※ 注意：請於答案卷上依序作答，並應註明作答之大題（部份）及其題號。

Please **answer** the following **questions in order.** Good Luck.

A. Read the following text and then please answer the questions (30 分)：

To examine the relation between recreational physical activity before and during pregnancy and risk of gestational diabetes mellitus, a group of researchers conducted the following study.

Study Population.

The population for the present analysis was drawn from participants of an ongoing study in the U.S.A. Women eligible for inclusion were those who initiated prenatal care prior to 16 weeks of gestation. Women were ineligible if they were younger than 18 years of age, did not speak and read English, did not plan to carry the pregnancy to term, and/or did not plan to deliver at either of the two research hospitals. Enrolled participants were asked to take part in a 45–60-minute interview in which trained research personnel used a structured questionnaire to elicit information regarding maternal sociodemographic characteristics, lifestyle habits, and medical and reproductive histories. In 1996-2000, 1,219 eligible women were approached, and 1,000 (approximately 82 percent) agreed to participate. Thirty-six women who were lost to follow-up (moved, delivered elsewhere, records not found, etc.) were excluded from the analysis. Also excluded were women who experienced a spontaneous ($n = 25$) or induced ($n = 6$) abortion, those for whom glucose tolerance test data were missing ($n = 3$), those with preexisting diabetes mellitus ($n = 6$), and those for whom physical activity data were incomplete ($n = 15$). Hence, a cohort of 909 women remained for analysis.

Exposure Assessment.

Maternal recreational physical activity status was assessed for two periods: during the year before pregnancy and during the index pregnancy. **Three types of measurements** for recreational physical activity were used in this study: 1) women were categorized into two groups (not active and active) with respect to participation in any recreational physical activity during each assessment period; 2) amount of time engaged in recreational physical activities; and 3) energy expended during the performance of those activities.

Outcome Assessment.

Maternal and infant medical records were reviewed approximately 7–9 months after participants were enrolled in the study to collect detailed information concerning antepartum, labor, and delivery characteristics as well as conditions of the newborn.

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Women were classified as having gestational diabetes mellitus if two or more of the following plasma glucose concentrations obtained during the 100-g, 3-hour oral glucose tolerance test were abnormal according to National Diabetes Data Group criteria: fasting, ≥105 mg/dl; 1-hour, ≥190 mg/dl; 2-hour, ≥165 mg/dl; 3-hour, ≥145 mg/dl. Women in this cohort underwent routine screening for diabetes between 24 and 28 weeks of gestation.

Major Findings.

Compared with inactive women, women who participated in any physical activity during the year before experienced a 56% risk reduction (adjusted relative risk (RR) = 0.44, 95% confidence interval (CI): 0.21, 0.91). Women spending ≥4.2 hours/week engaged in physical activity experienced a 76% reduction in gestational diabetes mellitus risk (adjusted RR = 0.24, 95% CI: 0.10, 0.64), and those expending ≥21.1 metabolic equivalent-hours/week experienced a 74% reduction (adjusted RR = 0.26, 95% CI: 0.10, 0.65) compared with inactive women. Physical activity during pregnancy was also associated with reductions in gestational diabetes mellitus risk. Women who engaged in physical activity during both time periods experienced a 69% reduced risk (adjusted RR = 0.31, 95% CI: 0.12, 0.79).

Questions:

1. What is the **design** of this **study**? What are its **strengths** and **weaknesses** in this **context**? (10 分)

2. How many **subjects** who were eligible and agreed to participate in the initial study were **deleted** from this analysis? Why? (5 分)

3. The following covariates were considered as possible confounders in this analysis: maternal age, race, parity, smoking during pregnancy, first-degree family history of type 2 diabetes, prepregnancy adiposity, and annual household income. To obtain a RR estimate with adjustment for these potential confounders, what kind of **statistical analysis** would you recommend? **Why**? (10 分)

