



臺北市立萬芳醫院 - 委託財團法人臺北醫學大學辦理
Taipei Municipal Wan Fang Hospital (Managed by Taipei Medical University)

Safety of coffee consumption after myocardial infarction: A systematic review and meta-analysis

Eduardo M. Ribeiro, Mariana Alves, João Costa, Joaquim J. Ferreira, Fausto J. Pinto, , Daniel Caldeira

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引言人：簡美麗

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背景

* 根據WHO在2019年統計資料，全球5540萬死亡病例中，MI是缺血性心臟病排名第一的死亡原因，佔世界總死亡人口的16%。

* 台灣110年十大死因：

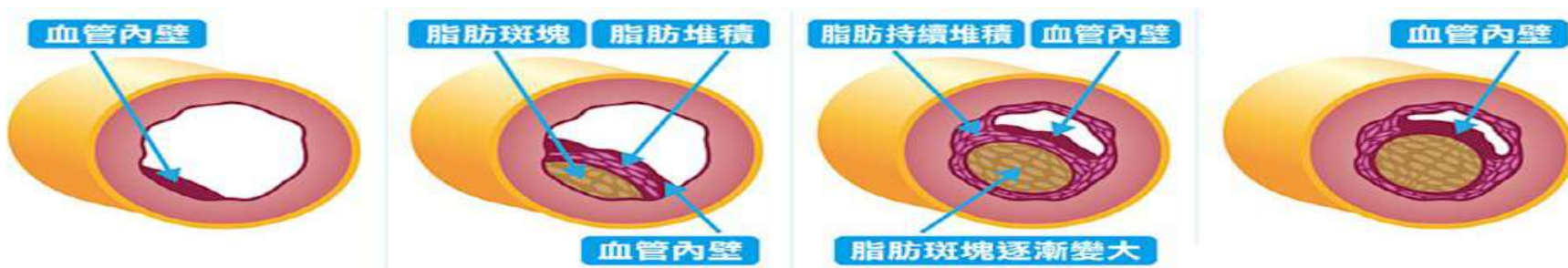
死因別	死亡人數 (人)		死亡率 (每十萬人口)		標準化死亡率 (每十萬人口)	
		年增率 (%)		年增率 (%)		年增率 (%)
所有死亡原因	184,172	6.4	784.8	6.9	405.5	3.8
1.癌症	51,656	3.0	220.1	3.5	118.2	0.7
2.心臟疾病(高血壓性 疾病除外)	21,852	6.8	93.1	7.3	45.6	4.3
3.肺炎	13,549	-1.4	57.7	-0.9	25.3	-4.0
4.腦血管疾病	12,182	3.1	51.9	3.6	25.2	-0.3
5.糖尿病	11,450	11.0	48.8	11.6	23.8	8.1
6.高血壓性疾病	7,886	17.6	33.6	18.2	15.2	13.2
7.事故傷害	6,775	0.1	28.9	0.6	20.0	-1.4
8.慢性下呼吸道疾病	6,238	10.3	26.6	10.8	11.7	6.1
9.腎炎、腎病症候群 及腎病變	5,470	7.3	23.3	7.9	10.9	4.2
10.慢性肝病及肝硬化	4,065	2.5	17.3	3.0	10.4	0.6
19.嚴重特殊傳染性肺炎 (COVID-19)	896	-	3.8	-	2.0	-



急性心肌梗塞簡介⁻¹

(acute myocardial infarction, AMI)

* **急性心肌梗塞**是指供應心肌血液之冠狀動脈，因斑塊破裂並在冠狀血管中形成血栓或**粥狀動脈硬化**導致心肌供血急劇減少不足以應付氧氣需求，而導致心肌梗塞 (MI) 造成不可逆轉的損害。



藥物

心導管

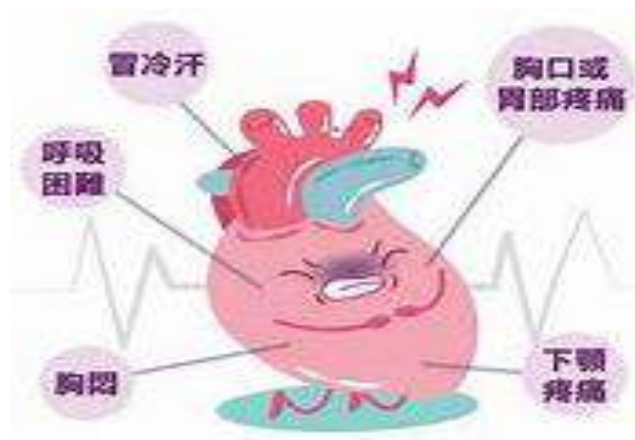
繞道手術

急性心肌梗塞簡介-2

(acute myocardial infarction, AMI)

*症狀:

- 在**休息**或**勞動**狀態下，引發的胸悶、心悸、呼吸急速，上肢疼痛，下顎痛或上腹疼痛不適，且症狀是**持續性**、至少**二十分鐘**。
- 發生部位通常範圍較廣，**並非局部性**的，不會因姿勢不同，或者身體部位移動而有所改變，有時會伴隨嘔心、呼吸困難、盜汗、昏厥，甚至**死亡**。



(廖、駱，2022)

急性心肌梗塞簡介⁻³

(acute myocardial infarction, AMI)

