循证医学与证据检索

主要内容

1. 循证医学概况
2. 循证医学实践
3. 循证医学的证据检索

1.1 定义与先驱

Evidence Based Medicine (EBM)

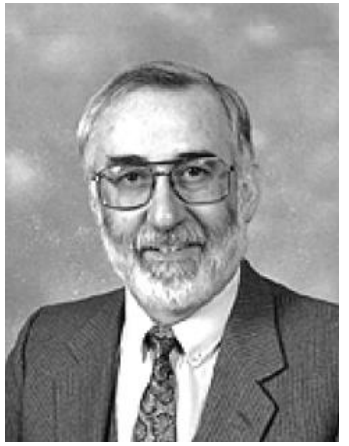
- 1991年，加拿大流行病学专家Gordon Guyatt发表单一著者论文，文中首次出现Evidence Based Medicine一词【1】。
- 1992年，以Guyatt为首的 McMASTER大学临床流行病教学组在期刊*JAMA*上首次提出循证医学的概念【2】。

【1】 Guyatt GH. Evidence-Based Medicine [editorial]. ACP Journal Club 1991:A-16. (Annals of Internal Medicine; vol. 114, suppl. 2).

【2】 Guyatt G, Cairns J, Churchill D, et al. (November 1992). "Evidence-based medicine. A new approach to teaching the practice of medicine". JAMA. 268 (17): 2420–5.

循证医学定义

- David L. Sackett（1934-2015），美国裔加拿大人，流行病学家，循证医学之父。



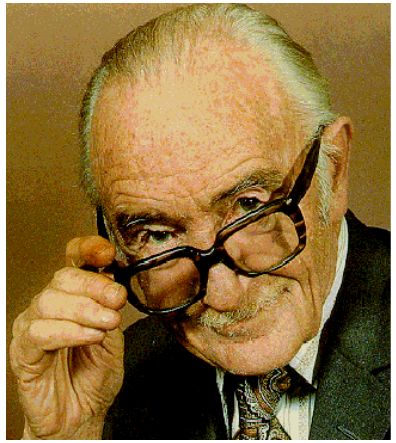
- 加拿大 McMaster 大学临床流行病学部、牛津循证医学中心创始人。
- 1995年，Sackett等出版专著*Evidence-based medicine: how to practice and teach EBM*，陈述循证医学定义及方法。

循证医学定义

慎重、准确、明智地应用目前可获取的最佳研究证据，同时结合临床医师个人的专业技能和长期临床经验，考虑患者的价值观和意愿，完美地将三者结合在一起，制定出具体的治疗方案【1】。—David L. Sackett

【1】***Evidence-based medicine: how to practice and teach EBM, 2nd ed.*** Edinburgh & New York: Churchill Livingstone, 2000.

循证医学先驱



Archie Cochrane（1909–1988），英国，临床流行病学先驱之一，循证医学思想的鼻祖。

主张使用随机对照试验，使治疗更有效。催生了循证医学、Cochrane系统评价和协作网的诞生。

1972年出版专著 *Effectiveness and Efficiency: Random Reflections on Health Services*，临床流行病学发展史上里程碑式的经典巨著。

1993.10 为纪念其成就，以其姓氏Cochrane命名的循证医学国际协作网宣布正式成立。

循证医学先驱

Iain Chalmers(1943-)，英国循证医学专家，循证医学创始人之一。

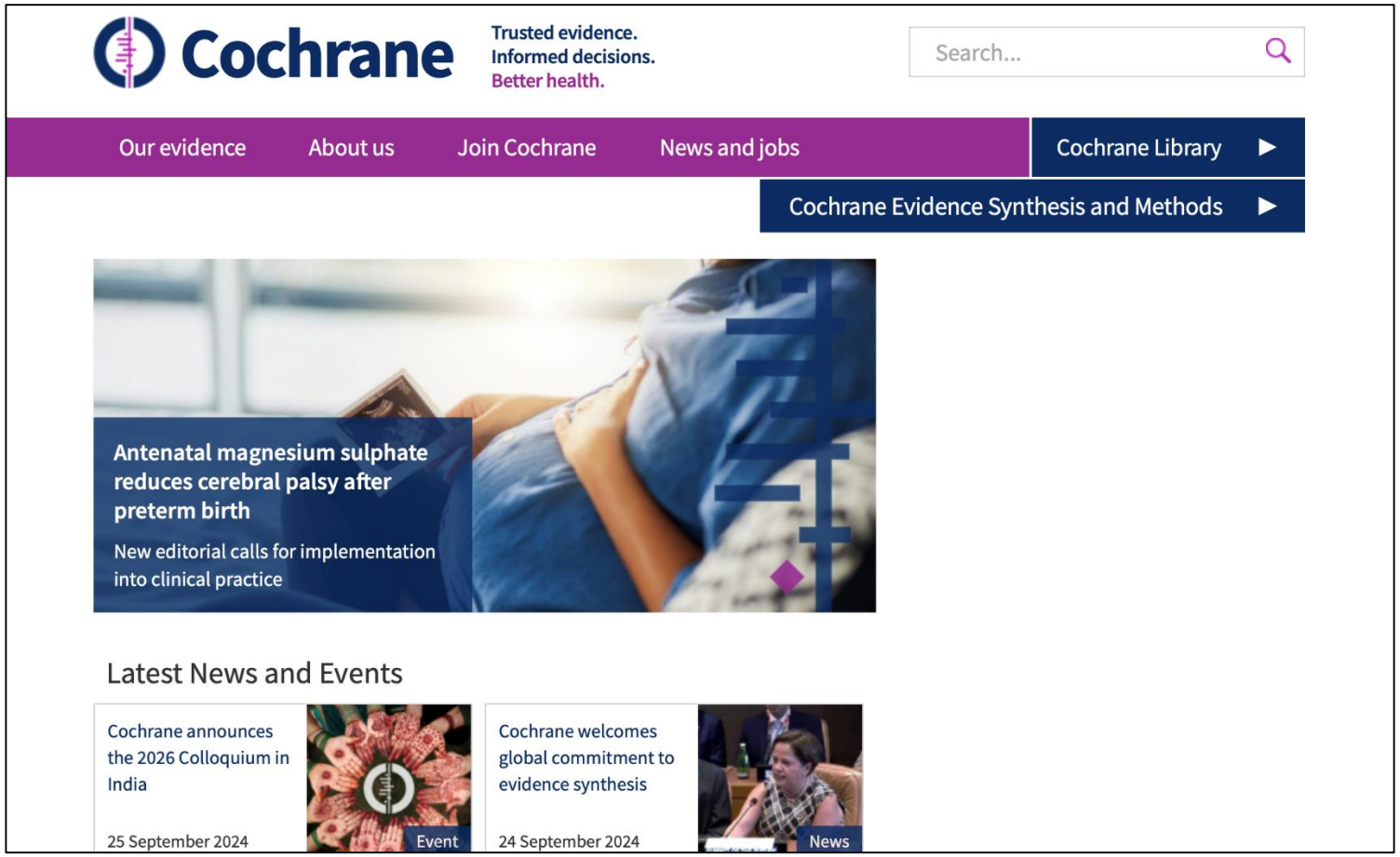
长达20余年对妊娠和分娩后随访，根据大样本随机对照试验结果进行系统评价研究，获得了令人信服的证据。

1989年，在其专著中明确肯定：皮质激素可以降低新生儿死于早产并发症的危险，使早产儿死亡率下降30%～50%【1】。

此前没有相关的系统评价分析和报道，多数产科医师并未认识到该项治疗措施的效果，导致成千上万早产儿死亡，耗费更多不必要的治疗费用。

【1】Chalmers Iain; Murray Enkin; Marc J.N.C. Keirse (1989). Effective Care in Pregnancy and Childbirth. Oxford University Press.

1.2 Cochrane协作网 （www.cochrane.org）



Cochrane标志：森林图

- 每一**横线**代表一个试验结果的可信区间，横线**越短**试验**精度越高**，**结果越肯定**；
- **垂直线**将圆一分为二，可判断结果差别有无统计学意义，区别治疗效果；
- 横线与垂直线**相接触或相交**，表明该试验的不同治疗措施间**差异无统计学意义**；
- 横线落在垂直线**右侧**，表明该措施会**增加**研究事件（如：导致痴呆）的**发生概率**；
- 横线落在垂直线**左侧**，表明该措施会**减少**研究事件（如：导致痴呆）的**发生概率**；
- 圆形图内下方的**菱形**符号代表7个试验的**综合结果。**

论文中的森林图

was 5.80, $P < 0.000\ 01$; Figure 2). The *OR* value of the C/A allele was 1.80 (95% *CI*: 1.47–2.22, $Z = 5.59$, $P < 0.000\ 01$; Figure 3).

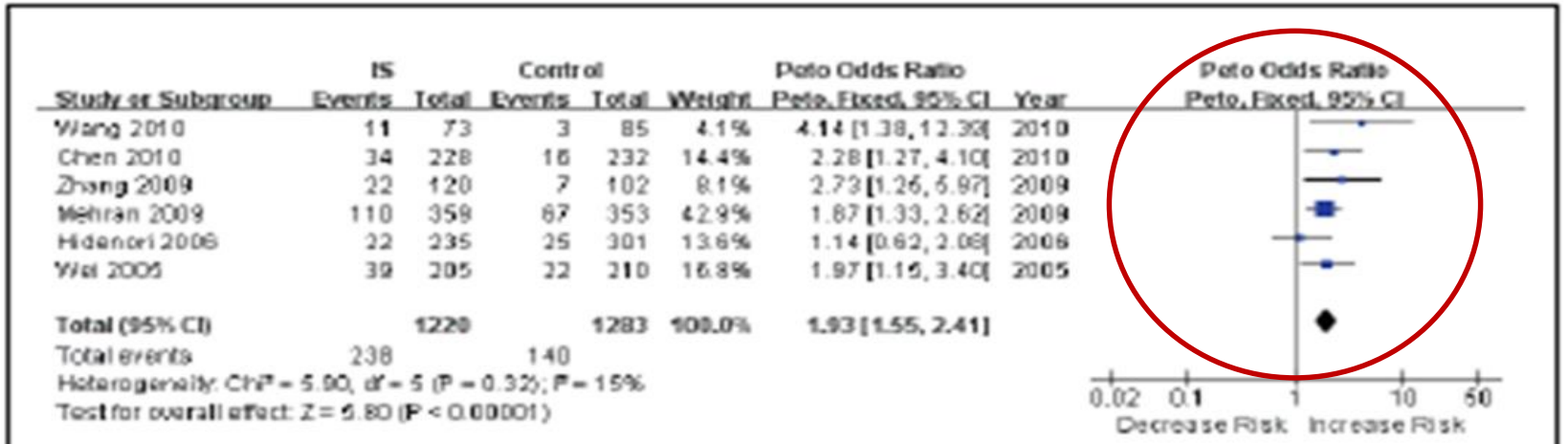
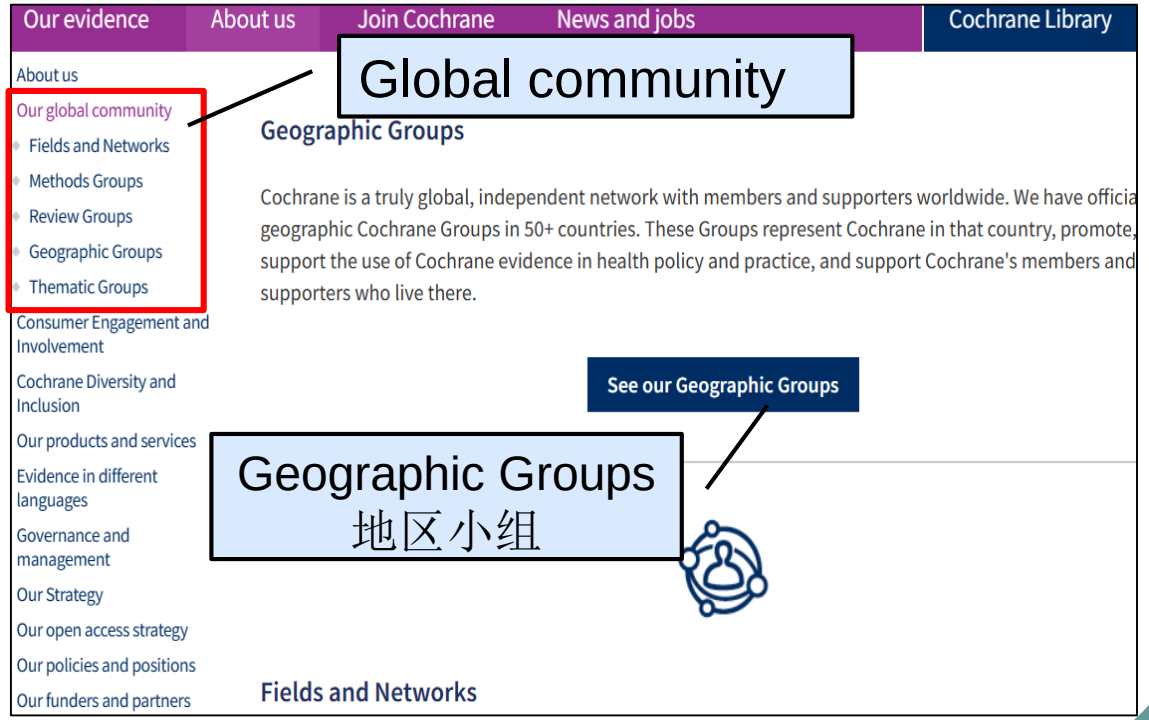


Figure 2 Forest map of the (AC+CC)/AA genotype in the E-selectin S128R gene A/C locus and ischemic stroke.

Cochrane协作网组织结构

- Central Executive Team执行团队
- Global community全球团队
- 50多个国家设有Cochrane中心或分支机构
- 18个方法学组
- 32个Active Cochrane系统评价小组



数据来源：https://www.cochrane.org/about-us/our-global-community/review-groups 访问日期：2024年4月10日

1.3 我国的循证医学

- 1999.3.31，中国经Cochrane协作网指导委员会正式批准，注册成为Cochrane协作网的第十四个成员国。**总部设在四川大学华西医院。**

- 设有北京大学、复旦大学、兰州大学等分中心。

2. 循证医学实践的步骤

2.1 构建临床问题

2.2 检索相关文献

2.3 严格评价文献

2.4 应用最佳证据

2.5 评价改进效果

2.1 构建临床问题

Patients/Population/Problem
病患/人群/问题

Intervention
干预措施或暴露因素

Comparison
比较干预或暴露

Outcome
临床结局

- **研究设计：Diagnosis, Etiology/Harm, Therapy, Prognosis, Prevention**

PICO模型的扩展

表 1　PICO 模型的扩展模式

字母	英文全称	中文意义
P	Population/Problem	某疾病的患病人群 / 需要解决的问题
I	Intervention/Exposure	实施的干预措施 / 危险因素暴露的情况
C	Comparison/Control	比较组 / 对照组
O	Outcome	产生的结局
E	Environment	患者的诊治环境、服务条件或是某种疾病发生的特定区域等外界环境因素
T	Time of frame	疾病研究进程
Q	Type of question being asked	问题的类型（诊断、病因、治疗、预后等）
D	Type of study design	需要检索研究的设计类型（RCT、队列、病例 - 对照等）

- 资料来源：DOI：10.7507/1672-2531.20140087

各类临床问题举例

表 2　各类临床问题举例

类型	临床问题举例	P	I	C	O	E	T	Q	D
病因问题	患者吴某，女，36 岁，妊娠 10 周，初产妇；经查体，身高体重指数（BMI）=34.5；经询问，家庭经济条件差。该患者向医生提问："我有可能得妊娠期高血压么？"	高龄初产妇	BMI 值较高		妊娠期高血压	家庭经济条件较差，营养状况较差	妊娠 10 周	病因 / 危险因素	队列研究 / 病例 - 对照研究
诊断问题	患者王某，女，68 岁，血红蛋白值 95 g/L，平均红细胞容积 80 fL。外周血涂片示血红蛋白减少，其余正常，未使用其他造血系统的药物。既往检查结果显示 6 个月前其血红蛋白值为 105 g/L，未发现贫血。铁蛋白检测值为 40 mmol/L。患者希望了解铁蛋白检查结果能否诊断贫血，诊断价值多大？	老年女性小细胞低色素性贫血患者	低铁蛋白		缺铁性贫血			诊断	横断面研究
治疗问题	患者张某，男，19 岁，因发热胸痛呼吸困难前来某县级医院就诊；经检查，拟诊为结核性胸膜炎；接诊医生按常规给予如下治疗：① 利福平、异烟肼、链霉素、吡嗪酰胺；② 抽胸水；③ 考虑患者自身情况，给予泼尼松治疗。患者问："用药后多长时间能退烧？"	年轻结核性胸膜炎患者	糖皮质激素类药物治疗	安慰剂	结核性胸膜炎症状，如发热等	县级医院		治疗	随机对照研究
预后问题	患者林某，女，32 岁，左侧乳房肿块，前来某三甲医院就诊。经检查，肿块质地较硬，比较固定；行左侧乳腺癌根治术；术后病理结果：浸润性导管癌，3 cm×4 cm，ER（-），PR（-），Her-2（+），左腋窝下淋巴结清扫 20 个，12 个见转移。患者问："术后 2 年内复发的机会有多大？还能活多久？"	年轻女性，乳腺癌，TNM 分期为 Ⅱ a 期	行左侧乳腺癌根治术	未行乳腺癌根治术	复发时间 / 生存时间	三级甲等医院	术后 2 年随访	预后	队列研究

- 资料来源：DOI：10.7507/1672-2531.20140087

临床问题举例

PICO

一位64岁肥胖的男性病人，尝试用各种方式减轻体重。他向王医师呈交一篇报道：“肥胖者的福音”—壳聚糖（chitosan），患者想了解服用壳聚糖对他减肥是否有效，但王医师凭借以往经验无法给出答案。

P	I	C	O
肥胖病人 Obesity overweight	壳聚糖 chitosan	是否有对照组 (not clear)	减轻体重 Weight

S 治疗 therapy

临床问题举例

- 构建不够好的问题

  壳聚糖对肥胖病人有效吗?

  I P

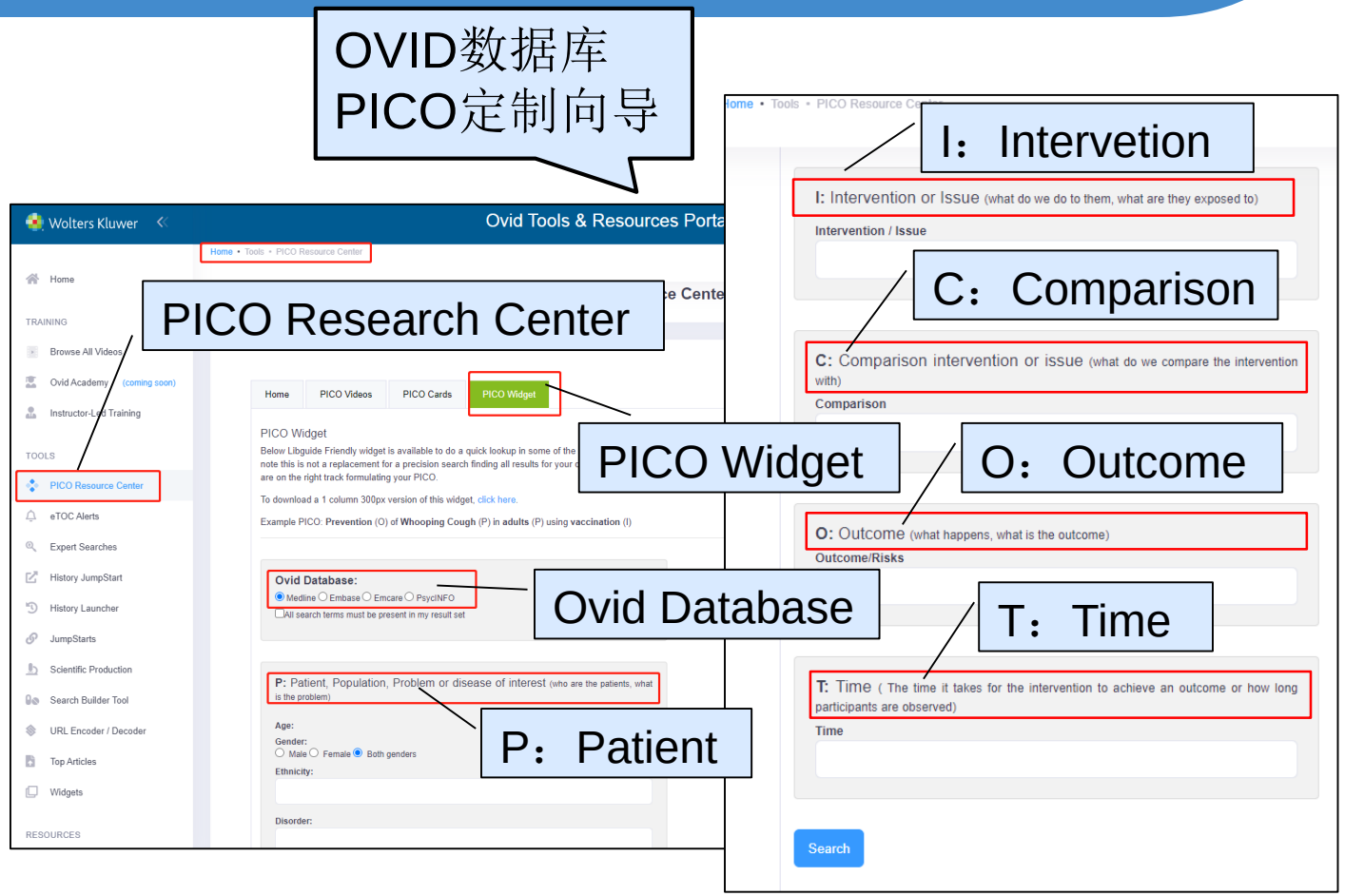
- 构建良好的问题

  壳聚糖与奥利斯他相比是否更能降低肥胖病人的脂肪吸收?

  I C P O

2.2 检索相关文献

- 根据临床问题，确定“检索词”
- 检索相关文献。找出密切相关资料，作为分析评价之用。
  - ✓ 原始研究
  - ✓ 二次研究（汇总分析不同研究者的原始研究结果，得出综合结论）
- **文献检索虽是循证医学实践中的一个环节，检索策略的制定很重要。**



2.3 严格评价文献

- 应用临床流行病学及EBM质量评价标准，对收集到的文献从证据的真实性、可靠性、临床价值及其适用性作出具体的评价。
- 如果收集的合格文献较多的话，可以作系统评价(systematic review) 和Meta-分析(meta-analysis)
- 学习循证医学最好的方法是写一篇系统评价

2.4 应用最佳证据

- 将获得的真实可靠的，并有临床应用价值的最佳证据，用于指导临床决策。
- 否定经严格评价认为乏效，甚至有害的治疗措施。
- 对于尚难定论并有期望的治疗措施，可为进一步研究提供信息。
- 遵循个性化原则

2.5 评价改进效果

- 通过对患者的实践，总结应用证据的经验教训，从中获益；
- 为临床研究设计和改进提供实证依据；
- 促进学术水平和医疗质量的提高。

3. 循证医学证据的检索

3.1 循证医学的证据

“证”就是对临床研究的文献，应用临床流行病学的原则和方法，经过认真的分析和评价获得的新近的最真实可靠且有临床重要应用价值的研究成果。

3.1.1 证据分类

按研究方法分类	按研究问题	按用户需要分类	按获得渠道分类
原始临床研究证据 随机对照试验 队列研究 病例—对照研究 无对照的研究 二次临床研究证据 系统评价 Meta分析 临床实践指南 卫生技术评估	病因临床研究证据 诊断临床研究证据 预防临床研究证据 治疗临床研究证据 预后临床研究证据	系统评价 临床实践指南 卫生技术评估 健康教育材料 在研临床研究证据	公开发表的临床研究证据 灰色文献

1、系统评价(Systematic Review)与Meta-分析

是针对某一具体临床问题，全面搜集相关文献，并从中筛选出符合标准的文献，运用统计学原理和方法，对这些文献进行综合和研究而产生的新文献。

［例］非小细胞肺癌完全切除术后的放射治疗，地位不明确、存在争议。

20世纪90年代，有meta分析明确表明：术后放射治疗不适合完全切除的早期非小细胞肺癌病人。

系统评价的格式

- 题目
- 摘要：结构式
- 课题背景
- 研究目的
- 检索策略
- 选择标准
- 结果
- 结论

房颤卒中预防的新型抗凝剂：成本效益模型系统评价

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0062183

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Novel Anticoagulants for Stroke Prevention in Atrial Fibrillation: A Systematic Review of Cost-Effectiveness Models

Brendan L. Limone, William L. Baker, Jeffrey Kluger, Craig I. Coleman

Published: April 23, 2013 • https://doi.org/10.1371/journal.pone.0062183

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Abstract
Introduction
Patients and Methods
Results
Discussion
Supporting Information
Author Contributions
References

Reader Comments
Figures

Abstract

Objective

To conduct a systematic review of economic models of newer anticoagulants for stroke prevention in atrial fibrillation (SPAF).

