

# 选题

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首先我们来看一下临床idea产生

## 临床idea来源主要为



首先临床idea的来源可以来源于文献，临床的实际工作以及指南。对于刚接触临床研究的初学者而言，以文献还有指南作为选题idea的来源最为安全。

“

指南中C级证据和专家推荐是一个非常好的发力点。此外，对于指南中未覆盖的空白点也是必中的、好的IDEA。

”

## 题目

**Mildly Abnormal Lipid Levels, but Not High Lipid Variability, Are Associated with Increased Risk of Myocardial Infarction and Stroke in 'Statin-Naive' Young Population: A Nationwide Cohort Study**

Circ Res | 126 (7) 2020, IF: 15.8620

## 追指南

这个例子主要讲的是血脂的水平以及血脂变异度与中风及心梗的关系，研究人群比较特殊，是没有服用过他汀类药物的年轻人。

## 摘要的目的

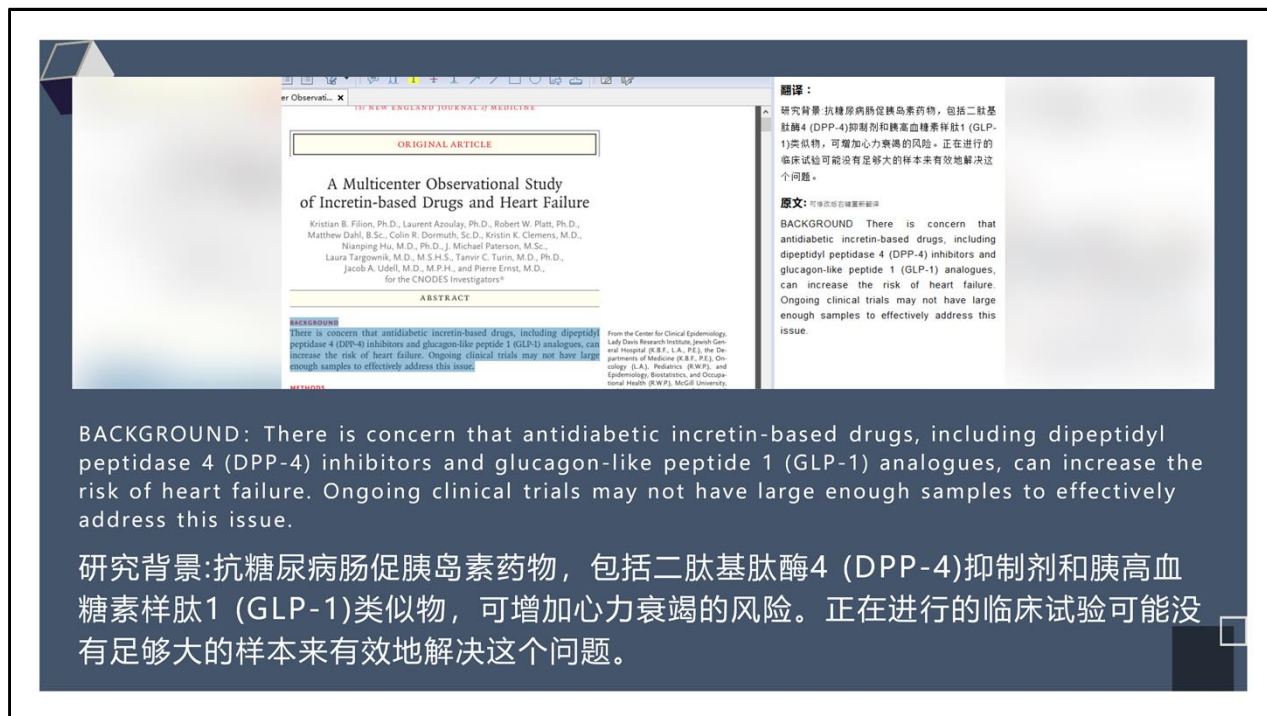
**Objectives:** 在年轻人中，轻度异常的血脂水平和血脂变异在动脉粥样硬化性心血管疾病(ASCVDs)风险中的作用仍不确定。因此，本研究研究这些血脂异常与年轻人群心肌梗死(MI)和卒中风险的关系。

## 追指南

这篇研究就是典型的追指南，因为在指南中并没有讲到，对于20~39岁的年轻患者，如果其血脂异常，该不该服用降血脂的药物，以控制未来发生不良事件的风险。而这篇研究就是弥补了这个空白，其选题非常有临床价值。

**TIPS: 越是高分的临床型研究, IDEA就越清晰,  
越简单**





这是另一篇例文，其主要描述的是一种新的药物，ddp4抑制剂会不会增加心力衰竭的风险？其选题的来源是因为此前的很多高分研究得到了矛盾的结果。



## 前言 (译文)

基于肠促胰岛素的药物，包括二肽基肽酶4 (DPP-4)抑制剂和胰高血糖素样肽1 (GLP-1)类似物的安全性是有争议的。尽管人们对不良胰腺事件的关注越来越多，但对心力衰竭风险的增加也有新的关注的确，血管Saxagliptin评估的结果记录在糖尿病患者的心肌梗死Mellitus-Thrombolysis 53 (SAVOR-TIMI 53)试验,2、3的患者被随机分配到DPP-4抑制剂Saxagliptin增加了27%在因心脏衰竭而住院治疗的风险比那些接受安慰剂。相比之下，阿格列汀与护理标准(检验)心血管结局试验4和西格列汀心血管结局评估试验(TECOS)5显示，在分别随机分配给阿格列汀和西格列汀的患者中，因心力衰竭住院的总体风险没有增加。这些试验和其他正在进行的试验都不足以有效地解决这个问题，而针对这个问题的少数观察性研究得出了不同的结果。6-10我们检查了来自多个队列患者的现有数据，以确定在常规临床实践中，与口服降糖药联合使用相比，以肠促胰岛素为基础的药物的使用是否与心力衰竭风险增加相关。该研究是加拿大观察性药物效应研究网络(CNODES)的一部分

从前沿的译文中，我们可以看到这些研究得到的结果是完全相反的，而这种完全相反的结果所带来的争议就是他选题的理由。

## 为什么要做这个研究（理由、研究意义、 立项依据）



- DDP-4抑制剂对于心脏的不良影响目前仍有争议。国外的几项来自于新英格兰及循环杂志的RCT研究产生了分歧。而一项多中性的观察性研究则发现无关。然而，这些研究都是基于国外的人群，少有基于中国人群的证据。鉴于中国糖尿病患者人数逐年递增，且DDP-4也已经写入中国的糖尿病治疗指南，因此我们想.....

如果我们现在想要做一模一样的研究，其实很简单，只要在他的基础上多加两句话，第一，此前的研究均是针对外国人群。第二，中国糖尿病患者的数量每年都在递增。可想而知，又没有中国人的数据，而且又非常的重要，我们的选题临床价值就可以得到非常大的保证。

## 总结：

- 一. 临床最稳靠的 IDEA来源为高分SCI临床文献以及我国指南中的漏洞或未覆盖的人群。
- 二. 相比指南，高分SCI文献更为直接，方便。
- 三. 高分SCI如何明确IDEA的理由？看摘要的目的部分（简），看前言部分（详细）
- 四. 在获取老外IDEA后，只需要补刀“上述证据来自老外，少于中国人的证据”
- 五. 再扯一句：鉴于病的人越来越多，所以，搞清楚，好处大。

## 特别注明：

刚接触临床研究的学友尽可能不要碰治疗相关的选题。因为，真实世界研究的数据分析非常繁琐及困难。特殊人群中的标志物是一个很好的方向来源。



02

**临床IDEA的校正**

RESEARCH ARTICLE

# Leukocyte Telomere Length in Relation to 17 Biomarkers of Cardiovascular Disease Risk: A Cross-Sectional Study of US Adults

David H. Rehkopf<sup>1\*</sup>, Belinda L. Needham<sup>2</sup>, Jue Lin<sup>3</sup>, Elizabeth H. Blackburn<sup>3</sup>, Ami R. Zota<sup>4</sup>, Janet M. Wojcicki<sup>5</sup>, Elissa S. Epel<sup>6</sup>

这些问题  
是否需要  
解决

你解决了  
什么样的  
临床问题

## Why Was This Study Done?

- Leukocyte telomere length (LTL) is a biomarker of white blood cell division and is strongly associated with age.
- There are still mixed findings on how LTL is related to different types of mortality.
- Observational evidence and quasi-experimental studies suggest that there is an association between shorter LTL and cardiovascular disease mortality.