* 世界衛生組織於美國及歐洲心臟學會對急性心肌梗塞的診斷標準，需符合其中兩項包括：

(一)急性缺血性胸痛：強烈的胸悶痛，輻射至手臂、肩頸與背部、血壓降低、呼吸急促、冒冷汗。

(二)心電圖變化：急性期ST段上升或下降、T波倒置及Q波出現。

(三)CK、CK-MB心肌標記升高

* 心肌梗塞在10 分鐘內完成心電圖檢查及判讀，在 90 分鐘內以心導管執行第一次氣球擴張術，給予血栓溶解劑，若三條以上冠狀動脈嚴重阻塞者則施行冠狀動脈繞道手術。

(張、胡，2018)



心肌梗塞後護理指導-1

- * 調整**飲食**和**生活型態**，可減少 92% AMI風險。
- * 運動及飲食控制可降低血脂，規律的運動可控制體重、增加心肺耐力，減少心因性死亡之危險。
- * 按時回診、正確服藥可**降低 46%**心血管罹患率及 **22%**死亡率。
- * 抽菸會增加血栓及血管收縮，故須戒菸，除此之外，控制體重、血壓與血脂、血糖以及注意保暖也是十分重要的。



(鄭、孫、白，2018)

心肌梗塞後護理指導-2

- * **咖啡**是人們常飲用的飲料，國人的飲料一直以來都是以茶為主，但喝咖啡習慣近年也有大幅成長，每人每年平均喝**100 杯**。
- * 咖啡可引起**心悸、血壓高、心律不整**（特別是原本有心臟病者），血液總膽固醇以及低密度脂蛋白膽固醇、三酸甘油酯濃度升高。
- * 亦有研究顯示，每天喝 3-5 杯咖啡，可以減少**15%**心血管疾病的風險。

(顏，2017)



動機

➤ 病患常會問~~~

心肌梗塞後，能否喝咖啡？

心臟不好的人，是不是就不能喝咖啡？

➤ 喝咖啡是否會引發心肌梗塞的發生？

➤ 心肌梗塞後，攝入咖啡對患者的影響？

➤ 臨床醫療人員是否能將咖啡衛教，加入心肌梗塞後的飲食衛教項目？



臨床現況

當您發生心肌梗塞後，你/妳的選擇?.....



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快速評讀[FAITH的工具]

FAITH tools

[Meta-analysis]

步驟1：研究探討的問題為何？ (PICO)
(內在效度)

步驟2：研究的品質如何？ (效益)

步驟3：研究結果之意義為何？

步驟1: 文獻回顧探討問題為何？

P

- Patients with cardiac infarction

I

- Coffee intake

C

- **NO** Coffee intake

O

- Incidence of cardiovascular events(事件)

問題類型：●治療型 ○預後型 ○診斷型 ○傷害型



快速評讀[FAITH的工具]

FAITH tools

[Meta-analysis]

步驟1：研究探討的問題為何？ (PICO)

步驟2：研究的品質如何？
(內在效度)
(效益)

步驟3：研究結果之意義為何？



F (Find)—研究是否找到所有相關證據

? Unclear

Information sources and search strategy

Electronic identification of studies was conducted by two authors (DC and ER), searching in MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science Core Collection, SciELO Citation Database, Current Contents Connect®, KCI Korean Journal Database, African Index Medicus, and LILACS, lastly updated in April 2020. Reference lists and systematic reviews evaluating coffee/caffeine exposure and cardiovascular diseases or cardiovascular risk factors were comprehensively assessed to ensure the sensitivity of the search.

P.2147

良好的文獻搜尋至少應包括二個主要的資料庫(如：Medline, Cochrane 考科藍實證醫學資料庫, EMBASE 等)，並且加上文獻引用檢索、試驗登錄資料等。文獻搜尋應不只限於英文，並且應同時使用 MeSH 字串及一般檢索詞彙。

Information sources and search strategy
Electronic identification of studies was conducted by two authors (DC and ER), searching in MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science Core Collection, SciELO Citation Database, Current Contents Connect, KCI Korean Journal Database, African Index Medicus, and LILACS, lastly updated in April 2020. Reference lists and systematic reviews evaluating coffee/caffeine exposure and cardiovascular diseases or cardiovascular risk factors were comprehensively assessed to ensure the sensitivity of the search.

Web of Science、Medline和Cochrane圖書館的電子數據庫使用和關鍵詞進行了搜索

文獻中未寫到有用MeSH術語及語言限制



F(Find)—研究是否找到所有相關證據 (納入及排除條件)



1.

Study design and participants of interest

All longitudinal studies (clinical trials, cohort/nested casecontrol studies, casecontrol studies) were **included**, provided that they reported data or estimates about the coffee exposure and new cardiovascular events in patients that have or had myocardial infarction. History of myocardial infarction was defined according to clinical definitions , administrative codes, or autoreporting.

納入條件

2.

Studies addressing the effects of short-term exposure to coffee (<1 year) as well as studies evaluating coffee exposure in patients who had not prior MI were **excluded**. Studies that met inclusion criteria were not excluded apriori on the basis of weakness of design or data quality.