Patients and Methods

We searched Medline, Embase, NHSEED and HTA databases and the Tuft's Registry from January 1, 2008 through October 10, 2012 to identify economic (Markov or discrete event simulation) models of newer agents for SPAF.

Results

Eighteen models were identified. Each was based on a lone randomized trial/new agent, and these trials were clinically and methodologically heterogeneous. Dabigatran 150 mg, 110 mg and

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房颤卒中预防的新型抗凝剂：成本效益模型系统评价

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0062183

Introduction

Atrial fibrillation (AF) affects approximately 3 million people in the Unites States (U.S.), and this number may reach as high has 12 million by 2050 [1]. AF is associated with a significant financial burden, costing the U.S. healthcare system about $26 billion annually [2]. While hospitalizations are the primary driver of these costs (52%); the cost of pharmacologic management of AF is also noteworthy (23%) [3].

One of the primary concerns accompanying the diagnosis of A old increase in ischemic stroke risk [4]. Guidelines for the manage use of pharmacologic agents for the prevention of stroke dependin or patients at moderate-to-high risk of stroke, a vitamin K antagonist such as warfarin has traditionally been recommended. However, its use has been limited by its narrow therapeutic index and food and drug interactions [8], [9]. Therefore, alternative anticoagulants have been evaluated in recent years. To date, two agents (dabigatran, rivaroxaban) have received approval by the United States Food and Drug Administration (FDA) for prevention of stroke and systemic embolism in patients with AF, with a third (apixaban) currently under consideration. Clinical trials have demonstrated these agents to have at least similar impact on reducing stroke rates compared to warfarin with comparable or improved safety profiles [10]–[12].

课题背景

An important step in determining the place of these newer anticoagulants in clinical practice is to evaluate their cost-effectiveness. This fact is highlighted by the discussion of cost-effectiveness data (although not exhaustive) in recent national guidelines for pharmacologic stroke prevention in AF (SPAF) [7]. Numerous economic models have been published to evaluate the cost-effectiveness of these newer oral anticoagulants for SPAF [13]–[30]. Accordingly, we undertook a systematic review of economic models of dabigatran, rivaroxaban and apixaban for SPAF.

Patients and Methods

Data Sources and Searches

We searched the MEDLINE, EMBASE, National Health Service Economic Evaluation Database (NHS EEDS) and Health Technology Assessment (HTA) bibliographic databases along with the Tufts Cost-Effectiveness Analysis Registry. Searches were conducted for economic studies published between January 2008 and October 10, 2012. The start date of our search corresponded with the first published outcomes study of dabigatran. Our searches utilized Medical Subject Heading (MeSH) terms and keywords for AF, economic modeling and the newer anticoagulants (**see Text S1**). Finally, we also reviewed references from included models to identify additional relevant citations.

检索策略

选择标准

数据提取与分析

质量评估

Abstract
Introduction
Patient
Results
Discussion
Supporting Information
Author Contributions
References

Reader Comments (0)
Figures

Patients and Methods

Data Sources and Searches

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Text S1). F
viewed referen

Study Selection

Two investigators independently reviewed a
inclusion in a parallel manner using *a priori*
pharmacologic agents for SPAF using a M
to evaluate both cost (in monetary units) a
(QALYs)). Models had to be available as a
Manufacturer's models reported as part of
(NICE) or Canadian Agency for Drugs and
models presented solely at professional m

Data Extraction

Two investigators used a standardized data
disagreement resolved by discussion. We
made; 2) characteristics of the base-case
"progenitor" models, health states, study p
analysis, willingness-to-pay threshold(s) (V
of the models themselves and that of the randomized trials un
blinding, intention-to-treat methods, inclusion/exclusion criteri
the therapeutic international normalized ratio (INR) range, etc.
analyses. For the purpose of this review, a "progenitor" model
distinct structure and serving as a template for future models.

Quality Assessment of Economic Mo

We conducted a critical appraisal of the methodology and rep
government reports) using the Quality of Health Economic Studies (QHES) rating scale [31], [32]. The QHES is a validated assessment of quality for cost-effectiveness analyses and contains 16 evaluable items. Each item carries a weighted point value, with total possible scores ranging from 0 (lowest quality) to 100 (highest quality). An explanation of our QHES scoring of included models is available in **Supporting Information:** Text S2. In addition, we evaluated the internal validity of the models using the Jadad scale [33]. For the purpose of this review,

Text S1.
MEDLINE Search Strategy.
https://doi.org/10.1371/journal.pone.0062183.s005
(DOCX)

Text S2.
Explanati
https://doi
(DOCX)

Checklist
PRSIMA
https://doi
(DOC)

Author

pone.0062183.s005.docx - Microsoft Word

文件 开始 常用按钮 插入 页面布局 引用 邮件 审阅 视图 美化大师 EndNote X2

Text S1: MEDLINE Search Strategy

Atrial fibrillation AND (markov OR semi-markov OR markov state transition model OR markov simulation OR markov chain OR markov processes OR decision analysis OR decision analyses OR decision analytic OR decision tree OR decision model) AND (warfarin OR coumarins OR vitamin K antagonists OR dabigatran OR apixaban OR rivaroxaban OR ximelagatran OR anticoagulants OR aspirin OR clopidogrel OR antiplatelet)

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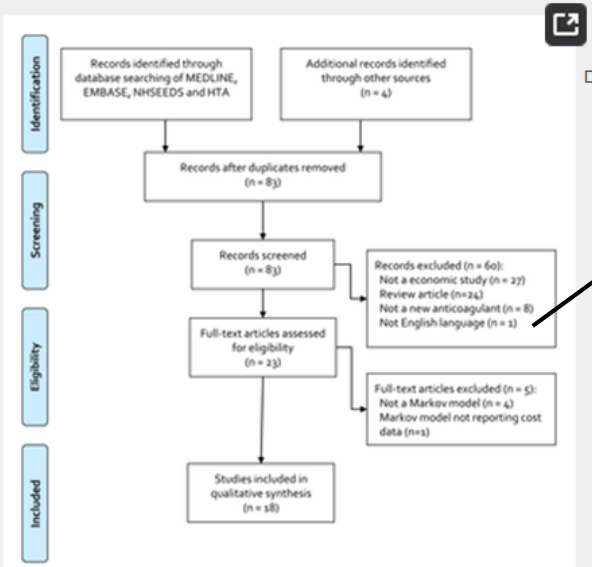
means ± standard deviations. The authors have followed the PRISMA Statement in reporting this systematic review (see Checklist S1).

Results

数据识别、筛选、合格入选、综合

The literature search initially identified 83 non-duplicate citations (Figure 1). Upon title and abstract review, 60 citations were excluded, leaving 23 articles for full-text review. Upon full-text review, 5 articles were excluded, leaving a total of 18 models for inclusion in our systematic review (Table 1) [13]–[30].



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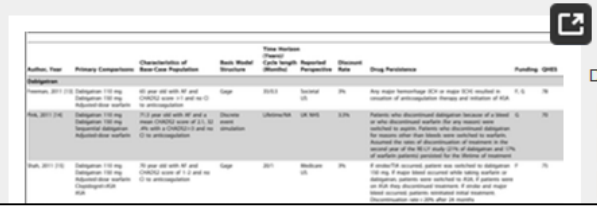
文献筛选流程

Figure 1. Results of Literature Search.
doi:10.1371/journal.pone.0062183.g001



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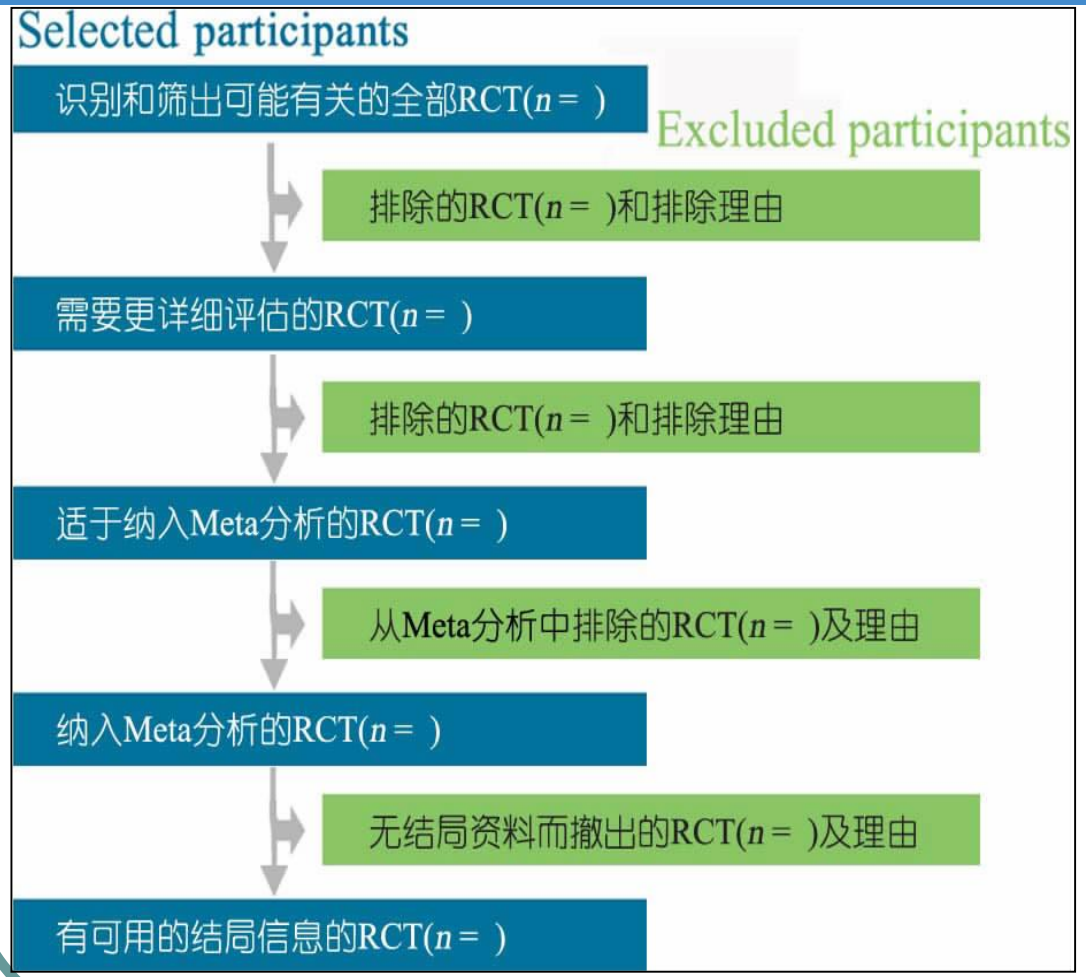
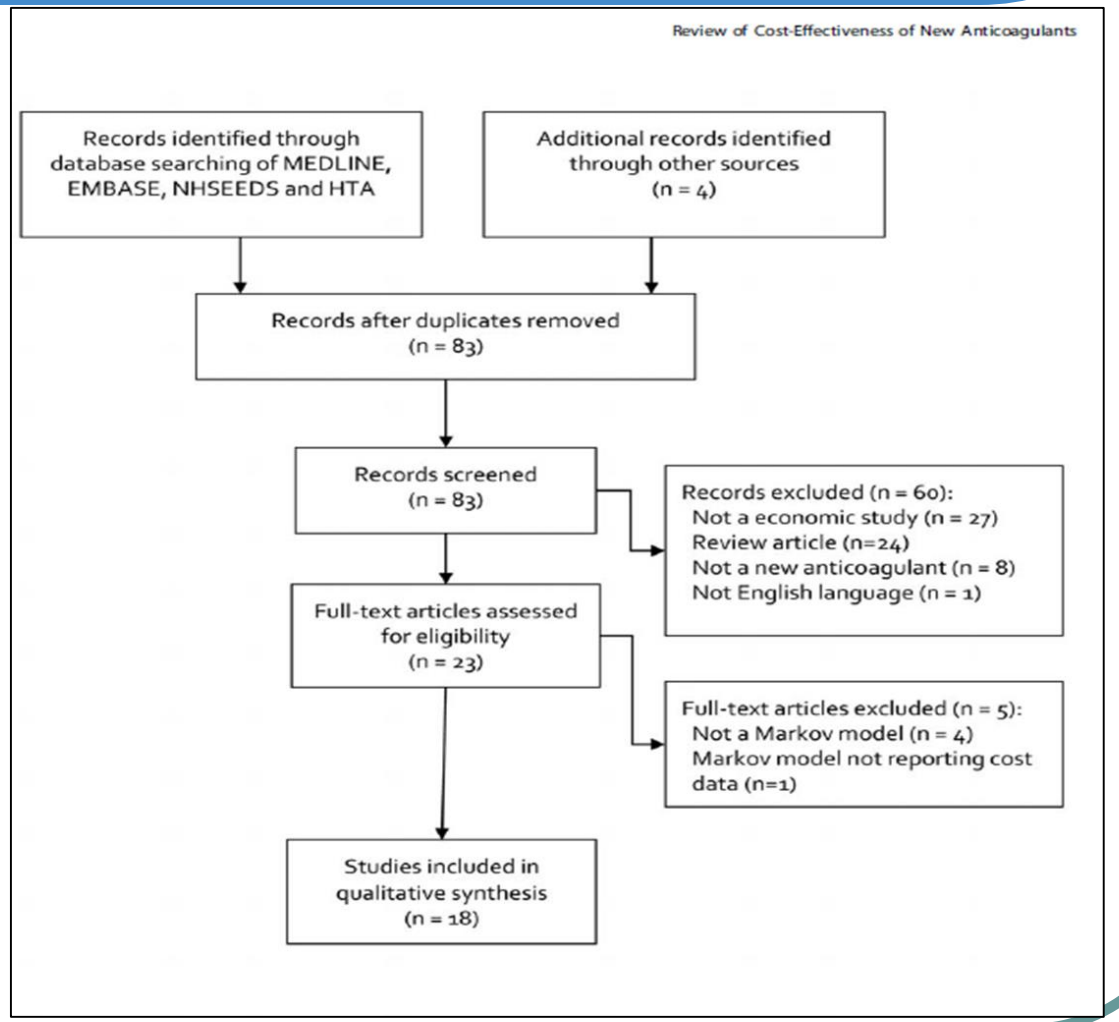
RCT的Meta分析文献纳入和排除流程图





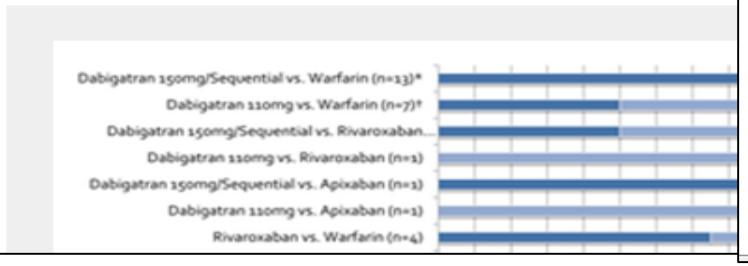
- 资料来源：DOI：10.3969/j.issn.1673-5501.2010.01.009

Prevention in Atrial Fibrillation: A Systematic Review of Cost-Effectiveness Models

ey Kluger, Craig I. Coleman

Dabigatran Models

Of the 13 models that directly compared dabigatran to warfarin, 8 as
110 mg, and 8 assessed sequentially-dosed dabigatran. Seven mod
al. [16] were very similar in terms of model characteristics, with sligh
(e.g., country-specific costs, discount rates, life tables to model nor
based on Gage et al. [34] had more variation in model properties and
population characteristics, health states modeled). Of note, one mo
with a prior stroke or transient ischemic attack (TIA) [20], while the
patients with or without a prior stroke or TIA (typically around 20%).
discrete event simulation, and the other exhibited a unique model st
myocardial infarction (MI) health state, 11 included a minor bleed he
control on the results. Eight of the 13 models included a systemic e
derivatives of Sorensen et al.), but only two of 13 modeled a dyspep
significantly differing in incidence between treatment groups in RE-L
from the RE-LY trial. In total, 78% of dabigatran vs. warfarin ICERs w
thresholds (four dabigatran 110 mg and two 150 mg comparisons vs
WTPs) and ranged from $3,547–$86,000 for dabigatran 150 mg; $20
$21,466 for sequentially-dosed dabigatran (**Table 3, Figure 2**). The
cost-effective, perhaps due to the chosen cost of dabigatran. The au
median cost of USD$9 per day, whereas other models typically use
[13] also utilized a higher cost for dabigatran which may have pushe
threshold. Though dabigatran 150 mg was cost-effective in their origi
on a lower cost of dabigatran 150 mg which decreased the ICER fro
13 models comparing dabigatran to warfarin, 9 performed probabilist
dabigatran 150 mg to be cost-effective in 44.9%–93% of iterations; c
sequentially-dosed dabigatran in 82%–100% of iterations at the lowe
All 13 models performed one-way sensitivity analyses and the result
risks of ischemic stroke or ICH on dabigatran/warfarin, time in thera
long term disability care.



Discussion

There has been a rapid dissemination of newer oral anticoagulants SPAF cost-effectiveness analyses in the last few years [13]–[30]. Fourteen models evaluated dabigatran [13]–[23], [28]–[30], four evaluated rivaroxaban [24], [28]–[30] and four evaluated apixaban [25]–[27], [30]. Moreover, three models provided comparative the cost-effectiveness of two or more of the newer oral anticoagulants [28]–[30]. Six of eight models found dabigatran 150 mg to be cost effective, three of seven found dabigatran 110 mg to be cost-effective, and seven of eight found sequential dabigatran to be cost-effective versus adjusted-dose warfarin. The earlier dabigatran models generally had higher ICERs due to an over-estimation/high cost of dabigatran. Studies evaluating sequential dabigatran dosing generally showed lower ICERs than traditional dosing, although it is noteworthy that sequential dosing is not supported by the RE-LY trial and is not an approved regimen in the United States. Three apixaban models showed it to be either dominant [26] or cost-effective compared with warfarin [25], [30], whereas compared to aspirin, apixaban was dominated in a 1-year trial length model, but dominant in a longer 10-year model [27]. Commonly reported sensitive or influential variables included the cost of the newer agents, the rates of stroke/ICH versus various comparators, the time horizon, the quality of warfarin control and the costs of acute events and long term disability care.

One of the challenges in attempting to evaluate the comparative cost-effectiveness of newer oral anticoagulants is the difficulty in making cross-model comparisons. This is likely true in the case of these newer SPAF models, even though a majority of them used the basic and common structures of Gage [34] or Sorensen [16]. This is because the models had some differences in health states included, made different assumptions and used varying inputs. In some instances, similar models were performed from the perspective of varying countries, this was necessary in order to not only address differences in costs, discount rates and average life spans (life tables), but also to address the varying approved dosing schemes from country-to-country (i.e., sequentially-dosed dabigatran is not an FDA approved regimen). Three models used data from either adjusted indirect comparison meta-analyses or network meta-analyses [28]–[30]; however, even the results of these models must be interpreted with caution due to important differences in the studies that underlie the comparisons and the conduction of the indirect comparisons themselves. Of importance, the 3 major clinical trials evaluating the newer oral anticoagulant agents vs. warfarin differ in notable ways [10]–[12].The ROCKET-AF trial enrolled patients at higher baseline ischemic stroke risk than the RE-LY or ARISTOTLE trials, with mean $CHADS_2$ scores of 3.5, 2.1, and 2.1, respectively. In addition, the quality of warfarin dosing was not consistent across studies with patients spending less time within the therapeutic INR range in ROCKET-AF (55%) versus either RE-LY (64%) or ARISTOTLE (62%). In fact, methodological guidance documents would suggest this may be an inappropriate situation for indirect comparison due to the lack of comparability/heterogeneity of the trials to be pooled [37]–[39]. Also, as alluded to previously, endpoint data used both within and across the indirect comparisons were not always based on the same trial populations/analysis methods, some using ITT populations and others using SOT populations. Thus, it is not surprising that these indirect comparison meta-analyses had disparate effect size estimates for many of the key model inputs [29], [30], [40]–[42]. In 5 identified meta-analyses making indirect comparison of at least 2 of the newer agents, marked variation in relative effect size estimates can be observed. For example, odds ratios of dabigatran versus rivaroxaban ranged from: 0.74–0.85 for stroke/systemic embolism, 0.95–1.06 for all-cause mortality, and 1.59–1.76 for acute MI. Similarly hazard ratios ranged from 0.96–1.04 for all-cause mortality, 1.40–1.57 for acute MI and 0.48–0.63 for ICH.

Importantly, all of the identified models in this review utilized a lone RCT (or an indirect comparison in which only a lone study existed for a given direct comparison) to characterize the main efficacy and safety comparisons between treatments. Data from these short-term clinical trials had to be extrapolated to longer time horizons in order to estimate

Novel Anticoagulants for Stroke Prevention in Atrial Fibrillation: A Systematic Review of Cost-Effectiveness Models

Brendan L. Limone, William L. Baker, Jeffrey Kluger, Craig I. Coleman

assessment, and therefore interpretation of the results and conclusions of these analyses. The use of outdated non-drug specific may reduce the validity of some of these models. Variations in the inclusion of health states, even across models assessing similar drugs, also presents difficulties in translating results, especially in cases of disagreement in the conclusions of those models. Decision makers must be aware of these caveats when clinical and coverage decisions are formed on the basis of these economic analyses.

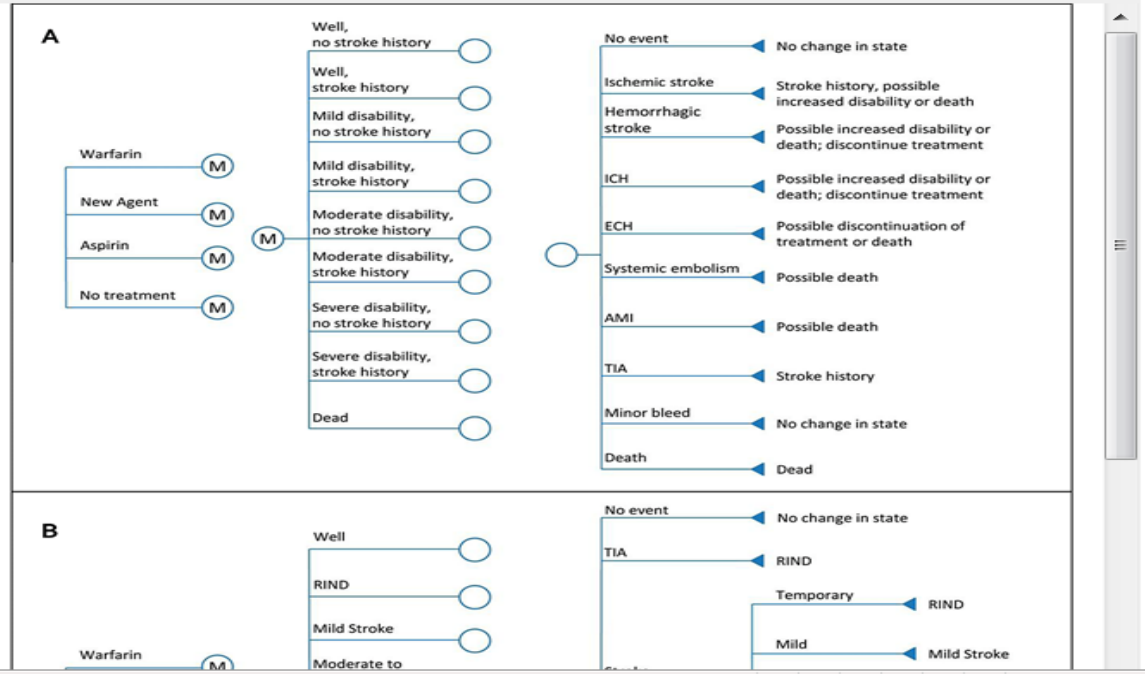
Conclusions

结论

Many researchers have published cost-effectiveness models of the novel anticoagulants for SPAF. These models suggest that the novel anticoagulants are cost-effective, but do not provide adequate data for direct comparison of the individual agents. For now, it seems prudent to choose anticoagulation therapy on a patient-specific basis. Standardization of the structure and inputs to assure that important health states are not being ignored and the best and most recent inputs are utilized would improve future comparisons between SPAF models. In addition, head-to-head trials of the newer oral anticoagulants would aid health economists to assess their comparative cost-effectiveness.

