§ **SAS : homework 10 ：**

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一. **Effect-measure modification ：**

(一) Result ：

1. RR difference ：- 0.0336
2. RR ratio = 0.975

(二) Figure ：

Statistics for Table 1 of sex by caco
Controlling for apo4car=0

Odds Ratio and Relative Risks			
Statistic	Value	95% Confidence Limits	
Odds Ratio	1.3265	0.8888	1.9796
Relative Risk (Column 1)	1.2145	0.9206	1.6023
Relative Risk (Column 2)	0.9156	0.8087	1.0366

Statistics for Table 2 of sex by caco
Controlling for apo4car=1

Odds Ratio and Relative Risks			
Statistic	Value	95% Confidence Limits	
Odds Ratio	1.2929	0.6644	2.5159
Relative Risk (Column 1)	1.1055	0.8475	1.4420
Relative Risk (Column 2)	0.8550	0.5724	1.2770

rr_nonAPOEe4	rr_APOEe4	rr_diff
1.3265	1.2929	-0.0336

rr_nonAPOEe4	rr_APOEe4	rr_ratio
1.3265	1.2929	0.9746702

Breslow-Day Test for Homogeneity of Odds Ratios	
Chi-Square	0.0042
DF	1
Pr > ChiSq	0.9485

(三) Descriptions ：

Strata1 ：non-APOE e4 carrier			Strata 2 ：APOE e4 carrier		
	Case	Control		Case	Control
women	n00 = 84	n10 = 161	women	N00 = 64	N10 = 36
Men	n01 = 59	n11 = 150	Men	N01 = 33	N11 = 24
OR(n)	OR = $\frac{(n00 \times n11)}{(n10 \times n01)}$		OR(N)	OR = $\frac{(N00 \times N11)}{(N10 \times N01)}$	
OR difference = OR(n) – OR(N)					

1. 以 APOE e4 status 分層，觀察兩層中 gender 與 AD 的關係。定義 women 為 exposure，men 為 non-exposure；發生 AD 為 disease。
2. 以上述公式計算兩層的 OR。在 non-carrier 層的 OR 為 1.3265（95% CI：0.8888 – 1.9796）；在 carrier 層的 OR 為 1.2929（95% CI：0.6644 – 2.5159）
3. 在抽樣與暴露與否相互獨立的前提下，可以 OR 推論 RR。
4. 計算兩層 RR difference，將 non-carrier 層與 carrier 相減，得 RR difference = -0.0336。以 RR difference 判斷兩層的 RR 相差不大（接近 1），APOE e4 status

應不造成 effect-measure modification。

5. 計算兩層 RR ratio，將 non-carrier 層與 carrier 相除，得 RR ratio = 0.9746702。兩層的 RR 相差不大，APOE e4 status 應不造成 effect-measure modification。
6. 以 Breslow-Day test 檢定兩層之 OR 是否相等，檢定結果 p-value 為 0.9485，無法拒絕虛無假說，兩層 OR 無顯著不同。表示 APOE e4 status 與 gender 較不可能有交互作用。

Code：

```
/* homework 10 */
dm "odsresult" clear;
dm "log" clear;
/* import data of sasdataset*/
libname data "\\Mac\Home\Desktop\";

/* q1 : effect-measure modification ,  E1 ( women),  DZ( AD) , stratified by APOE
status*/
title "q1";
    data ad;
        set data.ad_dataset_new;
    run;
    /* Risk difference */
    proc sort data = ad;
        by apo4car sex descending caco;
    run;

    proc freq data = ad order = data;
        tables apo4car * sex * caco / or nocol nopercent cmh;
    run;

    proc iml;
        rr_nonAPOEe4 = 1.3265;
        rr_APOEe4 = 1.2929;
        rr_diff = rr_APOEe4 - rr_nonAPOEe4;

        print rr_nonAPOEe4 rr_APOEe4 rr_diff;
    run;
    /* Rate difference */
        proc iml;
        rr_nonAPOEe4 = 1.3265;
        rr_APOEe4 = 1.2929;
        rr_ratio = rr_APOEe4 / rr_nonAPOEe4;

        print rr_nonAPOEe4 rr_APOEe4 rr_ratio;
    quit;
```

二. **Statistical interaction（adjusted for age , years of education）**

(一) RR of gender and APOE e4 status and both

1. Result：

   (1) RR of APOE e4 status alone：3.495 (95% CI ：1.907 – 6.406)

   (2) RR of gender alone：1.326 (95% CI ：0.889 – 1.979)

   (3) RR of both APOE e4 status and gender： 4.518 (95% CI : 2.720 – 7.504)

2. Figure：

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
group A vs U	1.326	0.889	1.979
group AB vs U	4.518	2.720	7.504
group B vs U	3.495	1.907	6.406

3. Descriptions：

	Men (A′)	Women (A)
Non APOE e4 carrier (B′)	RR_U	RR_A
APOE e4 carrier (B)	RR_B	RR_{AB}

   (1) $RR_A / RR_U = 1.326$，單純 gender 這個變項的 RR 為 1.326。

   (2) $RR_B / RR_U = 3.495$，單純 APOE status 的 RR 為 3.495。

   (3) 若不存在統計上的交互作用，則 RR_{AB} 應為 $RR_A \times RR_B = 4.634$。而 RR_{AB} = 4.518。兩者差異不大，叫不可能有統計上的交互作用

