# 統合分析新手之心路歷程分享

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# 自我介紹

## 學歷

- 國立成功大學 臨床藥學與藥物科技研究所 碩士　2014.9-2016.6
- 台北醫學大學 藥學系 藥學士　2010.9-2014.6

## 經歷

- 亞東紀念醫院 | 藥師　2016.9–2023.10, 2024.7-
  - 處方審議小組成員
  - 臨床藥學科藥事照護組藥師 2021.11-
    - 呼吸照護病房 (RCC)、其他一般病房
    - 藥師門診、記憶門診
    - 藥學系實習生指導、院外專題演講
  - 參與醫策會第19屆實證醫學文獻查詢競賽、2021藥師臨床高血脂照護競賽
  - 學術研究投稿（國內壁報3篇、臨床藥學雜誌orignial article：1篇）
  - COVID疫苗施打站協助疫苗抽取、曾參與社區正確用藥推廣活動

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綜合評述

# 第一代 EGFR 酪氨酸激酶抑制劑併用胃酸抑制劑對於肺癌病人存活率的影響：系統性回顧與統合分析

# Effects of Concomitant Use of Acid Suppressants and the First-Generation EGFR Tyrosine Kinase Inhibitors on Survival in Patients With Lung Cancer: A Systematic Review and Meta-Analysis

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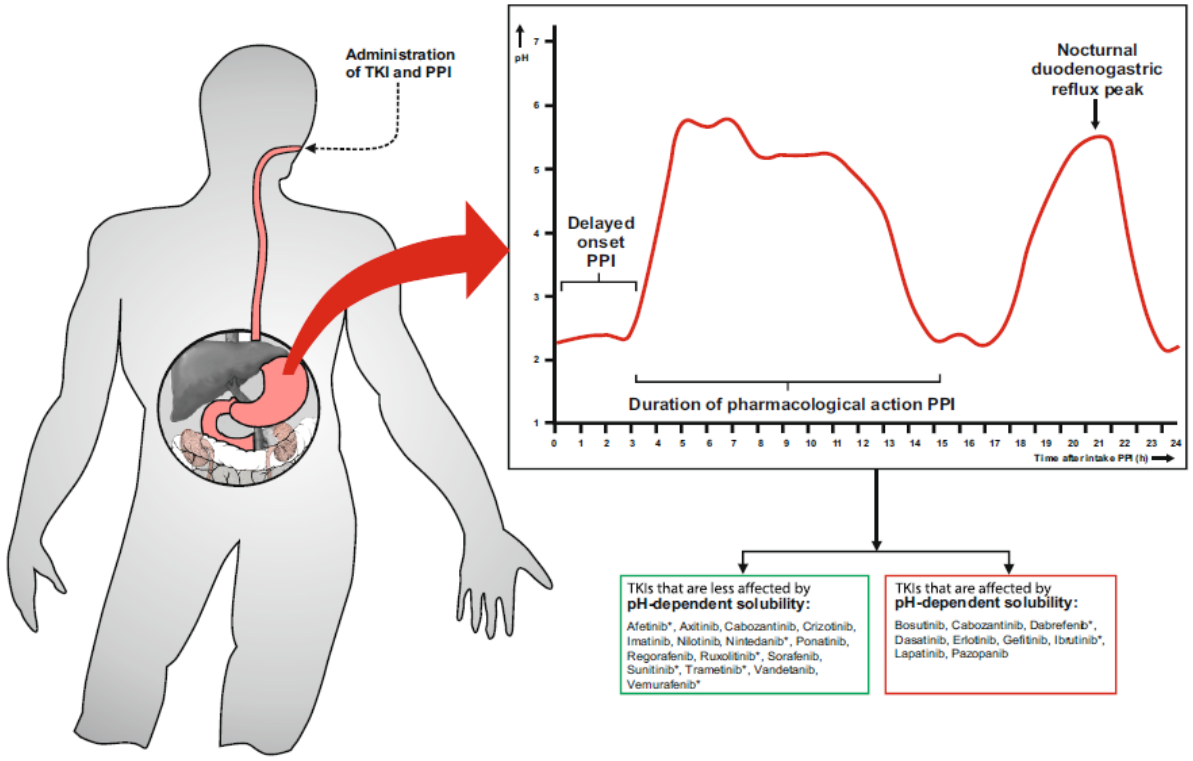
# 研究發想

