行政院國家科學委員會補助專題研究計畫 ■ 成果報告
□期中進度報告

生活品質與醫藥衛生成本效性評估—

環境與職業性危害之比較性風險評估—以吸菸相關之疾病為例〔3/3〕

計畫類別：□個別型計畫　■整合型計畫
計畫編號：NSC 91-2320-B-002-082-M56
執行期間：91 年 8 月 1 日至 92 年 7 月 31 日

計畫主持人：王榮德
共同主持人：姚開屏、劉錦添、謝清麟、郭壽雄、楊銘欽、
詹長權、黃景祥
計畫參與人員：鍾智文、游正芬

成果報告類型(依經費核定清單規定繳交)：□精簡報告　■完整報告

本成果報告包括以下應繳交之附件：
□赴國外出差或研習心得報告一份
□赴大陸地區出差或研習心得報告一份
■出席國際學術會議心得報告及發表之論文各一份
□國際合作研究計畫國外研究報告書一份

處理方式：除產學合作研究計畫、提升產業技術及人才培育研究計畫、列管計畫及下列情形者外，得立即公開查詢
□涉及專利或其他智慧財產權，□一年□二年後可公開查詢

執行單位：國立台灣大學公共衛生學院職業醫學與工業衛生研究所
中　華　民　國　92　年　10　月　31　日

摘要

本研究建立了肺癌、肝癌、中風、急性心肌梗塞、慢性阻塞性肺病等五種與吸菸有關之疾病的疾病世代並完成各疾病之存活分析。其中肺癌與肝癌造成最大之壽命損失，分別為 15.6 年及 18.9 年。以健保資料與吸菸之可歸因風險估計吸菸導致此 5 種疾病之醫療費用，一年約為 26.3 億元。每年由吸菸造成之新增病例的終生醫療成本，總和約為 128 億元。

另針對肺癌病人進行了間接醫療成本與生活品質之調查。綜合交通成本、時間成本、藥品補品的費用等，每一位肺癌病人除了直接之醫療費用（主要健保給付）外，每一年尚有約 62,597 元（男性 58,558 元，女性 65,785 元）之經濟損失。估計終生之經濟損失約 148,284 元（男性 127,506 元，女性 190,247 元）。相較於年直接醫療費用：男性 108,859 元、女性 95,184 元；終生醫療費用：男性 235,240 元、女性 278,634 元。間接疾病成本約為直接醫療成本之 50% 以上。

生活品質之測值也反應了較嚴重之病人的生活品質較差，以生理範疇最為明顯。與一般人之生活品質比較，癌症病患之綜合健康與綜合生活品質評量均較一般人差，癌症期別≧3B 者較期別≦3A 者差。

Abstract

This study has established the cohorts of five smoking related diseases: lung cancer, liver cancer, stroke, acute myocardial infarction (AMI), chronic obstructive pulmonary disease, (COPD). The survival analysis was conducted accordingly. The estimated lost of life for lung cancer is 15.6 years, and it is 18.9 years for liver cancer. Based on data from National Insurance Databank and calculated smoking attributable risk, we have estimated the direct medical cost due to cigarette smoking. The annual smoking attributable medical cost is about NT$2.63 billion for these five diseases altogether, and the estimated lifetime medical cost is about NT$12.8 billion (based on the monetary value of the year 2000).

A questionnaire survey was conducted on lung cancer patients to collect the information regarding indirect cost of illness and quality of life. The annual total indirect cost for a lung cancer patient is about NT$62,597 (male: NT$58,558, female: NT$65,785). Estimated lifetime indirect cost is about NT$148,284 (male: NT$127,506, female: NT$190,247). Comparing to the annual direct medical costs (male: NT$108,859; female: NT$95,184) and estimated lifetime medical costs (male: NT$235,240;; female: NT$278,634), there is a substantial sum of indirect cost for each lung cancer patient.

The overall quality of life for lung cancer patient is worse than that for general population. And, the quality of life for patients with stage $\geqq$ 3B is worse than that for patients with stage $\leqq$ 3A.

目錄

背景與目的

我們在日常生活或工作中可能會暴露於物理、化學、生物性等多重的環境危害，再加上個人生活行為（如吸菸、喝酒）的交互作用，則對身體的健康可能產生不同程度之傷害。比較健康風險評估（Comparative health risk assessment）乃是探討不同環境危害狀況與個人行為因子的組合所造成之健康傷害的程度及差異，其結果可協助我們制訂危害控管與預防策略的優先順序。然而在實際應用時，除了因病死亡或意外事故造成立即性傷害所導致的死亡或永久殘障可直接比較其健康效應外，其他有關的健康效應，因為欠缺健康計量的基本單位，往往無法直接比較。加上環境與職業性之健康傷害，需很長的時間才會造成可見的健康傷害，因此比較風險評估在職業與環境衛生方面之實用性就大受限制。此外各種毒性化學物質進入人體後，所引起之健康效應如果牽涉到的器官系統不同，亦無法直接比較，且很難分辨各毒物之相對毒性。近年來由於健康相關生活品質（Health-Related Quality of Life，HRQL）的觀念所衍生出來的健康測量基本單位，如「調整品質後人年」（Quality-Adjusted Life Year，QALY）已漸成熟，並被運用到總體健康政策與臨床決策的研究上。本研究將以這些研發的成果為基礎，將生活品質與成本效性評估之概念與方法引進環境風險評估中。

在眾多的環境與職業醫學領域中，我們將選擇以吸菸導致的疾病為例，來進行研究。呼吸系統是人體接受環境性與職業性危害物質的主要途徑，此與吸菸相似。與吸菸有關之疾病（如肺癌）也是主要的環境病與職業病之一。從公共衛生的角度看（Grievink 1988, Spengler and Wilson 1996, National Research Council 1983, Levy and Wegman 1983, Edward et al. 1991, National Research Council 1989），呼吸系統相關疾病（如肺癌、肺炎、支氣管炎支氣管炎、肺氣腫氣喘及結核病....等）每年約佔國人死亡人數的百分之十。因此這些呼吸系疾病總體健康損失的估計是一項極為重要的公共衛生議題。此外這類疾病的病因不論是環境性或職業性的（National Research Council 1986; U.S. Department of Health and Human Services 1984, 1985, 1990），相對於其他疾病都有病因較確定，暴露人群廣及具備完整的預防方式的特質，因此是值得積極介入並易於達到預防成效的疾病。

本研究之主要目標在比較引起主要呼吸系統相關疾病(如肺癌)的環境與職業性因子（如吸菸）的相對健康風險大小。並希望將研究方法推廣到其他環境與職業疾病與危害之評估。

文獻探討

吸菸會導致許多疾病已是公認之事實，一個由美國、芬蘭、日本等 7 國經 25 年追蹤之研究結果，發現一天抽 10 支菸者較之於不吸菸者之死亡率增加 30% （所有死因總和，all-causes），一天抽 20 支菸者則增加 80% 。若針對肺癌、其他癌症、中風、心臟血管疾病、慢性阻塞性肺病等疾病則死亡率增加更多。該研究也發現這樣之結果並不會因為不同的文化而有所差異，亦即是各國普遍之現象（Jacobs et al. 1999）。

在美國吸菸所造成之直接醫療花費約佔整體醫療費用之 5-8%（Miller et al. 1999, Warner et al. 1999, Zhang et al. 1999）。吸菸除了直接傷害吸菸者之健康外，也導致吸菸者之缺勤或早逝，間接造成生產力之降低或喪失。同時吸菸也可能引起火災，而造成財務之損失。此外經由二手菸，吸菸者之家人與同事等之健康亦受到威脅。因此菸害一直是各國重視之問題，而估計戒菸帶來之利益亦遠高於推動戒菸之成本(Parrott et al. 2000)。同時，經由課徵菸稅來達到抑制吸菸人口之增加、以稅款推動戒菸措施或補助相關之醫療費用等，均為各界長期關切之議題(Galbraith and Kaiserman, 1997; Warner, et al. 1995, Guindon et al. 2002)。

我國之男性吸菸盛行率一向偏高，李蘭與潘怜燕（2000）在 1999 年全國性之調查研究顯示，男女性之吸菸盛行率分別為 47.29% 和 5.23% 。第一次吸菸之年齡大多在 18 至 20 歲之間。男性之吸菸率在近年來是下降的，而女性反呈現上昇趨勢。一個本國 12 年之追蹤研究顯示，男女性吸菸者較之不吸菸者而言死於肺癌之相對風險為 3.7 和 3.6，總死因之相對風險則為 1.3 和 1.8。男性總死亡人數之 13.9% 可歸因於吸菸，而女性總死亡人數之 3.3% 為吸菸所造成（Liaw and Chen, 1998）。因此吸菸對本國人民之健康造成極大之傷害。依據行政院主計處公告之國情統計通報，在 2000 年底健保的納保率約為 96.2% ，因此可以相信目前之納保率將更高，所以吸菸造成之醫療成本將主要由健保來支付，無形中也增加健保之負擔。但是本國有關吸菸造成之經濟成本尚未有完整之研究，因此難以顯示菸害之程度。所以當務之急乃建立一套評估方法並實際估計與吸菸相關之疾病成本，作為推動戒菸措施或菸稅之資源運用的參考。

研究方法

醫療衛生之經濟評估乃為以經濟之理論為基礎對醫療衛生之成本加以估計，為了要以量化的方式來表達經濟評估的結果，通常以貨幣化價值作為經濟評估之基本單位。

評估疾病所造成之成本或損失常用的方法有假設市場評價法（contingent valuation method）及罹病成本法（cost-of-illness）。假設市場評價法根據福利經濟學理論，以在不同的假設狀況下（如不同治療方法或死亡率等），探討受訪者為維持個人效用（如健康等）或避免效用降低所願意支付的最高價格（willingness to pay），或願意降低效用所接受之最低補償金額（willingness to accept），再依此估計健康的價值或疾病之成本。罹病成本之估計方法則是比較直覺的方式，將疾病可能造成之所有金錢及時間等之損失換算成貨幣，再加總起來以估算該疾病之成本。其中有關金錢之花費資料可經由患者本人、陪伴者、有關之醫療機構及健保體系取得，可直接以貨幣價值表示。時間成本則依據患者本人及陪伴者提供的時間損失量，再乘以患者本人及陪伴者每單位時間之平均收入，其乘積即為時間成本。本研究乃是以罹病成本法來估算與吸菸有關之疾病所造成的經濟成本。

疾病所造成的成本或損失，一般可分為直接成本（direct costs）、間接成本（indirect costs）、無形成本（intangible costs） [Rice et al, 1985] 及其他可能之成本等。由於無形成本及其他可能之成本較難以貨幣量來進行估計，因此一般在估計疾病成本時往往僅計算直接及間接成本。因此，一般經濟學家認為它低估了疾病之成本，且所估之價值大約是用願付法估計出來之下限。但是由於此法估計較快且再現性高，故仍是公共衛生學者愛用的方法 [Kenkel, 1994]。

直接成本包含了患者個人醫療的費用如診斷、治療、照護、復健、臨終的照護等、以及其他非醫療之費用。此外就整個醫藥衛生體系而言，疾病成本尚包含研究、教育訓練、建築、行政等，不論是公私單位或保險機構之成本，這些成本都可能被忽略而沒有直接反應到醫療費用[Hodgson, 1982]。直接成本的醫療費用資料可由醫療機構或健保單位取得。其他的醫療相關花費資料則可由病人或其家屬之問卷調查獲得。

間接成本主要包括患者本人就醫之交通費、陪伴者之交通費、患者門診或住院時之時間成本、陪伴者陪患者就醫之時間成本、聘僱看護照顧患者之費用等。間接成本中之時間成本，一般以換算為生產力損失來表示，再換算為貨幣價值來推估成本，所謂生產力的貨幣價值通常以收入來表示。所以患者因疾病而缺勤、失能、早逝等所造成的生產力損失，以及病人的主要照護者因照顧病人而導致之生產力損失，均可以貨幣價值來表示，這種估計生命或健康健康之方法稱為人力資本法（Human capital approach）。而患者之生產力損失又分為罹病成本（morbidity costs）及死亡成本（mortality costs）。罹病成本係指因罹患疾病而導致暫時或永久的生產力降低或喪失；

死亡成本乃因早逝而導致之生產力的喪失。

由於疾病本身或診斷治療過程，往往造成患者身體之疼痛、難受不適，或因為疾病使身體某些功能喪失或殘障，進而引起患者心理精神的痛苦、悲傷，也導致須依賴他人、親情友誼之困擾、人際關係的疏離、遭受歧視等不愉快的感受與情緒的低落等等。我們將這些問題歸類為無形成本，相較於直接或間接成本，無形成本較不易量測與量化，也不易貨幣化，因此在估計疾病成本時，往往被忽略。由於生活品質測量方法的逐漸發展與廣泛的被運用到無形成本之研究，本研究也進行了肺癌病患之生活品質的探討。

間接成本的生產力損失乃以人力資本法（human capital method）估計，即是將個人視為社會資產，其在勞動市場中具有生產價值，以其收入來代表其生產力，因此依照一定公式計算個人在一段期間之薪資所得，並以之表示其對社會之貢獻。基本之做法將醫療花費視為直接的罹病成本，因疾病或早逝造成收入之減少被視為間接之罹病成本，如此增進健康或避免早逝所帶來之價值就是這些可以減少的直接及間接罹病成本之總合。也就是可以避免之損害。

人力資本法基本上將人視為貨幣生產者，那麼人的預期生命價值即是個人終身所能賺取的金錢（Rice 1985）。因此疾病所造成之生產力損失，就是因疾病而少賺的金錢。Rice 與 Cooper (1967) 以下列七個假設為基礎，提出人力資本法的方法論：

(1) 預期餘命 (life expectancy)：例如以 1964 年之平均餘命為標準；
(2) 勞動力參與（labor force participation）：個人未來的勞動力與生產力和 1965 年情形相同；
(3) 所得（earning）：以估計之平均所得衡量個人的產出；
(4) 家庭主婦之勞務（housewife services）：以國內勞務者平均所得估計之；
(5) 折現（discount）：假設折現率為 4%；
(6) 生產力增加（Productivity increase）：來自生產力的所得時間增加而調整；
(7) 消費津貼（the allowance for consumption）：由於個人本身亦須消費，所得不可能完全提供社會，故個人給予他人的產出小於所得的總產出。

疾病所造成之生產力損失，一般只計算預期終生薪資損失，其公式如下：

$$L_1 = \sum_{t=d}^{\infty} Yt\, P_d^t\, (1+r)^{-(t-d)}$$

其中，Yt 為個人在 t 年預期之所得毛額，但不包含非人力資本之所得，
Pt 為由當期（或 d 年）活至 t 年的機率；r 為折現率。

「人力資本法」之優點在於計算較方便，所計算的值較為直接，其缺點為：對於退休者、家庭主婦(夫)、失業或待業者、未開始工作之小孩的生命價值被視為零，或是相當低，此假設並不合理；當薪資估計不能反映真正的能力或勞力市場之價格並非完全符合自由經濟之情形下，造成高估或低估生命之價值；對於疾病或死亡所帶來的痛苦(肉體或精神)與病患個人及他人之苦難等均不予估計故會低估了生命或健康的價值。

嘗試以生活品質來探究無形成本，Klastersky 與 Paesmans（2001）經回顧許多有關化學治療與進行性非小細胞肺癌(advanced non-small-cell lung cancer, NSCLC)患者之存活與生活品質的研究，認為生活品質不失為評估新治療法的良好之輔助工具。我們以本研究團隊發展之世界衛生組織生活品質問卷之台灣簡明版（WHOQOL-BREF）為研究工具，來探討肺癌病患之生活品質。

執行方法

吸菸造成之直接疾病成本（醫療費用）

由於吸菸會導致許多不同之疾病，若僅考慮呼吸系統疾病之菸害成本時，會嚴重低估吸菸所造成之損失。因此我們以 5 種與吸菸相關之主要疾病：肺癌（Lung Cancer），肝癌（Liver Cancer）、中風（Stroke）、急性心肌梗塞（Acute Myocardial Infarction, AMI）、慢性阻塞性肺病（Chronic Obstructive Pulmonary Disease, COPD），來估計吸菸造成之醫療成本。以回溯方式從台大醫院之病歷中建立這些疾病之疾病世代，肺癌與肝癌回溯 5 年、中風回溯 6 年、急性心肌梗塞與慢性阻塞性肺病回溯 10 年，各疾病世代追蹤截止時間均為 2000 年（表 1）。將這些疾病世代與衛生署及財政部之死亡資料庫結合，以本研究團隊成員所發展之方法，進行存活分析，可得到各疾病之男女病患的存活曲線，作為後續計算終生成本之基礎。

以 2000 年健保資料庫之資料統計出各疾病之住院與門診費用，其中肺癌與肝癌之費用由癌症資料檔計算，中風費用由重大傷病資料檔計算，急性心肌梗塞與慢性阻塞性肺病費用則由承保抽樣歸人檔計算。癌症資料檔與重大傷病資料檔為完整資料，涵蓋所有申報個案。抽樣歸人檔為全國資料中分層隨機抽樣 20 萬人之資料，因此估算之病例個案數需再參考當年之人口數來估計全國之病例數。由上述之方法得到 2000 年各疾病之男性與女性的病例數、每一病例的平均年門診費用與年住院費用。可求出每一疾病全體男女性病患之總醫療費用，也可以每一個案的醫療花費與前述之存活曲線結合估計出每一病例的預期終生醫療費用。

估計吸菸造成之醫療成本，需先計算吸菸之可歸因風險（population attributable risk, PAR）。本國人口中由吸菸所造成之可歸因風險可由吸菸盛行率及吸菸之相對風險來估計，其計算公式如下：

$$PAR = \frac{P(RR-1)}{P(RR-1)+1}$$

P：吸菸盛行率（以 1990 年資料，男性：0.628, 女性：0.051）

RR: 吸菸導致疾病死亡之相對風險（Liaw and Chen, 1998； Lee, et al., 1995）

考慮需長時期吸菸才會導致疾病，因此以 1990 年的吸菸盛行率作為估計之依據。由可歸因風險與前述之醫療費用計算結果結合，估計吸菸每一年造成之醫療成本，及吸菸每一年導致之新增病例的總終生醫療成本。

終生直接醫療成本之估計

仿造前述人力資本法之終生薪資估計公式，則疾病之終生醫療成本可由下列之公式估計：

$$\mathrm{PVC} = \sum_{n=l}^{T^i_{l,s}} P^i_{l,s}(n)\,\mathrm{DC}^i_{l,s}(n-l+1)\left(\frac{1+m}{1+r}\right)^{n-l}$$

PVC = 以目前幣值表示之終生總直接成本

n = 個案當時年齡

l = 個案罹病年齡

$P^i_{l,S}(n)$ = 性別為 s 且在 l 歲罹病，至 n 歲仍存活之機率

$DC^i_{l,S}(n\text{-}l+1)$ =性別為 s 且在 l 歲罹病，在 n 歲時之年罹病成本

T^i_{ls} = 性別為 s 且在 l 歲罹病者之平均餘命

r = 年折現率（通貨膨脹率以綜合物價指數表示）

m= 醫療成本之年變化率

肺癌之間接疾病成本

對台大醫院之肺癌病人進行病患就醫之時間成本與陪伴者之時間成本、交通費用及額外之花費等之問卷調查。並調閱各病患之病歷，註明確診之期別以供分類分析。其中有關薪資之估計以行政院主計處之人力運用報告的受雇者平均月收入為計算依據。

生活品質

進行間接疾病成本調查時也同時做生活品質問卷之調查，以本研究團隊發展之世界衛生組織生活品質問卷之台灣簡明版為施測工具。所得結果再進行比較分析，並以國民健康局對全國 13,083 位 20 歲以上的成年人所做之生活品質調查資料作為比較之依據。有關生活品質與上述間接疾病成本之問卷附於附錄一。

結果與討論

存活分析

我們對這五種疾病病患作存活分析，各疾病病患之確診年齡、預期存活時間、預期減少之壽命等列於表 2。其中以癌症造成最多之壽命損失，肝癌導致約 18.9 年之壽命損失，肺癌約折損 15.6 年之壽命。慢性阻塞性肺病與急性心肌梗塞之預期存活時間較長，預期之壽命損失約 2 至 4 年。

吸菸之可歸因風險

本國吸菸的可歸因風險如表 3，由於男女之吸菸盛行率明顯不同，所以吸菸對於男性之影響很大，男性有相當大比率之死亡為吸菸所造成。其中男性死於肺癌者有 62.9%為吸菸造成，女性死於肺癌者有 11.7%為吸菸造成。男性死於其他四種疾病者，約有 30-43%為吸菸所造成。女性肝癌與 COPD 之死亡者由於研究之個案數較少所以沒有相對風險之估計。Liaw 與 Chen 之流行病學研究中沒有急性心肌梗塞之項目，所以我們以相類似分類之缺氧性心臟病（Ischemic heart disease）的 RR 值來代替。

直接疾病成本

吸菸造成之經濟成本可分為直接成本（如醫療費用、吃補品的花費等）與間接成本（如人力資本之損失、就醫之時間及交通費用等）。我們先以健保資料庫的醫療費用作為估計直接成本之基礎。

我們由國衛院健保資料庫（2000 年之資料）中計算五種疾病病患之每人年平均醫療成本（住院、門診）作為初步估計疾病之終身成本的依據。各疾病患者之年平均醫療費用詳列於表 4，COPD 之花費較少，男性約 7 千多元，女性約 3 千多元，其他四種疾病男性由 AMI 之 4 萬多到肺癌之 10 萬多元，女性由肝癌之 5 萬多到肺癌之 9 萬多元。肺癌之年平均醫療費用最高。合併病患人數與吸菸造成之可歸因風險加以估算，則吸菸在 2000 年所造成之總直接醫療成本（僅就五種疾病而言），男性約為 25 億元，女性約為 1.3 億元，合計 26.3 億元。

以 2000 年之醫療費用為計算基礎，各疾病之個案平均終生醫療成本列於表 5。其中綜合物價指數與醫療成本之年變化率採用最近 10 年（1993-2002）之數據的平均值及上下限值，如此分別作高中低之估計。中風與急性心肌梗塞由於預期存活時間較長（見表 2）所以終生成本較高，男女均約超過 70 萬元，肺癌與肝癌患者之平均預期存活時間為不到 3 年，所以終生成本較低。COPD 之年醫療費用較低所以終生成本也較低。

2000 年新增病例之個案數，癌症以最新版本之癌症登記報告（1999）為依據，中風、急性心肌梗塞則採用 2000 年新發生之住院個案（即健保完整住院資料檔中

1996-1999年均未曾出現該疾病，而到2000年首次以該疾病登錄之住院記錄者），COPD則以健保抽樣資料檔為依據（即1996-1999年均未曾出現該疾病，而到2000年首次以該疾病登錄之病患）。進一步估算可歸因於吸菸之新增病例數如表6。再合併表5之個案終生成本，則可得吸菸導致2000年新增病例之終生醫療成本，該數據乃是換算為2000年貨幣之立即經濟損失，總額約為128億元（表7）。

問卷調查

以我們先前發展的台灣簡明版世界衛生組織生活品質問卷（WHOQOL-BREF）、醫療費用支出問卷及標準賭博法(standard gamble)問卷，對台大醫院的胸腔外科、內科及腫瘤醫學部等單位之肺癌病人施以問卷調查，來評估生活品質及估計就醫成本，其結果進一步可作為成本效性評估之基礎。共收集241位病患之資料（表8），男女平均年齡皆高於60歲。大部分病人居住於北部地區（表9）。

間接疾病成本

疾病造成之損失，除了前述直接醫療成本外，尚有間接成本之損失。依據我們之調查每一位肺癌病患門診時平均約有1人陪病照護，就醫時間平均約需4小時（包含看診與交通時間）（表10、11）。以2000年健保資料庫為基礎，先算出肺癌病患之平均門診次數、住院次數及天數，再以前述之存活曲線估計終生門診次數、住院次數及天數（見表12），病患有工作之比率約為11至18%（表13），男性較高。以有工作之比率作為計算生產力損失之依據，再結合門診時間及陪病者資料估計每次門診、每年門診、終生門診所需之時間及陪病時間（表14-16）。以相同過程計算每天住院、每年住院、終生住院天數及陪病時間（表17-19）。再依據行政院主計處人力運用報告的受雇就業者月薪的資料（表20）估計出門診及住院之時間成本（門診：表21-23，住院：表24-26），每年之門診陪病費用約為3,432元（男性2,155元，女性4,607元），終生門診陪病費用約為8,167元（男性4,637元，女性13,419元）。每年之住院陪病費用約為18,528元（男性18,687元，女性16,994元），終生住院陪病費用約為44,037元（男性40,223元，女性49,425元）。其中無職業者被視為沒有收入，因此無職業者對家庭之貢獻就被忽略了。此外住院陪病之時間成本以小時估計，可能低估實際之時間成本，因為陪病者之交通成本（時間與金錢）等並沒有估計。

男性病患每日額外服用藥品補品或另類療法之費用約為88元，女性患者每日約為107元（表27），綜合交通成本、時間成本、藥品補品的費用等，每一位肺癌病人除了直接之醫療費用（主要健保給付）外，每一年尚有約62,597元（男性58,558元，女性65,785元）之經濟損失（表28）。估計終生之經濟損失約148,284元（男性127,506元，女性190,247元）（表29）。相較於表4之年醫療費用男性108,859元、女性95,184元；表5之終生醫療費用男性235,240元、女性278,634元。間接成本與直接醫療成本之比值約為0.5以上。

由於肺癌病人之罹病年齡男性為 65.4 歲，女性為 62.3 歲，因此並未估算其罹病喪失工作之損失。女性病患至退休年齡（65 歲）尚有 2.7 年，若以表 20 之月薪 26,189 元估計，女性罹患肺癌除了減少 18.5 年之壽命外，還有約 848,524 元之經濟損失。

這些都是疾病造成之損失，但不能完全從健保資料庫中反映。同時其他之人力資本的損失也尚未包含在內，因此一般醫療成本之估計值乃相當程度的低估了實際之損失。

生活品質

肺癌病人確診時癌症期別關係了爾後之治療方式及預後情形，一般而言癌症期別≦3A 者可施以外科手術，預後較好，癌症期別≧3B 則較嚴重，一般無法手術，多施以化學療法或放射性療法，預後往往較差。男性與女性之問卷調查結果分列於表 30 及表 31。男女患者各項生活品質之比較值，癌症期別≧3B 者均低於癌症期別≦3A 者，其中生理範疇、自覺個人健康、整體健康、整體快樂等四項之差異均有顯著的統計意義，心理範疇之差異在女性有顯著的統計意義，在男性接近於有顯著的統計意義。此結果反映了嚴重度較高之癌患者的生活品質較差，同時反映了與健康較直接相關之項目具有較好的區辨力。將病人與一般人（國民健康局對全國 13,083 位 20 歲以上的成年人所做之生活品質調查資料）之生活品質測值比較後列於表 32 及表 33，也反映了較嚴重之病人的生活品質較差，尤以生理範疇最為明顯。另自覺健康、快樂、標準賭博法之分數，嚴重之病患也較差。

結論與建議

本研究建立了肺癌、肝癌、中風、急性心肌梗塞、慢性阻塞性肺病等五種與吸菸有關之疾病的疾病世代並完成各疾病之存活分析。其中肺癌與肝癌造成最大之壽命損失，分別為 15.6 年 18.9 年。以健保資料與吸菸之可歸因風險估計吸菸導致此 5 種疾病之醫療費用，一年約為 26.3 億元。每年由吸菸造成之新增病例的終生醫療成本，總和約為 128 億元。

本研究針對肺癌病人進行了間接醫療成本與生活品質之調查。每一位男女患者一年之間接疾病成本約 5.8 萬元和 6.6 萬元（直接醫療費用為 10.9 萬元和 9.5 萬元），男女患者之終生間接疾病成本約 12.8 萬元和 19.0 萬元(直接醫療費用為 23.5 萬元和 27.9 萬元)。生活品質之測值也反映了較嚴重之病人的生活品質較差，以生理範疇最為明顯。

本研究以台大醫院之病例來建立疾病世代，其所求得之存活曲線難以代表全國之人口群，應有更多醫療院所之參與，才有更精準之估計值。急性心肌梗塞與慢性阻塞性肺病之醫療費用乃以健保資料之 20 萬承保抽樣歸人檔為基礎，其估計值也有失真之顧慮。就間接成本之計算而言，將無職業者與年齡超過 65 歲者視之為無生產力，因此會低估疾病之間接成本，男性肺癌之平均罹病年齡為 65.4 歲，因此沒有生產力損失之顧慮。其他之無形成本（如情感、痛苦等）均難以貨幣值表達與估計。

參考文獻

行政院主計處 2002 年人力運用報告，2002 年 5 月。

Edward J, Calabrese, Elaina M. Kenyon, Air Toxics and Risk Assessment, Chelesa, Michican, Lewis Publishers, INC., 1991.

Galbraith JW, Kaiserman M. Taxation, smuggling and demand for cigarettes in Canada: Evidence from time-series data. Journal of Health Economics 1997;16:287-301.

Grievink L. Antioxidants and air pollution in relation to indicate of asthma and COPD. Wageingen, Grafisch Service Centrum van Gils BV, 1988.

Guindon GE, Tabin S, Yach D. Trends and affordability of cigarette prices: ample room for tax increases and related health gains. Tabocco Control 2002;11:35-43.

Hodgson TA, Meiners MR (1982) Cost-of-illness methodology: a guide to current practices and procedures. Milbank Memorial Fund Quarterly – Health & Society 60(3):429-462, 1982 summer.

Jacobs DR, Adachi H, Mulder I, Kromhout D, Menotti A, Nissinen A, Backhurn H. Cigarette smoking and mortality risk. Arch Intern med. 1999;159:733-740.

Kenkel D. (1994) Cost of illness approach. In Valuing Health for Policy, An Economic Approach. Chapter 3. (Tolley G, Kenkel D and Fabian R.ed.). The University of Chicago Press. Chicago, USA.

Klastersky J, Paesmans M. Response to chemotherapy, quality of life benefits and survival in advanced non-small cell lung cancer; review of literature results. Lung Cancer 2001;34:s95-s101.

