guidelines & standards

求同尊异、和而不同的传统医药技术标准与指南

Standards & GxP
guidelines

标准与指南

More internationally harmonised

国际同化度较高的标准与规范

Regional guidelines with international
importance

具有国际影响力的区域性标准与规范

Who publishes more internationally harmonised standards?

制订高同化度标准与指南的国际组织

- International Standardization Organization (**ISO**)
国际标准化组织
- World Federation of Chinese Medicine Societies (**WFCMS**)
世中联
- World Health Organization (**WHO**)
世卫组织
- International consortia (e.g. **GP-TCM**, **EQUATOR**, etc)
国际协作组织

ISO/TC 249

ISO中医药技术委员会

- 2009-2023, ISO has collaborated with WFCMS in publication of **95 standards on quality, safety and processing procedures of TCM raw materials & products**;
- >30 ISO drafts are being developed.
- 2009-2023年，ISO与世中联等合作，发布了95个中医药原材料和生产成品质量、安全性和加工程序的国际标准。
- >30国际标准正在制定过程中

For details, please visit:

<https://www.iso.org/committee/598435.html>

ISO is a partner preferred by the Chinese government in its efforts promoting internationalization of TCM standards

中医药标准国际化是中国政府鼓励的重点工作之一。ISO/TC 249是推动对接的中医药标准制定国际平台。

一、优化中医药标准体系总体布局

二、加强重点领域标准供给

三、推动中医药标准与科技创新互动发展

四、推进中医药标准国际化

五、深化中医药标准改革创新

六、夯实中医药标准发展基础

七、保障措施

国家中医药管理局

国中医药综法监函〔2024〕271号

国家中医药管理局综合司关于印发 《中医药标准化行动计划（2024—2026年）》 重点任务分工方案的通知

各省、自治区、直辖市中医药主管部门，局机关各部门，全国中医药标准化技术委员会、ISO/TC249国内技术对口单位，中医药社会团体：

现将《中医药标准化行动计划（2024—2026年）》重点任务分工方案》印发给你们，请认真执行，确保如期完成各项任务。

各部门要加强组织领导，按照重点任务分工方案要求，进一步分解细化相关任务，抓紧制定具体措施，明确进度安排，逐项推进落实。



WFCMS partners with ISO and also publishes its own standards

世中联是ISO的主要伙伴，也独立发表的国际标准

No	WFCMS 国际标准与指南 (n=22 by Nov. 2022))	发布时间
22	SCM 54-2020 中药处方要求 (TCM prescription)	2022-08-23
21	SCM 54-2020 中药调剂要求 (Dispensing)	2022-08-24
20	SCM 54-2020 中药给付要求 (Delivery)	2022-08-24
19	SCM 55-2020 中药煎服要求 (Decoction and taking)	2022-08-24
18	SCM-C 0039-2020 温控红外灸疗垫	2022-05-05
17	SCM-C 0014-2019 糖脂代谢病（瘰疬）中西医结合诊疗技术规范	2022-05-05
16	SCM-C 0011-2018 牛胶原肽粉	2022-05-05
15	SCM0051-2019 国际中医远程会诊服务规范	2022-05-05
14	SCM-C 0008-2017 耳穴探测仪	2022-04-28
13	SCM0050-2019 国际中医远程教育服务规范	2022-04-28
12	SCM0041-2014 世界中医药学科体系类目	2022-04-28
11	SCM0027-2019 凉茶饮料 (Liangcha herbal drinks)	2022-04-28
10	SCM0026-2019 浮针疗法技术操作规范	2022-04-28
9	SCM0024-2018 标准化煎药中心基本要求 (Standardised decoction-making centre)	2022-04-28
8	SCM0023-2019 热敏灸技术操作规范	2022-04-28
7	SCM0020-2017 中医药健康旅游服务要求	2022-04-28
6	SCM0018-2017 国际中医临床实践指南 糖尿病	2022-04-28
5	SCM0012-2014 国际中医医师测试与评审规范	2022-04-28
4	SCM0010-2012 世界中医专业核心课程	2022-04-28
3	SCM0008-2011 国际中医医师专业技术职称分级标准	2022-04-28
2	SCM0004-2010 诊所设置与服务标准	2022-04-28
1	SCM0003-2009 世界中医医学本科（CMD 前）教育标准	2022-04-28

Please visit: <http://www.wfcms.org/index.php/list/52.html>

WFCMS drafts, e.g. Network Pharmacology Evaluation Method
世中联指南草案，比如网络药理学评价方法



Prof. LI Shao

Tsinghua University

Chair, WFCMS Specialty
Committee of Network
Pharmacology

Li S, et al. WFCMS Specialty
Committee of Network
Pharmacology.