01. 臨床問題

02. 文獻搜尋

03. 證據缺口




Clin Pharmacokinet (2017) 56:683–688

# 投稿過程

**2021/5初次投稿, 2021/8 初審意見**

- 格式、敘述、呈現方式
- 補充PRISMA
- 文獻品質評讀依據
- 副作用選擇的原因
- 漏斗圖限制

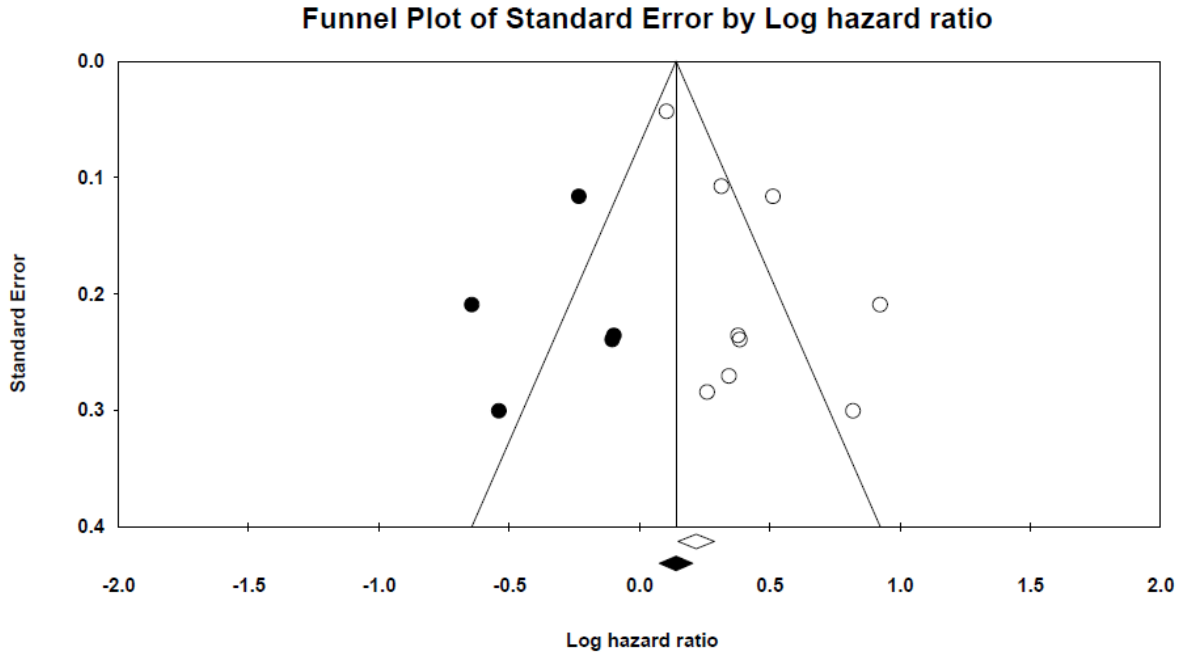



Figure 7. Funnel plot for overall survival of cohort studies
White circle (n=9) included cohort studies; black circle (n=5) imputed studies

# 投稿過程

**2021/5初次投稿, 2021/8 初審意見**

**2021/10 複審意見**

- 多種統計軟體目的
  - Cochrane Review Manager
  - Comprehensive Meta Analysis
- 僅將世代研究進行統合分析原因
  - 隨機分派事後分析 vs. 世代研究

# 投稿過程

**2021/5初次投稿, 2021/8 初審意見**

**2021/10 複審意見**

- 統計方法疑慮
  - 檢視控制組重複分析方式

**2021/12 複審(2)意見:**

先進行輔導再重新投稿

| Author | Study design | Country | Patient number (male) | TKI | Inclusion criteria | Definition of AS use | AS, n (%) | Mean age (yr) | PFS, months | OS, month |
|---|---|---|---|---|---|---|---|---|---|---|
| Chu et al., 2015 [15] | R 1-centered | Canada | 507 (46%) | erlotinib | Advanced NSCLC, TKI > 1 week | ≥ 20% overlap TKI course | 124 (25); PPI: 115 | 64 | PPI: 1.3<br>H2RA: 1.8<br>no AS: 2.3 | PPI: 12.8<br>H2RA: 12.6<br>no AS: 16.8 |
| Chen et al., 2016 [16] | R 1-centered | Taiwan | 269 (42%) | gefitinib, erlotinib | > 18 y/o, advanced NSCLC, mutated EGFR, TKI as first line | > 30% overlap TKI course | 57 (21.2)<br>PPI: 18 | 65 | PPI: 6.7<br>H2RA: 9.3<br>no AS: 11.2 | PPI: 11.3<br>H2RA: 15.5<br>no AS: 25 |
| Kumarakulasinghe et al., 2016 [17] | R 1-centered | Singapore | 157 (48%) | gefitinib, erlotinib | Advanced NSCLC, mutated EGFR | ≥ 30% overlap TKI course | 55 (35) | 62 | AS: 7.6<br>no AS: 8.7 | AS: 11.4<br>no AS 17.5 |