Lee TK. Huang ZS. Ng SK. Chan KW. Wang YS. Liu HW. Lee JJ. Impact of alcohol consumption and cigarette smoking on stroke among the elderly in Taiwan. *Stroke. 26(5):790-4, 1995 May*

Levy BS, Wegman DH, Occupational Health: Recognizing and Preventing. Work-Related Disease. Boston, Massachusetts, Little, Brown and Company, 1983.

Liaw KM, Chen CJ. Mortality attributable to cigarette smoking in Taiwan, a 12-year follow up study. Tobacco Control 1998;7:141-8.

Liaw KM, Chen CJ. Mortality attributable to cigarette smoking in Taiwan: a 12-year follow-up study. Tobacco Control 1998;7:141-8.

Miller VP, Ernst C, Collin F. Smoking-attributable medical care costs in the USA. Social Science & Medicine 1999;48:375-391.

National Research Council, Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects, Washington, D.C., National Academy Press, 1986.

National Research Council, Risk Assessment in the Federal Government: Managing the Process. Washington, D.C., National Academy Press, 1983.

National Research Council. Biologic Markers in Pulmonary Toxicology. National Research Council, National Academy Press,1989.

Parrott S, Godfrey C, Raw M. Cost of employee smoking in the workplace in Scotland. Tobacco Control 2000;9:187-192.

Rice DP, Hodgson TA, Kopstein AN. The economic costs of illness: a replication and update. Health Care Financing Review 1985; 7: 61-80.

Spengler J, WilsonR, Particles in Our Air: Concentration and Health Effects. Boston, Massachusetts, Harvard University Press, 1996.

U.S. Department of Health and Human Services, Public Health Service, Office on smoking and Health, The Health Consequences of Smoking: Chronic Obstructive Lung Disease. Washington, D.C.,U.S. Government Printing Office, 1984.

U.S. Department of Health and Human Services, Public Health Service, Office on smoking and Health, The Health Consequences of Smoking: Cancer and Chronic Lung Disease in the Workplace. Washington, D.C., U.S. Government Printing Office, 1985.

U.S. Department of Health and Human Services, Public Health Service, Office on smoking and Health, The Health Benefits of Smoking Cessation. Washington, D.C., U.S. Government Printing Office, 1990.

Warner KE, Chaloupka FJ, et al. Criteria for determining and optimal cigarette tax: the economist's perspective. Tobacco Control 1995;4:380-6.

Warner KE, Hodgson TA, Carroll CE. Medical costs of smoking in the United States: estimates, their validity, and their implication. Tobacco Control 1999;8:290-300.

Zhang X, Miller L. Max W, Rice DP. Cost of smoking to the Medicare Program, 1993. Health Care Financing Review 1999;20(4):179-196.

附表

表 1. 各疾病世代組成時期及追蹤時限

疾病別	COHORT 開始年代	COHORT 結束年代	追蹤截止時間
肺癌 Lung cancer	1996*	2000	2000
肝癌 Liver cancer	1996	2000	2000
中風 Stroke	1995	2000	2000
急性心肌梗塞 AMI	1989	1999	2000
慢性阻塞性肺病 COPD	1991	2000	2000

表 2. 各疾病病患之預期存活時間與估計損失壽命

Diseases (N %)	age of onset	life expectancy	estimated LE without disease	expected life year lost
Lung Cancer (2169)	64.5±12.2	1.8±0.1	17.4±0.1	15.6
Male (1394, 64.3%)	65.4±12.0	1.6±0.1	15.2±0.1	13.6
Female(775, 35.7%)	62.3±12.2	2.4±0.4	20.8±0.1	18.5
Liver Cancer (2598)	57.8±13.9	2.2±0.2	21.1±0.2	18.9
Male (1986, 76.4%)	56.6±13.7	2.4±0.2	21.6±0.2	19.3
Female(612, 23.6%)	61.5±13.9	2.4±0.2	20.4±0.1	18.0
Stroke (6425)	64.2±14.7	8.2±0.4	17.7±0.2	9.5
Male (3779, 58.8%)	63.1±14.5	8.0±0.4	17.7±0.1	9.7
Female(2646, 41.2%)	65.7±14.8	8.2±0.6	17.8±0.1	9.6
AMI (1586)	62.2±12.6	14.5±0.8	18.0±0.1	3.5
Male (1255, 79.1%)	60.7±12.5	16.0±0.9	18.3±0.1	2.3
Female (331, 20.9%)	68.1±11.0	9.8±1.3	15.4±0.1	5.5
COPD (3651)	69.7±11.0	11.0±0.7	13.4±0.1	2.4
Male (2812, 77.0%)	69.7±10.7	10.7±0.5	12.9±0.1	2.3
Female (839, 23.0%)	69.6±11.8	10.8±1.2	14.9±0.1	4.0

表 3. 五種吸菸相關疾病之相對風險(Relative risk, RR)及人口可歸因風險(population attributable risk)

Diseases	Male		Female	
	RR[a]	population smoking attributal risk[c]	RR[a]	population smoking attributal risk[c]
Lung cancer	3.70	0.629	3.60	0.117
Liver cancer	2.20	0.430		
COPD	1.90	0.361		
Ischemic heart disease	1.80	0.334	1.90	0.044
Stroke[b]	1.71	0.308	1.71	0.035

a: Liaw and Chen, 1998.

b: Lee, et al., 1995.

c: Based on the smoking prevalence rate in 1990: 0.628 (male), 0.051(female)

表 4. 2000 年疾病病患每人之年平均醫療成本及吸菸造成之總醫療成本

	Male				Female			
疾病	個案數	年平均費用（住院費用%）	總計（百萬）	吸菸造成之損失（百萬）	個案數	年平均費用（住院費用%）	總計（百萬）	吸菸造成之損失（百萬）
Lung cancer	13,893	108,859 (70%)	1,512	951	7,567	95,184 (65%)	720	84
Liver cancer	19,477	71,939 (78%)	1,401	603	9,727	52,269 (78%)	508	
Stroke	15,063	77,451 (98%)	1,167	359	11,643	85,340 (98%)	994	35
AMI	5,409	42,093 (83%)	228	76	2,887	68,687 (95%)	198	9
COPD	191,121	7,422 (61%)	1,419	512	160,201	3,728 (53%)	597	
			Sum	2,501			Sum	128
							總計	2,629

% of inpatient cost

表 5. 每一新發生個案之平均終生醫療成本及計算時採用之數據

	Male			Female		
	Low estimation	Median estimation	High estimation	Low estimation	Median estimation	High estimation
lung cancer	222,182	235,240	253,193	253,408	278,634	316,507
liver cancer	189,041	203,994	224,626	146,694	156,815	170,119
Stroke	576,844	718,316	972,233	637,862	791,235	1,062,218
AMI	511,984	712,389	1,136,073	598,193	792,664	1,189,283
COPD	73,505	98,277	150,312	32,953	41,911	58,588
Discount rate (%)	4.10	1.76	-0.20	4.10	1.76	-0.20
Annual increment of medical cost (%)	0.93	1.97	3.75	0.93	1.97	3.75

表 6. 2000 年歸因於吸菸之新病例數估計值

	Incidence cases		Smoking Attributable cases	
Year	Male	Female	Male	Female
Lung cancer[a]	4,368	1,947	2,748	228
Liver cancer[a]	5,659	2,070	2,432	
Stroke[b]	11,691	9,373	3,605	328
AMI[b]	4,527	1,514	1,514	66
COPD[c]	215,747	210,135	77,907	

a: 1999 癌症登記報告; b: 完整住院檔 (2000); c: 抽樣檔換算 (2000)

表 7. 五種疾病在 2000 年所有新發生病例之預期總終生醫療成本

	Male			Female		
	Low estimation	Medain estimation	High estimation	Low estimation	Medain estimation	High estimation
lung cancer	610,463,493	646,341,274	695,668,808	57,763,359	63,513,632	72,146,746
liver cancer	459,733,659	496,098,255	546,272,222			
Stroke	2,079,676,348	2,589,719,402	3,505,159,451	208,922,767	259,157,978	347,914,972
AMI	775,052,597	1,078,429,305	1,719,810,933	39,745,688	52,666,875	79,019,378
COPD	5,726,521,585	7,656,500,484	11,710,331,571			
Sum	9,651,447,682	12,467,088,720	18,177,242,986	306,431,814	375,338,485	499,081,096
Grant total (male and female)	Low estimation	Medain estimation	High estimation			
	9,957,879,496	12,842,427,205	18,676,324,082			

表 8. 問卷調查之受訪肺癌病患基本資料

	個案數	百分比	平均年齡	平均確診年齡	≧40 歲	≧50 歲	≧60 歲	≧70 歲
男	144	59.8	65.90	64.60	97.1%	93.5%	71.2%	33.1%
期別≦3A	73		67.81	65.88	98.6%	94.5%	74.0%	37.0%
期別≧3B	60		63.28	62.50	93.2%	89.8%	64.4%	27.1%
女	97	40.2	61.18	59.18	95.3%	76.7%	47.7%	18.6%
期別≦3A	38		62.72	60.09	94.7%	76.3%	55.3%	26.3%
期別≧3B	53		60.03	58.28	95.7%	76.6%	40.4%	12.8%
總和	241	100	63.99	62.53	96.4%	87.1%	62.2%	27.6%

表 9. 問卷調查之受訪病患居住地區

	門診			住院		
	次數	百分比	累積百分比	次數	百分比	累積百分比
台北市區	46	21	21	8	21	21
台北市郊、台北縣	104	49	70	18	47	68
桃竹苗	37	17	87	8	21	89
雲嘉地區	20	9	97	2	5	95
其他	7	3	100	2	5	100
總和	214	100		38	100	

表 10. 門診之時間成本

	個數	平均數
就醫單程時間〔分〕	205	56.44
門診時間(分)	185	142.37
返家單程時間〔分〕	203	55.44

表 11. 門診陪伴人數

	個數	平均數
男	126	0.94
女	90	1.04
總計	216	0.99

表 12. 2000 年健保資料庫肺癌病患平均門診、住院次數及天數之統計值及終生估計值

	年平均門診次數	終生門診估計次數	年住院平均值		終生住院估計值	
			次數	天數	次數	天數
總計	7.9	18.8	1.3	13.3	3.1	31.6
男性	7.9	17.0	1.3	14.1	2.8	30.4
女性	8.0	23.3	1.2	12.0	3.5	34.9

表 13. 病患有工作比率

	門診	住院
總計	0.116	0.161
男	0.123	0.182
女	0.106	0.111

表 14. 每次門診之就醫時間（時）

病患	病患每次門診時間	每次門診配偶陪伴人時		每次門診其他家人陪伴人時		每次門診看護人次
		有職	無職	有職	無職	
總計 216	4.1	0.43	0.84	1.39	0.84	0.09
男 126	3.9	0.10	1.14	1.19	1.01	0.05
女 90	4.1	0.40	0.89	1.67	0.59	0.14

表 15. 每年門診之就醫時間（時）

病患	病患每年門診時間	每年門診配偶陪伴人時		每年門診其他家人陪伴人時		每年門診看護人次
		有職	無職	有職	無職	
總計	32.1	3.40	6.64	10.98	6.64	0.71
男	30.9	0.79	9.01	9.40	7.98	0.40
女	33.0	3.20	7.12	13.36	4.72	1.12

表 16. 終生門診時間估計值（時）

病患	病患終生門診時間	終生門診配偶陪伴人時		終生門診其他家人陪伴人時		終生門診看護人次
		有職	無職	有職	無職	
總計	76.3	8.08	15.79	26.13	15.79	1.69
男	66.5	1.70	19.38	20.23	17.17	0.85
女	96.1	9.32	20.74	38.91	13.75	3.26

表 17. 每天住院陪病人數及陪伴時間（時）

病患	平均每天陪伴人數	每天配偶陪伴人時		每天其他家人陪伴人時		每天看護人次
		有職	無職	有職	無職	
總計(38)	2.89	1.41	4.69	7.05	4.53	0.11
男 (26)	2.77	1.46	6.86	6.81	5.38	0.12
女 (12)	3.15	1.31	0.5	7.58	2.68	0.08

表 18. 每年住院天數與陪伴時間（時）

病患	每年住院天數	每年配偶陪伴人時		每年其他家人陪伴人時		每年看護人次
		有職	無職	有職	無職	
總計	13.3	18.75	62.38	93.77	60.25	1.46
男	14.1	20.59	96.73	96.02	75.86	1.69
女	12.0	15.72	6.00	90.96	32.16	0.96

表 19. 終生住院天數與陪伴時間（時）

病患	終生住院天數	終生配偶陪伴人時		終生其他家人陪伴人時		看護人次
		有職	無職	有職	無職	
總計	31.6	44.57	148.25	222.85	143.19	3.48
男	30.4	44.31	208.20	206.68	163.28	3.64
女	34.9	45.72	17.45	264.54	93.53	2.79

表 20. 受雇就業者之薪資（行政院主計處人力運用報告）

性別	年齡	月薪	日薪	時薪
總計	20-44 歲	32,716	1,091	136
	≧45 歲	36,527	1,218	152
男性	20-44 歲	35,920	1,197	150
	≧45 歲	41,234	1,374	172
女性	20-44 歲	28,564	952	119
	≧45 歲	26,189	873	109

表 21. 每次門診時間成本

病患	本人時間成本	配偶陪伴成本		其他家人陪伴成本		每日看護費用	每次門診總陪病費用
		有職	無職	有職	無職		
總計	72	65	0	189	0	180	434
男	83	11	0	162	0	100	273
女	48	69	0	227	0	280	576

表 22. 每年門診時間成本

病患	本人每年門診之費用	每年配偶陪伴費用		每年其他家人陪伴費用		每年看護費用	每年門診總陪病費用
		有職	無職	有職	無職		
總計	565	516	0	1,493	0	1,422	3,432
男	654	86	0	1,279	0	790	2,155
女	381	550	0	1,817	0	2,240	4,607

23. 終生門診時間成本

病患	本人終生門診之費用	終生配偶陪伴費用		終生其他家人陪伴費用		終生看護費用	終生門診總陪病費用
		有職	無職	有職	無職		
總計	1,345	1,229	0	3,554	0	3,384	8,167
男	1,408	185	0	2,751	0	1,700	4,637
女	1,111	1,603	0	5,292	0	6,524	13,419

表 24. 每天住院時間成本

病患	本人每日之費用	每日配偶陪伴費用		每日其他家人陪伴費用		每日看護費用	每日住院總陪病費用
		有職	無職	有職	無職		
總計	196	214	0	959	0	220	1,393
男	250	159	0	926	0	240	1,325
女	97	225	0	1,031	0	160	1,416

表 25. 每年住院時間成本

病患	本人每年之費用	每年配偶陪伴費用		每年其他家人陪伴費用		每年看護費用	每年住院總陪病費用
		有職	無職	有職	無職		
總計 l	2,608	2,850	0	12,752	0	2,926	18,528
男	2,765	2,244	0	13,059	0	3,384	18,687
女	2,353	2,704	0	12,371	0	1,920	16,994

表 26. 終生住院時間成本

病患	本人終生之費用	終生配偶陪伴費用		終生其他家人陪伴費用		終生看護費用	終生住院總陪病費用
		有職	無職	有職	無職		
總計	6,199	6,775	0	30,308	0	6,954	44,037
男	5,952	4,830	0	28,109	0	7,284	40,223
女	6,844	7,864	0	35,978	0	5,584	49,425

表 27. 額外服用藥品補品或另類療法之費用（元）

	個數	日平均花費
男	144	88
女	95	107
總計	239	95

表 28. 平均每一病患每年健保以外之花費

病患	門診			住院			額外服用藥品補品	總和
	門診薪資損失	門診總陪病費用	往返總交通費用	住院薪資損失	住院總陪病費用	往返總交通費用		
總病患	565	3,432	2,251	2,608	18,528	370	34,841	62,597
男	654	2,155	1,910	2,765	18,687	310	32,078	58,558
女	381	4,607	2,099	2,353	16,994	319	39,031	65,785

表 29. 平均每一病患終生健保以外之花費

病患	門診			住院			額外服用藥品補品	總和
	門診薪資損失	門診總陪病費用	往返總交通費用	住院薪資損失	住院總陪病費用	往返總交通費用		
總病患	1,345	8,167	4,845	6,199	44,037	881	82,811	148,284
男	1,408	4,637	5,562	5,952	40,223	668	69,057	127,506
女	1,111	13,419	4,995	6,844	49,425	927	113,525	190,247

表 30. 男性肺癌病患生活品質調查值

	期別≦3A			期別≧3B			T-test	
範　　疇	人數	平均數	標準差	人數	平均數	標準差	t	顯著性
生理範疇	72	13.7	2.1	60	12.3	2.6	3.27	0.001**
心理範疇	72	13.5	2.0	60	12.9	1.9	1.96	0.052
社會範疇	72	14.3	1.9	60	14.0	2.1	0.87	0.384
環境範疇	72	13.8	1.8	60	13.4	2.0	1.10	0.275
自覺個人健康	73	3.0	0.9	60	2.5	1.0	2.63	0.010**
整體生活品質	73	3.3	0.7	60	3.2	0.7	0.45	0.655
整體健康	73	3.1	1.0	60	2.6	0.8	2.70	0.008**
整體快樂	73	3.3	0.8	60	3.0	0.9	2.35	0.020*
標準賭博法	66	72.0	35.0	56	66.9	31.8	0.85	0.399

*: p≦0.05；**: p≦0.01

表 31. 女性肺癌病患生活品質調查值

	期別≦3A			期別≧3B			T-test	
範　　疇	人數	平均數	標準差	人數	平均數	標準差	t	顯著性
生理範疇	38	13.8	3.0	53	12.1	3.2	2.6	0.010**
心理範疇	38	13.2	2.4	53	11.8	2.9	2.6	0.012*
社會範疇	38	14.5	2.1	53	14.7	2.1	-0.3	0.745
環境範疇	38	13.8	2.0	53	13.2	2.3	1.3	0.198
自覺個人健康	37	3.0	0.8	53	2.5	1.0	2.3	0.024*
整體生活品質	38	3.3	0.8	53	2.9	0.9	1.7	0.089
整體健康	38	2.9	0.9	53	2.4	0.9	2.8	0.006**
整體快樂	37	3.4	0.8	53	2.9	1.1	2.4	0.021*
標準賭博法	35	81.5	26.4	49	70.4	32.9	1.7	0.089

*: p≦0.05；**: p≦0.01

表 32. 與一般人比較後之各層面測值

範疇	層面	期別≦3A		期別≧3B		T-test	
		Mean	SD	Mean	SD	t	顯著性
生理	疼痛不適	1.04	0.27	0.91	0.33	3.31	0.001
	日常活動	0.99	0.21	0.89	0.28	3.02	0.003
	醫療的依賴	0.89	0.30	0.77	0.31	3.05	0.003
	工作能力	1.01	0.22	0.88	0.29	3.67	0.000
	活力	0.95	0.26	0.81	0.29	3.99	0.000
	睡眠	0.98	0.30	0.91	0.32	1.68	0.095
	活動能力	0.95	0.28	0.83	0.29	3.00	0.003
心理	靈性/個人信念	1.02	0.30	1.01	0.28	0.29	0.771
	正面感覺	1.08	0.40	0.90	0.40	3.30	0.001
	思考學習記憶	0.99	0.28	0.93	0.28	1.43	0.155
	自尊	0.97	0.20	0.89	0.27	2.54	0.012
	身體意像	1.00	0.25	0.89	0.31	2.94	0.004
	負面感覺	1.13	0.30	1.03	0.30	2.43	0.016
社會	個人關係	1.04	0.17	1.03	0.19	0.19	0.846
	社會支持	1.07	0.17	1.08	0.18	-0.44	0.657
	性生活	1.04	0.22	0.98	0.29	1.45	0.150
	被尊重	1.06	0.20	1.07	0.24	-0.19	0.849
環境	身體安全保障	1.08	0.25	1.01	0.28	1.85	0.065
	家居環境	1.01	0.20	1.06	0.20	-1.81	0.072
	財務資源	1.16	0.39	1.14	0.38	0.44	0.663
	社會照護	1.07	0.20	1.09	0.21	-0.43	0.666
	資訊技能	1.16	0.26	1.04	0.30	3.17	0.002
	娛樂休閒	1.01	0.41	0.89	0.43	2.18	0.030
	物理環境	1.01	0.31	0.99	0.31	0.60	0.548
	交通	1.12	0.17	1.07	0.19	2.22	0.027
	飲食	1.08	0.23	1.11	0.26	-0.86	0.388

表 33. 與一般人比較後之各範疇測值

範疇/層面	期別≦3A		期別≧3B		T-test	
	Mean	SD	Mean	SD	t	顯著性
綜合生活品質	1.03	0.23	0.96	0.26	2.03	0.044
綜合健康	0.93	0.30	0.78	0.28	3.85	0.000
生理範疇	0.97	0.17	0.86	0.21	4.59	0.000
心理範疇	1.03	0.17	0.94	0.19	3.67	0.000
社會範疇	1.04	0.14	1.03	0.15	0.52	0.606
社會範疇 tw	1.04	0.13	1.04	0.15	0.33	0.743
環境範疇	1.08	0.15	1.04	0.16	1.94	0.053
環境範疇 tw	1.08	0.13	1.05	0.16	1.69	0.093
QOL_綜合評量	0.92	0.20	0.83	0.24	2.90	0.004
自覺個人健康	2.97	0.84	2.54	1.01	3.49	0.001
整體快樂	3.32	0.79	2.91	0.99	3.39	0.001
標準賭博法分數	75.31	32.44	68.50	32.22	1.51	0.132

計畫成果自評

本計畫研究之目標乃以吸菸為例來探討其相關之疾病患者之生活品質及醫藥衛生成本效性評估，原計畫以肺癌為研究對象來估計吸菸所造成之經濟成本。因為考量吸菸會導致許多之疾病，因此在實際進行研究時，又加入其他與吸菸有關之主要疾病：肝癌、中風、急性心肌梗塞、慢性阻塞性肺病。所涵蓋之疾病較原計畫範圍更廣，也更能反映吸菸造成之影響，已達成原訂之目標。此外針對肺癌患者，我們也進行了就醫的時間成本及其他間接成本之問卷調查，透過這些研究可以估算醫療成本以外之疾病成本，對於瞭解疾病對病人及其家人造成之經濟影響大有助益。也有助於對菸害之評估提供實際的數據，可作為關政策研訂之參考。

研究之結果預期很適合在期刊發表，目前正撰寫吸菸造成五種主要疾病的醫療成本之論文；另將撰寫其他研究論文，主題分別為有關「肺癌病患之生活品質」、「肺癌病患之直接與間接的疾病成本」。同時預定於 2004 年上半年出版一本有關生活品質與成本效性評估之工具書。此外，本計畫執行期間也陸續在學術期刊發表了 8 篇文章及完成一篇手稿，條列如下（文章的影印本另附於附錄二）：

國科會計畫「生活品質研究與醫藥衛生成本效性評估-環境與職業性危害之比較性風險評估-以吸煙相關之疾病為例」三年期計畫論文產出

89-- NSC 89-2314-B-002-433-M56

- 張彧、王顏和、姚開屏、王榮德：脊髓損傷生活品質問卷之發展。台灣醫學 2002；6：209-214.
- 方啟泰、熊秉荃、游正芬、陳茂源、王榮德：如何設計一份特定疾病所適用之生活品質問卷-以愛滋病患為例。台灣醫學 2002；6：215-219.
- 台灣版世界衛生組織生活品質問卷發展小組：台灣版世界衛生組織生活品質問卷之發展簡介。中華衛誌 2000；19(4)：315-324。
- Liu YH, Du CL, Lin CT, Chan CC, Chen CJ, Wang JD. Increased morbidity from nasopharyngeal carcinoma and chronic pharyngitis or sinusitis among workers at a newspaper printing company. Occup Environ Med 2002; 59:18-22.
- Fang CT, Hsiung PC, Yu CF, Chen MY, Wang JD. Validation of the World Health Organization Quality of Life (WHOQOL) instrument in patients with HIV infection. Quality of Life Research 2002; 11:753-62.
- Hwang JS, Wang JD. Integrating health profile with survival for quality of life assessment. Quality of Life Research 2003 (in press)

90-- NSC 90-2320-B-002-127-M56

- Lee LJH, Chan CC, Chung CW, Ma YC, Wang GS, Wang JD. Health risk assessment on residents exposed to chlorinated hydrocarbons contaminated in groundwater of a hazardous waste site. J Toxicol Environ Health 2002; 65: 219-235.
- 謝功毅、陳保中、王榮德：公元 1980 至 1997 年本國衛生署死因資料庫準確性之確認與

補正。台灣衛誌 2003；21(5)：329-338.

91 --NSC 91-2320-B-002-082-M56

- Lee LJH, Chen CH, Yao Grace, Chung CW, Sheu JC, Lee PH, Tsai YJ, Wang JD. Assessing Health-Related Quality of Life in Patients with Hepatocellular Carcinoma. (manuscript)

附錄一

肺癌病患生活品質及疾病間接成本問卷

附錄一

病歷號：_____ 填答日期：_____

世界衛生組織生活品質問卷

（台灣簡明版）

同意書

本人同意參加『肺部疾病健康相關生活品質』研究計畫，並同意該計畫基於研究之需要，可由臺大醫院病歷取得相關之資料，本人瞭解上述資料僅供學術研究，不作其他用途；且絕不會有本人或其他個人姓名出現在最後報告中。

受訪者簽名：_____

受訪日期：_____

第一部份　生活品質問卷

問卷說明：

這份問卷詢問您對於自己的生活品質、健康、以及其他生活領域的感覺。請您回答所有的問題。如果您對某一問題的回答不確定，請選出五個答案中最適合的一個，通常會是您最早想的那個答案。

我們的問題所關心的是您最近兩星期內的生活情形，請您用自己的標準、希望、愉快、以及關注點來回答問題。請參考下面的例題：

例題一：整體來說，您滿意自己的健康嗎?

□極不滿意　□不滿意　□中等程度滿意　□滿意　□極滿意

請選出最適合您在最近兩星期內對自己健康的滿意程度，如果您很滿意自己的健康，就在「很滿意」前的□內打「√」。請仔細閱讀每個題目，並評估您自己的感覺，然後就每一個題目選出最適合您的答案。謝謝您的協助！

國立台灣大學醫學院附設醫院　內科部　郭壽雄醫師、廖永祥醫師、王榮德醫師

外科部　李元麒醫師

腫瘤部　楊志新醫師

國立台灣大學公共衛生學院　王榮德教授、鍾智文博士

1. 整體來說，您如何評價您的生活品質？

□極不好 □不好 □中等程度好 □好 □極好

2. 整體來說，您滿意自己的健康嗎?

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

3. 您覺得身體疼痛會妨礙您處理需要做的事情嗎？

□完全沒有妨礙 □有一點妨礙 □中等程度妨礙 □很妨礙 □極妨礙

4. 您需要靠醫療的幫助應付日常生活嗎?

□完全沒有需要 □有一點需要 □中等程度需要 □很需要 □極需要

5. 您享受生活嗎？

□完全沒有享受 □有一點享受 □中等程度享受 □很享受 □極享受

6. 您覺得自己的生命有意義嗎？

□完全沒有 □有一點有 □中等程度有 □很有 □極有

7. 您集中精神的能力有多好？

□完全不好 □有一點好 □中等程度好 □很好 □極好

8. 在日常生活中，您感到安全嗎?

□完全不安全 □有一點安全 □中等程度安全 □很安全 □極安全

9. 您所處的環境健康嗎? (如污染、噪音、氣候、景觀)

□完全不健康 □有一點健康 □中等程度健康 □很健康 □極健康

10. 您每天的生活有足夠的精力嗎?

□完全不足夠 □少許足夠 □中等程度足夠 □很足夠 □完全足夠

11. 您能接受自己的外表嗎?

□完全不能夠 □少許能夠 □中等程度能夠 □很能夠 □完全能夠

12. 您有足夠的金錢應付所需嗎?

□完全不足夠 □少許足夠 □中等程度足夠 □很足夠 □完全足夠

13. 您能方便得到每日生活所需的資訊嗎？

□完全不方便 □少許方便 □中等程度方便 □很方便 □完全方便

14. 您有機會從事休閒活動嗎?

□完全沒有機會 □少許機會 □中等程度機會 □很有機會 □完全有機會

15. 您四處行動的能力好嗎？

□完全不好 □有一點好 □中等程度好 □很好 □極好

16. 您滿意自己的睡眠狀況嗎?

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

17. 您對自己從事日常活動的能力滿意嗎?

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

18. 您滿意自己的工作能力嗎？

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

19. 您對自己滿意嗎?

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

20. 您滿意自己的人際關係嗎?

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

21. 您滿意自己的性生活嗎?

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

22. 您滿意朋友給您的支持嗎?

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

23. 您滿意自己住所的狀況嗎?

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

24. 您對醫療保健服務的方便程度滿意嗎？

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

25. 您滿意所使用的交通運輸方式嗎？

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

26. 您常有負面的感受嗎？（如傷心、緊張、焦慮、憂鬱等）

□從來沒有 □不常有 □一半有一半沒有 □很常有 □一直都有

27. 您覺得自己有面子或被尊重嗎?

□完全沒有 □有一點有 □中等程度有 □很有 □極有

28. 您想吃的食物通常都能吃到嗎?

