流行病學方法論及實驗
The Methods of Epidemiology and Practices
觸媒流行病學故事與護理照護

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咖啡為什麼這麼香？咖啡烘培時的焦糖化與梅納反應

2012/12/25 | 分析 / 評論 專欄 泛科授權 2.0 活得科學 萬物之理 | 標籤： 咖啡 梅納反應 焦糖化 香氣







http://pansci.asia/archives/33203
https://kknews.cc/food/85le8yq.html

美拉德反應（Maillard reaction），又稱麥拉德反應、梅拉德反應、梅納反應、羰胺反應，是廣泛分布於食品工業的非酶褐變反應，指的是食物中的還原糖（碳水化合物）與胺基酸／蛋白質在常溫或加熱時發生的一系列複雜反應，其結果是生成了棕黑色的大分子物質類黑精或稱擬黑素。除產生類黑精外，反應過程中還會產生成百上千個有不同氣味的中間體分子，包括還原酮、醛和雜環化合物，這些物質為食品提供了宜人可口的風味和誘人的色澤。



如果當糖與蛋白質或胺基酸等一起烹煮，就會發生梅納反應（Maillard reaction），或稱美拉德反應。含糖食材除了焦糖化，部份糖份會和後者交互發生一系列化學反應，產生更多樣化的化合物，簡而言之就是風味比焦糖化更豐富，巧克力、咖啡、楓糖漿、釀造啤酒等都是梅納反應的成品。