Supporting Information

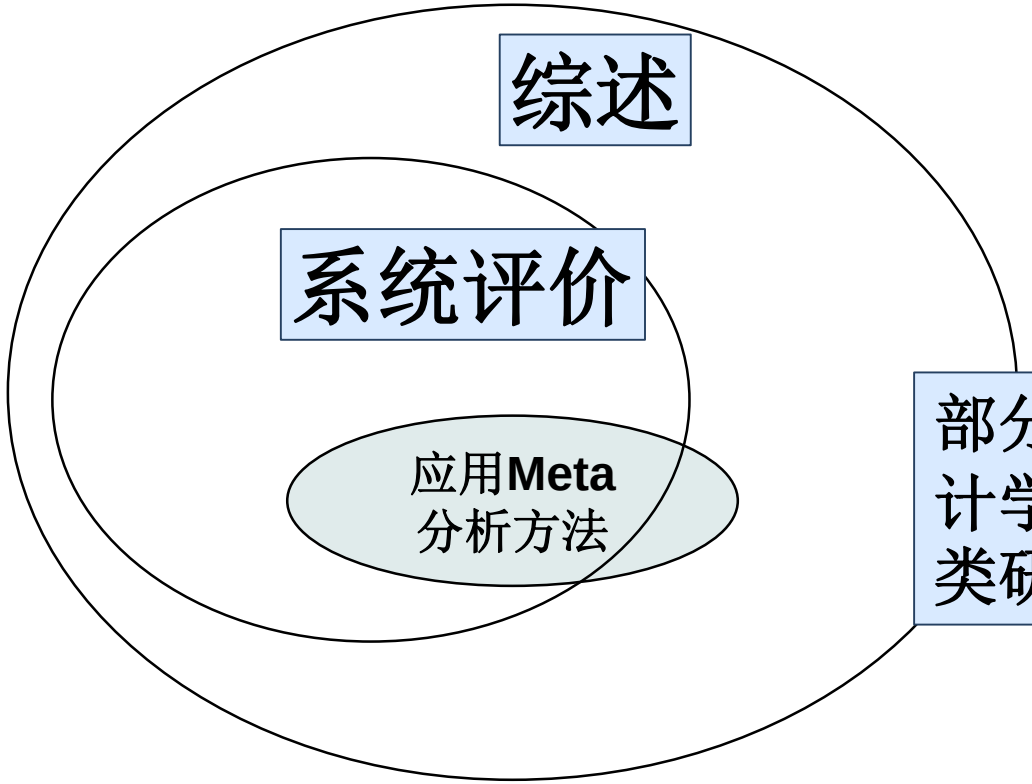
Figure_S1.tif



系统评价和一般综述的区别

	系统评价	一般综述
研究问题：	常集中于某一问题	涉及范围较广
文献来源：	明确，常为多渠道	不够全面
检索方法：	有明确检索策略	常未说明
文献选择：	有明确选择标准	有潜在偏倚
文献评价：	有严格评价方法	方法不统一
结果合成：	定量研究	定性研究
结论推断：	大多遵循研究依据	有时遵循研究依据
结果更新：	依据新试验定期更新	不更新

系统评价和一般综述的区别



部分系统评价应用了Meta分析统计学方法，将多个不同结果的同类研究合并为一个量化指标。

制作Cochrane系统评价的过程

1、提出问题，确定系统评价的题目
2、与相关Cochrane系统评价组联系，申请注册题目
3、批准后，按协作网提供的软件和Handbook制作protocol
4、计划书完成后提交协作网，接受评价组的修改
5、修改到编辑部满意后，发表在Cochrane Library上
6、完成系统评价全文并送协作网审批
7、再修改直到发表在CL上
8、跟踪本课题的进展，随时更新。

Cochrane系统评价手册

例：Cochrane Handbook for Systematic Reviews of Interventions

Online learning | Learning events | Guides and handbooks | Trainers' Hub | Log in

Cochrane Handbook for Systematic Reviews of Interventions

Search Handbook

Version 6.5, 2024

2024年6.5版

- Overview
- Part 1: About Cochrane Reviews
- Part 2: Core methods
- Part 3: Specific perspectives in reviews
- Part 4: Other topics

Senior Editors: Julian Higgins[1], James Thomas[2]

Associate Editors: Jacqueline Chandler[3], Miranda Cumpston[4,5], Tianjing Li[6], Matthew Page[4], Vivia

Part 1: About Cochrane Reviews

I. Introduction
II. Planning a Cochrane Review
III. Reporting the review
IV. Updating the review
V. Overviews of Reviews

Part 3: Specific perspectives in r

16. Equity
17. Intervention complexity
18. Patient-reported outcomes
19. Adverse effects
20. Economic evidence
21. Qualitative evidence

第2部分：核心方法

文献检索与研究筛选

Part 2: Core methods

1. Starting a review
2. Determining the scope and questions
3. Inclusion criteria & grouping for synthesis
4. Searching & selecting studies
5. Collecting data
6. Effect measures
7. Bias and conflicts of interest
8. Risk of bias in randomized trials
9. Preparing for synthesis
10. Meta-analyses
11. Network meta-analyses
12. Synthesis using other methods
13. Bias due to missing results
14. 'Summary of findings' tables & GRA
15. Interpreting results

Part 4: Other topics

22. Prospective approaches
23. Variants on randomized trials
24. Including non-randomized studies
25. Risk of bias in non-randomized studies
26. Individual participant data

C25: Searching specialist bibliographic databases (**Highly desirable**)

Search appropriate national, regional and subject-specific bibliographic databases.

Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. Databases relevant to the review topic should be covered (e.g. CINAHL for nursing-related topics, APA PsycInfo for psychological interventions), and regional databases (e.g. LILACS) should be considered.

C19: Planning the search (**Mandatory**)

Plan in advance the methods to be used for identifying studies. Design searches to capture as many studies as possible that meet the eligibility criteria, ensuring that relevant time periods and sources are covered and not restricted by language or publication status.

Searches should be motivated directly by the eligibility criteria for the review, and it is important that all types of eligible studies are considered when planning the search. If searches are restricted by publication status or by language of publication, there is a possibility of publication bias, or language bias (whereby the language of publication is selected in a way that depends on the findings of the study), or both. Removing language restrictions in English language databases is not a good substitute for searching non-English language journals and databases.

C24: Searching general bibliographic databases and CENTRAL (**Mandatory**)

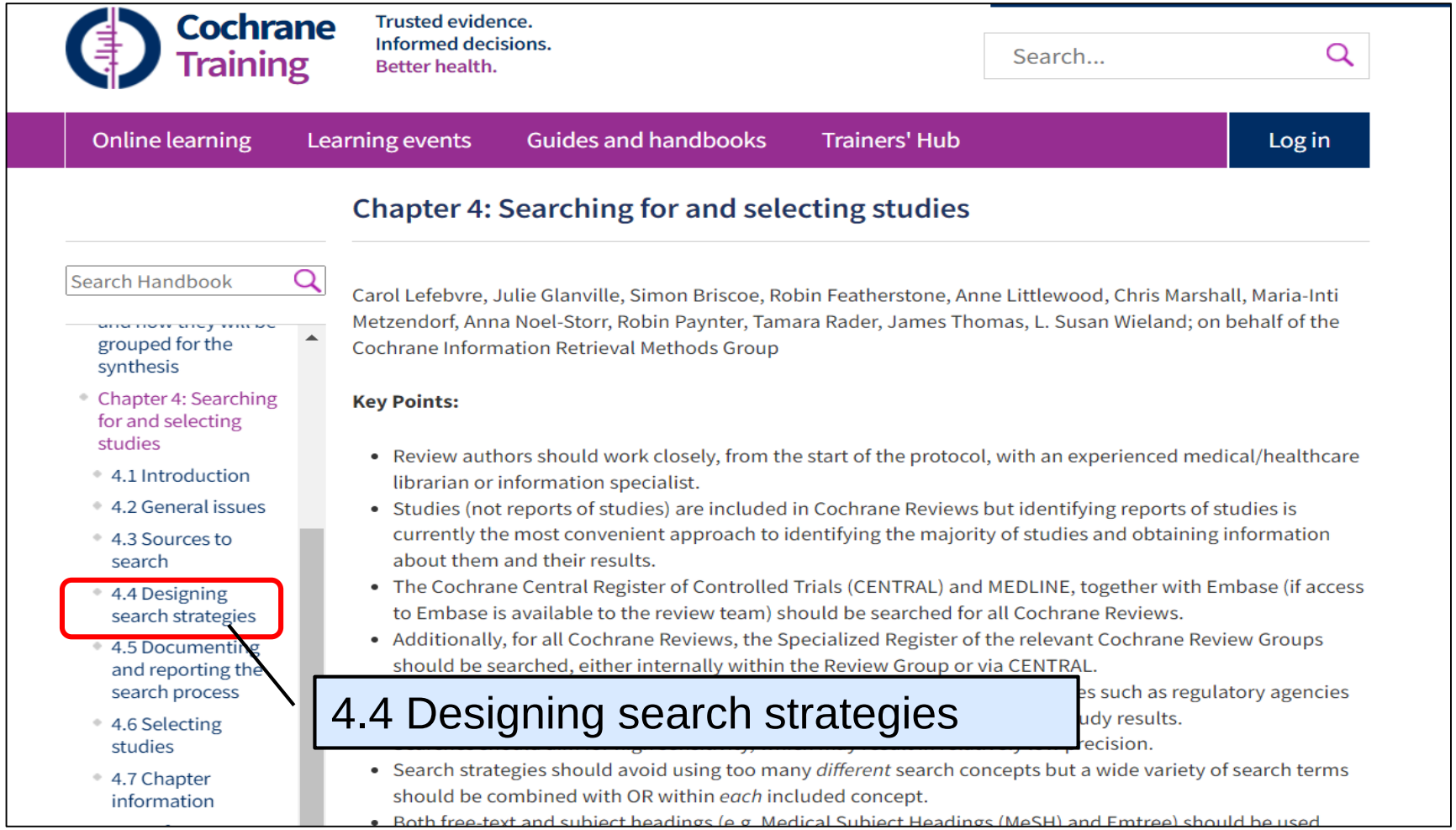
Search the Cochrane Review Group's (CRG's) Specialized Register (internally, e.g. via the Cochrane Register of Studies, or externally via CENTRAL). Ensure that CENTRAL, MEDLINE and Embase (if Embase is available to either the CRG or the review author), have been searched (either for the review or for the Review Group's Specialized Register).

Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. The minimum databases to be covered are the CRG's Specialized Register (if it exists and was designed to support reviews in this way), CENTRAL, MEDLINE and Embase (if Embase is available to either the CRG or the review author). Expertise may be required to avoid unnecessary duplication of effort. Some, but not all, reports of eligible studies from MEDLINE, Embase and the CRGs' Specialized Registers are already included in CENTRAL.

英文版：https://training.cochrane.org/handbook/current 访问日期：2024.9.28

Cochrane干预措施系统评价手册

https://training.cochrane.org/handbook/current



Cochrane Information Specialists ‘ Handbook
检索策略结构范例

检索策略范例参见
Cochrane信息专家手册

Cochrane review(CENTRAL数据库)检索策略结构范例

https://training.cochrane.org/handbook/current/chapter-04#section-4-4-2

- Chapter 4: Searching for and selecting studies
  - 4.1 Introduction
  - 4.2 General issues
  - 4.3 Sources to search
  - 4.4 Designing search strategies
    - 4.4.1 Introduction to search strategies
    - 4.4.2 Structure of a search strategy
    - 4.4.3 Sensitivity versus precision
    - 4.4.4 Controlled vocabulary and

be conducted for different types of evid

4.4.2 Structure of a search strategy #section-4-4-2

The starting point for developing a search strategy is to consider the main concepts being examined in a review. This is often referred to as PICO – that is Patient (or Participant or Population or Proble Comparison and Outcomes (Richardson et al 1995): see also Chapter 2 and Chapter 3 f and refining PICO definitions that will be operationalized in the search strategy. Examp appendices to th Cochrane Information Specialists' Handbook (Cochrane Informatio 2021d). For ochrane Review, the review objective should provide the PICO concepts for stu to be included will further assist he selection of appropriate subject hea th earch strategy.

The structure of search strategies in bib graphic databases should be informed by the review (see Chapter 3), using appropri elements from PICO and the study design (se usually unnecessary, however, and n even be undesirable, to search on every aspec question (Frandsen et al 2020). Alth gh a research question may specify particular co these concepts may not be well d ibed in the title or abstract of an article and are o

Appendix 8. Template for a Search Report Form

- 1. Role of a Cochrane Information Specialist
- 2. Specialised Registers
- 3. The Cochrane Register of Studies (CRS)
- 4. Maintaining and developing a Specialised Register
- 5. Handsearching
- 6. Author support
- 7. Editorial process

A template for a Search Report Form is available to download and adapt to reflect a Gr

‹ Appendix 7. Example of the structure of a search strategy for a Cochrane review (CENTRAL)

up

Share

- 1. Role of a Cochrane Information Specialist
- 2. Specialised Registers
- 3. The Cochrane Register of Studies (CRS)
- 4. Maintaining and developing a Specialised Register
- 5. Handsearching
- 6. Author support
- 7. Editorial process
- 8. Cochrane Review Production Tools
- 9. Communication
- 10. Professional development
- 11. Key Resources for Cochrane Information Specialists
- 12. PICO Annotation
- Appendix 1. Example of how studies with multiple reports are cited in Cochrane reviews

Example of the structure of a search strategy for a Cochrane review (CENTRAL)

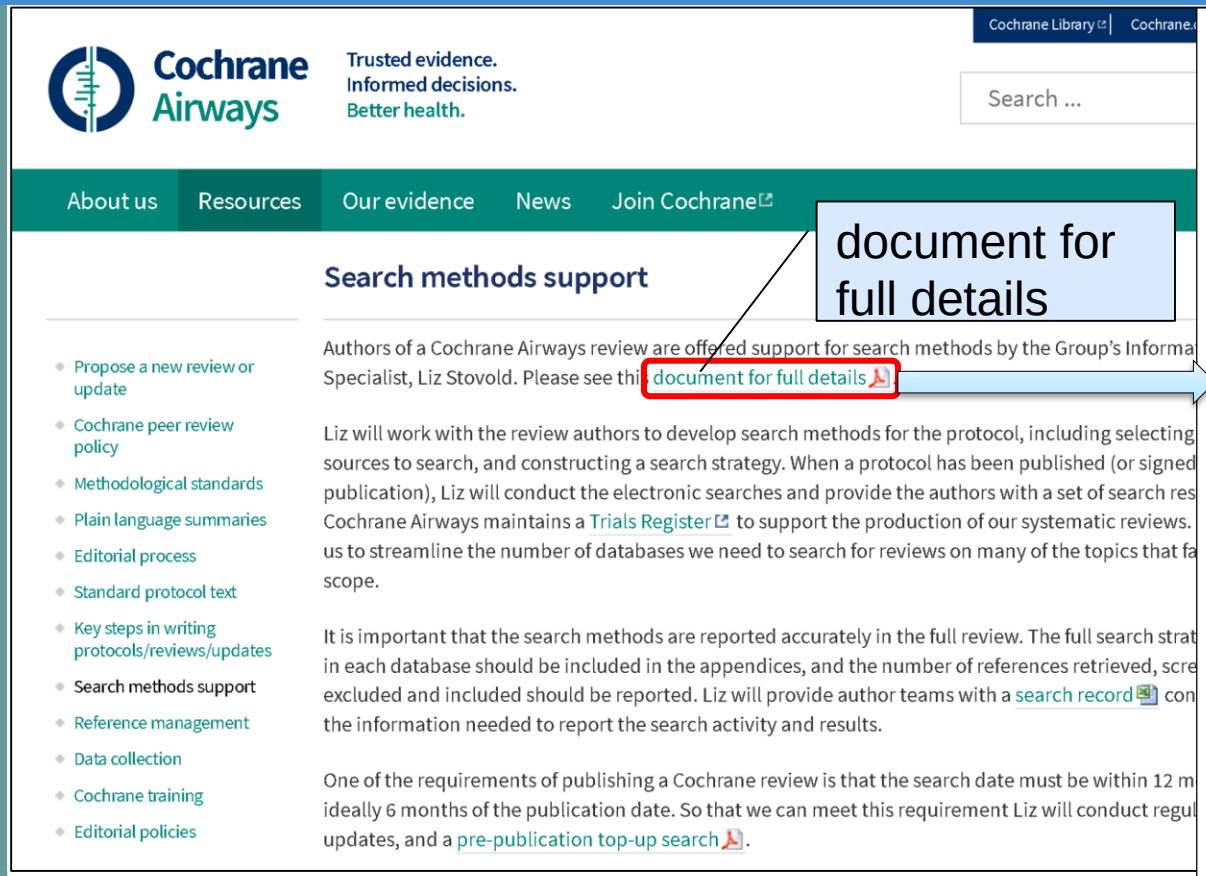
Helmets for preventing head and facial injuries in bicyclists

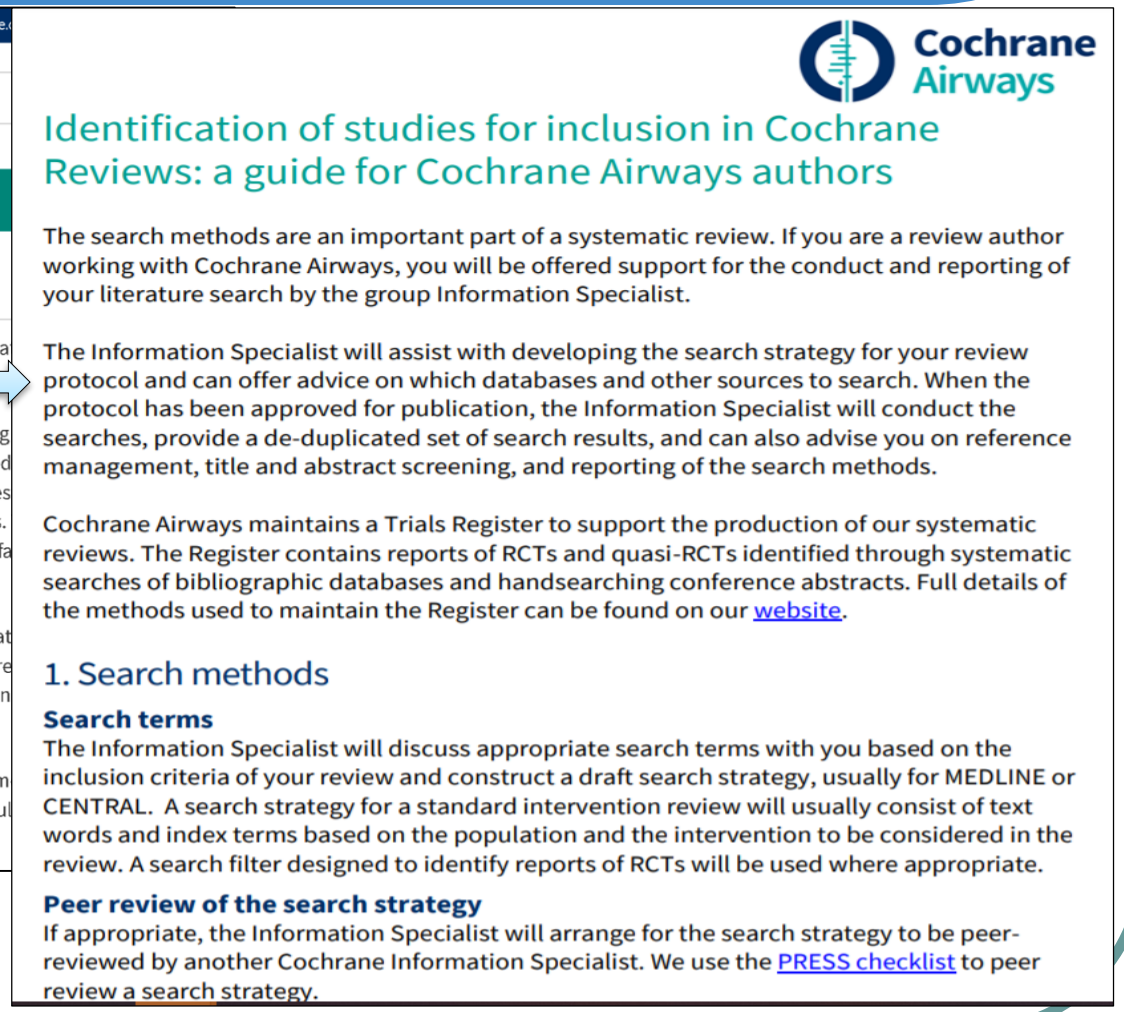
Sets 1-3 are the **MeSH terms & text words [words found in the TITLE or ABSTRACT of a record]** for the **population** (i.e bicyclists). They are combined using **OR**	1. bicycl* or cycling or cyclist* :ab,ti,kw 2. [mh Bicycling] 3. #1 or #2	**Population (P)**
Sets 4-6 are the **MeSH terms & text words [words found in the TITLE or ABSTRACT of a record]** for the **intervention** (i.e helmets). They are combined using **OR**	4. helmet*:ab,ti,kw 5. [mh “Head Protective Devices”] 6. #4 or #5	**Intervention (I)**
Set 7 is the combination of **Population, intervention**. No study design is required as CENTRAL contains RCTS & CCTS	7. #3 and #6	**Combination of P & I**

https://training.cochrane.org/resource/cochrane-information-specialists-handbook/appendix-7-example-structure-search-strategy

Reviews-Airways Group关于检索的说明

https://airways.cochrane.org/literature-searching





2、随机对照试验(Randomized Controlled Trial)

采用随机分配的方法，将符合要求的研究对象分别分配到试验组或对照组，然后接受相应的试验措施，在一致的条件或环境里，同步地进行研究和观察试验效应，并用客观的效应指标，对试验结果进行测量和评价的试验设计。

奥美沙坦酯与氯沙坦钾治疗中国轻、中度原发性高血压患者 8 周的疗效与安全性比较

诸骏仁　蔡颖绳　范维琥　朱鼎良　何奔　吴宗贵
柯元南　郭静莹　马虹　黄峻　李新立　陈运贞

【摘要】 **目的**　通过与氯沙坦钾比较评价奥美沙坦酯治疗轻、中度原发性高血压患者的疗效和安全性。**方法**　采用随机、双盲、双模拟、阳性对照、平行分组、多中心临床试验方法。共入选 287 例轻、中度原发性高血压患者，按照 1∶1 的比例随机分组，分别接受奥美沙坦酯 20 mg 或氯沙坦钾 50 mg，每天 1 次口服治疗。在用药 4 周后对患者进行血压评价，如果患者舒张压(DBP)仍≥ 90 mm Hg (1 mm Hg = 0.133 kPa)，则试验药物剂量加倍，直至 8 周试验结束；治疗 4 周后 DBP < 90 mm Hg 的患者则维持原剂量继续治疗至第 8 周。**结果**　(1) 治疗 4 周后，奥美沙坦酯组坐位 DBP 谷值平均下降 11.72 mm Hg，氯沙坦钾组平均下降 9.23 mm Hg，两组间比较 $P = 0.004$。(2)治疗 8 周后，奥美沙坦酯组坐位 DBP 谷值平均下降 12.94 mm Hg，氯沙坦钾组平均下降 11.01 mm Hg，两组间比较 $P = 0.035$。(3)治疗 4 周后，奥美沙坦酯组有效数为 81 例(65.3%)，氯沙坦钾组有效数为 68 例(52.7%)，两组间比较 $P = 0.028$；治疗 8 周后，两组有效病例数和有效率相当，$P > 0.05$。(4)治疗 8 周后，24 h 动态血压监测显示，奥美沙坦酯组 DBP 和 SBP 的个体和总体谷/峰比值均高于氯沙坦钾组，奥美沙坦酯在 24 h 内的作用持续时间比氯沙坦钾组长。(5)奥美沙坦酯组和氯沙坦钾组发生的与试验药物有关的不良事件的发生率分别为 10.5% 和 13.9%，$P > 0.05$。**结论**　奥美沙坦酯每日口服 20 ~ 40 mg 能够有效、安全地治疗高血压。与氯沙坦钾每日口服 50 ~ 100 mg 相比，奥美沙坦酯的降压效果优于氯沙坦钾。

【关键词】 高血压；　抗高血压药；　治疗结果

3、卫生技术评估(Health Technology Assessment)