**Network Pharmacology
Evaluation Method
Guidance - Draft.**

World J Tradit Chin Med
2021;7:146-54

<https://www.wjtcm.net/text.asp?2021/7/1/146/310934>

WHO standards in acupuncture nomenclature and benchmark series on TM training & practice (2022): acupuncture, tuina, Ayurveda, and Unani.

世卫针灸术语, 以及针灸、推拿、印度传统医学指南

WHO Standards of TM terms and translation

世卫组织引领传统医学术语翻译的标准化

- WHO international standard terminologies on **traditional medicine in the Western Pacific Region**. 2007
- WHO international standard terminologies on **traditional Chinese medicine** (2022) and **traditional Indian medicines** (siddha, ayurveda, unani) (2023)

WHO standardises TM diagnosis, bringing it in ICD-11

世卫组织标准化传统医学诊断，并将其带入国际疾病分类目录

- WHO. Chapter 26. Supplementary Chapter Traditional Medicine Conditions - Module I. ICD-11. International Classification of Diseases 11th Revision; The global standard for diagnostic health information. 1999; in effect, Jan. 2022.

WHO guidelines on TM research & evaluation and herbal
GMP was the foundation of the FP7 GP-TCM collaboration
世卫组织传统医药研究评估方法指南与草药生产规范

- WHO **General Guidelines** for Methodologies on Research and Evaluation of Traditional Medicine. 2000; p1-74 (>1000 citations)
- WHO Guidelines for Selecting Marker Substances of Herbal Origin for **Quality Control of Herbal Medicines** (2017)
- WHO Guidelines on **Good Herbal Processing Practices** for Herbal Medicines (2018)
- Guidelines on **Good Manufacturing Practices** for the Manufacture of Herbal Medicines (2018)
 - replacing the 2007 WHO Guidelines on GMP for Herbal Medicines.

Good Practice in TCM Research in the Post-genomic Era (GP-TCM, 2009-2012)

后基因组时代中医药研究的良好实践

- A €1m project funded by the European Commission, under its 7th Programme Framework
- 25 countries, 110 institutions & enterprises, >200 members
- Aimed at promoting EU-China collaboration in modernisation of TCM research





Prof. Kelvin Chan
University of Sydney



Prof. Pierre Duez
University of Mons



Prof. Monique Simmonds
Royal Botanic Gardens

Chan K, et al.

Good practice in reviewing and publishing studies on herbal medicine, with special emphasis on traditional Chinese medicine and Chinese materia medica.

J Ethnopharmacol. 2012;140(3):469-75.

(203 citations)

World Flora Online - The WFO Plant List

<https://wfoplantlist.org/plant-list>

Consensus-based reporting guidelines for **Phytochemical** Characterisation of **Medicinal Plant** extracts (ConPhyMP)



药用植物鉴定、命名、提取、化学分析的指南

- Heinrich M, et al. **Best Practice in the chemical characterisation of extracts used in pharmacological and toxicological research: The ConPhyMP Guidelines.** Front Pharmacol. 2022;13:953205.