風味優劣

豆種: A 豆 vs B豆

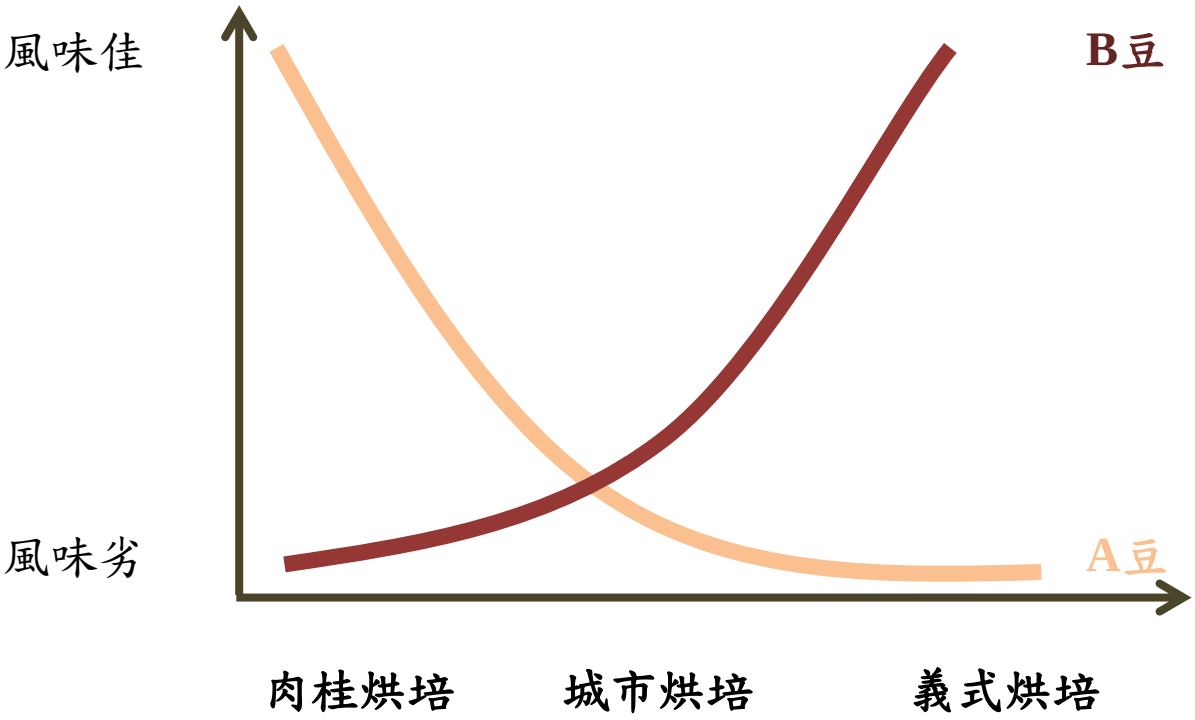
烘培程度: 淺、中、深

https://zh.wikipedia.org/wiki/%E7%BE%8E%E6%8B%89%E5%BE%B7%E5%8F%8D%E5%BA%94

http://pic.pimg.tw/mayaroast/4a799d8e0bab7.jpg

https://nommagazine.com/梅納反應跟焦糖化到底差在哪？一次搞懂原理與五/

咖啡風味與烘培程度



A豆風味優於B豆

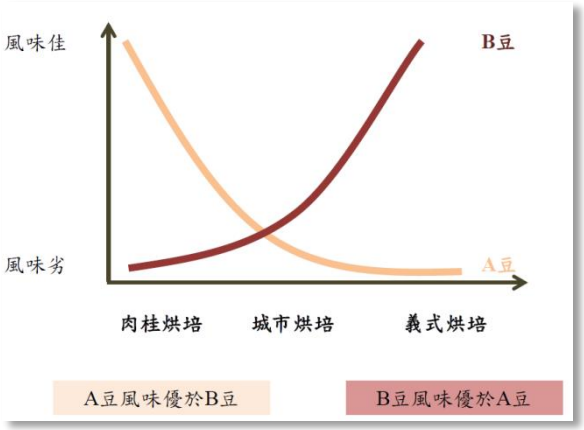
B豆風味優於A豆



效果修飾(Effect Modification)–定義

若X與Y的關係會隨著Z而改變，Z則可能為一效果修飾因子(effect modifier)。此亦代表對於結果Y，X與Z之間具有交互作用。

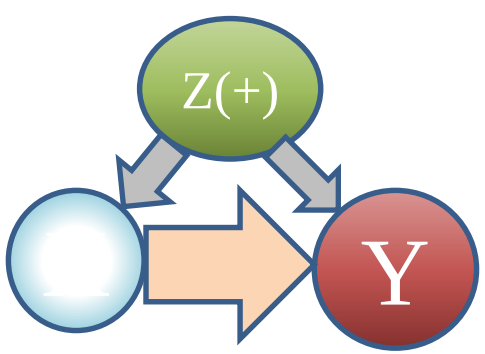


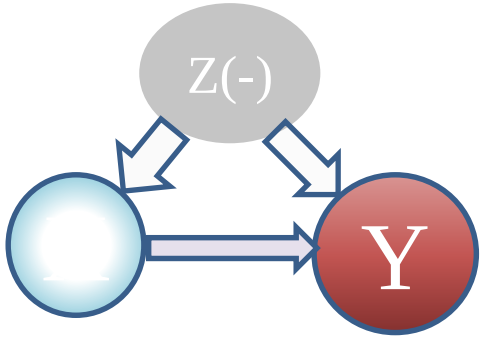


風味優劣
豆種: A 豆 vs B豆
烘培程度: 淺、中、深