是对卫生技术的技术特性、安全性、有效性（效能、效果和生存质量）、经济学特性（成本效果）和社会的适应性（法律、伦理）进行评价，为决策者提供合理选择卫生技术的证据。

卫生技术评估

国产永磁型磁共振成像设备的卫生技术评估

Health Technology Assessment of Domestic Permanent Magnetic Type Magnetic Resonance Imaging Equipment

邱晓力[1]，钱兵[1]，包家立[2]，姚赛苗[1]
1.浙江现代生物技术发展中心，浙江 杭州 310002；2.浙江大学医学院 浙江省生物电磁学重点实验室生物物理与医学工程研究组，浙江 杭州 310058

[摘 要] 对国产永磁型磁共振成像设备进行卫生技术评估，为政府制定公共卫生政策、产业发展规划、技术创新指南提供科学依据。采用公开文献、企业调查、医院问卷等方式，对某家国产永磁型磁共振成像设备的图像质量、安全性能、有效性、利用率、经济性、社会性等六方面进行评价。结果显示该型设备图像质量和安全性能符合技术标准；诊断检查多数比CT、MSCT、US、X线等检出率高；设备使用率达到95%以上，适合各级别医院使用，尤其是二甲医院；成本-效益远高于进口同类设备；社会已有较好的认可度。
[关键词] 磁共振成像设备；永磁型；卫生技术评估

QIU Xiao-li[1], QIAN Bin[1], BAO Jia-li[2], YAO Sai-miao[1]
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Abstract: A domestic permanent magnet magnetic resonance imaging (MRI) was evaluated by health technology assessment (HTA) so as to provide the scientific basis for the public health policies, the industrial development planning, and the guide of technological innovation for China government. The paper assessed the image quality, safety, effectiveness, efficiency, economy, sociality of the domestic MRI equipment by analyzing data from the public literature and surveys to the company and hospital. Results showed that image quality and safety performance of the MRI met technical standards; the relevance ratio of diagnostic was more than that of CT, MSCT, US and X-ray; utilization rate of the MRI was above 95%, which made it suitable for hospitals at all levels, especially second senior-class hospitals. And the cost-benefit was much higher than similar imported equipment.
Key words: magnetic resonance imaging; permanent magnet; health technology assessment

[中图分类号] R197.39 [文献标志码] A
doi：10.3969/j.issn.1674-1633.2016.04.003
[文章编号] 1674-1633(2016)04-0014-04

0 引言

近年来，随着医疗器械产业的发展，医疗设备的支付持续增长，增加了社会负担，严重影响了医改。世界卫生组织（WHO）在2007年世界卫生大会上有议程表达医疗器械对卫生资源侵占的关注，认为过渡医疗设备的投入剥夺了其他卫生资源的配置，从而破坏了整个卫生服务体系[1]。提出基于流行病学和人口数据对医疗器械的可及性和使用率、使用人员的能力、购置的成本效益分析，以及适宜卫生技术中的应用进行评估[2]。

医用磁共振成像设备（MRI）是一种高值乙类大型医疗设备，价格从几百万到上千万不等。我国目前主要依靠进口，与我国日益增长的医疗需求与现实支付能力形成了一对矛盾。国产MRI具有价格低、成本效益高、备件易得等特点，正被国内医疗机构所接受。并且经过十多年的发展，已经涌现了如鑫高益、贝斯达、安科、万东、东软、联影等一批国产MRI产品。然而，国产MRI因缺少客观的评估，社会认可度还不高，阻碍了我国卫生事业的发展。因此，对国产MRI进行全性能评价具有现实意义。

本文采用卫生经济学公认的卫生技术评估（Health

收稿日期：2016-03-08
基金项目：浙江省科技厅“十二五”国家创新医疗器械产品与技术成果转化工程重大专项(2013T301-16)。
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对MRI的比吸收率（SAR）作出了限制，3台抽检设备的全身SAR比标准低2个数量级。静磁场的生物效应相对较弱，限值可以达到8 T，本评价MRI属低场。因此，抽检设备所有检测项目均满足标准要求，在用设备也没有电磁安全不良事件报告。

表2 某国产品牌永磁型MRI安全特性

	限值标准	抽检1	抽检2	抽检3
有效刺激持续时间（ms）	0.30	0.28	0.28	0.30
梯度感应电场（V/m）	21.02	19.00	19.50	20.00
梯度磁场变化率（T/s）	210			
SAR限值（W/kg）				
全身				
正常运行模式	头和躯干	10		
		20		

有效性

2.3 有效性

[文献分析] 低场永磁型MRI在肿瘤、骨科、脑等检查与CT、螺旋CT（MSCT）、超声（US）、X线比较，见表3，表明MRI检查多数比CT、MSCT、US、X线等检出率高，但在颅脑外伤检查CT比MRI占优。有研究表明MRI的脑部检查一致性比CT高，椎体要低[30]。然而，表3表明其不具这种特性，表明制定MRI诊断的“金标准”具有重要意义。

表3 诊断疾病类型及检出率（%）

疾病类型	病例数	检出率	其他检出率
直肠癌[15]	79	72.15	
鼻咽癌[16]	36	72.2	38.9（CT）
鼻咽癌[17]	23	91.3	78.3（CT）
颅脑淋巴瘤[18]	9	100	
脑白质变[19]	77	98.7	
垂体瘤[20]	6	100	
肝肿瘤[21]	78	100	97.06（US）
椎管内占位性病变[22]	22	90.0	
腰椎间盘突出[23]	40	95.0	92.5（CT）
颅面骨病变[24]	57	96	84（CT）
股骨头缺血性坏死[25]			
隐匿性骨折[26]			
膝关节应力性骨折[27]			
颅脑外伤[28]			
乳腺肿瘤[29]	5	100	60（US）

利用率

2.4 利用率

在9家有某国产品牌永磁型MRI的医疗机构（1家三甲医院，7家二甲医院，1家民营医院）进行关于MRI利用率和经济效益的问卷调查，结果见表4和5。调查表明：某国产品牌永磁型MRI使用率达到95%以上，表明该型设备适合各级别医院使用，尤其是二甲医院。外地患者承担指数很低，表明该型设备完全适应于本地卫生资源配置。我国MRI总体上使用合理，过度使用率较低[31]。高场MRI的使用率在50%左右[32]，而某国产品牌利用率高的因素之一是许多疾病可用该型机器诊断。

表4 某国产品牌永磁型MRI利用率

评估项目	数据
年检查人次（次）	5867±1075
人均检查时间（分钟）	20.0±4.3
年实际开机时间（小时）	1981±96
年实际可能工作时间	2080
外地患者检查数	很少
年开机使用率	98.7%
年时间利用率	94.0%
外地患者承担指数	很少

表5 某国产品牌永磁型MRI经济性

评估项目	数据
人均收费（元）	350±60
初次投资（万元）	318±47
年折旧	10%
单位变动成本	291±44
成本回收率（%）	
投资回收期（年）	
年保本服务量（人次）	
外地患者承担指数	

经济性

2.5 经济性

成本-效益分析是医院分级标准的必需指标[33]，运行成本结构包括人员工资、管理费、材料费、维修费、业务费、折旧费等[34]。某国产品牌永磁型MRI初次投资318万元，是进口机价格的一半[35]，[illegible]同收率37.9%、投资回收期[illegible]。而同类进口机的投资[illegible]要达到2984人次[illegible]。头部[illegible]效益要比同类进口机高。

社会性

2.6 社会性

在7家有某国产品牌永磁型MRI的医疗机构（余姚市人民医院、成都医学院第一附属医院、昆明骨科医院、民权县中医院、湖南岳阳广济医院、河南鹿邑真源医院、绛县红十字会医院）进行关于MRI社会性问卷调查，调查内容包括对某国产品牌永磁型磁共振成像设备在工程评价、可靠性、主观感受、经济性、适用性、厂家服务、创新性等7大类55个指标评价，结果见图1。

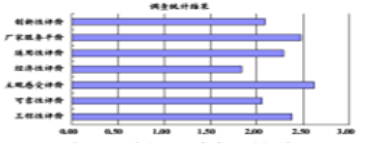


图1 医院对企业及其产品的评价

调查的主观结果是某国产品牌产品性能稳定，故障率低，图像质量良好，操作简单，主观感受满意，后续费用较低，厂家定期回访，跟踪指导，服务周到。

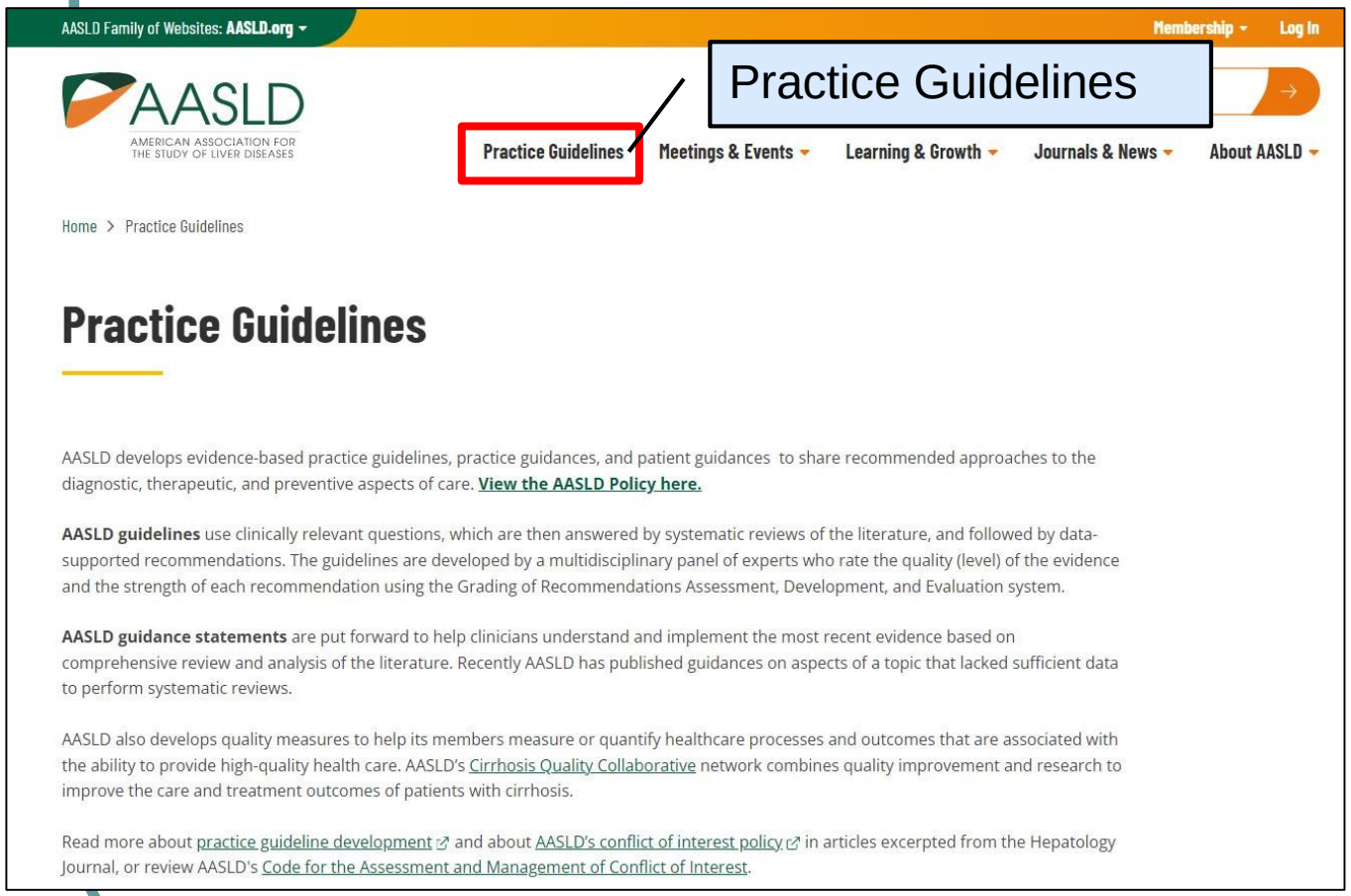
4、临床实践指南(Clinical Practice Guideline)

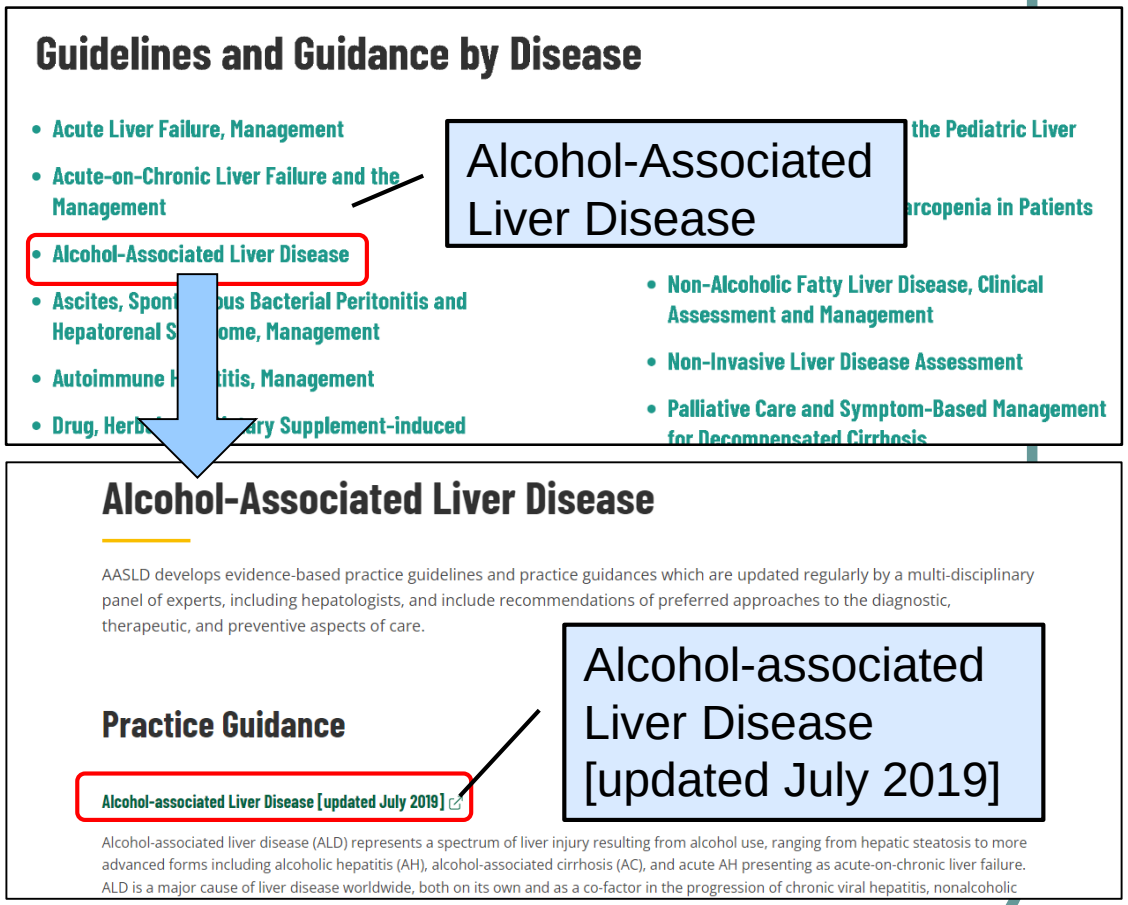
针对特定的临床问题，系统制定出的帮助临床医师和病人做出恰当处理的指导性意见 。

[例] AASLD (美国肝脏病学会) 酒精性肝疾病的临床实践指南

https://www.aasld.org/publications/practice-guidelines

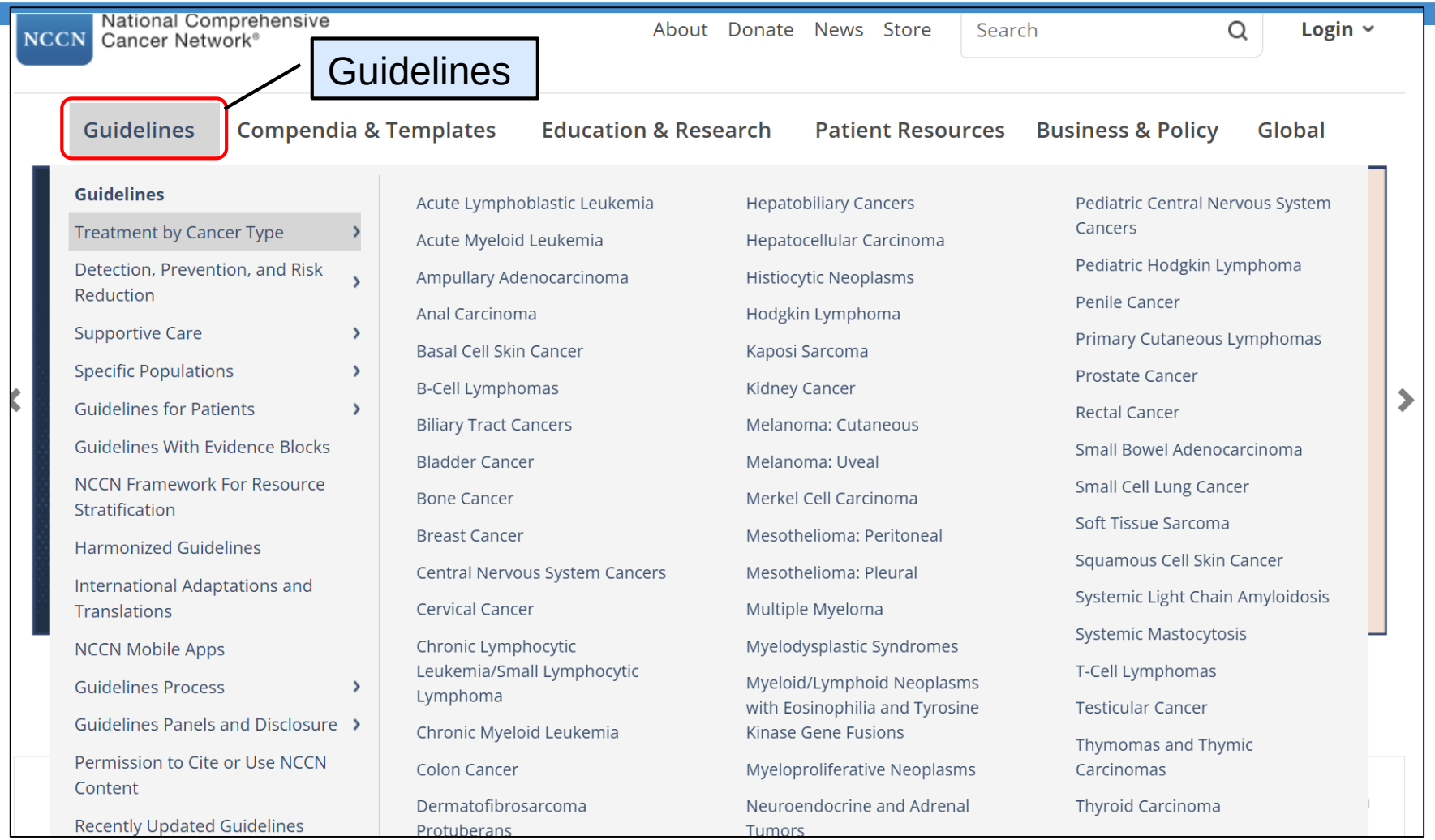
美国肝病研究学会 （AASLD https://www.aasld.org）





https://www.aasld.org/practice-guidelines/alcohol-associated-liver-disease

美国国立综合癌症网（NCCN https://www.nccn.org）



3.1.2 证据分级

来源：*Medical Research Library of Brooklyn - http://library.downstate.edu/ebm/2100.htm*

GRADE指南：证据质量分级

表 2　证据四个等级的含义

质量等级	当前定义	早前定义
高	我们非常确信真实的效应值接近效应估计值	进一步研究非常不可能改变我们对效应估计值的确信程度
中	对效应估计值我们有中等程度的信心：真实值有可能接近估计值，但仍存在二者大不相同的可能性	进一步研究有可能对我们对效应估计值的确信程度造成重要影响，且可能改变该估计值
低	我们对效应估计值的确信程度有限：真实值可能与估计值大不相同	进一步研究很有可能对我们对效应估计值的确信程度造成重要影响，且很可能改变该估计值
极低	我们对效应估计值几乎没有信心：真实值很可能与估计值大不相同	任何效应估计值都是非常不确定的

表 3　GRADE 证据质量分级方法概要

研究设计	证据集群的初始质量	如果符合以下条件，降级	如果符合以下条件，升级	证据集群的质量等级
随机试验	高 ⟹	偏倚风险 −1 严重 −2 非常严重	效应量大 +1 大 +2 非常大	高（4 个“+”：++++）
		不一致性 −1 严重 −2 非常严重	剂量反应 +1 梯度量效证据	中（3 个“+”：+++ ○）
观察性研究	低 ⟹	间接性 −1 严重 −2 非常严重	所有可能的剩余混杂因素 +1 降低所展示的效应 +1 如未观察到效应意味着是一种假效应	低（2 个“+”：++ ○○）
		不精确 −1 严重 −2 非常严重		极低（1 个“+”：+ ○○○）
		发表偏倚 −1 可能 −2 非常可能		

资料来源：DOI：10.3969/j.issn.1672-2531.2011.04.017

证据的检索资源

3.2.1　循证医学数据库

The Cochrane library

BMJ Best Practice

3.2.2　综合性数据库

PubMed；EMBASE；CBM；……

3.2.3　循证医学期刊

3.2.4　临床实践指南

医脉通指南；…

3.2.5　卫生技术评估

3.2.1 Cochrane Library数据库
www.cochranelibrary.com

- Cochrane协作网创建，获取循证医学证据的主要来源之一。
- 广域网免费检索，可获取我校订购的全文。
- 包含Cochrane Review (CDSR), Trials(CENTRAL), Clinical Answers三个子库。

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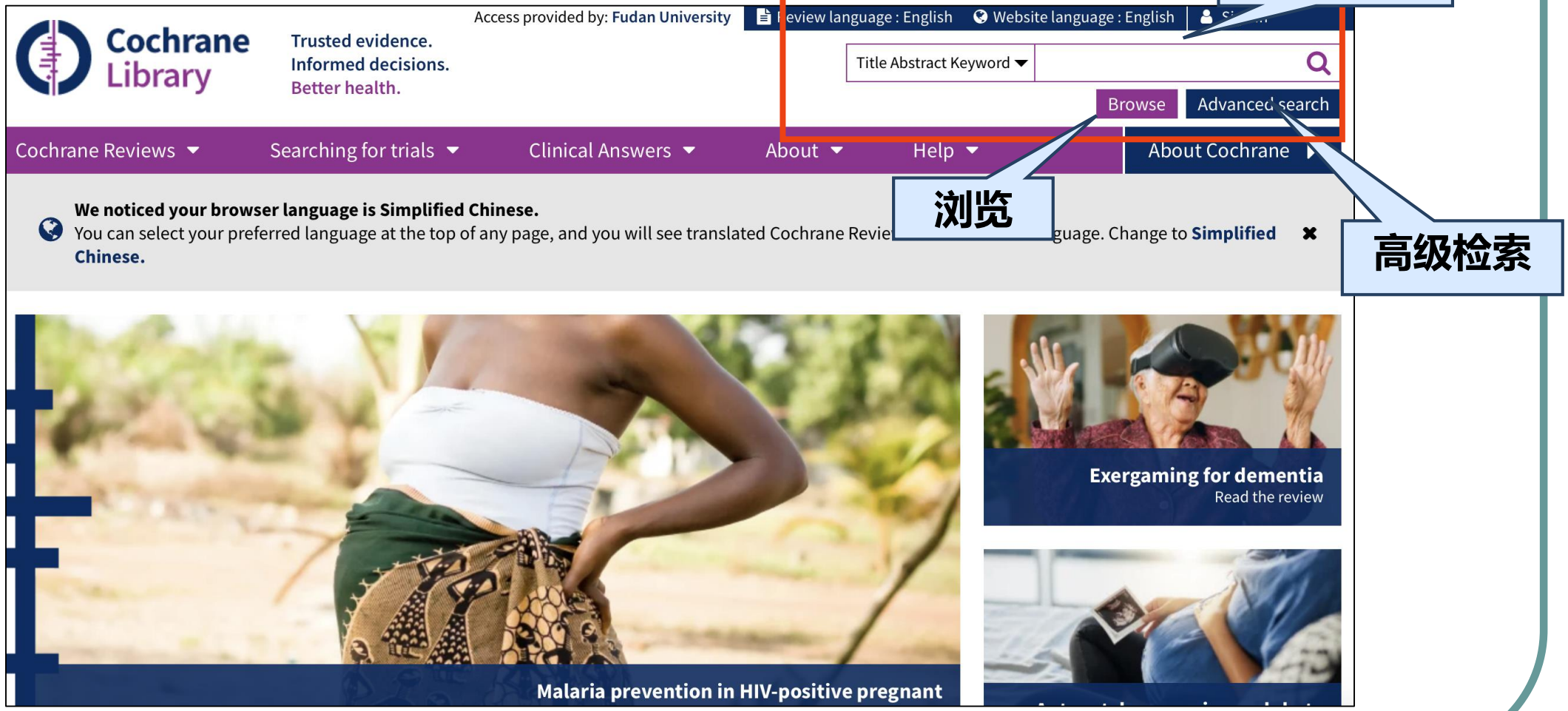