□從來沒有 □不常有 □一半有一半沒有 □很常有 □一直都有

29. 您是否會擔心您的健康會影響下一代的幸福？

□完全不擔心 □有一點擔心 □中等程度擔心 □很擔心 □極擔心

30. 您是否會擔心下一代的生活？

□完全不擔心 □有一點擔心 □中等程度擔心 □很擔心 □極擔心

31. 您滿意您的工作機會嗎？

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

32. 您常會覺得喘嗎？

□從來沒有 □不常有 □一半有一半沒有 □很常有 □一直都有

33. 喘的情形會造成您的困擾嗎？

□完全沒有困擾 □有一點困擾 □中等程度困擾 □很困擾 □極困擾

34. 您常有咳痰〔或帶血〕的情形嗎？

□從來沒有 □不常有 □一半有一半沒有 □很常有 □一直都有

35. 咳痰〔或帶血〕的情形會造成您的困擾嗎？

□完全沒有困擾 □有一點困擾 □中等程度困擾 □很困擾 □極困擾

36. 您對您的胃口好不好是否滿意？

□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

37. 您需要傳統醫療〔如中醫、國術館、草藥〕與健康食品來促進健康嗎？

□完全不需要 □有一點需要 □中等程度需要 □很需要 □極需要

38. 您的人生觀或信仰能幫助您面對人生的困難嗎？

□完全沒有幫助 □有一點幫助 □中等程度幫助 □很有幫助 □極有幫助

39. 您體重減輕的程度對您是否造成困擾？

□完全沒有困擾 □有一點困擾 □中等程度困擾 □很困擾 □極困擾

40. 您目前的日常生活狀況是

□完全臥床 □一天臥床時間大於50%〔不能照顧自己〕

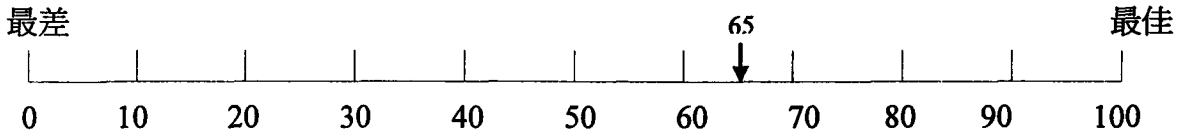
□一天臥床時間少於50%〔不能工作，但能留在家中，需要一些幫忙〕

□有症狀，但能行動、工作 □無症狀〔沒有臥床，可行動、工作〕

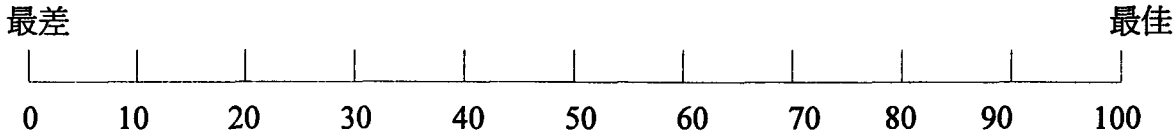
第二部份　綜合自我評估

請依您最近兩個星期的情況，回答下列題目；「0」端代表生活品質最差的狀態，「100」端代表生活品質最佳的狀態，根據此觀點，請在下列的長條圖中，以箭頭及數字的的方式，標出您的情況，謝謝。

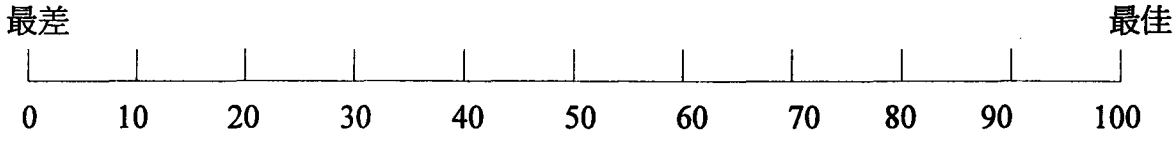
例如：　整體而言，您對自己健康相關生活品質的滿意程度。



1. 綜合而言，您對自己健康相關生活品質的滿意程度。



綜合而言，您在得肺病之前，您對健康相關生活品質的滿意程度。



您目前的日常生活狀況是

- ☐ 無症狀
- ☐ 正常活動，輕微症狀
- ☐ 正常活動，些微症狀
- ☐ 不能工作，可照顧自己
- ☐ 偶而需要協助
- ☐ 相當需要協助
- ☐ 失能，需要完全協助
- ☐ 需要一些積極性的支持照顧
- ☐ 非常虛弱，需要住院
- ☐ 即將死亡

第三部份　個人基本資料

〔1〕身分證字號：_____

〔2〕性別：1□男　2□女

〔3〕出生日期：西元_____年_____月_____日

〔4〕教育程度：1□不識字　2□國小/小學　3□國中/初中　4□高中/高職
5□大專/大學　6□研究所及以上　7□其他_____

〔5〕請問您目前從事什麼行業？

01□農林漁牧業　02□礦業及土石採取業　03□製造業
04□水電燃氣業　05□營造業　06□批發及零售業
07□住宿及餐飲業　08□運輸、倉儲及通信業　09□金融及保險業
10□不動產及租賃業　11□專業、科學及技術服務業　12□教育服務業
13□醫療保健及社會福利服務業　14□文化、運動及休閒服務業　15□其他服務業
16□公共行政業　17□家庭主婦　18□無工作
19□其他_____

〔6〕請問您的職業？請加註工作性質〔如自行開業〕：

01□現役軍人　02□民意代表、行政主管、企業主管及經理人
03□專業人員　04□技術員及助理專業人員
05□事務工作人員　06□服務工作人員及售貨員
07□農、林、漁、牧工作人員　08□技術工及有關工作人員
09□機械設備操作工及組裝工　10□非技術工及體力工
11□家庭主婦　12□無工作
13□其他_____

〔7〕宗教信仰：01□無　02□佛教　03□道教　04□基督教　05□天主教　06□無神論
07□回教　08□信有神但沒有特定宗教　09□一貫道　10□其他_____

〔8〕婚姻狀況：1□未婚/單身　2□已婚/同居　3□離婚/分居　4□喪偶　5□其他_____

〔9〕請問您目前患有哪些疾病？

1□無

2□若有，請列出:_____/_____/_____(依嚴重性列出前三項)

〔10〕自覺個人健康狀況：1□很差　2□差　3□不好不壞　4□好　5□很好

〔11〕整體來說，您覺得目前生活過得快樂嗎？

1□很不快樂　2□不太快樂　3□還算快樂　4□快樂　5□很快樂

〔12〕您過去一年的個人平均月收入多少元？請註明薪資計算單位：　　元／時／日／月

01□無收入　02□10,000 元以下　03□10,000-19,999 元

04□20,000-29,999 元　05□30,000-39,999 元　06□40,000-49,999 元

07□50,000-59,999 元　08□60,000-69,999 元　09□70,000-79,999 元

10□80,000-89,999 元　11□90,000-99,999 元　12□100,000-109,999 元

13□110,000-119,999 元　14□120,000-129,999 元　15□130,000-139,999 元

16□140,000-149,999 元　17□150,000-159,999 元　18□160,000-169,000 元

19□170,000-179,999 元　20□180,000-189,000 元　21□190,000-199,999 元

22□200,000 元以上

〔13〕您過去一年的全家平均月收入多少元？

01□無收入　02□10,000 元以下　03□10,000-19,999 元

04□20,000-29,999 元　05□30,000-39,999 元　06□40,000-49,999 元

07□50,000-59,999 元　08□60,000-69,999 元　09□70,000-79,999 元

10□80,000-89,999 元　11□90,000-99,999 元　12□100,000-109,999 元

13□110,000-119,999 元　14□120,000-129,999 元　15□130,000-139,999 元

16□140,000-149,999 元　17□150,000-159,999 元　18□160,000-169,000 元

19□170,000-179,999 元　20□180,000-189,000 元　21□190,000-199,999 元

22□200,000 元以上

〔14〕(a).您現在抽菸嗎？（最近六個月前還有抽菸也算）

1□是，何時開始抽？西元____年____月

2□否（如答「否」，請跳至第(15)題回答）

(b).平均來講，現在您一天抽多少菸？

1□1-5 支/每天　2□6-10 支/每天　3□11-15 支/每天

4□16-20 支/每天　5□21-30 支/每天　6□31 支以上/每天

〔15〕(a).如果您戒菸了（過去六個月都沒抽菸），何時戒的？西元____年____月

(b).戒菸前那段時間，平均每天抽多少支？

1□1-5 支/每天　2□6-10 支/每天　3□11-15 支/每天

4□16-20 支/每天　5□21-30 支/每天　6□31 支以上/每天

〔16〕您一般每週喝幾次酒？

1□天天喝　2□每週 5-6 次　3□每週 3-4 次　4□每週 1-2 次

5□每週一次以下　6□每月 1-2 次　7□一年 2-3 次　8□不喝

〔17〕您喝的是哪一種酒？每次喝酒的量有多少？

（以一般餐廳所使用之玻璃杯爲準，一杯的量約 150c.c.，以下括弧中所示爲酒精量）

1□啤酒(4.5%)，____杯

2□葡萄酒、玫瑰紅(10.5%)，____杯

3□紹興、花雕、紅露、烏梅、清酒(13-15%)，____杯

4□米酒(19.5%)，____杯

5□參茸(28.5%)、鹿茸(28.5%)、五加皮(34%)，____杯

6□白蘭地(40%)、威士忌(40%)、藍姆(40%)、竹葉青(43.5%)，____杯

7□高粱(54%)、茅台(54%)，____杯

8□大麴(65%)，____杯

9□其他（請註明_____，____杯）

〔18〕由誰填寫此份問卷：1□自己填寫　2□別人協助下自己填寫　3□別人填寫

〔19〕您花多少時間完成此問卷：_____分鐘

EORTC QLQ-C30 (version 3.0) 台灣中文版

我們很希望瞭解有關您和您的健康狀況。請您親自回答以下所有的問題，圈選最合適於您的答案。答案中沒有「對」或「錯」。您所提供的資料將完全保密。

請填寫您的姓名：_____

您的生日：____年____月____日

今天的日期：____年____月____日

	完全沒有	有一點	相當多	非常多
1. 您從事一些費力的活動，如攜帶重的購物袋或手提箱，是否有困難？	1	2	3	4
2. 您從事長距離步行，是否有困難？	1	2	3	4
3. 您在戶外從事短距離步行，是否有困難？	1	2	3	4
4. 您在白天是否需要待在床上或椅子上？	1	2	3	4
5. 您進食、穿衣、洗澡或上廁所需要別人幫助嗎？	1	2	3	4

在過去一星期內（過去七天內）：	完全沒有	有一點	相當多	非常多
6. 您在從事工作或日常活動上是否受到限制？	1	2	3	4
7. 您在從事嗜好或休閒活動上是否受到限制？	1	2	3	4
8. 您呼吸會喘嗎？	1	2	3	4
9. 您曾感到疼痛嗎？	1	2	3	4
10. 您需要休息嗎？	1	2	3	4
11. 您曾難於入睡嗎？	1	2	3	4
12. 您曾感到虛弱嗎？	1	2	3	4
13. 您曾缺乏食慾嗎？	1	2	3	4
14. 您曾感到噁心嗎？	1	2	3	4
15. 您曾嘔吐嗎？	1	2	3	4

請接下頁

在過去一星期內（過去七天內）：	完全沒有	有一點	相當多	非常多
16. 您曾便秘嗎？	1	2	3	4
17. 您曾腹瀉嗎？	1	2	3	4
18. 您疲倦嗎？	1	2	3	4
19. 疼痛干擾您的日常活動嗎？	1	2	3	4
20. 您曾否難將注意力集中在一些事情上，如看報紙或看電視？	1	2	3	4
21. 您覺得緊張嗎？	1	2	3	4
22. 您感到憂慮嗎？	1	2	3	4
23. 您覺得容易發怒嗎？	1	2	3	4
24. 您覺得情緒低落嗎？	1	2	3	4
25. 您曾感到記憶困難嗎？	1	2	3	4
26. 您的身體狀況或醫療過程是否曾干擾您的家庭生活？	1	2	3	4
27. 您的身體狀況或醫療過程是否曾干擾您的社交活動？	1	2	3	4
28. 您的身體狀況或醫療過程是否曾造成您財務上的困難？	1	2	3	4

以下問題，請在1到7之間圈選最適合您的答案。

29. 您如何評定過去一星期內（過去七天內）您整體的健康？

1	2	3	4	5	6	7
非常差						極好

30. 您如何評定過去一星期內（過去七天內）您整體的生活品質？

1	2	3	4	5	6	7
非常差						極好

EORTC QLQ - LC13 台灣中文版

病人有時會表示他們有下列的症狀，請您指出在過去一星期內（過去七天內），您所經驗到這些症狀的程度。

在過去一星期內（過去七天內）：	完全沒有	有一點	相當多	非常多
31. 您咳嗽的情形如何？	1	2	3	4
32. 您是否有咳血？	1	2	3	4
33. 您在休息時是否感到呼吸困難？	1	2	3	4
34. 您在走路時是否感到呼吸困難？	1	2	3	4
35. 您在爬樓梯時是否感到呼吸困難？	1	2	3	4
36. 您曾覺得口腔或舌頭疼痛嗎？	1	2	3	4
37. 您曾有吞嚥困難嗎？	1	2	3	4
38. 您的手腳曾有刺痛感嗎？	1	2	3	4
39. 您曾有掉頭髮嗎？	1	2	3	4
40. 您曾有胸痛嗎？	1	2	3	4
41. 您曾有手臂或肩膀疼痛嗎？	1	2	3	4
42. 您曾有身體其他部位的疼痛嗎？	1	2	3	4
如果有，是那裡 _____				
43. 您有無服用任何止痛藥物？（請圈選無或有）				
1 沒有　　2 有				
如果有，止痛藥有多大幫助？	1	2	3	4

第五部分：疾病費用支出問卷

您好！我們需要知道肺病對您經濟上、財務上所造成的影響，請仔細回答下列問題。
謝謝您的合作！

（1）請問您生病前是否有工作？　　1□沒有（請跳答第二題）　　2□有
您生病前最後一個工作的平均月收入（不包括投資、房租、利息、其他非工作就有報酬之收入）是：
01□無收入（□無工作、□退休、□家庭主婦、□學生、□其他_____）
02□5,000 元以下　　03□5,000-9,999 元　　04□10,000-14,999 元
05□15,000-19,999 元　　06□20,000-24,999 元　　07□25,000-29,999 元
08□30,000-34,999 元　　09□35,000-39,999 元　　10□40,000-44,999 元
11□45,000-49,000 元　　12□50,000-54,999 元　　13□55,000-59,999 元
14□60,000-64,999 元　　15□65,000-69,999 元　　16□70,000-74,999 元
17□75,000-79,999 元　　18□80,000-84,999 元　　19□85,000-89,999 元
20□90,000-94,999 元　　21□95,000-99,999 元　　22□100,000-104,999 元
23□105,000-109,999 元　　24□110,000-114,999 元　　25□115,000-119,999 元
26□120,000 元以上

（2）請問您最近一個月是否有工作上的收入？（不包括投資、房租、利息、其他非工作就有報酬之收入）
01□無收入（□無工作、□退休、□家庭主婦、□學生、□因病提前退休或辭職、
□其他_____）
02□5,000 元以下　　03□5,000-9,999 元　　04□10,000-14,999 元
05□15,000-19,999 元　　06□20,000-24,999 元　　07□25,000-29,999 元
08□30,000-34,999 元　　09□35,000-39,999 元　　10□40,000-44,999 元
11□45,000-49,000 元　　12□50,000-54,999 元　　13□55,000-59,999 元
14□60,000-64,999 元　　15□65,000-69,999 元　　16□70,000-74,999 元
17□75,000-79,999 元　　18□80,000-84,999 元　　19□85,000-89,999 元
20□90,000-94,999 元　　21□95,000-99,999 元　　22□100,000-104,999 元
23□105,000-109,999 元　　24□110,000-114,999 元　　25□115,000-119,999 元
26□120,000 元以上

（3）請問您最近二週曾經因肺病住院或動手術嗎？　　1□沒有　　2□有

住院次數	第一次	第二次	第三次
醫院名稱			
住院日期 （或住院日數）	入院日期 出院日期 （共　　日）	入院日期 出院日期 （共　　日）	入院日期 出院日期 （共　　日）
住院加休養，請幾天假	□沒有工作，不需請假 □沒有，因病提前退休或辭職 □有，共請假　　日 □其他，請說明 _____	□沒有工作，不需請假 □沒有，因病提前退休或辭職 □有，共請假　　日 □其他，請說明 _____	□沒有工作，不需請假 □沒有，因病提前退休或辭職 □有，共請假　　日 □其他，請說明 _____

陪伴者：

1. 父
2. 母
3. 配偶
4. 子
5. 媳婦
6. 女
7. 女婿
8. 兄弟
9. 姊妹
10. 親戚
11. 朋友
12. 看護
13. 其他___

交通方式及項目：

1. 機車
2. 轎車
3. 計程車
4. 火車
5. 長途客運
6. 飛機
7. 公車
8. 捷運
9. 停車費／過路費
10. 走路
11. 其他___

住院健保給付額			
住院自付額			
就醫時交通方式及交通費	交通方式___ 起訖點________ 單程交通　時　分 單程費用約　　元	交通方式___ 起訖點________ 單程交通　時　分 單程費用約　　元	交通方式___ 起訖點________ 單程交通　時　分 單程費用約　　元
就醫時的陪伴者	陪伴者_____ □在職___人 □請／休假___人 註：________	陪伴者_____ □在職___人 □請／休假___人 註：________	陪伴者_____ □在職___人 □請／休假___人 註：________
返家時交通方式及交通費	交通方式___ 起訖點________ 單程交通　時　分 單程費用約　　元	交通方式___ 起訖點________ 單程交通　時　分 單程費用約　　元	交通方式___ 起訖點________ 單程交通　時　分 單程費用約　　元
返家時的陪伴者	陪伴者_____ □在職___人 □請／休假___人 註：________	陪伴者_____ □在職___人 □請／休假___人 註：________	陪伴者_____ □在職___人 □請／休假___人 註：________
住院期間之成年照顧者（18 歲以上）照顧的人次、時間、單程往返交通之時間與費用			
看護	每日　　人次 每人次　　小時 ________元/時日月	每日　　人次 每人次　　小時 ________元/時日月	每日　　人次 每人次　　小時 ________元/時日月
特別護士	每日　　人次 每人次　　小時 ________元/時日月	每日　　人次 每人次　　小時 ________元/時日月	每日　　人次 每人次　　小時 ________元/時日月
志工	每日　　人次 每人次　　小時	每日　　人次 每人次　　小時	每日　　人次 每人次　　小時
住院期間之成年照顧者照顧情形	住院日期：	照顧者___　□在職　□請／休假___小時　照顧___小時 往返交通方式___　起訖點________ 單程交通　時　分　單程費用約　　元 註：________	
		照顧者___　□在職　□請／休假___小時　照顧___小時 往返交通方式___　起訖點________ 單程交通　時　分　單程費用約　　元 註：________	
		照顧者___　□在職　□請／休假___小時　照顧___小時 往返交通方式___　起訖點________ 單程交通　時　分　單程費用約　　元 註：________	
	訪問時間：	照顧者___　□在職　□請／休假___小時　照顧___小時 往返交通方式___　起訖點________ 單程交通　時　分　單程費用約　　元 註：________	
		照顧者___　□在職　□請／休假___小時　照顧___小時 往返交通方式___　起訖點________ 單程交通　時　分　單程費用約　　元 註：________	

陪伴者：

1. 父
2. 母
3. 配偶
4. 子
5. 媳婦
6. 女
7. 女婿
8. 兄弟
9. 姊妹
10. 親戚
11. 朋友
12. 看護
13. 其他

——

交通方式及項目：

1. 機車
2. 轎車
3. 計程車
4. 火車
5. 長途客運
6. 飛機
7. 公車
8. 捷運
9. 停車費／過路費
10. 走路
11. 其他__

	住院日期：	照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
	住院日期：	照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
	住院日期：	照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________
		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點________ 單程交通 時 分 單程費用約 元 註：________

		照顧者____ □在職 □請／休假____小時 照顧____小時 往返交通方式____ 起訖點_____ 單程交通 時 分 單程費用約 元 註：_____	
其他情形：			

（4）請問您最近二週有因肺病而到醫院看病（包括門診、急診、看中醫及其他另類療法）嗎？

1□沒有 2□有

陪伴者：
1.父
2.母
3.配偶
4.子
5.媳婦
6.女
7.女婿
8.兄弟
9.姊妹
10. 親戚
11. 朋友
12. 看護
13. 其他
____

交通方式及項目：
1.機車
2.轎車
3.計程車
4.火車
5.長途客運
6.飛機
7.公車
8.捷運
9.停車費／過路費
10. 走路
11. 其他__

看病次數	第一次	第二次	第三次
醫院名稱			
就醫日期			
請假看病	□沒有工作，不需請假 □沒有，因病提前退休或辭職 □共請假 日 □其他， 請說明_____	□沒有工作，不需請假 □沒有，因病提前退休或辭職 □共請假 日 □其他， 請說明_____	□沒有工作，不需請假 □沒有，因病提前退休或辭職 □共請假 日 □其他， 請說明_____
健保給付額			
自付額			
就醫時交通方式及交通費	交通方式____ 起訖點_____ 單程交通 時 分 單程費用約 元	交通方式____ 起訖點_____ 單程交通 時 分 單程費用約 元	交通方式____ 起訖點_____ 單程交通 時 分 單程費用約 元
就醫時的陪伴者	陪伴者_____ □在職____人 □請／休假____人 註：_____	陪伴者_____ □在職____人 □請／休假____人 註：_____	陪伴者_____ □在職____人 □請／休假____人 註：_____
門診看病所需時間（不含交通時間）	時 分	時 分	時 分
門診時的陪伴者： 是否和就醫時的陪伴者相同 □不是 □是〔跳到返家時交通方式及交通費〕	陪伴者_____ □在職____人 □請／休假____人 註：_____	陪伴者_____ □在職____人 □請／休假____人 註：_____	陪伴者_____ □在職____人 □請／休假____人 註：_____
返家時交通方式及交通費	交通方式____ 起訖點_____ 單程交通 時 分 單程費用約 元	交通方式____ 起訖點_____ 單程交通 時 分 單程費用約 元	交通方式____ 起訖點_____ 單程交通 時 分 單程費用約 元

返家時的陪伴者： 是否和就醫時的陪伴者相同 □不是 □是〔跳到下一題〕	陪伴者_____ □在職____人 □請／休假____人 註：_____	陪伴者_____ □在職____人 □請／休假____人 註：_____	陪伴者_____ □在職____人 □請／休假____人 註：_____
其他情形：			

（5）請問您最近二週除了門診及住院外，是否有因肺病在家中聘請看護照顧您的生活？

1□沒有

2□有，每日　　人次，每人次　　小時，_____元/時日月

（6）請問您最近二週有因肺病在醫院療程外另行購買並服用或使用藥品（含中醫藥）／補品／維他命／醫療儀器設備等，或參加衛教課程？

1□沒有

2□有

□ 藥品（西藥）　_____ 次， 共 _____ 元

□ 中藥　_____ 次， 共 _____ 元

□ 補品／維他命　_____次， 共 _____ 元

□ 醫療儀器設備　_____次， 共 _____ 元

□ 參加衛教課程　_____次， 共 _____ 元

□ 其他〔如另類療法〕　_____次， 共 _____ 元

請註明：_____

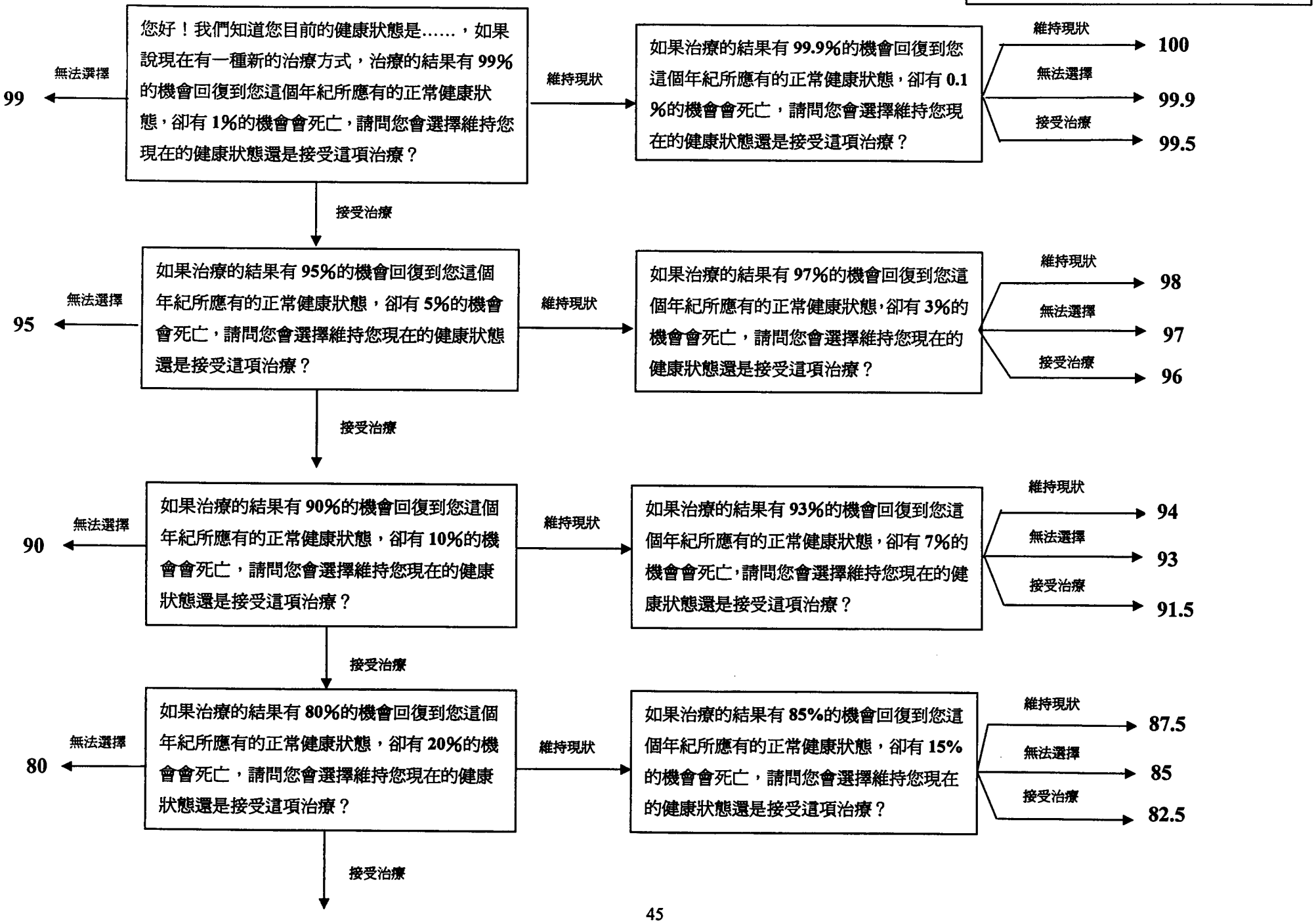
總計_____元

（7）本次住院除了健保外，請問您是否有其他商業醫療保險來分擔您的住院醫療支出？〔非住院者不填〕

1□沒有

2□有

病患是否可以了解題意？□是□否



附錄二

計畫論文產出

脊髓損傷生活品質問卷之發展

張彧* 王顏和** 姚開屏*** 王榮德****

國立台灣大學醫學院職能治療學系* 醫學系復健科** 國立台灣大學心理系***
國立台灣大學公共衛生學院職業醫學與工業衛生研究所暨醫學院附設醫院內科*****

前言

脊髓損傷(spinal cord injury)會造成永久的神經傷害及龐大的醫療支出。近年來，由於醫學的進步，改進了對於脊髓損傷者的處理，減少合併症的發生，縮短其住院時間，不但增進其生活功能，也降低能力障礙(disability)的嚴重度，脊髓損傷者早期死亡的情形逐漸減少，而其預期壽命有明顯的增加[1]。生活品質漸漸成爲脊髓損傷者復健計畫之主要目標及復健計畫成果評量的重要指標之一[2-5]。

「生活品質」一詞對不同的人代表不同的意義，每個人的感受與認知也不盡相同。在探討脊髓損傷者生活品質的研究中，通常有兩種方式：主觀的及客觀的方式[6-9]。主觀的方式定義生活品質與個人主觀感覺的希望及成就一致，生活品質被描述爲生活滿意度或幸福感；而客觀的方式是藉由評估個案的損傷及/或能力障礙來預測其主觀的生活品質。目前大多數的學者認爲只有個體的主觀感受可用以直接評估生活品質，客觀的生活品質測量只能描述生活狀況及經驗，但不能直接的測量生活品質[7,9]。

脊髓損傷患者生活品質曾以不同層面來加以探討，Dijkers[8]及 Fuhrer 等[9]所做的 meta analysis 研究發現生活品質與損傷(如傷害程度等)只有極少的相關性，與能力障礙(如自我照顧能力等)的相關性雖然比損傷較高，但並沒有一致性，然而社會環境角色的扮演在許多研究中卻是與生活品質有一致的相關性；影響脊髓損傷患者生活品質相關的因素包括：對生活的態度、自尊、自覺健康、生理能力、獨立程度、自主權、社會與家庭的支持、活動能力、日常生活活動能力、參與休閒活動與工作的機會與能力、資源的獲得[10-12]，這些因素涵蓋了生活品質中的生理、心理、社會、環境等層面。

雖然近年來有許多工具用來測量生活品質，如：Sickness Impact Profile，MOS SF-36，Nottingham Health Profile，EuroQol，世界衛生組織生活品質問卷等[13-16]。這些量表主要仍是作爲一般性(generic)問卷之用，並非針對某一種疾病(disease specific)而設計的，用來作跨病比較還可以，如果用來作特定疾病之生活品質研究，則恐怕反應性(responsiveness)會有所不足；因此，仍有發展特定疾病之生活品質問卷之必要，以作更深入之探討。

因爲世界衛生組織之生活品質問卷具有跨文化特色、容許外加適合本土文化特色的題目、及容許外加適合各種疾病特殊的題目等特色[14-16]，因此，本研究的目的是以「台灣簡明版世界衛生組織生活品質問卷」爲基礎[16]，並參照世界衛生組織生活品質小組發展「世界衛生組織生活品質問卷」的程序[14-15]，發展出適合測量脊髓損傷者的生活品質問卷。

Title: Development of a Quality of Life Questionnaire for Persons with Spinal Cord Injury