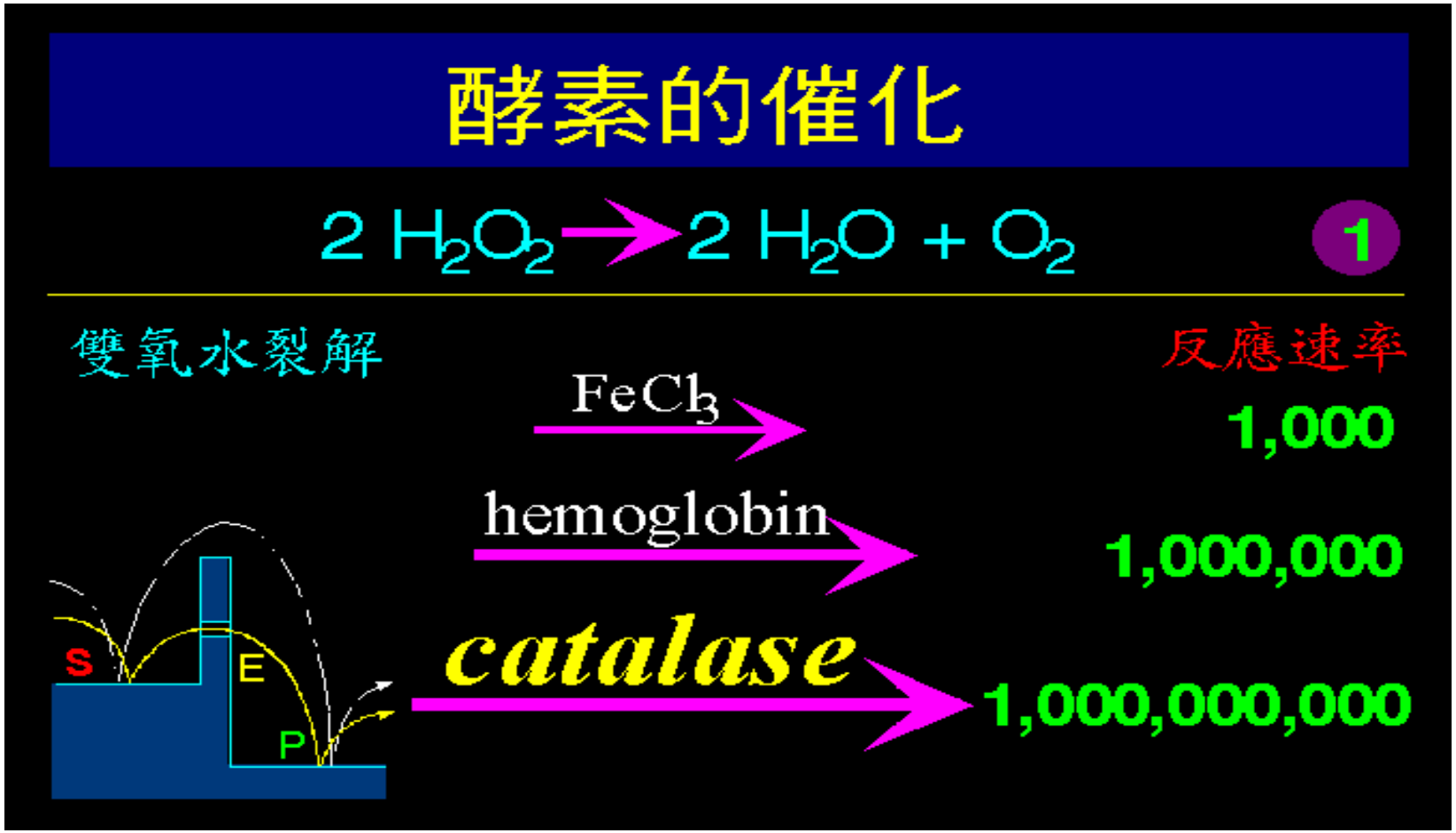
效果修飾–說明

1. X對於Y的效果會由於Z存在與否有所改變。描述X與Y關係之對數比(Odds ratio)，相較於Z不存在，會於Z存在時效果較大。
2. 相反效果亦可由Z存在與否進行說明闡述。
3. **一旦有效果修飾因子存在，報導調整後的總效果並不恰當(aggregate results)。**





酵素與化學反應速率

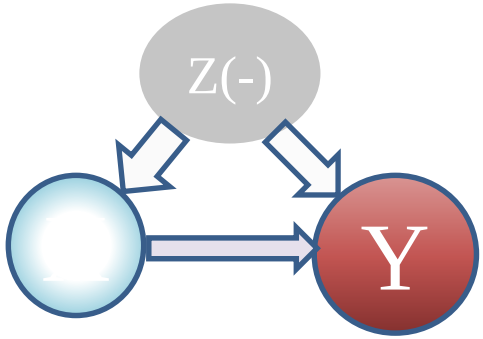


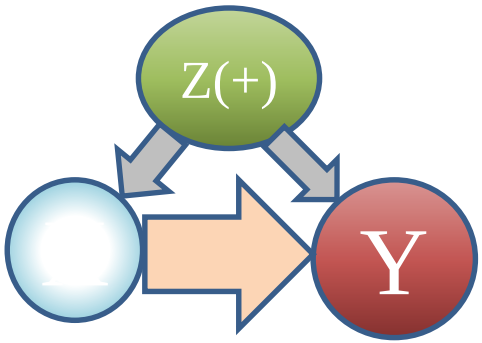
http://juang.bst.ntu.edu.tw/BCbasics/Enzyme12xx.htm#E103

效果修飾–範例一

(1) 由於Z所產生之效果修飾作用

	Z(-)			Z(+)			Aggregated	
	X(+)	X(-)		X(+)	X(-)		X(+)	X(-)
Y(+)	80	20		50	30		130	50
Y(-)	60	20		40	90		100	110
	OR=1.33			OR=3.75			OR=2.86 (Crude)	