排除條件

Intervention/exposure and control

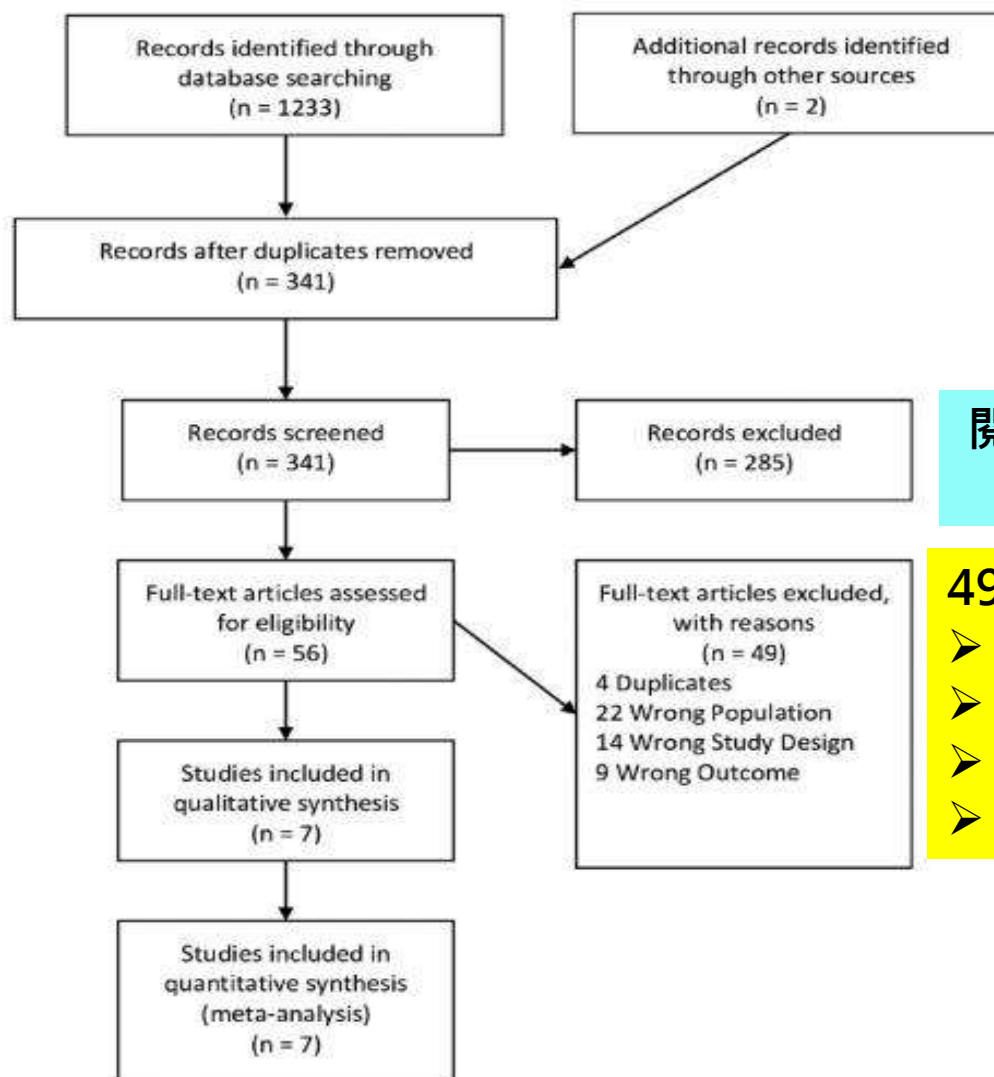
Studies had to appraise the coffee consumption after the myocardial infarction and had to include a control group.

The control group had to include patients who were coffee abstainers, low-dose coffee drinkers or decaffeinated coffee consumers. We were flexible about the definition of low-dose coffee, accepting the definition of each study.

p.2147



文獻納入的流程 PRISMA flow diagram



閱讀標題及摘要後排除文章

49篇文章排除：

- 4篇:重複文章
- 22篇:研究對象不符合
- 14篇:研究設計不符合
- 9篇:研究結果不符合

A(Appraisal)---文獻是否經過嚴格評讀

? Unclear

表三 列出納入的試驗研究的偏差風險

Risk of bias assessment

The risk of bias of individual studies was evaluated using the **ROBINS-I** (Risk Of Bias In Non-randomized Studies - of Interventions) tool [11], using the following domains: confounding, selection of participants into study, classification of intervention, deviations from intended intervention, missing data, measurement of outcome and selection of reported results. These domains were qualitatively classified as serious, moderate or low risk of bias.

Disagreements were solved **by consensus.**

Assessment of confidence in cumulative evidence

The Grading of Recommendation, Assessment, Development and Evaluation (GRADE) criteria was used to grade the quality of the pooled evidence for each outcome. The **GRADE** approach was independently assessed by two investigators (DC and ER) in the following domains: risk of bias, inconsistency, indirectness, imprecision and publication bias. **Discrepancies were solved by consensus.** The confidence on the pooled evidence accounted for all the factors and was graded as very low, low, moderate or high. **The pooled risk difference with coffee and the confidence on the pooled evidence were reported in the Summary of findings table.**

P.2148

經由2位作者嚴格評讀，在遇到評讀結果不一致時，採用溝通協調方式達到共識，未有第三位作者意見。

I(Included)----是否只納入具有良好效度文章?