## What Did the Researchers Do and Find?

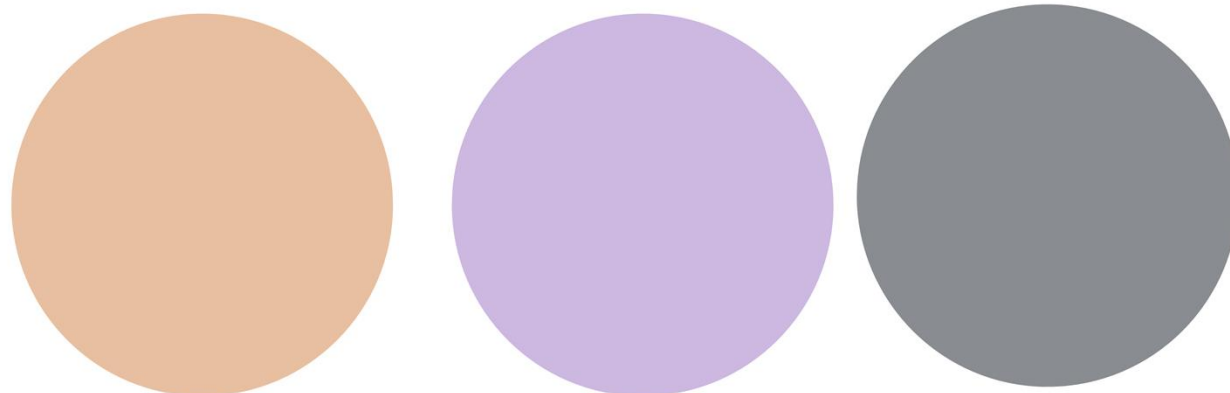
- We examined US nationally representative data on participants ages 25 to 84 that had LTL measured along with 17 other cardiovascular risk biomarkers.
- We found associations between LTL and measures of adiposity (BMI, waist circumference, percentage of body fat), along with C-reactive protein, cystatin C, high-density lipoprotein (HDL) cholesterol, triglycerides, insulin resistance, systolic blood pressure, diastolic blood pressure, and pulse rate.

问题解决了  
有什么  
好处

## What Do These Findings Mean?

- Our findings suggest that LTL is associated with cardiovascular risk factors across different physiological systems.
- The study findings do not have any implications for whether LTL is a cause of cardiovascular disease.

其实这三个问题，可以归纳成一个



基于现状，有新发现，并改变（改善）现状

临床研究选题上回答的三个问题，其实可以归纳为一个那就是现状。

如何知道我选的**XYZ**是否有临床价值

有新发现  
(数据分析)

**基于现状**

改变现状  
(现状)

只有基于现状，我们能够评估我们所要做的临床研究，到底有没有临床价值。这是临床研究选题的核心，也是临床研究的根基。



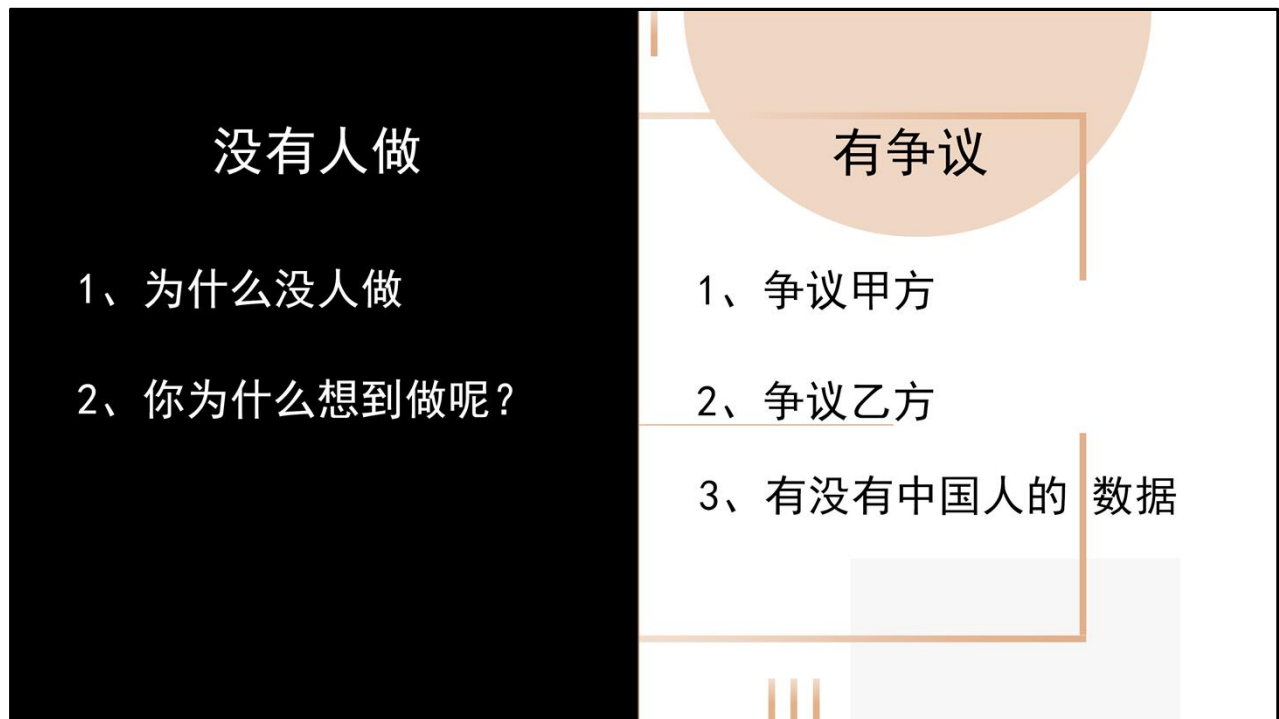


“

**选题的第二个阶段“校正”指的是对选取的  
IDEA进行基于现状的评估**

”





临床研究的现状可以分为两类，第1类没有人做，第2类有争议。没有人做，指此前没有和你同X同Y的研究，那么你要解决两个问题。第一，为什么没有人做呢？第二，既然无人做，你是怎么想到做的。如果有争议，那么我们要关注的是争议的甲方是什么观点，争议的乙方是什么观点？有没有中国人的数据？

## 当你的idea此前无相同研究时：为什么无人做

- 新手中，几乎全部都不知道为什么无人做 **(极度危险)**
- 高手中，需要运气 **(难度大)**
- 天灾 **(极小概率)**

当此前并不能发现与我们同X同Y的研究，这并不是好事情，因为我们必须要搞清楚为什么没有人做？初学者几乎大多数人都不会去解决为什么之前没有人做，这无疑是非常危险的，因为没有人做，并不意味着新颖，反而很有可能是因为没有临床价值。某些高手可以找到此前没有人做的原因，但难度很大而且概率很低。还有一种情况，譬如说新冠的感染此前就没有发生过，但是这种概率就更小了。



### 从基础机制着手

很多时候当你选的X、Y此前没有人报道，你必须得找个理由。而理由最常见来自于此前的基础研究，通过层层推断，从而找出这么一个似乎“可能”的理由。

## 当你的idea此前无相同研究时：理由2



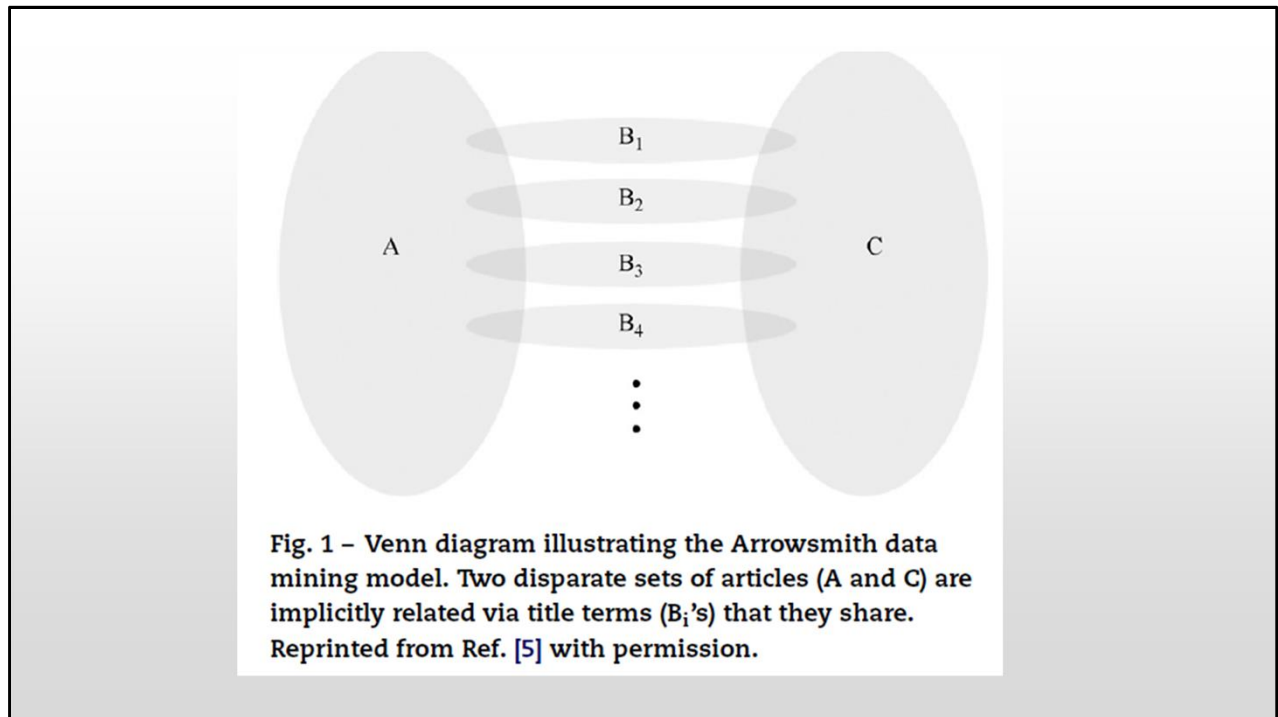
### 从同类文献着手

- 譬如你研究PLR和肺癌的关联，你可以看看关于PLR和肝癌（因为Y同类，都是癌症），或者看一下炎症因子与肺癌的关系（因为X同类，都是炎症标志物），看看他们的前言是怎么写的。



