單選題 （每小題2分共26分）

1. 某研究想要瞭解C型肝炎病毒（hepatitis C virus；HCV）感染和發生肝癌的關係，利用台灣地區368鄉鎮各鄉鎮成人健檢所獲得HCV血清標記陽性率和各鄉鎮近三年肝癌平均發生率進行相關性分析，根據此敘述，請回答以下問題：

(a)此研究設計為：(A) 病例對照研究(case-control study)(B)病例世代研究(case-cohort study) (C) 世代研究 (cohort study) (D)生態相關性研究 (ecological correlation study)

(b)在進行HCV和肝癌發生率相關性分析之前，你需要以下何種資料：(A)全台灣人口男女比例 (B) 各鄉鎮人口結構（即各年齡層所佔總人口比例）(C)世界標準人口結構（即世界人口各年齡層所佔總人口比例）(D)世界肝癌年齡標準化發生率 (age-standardized liver cancer incidence rate)

(c)相關係數(correlation coefficient)分析結果為0.5 ($p<0.01$)則推論：(A)HCV可能會導致肝癌發生 (B) HCV可能不會導致肝癌發生 (C) 肝癌發生率在不同地理區域的變化可能和各鄉鎮HCV陽性率的差異有關 (D) 肝癌發生率在不同地理區域的變化可能和各鄉鎮HCV陽性率的差異無關

(d)此研究在因果相關的判斷上容易產生以下何種偏差：(A) 干擾作用 (confounding effect) (B) 時序偏差 (temporal bias) (C) 生態謬誤 (ecological fallacy) (D)以上皆是

2. 某研究者在2014年欲探討糖尿病和罹患冠心病危險性的關係，選擇北部三家大型醫院為個案來源，經由病歷資料選定1990年診斷為糖尿病但無冠心病的病人，以及無糖尿病亦無冠心病的病人作為研究個案，並利用病歷記載，分析比較糖尿病病人和非糖尿病病人24年來的冠心病罹病狀況，根據此敘述，請回答以下問題：

(a)此研究可獲得以下何種流行病學指標：(A)糖尿病盛行率 (prevalence) (B) 糖尿病和冠心病的相對危險性 (C) 冠心病的累積發生率 (D)以上皆是

(b)此研究設計是：(A)病例對照研究(case-control study)(B)回溯世代研究(retrospective cohort study) (C)橫斷研究 (cross-sectional study) (D) 前瞻式世代研究 (prospective cohort study)

(c)此研究在因果相關的判斷上容易產生以下何種偏差：(A) 干擾作用 (confounding effect) (B) 時序偏差 (temporal bias) (C) 生態謬誤 (ecological fallacy) (D)以上皆是

3. 擬在社區進行30歲以上成年人大腸癌篩檢，篩檢的敏感度 (sensitivity) 為0.8，特異度 (specificity) 為0.8，估計一般30歲以上成年人的大腸癌比率2 per 10000 (2/10000)，根據以上數據回答下列問題：

(a) 陽性預測值(positive predictive value)為：(A) 0.0008 (B) 0.64 (C) 0.80 (D) 0.08

(b) 以上所獲得的陽性預測值反映：(A) 篩檢效度(validity)良好 (B) 篩檢成效(yielding)良好 (C) 篩檢效度(validity)不好 (D) 篩檢成效(yielding)不好

(c) 若要增進篩檢計畫效能 (cost-effectiveness)，首先你會如何建議：(A) 建議篩檢條件為50歲以上的中老年人 (B) 透過媒體加強全民篩檢預防大腸癌觀念 (C) 建立多家醫學中心大規模大腸內視鏡檢查系統 (D) 以上皆是

見背面

4. 已知某病原在我國的 Ro(基礎再生數)值為 3，針對該病原的疫苗在全國民眾的施打覆蓋率為 80%，但只有 80%的疫苗者可產生足夠抗體效價使其免疫。請問此病的有效再生數(effective reproductive number)為？