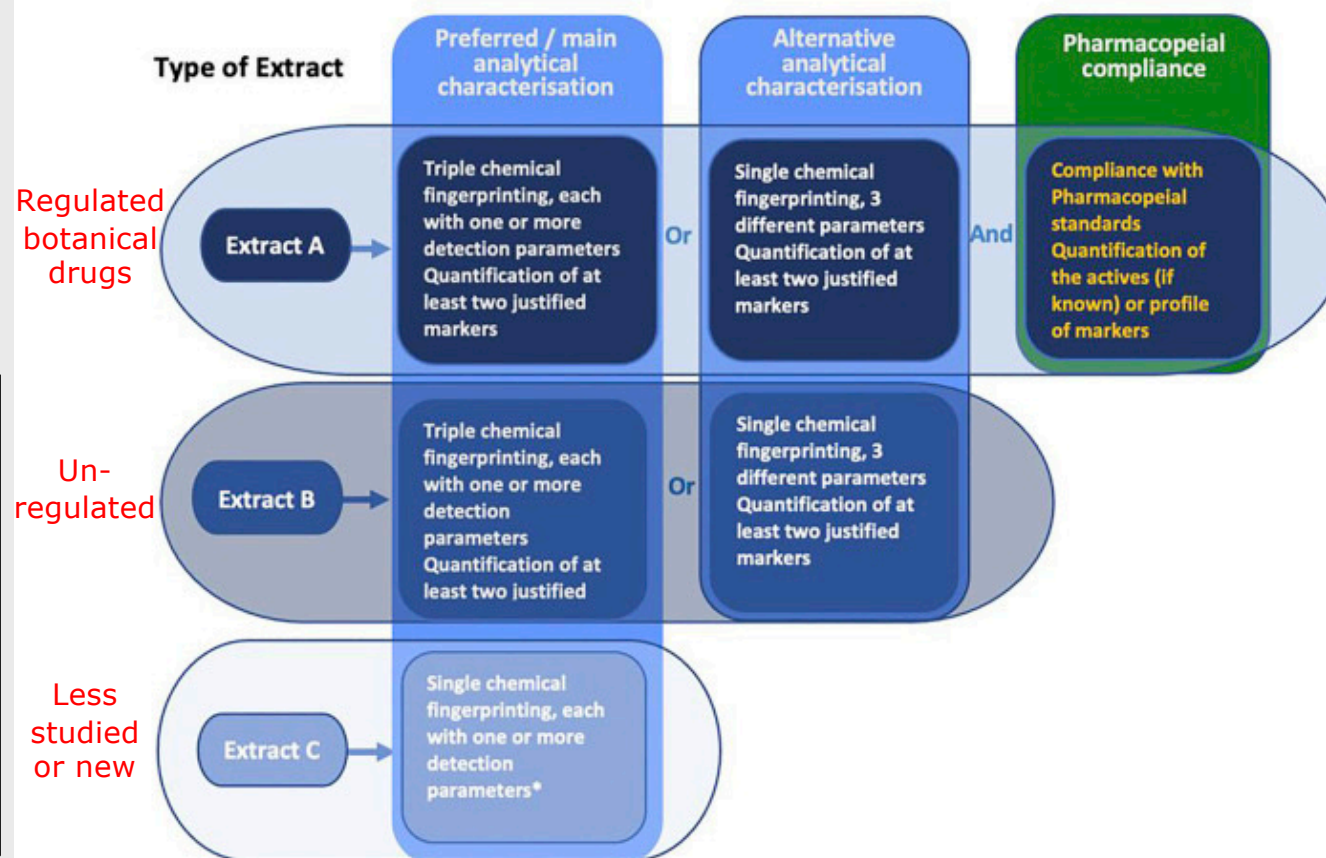


Prof. Michael Heinrich
University College London

ConPhyMP offers an online interactive tool for what is needed in the reporting pharmacology, toxicology and clinical effects of herbals:

<https://ga-online.org/best-practice/>

A strategic overview of levels of requirements for phytochemical analysis of different types of extracts





Prof. Zhaoxiang Bian
Chair, Clinical Studies
Interest Group
GP-TCM RA

CONSORT Extension for Chinese Herbal Medicine Formulas 2017: Recommendations, Explanation, and Elaboration.

Cheng CW, et al; CONSORT-CHM Formulas 2017 Group.
Ann Intern Med. 2017;167(2):112-121.

(186 citations)



Flower A, et al.
**Guidelines for randomised controlled trials
investigating Chinese herbal medicine.**
J Ethnopharmacol. 2012;140(3):550-4.

(96 citations)



Hugh MacPherson
Professor of Acupuncture Research
University of York

Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): extending the CONSORT statement.