? Unclear

Study	Outcomes	混淆 Bias due to confounding	研究參與者選擇 Bias in the selection of participants into the study	介入分類 Bias in the classification of interventions	偏離預期干預 Bias due to deviations from intended interventions	結果測量 Bias due to missing data	報告結果選擇 Bias in the measurement of outcome	報告結果選擇 Bias in the selection of reported result	Overall risk of bias
Makani 2004	All-cause Mortality	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
	Recurrent AMI	Moderate	Moderate	Moderate	No information	Low	Low	No information	Moderate
Silletta 2007	Stroke	Moderate	Moderate	Moderate	No information	Low	Low	No information	Moderate
	Sudden death	Moderate	Moderate	Moderate	No information	Low	Low	No information	Moderate
	MACE	Moderate	Moderate	Moderate	No information	Low	Low	No information	Moderate
	All-cause mortality	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
Makani 2009	CV Mortality	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
	Recurrent AMI	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
	Stroke	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
	Heart Failure	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
Forrester 2010	MACE	Moderate	Moderate	Moderate	No information	No information	Moderate	No information	Moderate
van Dungen 2017	All-cause Mortality	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
	CV Mortality	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
Notara 2015	Recurrent AMI	Moderate	Moderate	Serious	No information	Low	Low	No information	Serious
	All-cause Mortality	Moderate	Moderate	Serious	No information	No information	Low	No information	Serious
Suri 2015	Stroke	Moderate	Moderate	Serious	No information	No information	Serious	No information	Serious
	Recurrent AMI	Moderate	Moderate	Serious	No information	No information	Serious	No information	Serious
	CV mortality	Moderate	Moderate	Serious	No information	No information	Serious	No information	Serious

Risk of bias within studies

According to the ROBINS-I tool (Supplementary Table 3), the overall risk of bias was serious, with only two studies being considered as having moderate risk of bias [22,25]. The key element for downgrading the evidence was the bias in the classification of intervention/exposure, because just a baseline assessment is clearly insufficient to retrieve a reliable estimate of coffee exposure overtime. The studies that evaluated at least twice overtime were considered with moderate risk of bias [22,25].

P.2152

採用ROBINS評讀工具，把每一篇細項偏差評分，評讀結果有2篇為中度偏差、5篇是嚴重的偏差



I(Included)----是否只納入具有良好效度文章?

? Unclear

Table 2 Summary of findings according to the GRADE criteria, depicting the primary and the secondary outcomes.

Outcomes	Number and type of studies	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated yearly absolute effects**	
				Risk with no coffee***	Risk difference with coffee*
All-cause mortality	3 observational studies	⊕○○○ VERY LOW ^{a,b,c}	0.85 (0.63–1.13)	43 per 1000	6 fewer per 1000 (16 fewer to 6 fewer)
CV mortality	2 observational studies	⊕⊕○○ LOW ^a	0.70 (0.54–0.91)	18 per 1000	5 fewer per 1000 (8 fewer to 2 fewer)
Sudden death	1 observational study	⊕○○○ VERY LOW ^{d,e,f}	0.80 (0.55–1.17)	10 per 1000	2 fewer per 1000 (5 fewer to 2 more)
Myocardial infarction	3 observational studies	⊕○○○ VERY LOW ^{a,f}	0.99 (0.80–1.22)	16 per 1000	0 fewer per 1000 (3 fewer to 3 more)
Stroke	2 observational studies	⊕○○○ VERY LOW ^{a,f}	0.77 (0.42–1.43)	5 per 1000	0 fewer per 1000 (2 fewer to 3 more)
Heart failure	1 observational study	⊕○○○ VERY LOW ^{a,f,g}	0.71 (0.42–1.18)	40 per 1000	12 fewer per 1000 (23 fewer to 7 more)
MACE	2 observational studies	⊕○○○ VERY LOW ^{a,c}	0.96 (0.86–1.07)	39 per 1000	2 fewer per 1000 (6 fewer to 3 more)

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**The anticipated yearly absolute risks were calculated assuming a constant risk of events overtime.

***Data calculated from the control group in the largest study in each outcome: All-cause mortality and CV mortality (Van Dongen et al. [21]); Sudden death, myocardial infarction, stroke and MACE (Silletta et al. [22]); Heart failure (Mukamal et al. [20]).

Explanations: **a.** The risk of bias strata of most studies corresponds to very serious. **b.** Statistical heterogeneity was substantial with I^2 statistic of 50%. **c.** The confidence interval overlaps the HR 1.0. However, it excludes substantial harm. **d.** The risk of bias of the study was moderate. **e.** Only one study (Silletta et al. [22]). **f.** The confidence interval overlaps the HR 1.0. **g.** Only one study (Mukamal et al. [20]).

根據證據確定性 (GRADE) 獲得的結果。咖啡攝取對心血管死亡率的確定性很低



納入文獻特徵(Table I)

Table 1 Main characteristics of included studies.