Authors: Yuh Jang*, Yen-Ho Wang**, Grace Yao***, Jung-Der Wang****
School of Occupational Therapy*, Department of Physical Medicine and Rehabilitation, School of Medicine**, Department of Psychology***, Institute of Occupational Medicine and Industrial Hygiene, Department of Internal Medicine, National Taiwan University Hospital, Natioanl Taiwan University****

Key Words: quality of life, spinal cord injury, WHOQOL

表一：脊髓損傷特定 22 題之分析結果

題號	與假設所屬範疇之相關	與其他範疇之相關[a]	平均值	變異數	與整體生活品質之相關	與整體健康評價之相關	內部一致性 (Cronbach α)[b]
生理健康範疇							
29	.55	-	3.06	1.39	.17	.35**	.79
31	.28	-	1.94	1.18	.23*	.09	.75
34	.58	心理 (.49)	3.12	1.29	.35**	.18	.79
42[c]	.53	心理 (.42)	3.11	1.60	.28**	.21*	.78
44	.43	-	2.66	1.84	.17	.18	.77
46	.59	心理 (.54) 環境 (.49)	2.45	1.49	.37**	.21*	.79
48	.39	心理 (.42)	3.17	1.44	.32**	.21*	.77
心理範疇							
30[c]	.66	生理 (.47) 社會 (.47) 環境 (.42)	2.67	1.33	.50**	.41**	.80
33	.48	-	3.89	1.06	.17	.15	.78
41	.31	-	3.56	1.25	.15	.10	.75
45	.49	環境 (.41) 生理 (.41)	2.76	1.59	.52**	.29**	.78
49	.21		2.47	1.75	.20*	.06	.73
社會關係範疇							
35	.43	-	3.93	0.62	.13	.25**	.63
36[c]	.46	心理 (.41)	3.76	0.96	.22*	.40**	.64
37	.48	心理 (.41)	3.09	1.20	.15	.27**	.65
環境範疇							
32	.20	-	2.68	1.00	.13	.02	.78
38	.43	-	4.08	1.19	.37**	.16	.81
39	.27	-	4.17	0.94	.34**	.18	.79
40	.22	-	2.38	0.96	.11	.04	.78
43	.30	-	4.06	1.02	.38**	.04	.80
47	.42	-	3.37	1.22	.34**	.28**	.81
50	.35	-	2.52	1.20	.20*	.25**	.80

[a]表題目與範疇之相關係數大於.40；[b]表加入此題之 Cronbach's α 值；[c]最後選進「脊髓損傷生活品質問卷」之題目。*表 $p < 0.05$； **表 $p < 0.01$*。

是以參與者受訪時間爲基準，最近兩個星期的感受來評斷自己的生活品質。

依據「台灣簡明版世界衛生組織生活品質問之發展及使用手冊所述決定有效問卷，處理資料的缺失及轉換反向題目的分數。然後，將各範疇內每個題目的分數加起來之後，除以各範疇之題數，然後乘以 4 即可得到「脊髓損傷生活品質問卷」各範疇的分數。

所有的資料乃是採用 Statistical Package for the Social Sciences (SPSS) 視窗 8.0 版本來進行各種統計分析。

題目選擇之方法與標準

採用下面幾種分析方法來篩選：1.脊髓損傷特定題目之各個題目必須與其假設所屬範疇之相關性高於其他範疇的相關性，且皮爾森相關係數 r 必須大於.40 來表示。2.脊髓損傷特定題目應該要與「整體生活品質」及「整體健康評價」兩個一般性題目相關。3.題目平均數必須在二與四之間，題目之變異數必須大於同層面內原核心

表二：WHOQOL-BREF 與「脊髓損傷生活品質問卷」間之 Pearson *r* 相關係數

WHOQOL-BREF	脊髓損傷生活品質問卷			
	生理健康	心理	社會關係	環境
生理健康	**.98**	.70	.49	.67
心理	.71	**.99**	.69	.67
社會關係	.50	.63	**.89**	.55
環境	.64	.64	.56	**.99**

粗體部分表示收斂效度。

表三：「脊髓損傷生活品質問卷」 各範疇之內部一致性及再測信度*

範疇(題數)	內部一致性 Cronbach α	再測信度 Pearson r
1 生理健康(8)	.79	.75
2 心理(7)	.80	.82
3 社會關係(5)	.64	.77
4 環境(10)	.79	.82

*刪除「脊髓損傷生活品質問卷」中兩題一般及整體性題目。

題目中最大的變異數。4.求出題目所在層面的內部一致性(Cronbach's α)及刪除該題目後的內部一致性。若刪除該題目後 α 值反而比整體 α 值高的話，則表示此題目不是一個好的題目。

結 果

「脊髓損傷生活品質問卷」題目篩選的結果列在表一。題目與範疇之相關顯示：題號 31，32，39，40，41，43，48，49，及 50 因爲與假設所屬範疇之相關係數低於.40，且有些題目與假設所屬範疇之相關係數低於其他範疇。與「整體生活品質」具有相關性的題目有 13 題。與「整體健康評價」具有相關性的題目有 13 題。通過平均數測試的共有 16 題；通過變異數測試的有 7 題。信度分析：「台灣簡明版世界衛生組織生活品質問卷」生理健康及心理範疇之 Cronbach's alpha 值爲 0.75，社會關係範疇爲 0.55，環境範疇爲 0.79。如表 1 所示，在生理健康範疇中僅有第 31 題「您主動參與社區活動的頻率有多少？」一題刪去後，此範疇的整體 Cronbach α值會提高，因此，只有此題，在生理健康範疇中沒有通過測試。在心理範疇中僅有第 41 題「您有獲得社會福利及政策資訊的困難嗎？」及第 49 題「您個人的宗教信仰能幫助您面對人生的困難嗎？」此二題沒有通過測試。在社會關係範疇中的三個新增加的題目都通過此項測試。在環境範疇中僅有第 32 題「當您需要協助時，您會主動要求他人的協助嗎？」、第 39 題「您滿意您所接受到的復健服務嗎？」及第 40 題「您滿意政府對於脊髓損傷患者的政策或社會福利嗎？」三題沒有通過測試。

綜合各項分析結果在生理健康範疇選擇出第 42 題「您有獲得新技能機會的困難嗎？」；心理範疇選擇出第 30 題「您對自己的未來樂觀嗎？」；社會關係範疇第 36 題「您覺得家庭對您的支持足夠嗎？」等三題加入最後版本的「脊髓損傷生活品質問卷」，最後版本的問卷共有 31 題。

「脊髓損傷生活品質問卷」之信效度

收斂效度(convergent validity)：正如同我們所期待的，「脊髓損傷生活品質問卷」與 WHOQOL-BREF 具備高度的相關性(表二)。

內部一致性及再測信度：在 109 位參與研究之脊髓損傷個案中隨機選取 32 位個案進行再測信度的研究，這 32 位個案在接受第一次調查之後的 2-8 個星期之內，再接受一次的調查，利用 Pearson *r* 求得兩次調查結果的相關性，結果顯示(如表三所示)，所有的範疇都具備高的再測信度。

討 論

復健的目標是讓病患能夠在社會扮演主動

附錄：脊髓損傷患者生活品質問卷(新加入之 22 題)題目內容、所屬範疇/層面、量尺類型、題目正反向性質

題號	所屬層面	所屬範疇	量尺類型	題目方向	題目內容
29	疼痛及不適	生理健康	強度	反向	您的疼痛或不舒服，會造成您從事日常活動的困擾嗎？
30	靈性/宗教/個人信念	心理	強度	正向	您對自己的未來樂觀嗎？
31	移動能力	生理健康	頻率	正向	您主動參與社區活動的頻率有多少？
32	身體安全及保障	環境	能力	正向	當您需要協助時，您會主動要求他人的協助嗎？
33	身體意像及外表	心理	強度	反向	您對自己的外表感到不自在嗎？
34	日常生活活動	生理健康	強度	反向	您處理日常活動的限制，會造成您的困擾嗎？
35	個人關係	社會關係	評估	正向	您滿意照顧者對您的支持嗎？
36	個人關係	社會關係	強度	正向	您覺得家庭對您的支持足夠嗎？
37	個人關係	社會關係	評估	強度	您滿意自己的感情生活嗎？
38	健康及社會照護	環境	強度	反向	您有獲得醫療保健服務的困難嗎？
39	健康及社會照護	環境	評估	正向	您滿意您所接受到的復健服務嗎？
40	健康及社會照護	環境	評估	正向	您滿意政府對於脊髓損傷患者的政策或社會福利嗎？
41	負面感受	心理	強度	反向	您有獲得社會福利及政策資訊的困難嗎？
42	移動能力	生理健康	強度	反向	您有獲得新技能機會的困難嗎？
43	交通	環境	強度	反向	您有獲得輔助器具方面的困難嗎？
44	工作能力	生理健康	強度	反向	您有取得工作機會的困難嗎？
45	靈性/宗教/個人信念	心理	能力	反向	您覺得自己會拖累家人嗎？
46	移動能力	生理健康	能力	正向	您能夠參與自己想要參與的休閒及娛樂活動嗎？
47	取得新資訊及技能的機會	環境	強度	反向	您週遭的環境，會造成您從事日常活動及工作的困擾嗎？
48	日常生活活動	生理健康	強度	反向	您在交通方面的限制，會對您的生活造成困擾嗎？
49	靈性/宗教/個人信念	心理	強度	正向	您個人的宗教信仰能幫助您面對人生的困難嗎？
50	健康及社會照護	環境	能力	正向	您的家人或社會人士能方便取得有關脊髓損傷方面的資訊嗎？

的、獨立的、具生產性的角色，並對生活品質有高度的滿足感。本研究遵循世界衛生組織生活品質小組發展「世界衛生組織生活品質問卷」的步驟，發展出屬於脊髓損傷者的生活品質問卷，且此問卷經過初步的信效度分析顯示出具備相當的信效度。相信此「脊髓損傷生活品質問卷」將可應用在日後對於脊髓損傷者治療或服務的一種指標及依據。

誌 謝

感謝國科會 NSC 89-2314-B-002-433-M56 研究人員的技術支持，以及國科會 NSC 89-2614-B-002-008-M47 之經費支持，使得本研究得以順利完成。

推薦讀物

1. Trieschmann RB: Spinal Cord Injuries: Psychological, Social, and Vocational Rehabilitation, 2nd ed. New York: Demos Publications, 1988.
2. Tam SF: Quality of life: Theory and methodology in rehabilitation. Int J Rehabil Res 1998; 21:365-74.
3. Clayton KS, Chubon RA: Factors associated with the quality of life of long-term spinal cord injured persons. Arch Phys Med Rehabil 1994; 75:633-8.
4. Fabian ES: Quality of life: A review of theory and practice implications for individuals with long-term mental illness. Rehabil Psychol 1990; 35:161-9.
5. Gill TM, Feinstein AR: A critical appraisal of the quality of life measurements. J Am Med Assoc 1994; 272:619-25.
6. Kennedy P, Rogers B: Reported quality of life of people with spinal cord injuries: a longitudinal analysis of the first 6 months post-discharge. Spinal Cord 2000; 38:498-503.
7. Campbell A: Subjective measures of well-being. Am Psychol 1976; 2:171-7.
8. Dijkers M: Quality of life after spinal cord injury: A meta analysis of the effects of disablement component. Spinal Cord 1997; 35:829-40.
9. Fuhrer MJ, Rintala DH, Hart KA, Clearman R, Young ME: Relationship of life satisfaction to impairment, disability, and handicap among person with spinal cord injury living in the community. Arch Phys Med Rehabil 1992; 93:552-7.
10. Whiteneck OG: Measuring what matters: Key rehabilitation outcomes. Arch Phys Med Rehabil 1994; 75:1073-6.
11. Boswell BB, Dawson M, Heininger E: Quality of life as defined by adults with spinal cord injuries. J Rehabil 1998; 64:27-32.
12. Robnett RH, Gliner JA: Qual-OT: A quality of life assessment tool. Occup Ther J Res 1995; 15:198-214.
13. Kaplan RM: Profile versus utility based measures of outcome for clinical trials. In: Staquet MJ, Hays RD, Fayers PM eds. Quality of Life Assessment in Clinical Trials: Methods and Practice. Oxford: Oxford University Press, 1999:69-90.
14. WHOQOL group: Development of the WHOQOL: Rationale and current status. Int J Ment Health 1994; 23:24-56.
15. WHOQOL group: Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med 1998; 28:551-8.
16. 台灣版世界衛生組織生活品質問卷發展小組：台灣版世界衛生組織生活品質問卷之發展簡介。中華衛誌 2000; 19:315-24.
17. 張彧、王顏和、游正芬、鍾智文、王榮德：以焦點團體方式探討影響脊髓損傷者生活品質之因素。中華復健醫誌 2000; 28:87-95.
18. 林茂榮、姚開屏、黃景祥、王榮德：台灣版世界衛生組織生活品質問卷量尺語詞的選擇。中華衛誌 1999; 18:262-70.

如何設計一份特定疾病所適用之生活品質問卷—以愛滋病患為例

方啓泰* 熊秉荃** 游正芬*** 陳茂源* 王榮德*,***
臺灣大學醫學院附設醫院內科部* 臺灣大學醫學院護理學系**
臺灣大學公共衛生學院職業醫學及工業衛生研究所***

愛滋病(後天免疫不全症候群)簡介

後天免疫不全症候群(acquired immunodeficiency syndrome, AIDS)簡稱愛滋病，是由人類免疫不全病毒 (human immunodeficiency virus, HIV) 所引起的一種慢性病毒感染症。愛滋病很可能在 1970 年代起源於熱帶非洲，經輾轉傳播，跨洋傳到歐美地區。目前全世界現約有 4000 萬人感染 HIV 病毒，而且病患數目快速增加，僅 2000 年一年中即新增約 6 百萬感染者。已有 2100 萬人因愛滋病死亡。流行地區遍及每一個國家。非洲的病患最多(占 70%)，但亞洲地區的感染者數目正在快速增加中。首例本土愛滋病例出現於 1986 年。至 2001 年 9 月底我國 HIV 感染者人數累計已達 3740 人。初感染 HIV 時，可能會出現發燒、紅疹、淋巴腺腫大，持續數週，然後自然消退。無症狀期可能長達二、三年或十幾年 (平均七-八年)，這段期間內感染者自覺並無異狀，但有傳染性。HIV 病毒主要侵襲在人體免疫系統中擔任中心角色的 CD4+淋巴球，當 CD4+淋巴球數目逐漸減少，到低於 200/ μL 時，免疫系統即不易應付環境中各種原蟲、細菌、黴菌及病毒的挑戰。首先出現的伺機性感染是口腔念珠菌症，嚴重時可蔓延到食道，造成吞嚥疼痛。其次為肺囊蟲肺炎，以漸進性發燒、呼吸困難、咳嗽來表現。其他常見的併發感染包括：肺結核、肺外結核、巨細胞病毒視網膜炎(造成失明)、卡波西氏肉瘤、帶狀庖疹、及其他各種罕見的感染。患者最後因難以控制的反覆感染而形銷骨立，逐漸衰弱而死亡。

1995 年何大一博士提出高效抗反轉錄病毒療法 (highly active antiretroviral therapy) — 以一種蛋白胨抑制劑 (protease inhibitor) 加上二種反轉錄胨抑制劑 (nucleoside reverse transcriptase inhibitors) 合併治療，能將 HIV 在人體內的增殖完全抑制。但是高效抗反轉錄病毒療法並不能根治愛滋病，HIV 病毒僅是被藥物壓抑而已，一旦停藥即會再度活躍起來，因此須終生服用。而且藥物服用方式很複雜，有些處方一天需五次定時服藥，服藥時間又須與用餐時間配合，嚴重干擾生活作息。此外藥物副作用甚多：包括上吐下瀉、腎結石、神經病變、貧血等，許多病患難以忍受。但若未好好服藥，HIV 病毒會產生抗藥性而最終使治療失敗。

世界衛生組織生活品質問卷愛滋病版 (WHOQOL-HIV) 之發展：質性研究

國外對愛滋病患生活品質之測量雖已有

Title: How to Design a Disease-Specific Quality of Life Questionnaire for Patients with HIV Infection
Authors: Chi-Tai Fang*, Ping-Chuan Hsiung**, Cheng-Fen Yu***, Mao-Yen Chen*, Jung-Der Wang*,***
Department of Internal Medicine, National Taiwan University*; School of Nursing, College of Medicine, National Taiwan University**; Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University***
Key Words: quality of life, WHOQOL, human immunodeficiency virus

許多特定疾病版 (disease-specific)問卷量表問世，包括 MOS-HIV[1]、MQoL-HIV[2]、 HIV-QL31[3]、HIV Overview of Problem- Evaluation System (HOPES)[4]、 HIV/AIDS- targeted quality of life (HAT-QoL)[5]、Functional Assessment of Human Immunodeficiency Virus Quality of Life Questionnaire(FAHI)[6] 等等。但這些量表有兩個共同缺點：一爲這些量表發展時缺乏對「生活品質」的良好定義及理論基礎；二爲這些量表在西方社會開發，未必適用於其他文化。國外問卷量表尚有可能需繳交使用費問題。由於世界衛生組織生活品質問卷量表 (World Health Organization Quality of Life Assessment, 簡稱爲 WHOQOL) [7,8]在「生活品質」的觀念上已相當完整，且其心理計量特性較其他一般性問卷爲佳，更重要的是具有跨文化效度，又不必擔心未來應用時被收專利費，故我們選擇 WHOQOL 爲基礎來發展 HIV 感染者之特定疾病版生活品質問卷量表。

特定疾病版問卷之發展方法，乃是以質性研究 (qualitative research) 找出影響愛滋病感染者生活品質的因素，與台灣版世界衛生組織生活品質問卷簡明版[9] 之內容比對，加入增補性的特定疾病題目(disease-specific items)。質性研究係以焦點團體(focus group)討論的方式來進行。爲能充分瞭解問題的各種不同面向，焦點團體之選擇包括病患代表及專家委員會。病患代表包含處於疾病各種階段及不同性別背景之病患。專家委員則包括與病患接觸最密切的護理人員及志工。訪談全程以錄音記錄，以錄音帶方式收集資料後，整理成逐字稿(transcript)，再將逐字稿內容依其表達意思做小歸類，做一步分析。共 11 位經西方墨點法(Western blot)診斷確定之 HIV 感染者參與前後四次的焦點團體訪談。訪談時間爲 30 分鐘至 1 小時。包括早期無症狀病患 5 人，晚期已發病病患 6 人。就醫期間最短者爲二個月，最長爲六年。10 位爲男性，1 位爲女性。10 位病患正接受雞尾酒療法，位則尚未接受藥物治療。專家委員會包括一位醫師，一位護理學家，一位直接照護病人之護士，及一位義工，均爲愛滋病醫療團隊之成員。

接受訪談的病患均指出，初期幾乎全無不適，但疲倦、體重減輕等症狀。一旦發病，出現伺機性感染，各種症狀就常會困擾病患的生活品質，其中在心理及社會方面，常遭家庭及社會歧視及排斥，尤其在就業機會、醫療照護、及交友感情遭歧視及排斥影響最大。對死亡的恐懼、對病痛的害怕，則是心理上的莫大壓力。高效抗反轉錄病毒療法出現，有效的舒緩生理上死亡病痛的威脅，但對社會歧視的問題則無幫助。另一方面，藥物治療由於吃藥種類多、頻率高，且有各種程度的特定藥物副作用，反而影響生活品質。病患所提及會影響生活品質的藥物特定副作用症狀，包括拉肚子、嘔吐、起疹子、影響睡眠、口渴、外觀改變等等。

依病患所提影響因素與世界衛生組織生活品質問卷所包含層面做比較，找出對愛滋病患較特殊的生活品質影響層面，經過專家焦點團體會商，最後選出四個因素：吃藥引起的副作用、吃藥的頻率、工作機會、醫護人員提供的服務，並據當初病患提及此四因素影響的方式，決定選用「頻率」、「能力」、「強度」、「評估」中其一的方式來擬定題目。最後擬訂出來的 HIV 特定疾病題目共四題如下：

1.吃藥引起的副作用會造成您的困擾嗎？(屬生理範疇)
□完全沒有困擾 □有一點困擾 □中等程度困擾 □很困擾 □極困擾

2.您滿意自己的工作機會嗎？(屬環境範疇)
□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

3.整體而言，您滿意醫護人員所提供的服務嗎？(屬環境範疇)
□極不滿意 □不滿意 □中等程度滿意 □滿意 □極滿意

4.您吃藥的頻率會給您帶來困擾嗎？(屬生理範疇)
□完全沒有困擾 □有一點困擾 □中等程度困擾 □很困擾 □極困擾

按台灣版世界衛生組織生活品質問卷簡明版原有 28 題[9]。加入愛滋病特定疾病題目

表一：WHOQOL-HIV 之內部一致性(n = 136)

範疇	Cronbach's alpha
生理	0.74
生理 (含愛滋病特定疾病題目)	0.71
心理	0.81
社會	0.76
環境	0.85
環境 (含愛滋病特定疾病題目)	0.86
26 題問卷	0.92
28 題問卷 (含本土題目)	0.93
32 題問卷 (含愛滋病特定疾病題目)	0.93

4 題後(依序編爲第 29 至 32 題)，台灣版 WHOQOL-HIV 共有 32 題。

WHOQOL-HIV 之信效度

台灣版 WHOQOL-HIV 之信效度爲對 136 位在台大醫院及台北市立性病防治所就診的愛滋病患進行測試。136 位病患均經西方墨點法診斷確定。其中 44 位接受前後二次問卷施測，間隔 1 至 8 週(平均 4 週)。測試項目包括內部一致性(internal consistency)、再測信度(test-retest reliability)、內容效度(content validity)、建構效度(construct validity)、效標關連效度(criterion validity)及區辨效度(discriminative validity)。統計分析軟體採用 SPSS 9.0 for WINDOW。136 位病患中絕大多數(96%)爲男性，年齡層以 30 - 40 歲最多。90% 病患正接受高效抗反轉錄病毒療法，其他爲新診斷病患。62% 病患受到 10 個以上症狀困擾。136 位病患之 WHOQOL-HIV 各範疇之平均得分 ± 標準差(得分範圍)分別爲：生理 13.74 ± 2.00 (9.33–17.78)；心理 12.49 ± 2.75 (6.67–18.67)；社會 12.85 ± 2.70 (6.00–20.00)；環境 13.36 ± 2.26 (8.00–18.55)。(各範疇得分滿分均爲 20 分)。

在內部一致性方面，採用 Cronbach's α 評估，四個範疇以及問卷整體的內部一致性如表一。結果顯示本問卷各範疇內部一致性極佳，各範疇 Cronbach's α 介於 0.74 到 0.85 之間，整體問卷之內部一致性值高達 0.93。在再測信度方面，32 題中，除了三題(物理環境、被尊重及接受、及醫護人員提供之服務)之外，其他各題之相關係數均達統計上顯著水準。絕大多數題目前後測得分之相關係數介於 0.52–0.78 之間。這個結果和 WHOQOL 原版及 WHOQOL 台灣版測試結果相似。所加入的 4 個愛滋病特定疾病題目中，吃藥引起的副作用(相關係數 0.609)，工作機會(相關係數 0.626)，吃藥頻率(相關係數 0.657)都有很好的再測信度，而醫護人員提供的服務(相關係數 0.295)則前後測得分相關性較低。32 題中，有 5 題(物理環境、被尊重及接受、對醫藥之依賴、疼痛、醫護人員提供之服務)前後測得分相關較差，可能係前後測間隔期間(1 至 8 週，平均 4 週)狀況有所改變所致。

在確認本問卷的信度後，我們進一步分析其效度。在內容效度方面，我們採用皮爾森相關法(Pearson correlation)。結果發現所有題目與所屬範疇分數之相關均介於 0.42–0.82 之間，算是相當好的內容效度。除第 32 題之外，所加入的愛滋病特定疾病題目與 G1 題(整體生活品質)分數皆有合理的相關性，係數介於 0.20–0.50 之間。第 32 題(服藥頻率)與 G1 題(整體生活品質)分數相關係數僅有 0.13。這可能是由於若服藥頻率超過病患能忍受的限度，病患乾脆不予配合或要求醫師更改處方。結果導致服藥頻率高低對長期生活品質影響很小。由於內容效度較差，在接下來之分析中第 32 題予以排除。在建構效度方面，我們使用探索性因素分析方法(exploratory factor analysis)來看是否本問卷在 HIV 感染者生活品質的測量

表二：探索性因素分析結果 (n = 136)

範疇	WHOQOL 層面	題號	因子 1 心理/活力	因子 2 社會	因子 3 環境	因子4 生理/症狀
生理	F1. 疼痛	3	0.174	0.000	-0.073	0.735
生理	F2. 活力	10	0.447	0.073	0.305	0.114
生理	F3. 睡眠	16	0.437	-0.205	0.430	-0.189
生理	F9. 行動能力	15	0.380	0.546	-0.167	-0.024
生理	F10. 日常活動	17	0.607	0.130	0.203	0.035
生理	F11. 對醫療之依賴	4	-0.172	0.349	-0.164	0.742
生理	F12. 工作能力	18	0.526	0.218	0.109	-0.024
生理	藥物副作用	29	0.163	-0.290	0.364	0.495
心理	F4. 正面感覺	5	0.332	0.263	-0.064	-0.070
心理	F5. 思考學習記憶	7	0.696	-0.140	0.194	0.098
心理	F6. 自尊	19	0.775	0.080	-0.023	-0.079
心理	F7. 身體意象	11	0.710	0.193	-0.213	0.200
心理	F8. 負面感覺	26	0.752	-0.337	0.045	0.119
心理	F24. 靈性/個人信念	6	0.840	-0.070	-0.068	-0.014
社會	F13. 人際關係	20	0.059	0.538	0.142	-0.214
社會	F14. 社會支持	22	0.076	0.584	0.030	0.093
社會	F15. 性生活	21	0.073	0.053	0.556	0.174
社會	F25. 被尊重	27	0.126	0.501	0.277	0.080
環境	F16. 身體安全	8	0.578	0.234	0.011	0.041
環境	F17. 居家環境	23	-0.118	0.166	0.719	-0.138
環境	F18. 財務資源	12	0.426	0.371	0.049	-0.039
環境	F19. 社會照護	24	-0.124	0.231	0.567	0.163
環境	F20. 資訊技能	13	0.648	0.307	-0.223	-0.180
環境	F21. 休閒娛樂	14	0.354	0.337	0.175	-0.146
環境	F22. 物理環境	9	-0.040	0.194	0.593	-0.212
環境	F23. 交通	25	0.035	0.045	0.732	-0.038
環境	F26. 飲食	28	-0.120	0.755	0.194	0.120
環境	工作機會	30	0.388	0.355	-0.018	0.143
環境	醫療品質	31	-0.232	0.777	0.129	0.110

上會符合 WHOQOL-BREF 原來的四個範疇架構。因素分析採取主因子法(principal factor)及斜交轉軸(promax rotation)進行分析。因素分析的結果顯示：一個含四因子的解最爲恰當(表二)，能解釋 52.6% 總變異量。這四個因子基本上呼應 WHOQOL-BREF 原來的四個範疇，表明 WHOQOL-HIV 有良好的建構效度。某些題目未能在因素分析中歸屬於原本所屬範疇，可能是由於四個範疇在概念上原本就有若干重疊之處，若考慮病患的特殊處境，某些題目歸屬於其他範疇可能更爲合理。

在效標關連效度方面，各範疇之平均得分和病患自覺健康狀態及自覺快樂均有正相關(相關係數 0.52~0.73)，而和身體症狀數及以 SSC-HIV 症狀量表[10]測量之症狀嚴重度呈負相關(相關係數-0.39 ~ -0.56)，表示效標關連效度良好(表三)。在區辨效度上，我們比較 136 位病患資料與213位健康人以台灣版WHOQOL施測的結果，發現兩組在生理、心理、社會範疇之得分，均呈現有意義之差別 ($p < 0.01$, Student's t test)。在上述範疇，健康人之範疇平均得分顯著高於愛滋病患。這表明 WHOQOL

表三：效標關連效度 (n = 136)

	自覺健康狀態	自覺快樂	症狀數	症狀嚴重度
範疇得分				
生理	0.53	0.55	-0.46	-0.52
生理*	0.55	0.57	-0.48	-0.56
心理	0.60	0.73	-0.47	-0.49
社會	0.52	0.59	-0.40	-0.41
環境	0.57	0.55	-0.41	-0.43
環境*	0.57	0.56	-0.39	-0.41

全部相關係數 $p < 0.01$, *含愛滋病特定疾病題目

對 HIV 感染者有良好的區辨效度。

結 語

本文以愛滋病患爲例，說明如何以 WHOQOL 爲基礎，設計一份特定疾病所適用之生活品質問卷及驗證其信效度。WHOQOL-HIV 在測定 HIV 感染者的生活品質上具有良好的信度和效度，可作爲進一步研究愛滋病患生活品質問題的有用工具。

誌 謝

本研究係由國科會計畫 NSC 89-2314-B-002-433-M56 經費補助。

推薦讀物

1. Wu AW, Revicki DA, Jacobson D, Malitz FE: Evidence for reliability, validity and usefulness of the Medical Outcomes Study HIV Health Survey (MOS-HIV). Qual Life Res 1997; 6: 481-93.
2. Smith KW, Avis NE, Mayer KH, Swislow L: Use of the MQoL-HIV with asymptomatic HIV-positive patients. Qual Life Res 1997; 6: 555-60.
3. Leplege A, Rude N, Ecosse E, Ceinos R, Dohin E, Pouchot J: Measuring quality of life from the point of view of HIV-positive subjects: the HIV-QL31. Qual Life Res 1997; 6: 585-94.
4. De Boer JB, Sprangers MA, Aaronson NK, Lange JM, van Dam FS: A study of the reliability, validity and responsiveness of the HIV overview of problems evaluation system (HOPES) in assessing the quality of life of patients with AIDS and symptomatic HIV infection. Qual Life Res 1996; 5: 339-47.
5. Holmes WC, Shea JA: A new HIV/AIDS -targeted quality of life (HAT-QoL) instrument: development, reliability, and validity. Med Care 1998; 36: 138-54.
6. Peterman AH, Cella D, Mo F, McCain N: Psychometric validation of the revised Functional Assessment of Human Immunodeficiency Virus Infection (FAHI) quality of life instrument. Qual Life Res 1997; 6: 572-84.
7. WHOQOL Group: The World Health Organization quality of life assessment (WHOQOL): Development and general psychometric properties. Soc Sci Med 1998; 46: 1569-85.
8. WHOQOL Group: Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med 1998; 28: 551-8.
9. The WHOQOL-Taiwan Group: The User's manual of the development of the WHOQOL -BREF Taiwan version. 1st ed. Taiwan, Taipei, 2000.
10. Holzemer WL, Henry SB, Nokes KM, et al: Validation of the sign & symptom check-list for persons living with HIV disease (SSC-HIV). J Adv Nurs 1999; 30: 1041-9.