(A) 3.0

(B) 2.4

(C) 1.9

(D) 1.1

5. 以下哪個因子不會影響有效再生數 effective reproductive number (Re) ？

(A) 潛伏期(latent period)長短

(B) 族群中易感受(susceptible)人口的比例

(C) 人與人之間的接觸頻率

(D) 可傳染期長短

6. 關於干擾因子以及修飾因子的敘述，以下何者正確？

(A) 世代研究中的配對(matching)可以避免干擾因子以及修飾因子的發生

(B) 當疾病的危險因子在暴露族群與非暴露族群當中的分布情形一致時，不會發生干擾或是修飾現象

(C) 當我們研究特定暴露與疾病的相關性時，某個因子可能同時為干擾因子以及修飾因子

(D) 以上皆不正確

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7. 題組:請閱讀下列期刊文章摘要與圖表後回答下列問題

The Lancet Infectious Diseases, Volume 13, Issue 1, Pages 36 - 42, January 2013

Assessment of the Xpert MTB/RIF assay for diagnosis of tuberculosis with gastric lavage aspirates in children in sub-Saharan Africa: a prospective descriptive study

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Summary

Background

Rapid and accurate diagnosis of pulmonary tuberculosis in children remains challenging because of difficulties in obtaining sputum samples and the paucibacillary nature of the disease. The Xpert MTB/RIF assay is useful for rapid diagnosis of childhood tuberculosis with sputum and nasopharyngeal samples. We assessed this assay for the detection of tuberculosis and multidrug resistant (MDR) tuberculosis with gastric lavage aspirate (GLA) samples in children admitted to hospital.

Methods

We did a prospective study to assess the sensitivity and specificity of the Xpert MTB/RIF assay with GLA samples for the detection of pulmonary tuberculosis and MDR tuberculosis in new paediatric inpatient admissions at the University Teaching Hospital, Lusaka, Zambia. Children aged 15 years or younger were recruited between June, 2011, and May, 2012. GLA and sputum were analysed by standard smear-microscopy, mycobacterial growth indicator tube (MGIT) culture, MGIT drug-susceptibility testing, and the Xpert MTB/RIF assay. Sensitivity of the Xpert MTB/RIF assay was assessed with the Pearson x^2 or Fishers exact test.

Findings

Of 930 children, 142 produced sputum and GLA was obtained from 788 non-sputum producers. Culture-positive tuberculosis was identified in 58 (6·2%) of 930 children: ten from sputum producers and 48 from GLA of non-sputum producers. The sensitivity and specificity of the Xpert MTB/RIF assay were similar: sensitivity was 68·8% (95% CI 53·6—80·9) for GLA versus 90·0% (54·1—99·5; p=0·1649) for sputum samples; specificity was 99·3% (98·3—99·8) for GLA and 98·5% (94·1—99·7; p=0·2871) for sputum samples. The Xpert MTB/RIF assay detected an extra 28 tuberculosis cases compared with smear microscopy and was significantly more sensitive than smear microscopy for both sputum (90·0% [54·1—99·5] *vs* 30·0% [8·1—64·6], p=0·01) and GLA (68·8% [53·6—80·9] *vs* 25·0% [14·1—40·0], p<0·0001). The assay load did not differ significantly by sample type (p=0·791). 22 children were infected with HIV and tuberculosis and significant differences in assay performance could not be detected when stratifying by HIV status for either sample type. The Xpert MTB/RIF assay detected rifampicin resistance in three GLA samples: two confirmed as MDR tuberculosis and one false positive.

Interpretation

Analyses of GLA samples with the Xpert MTB/RIF assay is a sensitive and specific method for rapid diagnosis of pulmonary tuberculosis in children who cannot produce sputum. The single site nature of our study invites caution.