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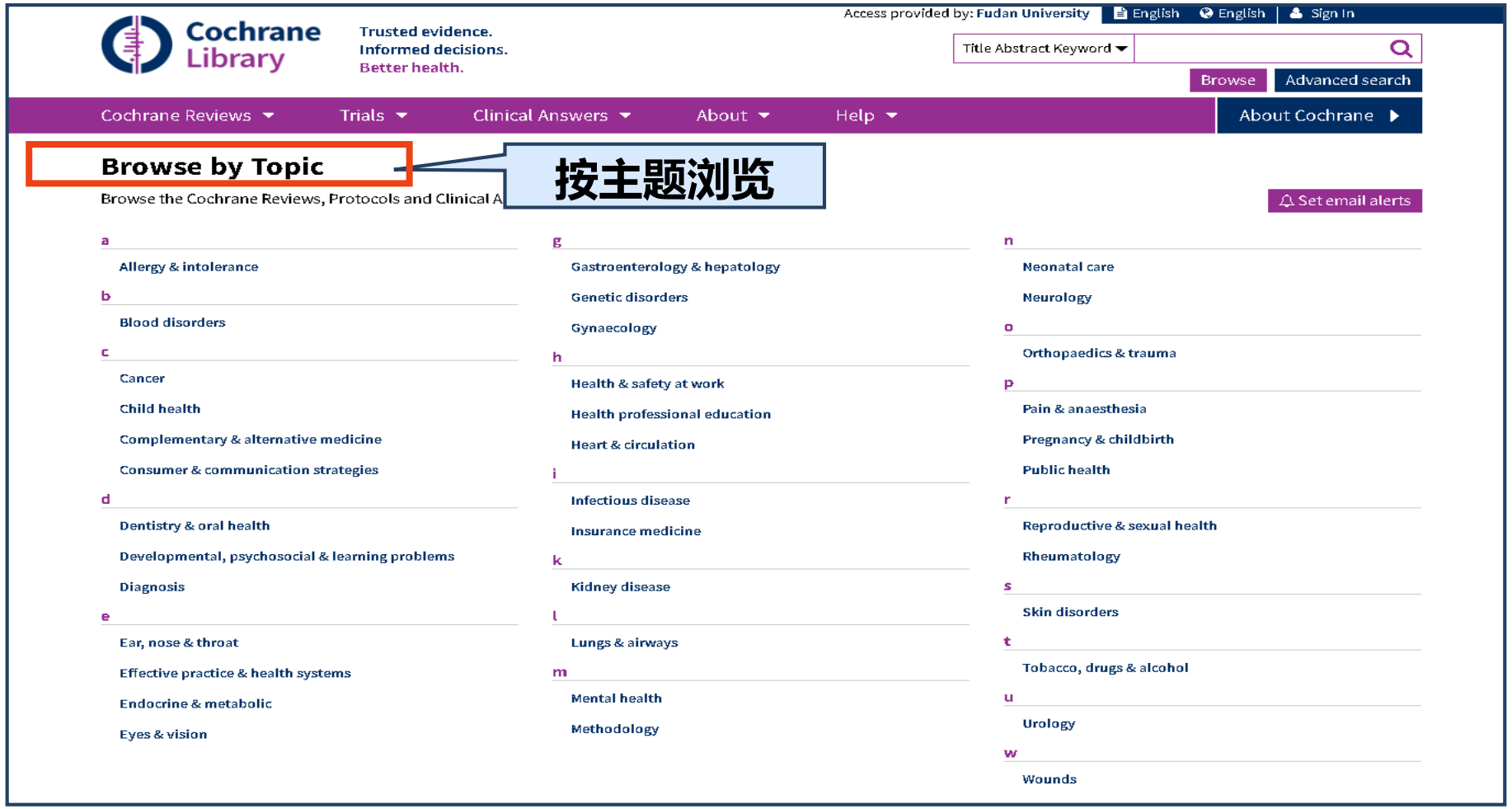


CL检索规则

1. 支持布尔算符，运算符大写，优先运算用括号

   如：liver AND (fibrosis OR cirrhosis)

2. 默认空格为AND运算，强迫词组用双引号

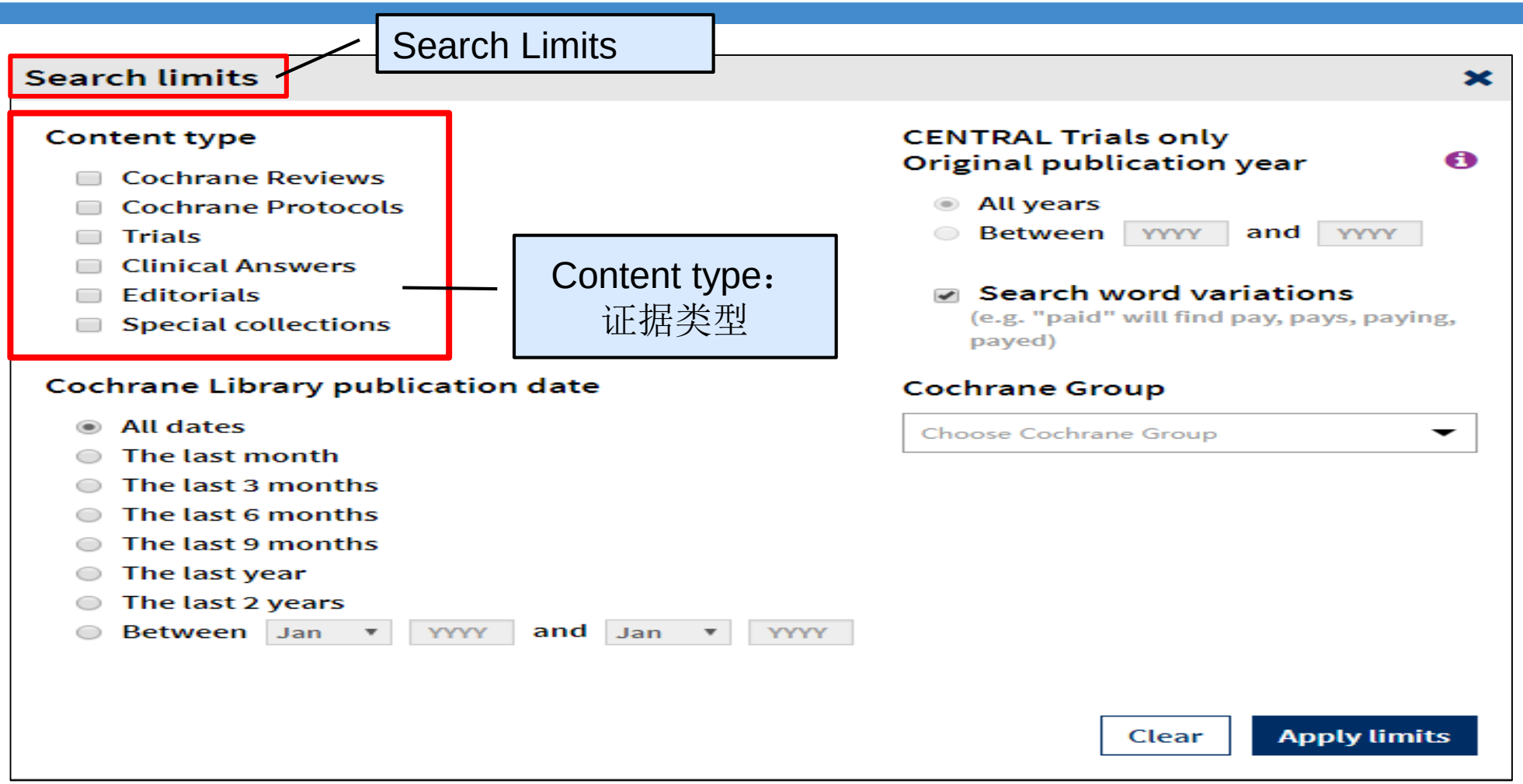
   如：“Molecular targeted therapy”

3. * 号可用作截词、？号可用作替代检索。

4. 检索词大小写皆可

5. 支持临近检索（near/x）

Advanced Search



Content Type

1. Cochrane Reviews

由Cochrane协作网系统评价组在统一工作手册(The Reviewer’s Handbook)指导下完成的系统评价，并随着读者的建议、评论以及新的临床试验的出现不断补充更新。

Content Type

2. Cochrane Protocols

由Cochrane协作网系统评价组在统一工作手册(The Reviewer’s Handbook)指导下完成的研究方案(Protocol)。

Content Type

3. Trials

来源于协作网各系统评价小组和其它组织的专业临床试验资料库以及在MEDLINE上被检索出的随机对照试验（RCT）和临床对照试验（CCT）。还包括了全世界Cochrane协作网成员从有关医学杂志会议论文集和其他来源中收集到的CCT报告。

Content Type

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从Cochrane系统评价中提取出基本信息，形成简短的问题和答案，非常适合在护理时使用。

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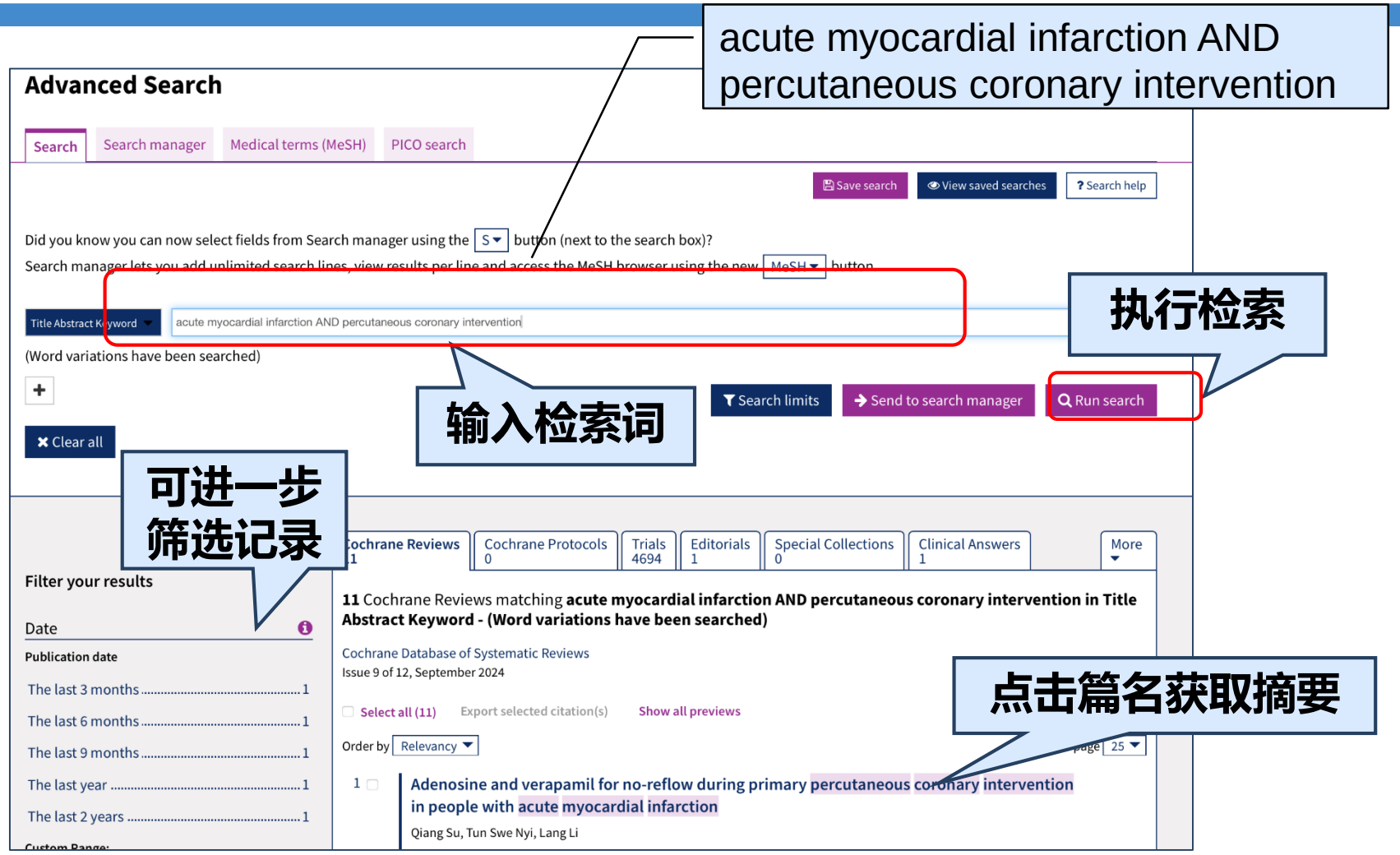
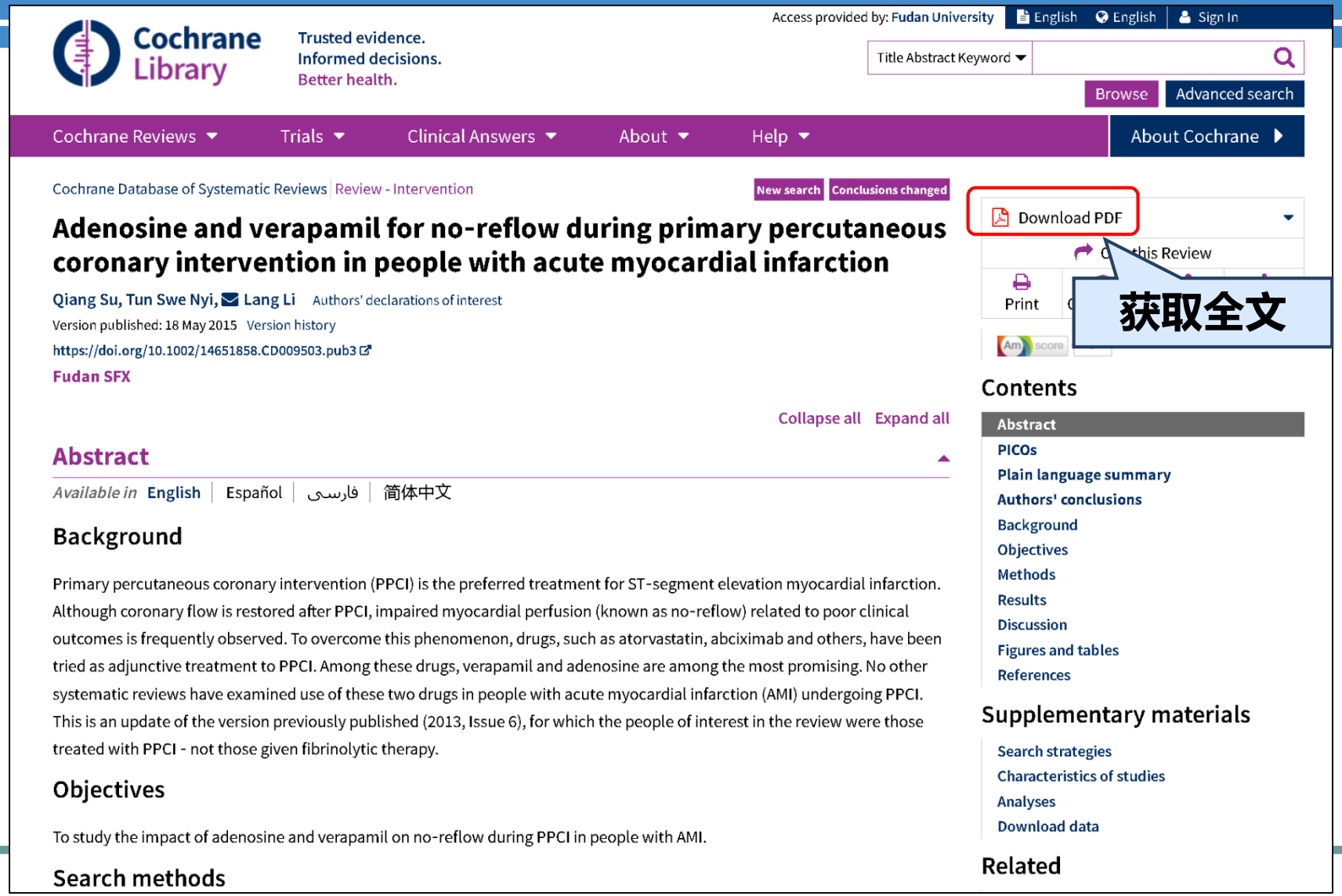
经皮冠状动脉介入治疗急性心肌梗死



摘要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Adenosine and verapamil for no-reflow during primary percutaneous coronary intervention in people with acute myocardial infarction
Qiang Su, Tun Swe Nyi, Lang Li
Authors' declarations of interest
Version published: 18 May 2015
Version history
https://doi.org/10.1002/14651858.CD009503.pub3
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简体中文
Background
Primary percutaneous coronary intervention (PPCI) is the preferred treatment for ST-segment elevation myocardial infarction. Although coronary flow is restored after PPCI, impaired myocardial perfusion (known as no-reflow) related to poor clinical outcomes is frequently observed. To overcome this phenomenon, drugs, such as atorvastatin, abciximab and others, have been tried as adjunctive treatment to PPCI. Among these drugs, verapamil and adenosine are among the most promising. No other systematic reviews have examined use of these two drugs in people with acute myocardial infarction (AMI) undergoing PPCI. This is an update of the version previously published (2013, Issue 6), for which the people of interest in the review were those treated with PPCI - not those given fibrinolytic therapy.
Objectives
To study the impact of adenosine and verapamil on no-reflow during PPCI in people with AMI.
Search methods
Contents
Abstract
PICOs
Plain language summary
Authors' conclusions
Background
Objectives
Methods
Results
Discussion
Figures and tables
References
Supplementary materials
Search strategies
Characteristics of studies
Analyses
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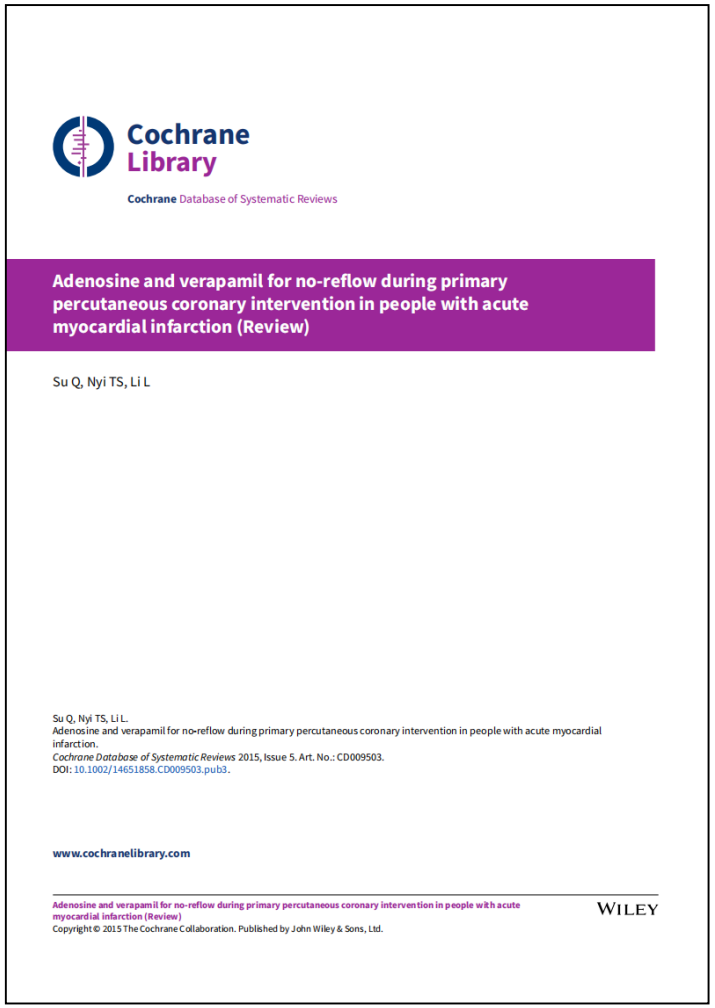

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Adenosine and verapamil for no-reflow during primary percutaneous coronary intervention in people with acute myocardial infarction (Review)

Su Q, Nyi TS, Li L

Su Q, Nyi TS, Li L.
Adenosine and verapamil for no-reflow during primary percutaneous coronary intervention in people with acute myocardial infarction.
Cochrane Database of Systematic Reviews 2015, Issue 5. Art. No.: CD009503.
DOI: 10.1002/14651858.CD009503.pub3.

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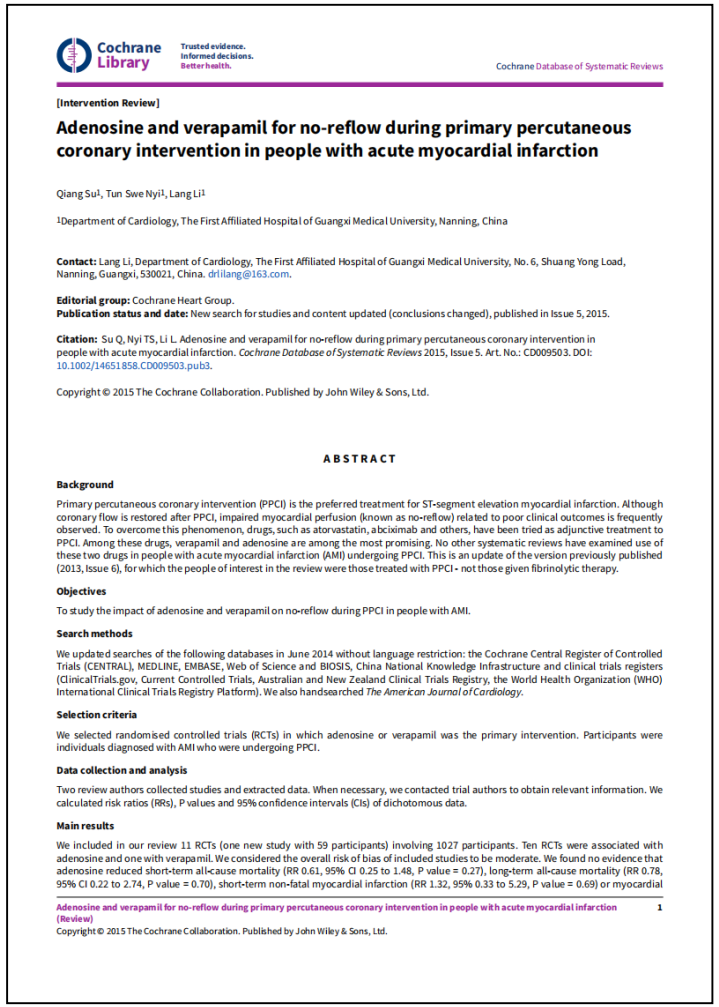

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[Intervention Review]

Adenosine and verapamil for no-reflow during primary percutaneous coronary intervention in people with acute myocardial infarction

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Editorial group: Cochrane Heart Group.
Publication status and date: New search for studies and content updated (conclusions changed), published in Issue 5, 2015.

Citation: Su Q, Nyi TS, Li L. Adenosine and verapamil for no-reflow during primary percutaneous coronary intervention in people with acute myocardial infarction. *Cochrane Database of Systematic Reviews* 2015, Issue 5. Art. No.: CD009503. DOI: 10.1002/14651858.CD009503.pub3.

ABSTRACT

Background

Primary percutaneous coronary intervention (PPCI) is the preferred treatment for ST-segment elevation myocardial infarction. Although coronary flow is restored after PPCI, impaired myocardial perfusion (known as no-reflow) related to poor clinical outcomes is frequently observed. To overcome this phenomenon, drugs, such as atorvastatin, abciximab and others, have been tried as adjunctive treatment to PPCI. Among these drugs, verapamil and adenosine are among the most promising. No other systematic reviews have examined use of these two drugs in people with acute myocardial infarction (AMI) undergoing PPCI. This is an update of the version previously published (2013, Issue 6), for which the people of interest in the review were those treated with PPCI - not those given fibrinolytic therapy.