台灣版世界衛生組織生活品質問卷之發展簡介

台灣版世界衛生組織生活品質問卷發展小組

THE WHOQOL-TAIWAN GROUP

請參考附註一的台灣版問卷發展小組成員名單

通訊作者Correspondence author. 姚開屏 E-mail: kaiping@ccms.ntu.edu.tw

世界衛生組織(World Health Organization, WHO)結合了世界上不同的國家或地區的學者，於1995年完成「世界衛生組織生活品質問卷(WHOQOL-100)」的發展，稍後也簡化發展成只有26題的簡明版問卷(WHOQOL-BREF)。此問卷有100題測各文化共通的一般性健康相關生活品質的題目，此外並允許各國另外加入各文化特有的題目。我們於1997年取得授權後，開始了台灣版問卷的發展，本篇即是介紹此問卷於台灣的發展經過及結果。臺灣版問卷在發展時，有考慮到如何處理問卷內容的翻譯、問卷量尺語詞的選用，以及本土題目的選擇等問題。我們將臺灣版預試問卷施用於全省十七家醫院，而收集到1068位受訪者的資料，以分析問卷的信、效度，結果發現整份問卷的內部一致性達0.97而再測信度達0.86($p<.01$)；內容效度及同時效度亦皆達到統計上的顯著水準($p<.01$)；在區辨效度方面，大多數的題目皆可區辨健康人與不健康的人；在預測效度方面，各範疇分數能解釋64.2%整體生活品質及一般健康狀態層面分數變異量；在建構效度方面，我們發現四個因素(生理健康、心理、社會關係、環境)是最佳的模式。此臺灣版問卷的信度與效度的結果良好且與全球版問卷相近，因此正式確立了臺灣版問卷的形成。(中華衛誌 2000；19(4)：315-324)

關鍵詞：世界衛生組織生活品質問卷、簡明版世界衛生組織生活品質問卷、台灣版本。

Introduction to the development of the WHOQOL-Taiwan version

The World Health Organization (WHO) initiated a cross-cultural project on the development of the WHOQOL-100 questionnaire in 1991 and finished it in 1995. Later, the questionnaire was simplified to the WHOQOL-BREF containing 26 items. The long form of the questionnaire contains 100(culturally comparable) generic core questions. However, it allows each nation/culture to add culture-specific questions. We started to develop the questionnaire-Taiwan version in 1997. This paper briefly introduces the development of the WHOQOL-Taiwan Versions. The procedures of translating the questionnaire, selecting the appropriate scale descriptors, and proposing suitable culture-specific items were seriously designed. We collected the data on 1068 subjects from 17 hospitals in Taiwan to conduct reliability and validity analyses. The results showed that the internal consistency (Cronbach's α) and the test-retest reliability coefficients of the questionnaire were 0.97 and 0.86 respectively; the indices of content validity and concurrence validity achieved statistically significant ($p < .01$); most of the items could discriminate between healthy and unhealthy subjects; Facet-G score (for measuring general QOL and health) was well predicted by the six domain scores and the explained variance was about 64.2%. Moreover, four-factor model (i.e., physical capacity, psychological, social relationship, and environment) was the most plausible model. Based on our data analysis, the psychometric properties of the questionnaire for Taiwan version were convincing and were comparable to the global study.*(Chin J Public Health. (Taipei): 2000;19(4):315-324)*

Key words: WHOQOL-100, WHOQOL-BREF, Taiwan-Version.

世界衛生組織生活品質問卷的發展

一、源起

隨著時代的變化、社會及經濟的發展，以及醫療水準的提升，我們對「健康」的定義已不再僅關注於死亡率(mortality)的變化或罹病率(morbidity)的多寡；雖然近年來有些測量健康的工具已相繼發展，如：Sickness Impact Profile, Nottingham Health Profile, MOS SF-36等，然而這些工具並未完全針對生活品質的概念來設計，而只是測量疾病或失能所造成的衝擊[1-7]；而過去對健康或生活品質(quality of life, QOL)的測量，多限於歐美文化體系之下，若要將該測量工具使用於另一文化，在翻譯方面及文化適用性都是一大挑戰；另外，目前健康照顧方面也越來越重視「人」而非疾病本身，亦即是重視全人的照顧(holistic approach)，有鑑於以上這些原因，世界衛生組織(World Health Organization, WHO)欲發展一份由多個地區、多種背景的人參與合作，並可做跨文化比較研究的測量生活品質的工具，以作爲研究、醫藥療效分析、臨床及衛生決策分析、擬定及評估等的參考[1,2,4,6-8]，因此於1991年開始，WHO展開了研究QOL的計畫。研究之初他們同時結合了15個不同的國家或地區，作爲此研究計畫的分部(division)，而後數年針對此研究議題進行一連串的研究、開會、討論，最後經過綜合彙整之後，發表了研究QOL的成果，即一份健康相關生活品質問卷，定名爲「世界衛生組織生活品質問卷(WHOQOL-100)」[9,10]，其內含有100題測各文化共通的一般性健康相關生活品質的題目，稱之爲一般性題目(generic items)，這些題目可被用來做爲跨文化的比較。WHOQOL問卷並允許各國依照所訂定出來的嚴格標準，將WHOQOL-100原始問卷翻譯爲本國文字後，並加入各文化特有的題目，稱之爲國家性題目(national items，在台灣我們慣稱爲本土性題目)，這些題目能補足一般性題目無法測到屬於各文化特色之下的生活品質概念。

投稿日期：89年2月24日
接受日期：89年7月26日

二、發展過程

WHOQOL-100問卷發展的過程是經由許多的階段所逐漸完成的，表一乃該問卷發展過程之簡單總整理，一共分爲四個階段，每個階段都有清楚的目標及達成的方法及成果。值得注意的是，於第一階段時，WHO將「生活品質」定義成「生活品質是指個人在所生活的文化價值體系中的感受程度，這種感受與個人的目標、期望、標準、關心等方面有關。它包括一個人在生理健康、心理狀態、獨立程度、社會關係、個人信念以及環境六大方面」。於第二階段，採用專家回顧、焦點團體等方式，對於健康相關生活品質議題的各範疇(domains)及次範疇(sub-domains，或稱爲facets即「層面」的意思)做清楚的定義，並建立問卷反應量尺(response scale)。而後每一個參與研究的分部開始編寫題目，並建立全球性的題目庫(global question pool)。題目編寫同時考慮到受測者的客觀感受(perceived objective)，及主觀自評(self-report subjective)兩部分。在經過專家們對題庫題目依照刪減題目的標準(例如：題意相似或重複者需被刪除)，以及研究者就各文化中題目所能提供的生活品質訊息之排序研究後，所有題目由最初的1,800題刪減至236題。於第三階段，以WHOQOL預試問卷(pilot form)的236題題目，另外並加入各國家本土性題目，分別對15個研究分部所在地進行預試，經由對預試對象考慮病人/健康人口、性別、年齡等適當的比率後，總共有將近五千人參與預試。經資料的心理計量分析後(包括對各題目的分析及問卷的各種信度及效度探討)，確立最後的WHOQOL問卷的100題一般性題目(此部分並未包括各國家的本土性題目)，並修正生活品質向度架構，從原先的六大範疇(domains)、29個層面(facets)，精簡成爲六大範疇、24個層面。第四階段則對被選出的一百題問卷題目再進行一系列的研究測試，以建立再測信度、改變感應度(responsiveness to change)以及測驗效度(包括收斂效度、區辨效度及預測效度)等心理計量特質。

表一　世界衛生組織生活品質問卷的發展過程

階段	方法	產品	目標
(1)概念釐清	國際間專家回顧文獻	1. 定義QOL 2. 建立研究步驟	建立符合QOL定義及方法以進行國際間的QOL評估
(2)質性先期研究	1. 專家回顧 2. 焦點團體 3. 成立題目編寫小組	1. 定義QOL的範疇及層面 2. 建立全面性題庫	探索跨文化的QOL概念及編寫題目
(3)發展階段的預試	於15個地區各至少對250名病人及50名健康人施測	300題標準化題目的問卷(含一般性及各國家性題目)	1. 精修WHOQOL架構 2. 減小全面性題庫
(4)實地測試	一連串小型研究： 1. 使用同質團體 2. 縱貫性研究設計 3. 平行使用國內或國際間的其他QOL測驗	1. 核心向度架構 2. 共通及各國特殊問題題庫 3. 標準化及跨國性問卷量尺等化研究	建立WHOQOL心理計量特性

三、問卷的架構

WHOQOL-100問卷的內容一共可分爲六大範疇(domains)，其內共分爲24個層面(facets)，另外還有一個綜合對整體生活品質(overall QOL)及一般健康狀態(general health)評量的「一般層面(Facet G)」。此問卷的六大範疇分別爲：(1)生理範疇(physical domain)，共有三個層面、(2)心理範疇(psychological domain)，共有五個層面、(3)獨立程度(level of independence)，共有四個層面、(4)社會關係(social relationship)，共有三個層面、(5)環境(environment)，共有八個層面、(6)心靈／宗教／個人信念(Spirituality／Religion/Personal Beliefs)，有一個層面，此架構請見表二。每一個層面各有四個題目，連同綜合對整體QOL及一般健康狀態層面評量的四題(合稱爲「一般層面」)，共計有100題。

四、問卷的施測與計分

原則上，此問卷主要是採用自填(self-administered)的方式來進行施測，在必要時才以施測者協助填寫或代填的方式進行。受訪者被要求以最近兩個星期爲時間參考點(time reference)來評斷自己主觀的生活品質。WHOQOL-100問卷中的每一題皆是採用五點式量尺來計分，分數越高表示生活品質越好。除了每個題目可計分外，還可將各層面內的題目分數相加，而得各層面分數，並且可將各範疇內的層面分數求平均，而得各範疇分數。

五、簡明版世界衛生組織生活品質問卷的發展

由於WHOQOL-100問卷太長，並不適合作爲需考慮時間及實用性的臨床試驗或流行病學調查用，因此WHOQOL研究總部嘗試將其簡化成簡明版問卷(稱做WHOQOL-BREF)。WHOQOL研究總部收集來自18個國家的20個研究中心的一萬多名受訪者資料來篩選題目。由於簡明版問卷考慮到需能維持測量生活品質的「全面性(comprehensiveness)」，因此問卷的題目是從24個層面的每一個層面中，依照心理計量的分析結果而各選出一個題目，並且也從一般層面中挑選出兩題分別與整體生活品質及一般健康相關的題目，如此使得問卷一共有26個題目。於各層面選題的標準乃採用計量分析的方式，使得題目能解釋相當比率的WHOQOL整體變異量(total variance)及一般層面的整體

表二　世界衛生組織生活品質問卷的範疇及層面架構

整體性的生活品質及健康	
範疇一 —	生理
	層面1. 疼痛及不適
	層面2. 活力及疲倦
	層面3. 睡眠及休息
範疇二 —	心理
	層面4. 正面感覺
	層面5. 思考、學習、記憶及集中注意力
	層面6. 自尊
	層面7. 身體心象及外表
	層面8. 負面感覺
範疇三 —	獨立程度
	層面9. 活動能力
	層面10. 日常生活活動
	層面11. 對藥物及醫療的依賴
	層面12. 工作能力
範疇四 —	社會關係
	層面13. 個人關係
	層面14. 實際的社會支持
	層面15. 性生活
範疇五 —	環境
	層面16. 身體安全及保障
	層面17. 家居環境
	層面18. 財務資源
	層面19. 健康及社會照護：可得性及品質
	層面20. 取得新資訊及技能的機會
	層面21. 參與娛樂及休閒活動的機會
	層面22. 物理環境：(污染／噪音／交通／氣候)
	層面23. 交通
範疇六 —	靈性／宗教／個人信念
	層面24. 靈性／宗教／個人信念

變異量，且題目能形成好的因素結構，並區辨出不同群體的人(例如：健康人與不健康人)。經由探索性及驗證性因素分析，這個由26個題目所組成的簡明版問卷可將原來的六大範疇簡化成四個主要的範疇：生理健康範疇(physical health domain，包括原先的生理及獨立程度範疇)、心理範疇(psychological domain，包括原先的心理及心靈／宗教／個人信念範疇)、社會關係範疇(social relationships domain)，以及環境範疇(environment domain)。WHOQOL-BREF問卷至1996年底，已經有十九種語言的版本被發展出來[7]，而至2000年初，在由中國大陸主辦的生活品質學術研討會中，WHO官員口頭報告則已有近四十種語言版本被發展完成，並且還在陸續增加中。

六、問卷的特點

從過去的文獻中，我們可發現有數個常被用來測量健康相關生活品質的工具，如：Sickness Impact Profile(SIP)、EuroQOL、MOS SF-36、Index of Health-Related Quality of Life(IHQOL)等，綜合而言，這些工具可能有的缺點如下：量表未配合各文化的特色加以修改或作跨文化之比較；對健康相關生活品質的定義不夠完全；題目太多到讓受訪者疲累，或太少到不足以涵蓋健康相關生活品質之全貌；題目的形式太過於複雜或混亂，可能降低受訪者的回答意願；同份量表內使用的量尺尺度不一致，使受訪者回答不易或會產生統計計分上的困擾；量尺標示語沒有考慮到使用本土語詞及等距特性，對分析的結果造成懷疑。

相對而言，我們則可將WHOQOL-100問卷歸納出下列幾個特點：編製時考慮到跨文化性；能反映出健康相關生活品質的多面性及精緻性；容許外加適合各本土文化特色的題目；編製的過程系統化、科學化及符合心理計量的重要原則，包括各文化必須先作研究以找出適當且具有等距性的量尺標示語詞(response scale descriptors)；從不同角度來問同一概念，因此使用到四大類型量尺(包括能力、頻率、強度、評估)；內容強調個體對自己生活品質的感受(perception)；可發展簡明版本(brief form)的生活品質問卷，使得應用上更具彈性；WHOQOL研究總部出版許多詳盡的發展此問卷的文件可供參考；有各國的問卷發展小組負責監督各國版本問卷的使用及提供技術性的支持。關於WHOQOL問卷的相關訊息，讀者可參考WHOQOL網頁：http://www.who.int/msa/mnh/mhp/ql.htm。

台灣版世界衛生組織生活品質問卷的發展

一、發展過程

WHOQOL台灣版問卷發展小組於1997年中，向WHOQOL瑞士日內瓦研究總部取得台灣版本的發展權，並獲得國科會在研究經費上的支持，著手進行生活品質各層面的定義及問卷題目的翻譯工作。本小組先後參與的人來自各種背景，包括：各科專科醫生、護理師、藥學專家、物理治療師、職能治療師、健康行為專家、健康人類學家、心理計量學家、流行病學家、生物統計專家、公共衛生學者等專家、教授們(見附註一)。我們根據WHOQOL研究總部的規定[6,11,12]，對生活品質各層面的定義及問卷中的各題目進行逐字逐句反覆地討論，期望在文字、概念及語意的翻譯上能達到適當性、對等性(equivalence)及符合本土文化的標準，翻譯後的文件先後除了讓一般人閱讀外，最後並由兩位雙語外籍人士(bilingual translators)進行回翻英文的步驟(back translation)，並再進行討論及修改，以確定最後台灣版本的世界衛生組織生活品質問卷。

二、問卷量尺的發展

原WHOQOL-100問卷中所採用的量尺共分為四大類型，包括：能力(capacity)類型、頻率(frequency)類型、強度(intensity)類型, 以及評估(evaluation)類型，每類型量尺皆是採用李克氏(Likert's)五點量尺的形式。為了要選擇符合本土性量尺標示語詞，且克服過去所採用的不等距(un-equidistance)量尺的缺點，WHOQOL研究總部鼓勵各國對自己文化所使用的量尺語詞從事研究。我們也進行了本土量尺標示語詞的研究，找出了四大類型本土性的量尺標示語詞，作為台灣版問卷使用的量尺語詞，關於這方面的研究我們寫了兩篇報告[13,14]，談及我們如何進行此方面的研究，我們除了選定具等距性且適合台灣本土文化所使用的四大類型的量尺標示語詞外，還比較了同質團體(即大學生)與異質團體(較能代表一般大眾)在選用量尺標示語詞方面之差異。

三、本土性題目的設計

問卷除了一百題各文化共通的題目外，還可另外加入符合本國文化特性的本土性題目，我們依照WHOQOL研究總部建議的方法[15,16]，進行數次對專家、不同疾病及病情程度的病人與其家屬的焦點團體(focus groups)與討論，從他們的觀點來找出符合本

土文化特色之下所關注的生活品質議題，以便作爲編製本土性生活品質問卷題目的參考。我們最後決定於台灣版問卷中初步加入20題本土性題目，包括了新增加的兩個本土性新層面：「被尊重及接受(面子與關係)」以及「飲食」層面，一共有11個題目，以及分屬於其他原有層面的9個本土性題目。這些新編製出的題目還需經過實地收集受訪者資料的測試，而後依照各題目心理計量特性的好壞，來篩選出最好的本土性題目。

四、台灣版問卷的預試

接下來我們對這120個題目做測試，除了要瞭解原WHOQOL問卷的100題核心題目的心理計量特性外，還要從外加的20題題目中篩選出最適當的本土性題目。我們對全台灣東西南北共十六家區域級以上的醫院及一家大型診所進行訪視(見附註二)，針對不同疾病及不同病情程度的門診及住院病人以及健康人(如病人家屬、醫院員工、志工)收集資料，共收集到1068份有效問卷。

五、台灣版問卷的分析結果

我們對所收集到的問卷資料進行描述統計分析、信度(包括內部一致性、再測信度)及效度(包括內容效度、區辨效度、同時效度、預測效度、建構效度)的研究，發現台灣版問卷具有良好的信度及效度(其心理計量特性簡述於表三，詳細討論請參考我們所出版的問卷發展手冊)，並且結果也與世界其他各國的結果相近。例如：問卷各層面的內部一致性指標，用多元迴歸法以各範疇分數來預測整體生活品質之解釋變異量，在區辨健康人與不健康人方面的區辨情形，用探索性因素分析所找出來的因素組成、因素負荷量及解釋變異量，用驗證性因素分析所找出來的因素模式及適配度值等，都可發現與世界各國的研究結果能相呼應。

關於本土性題目的測試及篩選，依照WHOQOL研究總部的規定，這些被測試的本土性題目的心理計量特質，需要與全球性及本土版問卷中的核心題目的資料來做比較，以決定是否該被選取入正式的問卷中[6]。我們使用了十多種計量方法，包括各種描述性統計、因素分析、多元迴歸、題目信效度分析、群聚分析(cluster analysis)、多向度度量化方法(multidimensional scaling)等，最後由20題原設計的本土性題目中篩選出12題作爲台灣版問卷的本土性題目，包括了新增加的兩個本土性層面各四題，以及分屬於其他原有層面的4個本土性題目，因此台灣版世界衛生組織生活品質問卷包括了100題全球共通性題目及12題本土性題目，一共是112題。新增加的兩個層面「被尊重及接受(面子與關係)」以及「飲食」，在經由計量分析後可分別被歸爲「社會關係」及「環境」範疇。我們將這部分的研究出版了一本「台灣版世界衛生組織生活品質問卷之發展及使用手冊」供使用該台灣版問卷者做參考[17]。

六、台灣簡明版問卷的發展

依照WHOQOL研究總部的規定，台灣簡明版問卷除了採用全球共通的WHOQOL-BREF的26個題目外，還可加上所選出的本土性題目。我們自新增加的兩個本土性層面中，經由心理計量的分析，各挑選出一個最具代表性的題目，因此台灣簡明版問卷乃是由28個題目所組成。於這兩個新的本土性層面中篩選題目的標準，是採用世界衛生組織發展簡明版問卷相同的計量分析方法，使用的資料來源仍是於發展台灣版世界衛生組織生活品質問卷時所收集到的1068份有效問卷。我們將這部分的研究也出版了一本「台灣簡明版世界衛生組織生活品質問卷之發展及使用手冊」供使用該台灣版問卷者做參考[18]。

使用問卷的注意事項

台灣版世界衛生組織生活品質問卷對於施測者的資格並沒有嚴格的要求，然而鼓勵所有施測者能在施測前，熟讀我們所出版的問卷發展及使用手冊[17,18]，以瞭解問卷的架構、問卷中各層面及範疇的定義以及施測過程等。基本上對於受訪者乃限制爲需年滿

表三　臺灣版世界衛生組織生活品質問卷的心理計量特性簡述

信度	內部一致性[1]	以層面爲主：0.59~0.92 以範疇爲主：0.78~0.91 整份問卷：0.97
	再測信度[2] (皆達p<.01)	以題目爲主：0.36~0.78 以層面爲主：0.68~0.85 以範疇爲主：0.75~0.91 整份問卷：0.86
效度	內容效度[3] (皆達p<.01)	題目與所屬層面間：0.57~0.91 題目與所屬範疇間：0.41~0.85 範疇間：0.22~0.68 範疇與整體生活品質分數間：0.64~0.85
	區辨效度[4]	大多數的題目、層面、範疇及整體生活品質分數可區辨健康人與不健康人
	同時效度[5] (皆達p<.01)	與相對應範疇之一百點計分題間：0.49~0.62
	預測效度[6]	各範疇分數能解釋64.2%整體生活品質及一般健康狀態層面(Facet G)分數變異量
	建構效度[7]	探索性因素分析：選出四個因素(生理健康、心理、社會關係、環境)，能解釋58.3%變異量 驗證性因素分析：四因素模式適配度佳，CFI=0.86

簡述以上所採用的方法：

1. 計算層面、範疇及整份問卷的Cronbach's α 值。
2. 計算受訪者的各題目、層面、範疇及整份問卷於二至四星期間前後測的皮爾森相關值。
3. 計算變項(題目、層面、範疇及整體生品質分數)間的皮爾森相關值。
4. 用t檢定的方式來檢驗健康人與不健康人之間的差異。
5. 計算各範疇與相對應範疇之一百點計分題間的皮爾森相關值(例如：心理範疇與以一百點visual analog方式計分之題目「整體而言，我對自己心理健康的滿意程度」間之相關)。
6. 以各範疇分數爲預測變項，以Facet G 分數(整體生活品質及一般健康層面)爲效標變項來做多元迴歸。
7. 探索性因素分析乃採用主因子法(principal factor analysis)以抽取因素，並做斜交轉軸(promax)；驗證性因素分析乃使用EQS軟體，分別對三種模式來作分析，包括一個(即整體生活品質)、四個(歸類簡化後的四大範疇)及六個(歸類簡化前的六大範疇)因素的模式，以看出哪一種模式的適配度最佳且模式最簡約。

十八歲的成年人，並且需能讀得懂問卷，這是因爲本問卷的設計是以自填的方式爲主，因此受訪者的教育程度需達到某個水準，我們的經驗是國中及以上教育程度者在填寫本問卷時通常都沒有問題，而國小教育程度者則部分需要在別人協助下來填寫問卷，例如：一些不常接觸文字的老年人。不過台灣版問卷發展小組目前正在針對不識字的老年人發展台語簡明口頭施測版問卷，該版問卷日後應可彌補原先版本之不足。基本上，受訪者在回答問卷時，是以最近兩個星期爲標準來評斷自己的生活品質，然而對於一些慢性病患者，可考慮使用長一點的時間爲參考點，研究者可依研究對象而適時的調整時間參考點。由於世界衛生組織生活品質問卷有自己發展出來的一套計分方法，包括有效問卷的確定方式、缺失資料(missing data)的處理、層面分數及範疇分數的計算、本土修正後的分數轉換法等，因此建議問卷使用者於使用問卷前，先熟讀我們所出版的問卷發展及使用手冊，這兩本手冊可向本文作者聯絡購買。

台灣版世界衛生組織生活品質問卷(包括含112題的長篇版及含28題的簡明版)的版權是屬於世界衛生組織及台灣版世界衛生組織生活品質問卷發展小組所有，但各研究者可依照規定來免費使用該問卷，這些規定包括了：研究者不能任意更改問卷中的指導語、題目的字句、量尺形式、題目順序等，並且研究者在使用問卷前，需填寫「問卷使用同意書」(附於問卷發展及使用手冊中)通知該問卷發展小組，該小組有權負責監督該問卷在台灣的使用情形，以及提供各研究者必要的協助。研究者被鼓勵將所收集到的資料備份送回至該小組，以便該小組集中送回給WHO-QOL研究總部做全球性的生活品質研究，但資料所有權仍屬研究者本人。該問卷發展小組鼓勵研究者們做跨領域的合作研究，期能瞭解及改善台灣百姓的生活品質，以及促進醫藥衛生政策的施行。

研究者若對該問卷有任何疑問，請與該問卷發展小組對外代表人姚開屏聯絡，聯絡方式如下：

姚開屏
台北市羅斯福路四段一號
國立台灣大學心理系
Phone:(02)23630231轉2374再轉2375
Fax:(02)23629909
E-mail:kaiping@ccms.ntu.edu.tw

附註一：

台灣版問卷發展小組成員：(依姓氏筆畫排列)

王榮德　國立台灣大學公共衛生學院職業醫學與工業衛生研究所教授
林茂榮　私立中國醫藥學院公共衛生學系助理教授
林淑文　國立台灣大學醫學院藥學碩士、亞培藥廠臨床藥師
姚開屏　國立台灣大學理學院心理學系所副教授
施富金　國立台灣大學醫學院護理學系所副教授
曹昭懿　國立台灣大學醫學院物理治療學系所講師
游正芬　國立台灣大學公共衛生學院職業醫學與工業衛生研究所研究助理
黃景祥　中央研究院統計所副研究員
劉　鳳　國立台灣大學公共衛生學院職業醫學與工業衛生研究所碩士班學生、草屯佑民醫院婦產科醫師
鍾智文　國立台灣大學公共衛生學院職業醫學與工業衛生研究所博士後研究

研究期間提供意見及協助的同仁：(依姓氏筆畫排列)

Sr, Mary Ellen Kerrigan, M. M.(林惠仁修女)
國立台灣大學醫學院附設醫院護理部顧問
Francina Vander Schyff(萬義娜)
國立台灣大學醫學院附設醫院綜合病房義工
中華基督教內地會宣教士
丁志音　國立台灣大學公共衛生學院衛生政策與管理研究所副教授
王嘉寧　國立台灣大學理學院心理學研究所碩士班學生
王姍妮　美國賓州大學醫學院學生
李　蘭　國立台灣大學公共衛生學院衛生政策與管理研究所教授
李俊賢　國立台灣大學公共衛生學院職業醫學與工業衛生研究所博士班學生
吳淑瓊　國立台灣大學公共衛生學院衛生政策與管理研究所教授
陳燕惠　國立台灣大學醫學院藥學系所副教授
許秀梅　國立台灣大學理學院心理系研究助理、助教

陸玓玲　國立台灣大學公共衛生學院衛生政策與管理研究所博士班畢業
基隆市衛生局第一課課長
潘文涵　中央研究院生物醫學科學研究所研究員
藍忠孚　國立陽明大學公共衛生研究所教授
羅鈞令　國立台灣大學醫學院職能治療學系副教授

附註二：以下的醫院參與台灣版世界衛生組織生活品質問卷的發展

台大醫院	台北榮民總醫院	台北馬偕醫院
省立新竹醫院	台中榮民總醫院	中國醫藥學院附設醫院
彰化基督教醫院	埔里基督教醫院	嘉義基督教醫院
台南成大醫院	高雄榮民總醫院	高雄醫學院附設醫院
屏東基督教醫院	羅東博愛醫院	花蓮慈濟醫院
台東馬偕醫院	台東東和外科診所	

參考文獻

1. Leung KF, Tay M, Cheng SW, Lin F. Hong Kong Chinese version World Health Organization quality of life measure-abbreviated version (WHOQOL-BREF(HK)). Hong Kong, 1997.
2. Szabo S. The World Health Organization Quality of Life (WHOQOL) assessment instrument. In: Spiker B ed. Quality of Life And Pharmacoeconomics in Clinical Trials, Chapter 36. Philadelphia: Lippincott-Raven, 1996;355-62.
3. The WHOQOL Group. Development of the WHOQOL: Rationale and current status. Int J Mental Health 1994;**23**:24-56.
4. The WHOQOL Group. The Development of the World Health Organization Quality of Life assessment instrument (the WHOQOL) In: Orley J, Kuyen W eds. Quality of life assessment: International perspectives. Berlin: Springer-Verlag, 1994;41-57.
5. World Health Organization. Field trial WHOQOL-100 : Introduction and background. Geneva: WHO (MNH/PSF/95.1.A), 1995.
6. World Health Organization. Resources for new WHOQOL centers. Geneva: WHO (MNH/PSF/95.2), 1995.
7. World Health Organization. WHOQOL-BREF: Introduction, administration, scoring and generic version of the assessment--Field trial version. Geneva: WHO, 1996.
8. The WHOQOL Group. The World Health Organization Quality of Life assessment (WHOQOL): Position paper from the World Health Organization. Soc Sci Med 1995; **41**:1403-9.
9. World Health Organization. Field trial WHOQOL-100: The 100 questions with response scales. Geneva: WHO (MNH/PSF/95.1.D.Rev.1), 1995.
10. World Health Organization. Field trial WHOQOL-100: Scoring the WHOQOL. Geneva: WHO (MNH/PSF/95.1.F), 1995.
11. World Health Organization. WHOQOL protocol for new centers. Geneva: WHO (MNH/PSF/94.4), 1994.
12. Sartorius N, Kuyken W. Translation of health status instruments. In: Orley J, Kuyen W eds. Quality of Life Assessment: International Perspectives. Berlin: Springer-Verlag, 1994;3-18.
13. 林茂榮、姚開屏、黃景祥、王榮德：台灣版世界衛生組織生活品質問卷量尺語詞的選擇。中華衛誌1999；**18**：262-70。
14. 姚開屏、林茂榮、王榮德：同質團體與異質團體在量尺語詞選擇的的比較研究。中

華心理學刊2000；41：141-53。
15. World Health Organization. WHOQOL focus group moderator training. Geneva: WHO (MNH/PSF/92.9), 1992.
16. World Health Organization. WHOQOL: Focus group work. Geneva: WHO (MNH/PSF/93.4), 1993.
17. 台灣版世界衛生組織生活品質問卷發展小組：台灣版世界衛生組織生活品質問卷之發展及使用手冊。第一版，台北：台灣版世界衛生組織生活品質問卷發展小組，1999。
18. 台灣版世界衛生組織生活品質問卷發展小組：台灣簡明版世界衛生組織生活品質問卷之發展及使用手冊。第一版，台北：台灣版世界衛生組織生活品質問卷發展小組，2000。

ORIGINAL ARTICLE

1 80

Increased morbidity from nasopharyngeal carcinoma and chronic pharyngitis or sinusitis among workers at a newspaper printing company

Y-H Liu, C-L Du, C-T Lin, C-C Chan, C-J Chen, J-D Wang

Occup Environ Med 2002;**59**:18–2

Objectives: To determine the association between printing works and nasopharygeal carcinoma c well as other diseases.
Methods: Demographic data were obtained for those who had worked in a particular newspape company since its establishment in 1950. Through access to the data bank of the hospital records (the Labor Insurance Bureau for 1985–94, all workers were identified who had been admitted to ho pital during their employment in the newspaper company. Multiple logistic regressions were performe to estimate the adjusted morbidity odds ratio (OR) for various diseases among the printing workers wi cardiovascular diseases as the reference diseases. Biopsy specimens from patients wi nasopharyngeal carcinoma were all subjected to in situ hybridisation of Epstein-Barr virus (EBV), an colocalisation of EBV and secretor component protein.
Results: Of the 1564 people who had worked in this company, 579 of them were admitted to hosp tal at least once. Five out of 144 printing workers admitted to hospital were diagnosed wi nasopharyngeal carcinoma compared with none of the other 435 non-printing workers admitted hospital. The morbidity OR for nasopharyngeal carcinoma in printing workers was 57.0 (95% con dence interval (95% CI) 2.8 to 1155.3). The morbidity OR for benign skin tumours was 28.0 (95% C 2.7 to 293.1). Chronic pharyngitis or sinusitis also showed significant relations with printing wor with a morbidity OR 29.4 (95% CI 1.7 to 514.7). Using all other diseases as the reference disease for calculation of morbidity ORs still showed a similar trend. In situ hybridisation of EBV encoded smc nuclear RNA-1 (EBER-1) showed tumour cells free of the EBV in each biopsy specimen. Colocalisatic of EBER-1 and secretor component showed that some tumour cells contained both secretor compone and EBV signal in each case.
Conclusion: Printing works are associated with an increased risk of nasopharyngeal carcinom benign skin tumours, chronic pharyngitis or sinusitis, chronic liver diseases, and mechanical injurie Induction of the development of nasopharyngeal carcinoma is probably not related to EBV infection these patients.