Study Year	Design	Region	Population	Follow-up	Mean age/% female	Type of coffee	Coffee exposure	Outcomes	Outcome adjustments
Mukamal 2004 [19]	Prospective cohort	USA	1902 hospitalized with a confirmed AMI between 1989 and 1994 at 45 community hospitals and tertiary care centers in the United States, as part of the Determinants of Myocardial Infarction Onset Study	Median of 3.8 years	56–65 years/32%	Caffeinated coffee only	Standardized questionnaire by trained interviewers	All-cause mortality	Age, sex, previous MI, previous angina, hypertension, diabetes mellitus, BMI, current smoking, former smoking, educational attainment, race, household income, usual frequency of exertion, usual alcohol consumption, use of thrombolytic therapy, use of cardiac medications (aspirin, β blockers, calcium channel blockers, ACEi, digoxin diuretics, lipid-lowering agents), congestive heart failure or ventricular tachycardia during hospitalization
Sillelta 2007 [22]	Prospective cohort	Italy	11,231 participants in the GISSI-Prevenzione trial – a prospective study investigating the relationship between coffee intake and cardiovascular events in a cohort of patients who survived myocardial infarction	3.5 years	52.3–63.6 years/14.7%	Coffee only (not specified)	Dietary questionnaire administered by cardiologists/nurses during clinical visits at the baseline examination and at the 6th, 18th, and 42nd month of follow-up	Recurrent AMI Stroke Sudden Death	Age, gender, smoking, time from MI to enrollment, prior MI previous to index MI, BMI, history of hypertension, history of diabetes mellitus, peripheral vascular disease, electrical instability, results of exercise stress testing, left ventricular ejection fraction, New York Heart Association class, Canadian Cardiovascular Society angina symptoms, revascularization procedures, n-3 PUFA use, vitamin E use, antiplatelet agent use, angiotensin-converting enzyme inhibitor use, lipid-lowering medication use, β -blocker use and intake of cooked vegetables, raw vegetables, fruit, fish, olive oil, other oil, butter, cheese, and wine

納入文獻特徵(Table I)

Table 1 Main characteristics of included studies.

Study Year	Design	Region	Population	Follow-up	Mean age/% female	Type of coffee	Coffee exposure	Outcomes	Outcome adjustments
Mukamal 2009 [20]	Prospective cohort	Sweden	1369 hospitalized with a confirmed first acute myocardial infarction between 1992 and 1994 in Stockholm County, Sweden, as part of the Stockholm Heart Epidemiology Program	6.9–9.9 years	59.5 years/30%	Caffeinated coffee only	Standardized questionnaire distributed during hospitalization	All-cause mortality CV mortality Recurrent AMI Stroke Heart failure	Age, sex, diabetes, smoking, obesity, physical inactivity, alcohol consumption, tea consumption, education, intake of boiled coffee, hypertension and systolic blood pressure
Fornengo 2010 [25]	Prospective cohort	Italy	112 patients with ≤45 years admitted to the Coronary Care Unit with acute MI	5.3 years	41 years/10%	Coffee (not specified)	Standardized questionnaire at baseline and end of follow-up	MACE (defined as cardiac death, recurrent MI, heart failure needing hospitalization stroke and angina pectoris needing re-vascularization procedure)	Age, gender, current smoking, hypercholesterolemia, hypertriglyceridemia, family history, previous CV events, hypertension, heart rate, diabetes mellitus, BMI, obesity, diet, physical activity, alcohol consumption, end-diastolic and end-systolic ventricular diameter and LV ejection fraction
Notara 2015 [23]	Prospective cohort	Greece	2172 ACS consecutive patients hospitalized in the cardiology clinics or the emergency units of six major General Hospitals in Greece	10 years	65 ± 13 years/24%	Coffee only (not specified)	Validated semiquantitative Food Frequency Questionnaire	Recurrent AMI	Sex, age, physical activity, years of school, MedDietScore, current smoking, body mass index, CES-depression, family history of CV disease, hypertension, hypercholesterolemia and diabetes mellitus