(二) Create a product interaction term (apo4car * sex) and run a logistic regression model：

1. Figures：

Analysis of Maximum Likelihood Estimates					
Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	-0.6506	0.1346	23.3639	<.0001
apo4car	1	1.2259	0.2480	24.4274	<.0001
sex	1	-0.2823	0.2043	1.9093	0.1670
apo4car*sex	1	0.0254	0.3964	0.0041	0.9489

Analysis of Maximum Likelihood Estimates						
Parameter			DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept			1	-11.8578	1.5004	62.4590	<.0001
apo4car	1		1	1.6761	0.3926	18.2293	<.0001
sex	0		1	0.0938	0.2698	0.1209	0.7281
apo4car*sex	1	0	1	-0.2464	0.5000	0.2428	0.6222
age			1	0.1725	0.0190	82.8772	<.0001

2. Descriptions：

(1) 在加入 age, education year 這兩個變項前，apo4car * sex 這個 interaction term 的 p-value 為 0.9489，未達統計上顯著。

(2) 加入 age, education year 這兩個變項後，這個 interaction term 的 p-value 為 0.6222，依然未達統計上的顯著。

(3) 表示 APOE e4 status 與 sex 沒有統計上的交互作用。

(三) Code：

```
/* q2 : statistical interaction, Logistic regression */
    title "q2";
    data q2;
        set ad;
        if apo4car = 1 and sex = 0 then group = "AB";
        else if apo4car = 1 and sex = 1 then group = "B";
        else if apo4car = 0 and sex = 0 then group = "A" ;
        else if apo4car = 0 and sex = 1 then group = "U";
    run;
    proc print data = q2;
        var apo4car sex group;
    run;

    proc logistic data = q2;
        class group (ref = "U") / param = ref;
        model caco (event = "1") = group;
    run;

    proc iml;
        rr_a = 1.326;
        rr_b = 3.495;
        rr_ab = 4.518;
        diff = rr_ab - (rr_a * rr_b);
        percent_diff = abs(diff) / rr_ab;

        print rr_a rr_b rr_ab diff percent_diff;
    quit;

    /* unadjusted model */
    proc logistic data = q2;
        class group (ref = "U") / param = ref;
        model caco ( event = "1") = apo4car sex apo4car * sex;
    run;

    /* adjusted model */
    proc logistic data = q2;
        class apo4car (ref = "0") sex ( ref = "1") / param = ref;
        model caco (event =  "1") = apo4car sex apo4car * sex age eduyr;
    run;

    proc logistic data = q2;
        class apo4car (ref = "0") sex ( ref = "1") / param = glm;
        model caco (event =  "1") = apo4car sex apo4car * sex;
        lsmeans apo4car * sex / diff oddsratio;
    run;
```

三. Biological interaction

(一) $((RR_{AB}-1)-(RR_A-1)-(RR_B-1)\neq 0$

1. Result：

   (1) $(RR_{AB}-1)-(RR_A-1)-(RR_B-1)=0.697$

   (2) $\frac{(RR_{AB}-1)-(RR_A-1)+(RR_B-1)}{RR_{AB}}=15.43\%$

2. Figure：

rr_a	rr_b	rr_ab	diff	percent_diff
1.326	3.495	4.518	0.697	0.1542718

3. Descriptions：

	Men (A′)	Women (A)
Non APOE e4 carrier (B′)	$RR_U = 1$	$RR_A = 1.326$
APOE e4 carrier (B)	$RR_B = 3.495$	$RR_{AB} = 4.518$

   (1) 若 biological interaction 不存在，則$(RR_{AB}-1)-(RR_A-1)-(RR_B-1)=0$

   (2) 本題上式相減為 0.697，佔 RR_{AB} 的 15.43%。代表有 15.43% 的 case 是因為生物交互作用而產生。

(二) Statistical interaction ←→ biological interaction ：

1. 若沒有 statistical interaction，則 RR_{AB} 應為 4.634。
2. 若沒有 biological interaction，則 RR_{AB} 應為 3.785。
3. 3.785 (no biological interaction) < 4.515 (observed) < 4.634 (no statistical interaction)，代表生物交互作用與統計交互作用的影響方向是反向的。
4. 首先，是否具有生物交互作用，取決於其生理機轉及生物的本質。在本題中，APOE status 與性別之間的交互作用不一定單純地符合相加效應，而可能有更複雜的機轉。是故本題計算生物交互用的方向及大小，不一定可真實反應其兩變項生理機轉的本質。
5. 此外，統計的交互作用是否存在取決於模型的選擇，本題之模型為羅吉斯回歸，兩變項是否具有統計交互作用視其是否偏離相乘效應而定。受限於資料樣態和格式，羅吉斯回歸或為本題最適合的模型，然而此模型不一定可真實反應兩變項與 AD 的關係。

(三) Code：

```
/* q3 : biological interaction */
title "q3" ;
proc iml;
    rr_a = 1.326;
    rr_b = 3.495;
```

```
    rr_ab = 4.518;
    diff = (rr_ab - 1) - ((rr_a - 1) + (rr_b - 1));
    percent_diff = abs(diff) / rr_ab;

    print rr_a rr_b rr_ab diff percent_diff;
quit;
```