MacPherson H, et al; STRICTA Revision Group.
Acupunct Med. **2010**;28:83-93.

(1565 citations)



Standards for reporting interventions in controlled trials of acupuncture: the STRICTA recommendations.

MacPherson H, et al.
Complement Ther Med. **2001**;9:246-9.

(262 citations)

CONSORT是Equator网络的一部分。后者发布一系列指南与**延伸指南**，旨在提升各种类型临床与实验研究的质量与透明度。

CONSORT is part of the Equator network, which publishes a **series of guidelines** and **extensions** aimed at enhancing the quality and transparency of various types of health research.



Reporting guidelines for main study types

Randomised trials CONSORT Extensions

Observational

studies STROBE Extensions

Systematic reviews PRISMA Extensions

Study protocols SPIRIT PRISMA-P

Diagnostic/prognostic

studies STARD TRIPOD

Case reports CARE Extensions

Clinical practice

guidelines AGREE RIGHT

Qualitative research SRQR COREQ

Animal pre-clinical

studies ARRIVE

Quality improvement

studies SQUIRE Extensions

Economic

evaluations CHEERS

延伸指南： 与传统医药研究密切相关

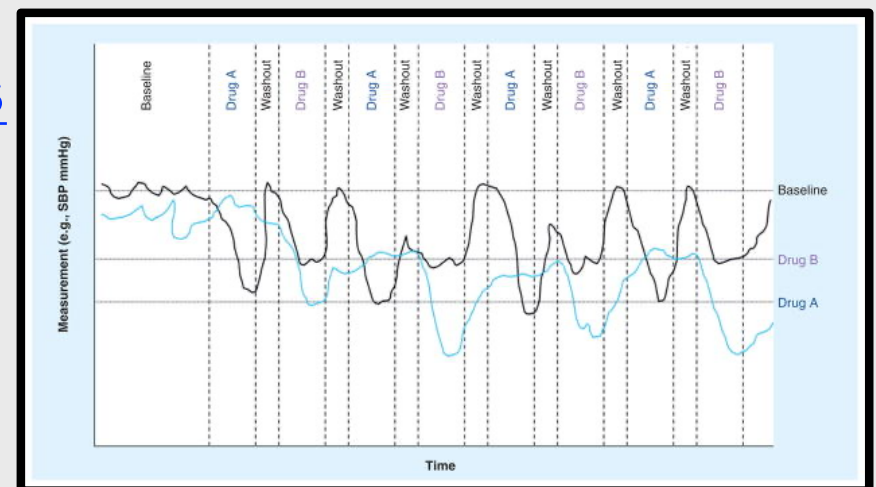
CONSORT extensions (n=35): Cutting-edge and relevant!

Six extensions directly related to TM:

- [Acupuncture \(STRICTA\)](#),
- [Cupping \(STRICTOC\)](#),
- [Tuina/Massage \(STRICTOTM\)](#),
- [Herbal interventions](#)
- [Chinese Herbal Medicine Formulas](#)
- **N-of-1 and N-of-1 TCM**

(单个患者的多重交叉设计)

(Single patient, multiple cross-over design)