从一些软件着手

● **ARROWSMITH**



该软件的原理是找到和A有关的文献，找到和C有关的文献，而同时和A和C有关的文献，其并集被软件罗列出来。

http://arrowsmith.psych.uic.edu/arrowsmith\_uic/index.html

The Arrowsmith Project Home x AB and BC Context x +

# ARROWSMITH LINKING

DOCUMENTS, DISCIPLINES, INVESTIGATORS AND DATABASES

- [Go](#) **Arrowsmith:** Identify meaningful links between two sets of Medline articles
- [Go](#) **Author-ity:** Identify Medline articles written by a particular individual
- [Go](#) **Anne O'Tate:** Summarize, drill-down and browse the results of a PubMed query
- [Go](#) **ADAM:** Another database of abbreviations in Medline
- [Go](#) **Evidence-Based Medicine:** The project website for "Text Mining Pipeline to Accelerate Systematic Reviews in Evidence-Based Medicine"



### Start ARROWSMITH

This search mode will assist you in looking for items or concepts that may be present in common between two distinct sets of articles. Another context for using this search mode is when you want to find information that is present in one field that may be relevant to another field of inquiry. You will be guided through two PubMed searches to retrieve biomedical articles from the Medline database: the first search defines "literature A" and the second defines "literature C." The program then generates a "B-list" of words and phrases found in the titles of both literatures.

The B-list is displayed ranked by relevance, and can be restricted to certain semantic categories (e.g. anatomical regions, or disorders, or drugs). For each B-term of interest, one can view the titles containing A and B ("AB titles") juxtaposed to the titles containing B and C ("BC titles"). In this manner, one can readily assess whether there appears to be a biologically significant commonality or relationship between the two sets of articles.

**TUTORIAL:** Smalheiser NR, Torvik VI, Zhou W. [Arrowsmith two-node search interface: A tutorial on finding meaningful links between two disparate sets of articles in MEDLINE](#). *Comput Meth Program Biomed.* 2009; 94(2): 190-197. A preprint version of this paper is available [here](#).

#### Two-Node Literature Search:

Advanced\*  Basic\*\*  OR continue existing search:

\*Advanced - provides a list of B-terms with multiple options for manual filtering

\*\*Basic - provides a list of B-terms ranked by relevance

#### One-Node Literature Search:

OR continue existing search:

Start A-Literature C-Literature D-List Filter Liter

tinea pedis

Home | Two-Node Literature | Job ID: 90481  Show Options  Hide

Use 'tinea pedis' for ARROWSMITH?

Items 1 - 20 of 174 (Next)

- Dermatophyte Antigen Kit.**  
Medical mycology journal. 2017 ;58(2):J51-J54  
Tsunemi Y  
The dermatophyte antigen kit uses monoclonal antibodies that react with polysaccharides present in the dermatophyte cell wall to detect dermatophyte antigen by immunochromatography. Clinical studies showed that the kit was very useful in the diagnosis of tinea unguium but not tinea pedis. The kit was therefore approved for tinea unguium and was approved by the Pharmaceuticals and Medical Devices Agency of Japan. The kit's extraction solution can extract antigens from tinea unguium. If direct microscopy fails to detect fungal elements in a specimen of suspected tinea unguium, the kit can be used so that positive samples are re-examined by direct microscopy to avoid false-negative detection. In addition, in settings where direct microscopy is unavailable, the kit can be used so that treatment for dermatophytes is initiated. This can reduce both wasteful treatment and medical costs. It is important to note that the kit is used to complement conventional fungus testing methods and not replace the final morphological diagnosis of the pathogenic fungal infection. Use of a combination of direct microscopy and this kit should improve the accuracy of diagnosis. PMID: 28566667
- Treatment of Tinea Pedis in Elderly Patients Using External Preparations.**  
Medical mycology journal. 2017 ;58(2):J35-J41  
Otani M  
Infection rate of tinea pedis is high in the elderly, wherein treatment by a dermatologist should be considered to prevent infecting their family members. However, treatment is not only using external preparations. In treating the elderly with tinea pedis using external preparation, we should take into consideration that the elderly have various conditions. There are many kinds of dosage form (cream, ointments, lotion, spray, and so on) for external preparations to treat tinea pedis. Generally, liquid preparations cause irritation compared to ointments and creams, thus, caution should be taken for side effects when applying them to the elderly. Contact dermatitis is the most common side effect. Caution should also be taken for the type of additives used. The composition of the preparation should be checked when changing dosage forms, or when using different preparations. Since the adherence rate of external preparations is low, it is preferable to use those with strong antibacterial activity and only have to be applied once a day. PMID: 28566665

我们以香港脚作为范例，想研究香港脚和心梗的关系，查不到文献，然而通过该软件可以找到。我们在框中输入香港脚的英文单词，找到了大概174篇文章

myocardial infarction

Home | Two-Node Literature | Job ID: 90481 | Show Options | Hide

Use 'myocardial infarction' for ARROWSMITH?

Yes

Items 1 - 20 of 25000 (Next)

- Intralesional versus intracoronary administration of glycoprotein IIb/IIIa inhibitors during percutaneous coronary intervention in patients with acute randomized controlled trials.**

Medicine. 2017 ;96(40):e8223

Sun B, Liu Z, Yin H, Wang T, Chen T, Yang S, Jiang Z

IL administration yielded favorable outcomes in terms of myocardial tissue reperfusion as evidenced by the improved TIMI flow grade, CTFC, complete ST-segment elevation myocardial infarction (STEMI) without increasing in-hospital major bleeding events. The IL administration of GPIIs can be recommended as the preferred regimen to guard against no-reflow..

PMID: 28984776
- Expression of matrix metalloproteinases-12 in ST-segment elevation myocardial infarction: A case-control study.**

Medicine. 2017 ;96(40):e8035

Wang J, Wei G, Hu W, Li L, Ye Y, Wang H, Wan W, Li R, Li L, Ma L, Meng Z

Matrix metalloproteinases-12 (MMP12) can lead to degradation of elastin resulting in plaque destabilization and rupture. MMP12 also facilitates platelet aggregation. However, evidence in the literature related to the function of MMP12 in ST-segment elevation myocardial infarction (STEMI) is little. This study investigated the expression of MMP12 in human coronary thrombus and examined the relationship between plasma MMP12 and STEMI. Arterial plasma was obtained from 46 STEMI patients and 52 stable angina pectoris patients with angiographically normal coronary arteries. Coronary thrombi were obtained from 26 STEMI patients with a large thrombus burden (LTB). The expression levels of MMP12 were analyzed by immunohistochemistry and immunofluorescence, reverse transcription-polymerase chain reaction (RT-PCR), Western blotting (WB) and casein zymography. MMP12 concentration measured by enzyme-linked immunosorbent assay (ELISA) and activity measured by fluorescence resonance energy transfer (FRET) were used to confirm the expression of MMP12 in human coronary thrombus. MMP12 was secreted mainly in active form of 45 kDa in coronary thrombus. In plasma samples, MMP12 concentrations were found to be higher than the SAP group (5.030 ± 2.24 pg/mL vs 3.010 ± 1.99 pg/mL, P < .05) but with lower MMP12 activity (332 ± 77 RFU vs 454 ± 112 RFU, P < .05). In addition, the STEMI group had significantly higher tissue inhibitor of metalloproteinases-1 (TIMP1) concentration (573.40 ± 270.60 pg/mL vs 219.90 ± 154.80 pg/mL, P < .05). The imbalance in MMP12/TIMP1 ratio was observed in the STEMI group compared with SAP and control group.