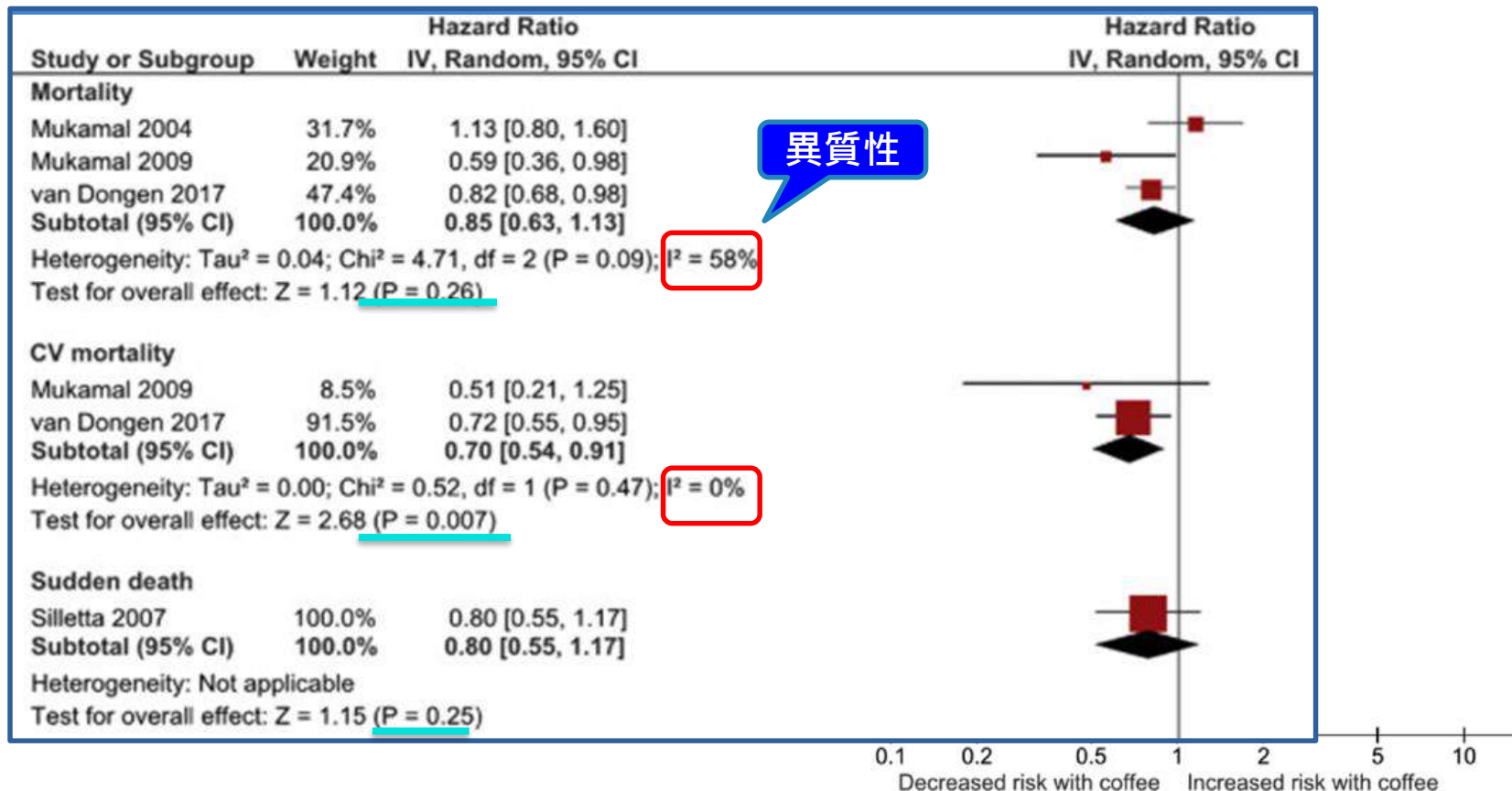


納入文獻特徵(Table I)

Table 1 (continued)

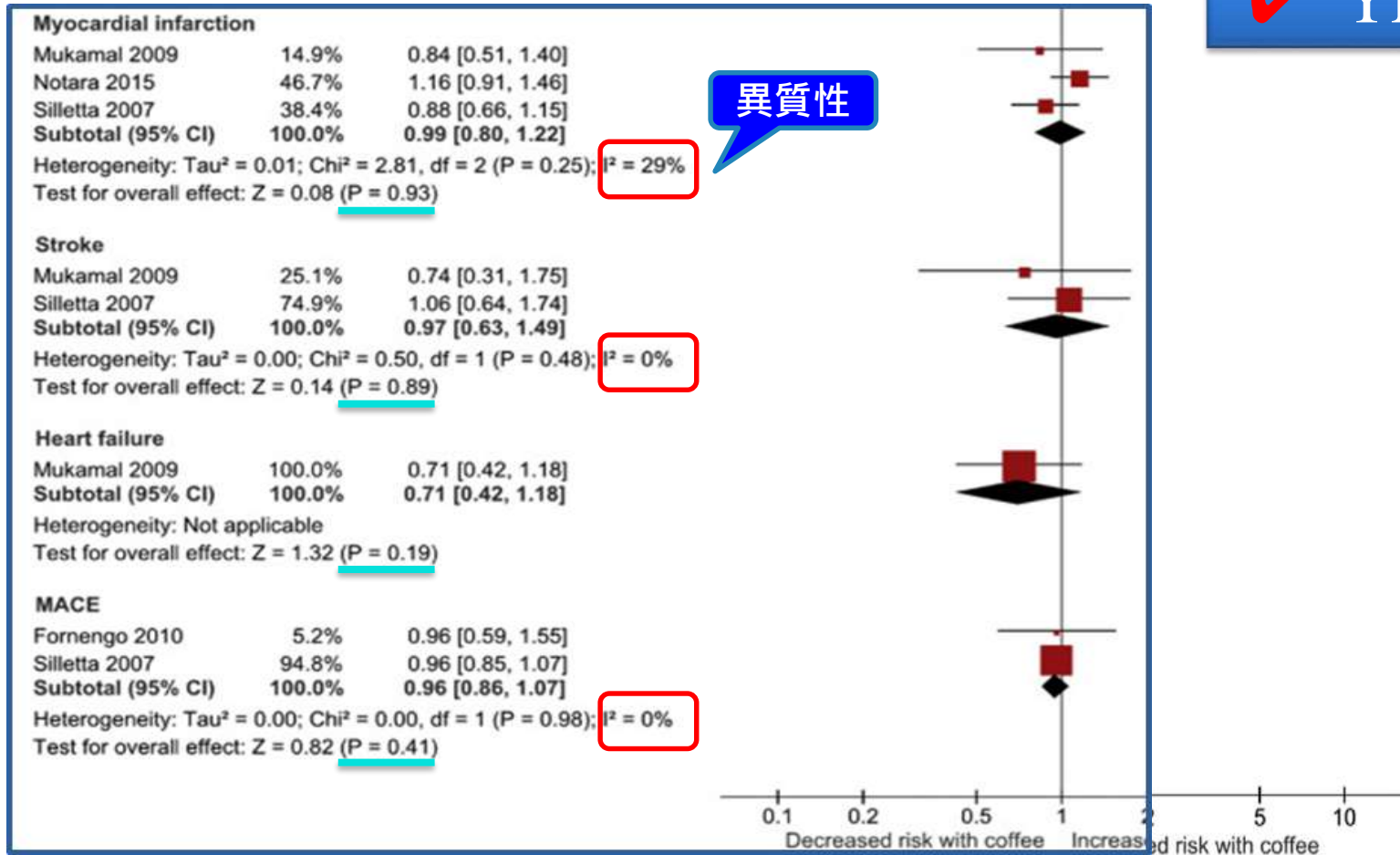
Study Year	Design	Region	Population	Follow-up	Mean age/% female	Type of coffee	Coffee exposure	Outcomes	Outcome adjustments
van Dongen 2017 [21]	Prospective cohort	Netherlands	4365 Dutch patients from the Alpha Omega Cohort between 60 and 80 years and that had experienced an MI less than 10 years before study	Median of 7.1 years	69.0 ± 5.6 years/21%	Caffeinated and decaffeinated coffee (total)	203-item validated food-frequency questionnaire by trained dietitians	All-cause mortality CV mortality	Age, sex, and type of intervention during the initial Alpha Omega Trial phase, prevalent diabetes, BMI, physical activity, educational level, smoking status, and alcohol use
Suri 2015 [24]	Prospective cohort	USA	739 survivors of AMI	9.0 ± 5.2 years	69 ± 17 years/41%	Caffeine intake divided into equivalent of 150-mg of coffee cups	Dietary interviews by trained dietary interviewers	All-cause mortality Fatal stroke Fatal recurrent AMI Fatal cardiovascular disease (CV mortality)	Age, sex, race/ethnicity, socioeconomic status group, smoking status, alcohol, history of diabetes mellitus, history of hyperlipidemia and history of hypertension