See end of article for authors' affiliations

Correspondence to: Dr J-D Wang, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; jdwang@ha.mc.ntu.edu.tw

Accepted 12 July 2001

There are various organic solvents, filler materials, and inks used in the printing factory. A survey of materials and substances used in the printing industry in 1978 showed that 2000 products were used, in which 300 chemicals were identified. Among the chemicals, 26 are known or suspected carcinogens according to the classifications made by the International Agency for Research on Cancer.[1] The printing occupations have been related to an increased mortality and morbidity from various diseases, including an increased mortality from lung cancer, bladder cancer, renal pelvis cancer, primary liver cancer, gall bladder cancer, and liver cirrhosis.[1–3] There has never been any report on the association between printing occupation and nasopharyngeal carcinoma.

Nasopharyngeal carcinoma is uncommon in most populations, but it occurs with a high frequency in Chinese people, especially in those from the southern provinces of China and Taiwan.[4] It has been the fifth leading malignant neoplasm for men and the sixth for women in Taiwan since 1983.[5] Environmental, genetic, and viral factors have been postulated as important determinants of nasopharyngeal carcinoma.[6–14] However, the pathogenesis of nasopharyngeal carcinoma still awaits further clarification.

At one particular newspaper printing factory there were reported cases of nasopharyngeal carcinoma identified during 1986 to 1993. We were requested by the labour union and the newspaper company to perform an epidemiological study to determine the associations between printing works and nasopharyngeal carcinoma as well as other diseases.

SUBJECTS AND METHODS

Data collection

Before 1995, the year the Taiwan government implemented national health insurance system, the Labor Insurance Bureau in Taiwan had provided medical insurance for all laborers who worked in a company with more than five workers. Nearly all the workers in public and private sectors joined the Labor Insurance Bureau. As the Labor Insurance Bureau coverage provides a free choice of doctors and hospitals, full coverage of medical service fees, and partial compensation (about 70%–80% depending on industrial sectors) for wages, our workers would use it whenever they have a major disease that requires admission to hospital. There were around 500 000 reimbursement records of admissions to hospital in the Labor Insurance Bureau each year from a population of about 7 million workers. Through access to the database of the Labor Insurance Bureau we retrieved the reimbursement data

Abbreviations: OR, odds ratio; EBV, Epstein-Barr virus; EBER-1, EBV encoded small nuclear RNA-1; ICD-9, ninth revision of the international classification of diseases; EBVCA, viral capsid antigen associated with the EBV; HBV, hepatitis B virus

admissions to hospital during 1985–94. The data items included national identification number, age, sex, occupation, hospital, total medical expense, medical record number, insurance number, date and duration of the stay in hospital, as well as the ninth revision of the international classification of diseases ICD-9 code of medical diagnosis.

We also obtained a complete list of workers who have worked in the company since its establishment in 1950. It contained information on demographic characteristics, history of working in a news printing factory, date and duration of employment, etc.

The reimbursement data and list of workers provided by the company were linked together to extract information of the workers who had been admitted to hospital during their employment in the company, regardless of the diagnosis. The relational query by example provided by the Microsoft database software Foxpro was applied for the extraction of information.[14] For any worker who had been repeatedly admitted to hospital due to the same disease we kept only one record.

Through the procedure we obtained the list of workers affected with nasopharyngeal carcinoma and interviewed them or members of their family about their working and health history. As all workers with nasopharyngeal carcinoma were extracted from the reimbursement data, we are confident that the reimbursement data are comprehensive. With their consent, we reviewed their medical records from different hospitals and summarised the initial symptoms and signs, date of diagnosis, clinical course, treatment received, pathological findings, clinical staging of the disease, and serological titre of antibodies against Epstein-Barr virus.

In situ hybridisation of EBER-1 and double localisation of EBER-1 and secretor component

Paraffin sections from four out of five patients with nasopharyngeal carcinoma were obtained from four different hospitals, including National Taiwan University Hospital, Kaoshuong Medical College Hospital, Macky Memorial Hospital and Veteran General Hospital (one of the paraffin blocks was missed in Tri-Service General Hospital). The paraffin sections after deparaffinisation were subjected to in situ hybridisation for localisation of EBV encoded small nuclear RNA-1 (EBER-1) with antisense riboprobe as described previously.[16] Some sections were counter stained with methyl green; others were not. In each case, stain with haematoxylin and eosin was also performed. At the same time we also performed double localisation of EBER-1 and secretor component protein (an IgA receptor) by immunohistochemistry with an antibody against secretor component and in situ hybridisation according to our previously published method.[17]

Table 1 Characteristics of workers in a newspaper company who had ever been admitted to hospital, and workers admitted to hospital for cardiovascular diseases (the reference group)

Workers	Printing	Non-printing
All workers:		
Men (n)	331	995
Women (n)	5	233
Age (y, mean (SD))	38.5 (6.4)	41.8 (10.0)
Employment (y, mean (SD))	11.7 (7.9)	13.7 (8.2)
Workers admitted to hospital:		
Men (n)	142	336
Women (n)	2	99
Age (y, mean (SD))	33.5 (5.6)	35.6 (10.1)
Employment (y, mean (SD))	9.0 (7.0)	10.3 (8.2)
Workers admitted to hospital for cardiovascular diseases:		
Men (n)	5	27
Women (n)	0	1
Age (y, mean (SD))	37.3 (7.0)	37.6 (10.4)
Employment (y, mean (SD))	13.6 (10.3)	11.9 (9.6)

Data analyses

Descriptive analysis of the demographic data and work history of all workers and the workers who had been admitted to hospital was performed. The morbidity odds ratios (ORs) of various diseases due to the exposure in a news printing factory was calculated as in a case-control study,[18] with the case being various diseases that resulted in admission to hospital of the worker. There were two control groups in this study. The first control group was workers admitted to hospital for cardiovascular diseases. We lumped all workers who were admitted to hospital due to diseases other than the diseases of interest and cardiovascular diseases as another control group. Multiple logistic regression analysis was used to estimate morbidity OR adjusted for age, duration of employment, sex, and other possible risk factors. The statistical package SAS/STAT PC 6.08 was used for data analyses.[19]

RESULTS

There were 1564 workers identified as having worked in the factory since its establishment in 1950. Of these workers there were 1326 men and 238 women; 336 of them had worked in the printing factory; 1228 workers worked in non-printing sectors. The mean (SD) age of the workers was 41.1 (9.4) years and the mean (SD) duration of employment in the company was 13.3 (8.2) years. Workers of printing factories were younger with shorter duration of employment than non-printing workers. The difference was not significant (table 1). A significantly higher proportion of men worked in printing than non-printing departments.

Of the 1564 people who had worked in this company, the total admissions to hospital was 796 during the observation period. After discounting repeated admission to hospitals with the same diagnosis, there were 579 workers who were admitted to hospital at least once. We first chose cardiovascular diseases as the reference. Morbidity ORs for nasopharyngeal carcinoma, benign skin tumours, chronic pharyngitis or sinusitis, chronic liver disease or cirrhosis, and mechanical injuries were significantly related to printing works. Five out of 144 printing workers admitted to hospital were diagnosed with nasopharyngeal carcinoma compared with none of the other 435 non-printing workers admitted to hospital. Because one of the 2×2 cells was zero, we added 1/2 to calculate the crude morbidity OR of nasopharyngeal carcinoma,[20] which was 57.0 (95% confidence interval (95% CI) 2.8 to 1155.3, Fisher's exact test, $p<0.001$).

When workers admitted to hospital due to diseases other than the disease of interest and cardiovascular disease as control group, all diseases of interest showed a significant trend except chronic liver disease or cirrhosis of the liver, as shown in table 2.

The mean (SD, range) duration of employment of the patients with nasopharyngeal carcinoma in this printing factory was 13.5 (7.2, 4.5–20.2) years. The mean age of these patients at the time of pathologic proof of nasopharyngeal carcinoma was 44.7 (14.5, 35.5–70.5) years, table 3.

The initial symptoms included bloody rhinorrhea, neck mass, nasal obstruction, hearing impairment, blurred vision, ptosis, and diplopia. Three out of five patients received the serological test for antibodies against EBV. Only one patient had a normal antibody titre of the viral capsid antigen associated with the EBV (EBVCA) in IgA class. The other two patients showed EBVCA IgA 1:20 and 1:160 respectively. Two patients died in 1993 and the other patients did not show any evidence of recurrence after radiotherapy and chemotherapy (table 3).

Table 2 Adjusted MORs for those diseases that showed significant relations with printing works*

Diseases	Printing workers	Non-printing workers	MOR†	95% CI†	MOR‡	95% CI‡
Nasopharyngeal carcinoma§	5	0	57.0	2.8 to 1155.3	33.8	1.9 to 613.8
Benign skin tumours	5	1	28.0	2.7 to 293.1	15.3	1.8 to 132.3
Chronic pharyngitis or sinusitis	4	1	29.4	1.7 to 514.7	6.9	1.2 to 39.2
Mechanical injuries	6	2	21.9	2.6 to 187.2	7.6	1.9 to 30.0
Chronic liver disease or liver cirrhosis	5	6	6.0	1.1 to 31.8	3.1	0.88 to 11.1
Lower respiratory tract infection	1	15	1.0			
Skin and subcutaneous disease	5	8	6.4			
Musculoskeletal disorder	6	17	1.9			
Cardiovascular diseases	5	28	1.0			
Other diseases						

*Adjusted for age, sex, and working duration; †Cardiovascular disease as the reference disease; ‡Diseases other than diseases of interest as the reference disease; §Crude morbidity odds ratio (MOR) with exact estimates for 95% CI.

Table 3 Characteristics and clinical findings of workers affected with nasopharyngeal carcinoma

	Patient No				
	1	2	3	4	5
Age at diagnosis	35.5	38.0	70.5	39.2	40.3
Year of diagnosis	1986	1987	1987	1990	1993
Working years	14.5	14.3	20.2	13.0	15.3
Initial symptoms	Hearing impairment, nasal obstruction	Neck mass, diplopia	Blurred vision, ptosis	Neck mass, bloody rhinorrhoea	Bloody rhinorrhoea
Histological finding	Undifferentiated carcinoma	Poorly differentiated carcinoma	Undifferetiated carcinoma	Undifferetiated carcinoma with feature of lympho-epitheliomatous carcinoma	Undifferetiated carcinoma
Clinical staging	T4N0M0	T4N1M1	T4N0M0	T2N2M0	T1N2M0
Epstein-Barr viruscapsid antigen:					
IgA	N/A	1:160	N/A	1:20	<1:10
IgG		1:640		1:160	1:160
Current status	No evidence of recurrence	Died in 1993 (brain metastasis)	Died in 1993 (stroke)	No evidence of recurrence	No evidence of recurrence

N/A=not available.

Four cases of nasopharyngeal carcinoma biopsy specimens showed a picture of undifferentiated nasopharyngeal carcinoma, and one of them seemed to have a lymphoepithelioma-tous carcinoma. In situ hybridisation of EBER-1 in the four cases showed some tumour cells without EBV signal. The EBV signal was found in a few tumour cells in two of them (cases 1 and 4) and was seen in more tumour cells in the other two (cases 3 and 5); in these some infiltrating lymphocytes also showed an EBV signal.

When double localisation of EBV and secretor component protein was performed, some tumour cells showed neither EBV signal nor secretor component protein; a few tumour cells showed both EBV signal and secretor component immuno-staining; other tumour cells either showed secretor compo-nent only or EBV signal with a very weak secretor component, a picture identical with our previously published data.[17]

DISCUSSION

The aetiology of nasopharyngeal carcinoma is probably multifactorial.[8 9 11–14 21] Although we have found an increased morbidity OR of nasopharyngeal carcinoma in printing work-ers, it does not necessarily follow that nasopharyngeal carcinoma was caused by printing works. Evidence and argu-ments strongly suggest such a possibility. Firstly, eating salty fish[12–14] and taking herbal drugs,[21] were reported to be risk fac-tors for nasopharyngeal carcinoma. But none of our patients had such habits. Secondly, smoking was reported to be associ-ated with a twofold to threefold increased risk of nasopharyn-geal carcinoma.[12] Yu *et al* found that smoking for more than 30 pack-years gave a twofold increase of nasopharyngeal carcinoma among ethnic Chinese.[11] Although all five patients in our series were smokers, they usually smoked less than 1 pack/day because the company policy prohibited smoking at the workplace for fear of explosion and fire. As four out of five patients were below 41 years of age at the time of diagnosis, they were unlikely to have accumulated more than 30 pack-years. Thus, smoking alone seemed inadequate to explain the increased risk of nasopharyngeal carcinoma among printing workers. Thirdly, as the income levels, which were major determinants for smoking and dietary habits,[22 23] seemed similar (800 US$/month for printers *v* 650 for non-printing workers). The likelihood of a major difference in these lifestyle habits may be low. Because both printing work-ers and non-printing workers had been working in an air con-ditioned system, the factor of merely poor ventilation cannot explain the difference of occurrence. Rather, workplace expo-sure must have contributed a significant portion, given that workers were under a closed air condition system to conserve energy. We conclude that all the suspected risk factors for nasopharyngeal carcinoma are not likely to be confounding factors in this study.

In the Chinese population, the incidence of nasopharyngeal carcinoma is unusually high. The annual incidence of nasopharyngeal carcinoma in Taiwan was 4.2/100 000.[9] In these 1564 workers with a mean duration of 13.3 working years, the total working years were around 20 800. The expected number of cases of nasopharyngeal carcinoma in the whole newspaper company should be 0.8 during this period. We identified five cases of nasopharyngeal carcinoma and all were printing workers. If the observed five cases were divided by the expected 0.15 cases of nasopharyngeal carcinoma in printing workers, the morbidity ratio was 32. The result was

very consistent despite selection of two different control groups, either cardiovascular disease or all diseases other than diseases of interest, as shown in table 2.

As infection with EBV has been proposed to be closely associated with the development on nasopharyngeal carcinoma,[14 26 27] and one of our patients has a high titre of IgA antibody against EBVCA (1:160), there is a possibility that nasopharyngeal carcinoma in this patient may have been induced by EBV infection. However, although a positive EBV signal was found in some tumour cells in each case, we found that all four specimens of nasopharyngeal carcinoma contained tumour cells free from EBV. This finding indicates that EBV infection is not the only causative factor for the development of nasopharyngeal carcinoma in these four cases, as we found previously.[16 17] Furthermore, the presence of EBV and secretor component positive cells in the sections indicates that EBV may infect the secretor component positive nasopharyngeal carcinoma tumour cells, instead of secretor component negative tumour cells, through the endocytosis of EBV-IgA-secretor component complex as we previously described, and possibly that EBV was not a causative factor in the induction of nasopharyngeal carcinoma in these patients.

Cancers of the lung, urinary bladder, and liver were once reported to be associated with printing works.[1-7] It is not surprising that such carcinogens might have a similar effect on the nasopharynx, especially in ethnic Chinese, of whom the structure of the nasopharynx is generally narrower and more easily deposited with aerosols compared with the nasopharynx of white people. Printing workers have been exposed to a panoply of potentially toxic substances, including pigments, inks, solvents, resins, driers, plasticisers and wetting agents,[7] which might have a direct irritative effect and produce chronic pharyngitis or sinusitis. Printing ink mixed with mineral oil might contain procarcinogens—such as benzoxy-a-pyrenes. Some printing pigments contain toxic heavy metals—such as chromium and lead. The environmental monitoring in the factory identified the presence of toxic solvents—such as tetrachloroethane, benzene, toluene, styrene, and *n*-hexane. We conducted an exposure assessment of chemicals in the printing workplace and detected trace concentration of formaldehyde (1.4–31.1 $\mu g/m^3$), sulfuric acid (0.03–0.13 mg/m^3), and aerosol of mineral oils (0.02–0.13 mg/m^3) after there had been some improvement in cleaning and ventilation of the workplace.[25] Although they were below the permissible concentrations, long term effects might still be hazardous, especially under a combined exposure to other potential carcinogens and in a closed system of indoor air conditioning. These toxic substances may coexist as aerosol and precipitate in the nasopharyngeal mucosa, causing repeated or chronic inflammation or even malignant change after a certain induction time.

More than 90% of nasopharyngeal carcinomas in Taiwan are undifferentiated, non-keratinising carcinoma diagnosed at a mean age around 45.[28 29] It was unusual to see that printing workers with undifferentiated, non-keratinising carcinoma had a mean age of 39.1 (table 3). One possible explanation was early carcinogenesis due to exposure of toxic substances. Among the workers with nasopharyngeal carcinoma, four had worked in the printing factory for more than 13 years before the date of diagnosis. One worker only spent 4.5 working years in the factory before the onset of nasopharyngeal carcinoma. However, this worker admitted that he had worked in another printing factory for 10 years before taking the current job. Thus the induction period of nasopharyngeal carcinoma would be more than 10 years.

Cardiovascular diseases were used as the reference diseases because cardiovascular diseases were not reported to be associated with printing works. We even used diseases other than the disease of interest as a second reference group. The result did not differ much. Except for chronic liver disease or cirrhosis of the liver, all diseases in table 2 remain significantly associated with printing works. The reason why OR decreased might be due to the effect of including some diseases that may also be related to printing. As we only had complete data from one newspaper company, the case number was relatively small and the estimated 95% CI of the morbidity OR was wide.

Both skin and the liver are vulnerable to toxic chemicals in printing factories because they are either the defence organ against toxic substance or the organ of detoxification. Primary liver cancer, cirrhosis of the liver, and skin cancer were reported to be increased in printing workers.[4 7] Organic solvents used in the printing factory might cause liver injury and the long term exposure to these solvents might contribute to the development of cirrhosis of the liver. In Taiwan, hepatitis B virus (HBV) caused most cases of cirrhosis of the liver and primary liver cancer.[30] As the prevalence of HBV carriers in printing and non-printing workers was similar (14.1% and 13.0%, respectively), the increased risk of cirrhosis of the liver was probably related to work. We thought that a longer duration of follow up or increased numbers in the study populations in the future might show a clearer tendency. Further study should identify whether these diseases progress to the development of nasopharyngeal carcinoma. Occupational injury remained a problem of concern in printing factories and most injuries were reported to occur during the process of cleaning or repair of machines.

Results from this study of a cohort containing a group of workers from a newspaper printing company support the conclusion that printing works are associated with an increased risk of nasopharyngeal carcinoma, chronic pharyngitis or sinusitis, cirrhosis of the liver, and mechanical injuries. Health surveillance, hazard control, and a programme of injury prevention should be implemented in all newspaper printing factories.

ACKNOWLEDGEMENTS

We are indebted to Professor Mow-Ming Hsu and Sister Mary Ellen Kerrigan for thorough review and helpful comments on the manuscript of the paper. The project is supported partially by a grant from the National Science Council of the Republic of China No NSC89-2314-B-002-433-M56.

Authors' affiliations

Y-H Liu, C-L Du, C-C Chan, J-D Wang, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health; and Department of Internal Medicine, National Taiwan University Hospital Taipei, No 1, Section 1, Jen-Ai Road, Taipei, Taiwan 10016

Y-H Liu, Department of Family Medicine, National Taiwan University Hospital and Cardinal Tien Hospital, Taipei, Taiwan

C-L Du, Institute of Occupational Safety and Health, Council of Labor Affairs, Executive Yuan, Taipei, Taiwan

C-T Lin, Department of Pathology, National Taiwan University Hospital, Taipei, Taiwan

C-J Chen, Graduate Institute of Epidemiology, National Taiwan University College of Public Health, Taipei, Taiwan

REFERENCES

1 **Lynge E**, Rix BA, Villadsen E, *et al.* Cancer in printing workers in Denmark. *Occup Environ Med* 1995;**52**:728–44.
2 **Moss E**, Scott TS, Atherley GRC. Mortality of newspaper workers from lung cancer and bronchitis 1952–66. *Br J Ind Med* 1972;**29**:1–14.
3 **Greenberg M.** A proportional mortality study of a group of newspaper workers. *Br J Ind Med* 1972;**29**:15–20.
4 **Leon DA.** Mortality in the British printing industry: a historical cohort study of trade union members in Manchester. *Occup Environm Med* 1994;**51**:79–86.
5 **Lloyd JW**, Decoufle P, Salvin LG. Unusual mortality experience of printing pressmen. *J Occup Med* 1997;**19**:543–50.
6 **Paganini-Hill A**, Glazer E, Henderson BE, *et al.* Cause-specific mortality among newspaper web pressman. *J Occup Med* 1980;**22**:542–4.
7 **Greene MH**, Hoover RN, Eck RL, *et al.* Cancer mortality among printing plant workers. *Environ Res* 1979;**20**:66–73.
8 **Hildesheim A**, Levine PH. Etiology of nasopharyngeal carcinoma: a review *Epidemiol Rev* 1993;**15**:466–85.

9 **Wang YF**, Tsai SF, Hsu KH, *et al.* Epidemiologic characteristics of malignant neoplasms in Taiwan: V. nasopharyngeal carcinoma. *Journal of the National Public Health Association of the Republic of China* 1989;**9**:46–57.
10 **Shanmugaratnam K.** Nasopharynx. In: Schottenfeld D, Fraumeni JF Jr, eds. *Cancer epidemiology and prevention.* Philadelphia: WB Saunders, 1982:536–53.
11 **Yu MC**, Garabrant DH, Huang TB, *et al.* Occupational and other non-dietary risk factors for nasopharyngeal carcinoma in Guangzhou, China. *Int J Cancer* 1990;**45**:1033–9.
12 **Lin TM**, Chen KP, Lin CC, *et al.* Retrospective study on nasopharyngeal carcinoma. *J Natl Cancer Inst* 1973;**51**:1403–8.
13 **Lin TM**, Chang HJ, Chen CJ, *et al.* Risk factors for nasopharyngeal carcinoma. *Anticancer Res* 1986;**6**:791–6.
14 **Chen CJ**, Liang KY, Chang YS, *et al.* Multiple risk factors of nasopharyngeal carcinoma: Epstein-Barr virus, malarial infection, cigarette smoking and familial tendency. *Anticancer Res* 1990;**10**:547–54.
15 **Slater LC**, Arnott SE, Jacobsen N, *et al. Using Foxpro 2.5 for windows.* Carmel: Que, 1993:187–344.
16 **Lin CT**, Dee AN, Chen W, *et al.* Association of Epstein-Barr virus, human papilloma virus and human cytomegalovirus in nine nasopharyngeal carcinoma cell lines. *Lab Invest* 1994;**71**:731–6.
17 **Lin CT**, Lin CR, Tan GK, *et al.* The mechanism of Epstein-Barr virus infection in nasopharyngeal carcinoma cells. *Am J Pathol* 1997;**150**:1745–56.
18 **Miettinen OS**, Wang JD. An alternative to the proportionate mortality ratio. *Am J Epidemiol* 1981;114–118.
19 **SAS Institute.** *SAS/STAT user's guide, release 6.03 edition.* Cray, NC: SAS Institute, 1988.
20 **Kahn HA**, Sempos CT. *Statistical methods in epidemiology.* Oxford. UK: Oxford University Press, 1989:57.
21 **Chen CJ**, Wang YF, Shieh TI, *et al.* Multifactorial etiology of nasopharyngeal carcinoma, *Epstein-Barr virus, familial tendency and environmental cofactors. Head and neck oncology research. Proceedings of the 2nd International Head and Neck Oncology Research Conference.* 1987;469–476.
22 **Sterling TD**, Weinkam JJ. Smoking characteristics by the type of employment. *J Occup Med* 1976;**18**:743–54.
23 **Covey LS**, Wynder EL. Smoking habits and occupation status. *J Occup Med* 1981;**23**:537–42.
24 **Ho CK**, Lo WCH, Huang PH, *et al.* Suspected nasopharygeal carcinoma in three workers with long-term exposure to sulfuric acid vapor. *Occup Environ Med* 1999;**56**:426–8.
25 **Tsai HJ.** *Exposure assessment of chemical hazards on newspaper printing workers* [master thesis]. Taipei: National Taiwan University of Public Health 1997:61–75.
26 **Henle W**, Henle G, Ho HC. Antibodies to Epstein-Barr virus in nasopharyngeal carcinoma, other head and neck neoplasms, and control groups. *J Natl Cancer Inst* 1970;**44**:225–30.
27 **Chen JY**, Chen CJ, Liu MY, *et al.* Antibodies to Epstein-Barr virus-specific DNAase in patients with nasopharyngeal carcinoma and control groups. *J Med Virol* 1987;**23**:11–21.
28 **Hsu MM**, Tu SM. Nasopharyngeal carcinoma in Taiwan: clinical manifestations and results of therapy. *Cancer* 1983;**52**:362–8.
29 **Hsu MM**, Lin BL. Characterisation of T cell subsets using monoclonal antibodies in nasopharyngeal carcinoma patients. *Ann Otol Rhinol Laryngol* 1986;**95**:298–301.
30 **Lin TM**, Tsu WT, Chen CJ. Mortality of hepatoma and cirrhosis of liver in Taiwan. *Br J Cancer* 1986;**54**:969–76.

184

Quality of Life Research 11: 753–762, 2002.

Validation of the World Health Organization quality of life instrument in patients with HIV infection☆

C.-T. Fang[1], P.-C. Hsiung[2], C.-F. Yu[3], M.-Y. Chen[1] & J.-D. Wang[1,3]
[1]*Department of Internal Medicine, National Taiwan University Hospital (E-mail: jdwang@ha.mc.ntu.edu.tw);* [2]*School of Nursing, College of Medicine;* [3]*Institute of Occupation Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Taipei, Taiwan, ROC*

Accepted in revised form 27 April 2002

Abstract

We studied the reliability and validity of the World Health Organization quality of life (WHOQOL) assessment instrument in patients with human immunodeficiency virus (HIV) infection. WHOQOL-BREF was used to assess 136 HIV-infected outpatients. The results were analyzed and compared with data from 213 healthy persons. The Cronbach's α for internal consistency ranged from 0.74 to 0.85 across domains in HIV-infected patients. The test–retest reliability ranged from 0.64 to 0.79 across domains at average 4-week retest interval. Factor analysis identified four major factors: social, psychological, environment, and physical, consistent with the four domains of the instrument. The scores of all four domains correlated positively with self-evaluated health status and happiness (r range: 0.52–0.60 and 0.55–0.73 across domains, respectively), and correlated negatively with the number and severity of symptoms (r range: −0.40 to −0.47 and −0.41 to −0.52, respectively). The scores of physical, psychological and social domains, but not the environment domain, discriminated between healthy persons and HIV-infected patients (all $p < 0.01$). We conclude that the WHOQOL-BREF can be a useful quality-of-life instrument in patients with HIV infection.