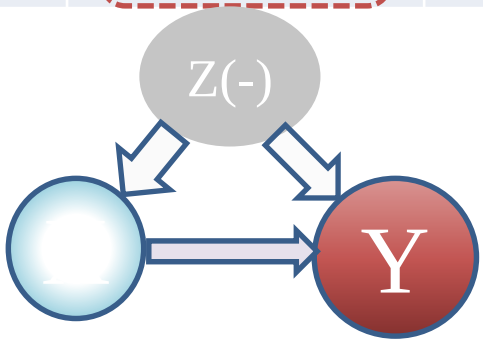


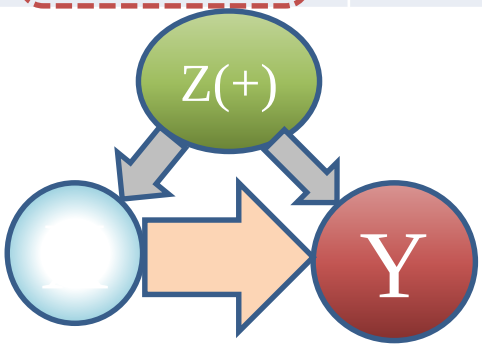


效果修飾–範例二

(2)由於Z所產生之反向效果作用

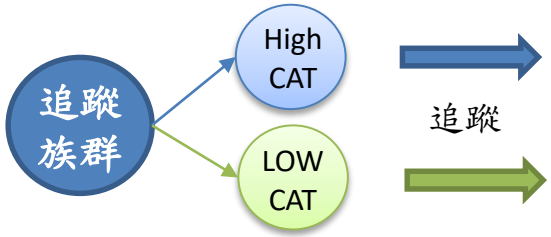
	Z(-)			Z(+)			Aggregated	
	X(+)	X(-)		X(+)	X(-)		X(+)	X(-)
Y(+)	40	140		180	60		220	200
Y(-)	80	110		120	90		200	200
	OR=0.39			OR=2.25			OR=1.10 (Crude)	





分層分析下的修飾效果評估

世代追蹤研究設計



心臟疾病(CHD)

在研究兒茶酚胺 (CAT) 與心臟疾病(CHD)之關係研究中，年齡的大小 (Age)及心電圖是否異常(ECG)為兩個可能的干擾因子

各分層及其RR

年輕組($Age < 55$),
心電圖無異常($ECG = 0$)

	High CAT	*Low CAT*	*Total*
CHD	1	17	18
No CHD	7	257	264
Total	8	274	282

$\hat{OR}_1 = 2.16(0.25 \sim 18.57)$

年輕組($Age < 55$),
心電圖有異常($ECG = 1$)

	High CAT	*Low CAT*	*Total*
CHD	3	7	10
No CHD	14	52	66
Total	17	59	76

$\hat{OR}_2 = 1.59(0.36 \sim 6.96)$

年老組($Age \geq 55$),
心電圖無異常(ECG) $= 0$

	High CAT	*Low CAT*	*Total*
CHD	9	15	24
No CHD	30	107	137
Total	39	122	161

$\hat{OR}_3 = 2.14(0.85 \sim 5.37)$

年老組($Age \geq 55$),
心電圖有異常 ($ECG = 1$)

	High CAT	*Low CAT*	*Total*
CHD	14	5	19
No CHD	44	27	71
Total	58	32	90

$\hat{OR}_4 = 1.71(0.56 \sim 5.31)$

Crude OR=2.86

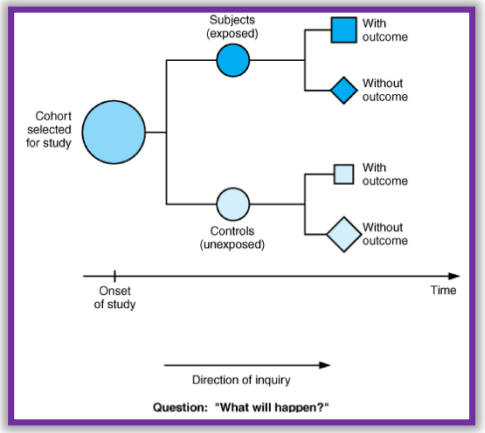
$$\sum_{i=1}^{k} \frac{\left\{ \log \hat{OR}_i - \log \hat{OR}_w \right\}^2}{Var\left\{ \log \hat{OR}_i \right\}}$$

評估因子是否造成效應修飾 (Effect modification)

效應修飾之評估
(Evaluation of effect modification)