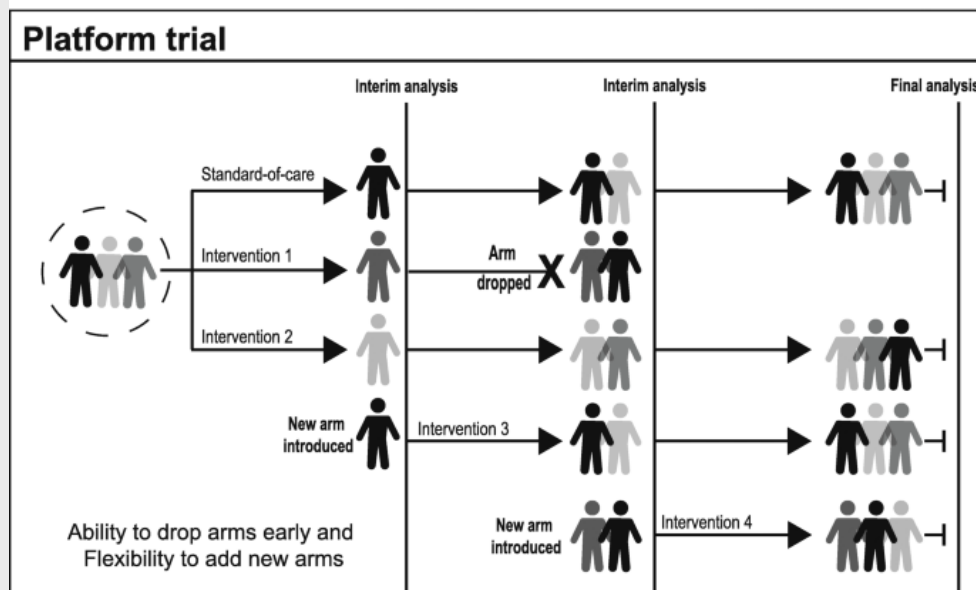
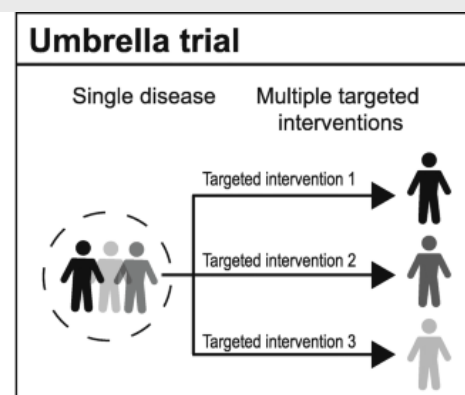
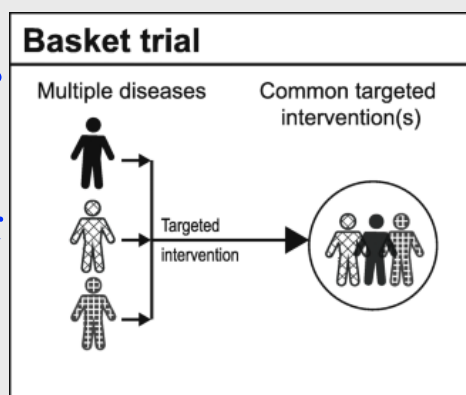
延伸指南： 与传统医药密切相关

Innovative RCTs of great relevance to TCM

- basket (篮子), umbrella (雨伞), Platform (平台) trials

篮子： 异病同治

Basket: One drug for 2 or more disorders



雨伞

同病异治

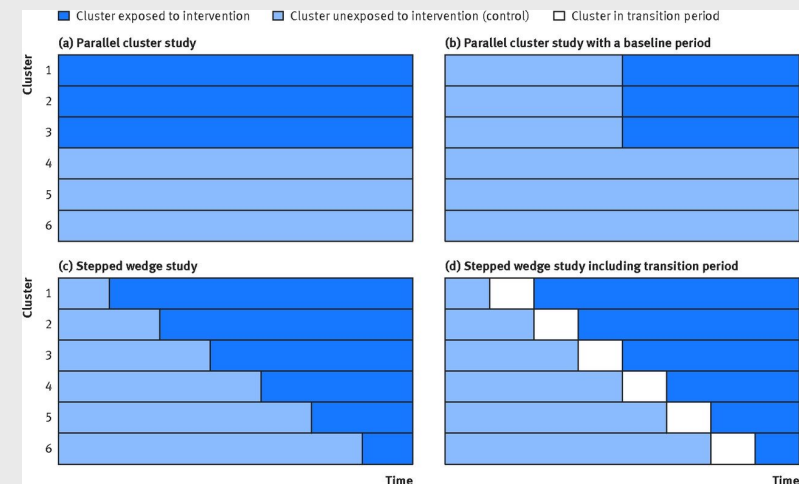
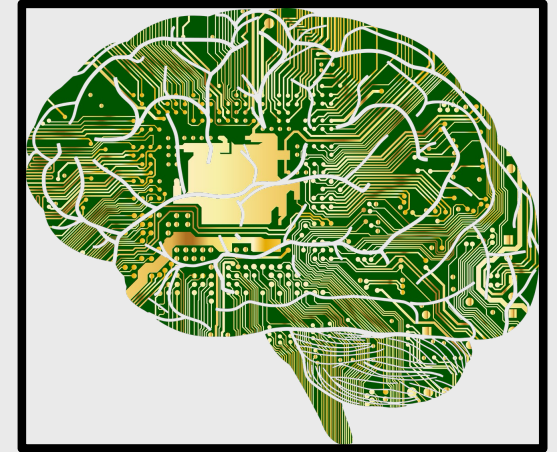
Umbrella & Platform:
2 or more
drugs for the
same disorder