T(Total up)作者是否以表格和圖表試驗結果？ +H-(Heterogeneity)研究結果異質性是否相近？



T(Total up)作者是否以表格和圖表試驗結果? +H-(Heterogeneity)研究結果異質性是否相近?

✓ YES



T(Total up)+ H----作者是否以表格和圖表試驗結果？

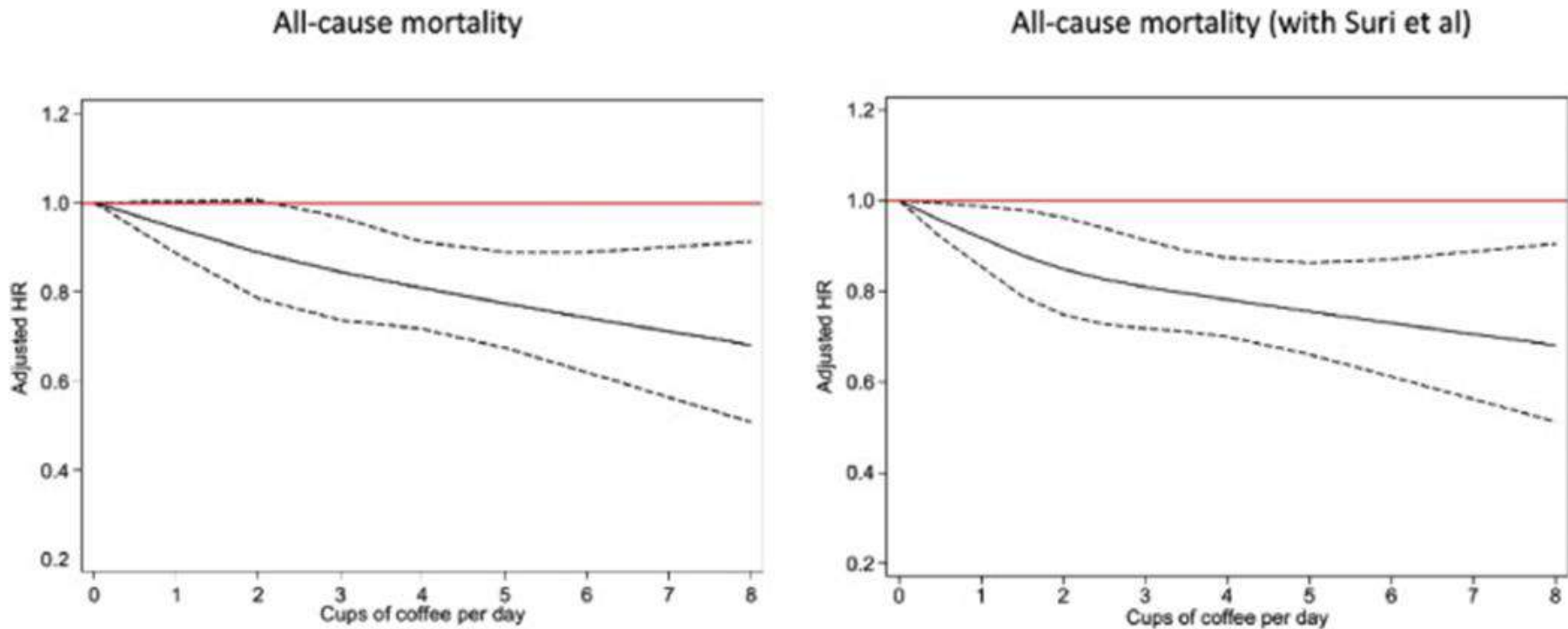
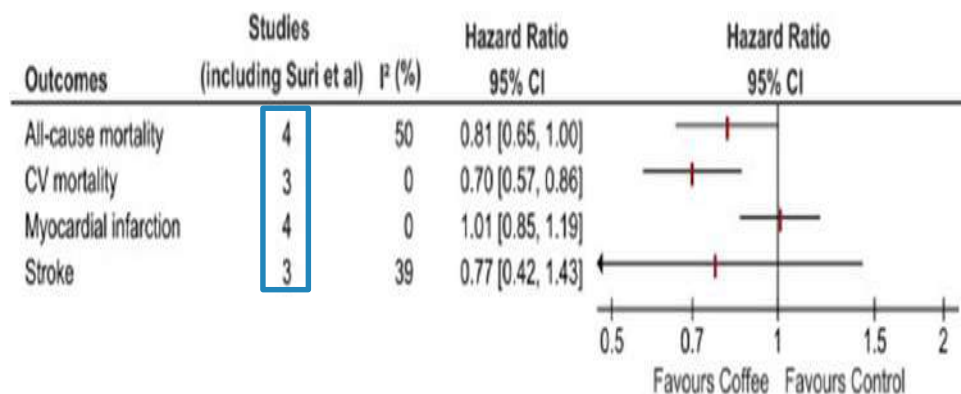