世代追蹤研究設計

在研究兒茶酚胺(CAT) 與心臟疾病(CHD)之關係的研究中，欲檢定各分層間**OR之同質性**:



檢定統計量

$$\sum_{i=1}^{k} \frac{(\log \hat{OR}_i - \log OR_W)^2}{Var(\log OR_i)}$$

(O - E)^2

$$= \frac{(0.770-0.637)^2}{1.205} + \frac{(0.465-0.637)^2}{0.567} + \frac{(0.761-0.637)^2}{0.220} + \frac{(0.541-0.637)^2}{0.331}$$

$$= 0.185$$

$$P(\chi_3^2 > 0.185) = 0.983$$

CAT及CHD間的關係不會被年齡及ECG所修飾(無效應修飾)，可繼續進行干擾因子的調整

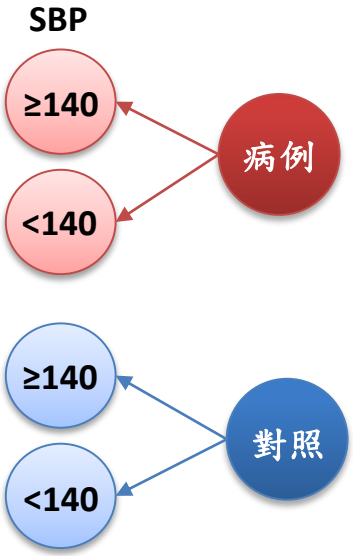






以病例-對照試驗設計研究：收縮壓與心肌梗塞之相關性 (Case-control study on SBP and MI)

	年齡≥60 歲 收縮壓 (SBP)			年齡<60 歲 收縮壓 (SBP)		
心肌梗塞	≥140	<140		≥140	<140	
發生 (Case)	9	6	15	20	21	41
未發生 (Control)	115	73	188	596	1,171	1,767
總人數	124	79	203	616	1,192	1,808



- 粗率 (Crude odds ratio) : 1.88 (1.10 ~ 3.20)
- 各年齡分層之勝算比:
  - 年齡≥60歲: 0.95 (0.33~2.79)
  - 年齡<60歲: 1.87 (1.01 ~ 3.48)

-調整年齡後的勝算比為:
- pooled: 1.58 (0.92,2.70)
- Mantel-Haenszel: 1.57 (0.91~2.69)

→調整年齡之效果後，收縮壓(SBP)與心肌梗塞 (MI) 之相關性不顯著。

以病例-對照試驗設計研究：收縮壓與心肌梗塞之相關性

粗率 (Crude odds ratio) : 1.88 (1.10 ~ 3.20)
年齡≥60歲: 0.95 (0.33~2.79)
年齡<60歲: 1.87 (1.01 ~ 3.48)

已知年齡可能為干擾因子

	年齡≥60 歲 收縮壓 (SBP)			年齡<60 歲 收縮壓 (SBP)		
心肌梗塞	≥140	<140	合計	≥140	<140	合計
發生(Case)	9	6	**15**	20	21	**41**
未發生(Control)	115	73	**188**	596	1,171	**1,767**
總人數	**124**	**79**	**203**	**616**	**1,192**	**1,808**

合併加權估計式 (Pooled estimator)

調整年齡後的勝算比為: $\hat{OR}_W = 1.58$

95%CI: $\exp(0.458 \pm 1.96 \times \sqrt{0.075}) = (0.92, 2.70)$

Mantel-Haenszel 方法

調整年齡後的勝算比為: $\hat{OR}_W = 1.569$

95%CI: $\exp(0.4504 \pm 1.96 \times \sqrt{0.0761}) = (0.91, 2.69)$

效應修飾之評估
(Evaluation of effect modification)

在研究收縮壓與心肌梗塞之關係的研究中，欲檢定不同年齡分層間OR之同質性:

檢定統計量

$$\sum_{i=1}^{k} \frac{\left\{ \log \hat{OR}_i - \log \hat{OR} \right\}^2}{Var\left\{ \log \hat{OR} \right\}}$$

$$\frac{(-0.049 - 0.458)^2}{0.3002} + \frac{(0.627 - 0.458)^2}{0.1002} = 1.141$$

$$P(\chi_1^2 > 1.141) = 0.285$$

收縮壓及心肌梗塞間的關係不會被年齡所修飾(無效應修飾)，可進行干擾因子的調整

羅吉斯迴歸分析:病例-對照研究

暴露與疾病之世代研究資料

	E	$\overline{E}$
	X=1	X=0
D	P_1	P_0
$\overline{D}$	$1-P_1$	$1-P_0$

$$\log(\frac{P}{1-P}) = \alpha + \beta X + \varepsilon$$

X=1 ➔ $\log\left(\frac{P_1}{1-P_1}\right) = \hat{\alpha} + \hat{\beta}$

X=0 ➔ $\log\left(\frac{P_0}{1-P_0}\right) = \hat{\alpha}$

＊ 無分母研究

$$\log(\frac{P_1/1-P_1)}{P_0/1-P_0)} = \hat{\beta}, \quad \hat{OR} = \exp\{\hat{\beta}\}$$

檢驗收縮壓與年齡間是否有交互作用

Y=1: 發生心肌梗塞(case, MI)

Y=0:未發生心肌梗塞(control, no MI)

X: 收縮壓 (SBP: ≥140 vs <140), 年齡 (Age: ≥60 vs <60)

$$\log it(P(Y=1)) = \alpha + \beta_1 \times SBP + \beta_2 \times Age + r(SBP \times Age)$$

$$H_0 : r = 0 \quad vs. \quad H_1 : r \neq 0$$

若存在交互作用 ($\gamma \neq 0$)

Age: ≥60 SBP=1, $\log(Odds_{Age\geq 60}) = \alpha + \beta_1 + \beta_2 + \gamma$

SBP=0, $\log(Odds_{Age\geq 60}) = \alpha + \beta_2$ ⇒ $OR_{Age\geq 60} = \exp(\beta_1 + \gamma)$

Age: <60 SBP=1, $\log(Odds_{Age<60}) = \alpha + \beta_1$

SBP=0, $\log(Odds_{Age<60}) = \alpha$ ⇒ $OR_{Age<60} = \exp(\beta_1)$

檢驗收縮壓與年齡間是否有交互作用

$$\log it(P(Y=1)) = \alpha + \beta_1 \times SBP + \beta_2 \times Age + r(SBP \times Age)$$

$$H_0 : r = 0 \quad vs. \quad H_1 : r \neq 0$$

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	age	1.522	.478	10.128	1	.001	4.583	1.795	11.705
	sbp(1)	.627	.316	3.920	1	.048	1.871	1.006	3.479
	age by sbp(1)	-.676	.633	1.140	1	.286	.509	.147	1.759
	Constant	-4.021	.220	333.571	1	.000	.018		

$$\hat{r} = -0.676, \quad sd(\hat{r}) = 0.633$$

$$\left(\frac{\hat{r}}{sd(\hat{r})}\right)^2 = 1.14, \quad p = 0.29$$

Wald test
大樣本理論 (Asymptotic property)

→無法推翻虛無假說（收縮壓與年齡不具交互作用，各年齡組間的勝算比具同質性）

Clare Bridge





Genetic predisposition, Western dietary pattern, and the risk of type 2 diabetes in men[1–3]

Lu Qi, Marilyn C Cornelis, Cuilin Zhang, Rob M van Dam, and Frank B Hu

- 第二型糖尿病的發生風險與西式飲食以及基因的感受性（genetic susceptibility）有關
- 對於gene-lifestyle interaction的證據仍不足

研究目標：評估飲食模式(dietary pattern)預測糖尿病風險是否會由於遺傳變異有所不同

Objective: The objective was to assess whether established genetic variants, mainly from genomewide association studies, modify dietary patterns in predicting diabetes risk.

Design: We determined 10 polymorphisms in a prospective, nested, case-control study of 1196 diabetic and 1337 nondiabetic men. A genetic risk score (GRS) was generated by using an allele counting method. Baseline dietary intakes were collected by using a semi-quantitative food-frequency questionnaire. We used factor analysis to derive Western and "Prudent" dietary patterns from 40 food groups.

西方飲食模式

- 紅肉、加工肉品、精緻食品





TABLE 1

Baseline characteristics of the diabetic patients and nondiabetic control subjects[1]

	Nondiabetic	Diabetic	*P*
No. of participants	1337	1196	—
Age (y)	55 ± 9[2]	56 ± 8	0.1
BMI (kg/m^2)	25 ± 2.8	27.8 ± 4.1	0.22
Obesity (%)[3]	5.3	25.5	<0.0001
Alcohol use (g/d)	12.2 ± 15.5	11.2 ± 16.6	0.01
Physical activity (MET/wk)	21.3 ± 27.4	14.6 ± 18.8	0.23
Current smoker (%)	7.0	11.3	0.0006
Family history of diabetes (%)	13.0	32.4	<0.0001
Total energy intake (kcal/d)	2039 ± 634	2031 ± 604	0.73

[1] MET, metabolic equivalent task. The geometric means of continuous variables were compared by using general linear models, and the proportions of categorical variables were compared by using chi-square tests.