今日优选 [http://arrowsmith.psych.uic.edu/cgi-bin/arrowsmith\\_uic/start.cgi](http://arrowsmith.psych.uic.edu/cgi-bin/arrowsmith_uic/start.cgi) 快剪辑 今日直播 热点资讯

再输入心梗的关键词找到了约25,000篇文章。

A-query: tinea pedis

C-query: myocardial infarction

The B-list contains title words and phrases (terms) that appeared in both the A and the C literature. 0 articles appeared in both literatures. The results of this search are saved under id # 90481 and can be accessed from the start page after you leave this session. There are 724 terms on the current B-list (88 are predicted to be relevant), which is shown ranked according to predicted relevance. The list can be further trimmed down using the filters listed in the left margin.

To assess whether there appears to be a biologically significant relationship between the AB and BC literatures for specific B-terms, please select one or more B-terms and then click the button to view the corresponding AB and BC literatures. Use Ctrl to select multiple B-terms.

Rank Prob B-term

1	0.76	dermcidin
2	0.82	comorbidity
3	0.82	medication adherence
4	0.82	retrospective cohort
5	0.82	pcr rflp
6	0.82	open label
7	0.82	sun exposure
8	0.80	diabetic patient
9	0.80	people diabetes
10	0.80	hiv infected
11	0.80	prevalence risk factor
12	0.79	patient outcome
13	0.79	patient diabetes
14	0.78	oxidative stress
15	0.77	randomized double
16	0.77	antibiotic prescribing
17	0.76	practice guideline
18	0.76	patient human immunodeficiency
19	0.75	diabetic foot

Restrict by semantic categories?

Yes

最后该软件会告诉你有724种说法可以把香港脚和心梗联系在一起，其中88种说法是比较有道理的。

The screenshot shows a search results interface. On the left, a list of semantic categories is displayed, each with a numerical value and a text label. The categories are:

57	0.55	retrospective study
58	0.55	mycosis fungoide
59	0.55	pharmacokinetic study
60	0.53	patient year
61	0.53	patient diabetic
62	0.52	cohort
63	0.51	nitric oxide releasing
64	0.51	poloxamer
65	0.51	psoriasis
66	0.51	controlled trial
67	0.50	cross sectional
68	0.50	sun
69	0.49	inpatient
70	0.49	recurrence patient
71	0.48	age sex
72	0.48	adherence
73	0.47	medication patient
74	0.46	elderly patient
75	0.46	randomized double blind
76	0.46	esophageal cancer

Below the list is a button labeled "View literature corresponding to highlight(s)". To the right of the list, a dialog box asks "Restrict by semantic categories?" with a "Yes" button.

此时我们就可以选择这些文献并且进行阅读。



tinea pedis	dermcidin	myocardial infarction
<p>1: Mycostatic effect of recombinant <b>dermcidin</b> against <i>Trichophyton rubrum</i> and reduced <b>dermcidin</b> expression in the sweat of <b>tinea pedis</b> patients. 2015  <a href="#">Add to clipboard</a></p>		<p>1: TRIAD system catalase, insulin, and low dose aspirin neutralize the effect of <b>dermcidin</b> isoform-2 and prevent cell death in acute <b>myocardial infarction</b> and recurrence of the disease. 2016  <a href="#">Add to clipboard</a></p> <p>2: [The significance of a 4,183 Da peptide of <b>dermcidin</b> protein in the early diagnosis and differential diagnosis of acute coronary syndrome]. 2015  <a href="#">Add to clipboard</a></p> <p>3: <b>Dermcidin</b> isoform-2 induced nullification of the effect of acetyl salicylic acid in platelet aggregation in acute <b>myocardial infarction</b>. 2014  <a href="#">Add to clipboard</a></p>

比如我们在其展示出来的文献中找到皮离蛋白，皮离蛋白及和香港脚有关，也和心梗有关，因此当我们研究香港脚和心梗之间的关系时，在前言中就可以指出为什么要研究香港脚和心梗，是基于皮离蛋白这个机制。

当你的idea此前有相同研究且有争议时：

- 
- 正方观点
  - 反方观点
  - 有无中国人的数据

## 包括七点

- 一. XY以及针对的研究人群是?
- 二. 结论是? (X与Y正相关? 负相关? 无关?)
- 三. 文献名称、年份、影响因子
- 四. 研究类型
- 五. 样本量
- 六. 表1中, 收集了哪些变量
- 七. 统计方法 (有没有用回归, 有没有得出独立作用, 有没有做曲线, 交互)





## **第一点：XY以及针对的研究人群是？**

明确XY是什么，何时测量的，有无使用盲法，其目的是用于超越。

明确研究人群，用于创新



(1) 人群在题目中

RESEARCH

Open Access



Triglyceride to high-density lipoprotein cholesterol (HDL-C) ratio and arterial stiffness in **Japanese population**: a secondary analysis based on a cross-sectional study

如果人群在题目中可以找到，一般都跟在“in”的后面

## (2) 人群在摘要的方法部分

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

A Multicenter Observational Study  
of Incretin-based Drugs and Heart Failure

### **METHODS**

We applied a common protocol in the analysis of multiple cohorts of patients with diabetes. We used health care data from four Canadian provinces, the United States, and the United Kingdom. With the use of a nested case-control analysis, we matched each patient who was hospitalized for heart failure with up to 20 controls from the same cohort; matching was based on sex, age, cohort-entry date, duration of treated diabetes, and follow-up time. Cohort-specific hazard ratios for hospitalization due to heart failure among patients receiving incretin-based drugs, as compared with those receiving oral antidiabetic-drug combinations, were estimated by means of conditional logistic regression and pooled across cohorts with the use of random-effects models.

## (2) 人群在摘要的方法学部分

Research

JAMA Otolaryngology-Head & Neck Surgery | [Original Investigation](#)

### Association of Subclinical Hearing Loss With Cognitive Performance

**DESIGN, SETTING, AND PARTICIPANTS** Cross-sectional study of 2 US epidemiologic studies (Hispanic Community Health Study [HCHS], 2008-2011, and National Health and Nutrition Examination Study [NHANES], 1999-2000, 2001-2002, and 2011-2012 cycles). The dates of analysis were November 2018 to August 2019. Multivariable generalized additive model (GAM) regression and linear regression were used to assess the association between HL (exposure) and cognition (outcome). Participants included 6451 individuals aged 50 years or older from the general Hispanic population (HCHS [n = 5190]) and the general civilian, noninstitutionalized US population (NHANES [n = 1261]).



## Tips:

- 一. 临床研究不用去在意此前有雷同的研究。因为你们的人群是不同的。
- 二. 临床研究对既往研究的X、Y进行详细的解读，可以保证你的研究质量，甚至可实现弯道超车

ORIGINAL ARTICLE

## IVF Transfer of Fresh or Frozen Embryos in Women without Polycystic Ovaries

Lan N. Vuong, M.D., Ph.D., Vinh Q. Dang, M.D., Tuong M. Ho, M.D., Bao G. Huynh, M.Sc., Duc T. Ha, M.D.,

ORIGINAL ARTICLE

## Fresh versus Frozen Embryos for Infertility in the Polycystic Ovary Syndrome

Zi-jiang Chen, M.D., Ph.D., Yuhua Shi, M.D., Ph.D., Yun Sun, M.D., Ph.D., Bo Zhang, M.D., Xiaoyan Liang, M.D., Ph.D., Yunxia Cao, M.D., Ph.D., Jing Yang, M.D., Ph.D., Jiayin Liu, M.D., Ph.D., Daimin Wei, M.D., Ph.D., Ning Weng, M.D., Lifeng Tian, M.D., Ph.D., Cuifang Hao, M.D., Ph.D., [et al.](#)

这是一个典型的换人群的临床研究，我们可以看到两篇临床研究的研究假设，也就是它的X和Y完全一致，不同的是一篇文章的研究人群是有多囊卵巢综合症的女性，而另外一篇文献是没有。因此当我们要研究的X和Y此前有争议时，一定要对研究人群进行采集。

## 采集既往文献XY的好处

- 既往的X是基线的，我们可以重复测量采集并计算变化率
- 既往的X只有一个单独指标，我们可以用多个指标集火判定。
- 既往的Y随访时间只有1月，我们尝试1年。
- 既往的Y只有一个，我们可以多个（临床可归为一类） .....



## 第二点：结论是？（X与Y正相关？负相关？无关？）

01

了解既往同类研究的结论，用于评估我们的发现，并据此作出超越。

02

投稿，可获得巨大的红利。



## A Multicenter Observational Study of Incretin-based Drugs and Heart Failure

Kristian B. Filion, Ph.D., Laurent Azoulay, Ph.D., Robert W. Platt, Ph.D.,

### CONCLUSIONS

In this analysis of data from large cohorts of patients with diabetes, incretin-based drugs were not associated with an increased risk of hospitalization for heart failure, as compared with commonly used combinations of oral antidiabetic drugs.