Objectives

To study the impact of adenosine and verapamil on no-reflow during PPCI in people with AMI.

Search methods

We updated searches of the following databases in June 2014 without language restriction: the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, Web of Science and BIOSIS, China National Knowledge Infrastructure and clinical trials registers (ClinicalTrials.gov, Current Controlled Trials, Australian and New Zealand Clinical Trials Registry, the World Health Organization (WHO) International Clinical Trials Registry Platform). We also handsearched *The American Journal of Cardiology*.

Selection criteria

We selected randomised controlled trials (RCTs) in which adenosine or verapamil was the primary intervention. Participants were individuals diagnosed with AMI who were undergoing PPCI.

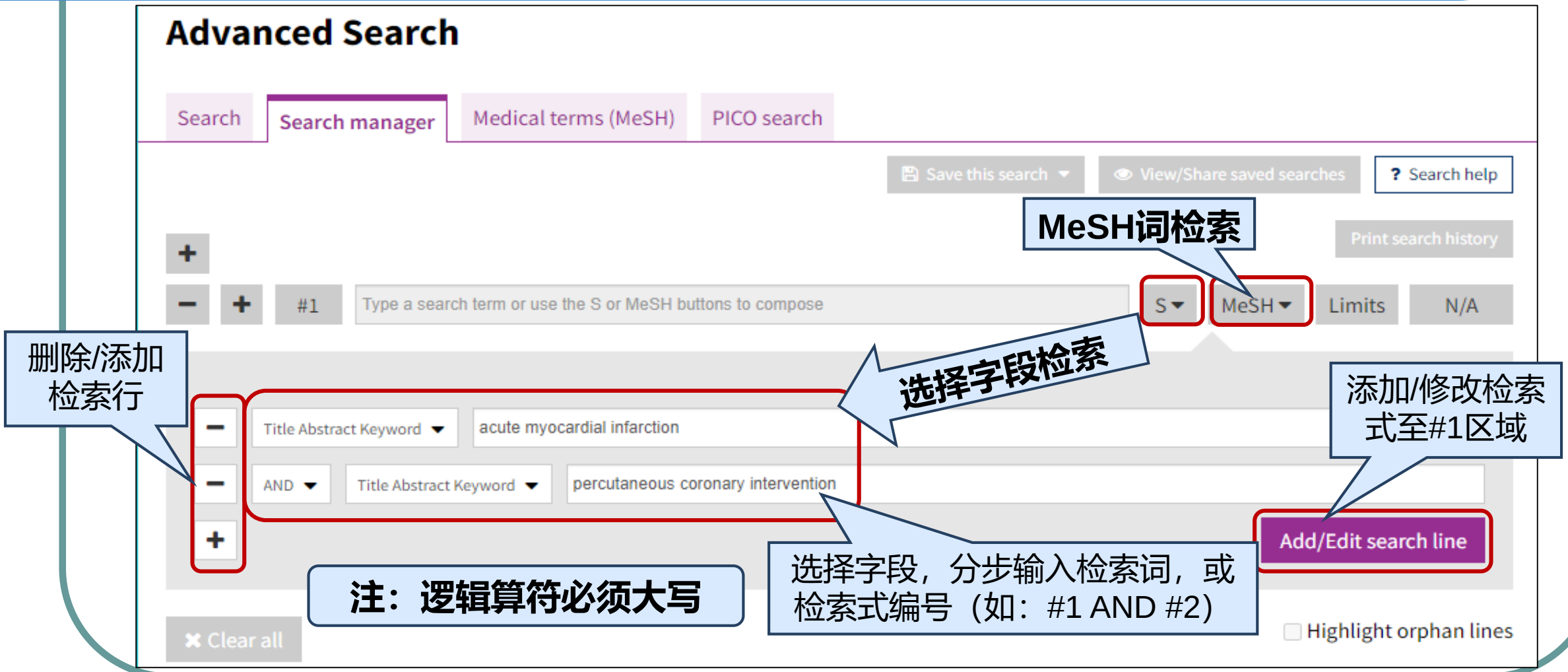
Data collection and analysis

Two review authors collected studies and extracted data. When necessary, we contacted trial authors to obtain relevant information. We calculated risk ratios (RRs), P values and 95% confidence intervals (CIs) of dichotomous data.

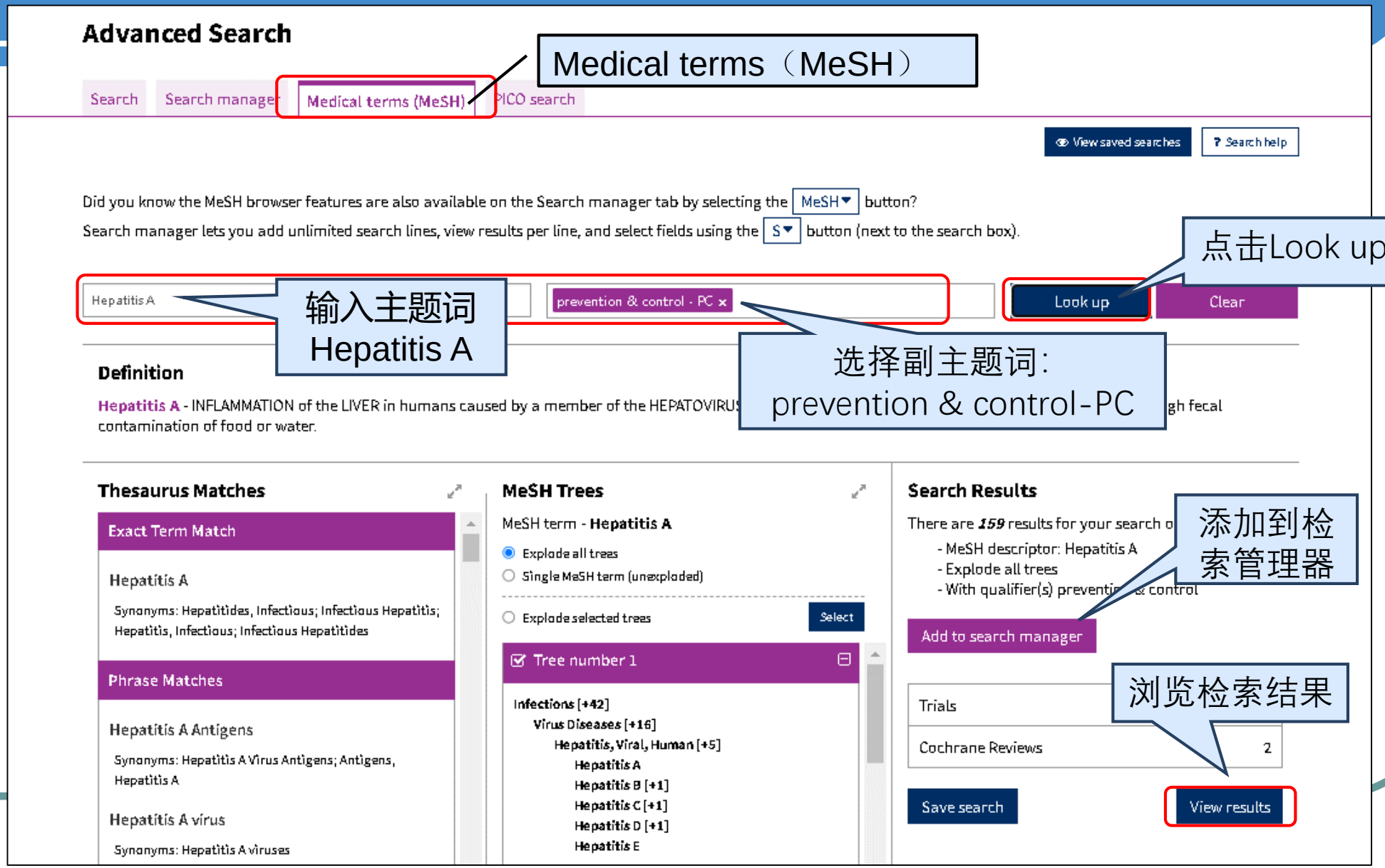
Main results

We included in our review 11 RCTs (one new study with 59 participants) involving 1027 participants. Ten RCTs were associated with adenosine and one with verapamil. We considered the overall risk of bias of included studies to be moderate. We found no evidence that adenosine reduced short-term all-cause mortality (RR 0.61, 95% CI 0.25 to 1.48, P value = 0.27), long-term all-cause mortality (RR 0.78, 95% CI 0.22 to 2.74, P value = 0.70), short-term non-fatal myocardial infarction (RR 1.32, 95% 0.33 to 5.29, P value = 0.69) or myocardial

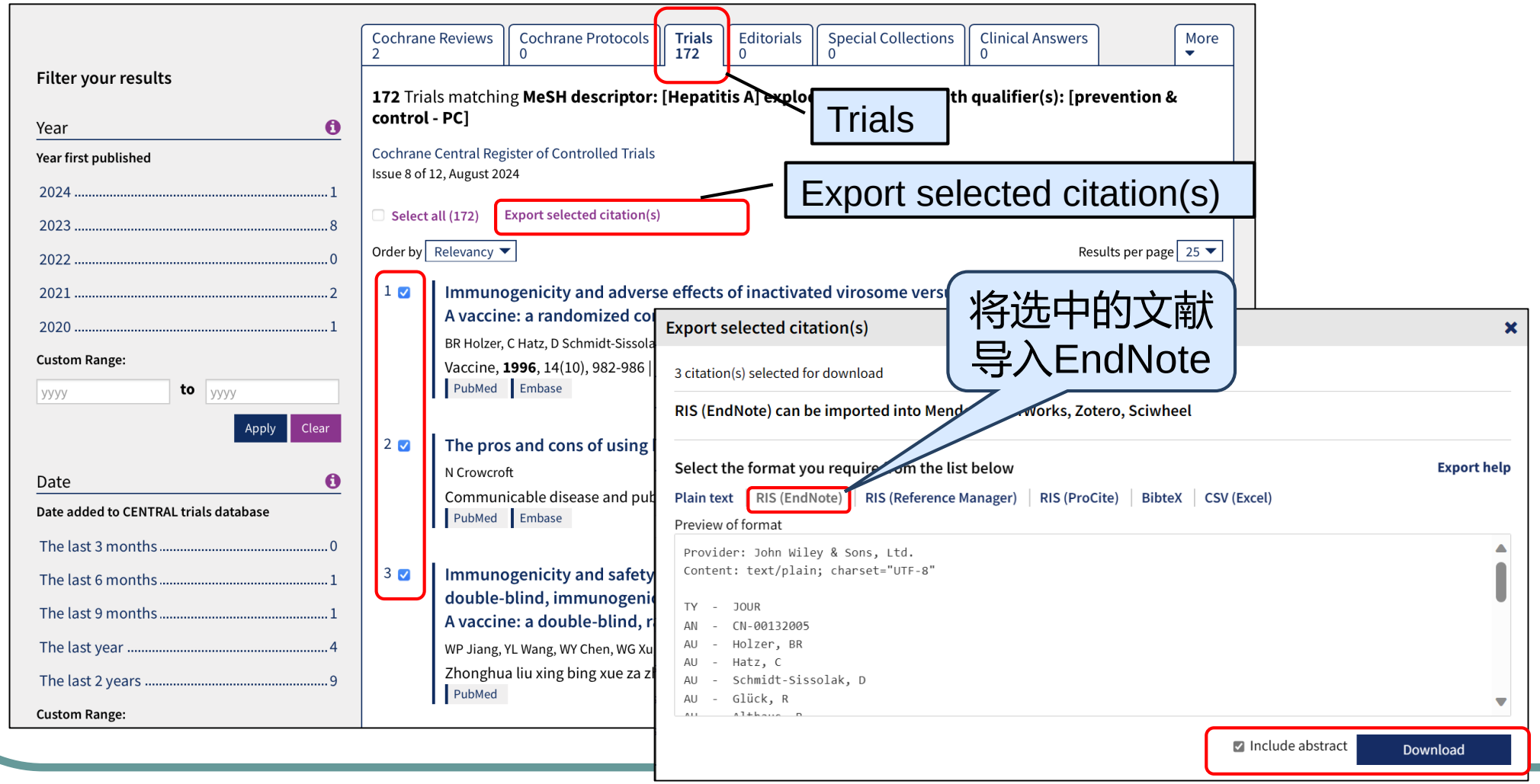
Search Manager：检索管理器



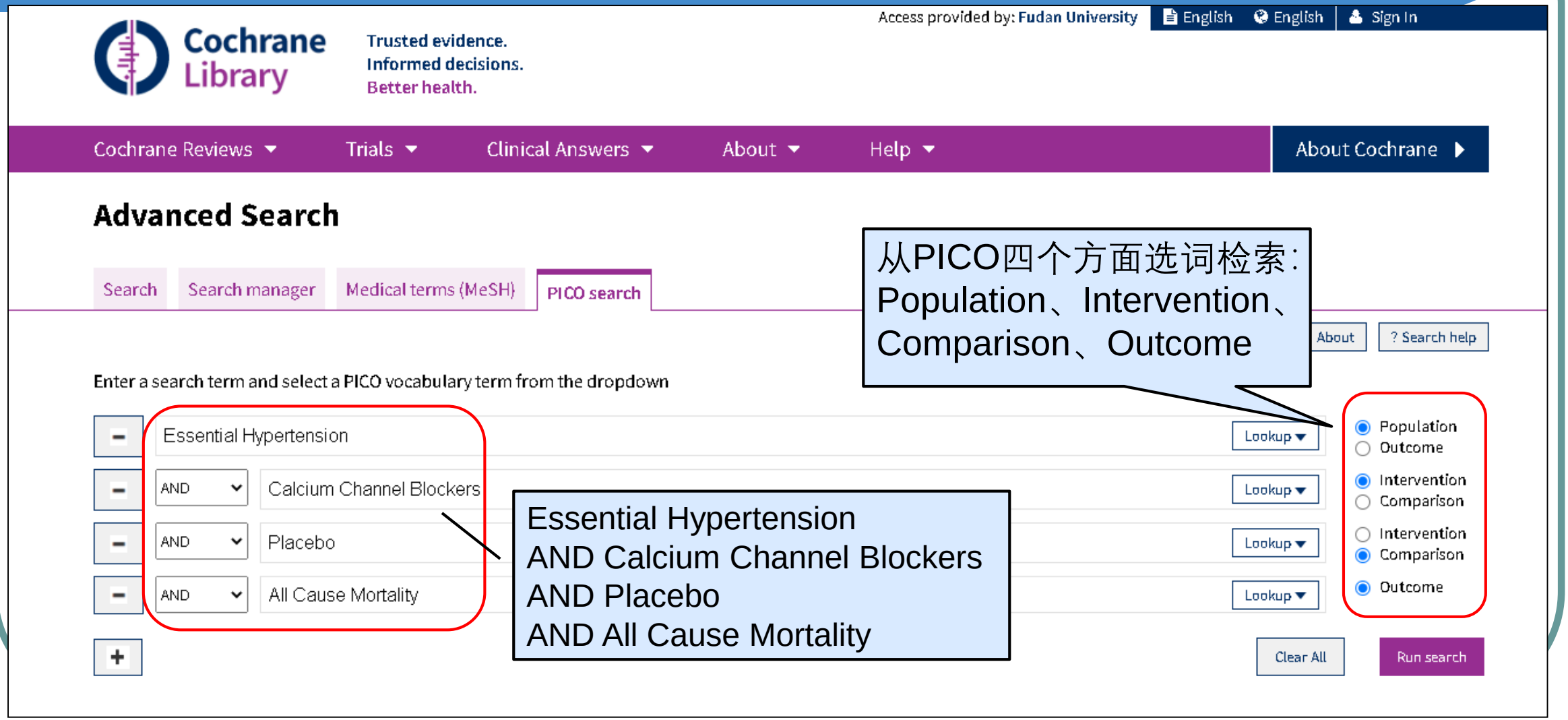
Medical Terms：甲型肝炎预防控制的临床试验证据



检索结果（Trials 临床试验）



PICO search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Informed decisions.
Better health.
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Trials
Clinical Answers
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Help
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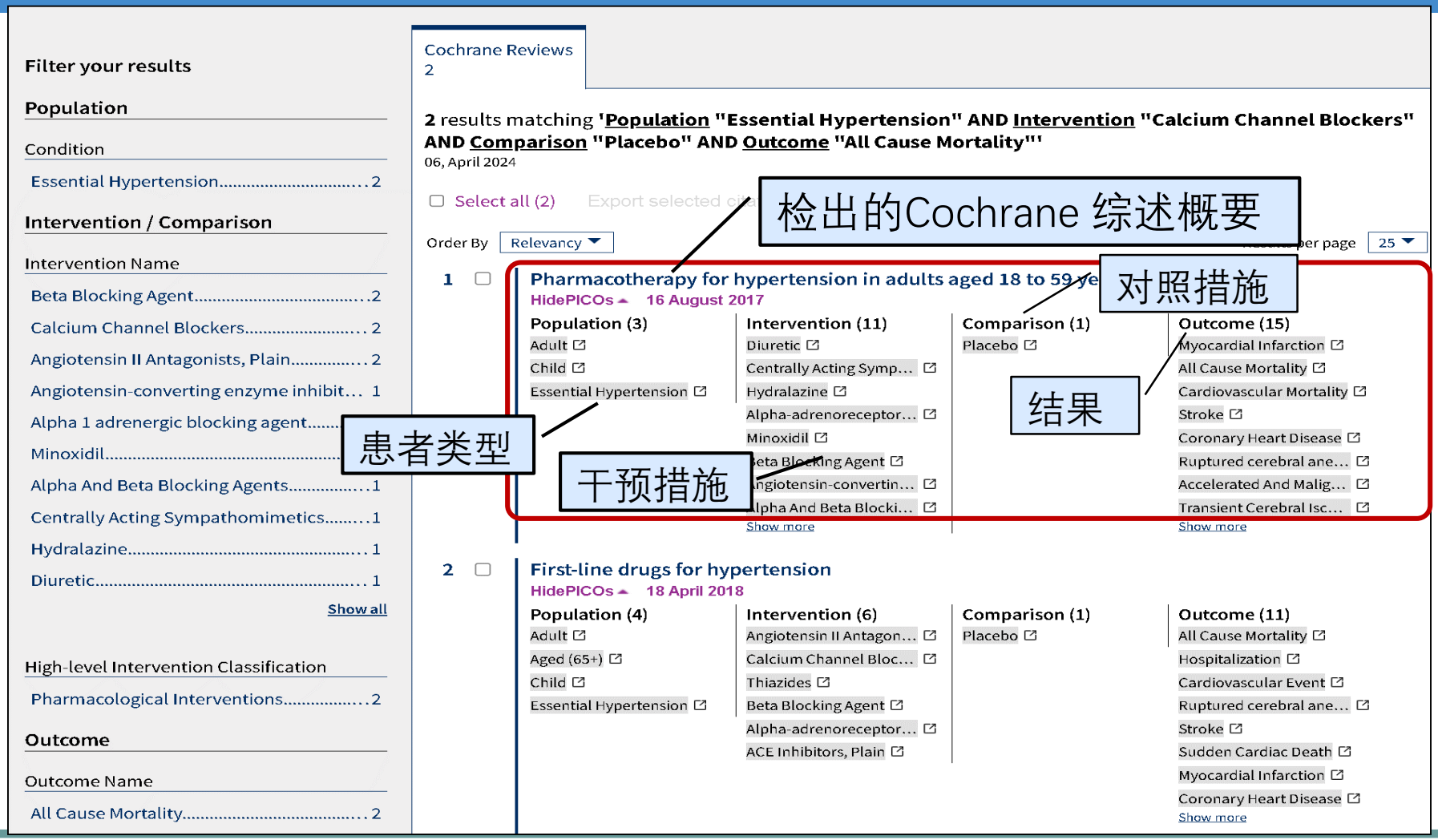
Advanced Search
Search
Search manager
Medical terms (MeSH)
PICO search
About
? Search help
Enter a search term and select a PICO vocabulary term from the dropdown
Essential Hypertension
Lookup
Population
Outcome
AND
Calcium Channel Blockers
Lookup
Intervention
Comparison
AND
Placebo
Lookup
Intervention
Comparison
AND
All Cause Mortality
Lookup
Outcome
Clear All
Run search
从PICO四个方面选词检索：
Population、Intervention、
Comparison、Outcome
Essential Hypertension
AND Calcium Channel Blockers
AND Placebo
AND All Cause Mortality