[2] Mean ± SD (all such values).

[3] Defined as a BMI ≥ 30.

TABLE 3

Interactions between dietary patterns and the genetic risk score in relation to diabetes risk[1]

	Dietary patterns[3]					
Genetic risk score[2]	Q1 (lowest)	Q2	Q3	Q4 (highest)	*P* for trend	*P* for interaction
Western dietary pattern						
<10 (n = 503)	1	0.79 (0.46, 1.38)	0.81 (0.48, 1.37)	1.07 (0.65, 1.76)	0.69	0.02
10–11 (n = 904)	1	0.98 (0.67, 1.44)	1.02 (0.69, 1.49)	1.40 (0.97, 2.01)	0.06	—
≥12 (n = 1126)	1	1.23 (0.88, 1.73)	1.49 (1.06, 2.09)	2.06 (1.48, 2.88)	0.01	—
Prudent dietary pattern						
<10 (n = 503)	1	0.85 (0.50, 1.44)	1.07 (0.65, 1.76)	1.29 (0.79, 2.11)	0.24	NS
10–11 (n = 904)	1	0.75 (0.52, 1.07)	0.81 (0.56, 1.18)	0.77 (0.53, 1.11)	0.21	—
≥12 (n = 1126)	1	0.81 (0.58, 1.14)	0.71 (0.51, 0.99)	0.81 (0.59, 1.13)	0.16	—

[1] The analyses were adjusted for age, BMI, smoking, alcohol consumption, physical activity, family history of diabetes, and total energy intakes. Q, quartile.

基因風險分數(genetic risk score)較高者，西式飲食會增加糖尿病的風險；而基因風險分數(genetic risk score)較低者（<10），西式飲食無顯著增加其罹患糖尿病風險

TABLE 5

Interactions between genetic risk score and individual foods and nutrients characterizing the Western dietary pattern[1]

	Western dietary patterns[2]					
Foods and genetic risk score	Q1 (lowest)	Q2	Q3	Q4 (highest)	*P* for trend	*P* for interaction
Red meat						
<10	1	0.54 (0.24, 1.23)	0.88 (0.39, 1.97)	0.81 (0.36, 1.80)	0.55	0.02
10–11	1	1.27 (0.75, 2.15)	1.16 (0.68, 1.97)	1.45 (0.86, 2.44)	0.23	—
≥12	1	1.03 (0.69, 1.54)	1.32 (0.87, 2.01)	2.42 (1.58, 3.70)	<0.0001	—
Processed meat						
<10	1	0.91 (0.45, 1.85)	0.70 (0.38, 1.28)	1.12 (0.66, 1.92)	0.76	0.029
10–11	1	0.98 (0.60, 1.61)	0.96 (0.62, 1.48)	1.47 (0.99, 2.20)	0.06	—
≥12	1	1.09 (0.72, 1.67)	1.88 (1.30, 2.71)	2.01 (1.41, 2.89)	<0.0001	—
Heme iron						
<10	1	1.06 (0.57, 1.96)	0.82 (0.45, 1.49)	0.87 (0.48, 1.56)	0.47	0.0004
10–11	1	1.19 (0.77, 1.85)	1.37 (0.89, 2.10)	1.85 (1.23, 2.77)	0.002	—
≥12	1	0.71 (0.49, 1.03)	1.24 (0.86, 1.80)	2.48 (1.72, 3.56)	<0.0001	—

[1] The analyses were adjusted for age, BMI, smoking, alcohol consumption, physical activity, family history of diabetes, and total energy intakes.

[2] Values are odds ratios (95% CIs) calculated by using an unconditional logistic regression model.



修飾因子(Effect Modifier)

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The Effect of Losartan Versus Atenolol on Cardiovascular Morbidity and Mortality in Patients With Hypertension Taking Aspirin

The Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Study





高血壓病患常見併發症：
中風
心肌梗塞

是否Losartan對於預防心血管疾病之效益會受到「阿斯匹靈」所影響

OBJECTIVES We conducted a subgroup analysis in the Losartan Intervention For Endpoint reduction in hypertension (LIFE) study to determine whether aspirin interacted with the properties of losartan, an angiotensin-II receptor antagonist.