Key words: Human immunodeficiency virus infection, Quality of life, WHOQOL

Introduction

Improvements in life expectancy of patients with human immunodeficiency virus (HIV) infection in recent years [1], due to advances in highly active antiretroviral therapy, have led to greater emphasis of quality of life among these patients [2–10]. Measurement of quality of life is now an essential component in both clinical trials and cost-effectiveness analysis for HIV disease [11–15]. A wide variety of quality-of-life instruments have been applied in the evaluation of HIV-infected patients, including the multiple versions of the Medical Outcome Study (MOS) [16–19], the Quality of Well-Being Scale [19, 20], the HIV-QL31 [21], the HAT-QoL [22], the AIDS-HAQ [23], the HOPES [24], the MQoL-HIV [25], and the FAHI [26]. However, because these instruments were developed in the context of western culture, they may not be readily applicable to patients from societies with different cultural background, although several of these instruments have been used with success in some Asian countries [27].

In 1991, the World Health Organization (WHO) initiated a project to develop a generic quality-of-life instrument in 15 countries simultaneously, which led to the WHO quality of life (WHOQOL) assessment [28–31]. The WHOQOL has two

☆ The preliminary abstract of this paper was presented at Pan-Pacific Conference of the International Society for Quality of Life Research, Tokyo, April 2001.

unique features. First, it is based on a well-clarified definition of quality of life and encompasses physical, psychological, social and environment domains comprehensively [28], and is not just a functional assessment. Second, it is a cross-culture instrument developed for use across patient groups in various countries [29]. Despite these advantages, the reliability and validity of WHOQOL have not yet been well studied in HIV-infected patients. It is also unclear whether disease-specific modifications are needed. This study sought to determine the reliability and validity of the WHOQOL when used for the evaluation of patients with HIV infection.

Methods

Subjects

A total of 138 consecutive HIV-infected patients treated and followed up regularly at the outpatient clinics at the National Taiwan University Hospital (NTUH) (Taipei, Taiwan) and the Taipei Municipal Venereal Disease Control Institute (TMVDC) (Taipei, Taiwan) were enrolled. To evaluate the test–retest reliability, 44 of the 138 patients were retested after an average interval of 4.6 weeks (range: 1–8 weeks). NTUH and TMVDC have the largest cohort of patients with HIV infection in Taiwan. The two institutes cooperate closely to provide these patients the best integrative medical service in Taiwan, including pharmacological therapy, medical and surgical services, counseling for both patients and family, and social support network. Inpatients were not enrolled because most of them were too ill to respond adequately to the questionnaire. The diagnosis of HIV infection was confirmed by Western blot in all of the enrolled patients. Informed consent was obtained for all of the participants.

Version of WHOQOL

The WHOQOL-BREF (Taiwan version) [31, 32] was used. The WHOQOL-BREF [31] consists of 26 items, including one item (G1) for general quality of life, one item (G4) for health-related quality of life, and 24 items belonged to four domains (physical, psychological, social and environment). There are seven items in the physical domain, six items in the psychological domain, three items in the social domain, and eight items in the environment domain. The Taiwan version of the WHOQOL-BREF [32] contains the 26 original items, plus two national items of Taiwan; one item belonged to the social domain and another belonged to the environment domain. The method of application, reference time point, and the scoring of items were performed as described for the original WHOQOL-BREF [31]. In brief, the questionnaire was self-administrated. The participants were required to evaluate their quality of life in recent 2 weeks. The item scores ranged from 1 to 5, with a higher score indicating a better quality of life on the corresponding item. Because the number of items are different for each domain, the domain scores were calculated by multiplying the average of the scores of all items in the domain by the same factor of 4. Thus, the domain scores would have the same range from 4 to 20.

Qualitative research

The content validity of WHOQOL-BREF in patients with HIV infection was studied through qualitative research. Eleven HIV-infected patients, of different age, gender, social background and disease stage, were enrolled to focus groups. Four medical professionals, experienced in the care of HIV-infected patients, were also invited to form an expert committee. Focus groups and the expert committee were interviewed separately to identify the determinants and major concerns of quality of life in HIV-infected patients. With the permission of participants, the content of the interview was tape-recorded and then transcribed for analysis. Factors influencing quality of life were then identified and extracted. The results were compared with the content and definition of WHOQOL-BREF.

Health status measures

The convergent validity was studied through measuring the strength of correlation between WHOQOL-BREF domain scores and health status measures. The health status measures used in study included: (1) the self-evaluated health status

and self-evaluated happiness, both measured by a five-point response scales (Table 1); (2) the number and severity of symptoms, measured by the University of California at San Francisco (UCSF) symptoms and signs checklist for persons living with HIV disease (SSC-HIV) [33].

Table 1. Characteristics of 136 patients with HIV infection

Characteristics	% (N = 136)
Age (years)	
≤30	34
31–40	42
>40	24
Male	96
Education of high school or more	82
HIV risk factor	
Men have sex with men	84
Heterosexual	15
Intravenous drug abuser	1
Presence of AIDS	35
Current antiretroviral therapy	
None[a]	10
PIs-based regimens[b]	80
NNRTIs-based regimens[c]	10
Self-evaluated health status	
Very poor	4
Poor	16
Fair	52
Good	25
Excellent	3
Self-evaluated happiness	
Very unhappy	2
Unhappy	19
Moderately happy	49
Happy	26
Very happy	4
Number of body symptoms	
None	4
1–10	34
11–20	40
21–30	22
Current CD4 cell count (/mm^3)	
≤200	10
201–500	44
> 500	46
Current plasma HIV RNA (copies/ml)	
≤5000	78
5001–20000	7
20001–100000	8
> 100001	7

[a] Including treatment-naive fresh cases and patients under structured treatment interruption.
[b] PIs – protease inhibitors.
[c] NNRTIs – non-nucleotide reverse transcriptase inhibitors.

We hypothesized that if WHOQOL-BREF accurately assessed quality of life in patients with HIV infection, then:
(1) WHOQOL-BREF domain scores should positively correlate with self-evaluated health status and happiness in these patients.
(2) WHOQOL-BREF domain scores should inversely correlate with number and severity of symptoms in these patients.

Severity of diseases

The discriminant validity was studied through comparing the WHOQOL-BREF domain scores between HIV-infected patients and healthy people, and between HIV-infected patients with different severity of diseases. The severity of HIV diseases were determined by (1) the number and severity of symptoms, measured by the UCSF symptoms and signs checklist for persons living with HIV disease (SSC-HIV) [33]; (2) the CD4 count, the plasma HIV RNA level, and the presence of acquired immunodeficiency syndrome (AIDS) assessed by the 1993 Centers for Disease Control and Prevention (CDC) criteria [34]. The data from 213 healthy persons, who were hospital volunteers or employees, or family members of non-HIV infected patients, were obtained for comparison.

We hypothesized that if WHOQOL-BREF accurately assessed quality of life in patients with HIV infection, then:
(1) Healthy persons should have better WHOQOL-BREF domain scores than HIV-infected patients.
(2) HIV-infected patients with milder disease should have better WHOQOL-BREF domain scores than HIV-infected patients with more severe disease.

Statistical analysis

The internal consistency reliability was evaluated using Cronbach's α. Test–retest reliability was evaluated using intraclass correlation coefficient (ICC). The construct validity was tested using exploratory factor analysis. The factor analysis was conducted through extracting factors by principal axis factoring, followed by Promax rotation with Kaiser normalization. Kaiser's 'eigenvalues greater than 1' rule was used to determine the number of

factors to rotate. Since this rule tends to include too many factors, solutions containing less numbers of factors were also sought. The significance of differences between domain scores was evaluated by Student's t test. All data was analyzed using SPSS for Windows Version 10.0. Two-tailed p values of <0.05 were considered to be statistically significant.

Results

Characteristics of subjects

Among the 138 enrolled patients, only two patients declined to participate. The response rate was 99% (136/138). The majority (114 of 136) of these patients were homosexual men. AIDS had been diagnosed in 47 patients (35%). Most (90%) of the patients were receiving highly active antiretroviral therapy, with current CD4 cell count $>200/mm^3$ and plasma HIV RNA <5000 copies/ml. A high percentage (62%) of patients reported more than 10 symptoms listed on SSC-HIV. The characteristics of the 136 HIV-infected patients are summarized in Table 1. The 213 healthy subjects included 97 men and 116 women, with age and education level distribution similar to that of 136 HIV-infected patients.

Descriptive statistics

Among the respondents (n = 136), the scores of items ranged from 1 to 5 in all but two items. The mean ± standard deviation (range) of the domain scores was 13.73 ± 2.24 (8.00–18.86) for the physical domain, 12.49 ± 2.75 (6.67–18.67) for the psychological domain, 12.85 ± 2.70 (6.00–20.00) for the social domain, and 13.14 ± 2.36 (7.50–19.11) for the environment domain.

Internal consistency and test–retest reliability

The Cronbach α values (n = 136) ranged from 0.74 to 0.85 across domains (Table 2). The α value of the entire questionnaire was as high as 0.93. All of the 44 patients tested twice were in apparently clinical stable condition, but there were variations in number of symptoms and SSC-HIV scores between the first and the second test ($r = 0.82$ and 0.78, respectively). Only eight patients showed no change in number of symptoms and signs on the checklist of SSC-HIV and only two patients showed no change in average SSC-HIV scores after an interval averaging 4 weeks (range 1–8 weeks). The majority of items had test–retest reliability ranging from 0.51 to 0.78 ($p < 0.01$, n = 44). In four of the items (pain, dependence on medical service, being respected by others, healthy environment), the response was less reproducible, probably because these items may not be stable during the 4 weeks. The test–retest reliability of domain scores was 0.72 (physical domain), 0.79 (psychological domain), 0.64 (social domain) and 0.71 (environment domain) (all $p < 0.01$, n = 44), respectively.

Table 2. Internal consistency of the WHOQOL-BREF in HIV-infected patients (n = 136)

	Cronbach's α
Physical domain	0.74
Psychological domain	0.81
Social domain	0.76
Environment domain	0.85
26 items	0.92
28 items (with two national items included)	0.93

Content validity

All of the focus groups and the expert committee gave the similar message. The early stage of HIV infection is often asymptomatic, but in the later stage, intractable fatigue and wasting syndrome can be disturbing. Loss of interpersonal relationships, particularly the relationship with family members, can be a painful experience. Potential discrimination in employment and medical service often forces patients to hide their HIV-positive status. A lot of varieties of symptoms, including nausea, vomiting, abdominal fullness, diarrhea, numbness, headache, insomnia, weakness, dry mouth, thirsty, shooting pain, flank pain, hematuria, skin rash, dizziness, insomnia, difficult to concentrate, loss of hair, and various kinds of lipodystrophy, etc. were experienced sooner or later under antiretroviral therapy. The types of symptoms were clearly associated with the types of medication prescribed. The complexity of some antiretroviral regimens was also troublesome. While fatigue, pain, body image, sleep, ability to

concentrate and personal relationships have been addressed in the WHOQOL-BREF, other symptoms due to adverse drug effects and the discrimination in workplace and medical service were not covered.

Construct validity

The scores of 26 items were all correlated with the scores of the corresponding domains (r range: 0.42–0.82 across items, all $p < 0.01$, n = 136). The scores of four domains were also all correlated with the scores for general quality of life (item G1) (r range: 0.49–0.64 across domains, all $p < 0.01$, n = 136) and the scores for health-related quality of life (item G4) (r range: 0.52–0.62 across domains, all $p < 0.01$, n = 136). Exploratory factor analysis of data from the 136 patients showed six factors with eigenvalues greater than 1, which explained 53% of total variance. However, the meanings of these six factors were fragmented, suggesting too many factors were used. Instead, a four-factor solution, which explained 47% of total variance, allowed meaningful interpretation for all four factors that were essentially corresponding to the four WHOQOL-BREF domains (Table 3).

Table 3. Exploratory factor analysis, principle axis factoring, Promax rotation with Kaiser normalization (n = 136)

Domains	Facets	Items	Factor 1 (Social)	Factor 2 (Psycho)	Factor 3 (Environ)	Factor 4 (Physical)
Physical	F1. Pain	3	−0.200	0.177	0.018	0.754
Physical	F11. Dependence on medical service	4	0.271	−0.202	−0.152	0.626
Physical	F2. Energy	10	0.128	0.239	0.399	0.153
Physical	F3. Sleep	16	−0.184	0.405	0.450	−0.082
Physical	F9. Ability to get around	15	0.674	0.147	−0.123	0.006
Physical	F12. Working ability	18	0.347	0.275	0.199	−0.047
Physical	F10. Daily activity	17	0.265	0.382	0.268	0.064
Psycho	F5. Ability to concentrate	7	0.002	0.585	0.175	0.078
Psycho	F6. Satisfied with oneself	19	0.171	0.743	−0.045	−0.103
Psycho	F8. Negative feelings	26	−0.107	0.533	0.092	0.070
Psycho	F24. Meaning of life	6	0.045	0.837	−0.118	−0.058
Psycho	F4. Enjoy life	5	0.353	0.113	0.022	0.055
Psycho	F7. Body image	11	0.470	0.444	−0.232	0.103
Social	F13. Personal relationship	20	0.547	0.010	0.082	−0.076
Social	F14. Social support	22	0.643	−0.051	−0.033	0.094
Social	F25. Respected by others	27	0.594	−0.052	0.228	0.065
Social	F15. Sexual life	21	0.021	0.148	0.387	0.193
Environment	F19. Accessibility to medical care	24	0.080	0.102	0.348	0.040
Environment	F22. Healthy environment	9	0.075	−0.176	0.732	−0.093
Environment	F23. Transportation	25	−0.069	0.099	0.688	−0.058
Environment	F17. Living condition	23	0.103	−0.075	0.602	−0.062
Environment	F16. Safety in daily life	8	0.389	0.378	0.030	0.045
Environment	F18. Enough money	12	0.512	0.116	0.145	−0.121
Environment	F20. Accessibility to daily information	13	0.580	0.320	−0.146	−0.157
Environment	F21. Leisure time	14	0.456	0.005	0.311	−0.083
Environment	F26. Get things like to eat	28	0.735	−0.274	0.185	0.091

Correlation between four factors

	Factor 1	Factor 2	Factor 3	Factor 4
Factor 1	1			
Factor 2	0.687	1		
Factor 3	0.624	0.604	1	
Factor 4	0.212	0.177	0.182	1

Table 4. Correlation between WHOQOL domain scores and health status measures (n = 136)

	Self-evaluated heath status	Self-evaluated happiness	Number of symptoms	Severity of symptoms
Domain scores				
Physical	0.53*	0.55*	−0.46*	−0.52*
Psychological	0.60*	0.73*	−0.47*	−0.49*
Social	0.52*	0.59*	−0.40*	−0.41*
Environment	0.57*	0.55*	−0.41*	−0.43*

*$p < 0.01$.

Convergent validity

The scores for the physical, psychological, social, and environment domains were all correlated positively with patients' self-evaluated health status and self-evaluated happiness (Spearman's r range: 0.52–0.60 and 0.55–0.73 across domains, respectively, all $p < 0.01$); and correlated negatively with the number and severity of symptoms (r range: −0.40 to −0.47 and −0.41 to −0.52 across domains, respectively, all $p < 0.01$) (Table 4).

Discriminant validity

The scores for the physical, psychological and social domains, but not the environment domain, discriminated between healthy persons and HIV-infected patients (all $p < 0.01$, Student's t test) (Table 5). This result remains valid if the 97 healthy men, rather than the total 213 healthy persons, were used as the healthy group for the comparison. The scores for all domains also discriminated between HIV-infected patients with more severe symptoms with an SSC-HIV score higher than the average (mean) and those with scores lower than the average (all $p < 0.01$, Student's t test), and between HIV-infected patients with a number of symptoms higher than the average (mean) and those with a number of symptoms lower than the average (all $p < 0.01$, Student's t test) (Table 5).

Under highly active antiretroviral therapy, the majority (72%) of the 47 patients initially with AIDS had a favorable clinical response, with a sustained rise in CD4 counts and durable suppression of plasma HIV RNA level, and remained free from opportunistic infections. With this im-

Table 5. Comparison of the WHOQOL domain scores (mean ± SD)

Domains	HIV-infected patients (N = 136)	Healthy persons (N = 213)	p-Value
(a) Between HIV-infected patients and healthy persons			
Physical	13.73 ± 2.24	15.39 ± 1.88	<0.01
Psychological	12.49 ± 2.75	13.74 ± 2.11	<0.01
Social	12.85 ± 2.70	14.00 ± 2.11	<0.01
Environment	13.14 ± 2.36	13.11 ± 2.21	0.124
(b) Between HIV-infected patients with different number of symptoms			
	More[a] symptoms (N = 73)	Less[b] symptoms (N = 62)	
Physical	12.94 ± 1.99	14.69 ± 2.18	<0.01
Psychological	11.54 ± 2.40	13.59 ± 2.75	<0.01
Social	12.06 ± 2.35	13.76 ± 2.81	<0.01
Environment	12.46 ± 2.20	13.92 ± 2.31	<0.01
(c) Between HIV-infected patients with different severity of symptoms			
	High[c] SSC-HIV scores (N = 57)	Low[d] SSC-HIV scores (N = 78)	
Physical	12.56 ± 1.87	14.60 ± 2.13	<0.01
Psychological	10.92 ± 2.15	13.58 ± 2.59	<0.01
Social	11.70 ± 2.32	13.67 ± 2.68	<0.01
Environment	12.08 ± 1.97	13.88 ± 2.34	<0.01

[a] Number of symptoms more than the average (mean).
[b] Number of symptoms less than the average (mean).
[c] SSC-HIV scores higher than the average (mean).
[d] SSC-HIV scores lower than the average (mean).

provement of clinical status and none of our patients were currently hospitalized, although the scores for all domains were still consistently worse in patients initially with AIDS than in those initially without AIDS, the differences were not statistically significant (data not shown).

Discussion

In the present study, we demonstrated that the WHOQOL-BREF, in its Taiwan national version, can be a useful generic quality-of-life instrument in patients with HIV infection. The internal consistency was good. The domain scores were well correlated with self-evaluated health status and self-evaluated happiness, and inversely correlated with number and severity of symptoms. The scores of physical, psychological, and social domains also discriminated between HIV-infected patients and healthy persons, and between HIV-infected patients with different number and severity of symptoms. To provide further information about validity in this group of patients, a better design would have been to compare the generic WHOQOL to an existing, previously tested, leading disease-specific instrument, such as MOS-HIV [18]. However, because up to the beginning of this study there was still no Taiwan version for such instruments, we were unable to use this strategy to corroborate the validity of WHOQOL in the present study.

Although a reliability level of 0.90 was advocated by Nunnally [35] as a minimum standard for measurement that is designed for individual assessment, in practice it may be too stringent and many highly regarded quality-of-life instruments fail to meet this standard [36]. Even the test–retest reliability (24 hour) for physiological measurement of blood pressure, 0.87 for systolic pressure and 0.67 for diastolic pressure [36, 37], did not meet this standard, either. Furthermore, real changes of status may occur during the retest interval. To minimize the effect of real changes, the ideal interval between the first and the second test for quality of life would have been 2 weeks or less. However, most participants in this study found it difficult to make an extra visit to the clinic before the scheduled monthly follow-up. Although all 44 patients tested twice were in apparently clinical stable condition, there were variations in number of symptoms and SSC-HIV scores between the first and the second test ($r = 0.82$ and 0.78, respectively). Only eight patients showed no change in number of symptoms and signs on the checklist of SSC-HIV, and only two patients showed no change in average SSC-HIV scores. It indicated that minor but real changes of symptoms and subjective feelings might have occurred during the long interval (average 4.6 weeks) between the first and the second tests in our study. Thus, we obtained a test–retest reliability of 0.51–0.79 for items and domains, which was slightly less adequate compared with the reliability between 0.56 and 0.84 of the original WHOQOL-BREF [31].

The results of qualitative research suggested that the content of WHOQOL-BREF might not cover some important issues for HIV-infected patients who were under regular highly active antiviral treatment. For example, pain (or discomfort) and fatigue are the only body symptoms listed in the WHOQOL-BREF physical domain. Other disturbing symptoms, such as gastrointestinal upset, hematuria, dry mouth, thirsty, dizziness, and skin rash, are not specifically listed. Similarly, discrimination to HIV-infected persons in workplace and medical service are not particularly mentioned in the content of WHOQOL-BREF. It is interesting to note that, although the content of WHOQOL-BREF may not be comprehensive for HIV-infected patients, there was a consistently good correlation between domain scores and symptoms (inverse correlation), and between domain scores and self-evaluated health status measures. The strength of correlation with validation variables was comparable to that reported in previous WHOQOL literature [32]. During the initial validation of WHOQOL Taiwan version in general population, the magnitude of correlations between WHOQOL domain scores and the validation variables ranged from 0.33 to 0.63 [32]. In the present study, the correlation between WHOQOL domain scores and symptoms ranged from −0.40 to −0.47 (number of symptoms) and from −0.41 to −0.52 (SSC-HIV scores of symptoms severity). And the correlation between WHOQOL domain scores and self-evaluated health status measures ranged from 0.52 to 0.60 (self-evaluated health status) and from 0.55 to 0.73 (self-evaluated happiness).

The results of factor analysis in this study showed that some items were not best correlated with their related domains. This is most likely due to the overlapping of constructs between the domains, especially when perceived from the viewpoints of HIV-infected patients. For example, to persons without fixed sexual partners, sexual life may be more suitably classified in the environment domain rather than the social domain. The grouping of money, accessibility to daily information, leisure time, and getting thing one like to eat into factor 1 (social) may reflect the perception that economic security, information and leisure activity are an integral part of social life.

Previous studies have consistently shown that the presence, number, and severity of symptoms are the major determinants of quality of life in HIV-infected patients [3–6]. Clinical stage has only a weak association with quality of life after adjusting for the number of symptoms [3]. Using number and severity of symptoms as the disease severity markers, we found that the WHOQOL-BREF has good discriminant validity among patients with different severity of HIV disease. The magnitude of difference in domain scores was comparable to that reported between sick and healthy persons in the original validation of WHOQOL [29]. We did not use current CD4 count as the marker in the testing of discriminative validity because only a very small proportion (<10%) of our patients had a low CD4 count ($\leqslant 200/mm^3$) when the questionnaire was applied (Table 1).

Although this study showed WHOQOL-BREF scores generally correlated well with validation variables in patients with HIV infection, it also showed some unique aspects of quality of life in HIV-infected patients were not covered. As a result, WHOQOL-BREF may be insensitive to the change of status in these aspects. It is thus worthwhile to formally develop a disease-specific module to enhance its sensitivity and responsiveness to clinical status [38]. This modular approach, initially proposed by Aaronson and coworker for cancer patients [39, 40], is a promising way to satisfy both the demand for cross-disease comparison for the purpose of resource allocation and the need for assessing the status of a particular disease in clinical trials. There are still no official guidelines for the development of a disease-specific module of the WHOQOL. To ensure cross-cultural validity, the official guidelines of The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 instrument mandates that the development of disease-specific modules should involve a number of countries, each representing a broadly defined geographic and culture category [41]. We suggest that if an HIV-specific module of the WHOQOL is to be formally developed, both the general guidelines for disease-specific instruments [38] and the guidelines to ensure cross-cultural validity [39–41] should be followed.

We conclude that the WHOQOL-BREF, in its national version, can be a useful generic quality-of-life instrument in patients with HIV infection. To further enhance the sensitivity and responsiveness to clinical status, it is worthwhile to formally develop an HIV-specific module for WHOQOL.

Acknowledgements

This work was supported by grants NSC 89-2314-B-002-433-M56 and DOH91-DC-1056. We are indebted to Dr Kai-Ping Yao for constructive comments. We would like to thank Dr Shou-Chien Chen, Dr Shiow-Ing Wu, and the Taipei Municipal Venereal Disease Control Institute for allowing us to recruit their patients for participation in this study. We also thank Miss Yu-Yin Chang for her help in statistical analysis. Dr Mao-Yen Chen and Dr Jung-Der Wang contributed equally to this work.

References

1. Palella FJ, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. N Engl J Med 1998; 338: 853–860.
2. Wu AW. Quality of life assessment comes of age in the era of highly active antiretroviral therapy. AIDS 2000; 14: 1449–1451.
3. Hays RD, Cunningham WE, Sherbourne CD, et al. Health-related quality of life in patients with human immunodeficiency virus infection in the United States: Results from the HIV Cost and Services Utilization Study. Am J Med 2000; 108: 714–722.
4. Cunningham WE, Shapiro MF, Hays RD, et al. Constitutional symptoms and health-related quality of life in patients with symptomatic HIV disease. Am J Med 1998; 104: 129–136.

5. Lorenz KA, Shapiro MF, Asch SM, Bozzette SA, Hays RD. Associations of symptoms and health-related quality of life: Findings from a national study of persons with HIV infection. Ann Intern Med 2001; 134: 854–860.
6. Bing EG, Hays RD, Jacobson LP, et al. Health-related quality of life among people with HIV disease: Results from the Multicenter AIDS Cohort Study. Qual Life Res 2000; 9: 55–63.
7. Low-Beer S, Chan K, Wood E, et al. Health-related quality of life among persons with HIV after the use of protease inhibitors. Qual Life Res 2000; 9: 941–949.
8. Osowiecki DM, Cohen RA, Morrow KM, et al. Neurocognitive and psychological contributions to quality of life in HIV-1-infected women. AIDS 2000; 14: 1327–1332.
9. Weinfurt KP, Willke RJ, Glick HA, Freimuth WW, Schulman KA. Relationship between CD4 count, viral burden, and quality of life over time in HIV-1-infected patients. Med Care 2000; 38: 404–410.
10. Call SA, Klapow JC, Stewart KE, et al. Health-related quality of life and virologic outcomes in an HIV clinic. Qual Life Res 2000; 9: 977–985.
11. Nieuwkerk PT, Gisolf EH, Colebunders R, Wu AW, Danner SA, Sprangers MA. Quality of life in asymptomatic and symptomatic HIV-infected patients in a trial of ritonavir/saquinavir therapy. The Prometheus Study Group. AIDS 2000; 14: 181–187.
12. Nieuwkerk PT, Gisolf EH, Reijers MH, Lange JM, Danner SA, Sprangers MA. Long-term quality of life outcomes in three antiretroviral treatment strategies for HIV-1 infection. AIDS 2001; 15: 1985–1991.
13. Bucciardini R, Wu AW, Floridia M, et al. Quality of life outcomes of combination zidovudine-didanosine-nevirapine and zidovudine-didanosine for antiretroviral-naive advanced HIV-infected patients. AIDS 2000; 14: 2567–2574.
14. Freedberg KA, Losina E, Weinstein MC, et al. The cost effectiveness of combination antiretroviral therapy for HIV disease. N Engl J Med 2001; 344: 824–831.
15. Schackman BR, Goldie SJ, Weinstein MC, Losina E, Zhang H, Freedberg KA. Cost-effectiveness of earlier initiation of antiretroviral therapy for uninsured HIV-infected adults. Am J Public Health 2001; 91: 1456–1463.
16. Smith MY, Feldman J, Kelly P, DeHovitz JA, Chirgwin K, Minkoff H. Health-related quality of life of HIV-infected women: Evidence for the reliability, validity and responsiveness of the Medical Outcomes Study Short-Form 20. Qual Life Res 1996; 5: 47–55.
17. Wachtel T, Piette J, Mor V, Stein M, Fleishman J, Carpenter C. Quality of life in persons with human immunodeficiency virus infection: Measurement by the Medical Outcomes Study instrument. Ann Intern Med 1992; 116: 129–137.
18. Wu AW, Revicki DA, Jacobson D, Malitz FE. Evidence for reliability, validity and usefulness of the Medical Outcomes Study HIV Health Survey (MOS-HIV). Qual Life Res 1997; 6: 481–493.
19. Anderson JP, Kaplan RM, Coons SJ, Schneiderman LJ. Comparison of the Quality of Well-being Scale and the SF-36 results among two samples of ill adults: AIDS and other illnesses. J Clin Epidemiol 1998; 51: 755–762.
20. Kaplan RM, Anderson JP, Patterson TL, et al. Validity of the Quality of Well-Being Scale for persons with human immunodeficiency virus infection. Psychosom Med 1995; 57: 138–147.
21. Leplege A, Rude N, Ecosse E, Ceinos R, Dohin E, Pouchot J. Measuring quality of life from the point of view of HIV-positive subjects: The HIV-QL31. Qual Life Res 1997; 6: 585–594.
22. Holmes WC, Shea JA. A new HIV/AIDS-targeted quality of life (HAT-QoL) instrument: Development, reliability, and validity. Med Care 1998; 36: 138–154.
23. Lubeck DP, Fries JF. Assessment of quality of life in early stage HIV-infected persons: Data from the AIDS Time-oriented Health Outcome Study (ATHOS). Qual Life Res 1997; 6: 494–506.
24. De Boer JB, Sprangers MA, Aaronson NK, Lange JM, van Dam FS. A study of the reliability, validity and responsiveness of the HIV overview of problems evaluation system (HOPES) in assessing the quality of life of patients with AIDS and symptomatic HIV infection. Qual Life Res 1996; 5: 339–347.
25. Smith KW, Avis NE, Mayer KH, Swislow L. Use of the MQoL-HIV with asymptomatic HIV-positive patients. Qual Life Res 1997; 6: 555–560.
26. Peterman AH, Cella D, Mo F, McCain N. Psychometric validation of the revised Functional Assessment of Human Immunodeficiency Virus Infection (FAHI) quality of life instrument. Qual Life Res 1997; 6: 572–584.
27. Thumboo J, Fong KY, Ng TP, et al. Validation of the MOS SF-36 for quality of life assessment of patients with systemic lupus erythematosus in Singapore. J Rheumatol 1999; 26: 97–102.
28. WHOQOL Group. The development of the World Health Organization Quality of Life Assessment Instrument (the WHOQOL). In: Orley J, Kuyken W (eds), Quality of Life Assessment: International Perspectives. New York: Springer-Verlag, 1994.
29. WHOQOL Group. The World Health Organization quality of life assessment (WHOQOL): Development and general psychometric properties. Soc Sci Med 1998; 46: 1569–1585.
30. Bonomi AE, Patrick DL, Bushnell DM, Martin M. Validation of the United States' version of the World Health Organization Quality of Life (WHOQOL) instrument. J Clin Epidemiol 2000; 53: 1–12.
31. WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med 1998; 28: 551–558.
32. The WHOQOL-Taiwan Group. The User's Manual of the Development of the WHOQOL-BREF Taiwan Version. 1st edn., Taiwan, Taipei, 2000.
33. Holzemer WL, Henry SB, Nokes KM, et al. Validation of the sign and symptom check-list for persons living with HIV disease (SSC-HIV). J Adv Nurs 1999; 30: 1041–1049.
34. Centers for Disease Control and Prevention. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR 1992; 41(RR-17): 1–19.
35. Nunnally JC. Psychometric Theory. New York: McGraw-Hill, 1967: 226.