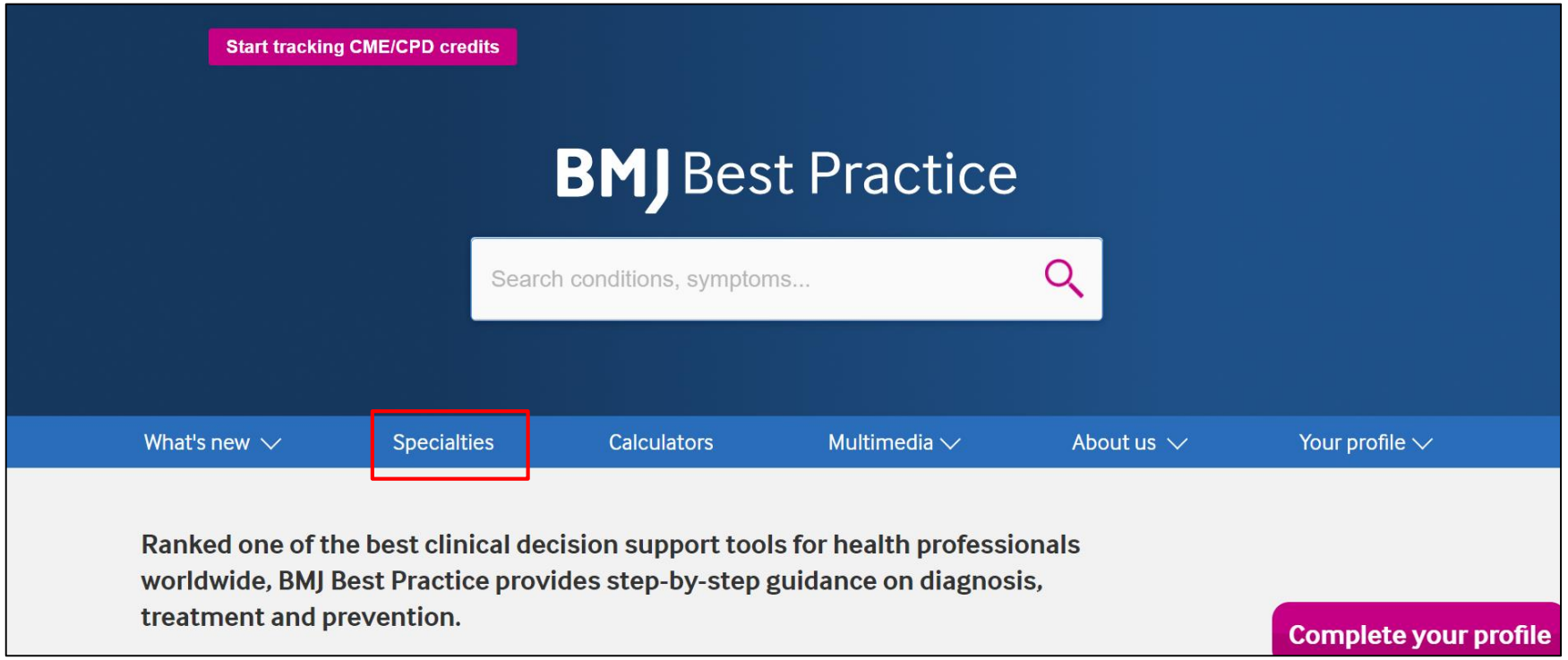
PICO search检索结果：2篇Cochrane综述



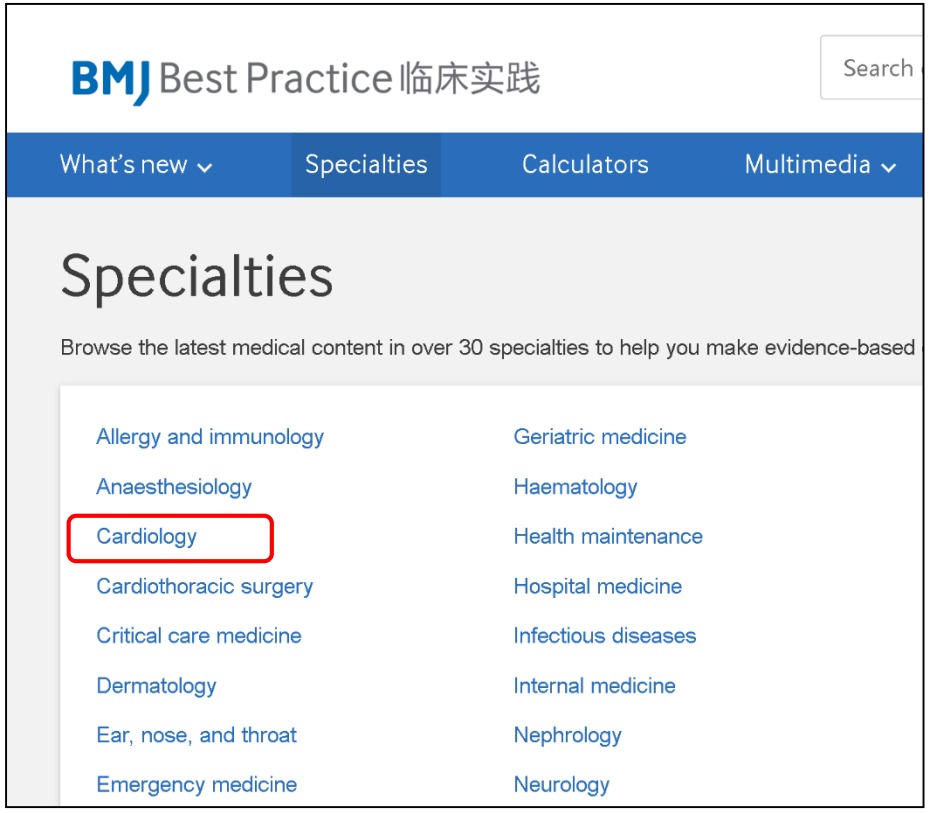
3.2.1 BMJ Best Practice

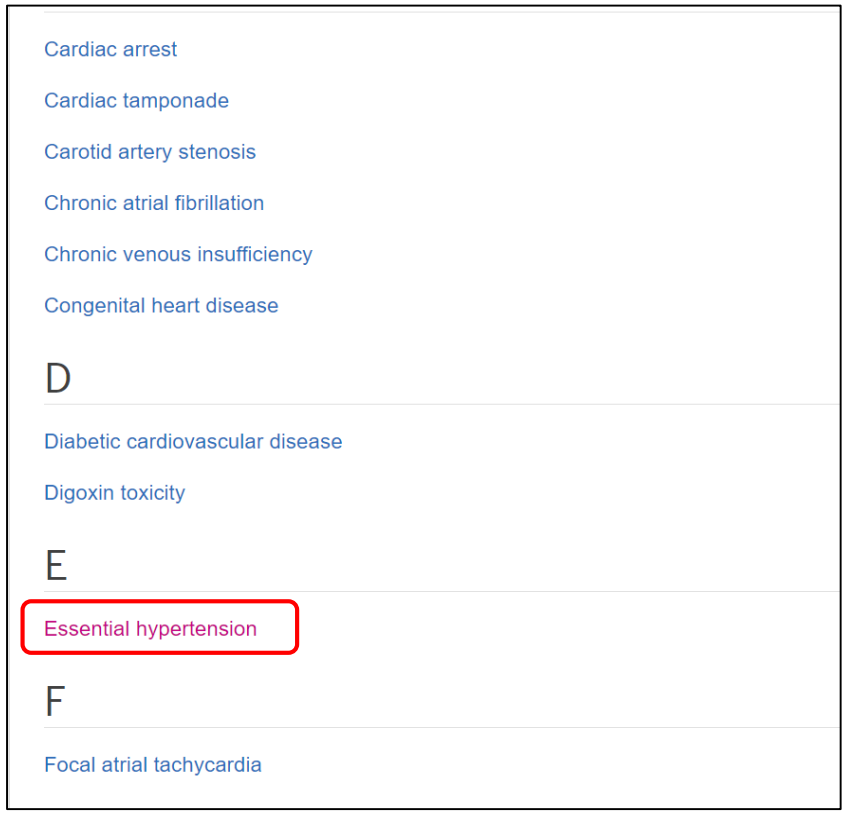
- 以疾病为单位，涵盖基础、预防、诊断、治疗和随访等各个环节的内容。
- 数千项的国际治疗指南和诊断标准，并可定制中文的临床指南和标准。
- 国际权威的药物处方数据库，提供最新的药物副反应和多种药物相互作用的最新证据。
- 大量的病症彩色图像和证据表格等资料。

Best Practice主页



Specialties专业





对每一种疾病都提供了标准结构内容

BMJ Best Practice 临床实践

Search conditions, symptoms...

What's new | Specialties | Calculators | Multimedia | About us | Your profile

Essential hypertension

Ver contenido en español

OVERVIEW	THEORY	DIAGNOSIS	MANAGEMENT	FOLLOW UP	RESOURCES
Summary	Epidemiology	Approach	Approach	Monitoring	Guidelines
	Aetiology	History and exam	Treatment algorithm	Complications	Images and videos
	Case history	Investigations	Emerging	Prognosis	References
		Differentials	Prevention		Calculators
		Criteria	Patient discussions		Evidence
		Screening			

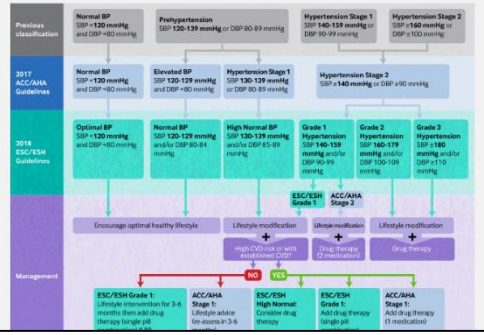
Last reviewed: 6 Mar 2024 Last updated: 17 Oct 2023

Summary

Essential hypertension is typically diagnosed by screening of an asymptomatic individual.

Treatment of uncontrolled hypertension reduces the risks of mortality and of cardiac, vascular, renal, and cerebrovascular complications.

Lifestyle changes are recommended for all patients: weight loss, exercise, decreased sodium

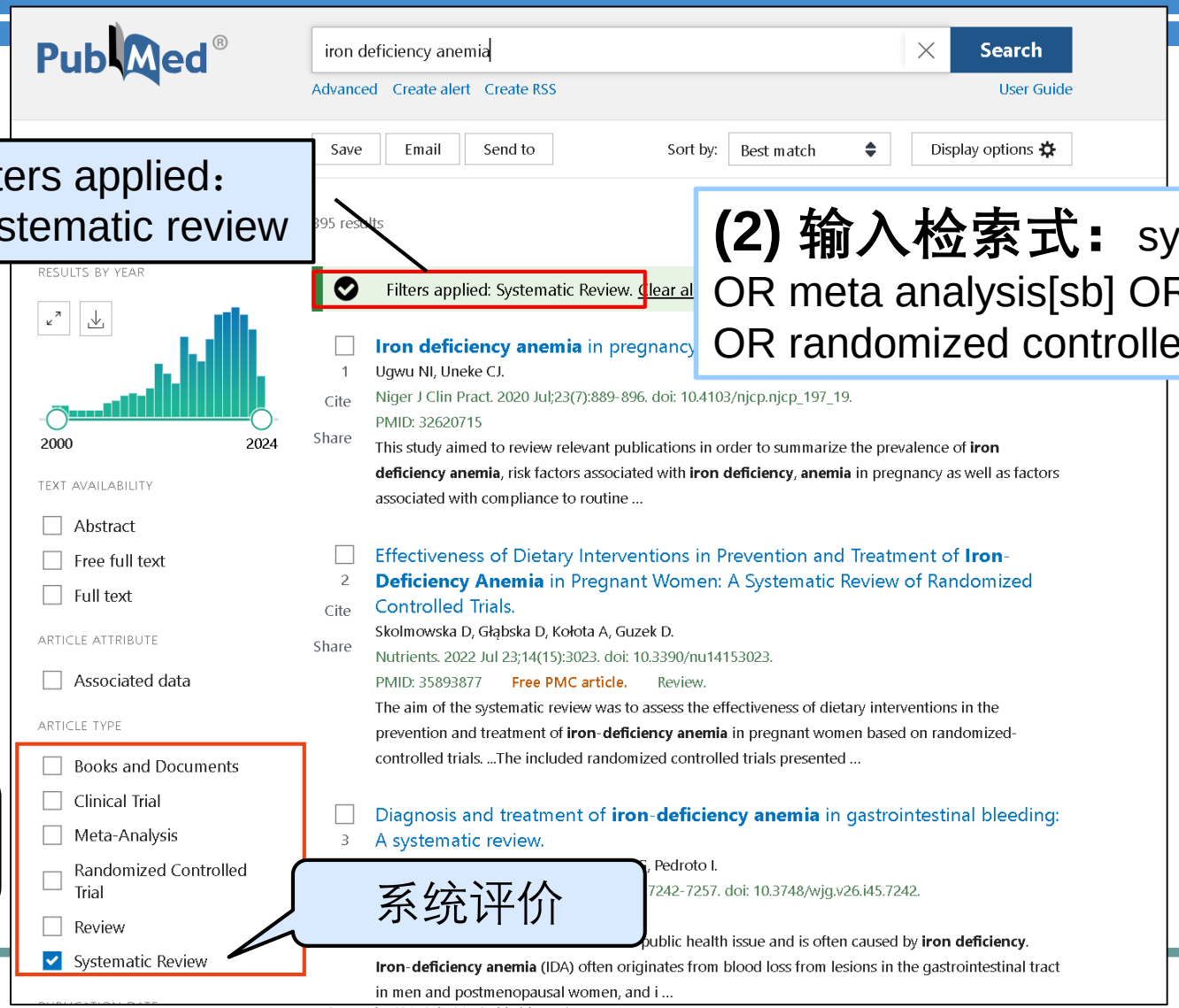


3.2.2 PubMed：通过文献类型筛选循证证据

(1) Filters：Article Type

- Systematic Review
- Meta Analysis
- Clinical Trials
- RCT
- ……

注：Review 只包含部分系统评价、Meta分析



Filters applied：Systematic review

系统评价

(2) 输入检索式： systematic review[sb] OR meta analysis[sb] OR clinical trial[sb] OR randomized controlled trial[sb] OR ……

随机对照试验的高敏感检索策略
(MEDLINE数据库，含文献类型与自由词检索)

- #1 randomized controlled trial [pt]
- #2 controlled clinical trial [pt]
- #3 randomized [tiab]
- #4 placebo [tiab]
- #5 drug therapy [sh]
- #6 randomly [tiab]
- #7 trial [tiab]
- #8 groups [tiab]
- #9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
- #10 animals [mh] NOT humans [mh]
- #11 #9 NOT #10

“他莫昔芬治疗乳腺癌”
Cochrane Library-Trials 检索策略

#1 MeSH descriptor Breast Neoplasms explode all trees

#2 breast near cancer*

#3 breast near neoplasm*

#4 breast near carcinoma*

#5 breast near tumour*

#6 breast near tumor*

#7 #1 OR #2 OR #3 OR #4 OR #5 OR #6

#8 MeSH descriptor Tamoxifen explode all trees

#9 tamoxifen

#10 #8 OR #9

#11 #7 AND #10

注意：在Trials中检索研究，纳入系统评价时，针对每个概念需要更多的检索词汇。

3.2.2 中国生物医学文献数据库： 自由词检索

循证医学综述文献的检索策略：

#1 系统评价 OR 系统综述 OR 系统性评价 OR 系统性综述 OR 系统评述 OR 系统性评述

#2 英文题目： systematic AND review

#3 循证医学 OR 证据医学 OR 实证医学

#4 meta分析 OR 荟萃分析 OR 汇总分析 OR 集成分析

#5 英文题目： meta AND analysis

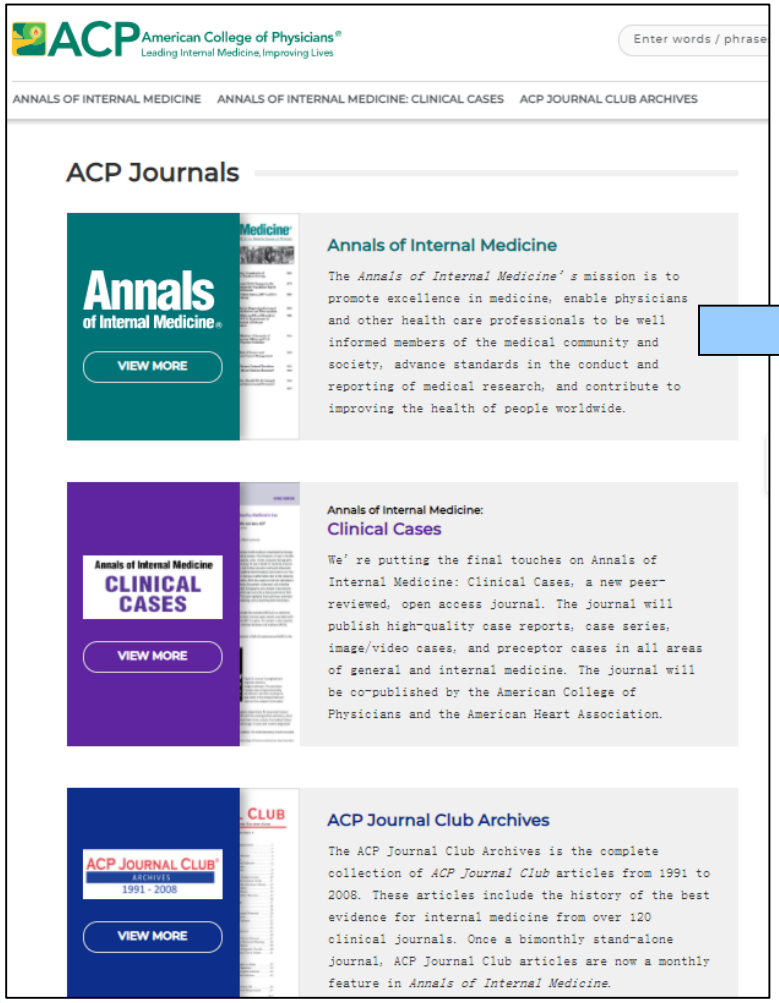
#6 #1 OR #2 OR #3 OR #4 OR #5

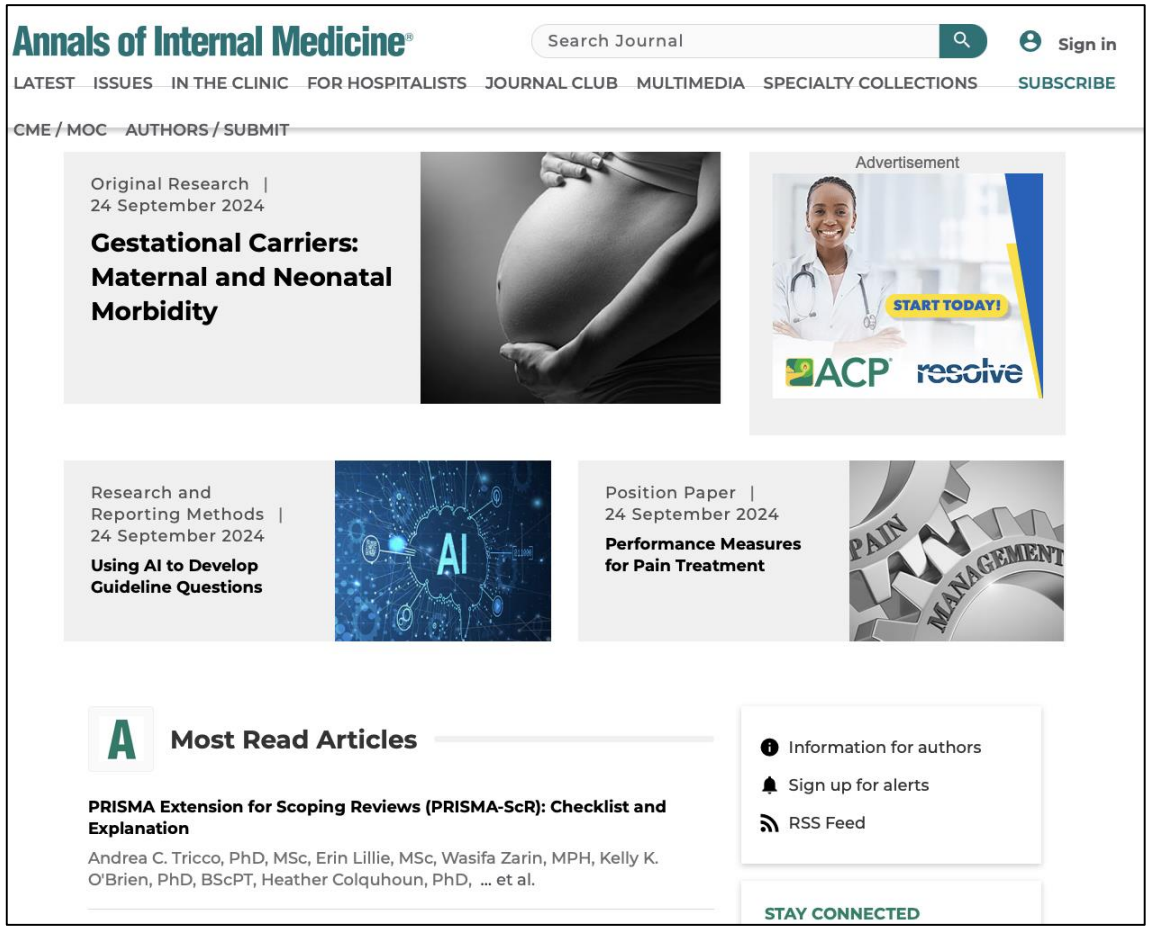
3.2.3 循证医学期刊

(1) ACP Journal Club 月刊

- 美国内科医师协会和美国内科协会联合主办
- 隶属于Annals of Internal Medicine
- https://www.acpjournals.org

ACP Journal Club





3.2.3 循证医学期刊

(2) Evidence-based Medicine

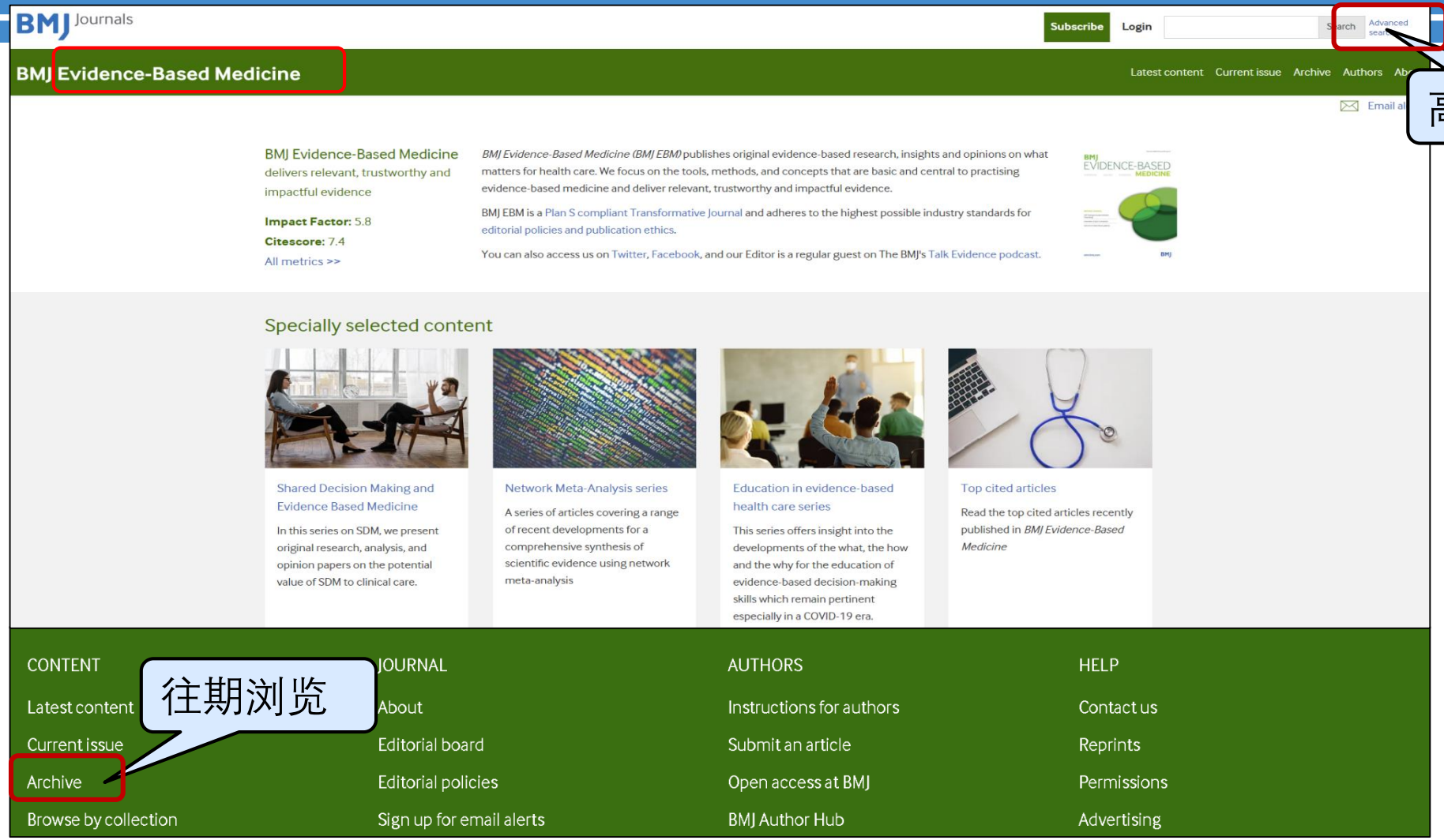
双月刊，BMJ出版

由英国医学杂志和美国内科医师协会联合主办。

https://ebm.bmj.com/

可在我校EBSCO平台中获取全文。

Evidence-based Medicine



3.2.3 循证医学期刊

(3)《中国循证医学杂志》

月刊

由中华人民共和国教育部主管，四川大学主办，中国循证医学中心和四川大学华西医院承办的医学类专业性学术期刊。

http://www.cjebm.com/

中国循证医学杂志


华西医学期刊出版社
WEST CHINA MEDICAL PUBLISHERS
首页 期刊 新闻 大刊解读 新冠肺炎 关于 搜索 登录 注册 English
《中国循证医学杂志》
主管：中华人民共和国教育部 主办：四川大学
主编：李幼平
刊期：月刊 ISSN：1672-2531 CN：51-1656/R
微信公众号
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当期目录 优先发表 过刊浏览
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3.2.4 临床实践指南： 医脉通指南

http://guide.medlive.cn

3.2.4 临床实践指南： 医脉通指南

截屏日期：2024年9月

3.2.4 临床实践指南： 医脉通指南全文

Clinical Practice Guidelines

2020 International Society of Hypertension Global Hypertension Practice Guidelines

Thomas Unger, Claudio Borghi, Fadi Charchar, Nadia A. Khan, Neil R. Poulter, Dorairaj Prabhakaran, Agustin Ramirez, Markus Schlaich, George S. Stergiou, Maciej Tomaszewski, Richard D. Wainford, Bryan Williams, Aletta E. Schutte

Table of Contents

Section 1: Introduction

Context and Purpose of This Guideline

Statement of Remit

To align with its mission to reduce the global burden of raised blood pressure (BP), the International Society of Hypertension (ISH) has developed worldwide practice guidelines for the management of hypertension in adults, aged 18 years and older.

The ISH Guidelines Committee extracted evidence-based content presented in recently published extensively reviewed guidelines and tailored ESSENTIAL and OPTIMAL standards of care in a practical format that is easy-to-use particularly in low, but also in high resource settings – by clinicians, but also nurses and community health workers, as appropriate. Although distinction between low and high resource settings often refers to high (HIC) and low- and middle-income countries (LMIC), it is well established that in HIC there are areas with low resource settings, and vice versa.

Herein optimal care refers to evidence-based standard of care articulated in recent guidelines[1,2] and summarized here, whereas ESSENTIAL standards recognize that OPTIMAL standards would not always be possible. Hence essential standards refer to minimum standards of care. To allow specification of essential standards of care for low resource settings, the Committee was often confronted with the limitation or absence in clinical evidence, and thus applied expert opinion.

Received March 6, 2020; first decision March 16, 2020; revision accepted March 27, 2020.