如何获取X和Y的确切关系，在摘要的结论部分就可以得到。



## 第三点：文献名称、年份、影响因子

calcium and HPV infection

文献(88) 知识图谱 看单(123) 中国临床试验(541) clinicaltrials(31751)

1. Could 25-OH vitamin D deficiency be a reason for HPV infection persistence in cervical premalignant lesions?  
作者: Özgü Emre, Yılmaz Nafiye, Başer Eralp, Güngör Tayfun, Erkaya Salim, Yakut Halil İbrahim  
期刊: Journal of experimental therapeutics & oncology  
日期: 2016-07-01  
Vitamin D is an essential precursor to the steroid hormone calcitriol which mainly regulates calcium homeostasis. Moreover anti- proliferative, pro- apoptotic, anti- angiogenic effects of Vitamin D support the ideas of preventive role in various cancer. This study aimed to determine if there is a relationship between...

影响因子: 5.962 免费全文

2. Human papillomavirus (HPV)-18 E6 oncoprotein interferes with the epithelial cell polarity Par3 protein.  
作者: Facciuto Florencia, Bugnon Valdano Marina, Marziali Federico, Massimi Paola, Banks Lawrence, Cavatorta Ana ...  
期刊: Molecular oncology  
日期: 2014-01-14  
DOI: 10.1016/j.molonc.2014.01.002  
High-risk human papillomavirus (HPV) infection is the principal risk factor for the development of cervical

共 88 条 < 1 2 3 4 5 >

结果排序  
最佳匹配 最新收录

检索字段  
全部字段 [All Fields]

文献类型  
不限

出版日期  
不限 3年 5年 10年

影响因子  
0 1 2 3 4 5 6 7 8 9 10 15 +

重置 搜索

建议反馈

通过很多的插件或者软件，都可以简单的获取文献的影响因子，发表年份。

访问官网即可

NCBI Resources How To Sign in to NC

PubMed lung cancer Search Top Cited 500

Format: Summary Sort by: Best Match Per page: 20

Search results

Items: 4001 to 4020 of 17830

Due to technical constraints, your results were generated using the standard Best Match algorithm.

The quality of supportive cancer care in the veterans affairs health system and targets for improvement.

Intern Med. 2014 Nov;174(11):1675.  
PMID: 24126685 Free Article

PUBMED IF: 16.5380 Cited: 23 Ref: 0 SciHub Free

SCI期刊筛选器, 按照期刊影响因子筛选文献

260元/年

Filter your results:

- All (329447)
- F1000 (1933)
- Published in the last 5 years (86287)
- Review (36207)
- IF:>10 (17830)
- IF:5-10 (57462)
- IF:2-3 (45037)
- IF:3-5 (61299)

工具条显示: 影响因子、施引文献、参考文献、SciHub链接、免费全文链接等

注: 引用自https://service.pubmedplus.com/pubmedplus-extension。如有侵权, 立即删除。

The image shows a screenshot of the PubMed website (ncbi.nlm.nih.gov/pubmed) with search results for 'lung cancer'. The page is annotated with several Chinese text boxes and arrows:

- 访问官网即可** (Visit the official website directly) - points to the URL bar.
- SCI期刊筛选器, 影响因子筛选文** (SCI journal filter, impact factor filter) - points to the 'Filter your results' sidebar.
- 260元** (260 Yuan) - a price tag next to the filter sidebar.
- 工具条显示: 影响因子、施引文献、参考文献、SciHub链接、免费全文链接等** (Toolbar displays: impact factor, citing literature, reference literature, SciHub link, free full-text link, etc.) - points to the article's metadata bar.

The search results show a list of items (4001 to 4020 of 17830). A specific article is highlighted:

**The quality of supportive cancer care in the veterans affairs health system and targets for improvement.**  
Intern Med. 2014 Nov;174(11):1675.  
PMID: 24126685 Free Article

The article's metadata bar includes: **PUBMED** IF: 16.5380 Cited: 23 Ref: 0 SciHub Free

The 'Filter your results' sidebar shows various filters:

- All (329447)
- F1000 (1933)
- Published in the last 5 years (36207)
- Review (36207)
- IF:>10 (17830)
- IF:5-10 (57462)
- IF:2-3 (45037)
- IF:3-5 (61299)

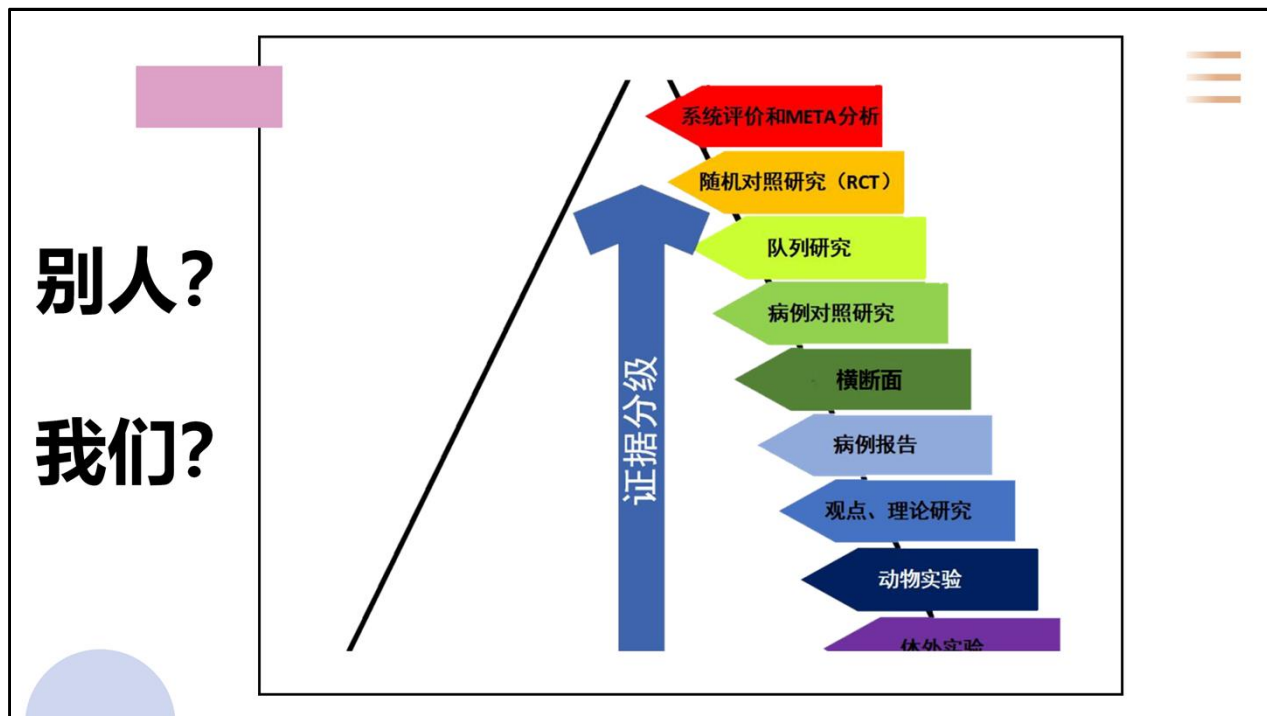


“

## 第四点：既往研究的研究类型

”





为何要采集既往同X同Y的研究类型，旨在看一下他们的证据级别。不同的临床研究类型，其证据级别有高有低。我们的临床研究证据级别至少不能比前人的差。

## 题目中，一般在study前。

RESEARCH

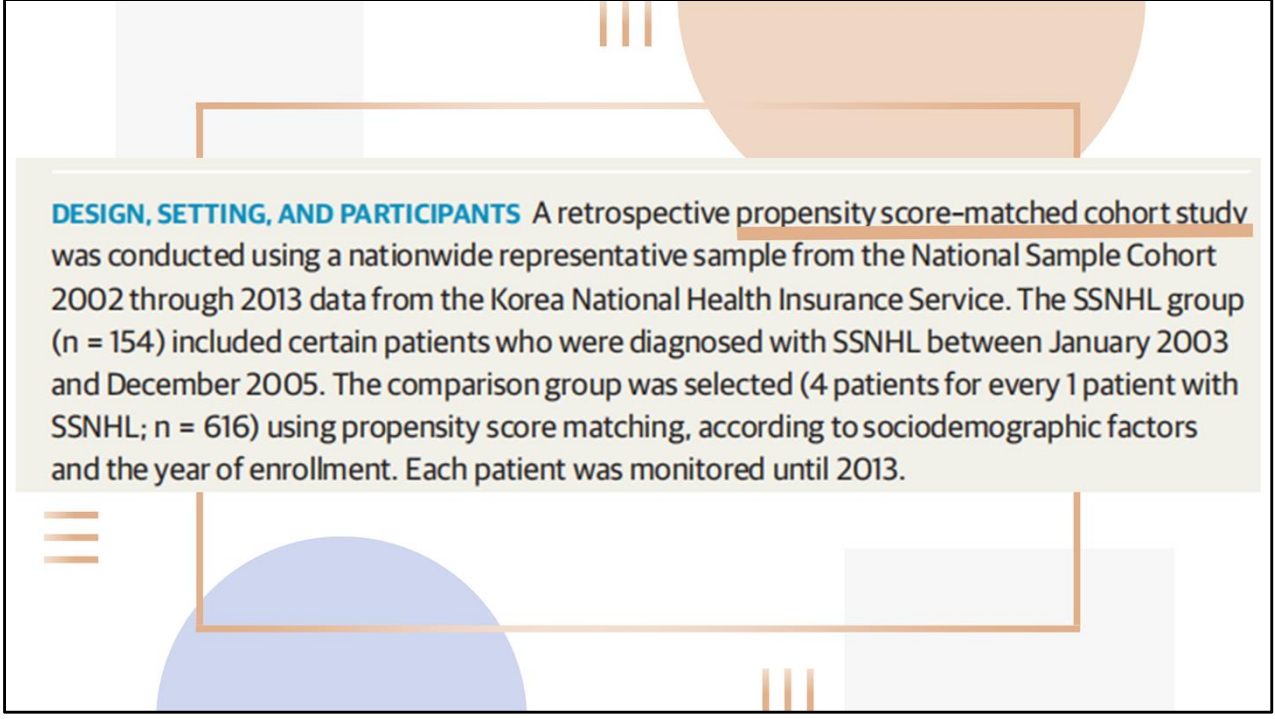
Open Access



Triglyceride to high-density lipoprotein cholesterol (HDL-C) ratio and arterial stiffness in Japanese population: a secondary analysis based on a cross-sectional study