4. What are the **conclusions** that can be drawn from these results? (5 分)

B. 某研究人員擬以下列四種方法探討飲食中微量元素和肺癌發生的關係 (30分)：

第一種：選擇臺灣地區 300 個鄉鎮，每個鄉鎮隨機選取 100 名 40-60 歲居民，抽血並做血清中各種微量元素濃度分析，再以每個鄉鎮居民血清微量元素濃度之平均值和各鄉鎮肺癌發生率作相關性分析。

第二種：選擇某大醫院 2000-2004 年間肺癌住院病例 500 名，對每名病例，選取 2 名年齡、性別和居住地區配對的社區健康對照個案總計 1000 名。對所有個案進行問卷調查，並比較病例組和對照組血清微量元素濃度平均值之差異，同時將血清濃度分成高、中、低三組，分析病例組和對照組分佈是否不同。

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第三種：利用臺灣地區 1997 年對 40 歲以上成人健檢所收集的十萬人血液檢體，建立血清檢體庫，同時以健檢問卷資料聯結全國癌症和死亡登記電腦檔案，追蹤這十萬人自 1997 年進入研究到 2004 年間肺癌發生或死亡的情形，結果有 150 名研究個案發生或死於肺癌。對每名病例，由這十萬人中未發生肺癌者中選取 2 名年齡、性別配對的對照個案，再取出病例和對照組 1997 年凍存的血液檢體，分析病例組和對照組血清微量元素濃度平均值之差異，並將血清濃度分成高、中、低三組，分析病例組和對照組分佈是否不同。

第四種：利用臺灣地區 1997 年對 40 歲以上成人健檢所收集的十萬人血液檢體，進行血中各種微量元素濃度分析，每年再以健檢問卷資料聯結全國癌症和死亡登記電腦檔案，追蹤這十萬人自 1997 年進入研究到 2004 年間肺癌發生或死亡的情形，結果有 150 名研究個案發生肺癌，再進行各種統計分析探討血清微量元素濃度和肺癌的關係。

請回答：

(1) 這四種方法各是何種研究設計？(4 分)

(2) 利用這四種方法各可求得何種流行病學指標，包括：暴露率、各種疾病率、相對和相差危險性指標，這些指標如何解釋或代表什麼意義？(10 分)

(3) 這四種方法探討此研究主題各自容易產生何種偏差？為什麼？(8 分)

(4) 這四種方法相比，探討此研究主題各有何優缺點？為什麼？(8 分)

C. 某研究者欲探討抽煙與肺癌間相對危險性(relative risk)大小。他（她）進行了一個很大的世代追蹤研究（共有 N 人，每人皆追蹤一年）。試問(30 分)：

1. 假如追蹤世代中，男性佔了 p 比率，女性佔了 1-p 比率。男性抽煙的比率為 q_1，女性抽煙的比率為 q_2。試分別算出該世代中男抽、男不抽、女抽及女不抽等四種人的人數。(5 分)

2. 承第 1.小題，假設女性不抽煙者的肺癌死亡率為 M；不論在抽煙者或不抽煙者中，男性比女性得肺癌的相對危險性皆為 RR_S；不論男性或女性，抽煙得肺癌的相對危險性皆為 RR_E。試分別算出男抽、男不抽、女抽、及女不抽的肺癌死亡人數。(5 分)

3. 該研究者若未調整性別，那麼他（她）得到抽煙與肺癌的粗相對危險性(crude relative risk，記為 RR_E^*)為何？（5 分）

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4. 定義 CRR(**confounding risk ratio**) $= \frac{RR_E^*}{RR_E}$。請問 CRR 如何闡釋？（比如其值若為 **1.3** 代表何意？若為 **0.6** 代表何意？）（5 分）

5. 當 $\mathbf{RR_S = 1}$ 時，**CRR** 為何？當 $q_1 = q_2$ 時，**CRR** 為何？（5 分）

6. 從第 5 小題的分析，您得到什麼結論？（5 分）

D. Surveillance of infectious disease becomes more important in emerging infectious diseases. Would you please write down the key approaches in **surveillance** that you would like to **decrease** the **incidence** of **high risk populations** for **two diseases selected** from the severe acute respiratory syndrome (**SARS**) or **avian influenza** or **mad cow** disease（10 分）