Table 2
Specificity and sensitivity of the Xpert MTB/RIF assay and smear microscopy versus culture in sputum and GLA samples

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Sensitivity (smear positive)	Sensitivity (smear negative)
Xpert MTB/RIF assay vs culture						
Sputum	9/10 (90·0%; 54·1–99·5)*	130/132 (98·5%; 94·1–99·7)	81·8% (47·8–96·8)	99·2% (95·2–100·0)	3/3 (100%; 31·0–100·0)	6/7 (85·7%; 42·0–99·2)
HIV positive	6/6 (100%; 51·7–100·0)	38/38 (100%; 88·6–100·0)	100% (0·52–100·0)	100% (88·6–100·0)	2/2 (100%; 20·100·0)	4/4 (100% 39·6–100·0)
HIV negative	3/4 (75·0%; 21·9–98·7)	84/86 (97·7%; 91·1–99·6)	60% (17·0–92·7)	98·8% (92·7–100·0)	1/1 (100%; 5·5–100)	2/3 (66·7%; 12·5–98·2)
Gastric lavage aspirate	33/48 (68·8%; 53·6–80·9)*†	735/740 (99·3%; 98·3–99·8)	86·8% (71·1–95·1)	98·0% (96·6–98·9)	11/12 (91·7%; 59·7–99·6)‡	22/36 (61·1%; 43·5–76·4)‡
HIV positive	10/16 (62·5%; 35·9–83·7)	217/219 (99·1%; 96·3–99·8)	83·3% (50·9–97·1)	97·3% (94·0–98·9)	5/5 (100%; 46·3–100·0)	5/11 (45·5%; 18·1–75·4)
HIV negative	23/31 (74·2%; 55·1–87·5)	470/473 (99·4%; 98·0–99·8)	88·5% (68·7–97·0)	98·3% (96·6–99·2)	6/7 (85·7%; 42·0–99·2)	17/24 (70·8%; 48·7–86·6)
Gastric lavage aspirate and sputum combined						
<2 years (1·5% sputum)	12/19 (63·2%; 38·6–82·8)	442/443 (99·8%; 98·5–100·0)	92·3% (62·1–99·6)	98·4% (96·7–99·3)	2/2 (100%; 19·8–100·0)	10/17 (58·8%; 33·5–80·6)
2–4 years (4·0% sputum)	12/18 (66·7%; 41·1–85·6)	182/183 (99·4%; 96·5–100·0)	92·3% (62·1–99·6)	96·8% (92·9–98·7)	5/6 (83·3%; 36·5–99·1)	7/12 (58·3%; 28·6–83·5%)
5–9 years (45·2% sputum)	3/6 (50·0%; 13·9–86·1)	115/118 (97·5%; 92·2–99·3)	50·0% (13·9–86·1)	97·5% (92·2–99·3)	1/1 (100%; 5·5–100·0)	2/5 (40%; 7·3–83·0)
10–15 years (50·0% sputum)	15/15 (100%; 74·7–100)	121/123 (98·4%; 93·7–99·7)	88·2% (62·3–97·9)	100% (96·2–100)	6/6 (100%; 51·7–100)	9/9 (100%; 62·9–100)
Smear vs culture						
Sputum	3/10 (30·0%; 8·1–64·6)	125/132 (94·7%; 89·0–97·7)	30% (8·1–64·6)	94·7% (89·0–97·7)	NA	NA
Gastric lavage aspirate	12/48 (25·0%; 14·1–40·0)†	717/740 (96·9%; 95·3–98·0)	34·3% (19·7–52·3)	95·2% (93·4–96·6)	NA	NA
Xpert MTB/RIF assay vs culture drug-susceptibility test						
All patients	2/2 (100%; 19·8–100·0)	38/39 (97·4%; 84·9–99·9)	66·6% (12·5–98·2)	100% (88·6–100·0)	NA	NA