如何获取临床研究类型，一般在题目中都是在study的前面。





**DESIGN, SETTING, AND PARTICIPANTS** A retrospective propensity score–matched cohort study was conducted using a nationwide representative sample from the National Sample Cohort 2002 through 2013 data from the Korea National Health Insurance Service. The SSNHL group (n = 154) included certain patients who were diagnosed with SSNHL between January 2003 and December 2005. The comparison group was selected (4 patients for every 1 patient with SSNHL; n = 616) using propensity score matching, according to sociodemographic factors and the year of enrollment. Each patient was monitored until 2013.

在摘要中也是一样。

# 第五点：样本量

RCT为何要计算样本量？

# 筹钱

## Original Contribution

### Lipid-Lowering Agents and High HDL (High-Density Lipoprotein) Are Inversely Associated With Intracranial Aneurysm Rupture

lipoprotein) values.<sup>1</sup> In addition, growing evidence from various experimental animal models and smaller clinical studies supports the inverse relationship between statin use and intracranial aneurysm rupture.<sup>2-4</sup> Here, we present the largest case-control study to date, to investigate the role of total cholesterol, HDL, LDL, and use of lipid-lowering agents on the risk of SAH in 4701 patients with 6411 intracranial aneurysms.

观察性研究不强求计算样本量，我们只需要了解此前同X同Y的研究，他们的样本量是多少，我们至少不能够比他们少。



第六点：既往同X同Y的文章中，表1收集的变量

Variable	No. (%)	
	Comparison Group (n = 616)	Sudden Sensorineural Hearing Loss Group (n = 154)
<b>Sex</b>		
Male	308 (50.0)	77 (50.0)
Female	308 (50.0)	77 (50.0)
<b>Age, y</b>		
<45	264 (42.9)	66 (42.9)
45-64	296 (48.1)	74 (48.1)
>64	56 (9.1)	14 (9.1)
<b>Residence<sup>a</sup></b>		
Seoul	136 (22.1)	34 (22.1)
Second area	212 (34.4)	53 (34.4)
Third area	268 (43.5)	67 (43.5)
<b>Household income<sup>b</sup></b>		
Low	144 (23.4)	36 (23.4)
Middle	228 (37.0)	57 (37.0)
High	244 (39.6)	61 (39.6)
<b>Comorbidities</b>		
No	504 (81.8)	126 (81.8)
Yes	112 (18.2)	28 (18.2)

JAMA Otolaryngology-Head & Neck Surgery | Original Investigation

### Association of Sudden Sensorineural Hearing Loss With Risk of Cardiocerebrovascular Disease A Study Using Data From the Korea National Health Insurance Service

如何知道此前同类研究他们用了哪些变量？我们可以在研究人群描述模块中快速获取。

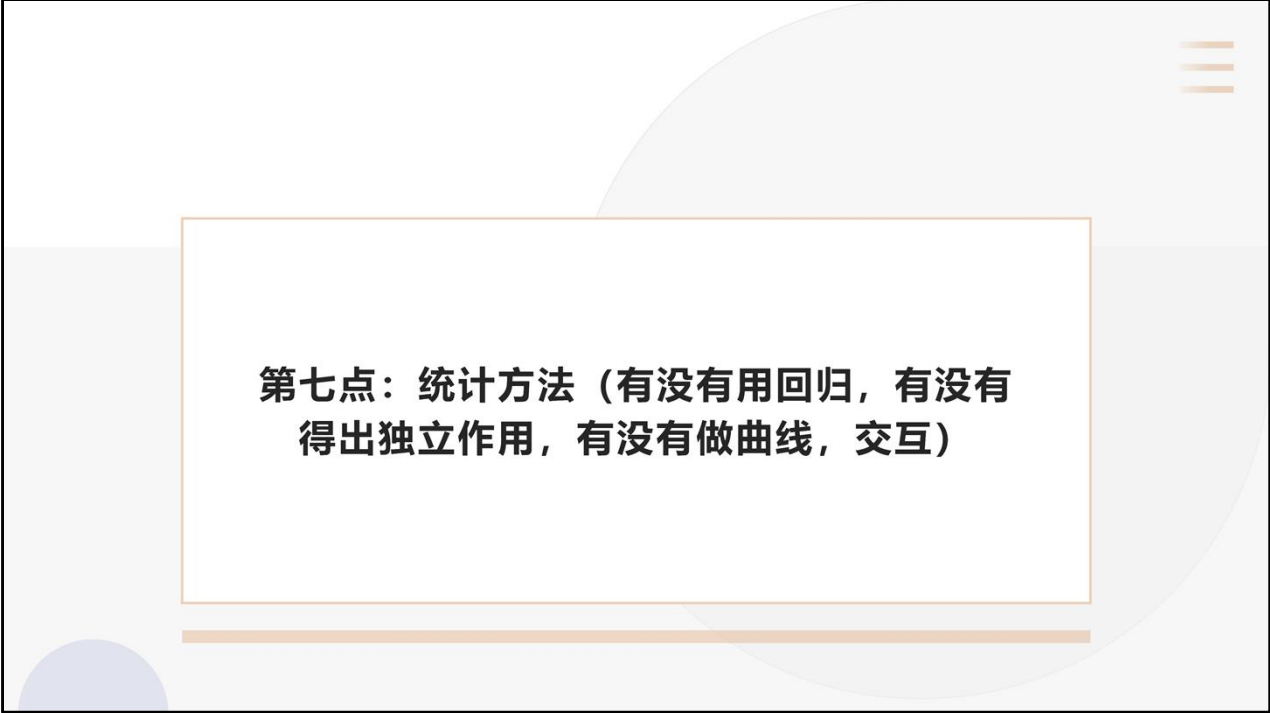
Published in final edited form as:

*Circulation*. 2015 October 27; 132(17): 1630–1638. doi:10.1161/CIRCULATIONAHA.114.014443.

**Depression and HIV Infection are Risk Factors for Incident Heart Failure Among Veterans: Veterans Aging Cohort Study**

Our covariates were selected apriori based on our prior work and studies from others examining risk factors for heart failure. The Framingham Heart Study and others have identified risk factors for heart failure including age, hypertension, diabetes, smoking, cholesterol, body mass index, substance use, atrial fibrillation and flutter, and renal disease.<sup>4, 21–24</sup> Administrative data were used to obtain age, sex, and race/ethnicity.