From the CARIM – School for Cardiovascular Diseases, Maastricht University, the Netherlands (T.U.); Department of Medical and Surgical Sciences, University of Bologna, Italy (C.B.); Federation University Australia, School of Health and Life Sciences, Ballarat, Australia (F.C.); University of Melbourne, Department of Physiology, Melbourne, Australia (F.C.); University of Leicester, Department of Cardiovascular Sciences, United Kingdom (F.C.); University of British Columbia, Vancouver, Canada (N.A.K.); Center for Health Evaluation and Outcomes Sciences, Vancouver, Canada (N.A.K.); Imperial Clinical Trials Unit, Imperial College London, United Kingdom (N.R.P.); Public Health Foundation of India, New Delhi, India (D.P.); Centre for Chronic Disease Control, New Delhi, India (D.P.); London School of Hygiene and Tropical Medicine, United Kingdom (D.P.); Hypertension and Metabolic Unit, University Hospital, Favaloro Foundation, Buenos Aires, Argentina (A.R.); Dobney Hypertension Centre, School of Medicine, Royal Perth Hospital Unit, University of Western Australia, Perth (M.S.); Neurovascular Hypertension & Kidney Disease Laboratory, Baker Heart and Diabetes Institute, Melbourne, Victoria, Australia (M.N.); Hypertension Center STRIDE-7, School of Medicine, Third Department of Medicine, Sotiria Hospital, National and Kapodistrian University of Athens, Greece (G.S.S.); Division of Cardiovascular Sciences, Faculty of Medicine, Biology and Health, University of Manchester, United Kingdom (M.T.); Division of Medicine and Manchester Academic Health Science Centre, Manchester University NHS Foundation Trust Manchester, United Kingdom (M.T.); Department of Pharmacology and Experimental Therapeutics, Boston University School of Medicine, MA (R.D.W.); The Whitaker Cardiovascular Institute, Boston University, MA (R.D.W.); Department of Health Sciences, Boston University Sargent College, MA (R.D.W.); University College London, NIHR University College London, Hospitals Biomedical Research Centre, London, United Kingdom (B.W.); Faculty of Medicine, University of New South Wales, Sydney, Australia (A.E.S.); The George Institute for Global Health, Sydney, Australia (A.E.S.); and Hypertension in Africa Research Team (A.E.S.) and South African MRC Unit for Hypertension and Cardiovascular Disease (A.E.S.), North-West University, Potchefstroom, South Africa.

This article has been copublished in the Journal of Hypertension.

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(*Hypertension*. 2020;75:00-00. DOI: 10.1161/HYPERTENSIONAHA.120.15026.)

Hypertension is available at https://www.ahajournals.org/journal/hyp DOI: 10.1161/HYPERTENSIONAHA.120.15026

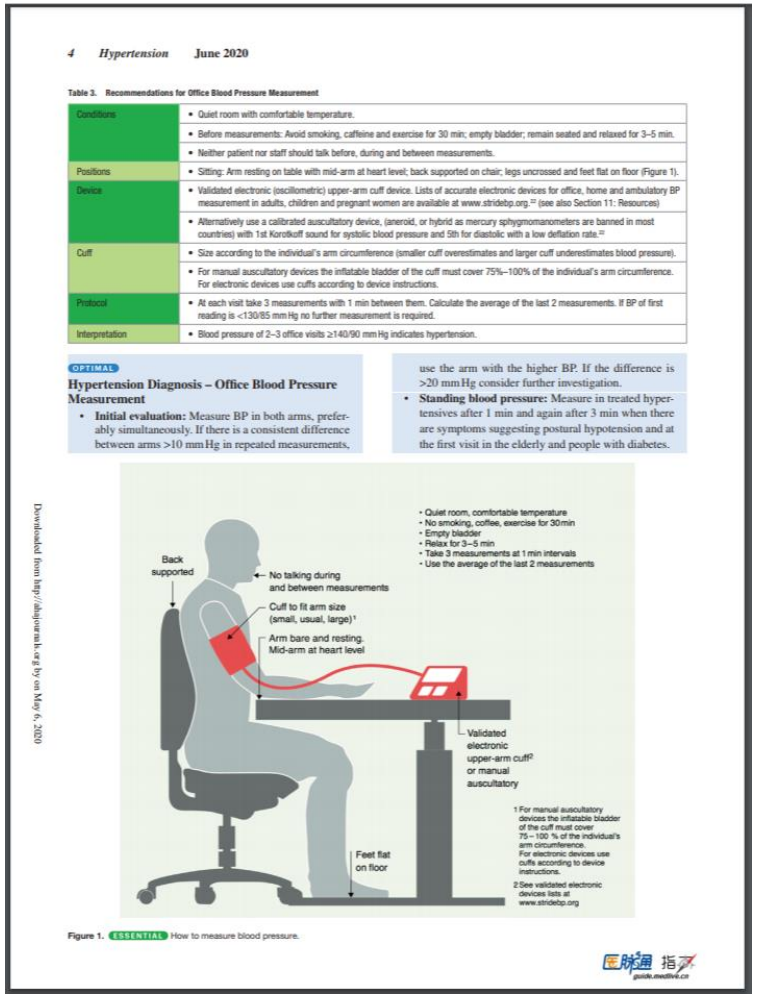


Table 3. Recommendations for Office Blood Pressure Measurement

Conditions	• Quiet room with comfortable temperature.
	• Before measurements: Avoid smoking, caffeine and exercise for 30 min; empty bladder; remain seated and relaxed for 3–5 min.
	• Neither patient nor staff should talk before, during and between measurements.
Positions	• Sitting: Arm resting on table with mid-arm at heart level; back supported on chair; legs uncrossed and feet flat on floor (Figure 1).
Device	• Validated electronic (oscillometric) upper-arm cuff device. Lists of accurate electronic devices for office, home and ambulatory BP measurement in adults, children and pregnant women are available at www.stridebp.org.[22] (see also Section 11: Resources)
	• Alternatively use a calibrated auscultatory device, (aneroid, or hybrid as mercury sphygmomanometers are banned in most countries) with 1st Korotkoff sound for systolic blood pressure and 5th for diastolic with a low deflation rate.[23]
Cuff	• Size according to the individual's arm circumference (smaller cuff overestimates and larger cuff underestimates blood pressure).
	• For manual auscultatory devices the inflatable bladder of the cuff must cover 75%–100% of the individual's arm circumference. For electronic devices use cuffs according to device instructions.
Protocol	• At each visit take 3 measurements with 1 min between them. Calculate the average of the last 2 measurements. If BP of first reading is <130/85 mm Hg no further measurement is required.
Interpretation	• Blood pressure of 2–3 office visits ≥140/90 mm Hg indicates hypertension.

OPTIMAL

Hypertension Diagnosis – Office Blood Pressure Measurement

- **Initial evaluation:** Measure BP in both arms, preferably simultaneously. If there is a consistent difference between arms >10 mm Hg in repeated measurements, use the arm with the higher BP. If the difference is >20 mm Hg consider further investigation.
- **Standing blood pressure:** Measure in treated hypertensives after 1 min and again after 3 min when there are symptoms suggesting postural hypotension and at the first visit in the elderly and people with diabetes.

Figure 1. ESSENTIAL How to measure blood pressure.

截屏日期：2024年9月

3.2.5 卫生技术评估

1.国际卫生技术评估机构网络(INAHTA)
(https://www.inahta.org/)

- 成立于1993年，秘书处在瑞典。
- 促进卫生技术评估机构之间的合作交流
- 促进信息的共享与比较
- 预防不必要的重复性研究。

3.2.5 卫生技术评估

2.欧洲卫生技术网络（EUnetHTA）
（https://www.eunethta.eu/）

- 成立于2006年
- 由欧盟组织支持,其目的是在欧洲各国之间建立合作关系，除了发展和共同利用HTA信息外,还包含交流和联合发展方法学。
- 共有国家级和地区级 81 个合作研究组织参加。

摘自——胡善联. 迎接新十年，HTA准备好了吗[N]. 医药经济报,2019-07-25(F03).

3.3 检索实例

- 一名内科医生在临床实践中提出问题
- 是否能够将溶栓联合冠状动脉介入治疗急性心肌梗塞，目前有无充分的相关证据?

3.3 检索实例

- **检索文献目的：获取解决临床问题的最佳证据，属循证医学实践范畴。**

- 从查全率和查准率的角度看，该医生的需求查准更为重要
- 检索时应首先查看是否有相关的高质量的临床实践指南、系统评价和Meta分析
- 若无，再查看其他等级证据，如：单个样本量足够的随机对照实验、设对照组但未用随机方法分组的研究等。

溶栓联合冠状动脉介入治疗急性心肌梗塞

- **选词**

  急性心肌梗塞（Acute myocardial infarction）

  血栓溶解疗法（Thrombolytic therapy）

  冠状动脉介入治疗（Primary coronary intervention）

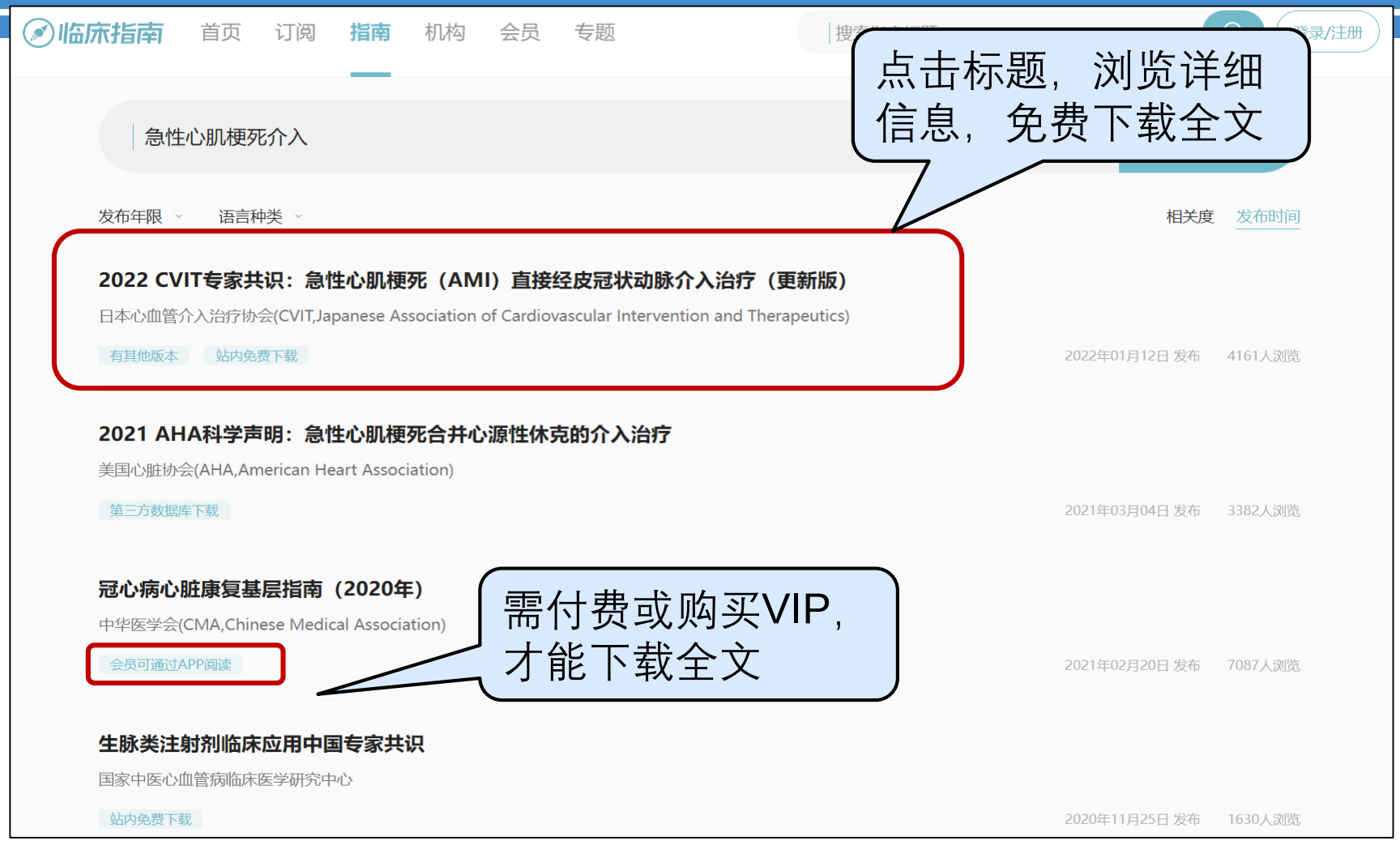
  经皮冠状动脉腔内成形术（Percutaneous transluminal coronary angioplasty）

- **逻辑关系**

  急性心肌梗塞 AND 血栓溶解疗法

  AND (冠状动脉介入治疗 OR 经皮冠状动脉腔内成形术)

医脉通 http://guide.medlive.cn



医脉通

必须注册，填写所有需提供的信息，登录后才能下载

医脉通-专家共识全文

Cardiovascular Intervention and Therapeutics
https://doi.org/10.1007/s12928-018-0516-y

EXPERT CONSENSUS DOCUMENT

CVIT expert consensus document on primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) in 2018

Yukio Ozaki[1] · Yuki Katagiri[2] · Yoshinobu Onuma[1,3] · Tetsuya Amano[4] · Takashi Muramatsu[1] · Ken Kozuma[5] · Satoru Otsuji[6] · Takafumi Ueno[7] · Nobuo Shiode[8] · Kazuya Kawai[9] · Nobuhiro Tanaka[10] · Kinzo Ueda[11] · Takashi Akasaka[12] · Keiichi Igarashi Hanaoka[13] · Shiro Uemura[14] · Hirotaka Oda[15] · Yoshiaki Katahira[16] · Kazushige Kadota[17] · Eisho Kyo[18] · Katsuhiko Sato[19] · Tadaya Sato[20] · Junya Shite[21] · Koichi Nakao[22] · Masami Nishino[23] · Yutaka Hikichi[24] · Junko Honye[25] · Tetsuo Matsubara[26] · Sumio Mizuno[27] · Toshiya Muramatsu[28] · Taku Inohara[29] · Shun Kohsaka[29] · Ichiro Michishita[30] · Hiroyoshi Yokoi[31] · Patrick W. Serruys[32] · Yuji Ikari[33] · Masato Nakamura[34] · The Task Force on Primary Percutaneous Coronary Intervention (PCI) of the Japanese Cardiovascular Interventional Therapeutics (CVIT)

Received: 23 February 2018 / Accepted: 27 February 2018

Abstract
While primary percutaneous coronary intervention (PCI) has significantly contributed to improve the mortality in patients with ST segment elevation myocardial infarction even in cardiogenic shock, primary PCI is a standard of care in most of Japanese institutions. Whereas there are high numbers of available facilities providing primary PCI in Japan, there are no clear guidelines focusing on procedural aspect of the standardized care. Whilst updated guidelines for the management of acute myocardial infarction were recently published by European Society of Cardiology, the following major changes are indicated; (1) radial access and drug-eluting stent over bare metal stent were recommended as Class I indication, and (2) complete revascularization before hospital discharge (either immediate or staged) is now considered as Class IIa recommendation. Although the primary PCI is consistently recommended in recent and previous guidelines, the device lag from Europe, the frequent usage of coronary imaging modalities in Japan, and the difference in available medical therapy or mechanical support may prevent direct application of European guidelines to Japanese population. The Task Force on Primary Percutaneous Coronary Intervention of the Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT) has now proposed the expert consensus document for the management of acute myocardial infarction focusing on procedural aspect of primary PCI.

Keywords ST elevation acute myocardial infarction · Acute coronary syndrome · Plaque rupture · Plaque erosion · Percutaneous ventricular assist devices · Guideline

Introduction

In ST segment elevation myocardial infarction (STEMI), primary PCI has been shown to reduce cardiac events, to convey earlier discharge and to contribute to hemodynamic stabilization in cardiogenic shock and subsequently to become a standard care in Japan [1–19]. Despite a high number of available facilities providing primary PCI in Japan, there are no guidelines focusing on procedural aspect of standardized care, which may further improve the quality of our practice.

Recently, updated guidelines for the management of acute myocardial infarction (AMI) were published by European Society of Cardiology (ESC) [20]. As major changes, (1) radial access and drug-eluting stent (DES) over bare metal stent (BMS) were recommended as Class I indication, (2) complete revascularization before hospital discharge (either the timing of angiography and revascularization should be based on patient risk profile, considering the significant difference between early and delayed strategies in short-term outcome.

Recently, GRACE risk score was applied to the patients with ACS in the Tokyo CCU (cardiovascular care unit) Network Database. A total of 9460 patients with ACS hospitalized at 67 Tokyo CCUs were retrospectively reviewed and there was a strong correlation between the GRACE risk score and in-hospital mortality for patients with STEMI or NSTEMI ($r = 0.99$, $P < 0.001$); however, the correlation was not significant for patients with unstable angina ($r = 0.35$, $P = 0.126$). We recommend use of GRACE score to identify high-risk patients with acute myocardial infarction [35].

Recommendations

- Primary PCI of the infarct-related artery (IRA) is indicated in STEMI.

In case of NSTEMI

- Urgent coronary angiography (< 2 h) is recommended in patients at very high ischemic risk (refractory angina, with associated heart failure, cardiogenic shock, life-threatening ventricular arrhythmias, or hemodynamic instability).
- An early invasive strategy (< 24 h) is recommended in patients with at least one primary high-risk criterion (Table 5).
- An invasive strategy (< 72 h after first presentation) is indicated in patients with at least one high-risk criterion (Table 5) or recurrent symptoms.
- Non-invasive documentation of inducible ischemia is recommended in low-risk patients without recurrent symptoms before deciding on invasive evaluation.

Table 5 Criteria for high risk with indication for invasive management [20]

Primary criteria
1. Relevant rise or fall in troponin
2. Dynamic ST- or T-wave changes (symptomatic or silent)
3. GRACE score > 140
Secondary criteria
4. Diabetes mellitus
5. Renal insufficiency (eGFR < 60 ml/min/1.73 m^2)
6. Reduced LV function (ejection fraction < 40%)
7. Early post-infarction angina
8. Recent PCI
9. Prior CABG
10. Intermediate to high GRACE risk score (http://www.gracescore.org)

CABG coronary artery bypass grafting, *eGFR* estimated glomerular filtration rate, *GRACE* Global Registry of Acute Coronary Events, *LV* left ventricular, *PCI* percutaneous coronary intervention

Practical recommendation for primary percutaneous coronary intervention

Loading dose DAPT

Prasugrel and ticagrelor reduce ischemic events and mortality in ACS patients compared to clopidogrel and are recommended by current guidelines [20, 36].

In TRITON-TIMI 38, 13608 patients with acute coronary syndromes with scheduled percutaneous coronary intervention were randomized to either prasugrel or clopidogrel. Prasugrel therapy was associated with significantly reduced rates of ischemic events, including stent thrombosis, but with an increased risk of major bleeding, including fatal bleeding. Overall mortality did not differ significantly between treatment groups [36]. In Japanese population, the PRASFIT-ACS study was conducted to confirm the efficacy and safety of prasugrel at loading/maintenance doses of 20/3.75 mg [37]. Japanese patients ($n = 1363$) with acute coronary syndrome undergoing percutaneous coronary intervention were randomized to either prasugrel (20 mg for loading/3.75 mg for maintenance) or clopidogrel (300 mg for loading/75 mg for maintenance). The incidence of MACE at 24 weeks was 9.4% in the prasugrel group and 11.8% in the clopidogrel group (risk reduction 23%, hazard ratio 0.77, 95% confidence interval 0.56–1.07). The incidence of non-coronary artery bypass graft-related major bleeding was similar in both groups (1.9 vs. 2.2%). The results were similar to TRITON-TIMI 38 with a low risk of clinically serious bleeding in Japanese ACS patients.

Regarding ticagrelor, clinical outcomes in a large real-world post-ACS population was studied in a Swedish prospective cohort study in 45073 ACS patients who were discharged on ticagrelor ($N = 11954$) or clopidogrel ($N = 33119$) [38]. The risk of the primary outcome (i.e. composite of all-cause death, re-admission with MI or stroke) with ticagrelor vs. clopidogrel was 11.7 vs. 22.3% [adjusted HR (HR) 0.85 (95% CI 0.78–0.93)], risk of death 5.8 vs. 12.9% [adjusted HR 0.83 (0.75–0.921)], and risk of MI 6.1 vs. 10.8% [adjusted HR 0.89 (0.78–1.011)] at 24 months. Re-admission for bleeding with ticagrelor versus clopidogrel was similar. Ticagrelor versus clopidogrel post-ACS was associated with a lower risk of death, MI, or stroke, as well as death alone. Risk of bleeding was higher with ticagrelor [38]. These real-world outcomes are consistent with the

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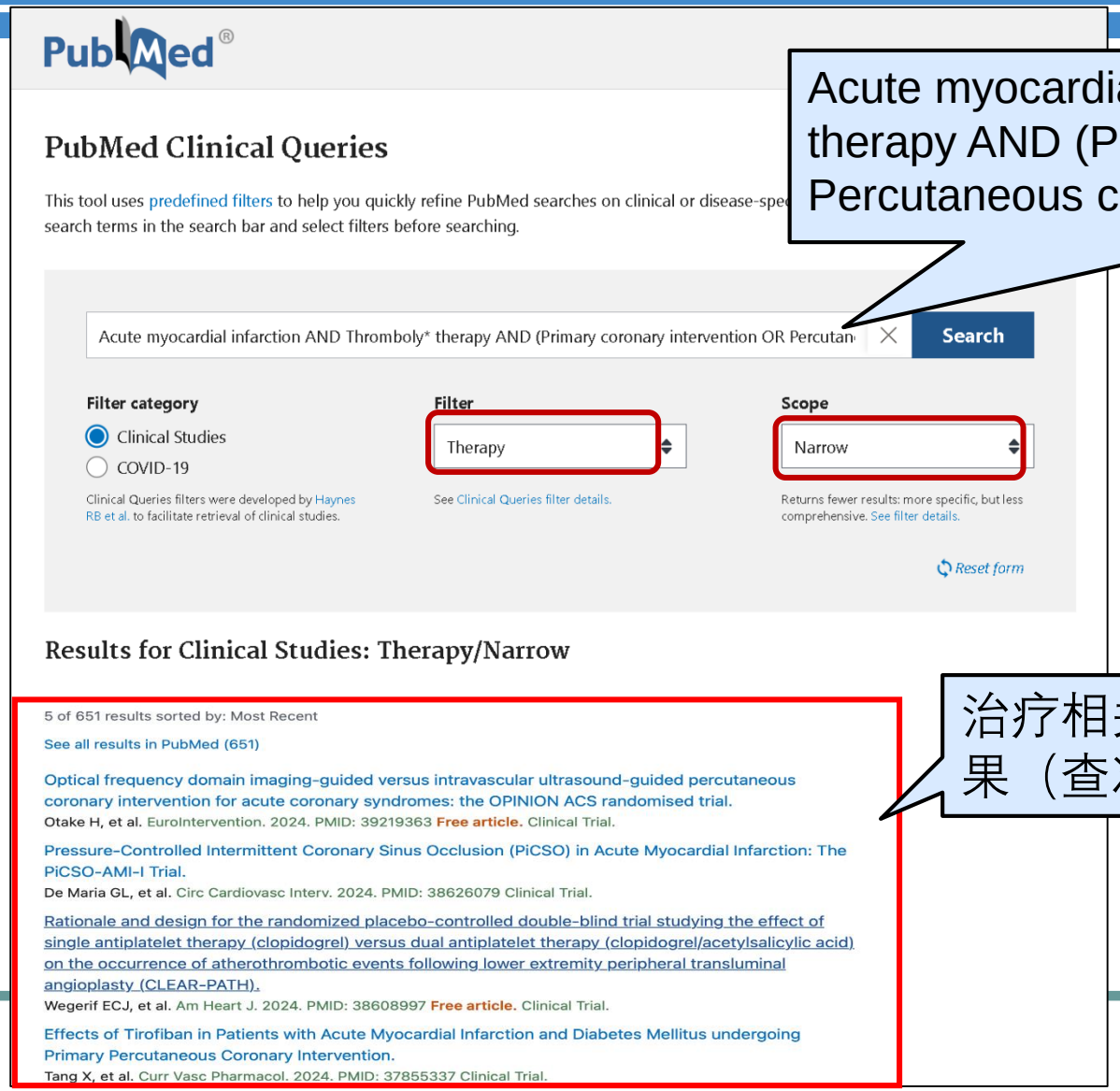

Acute myocardial infarction AND Thromboly* therapy AND (Primary coronary intervention OR Percutaneous coronary transluminal angioplasty)

治疗相关的结果（查准）