BACKGROUND Negative interactions between angiotensin-converting enzyme inhibitors and aspirin have been reported. There are no data reported from clinical trials about possible interactions between angiotensin-II receptor antagonists and aspirin.

METHODS The LIFE study assigned 9,193 patients with hypertension and left ventricular hypertrophy (LVH) to losartan- or atenolol-based therapy for a mean of 4.7 years, with 1,970 (21.4%) taking aspirin at baseline. The primary composite end point (CEP) included cardiovascular death, stroke, and myocardial infarction (MI). The present cohort was stratified by aspirin use at baseline.

RESULTS Blood pressures were reduced similarly in the losartan with aspirin (n = 1,004) and atenolol with aspirin (n = 966) groups. The CEP was reduced by 32% (95% confidence interval 0.55 to 0.86, p = 0.001) with losartan with aspirin compared to atenolol with aspirin, adjusted for Framingham risk score and LVH. The test for treatment versus aspirin interaction, excluding other covariates, was significant for the CEP (p = 0.016) and MI (p = 0.037).

CONCLUSIONS There was a statistical interaction between treatment and aspirin in the LIFE study, with significantly greater reductions for the CEP and MI with losartan in patients using aspirin than in patients not using aspirin at baseline. Further studies are needed to clarify whether this represents a pharmacologic interaction or a selection by aspirin use of patients more likely to respond to losartan treatment. (J Am Coll Cardiol 2005;46:770–5) © 2005 by the American College of Cardiology Foundation

相較研究起初未使用「阿斯匹靈」的人，Losartan對於起初有使用「阿斯匹靈」的人預防心血管疾病之效益較佳。

有吃aspirin者

End Point	Losartan (n = 1,004) n	%	Rate†	Atenolol (n = 966) n	%	Rate†	Adjusted* Hazard Ratio (95% CI)	p Value
Primary composite end point‡	128	12.7	28.3	180	18.6	42.1	0.68 (0.55–0.86)	0.001
Cardiovascular mortality	56	5.6	11.8	76	7.9	16.7	0.73 (0.52–1.03)	0.074
Stroke	61	6.1	13.4	94	9.7	21.8	0.63 (0.45–0.86)	0.004
Myocardial infarction	44	4.4	9.6	58	6.0	13.1	0.75 (0.51–1.11)	0.16
Other prespecified end points								
Total mortality	106	10.6	22.4	121	12.5	26.6	0.86 (0.66–1.12)	0.26
Hospitalization for								
Angina pectoris	53	5.3	11.6	48	5.0	10.9	1.10 (0.74–1.62)	0.64
Heart failure	45	4.5	9.8	53	5.5	12.1	0.84 (0.56–1.25)	0.39
Revascularization	100	10.0	22.5	109	11.3	25.5	0.91 (0.70–1.20)	0.51
New-onset diabetes§	58	6.9	15.3	57	7.1	15.6	0.98 (0.68–1.41)	0.91

沒有吃aspirin者

End Point	Losartan (n = 3,601) n	%	Rate†	Atenolol (n = 3,622) n	%	Rate†	Adjusted* Hazard Ratio (95% CI)	p Value
Primary composite end point‡	380	10.6	22.6	408	11.3	24.3	0.95 (0.82–1.09)	0.46
Cardiovascular mortality	148	4.1	8.5	158	4.4	9.1	0.96 (0.77–1.20)	0.71
Stroke	171	4.7	10.1	215	5.9	12.7	0.80 (0.66–0.98)	0.034
Myocardial infarction	154	4.3	9.0	130	3.6	7.6	1.21 (0.96–1.53)	0.11
Other prespecified end points								
Total mortality	277	7.7	15.9	310	8.6	17.8	0.91 (0.77–1.07)	0.24
Hospitalization for								
Angina pectoris	107	3.0	6.3	93	2.6	5.4	1.18 (0.89–1.56)	0.25
Heart failure	108	3.0	6.3	108	3.0	6.3	1.02 (0.78–1.34)	0.86
Revascularization	161	4.5	9.5	175	4.8	10.3	0.94 (0.76–1.17)	0.58
New-onset diabetes§	184	5.8	12.4	263	8.3	17.9	0.70 (0.58–0.85)	<0.001

King's College