此外在获取对方用了哪些混杂因素，哪些协变量的时候，还要注意一下他们为什么要使用这些协变量。



**第七点：统计方法（有没有用回归，有没有  
得出独立作用，有没有做曲线，交互）**

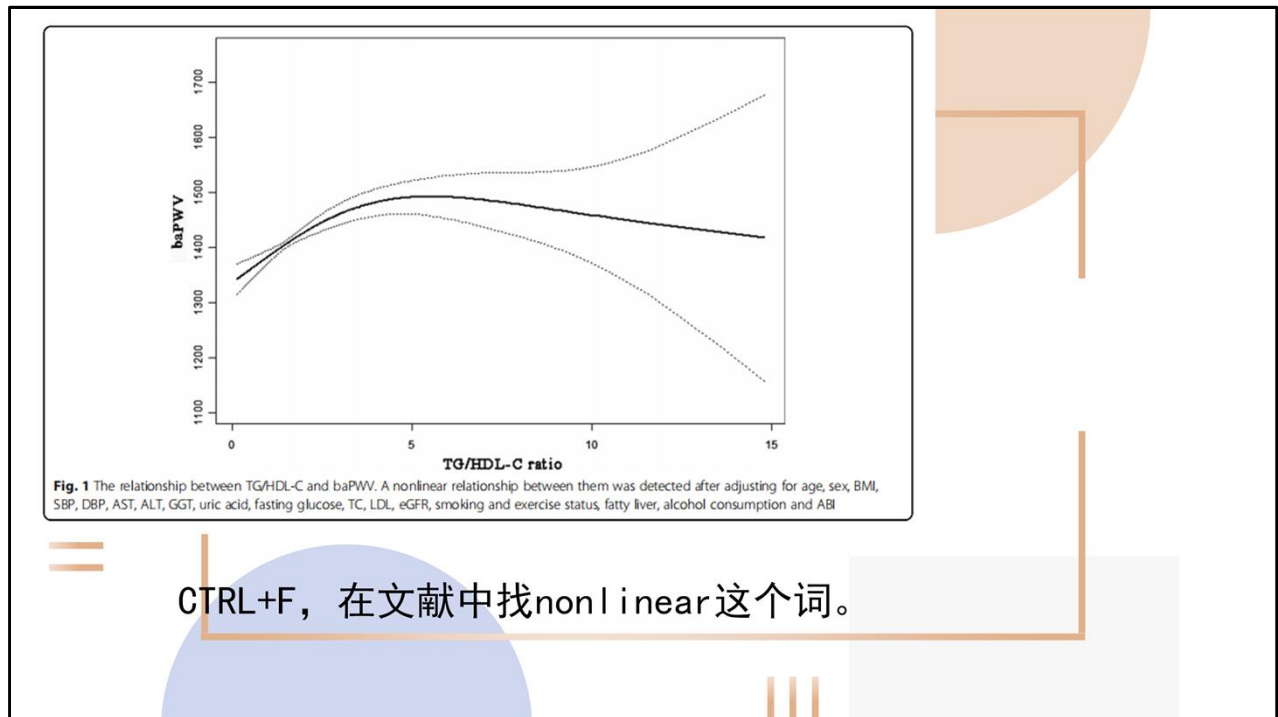


Table 2. Incidence per 1000 Person-years and Hazard Ratios (HRs) of Cardiocerebrovascular Disease During 11-Year Follow-up

Variable	No.	Cases, No.	Incidence, per 1000 Person-years	HR (95% CI)	
				Unadjusted	Adjusted
Group					
Comparison group	616	48	7.5	1 [Reference]	1 [Reference]
Sudden sensorineural hearing loss group	154	18	13.5	1.84 (1.06-3.18)	2.18 (1.20-3.96)
Sex					
Female	385	38	9.9	1 [Reference]	...
Male	385	28	7.1	0.72 (0.44-1.17)	...
Age, y					

ctrl+F, 查model这个词, 或adjuste这个词

最快速便捷的方法就是直接的查找，但凡是有adjust的这个词，一般就意味着使用了回归分析。



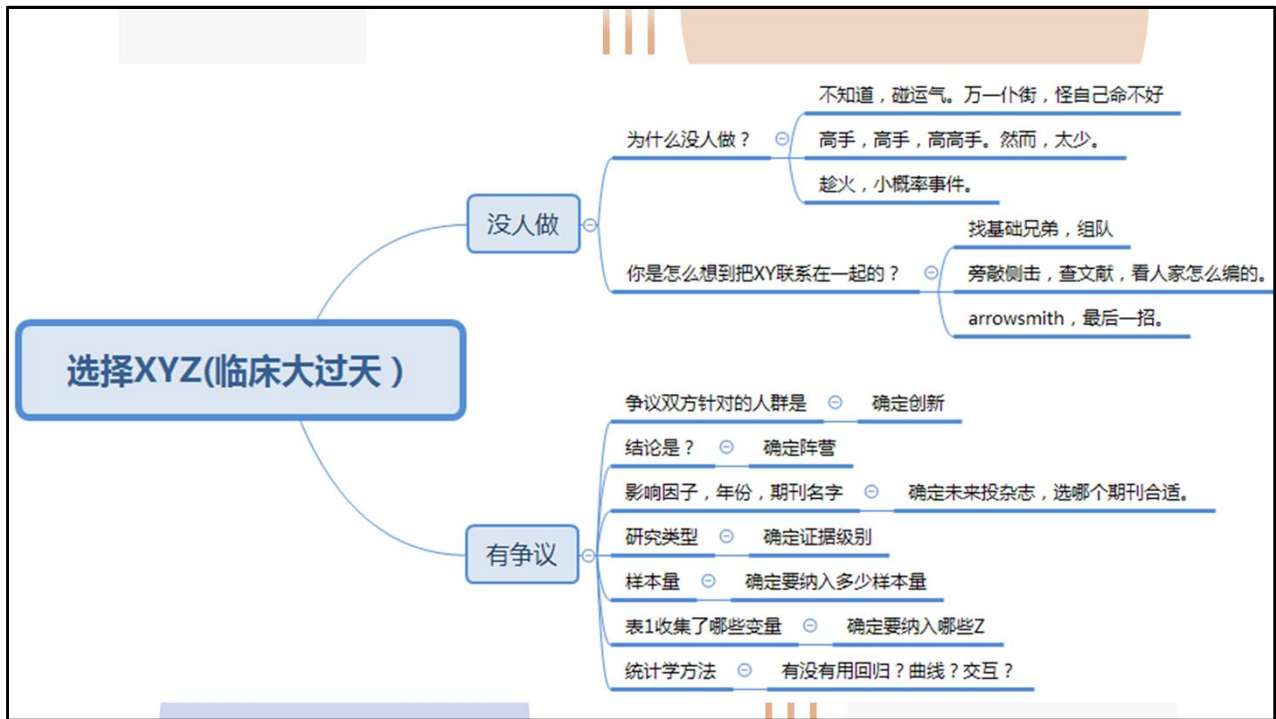
同理，如何知道对方有没有做曲线关系，看图便知。

**Table 5** Effect size of TG/HDL-C on baPWV in prespecified and exploratory subgroups

Characteristic	No of participants	Effect size(95%CI)	P for interaction
Age (year)			0.85
≤60	139	6.0 (- 12.3, 24.3)	
> 60	773	4.1 (- 3.8, 12.0)	
Sex			0.69
Male	592	3.2 (-4.8, 11.2)	
Female	320	7.2 (-11.4, 25.8) 8.0 (- 10.5, 26.5) <sup>a</sup>	

ctrl+F, 寻找subgroup, 或interaction这个词。

如何知道对方有没有做交互作用检验或者亚组分析？查interactiton这个词或查subgroup。同时也可以可以在文章的图表中看一下作者有没有进行分层分析。





03

**临床IDEA的提取**

## 基于未来前言的信息提取：

- X的特点，Y的特点，所研究的人群特点，所研究疾病的流行病学特点
- 要做X的理由：（1）此前无人做，请说出可能的机制；  
（2）此前有人做，请说出不同意见的特点

## 基于方法的信息提取：

- X如何定义，如何表示（连续/分类），何时测量，是否用盲法
- Y如何定义，如何表示（连续/分类），何时测量，是否用盲法
- Z包括哪些变量？为何要收集？何时采集的？
- 样本量
- 人群特征
- 纳排标准

## 基于数据分析的信息提取：

- 是否有独立作用？
- 是否有曲线？
- 是否有交互？
- 是否用了敏感性分析？如何做的？



## 基于讨论的信息提取：

- 与你相同的研究？
- 与你不同的研究，为什么不同？
- 这些研究的缺点有哪些？（文献的讨论中limitation部分）
- 这些研究的长处是什么？（文献的讨论中strength部分）



04

回顾性研究选题

## 流程8：回顾性研究选题



世界上没有绝对的东西。回顾性研究有可能是大家多块好省发SCI的快捷通道，也有可能是一个大坑。

# 流程8：回顾性研究特例

最安全的做法：二查三确定

## 二查

查文献，查病历。

## 三确定

确定病种、确定时间段、确定Y。

## 流程8：回顾性研究特例

最安全的做法：二查三确定

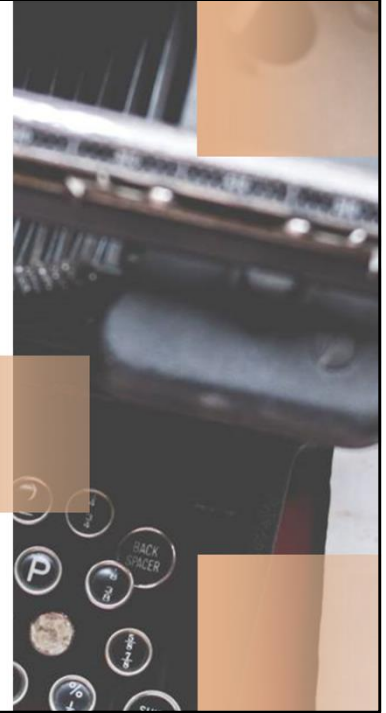
- 确定病种：常见病（保证样本量）、特色诊疗（保证有更多的东西可以挖掘）、诊疗比较规范的病种（缺失的数据和变量不会太多）
- 确定时间段：根据电子病历系统显示，并考虑实际情况，保证工作量和效率的平衡。
- 确定Y：预后？某个指标？治疗应答？疗效？