Figure 3 The pooled relative risk of all-cause mortality associated to the different coffee consumption strata. Note: The solid line represents the non-linear trend. Black dashed lines represent the 95% confidence intervals. Red dashed line represents HR = 1. HR, hazard ratio.

不同咖啡攝取量顯著反應反比關係，沒有明顯的不對稱

T(Total up)+ H----作者是否以表格和圖表試驗結果？

Publication bias and secondary analysis:








The inclusion of data from this study yielded similar results in the pooled analysis for every outcome that the study assessed: all-cause mortality (HR = 0.81; 95% CI 0.65–1.00; p -value for heterogeneity = 0.11; I^2 = 50%), CV mortality (HR = 0.70; 95% CI 0.57–0.86; I^2 = 0%), recurrent myocardial infarction (HR = 1.01; 95% CI 0.85–1.19; I^2 = 0%), and stroke (HR = 0.77; 95% CI 0.42–1.43; I^2 = 39%) (Fig. 4; Supplementary Fig. 2).

We also carried out the dose–response analysis for all-cause mortality (Fig. 3), cardiovascular mortality [20,21,24] and stroke [20,22,24] as these outcomes met the criteria of reported data in three or more studies. The all-cause mortality data overlapped the primary analysis. CV mortality was associated to a non-linear inverse relationship (p -value for non-linearity < 0.001) (Supplementary Fig. 3) while for stroke, there was not a significant change in the risk for each cup of coffee consumed.

P.2153-2154

我們還對全因死亡率、心血管疾病、心肌梗塞和中風 進行了分析，沒有顯著差異

綜整FAITH的結果

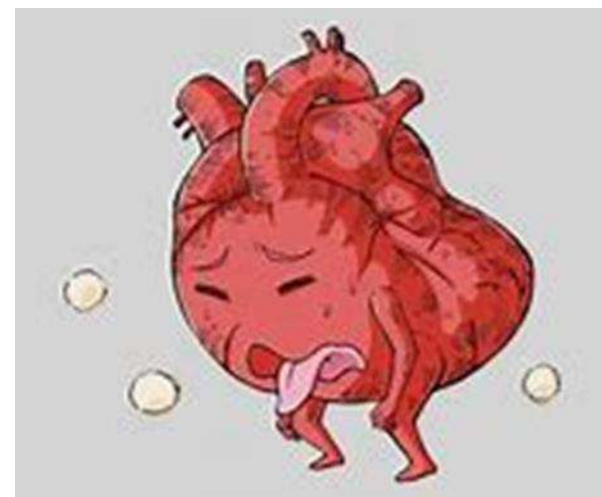
	Yes	No	Unclear
F			
A			
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結論

Consumption of coffee was not associated with an increased risk of all-cause mortality and cardiovascular events in patients with previous myocardial infarction.

The presence of a significant dose–response non-linear association between coffee consumption and risk of mortality in this population emphasize the relevancy for further observational studies to confirm our findings and to better elucidate the possible underlying mechanism of the impact of the consumption of coffee on mortality and other cardiovascular events in patients with previous myocardial infarction.

p.2156



喝咖啡在心肌梗塞患者中，發生死亡率和心血管事件的風險無相關性。

限制

The first limitation of this review is the small number of studies included in the single meta-analysis. There are also limitations inherent to the included studies themselves – given their observational nature, the possibility of residual or unmeasured confounding cannot be excluded, even though all studies had a multivariable outcome adjustment. Also, the control group was heterogeneous as included abstainer, low quantity drinkers or decaffeinated coffee drinker.

Regarding coffee exposure, all studies had equivalent assessment of coffee consumption – through a standardized dietary questionnaire/interview. However, the categories and classification regarding coffee doses were heterogeneous, as was the period of time in which coffee consumption was measured. The reference of coffee

p.2155



Q & A討論交流時間：

病人發生心肌梗塞後，是可以攝取咖啡？

同意 12票

不確定 12票

不同意 0票





謝謝聆聽

Thanks for your listening