見背面

(a)關於本研究的描述何者正確（4 分）
(A) 在本研究中大部分的兒童都能產生痰液檢體(sputum)而不需要使用到胃灌洗檢體(gastric lavage aspirate)
(B) 本研究發現使用 Xpert MTB/RIF 來檢驗痰液以及胃灌洗兩種不同檢體，其敏感度(sensitivity)在這兩種檢體當中並無統計上顯著差異
(C) 使用 Xpert MTB/RIF 來檢驗胃灌洗檢體，在診斷多重抗藥性結核(MDR tuberculosis)上偽陽性高達 2/3
(D) 以上皆錯誤

(b)若使用 Xpert MTB/RIF 來合併檢驗痰液以及胃灌洗兩種檢體，並且以細菌培養(culture)為標準，就整體族群來看(不作分層)，請問該檢驗的敏感度(sensitivity)與特異度(specificity)為何？(5 分) 陽性預測值與陰性預測值?(5 分)

8.社會上虐童、性侵幼童的事件層出不窮。隨著兒童保護的意識升高，研究者想瞭解（一）這些事件發生的頻率與嚴重程度近年來是否有改變？此外，（二）孩提時候遭遇到此類不良事件，對於孩童日後之行為或情緒問題的發生之影響，亦是時常受到關注的議題。若你是研究者，欲在台灣地區針對這兩大問題進行探討，必須小心規劃適當的研究設計，並進行詳細的測量。請問：

(a) 針對第一個議題，請簡述你將採用何種研究設計與方法（包括樣本之收案與測量工具），並利用哪些 outcome 指標來回答問題。進行此類研究的重要性為？ (10 分)

(b) 針對第二個議題，請簡述你將採用何種研究設計與方法（包括樣本之收案與測量工具），並利用哪些 outcome 指標來回答問題。此外，請簡述在進行結果推論時，你打算執行的研究可能產生的偏差？(10 分)

9.已知利用低劑量電腦斷層掃描針對40歲以上中年人來篩檢肺癌的敏感性是0.2，而其特異性是0.8。假設某研究對一家電子公司的500名40歲以上員工做了低劑量電腦斷層掃描，而肺癌在40歲以上人口的盛行率是4%。請問根據上述資料，研究者預期：
(a)有多少名員工其肺癌篩檢的結果會是陽性？(4分)

(b)其中有多少名員工其肺癌篩檢的結果會是偽陽性？(4分)

(c)有多少名員工其肺癌篩檢的結果會是陰性？(4分)

(d)其中有多少名員工其肺癌篩檢的結果會是偽陰性？(4分)

(e)該研究作者建議使用低劑量電腦斷層掃描在人群中來篩檢肺癌，這樣的結論合適嗎，請說明。(4分)

接次頁

國立臺灣大學 103 學年度碩士班招生考試試題

10. Simple Questions (8 points)

(a) What are differences in epidemiological characteristics of aerosol transmission versus air-borne transmission? You can give solid examples. (4 points)

(b) What are reservoirs for rabies and avian influenza, respectively? (4 points)

11. Thinking Questions (12 points)

(a) One 31-yaer-old surgeon died of H7N9 in Shanghai on January 18, 2014. This doctor had not touched any poultry nor visited to live-bird markets. What are the 3 most important hypotheses you like to ask? What data are you going to collect and which laboratory tests are you going to run? How are you going to do data analyses for better conclusion on which hypothesis is more right (6 points)

(b) A 20-year-old woman with influenza-like illness was confirmed as the world's first pneumonia case caused by low pathogenic avian influenza H6N1 by Taiwan-CDC in May of 2013. This woman lived in central Taiwan, worked as a waitress in a store for delivering dishes of breakfast to customers and getting payment but lacked of known poultry exposure. If you were governmental officials in central Taiwan, what are you going to do? What data would you like to collect and thus help you make better decision? Do you think whether other H6N1 human cases might appear in Taiwan later on? Please write your rationale of thinking for BEST judgment. (6 points)

試題隨卷繳回