## 流程8：回顾性研究特例

最安全的做法：二查三确定

二查：查文献，查病历。

- 查文献：只看表1，并把这些变量收集起来
- 查病历：看看科室病历中，这些变量全不全，差了多少，差的这些变量分布在哪些杂志的文章中。



## 举例

- 三确定：
- 病种：多发性骨髓瘤
- WHY?
  1. 白血病尽管较多，但很多患者的随访，治疗欠规范。
  2. 淋巴瘤亚型太多，反而不如骨髓瘤集中
  3. 骨髓瘤是血液科的特色诊疗项目，曾进行过多次的队列研究。
- 所以，病种，选择多发性骨髓瘤。

## 举例

- 三确定：
- 时间：2013年8月——至今
- WHY?
  1. 有827例次患者住院，样本量有保证。
  2. 有5名研究生进行数据录入工作，可以完成。
  3. 2013年8月开始，电子病历实施。此前的纸质病历，抄起来太累。。
- 所以，……。



## 举例

- 三确定：
- Y：多发性骨髓瘤的疗效，死亡
- WHY?
  1. 至少我所在的治疗组，所有患者都完成了疗效评估，较正规，至少可保证Y。
  2. 电子病历首页，有电话，患者死没有死，可以电话随访得知。

变量  
 年龄  
 种族  
 体重指数  
 血标本类型 (1血浆, 2加肝素, 3加Dedta)  
 空腹血糖  
 IGF-1  
 IGFBP-3  
 IGFBP-1  
 C-peptide  
 C反应蛋白  
 白介素6  
 超敏白介素6  
 性别  
 ECOG评分 (原文为ECOG performance status)  
 疾病状态 (1, 复发/进展的MM; 2, 复发/难治的MM) 注: 该文章针对的是难治, 复发的MM患者队列  
 此前接受的治疗方案 (手术, 放射) 注: 多发性骨髓瘤常出现病理性骨折, 故手术治疗, 放射治疗常有人做  
 此前的治疗药物 ( )  
 此前的治疗疗程  
 此前是否接受移植。注: 在省医, 基本没有患者接受骨髓移植治疗。极少此前在其他医院接受治疗。因此,  
 ISS积分 (评价骨髓瘤就诊时状态的评分, 相当于疾病的严重程度, 与ECOG类似)  
 IGG定量  
 IGM定量  
 IGA定量  
 IGD定量  
 IGE定量  
 初诊至进入队列的间隔时间 (主要针对老病人)

# 举例

二查:  
 查文献:

通过查阅关于多发性骨髓瘤的高分文献，我们收集了很多的变量，而这些变量就可用于本研究的数据库的构建素材，即四库攻略中的变量库。

# 举例



搜索结果

病案搜索 病案号 | 疾病 | 手术 | 科室 | 病人姓名 | 医生

王忠社 病人姓名搜索 结果中搜索

姓名] 包含 王忠社 符合条件总共有 5 记录

姓名	主要诊断	出院日期	住院次数	住院号	性别	出生日期	年龄	职业	出院科室	医
王忠社	多发性骨髓瘤Iga型II期a组	2015-2-15	1	550741	男	1970-10-20	44	农民	血液内科	
王忠社	1.多发性骨髓瘤Iga++型 II期a组 2...	2015-3-8	1	551797	男	1970-10-20	44	农民	血液内科	
王忠社	多发性骨髓瘤Iga型 II期a组	2015-4-2	1	556919	男	1970-10-20	44	农民	血液内科	
王忠社	多发性骨髓瘤Iga型 II期a组	2015-6-8	2	556919	男	1970-10-20	44	农民	血液内科	其他
王忠社	多发性骨髓瘤 Iga型 II期a组 疾病...	2015-12-5	3	556919	男	1970-10-20	45	农民	血液内科	其他

📁 最后一次住院

📄 说明.doc

二查：  
查病历：



05

**真实世界研究选题简介**

## 治疗：两种药物疗效比较



我们常说的真实世界研究其实是相对于RCT而言的一种狭义的真实世界研究。它指的是通过观察性研究去对两种药物疗效进行比较，药物的选择是基于临床实际场景，而非随机化。

## 真实世界研究的选题特点

01

定位是作为RCT的appendix, 是一种“假说”;

02

基于机制/临床基础;

03

此前有已报道的RCT, 为验证此前无报道RCT, 听过支撑

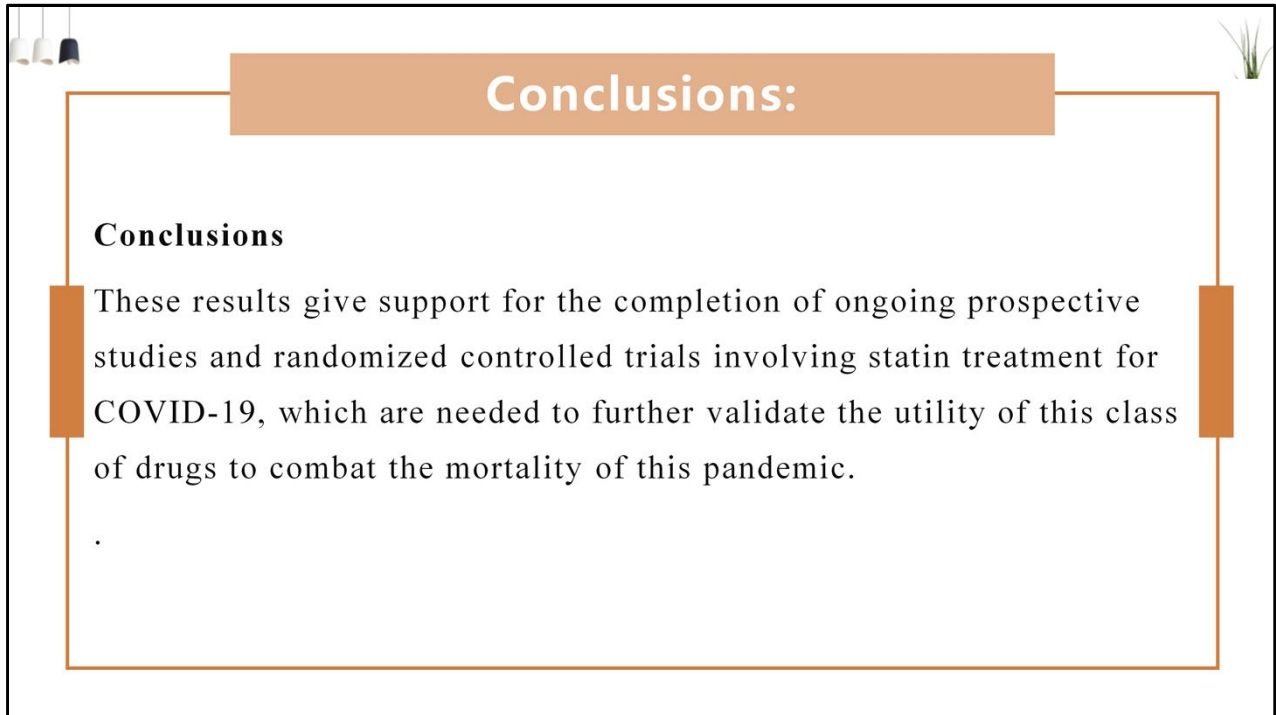
真实世界研究的选题有其特殊性，  
第一：真实世界研究的定位是作为RCT的验证。它的本质是一种假说。  
第二：真实世界研究最好是基于此前已有的机制或者已有的临床证据。  
第三，如果此前已有rct报道，那么真实世界研究就是对其进行验证，如果此前并没有rct报道，真实世界研究则是提供支撑。

题目

**In-Hospital Use of Statins Is Associated with a  
Reduced Risk of Mortality among Individuals with  
COVID-19**

Cell Metab 2020 Aug 4;32(2):176-187.e4. IF: 22.4150

这是一篇研究，对于新冠患者而言，服用他汀是否能够降低死亡率。



作者在结论部分明确指出：本研究为正在进行的前瞻性研究和RCT提供了证据，支撑。这就是这篇文章对自己的定位。



## NEJM范例

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Everolimus-Eluting Stents or Bypass Surgery for Multivessel Coronary Disease

CABG和PCI相比，既往研究证实比PCI好，但这是老黄历。  
新一代支架更好，但没有研究比CABG和PCI  
们的目的是评估冠脉搭桥与PCI和依维莫司洗脱支架在多血管  
冠状动脉疾病患者中的疗效

这篇NEJM的文章比较的是搭桥手术和PCI的疗效。作者提到了此前有类似RCT的研究，但指出这些研究是针对一代支架的，并非针对二代支架。然而，无论如何，作者仍然是基于此前的临床基础进行的选题。