# 投稿危機

Transl Lung Cancer Res. 2021 Aug;10(8):3567-3581. doi: 10.21037/tlcr-21-378.

**Interactions between epidermal growth factor receptor tyrosine kinase inhibitors and proton-pump inhibitors/histamine type-2 receptor antagonists in non-small cell lung cancer: a systematic review and meta-analysis**

統合截至2021 年1 月14 篇文獻共4,495 人

Review Int J Clin Pract. 2022 Jan 31:2022:3102641. doi: 10.1155/2022/3102641. eCollection 2022.

**Concomitant Gastric Acid Suppressants on the Survival of Patients with Non-Small-Cell Lung Cancer Treated with Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors: A Meta-Analysis**

統合截至2021 年6 月13 篇文獻共納入12,259 人

文獻搜尋不完整疑慮

將不同類型研究基礎研究一起統合分析

控制組重複分析

# 再次挑戰

**2023/1/15提交, 1/20預審不通過**

- 參考頂尖期刊摘要撰寫方式
- 檢索資料庫包含Embase
- 確認相同國家文獻是否族群重疊

| Author | Study design | Country | Patient number (male) | TKI | Inclusion criteria | Definition of AS use | AS, n (%) | Mean age (yr) | PFS, months | OS, month |
|---|---|---|---|---|---|---|---|---|---|---|
| Chen et al., 2016 [16] | R 1-centered 單一中心 | Taiwan | 269 (42%) | gefitinib, erlotinib | > 18 y/o, advanced NSCLC, mutated EGFR, TKI as first line | > 30% overlap TKI course | 57 (21.2) PPI: 18 | 65 | PPI: 6.7 H2RA: 9.3 no AS: 11.2 | PPI: 11.3 H2RA: 15.5 no AS: 25 |
| Fang et al., 2019 [22] | R database 健保資料庫 | Taiwan | 1114[b] (35%) | gefitinib | >18 y/o, NSCLC, TKI as first linea | PPI use > 20% overlap TKI course | 145 (13) | ≤ 65 (57.90%) | AS: 8.9 no AS: 10 | AS: 13.4 no AS: 21.8 |

# 再次挑戰

**2023/1/15提交, 1/20預審不通過**

**2023/3 初審修正稿件**

**2023/5 複審修正稿件**

**2023/6 接受!**

- 參考頂尖期刊摘要撰寫方式
- 檢索資料庫包含Embase
- 確認相同國家文獻是否族群重疊

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# 如何撰寫

- 研究目的、證據缺口
- 列出PICO及檢索策略
- 討論章節
  1. 主要發現
  2. 主要發現是否符合理論、事前假設
  3. 整體證據品質，影響證據品質的因素
  4. 本篇研究的優勢與弱點
  5. 本篇研究對於臨床的啟示

# 從中學到

- PRISMA for systematic review
- 統合分析中不同類型研究基礎處理
  - 分開探討
  - 合併分析→研究設計做次群組分析
- 多臂研究時的分析 (unit-of-analysis error)

  - Combine groups to create a single pair-wise comparison (recommended).
  - Select one pair of interventions and exclude the others.
  - Split the 'shared' group into two or more groups with smaller sample size, and include two or more (reasonably independent) comparisons.
  - Include two or more correlated comparisons and account for the correlation.
  - Undertake a *network meta-analysis* (see Chapter 11).

https://training.cochrane.org/handbook/current/chapter-23#section-23-3

# 給新手的建議

- 慎選題目
- 與時間賽跑
- 與有經驗者合作 / 參考優秀文章
- 將缺失轉化為進步的契機

# 統合分析新手之心路歷程分享

**Every expert was once a beginner — keep trying, and mastery will follow!**

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