平台

延伸指南：与真实世界研究密切相关

Extensions on more “real-world like” RCTs:

- Artificial intelligence (人工智能)
- De-centralized trials (去中心化临床研究)
- Adaptive designs (适应性设计)
- Pragmatic trials (实效性临床研究)
- Cluster & stepped wedge cluster (集簇设计、阶梯集簇设计)



A cross-sectional study of the endorsement proportion of reporting guidelines in 1039 Chinese medical journals.

Duan Y, et al. *BMC Med Res Methodol.* 2023;23:20.

- By 2022, 24.1% endorsed CONSORT; 0.8% endorsed CONSORT extensions.
- 14.8-17.2% endorsed STROBE, PRISMA, STARD, CARE:
- <0.7% endorsed SPIRIT, TRIPOD, AGREE and RIGHT:



Reporting guidelines for main study types

<u>Randomised trials</u>	<u>CONSORT</u>	<u>Extensions</u>
<u>Observational studies</u>	<u>STROBE</u>	<u>Extensions</u>
<u>Systematic reviews</u>	<u>PRISMA</u>	<u>Extensions</u>
<u>Study protocols</u>	<u>SPIRIT</u>	<u>PRISMA-P</u>
<u>Diagnostic/prognostic studies</u>	<u>STARD</u>	<u>TRIPOD</u>
<u>Case reports</u>	<u>CARE</u>	<u>Extensions</u>
<u>Clinical practice guidelines</u>	<u>AGREE</u>	<u>RIGHT</u>
<u>Qualitative research</u>	<u>SRQR</u>	<u>COREQ</u>
<u>Animal pre-clinical studies</u>	<u>ARRIVE</u>	
<u>Quality improvement studies</u>	<u>SQUIRE</u>	<u>Extensions</u>
<u>Economic evaluations</u>	<u>CHEERS</u>	

草药质控的指南落实情况令人担忧

Guidelines implementation is still far from satisfactory



Shepherd A, Brunckhorst O, Ahmed K, Xu Q.

Botanicals in health and disease of the testis and male fertility: A scoping review.

Phytomedicine. **2022**;106:154398.

- **Only 9%-23%** provided information on voucher samples, botanical authentication, extraction methods and chemical profiling!

草药临床研究规范落实也很堪忧

Poor guideline implementation in RCTs published in the past 5 years

- **Only 38% RCTs registered RCT protocols;**
- **Only 38% RCTs reported concealment of allocation and blinding of personnel involved in the trial.**
- **Only 43% RCTs reported ADR satisfactorily.**
- **Only 72% RCTs reported randomization methods.**
- **Only 78% RCTs reported ethical approval, but this was only 40% in those published in Chinese.**
- **Most RCTs reported written consent— only 2 RCTs published in Chinese did not report informed consent.**

Conclusions & Discussions

- Great progress has been made in the past decade in developing harmonised international guidelines & standards:
 - **GP-TCM, ConPhyMP and CONSORT** guidelines on herbal naming, QC, extraction & clinical studies.
 - **WHO** guidelines on TM terminology & diagnosis, herbal GMP, nomenclature, training & practice of acupuncture, etc;
 - **ISO and WFCMS collaborated** in publishing ~100 standards of TCM products;
 - **WFCMS** guidelines on TCM prescription, dispensing, delivery, decoction and taking, network pharmacology...
- These and many other general guidelines for scientists (**CONSORT**), publishers (**COPE**) and regulators (**ICH**) should be endorsed and implemented to safeguard quality of IM R&D.

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谢谢！