36. Hays RD, Anderson RT, Revicki D. Assessing reliability and validity of measurement in clinical trials. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998: 174–175.
37. Prisant LM, Carr AA, Bottini PB, Thompson WO, Rhoades RB. Repeatability of automatic ambulatory blood pressure measurements. J Family Practice 1992; 34: 569–574.
38. Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. Ann Intern Med 1993; 118: 622–629.
39. Aaronson NK, Bullinger M, Ahmedzai S. A modular approach to quality-of-life assessment in cancer clinical trials. Recent Results Cancer Res 1988; 111: 231–249.
40. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993; 85: 365–376.
41. Sprangers MA, Cull A, Groenvold M, Bjordal K, Blazeby J, Aaronson NK. The European Organization for Research and Treatment of Cancer approach to developing questionnaire modules: An update and overview. EORTC Quality of Life Study Group. Qual Life Res 1998; 7: 291–300.

Address for correspondence: Jung-Der Wang, Institute of Occupation Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Taipei 100, Taiwan, ROC
Phone: +886-2-23123456 ext. 2224; Fax: +886-2-23224660
E-mail: jdwang@ha.mc.ntu.edu.tw

191

Quality of Life Research 00: 000–000, 2003.

Integrating health profile with survival for quality of life assessment

Jing-Shiang Hwang[1] & Jung-Der Wang[2,3]
[1]*Institute of Statistical Science, Academia Sinica;* [2]*Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health, Taipei (E-mail: jdwang@ha.mc.ntu.edu.tw);* [3]*Department of Internal Medicine, National Taiwan University Hospital, Taiwan*

Accepted in revised form 10 January 2003

Abstract

In cohort studies or clinical trials, measurements of quality of life (QoL) were averaged across available individuals for each group at given points in time to produce single measures for comparisons. However, estimates of these single measures may be severely biased if substantial mortality occurs over time. The objective of this study is to develop a method that integrates QoL measurement and survival for long-term evaluation of health services. We defined a mean QoL score function over time for an index population as the average QoL score of all individuals both alive and dead at each time point in the population. While a living subject's QoL can be assessed by asking one's subjective preference, the score of a decedent can be assigned a fixed value depending on the specific facet on health profile. The mean QoL score function over time is reduced to a single measure of expected cumulative QoL score, which is the area under the curve of mean QoL score function over a given time interval and can be estimated by taking a random sample from a cross-sectional survey. For the QoL score function to be extrapolated to life-long, it requires the assumption that the disease causes premature death or a long-term moderate impairment of QoL. We provided methods and computer programs for estimating mean QoL score functions and the reduced single measures for use in comparisons. A cohort of 779 breast cancer patients from Chiangmai, Thailand were followed for 12 years to demonstrate the proposed methods. The data included the 12-year complete survival records and QoL scores on 233 patients collected from a cross-sectional survey using WHOQOL questionnaire and standard gamble method. The expected cumulative QoL scores using utility and psychometric scales were compared among patients in four groups of clinical stages in this cohort for time from onset up to 12 years and life-long. We conclude that such an integration of QoL measurement with survival can be useful for the evaluation of health service and clinical decision.

Key words: Health profile, Monte Carlo method, Quality-adjusted life year, Quality-adjusted survival

Introduction

Health-related quality of life (HRQoL) assessment is increasingly used in clinical trials and other health outcome evaluation [1]. HRQoL is generally defined as the individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [2]. It is a multidimensional concept incorporating both functional status and the individual's perception of health. Thus, many generic and condition-specific questionnaires have been proposed to assess these effects [3–5]. These QoL measures are similar in that each expresses the effects of medical care in terms that can be reported directly by a patient. However, the rationales for the methods differ considerably. Most of the available psychometric measures include multiple dimensions such as physical functioning, psychological status and social relationships in order to create a profile of patient outcomes. While utility-based methods

Journal : QURE SPS Article No. : 50001 | Dispatch : 1-8-2003 | Pages : 13
PIPS No. : 5118808 | ☐ LE | ☑ TYPESET
MS Code : QURE 50001 | ☑ CP | ☐ DISK

assign a value to a specific health state to reflect global impact of that state on the patient's overall QoL [6–9].

Since a patient's QoL continuously fluctuates or changes over time, many HRQoL studies have considered summarizing measurement and analysis from a time perspective. In clinical trials, HRQoL assessments were often conducted by administering profile questionnaires at multiple time points before, during, and after an intervention, with a focus on summarizing or showing the changes in QoL over time (or longitudinally) and across different individuals for group comparison [10]. In practice, the summary measures are often constructed to obtain population mean QoL score estimates at given time points using sampled data from each population. However, it has been a noteworthy problem that the estimates can be biased if there is a substantial proportion, say, 40%, of mortality in a study over time [11]. There is also argument regarding the assignment of scores to those who die in the study. Thus, so far there have been relatively few methods developed for summarizing health profile measures taking account of mortality or survival across time during longitudinal follow-up.

In this study, we first clarify the definition of mean QoL score function over time for an index population, which is a function of average score across all individuals both alive and dead at a given time in the index population. While a living subject's QoL can be assessed by asking one's subjective preference, the score of a decedent can be assigned a fixed value depending on the specific facet on health profile. We then show that the mean QoL score function can be presented in terms of survival function and average QoL score function of the sub population of living individuals. When the survival data are complete, the survival function can be estimated quite accurately using available techniques. The average QoL score function of the sub population of living individuals can be estimated by kernel-smoothing the data of a random sample from a cross-sectional survey of QoL on the living individuals, which was demonstrated in a previous simulation study by Hwang et al. [12]. When the data are not complete such as in follow-up studies with heavy censoring, the mean QoL score functions can be accurately estimated over time only up to the end of the follow-up. Then, the lifetime score for the whole population can also be extrapolated by a Monte Carlo method proposed by Hwang and Wang [13]. Therefore, we can obtain relatively accurate mean QoL score function estimates, which can be further plotted against the whole life span for specific QoL domain or item scales in different treatment groups. When the QoL score function is replaced by utility function, the area under the whole life span is the expected quality-adjusted life expectancy (QALE).

Data from a cohort of 779 cases of breast cancer from Chiangmai, Thailand followed for 12 years were used as an example to illustrate the proposed methods [14]. The cohort was stratified into four groups with different clinical stages. To the end of the follow-up, June 30, 1997, the survival and mortality of the 779 patients were well recorded. Measurements of QoL were obtained through a cross-sectional survey on 223 patients during 1996–1997 using utility measurement of standard gamble and the questionnaire of World Health Organization quality of life (WHOQOL). We computed and compared expected QALYs in utility and psychometric scores for the four groups of cancer patients for time up to 12 years and lifelong.

Methods

In this section, we first clarify the definition and interpretation of mean QoL function over time for an index population and then introduce methods for estimating the function. Let $q_i(t)$ be the unobserved QoL score at time t since the onset of a specific disease or health condition on the ith individual patient in an index population. The QoL score can be measured using the utility or health profile instrument. In most QoL measurement, we often can rescale the QoL score to a value between 0 and 1, in which 0 represents the worst health status and 1 represents the perfect health. If a patient dies during the study, a constant value between 0 and 1, denoted by δ, could also be assigned after that time point for the patient. The population mean QoL score at each time t is constructed straightforwardly by the population average, $Q(t) = \frac{1}{N}\sum_{i=1}^{N} q_i(t)$, where N is the size of the index population. Let $G(t)$ denote the set of

subjects in this index population who are still alive at time t. The size of $G(t)$ is denoted by $M(t)$. Note that in the beginning of time 0, $M(t) = N$. The mean QoL score function over time t for the index population can be rewritten as the sum of scores of those who are still alive plus those who die:

$$Q(t) = \frac{1}{N}\left(\sum_{i\in G(t)} q_i(t) + \sum_{i\notin G(t)} q_i(t)\right)$$
$$= \frac{M(t)}{N} \times \frac{1}{M(t)} \sum_{i\in G(t)} q_i(t) + \frac{N - M(t)}{N} \times \delta.$$

Note that $M(t)/N$ is the survival rate at time t for the index population, denoted by $S(t)$. We may denote $\frac{1}{M(t)}\sum_{i\in G(t)} q_i(t)$ by $Q_s(t)$ representing the average QoL score for the sub population of individuals still alive at time t. We then obtain the following simple equation

$$Q(t) = S(t) \times Q_s(t) + [1 - S(t)] \times \delta$$

which establishes the relationship between population mean QoL score function and survival function. Note that when QoL score is assigned with a constant value of 1 for all living individuals and $\delta = 0$, $Q(t)$ is the survival function for the index population. Therefore, we can interpret the mean QoL score function as quality-adjusted survival function when the QoL score is in the 0–1 scale. More importantly, this equation provides an alternative way of estimating $Q(t)$ by separately estimating the survival function and the mean QoL score function for the sub population of the living individuals. The area under the curve of the mean QoL score function $Q(t)$ plotted against time t over the period $[a, b]$, presented by

$$Q[a, b] = \int_a^b S(t)Q_s(t)\,dt + \delta\int_a^b [1 - S(t)]\,dt,$$

is a common single measure of QoL, with a unit of psychometric score-time, which is conceptually the same as quality-adjusted life year (QALY) for the time period except substituting the utility measurement with health profile scores. This useful measure $Q[a, b]$ is the expected cumulative QoL score, which can be also interpreted as expected quality-adjusted survival time adjusted for the specific score/utility for an index population over the time period $[a, b]$. If the QoL score is a utility measurement, then the measure $Q[0, \infty]$ is exactly the QALE with the unit of QALY. When the QoL is a score from psychometric measurement, then the unit is a score-time, say, score-month or score-year, etc. Namely, it is a psychometric score adjusted by survival function and should specify the time unit for comparative purpose. The proposed formula is a generalization from that derived by Hwang et al. using integration techniques in which δ is restricted to be 0 [12].

To estimate the expected cumulative QoL score $Q[a, b]$, we can conduct on discrete time by dividing the entire time period $[a, b]$ into K disjointed short intervals $[t_{k-1}, t_k)$, $k = 1, K, K$, where $t_0 = a$ and $t_K = b$. The estimate of survival at time t_k, denoted by $\hat{S}(t_k)$, can be easily obtained using common approaches such as Kaplan–Meier method when complete survival data are available. To obtain the estimate of mean QoL for the sub population, $\hat{Q}_s(t_k)$, we only need measurements from a cross-sectional survey on the living individuals, instead of the costly repeated measures, and using kernel smoothing techniques or fitting a non-linear curve to the interviewed scores. The estimate of population mean QoL at time t_k is $\hat{Q}(t_k) = \hat{S}(t_k) \times \hat{Q}_s(t_k) + [1 - \hat{S}(t_k)] \times \delta$. The expected quality-adjusted survival time over the period $[a, b]$ can be estimated using a trapezoidal approximation:

$$\hat{Q}[a, b] = \frac{1}{2}\sum_{k=1}^{K}(t_k - t_{k-1})[\hat{Q}(t_k) + \hat{Q}(t_{k-1})].$$

Extrapolation to lifetime with censored follow-up data

When the data are complete, simulation studies conducted by Hwang et al. showed the estimator is quite accurate [12]. However, especially for follow-up studies with heavy censoring, the mean QoL score function $Q(t)$ for the index population can be accurately estimated only over time up to the end of follow-up. Hwang and Wang have proposed a Monte Carlo extrapolation approach to provide estimate of $Q(t)$ for t beyond the close of follow-up [13]. The main idea of that approach is to borrow information of long-term survival from a reference population matched with the same age and gender

for every individual of the index population. In other words, we can generate a hypothetical reference population composed of exactly the same age and gender distribution through Monte Carlo simulation method from the vital statistics. Then, fit a simple linear regression to the logit of the ratio between $Q(t)$ of the index population and the simulated survival function of the reference population for a certain point in time to the end of the follow-up. Finally, use the predicted line to extrapolate $Q(t)$ beyond the follow-up. On this approach, one must assume that the mean QoL score function $Q(t)$ for the index population at time t should be no greater than that of the reference population [13], which only holds for any disease that results in premature death or affects QoL moderately on a long-term basis. A feedback plot to check the linearity assumption is also provided to assure the validity. Simulation studies have shown that this is a potential approach for estimating mean QoL score function and survival function beyond the follow-up with a certain degree of accuracy. The Bootstrap approach was also proposed to estimate standard errors of the estimates [15]. The authors have provided a free package of S-Plus functions for computing the estimates and standard errors of the estimates for $Q[a, b]$ and other applications [16]. Users only need to input files of survival data, cross-sectional survey data of QoL score, and sample of age and gender from the index population, in addition to a file of life table if extrapolation is needed.

Example of a breast cancer cohort

The detailed information of a cohort of 779 cases of breast cancer who were first diagnosed during 1985–1994 were followed regularly at Chiangmai cancer registry for 12 years was described elsewhere [14]. Briefly, the Chiangmai cancer registry is a population-based registry, co-sponsored by the Chiangmai University Faculty of Medicine and WHO, which actively collected data on cancer patients from one university hospital, 10 private hospitals, and 26 public hospitals in Chiangmai province, Thailand [17]. The cohort has been stratified into four groups with different clinical stages with group sizes 81, 330, 226 and 142, respectively. The average onset age of these 779 patients were 50.3 ± 13.0 years old with a range of 22–95. By the time of censoring, June 30, 1997, there were 75, 244, 106, and 28 patients still alive for stages I–IV, and the 12-year survival rates were 93, 74, 47, and 13%, accordingly. To establish the QoL function curve through time for each stage, we needed to obtain a random sample of 50 in size [12]. In addition, we added 15–25 patients whose duration-to-dates were less than 2 years, because the original cohort no longer collected patients by the end of 1994 and the QoL function was relatively unstable during the first 2 years after diagnosis. A cross-sectional survey was then implemented and the response rate was about 80%. In total, we collected 64, 72, 69 and 28 patients in stages I–IV for HRQoL interview during 1996–1997. Patients were asked to fill out the WHOQOL-100 questionnaire followed by standard gamble method conducted by an interviewer to elicit the utility value of her current health state [8].

The WHOQOL-100 was originally designed by the WHOQOL group, which intended to assess detailed health profile on four domains with 25 facets inquiring about physical/independent, psychological/spiritual, social relationship and environment [2, 18]. Each facet consists of 4 items in which a five point Likert scale (1–5 score) is used. The facet score, given by the sum of its four item scores, ranges from 4 to 20. The domain score is obtained by averaging the facet scores in that domain. In this study we rescaled the domain score by subtracting 4 and then dividing by 16 to a value between 0 and 1 corresponding to the worst and best health status of that domain, respectively. The rescaled score is still a preference measure. But it can be treated as a psychometric QoL score for comparison with the utility measurement obtained from standard gamble method, which also ranges between 0 and 1.

Results

Figure 1 shows the estimated survival, average scores of physical domain of WHOQOL obtained from living patients and the physical domain score-adjusted survival functions over the 12-year follow-up period for the four stages of breast cancer patients. The plots were produced from the free package in which the survival functions were

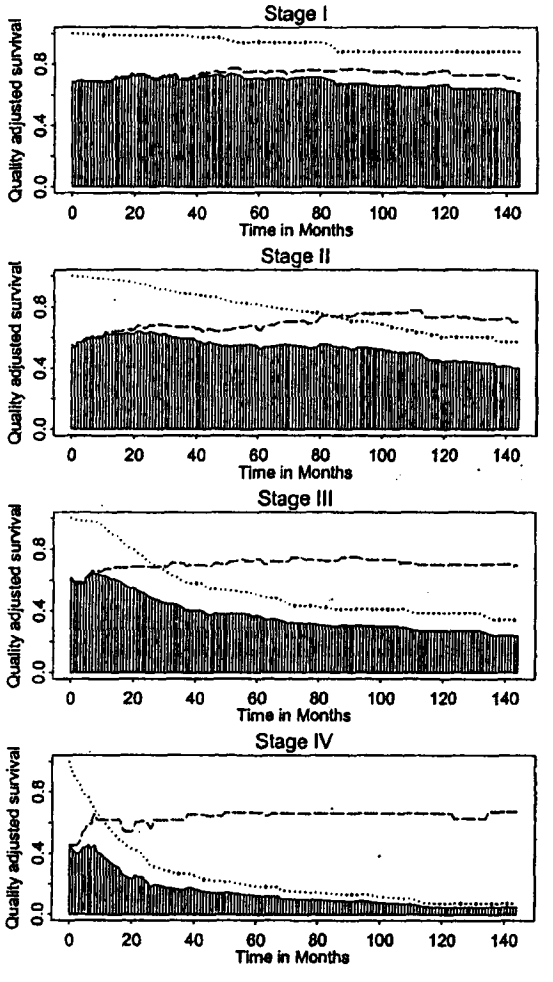


Figure 1. The estimated quality of life adjusted survival functions (solid curves) for stages I–IV breast cancer patients after 144 months of follow-up. Scores from the physical domain of WHOQOL were used for demonstration. The dotted curve is the estimated survival functions. The dashed curve is the estimated average quality of life score of living patients. The shaded area is the expected cumulative physical score-months over the 144 months of follow-up.

estimated using Kaplan–Meier method on the survival data of the breast cancer cohort. The estimated score function for physical domain of each subgroup of living individuals was obtained using kernel smoothing method on the sampled patients with different duration-to-dates. The shaded area under the estimated physical domain score-adjusted survival function in each plot was the expected cumulative physical domain score-time or physical domain adjusted survival time over the 12 years of follow-up. The average QoL scores of physical domain in living patients were usually lower in the first months of follow-up and then slowly increased to stable levels. Because only five stage IV patients survived for more than 5 years, the curve was over-smoothed after 5 years. However, the survival rates were very low for stage IV patients, and the estimated QoL adjusted survival function would not be greatly affected. Table 1 summarizes the results of estimated expected survival in months, expected quality-adjusted survival time adjusted for standard gamble utility, and for physical, psychological, social, and environmental domain scores, respectively, over the 12 years of follow-up and life-long. The estimated 12-year mean survival times are 134, 112, 77 and 33 months for the four stages, accordingly. The expected quality-adjusted survival time adjusted for utility, were higher than those adjusted with the psychometric scores in all the four stages. The 12-year cumulative psychometric adjusted survival for social domain seemed to be the worst domain compared with other QoL domains in WHOQOL, which indicates that social life is the most severely affected.

To extrapolate the mean QoL score function beyond the follow-up of 12 years, we have checked the linearity assumption for logit of the ratio between $Q(t)$ of the index population and the simulated reference population. As examples shown in Figure 2, the assumption seemed to be largely fulfilled for four stages for the last 60 months of 144-month follow-up. Figure 3 shows the estimated QoL adjusted survival functions up to 30 years for the stage I group. The curves against time beyond 144 months were extrapolated using the Monte Carlo approach on a reference group with age and gender matched for stage I group, which were generated from the general population using 1990 vital statistics of Thailand. The patterns of QoL adjusted survival functions over time were similar for utility measure, and psychometric scaling for physical and psychological domains, which shared a constant decreasing rate during this time period. The QoL adjusted survival functions for social and environmental domains behaved to have less decreasing rates. The lower half of Table 1 summarizes the results of estimated expected survival time, quality-adjusted survival

Table 1. The estimates of expected survival time (in months), quality-adjusted survival time (QAST) adjusted for standard gamble utility and psychometric scores obtained from physical, psychological, social and environmental domains during 144 months of follow-up and life-long for breast cancer patients in the four clinical stages.

QoL scale	Stage I		Stage II		Stage III		Stage IV	
	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
Over 144 months of follow-up								
Survival time	134.2	3.8	111.9	2.7	76.9	4.1	33.1	3.8
QAST adjusted for								
Standard gamble	117.7	3.6	92.4	2.9	62.1	3.5	26.7	3.3
Physical score	98.5	3.3	77.0	2.9	53.5	3.1	20.2	2.5
Psychological score	93.4	3.1	74.1	2.2	50.8	3.0	20.9	2.4
Social score	87.4	3.4	75.1	2.2	49.8	3.0	20.5	2.2
Environmental score	91.1	2.9	74.1	2.2	51.3	2.9	20.9	2.5
Extrapolated to life-long								
Survival time	277.5	59.8	166.2	15.3	118.6	17.1	36.9	6.1
QAST adjusted for								
Standard gamble	274.6	39.5	144.0	17.5	104.9	16.5	29.9	5.4
Physical score	215.5	33.2	122.3	16.0	84.0	13.3	22.8	4.1
Psychological score	203.5	30.6	111.9	12.0	74.6	10.4	23.5	4.3
Social score	213.5	42.4	122.9	14.2	82.7	12.3	23.2	3.9
Environmental score	221.8	31.7	118.7	12.9	77.6	12.1	23.5	4.3
Survival time for reference group	379.5	1.8	361.3	1.7	326.8	1.8	313.6	1.9

The standard errors were estimated using the Bootstrap approach. The reference group was created by matching onset ages of patients in each clinical stage group using female Thai vital statistics in 1990.

time adjusted for utility and for the four domain scores of WHOQOL after extrapolation to 50 years or life-long. The estimated life expectancies were 278, 166, 119 and 37 months for the four clinical stages of breast cancer patients. While the survival times for the four reference groups of people with perfect health (or QoL = 1) were 380, 361, 327 and 314 months, accordingly. The results revealed that psychological domain has the smallest life-long score-time for stages I–III, which implies that breast cancer patients need a long-term psychological care.

The results shown in Table 1 were based on the assumption of assigning the dead 0 score. To explore the sensitivity of assigning the death score, we calculated the expected psychological score-time adjusted survival time for the four stages with death score 0.1 and 0.2, respectively. We have chosen 0.2 because of the minimum psychological score of 0.22 found in the 233 sampled patients. The results are summarized in Table 2. The expected adjusted survival time increased as death scores increased. There were limited increased adjusted survival time for stage I patients because of a high survival rate. But the expected life-long adjusted survival time for psychological domain increased from 23.5 score-months with death score 0 to 130.3 score-months with death score 0.2 for the stage IV patients. The result indicates that expected quality-adjusted survival time was very sensitive to the assignment of death score for a disease with high mortality rate.

Discussions

In clinical trials, measured QoL scores using utility or psychometric health profile methods were usually compared for available patients at specific time points: before, during, and at the end of the trials. Summary measures over time were usually used for comparisons and reports. However, patient's survivorship is either ignored or considered separately from the observed QoL scores [19]. The ignorance of mortality has caused a serious problem of bias in the summarized QoL measures. In this study, we proposed a clear definition of mean QoL score function over time for an index population, which is the average score of all patients both alive and dead at a given time. Moreover, we

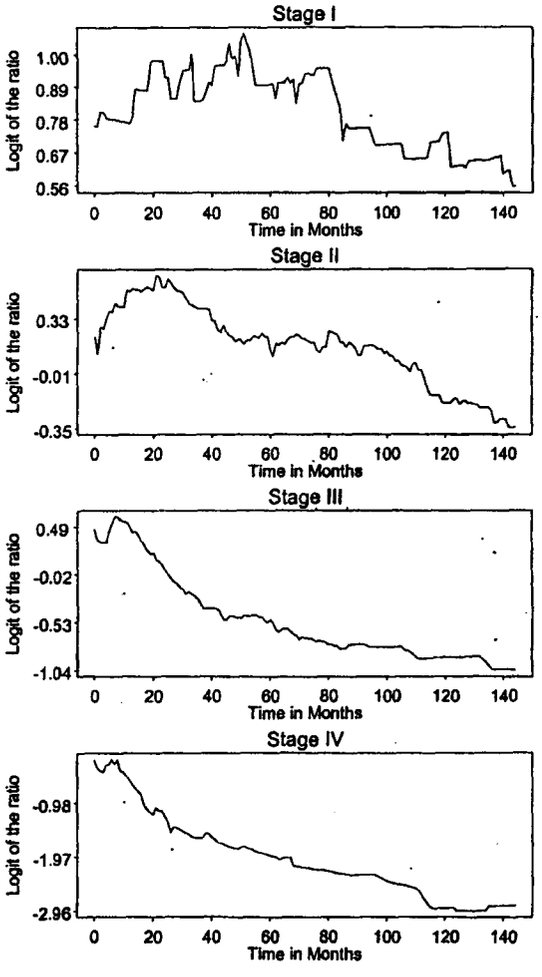


Figure 2. The logit of the ratio between the estimated mean physical QoL score function and survival function for reference population by clinical stages plotted against time over the 144 months of follow-up.

have also shown that the mean QoL score is the sum of following two products: the average score of surviving patients multiplied with population survival rate, and the mortality rate multiplied with the average score of decedents after assigning a fixed value. The survival of the population is then naturally integrated with QoL measure so that we can interpret the mean QoL score function as the QoL adjusted survival function. The QoL adjusted survival function is further extended to define the cumulative QoL score for an index population over a time duration, which can supplement the drawback of only comparing one or several specific time points. When the QoL score is rescaled to 0–1, life-long cumulative QoL score is equivalent to the commonly used expected quality-adjusted survival time in cost-effectiveness analysis [20]. We have provided a general form and procedures for calculating expected quality-adjusted survival time using both utility and health profile measures. Most HRQoL studies have assigned 0 score to the dead, although many people may disagree and there seems to have no consensus. Our proposed method allowed researchers to assign different constant values to the decedents according to different items or domains in health profile assessment. We propose that such a value had better be less than the lowest value of those alive during sensitivity analysis. Since the lowest possible score in our study for different domains was 0.22, we decided to assign scores of 0, 0.1 and 0.2 for sensitivity analysis of scoring the dead subjects, which therefore can be implemented to provide additional information for a more delicate clinical decision-making.

Although we have provided a clear interpretation of the combination of QoL with survival through the definition of population mean QoL, some practical problems are worth further clarification. The major critique on the combination of QoL and survival is the potential dependence of QoL on survival [19]. In general, patients who are about to die or to be lost to follow-up tend to have worse current scores, whereas those who survive longer tend to have somewhat better current scores [11, 20]. It indicates that the average scores obtained from a sample of the surviving patients might produce a positive bias because patients with worse scores may be less represented in the sample. Hence, a (stratified) random sample of currently surviving patients, which cover all different duration-to-dates or times-after-diagnosis, should be essential to an accurate measure for the combination of QoL measures and survival. In other words, our current approach of conducting a cross-sectional survey with kernel-smoothing the data to estimate the mean QoL function at different duration-to-dates may not be very accurate. It can be further improved by repeated measurements for the same cohort followed by constructing a mixed-effects model and adding more predictors of QoL as fixed factors.

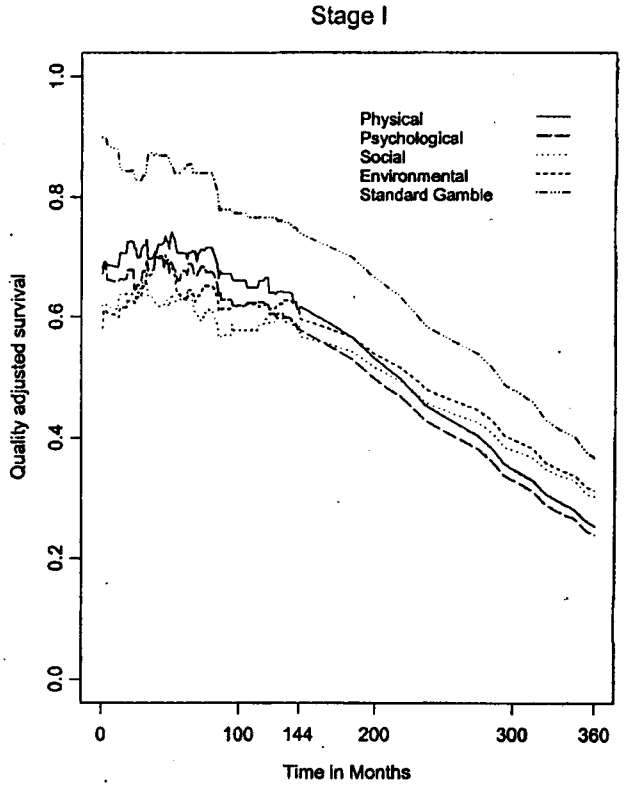


Figure 3. The estimated quality of life adjusted survival functions for stage I breast cancer patients using physical, psychological, social and environmental measures of WHOQOL and standard gamble utility.

By doing so, we can actually improve the estimates of QALE as well as lifetime psychometric scores.

Another concern is the choice of an appropriate reference population. While it is very convenient to use the life table of general population on vital statistics, one can only match with the index population on age and gender. A more accurate estimation may be achieved through a more deliberate selection of a reference population that are comparable with the index population on other determinants of outcome [21], because then the

Table 2. Results of sensitivity analysis for assigning scores of 0, 0.1 and 0.2 to the state of death on the estimates of expected cumulative psychometric score-months obtained from psychological score of four clinical stages of breast cancer for 144 months of follow-up and life-long

Time duration	Death Score	Stage I		Stage II		Stage III		Stage IV	
		Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
144 months	$\delta = 0$	93.4	3.1	74.1	2.2	50.8	3.0	20.9	2.4
	$\delta = 0.1$	94.4	3.0	77.3	2.0	57.5	2.6	32.0	2.2
	$\delta = 0.2$	95.4	2.5	80.6	1.8	64.2	2.2	43.1	1.7
Life-long	$\delta = 0$	203.5	30.6	111.9	12.0	74.6	10.4	23.5	4.3
	$\delta = 0.1$	213.3	27.4	135.2	11.0	111.3	8.4	76.9	2.7
	$\delta = 0.2$	216.1	29.1	156.5	8.6	148.1	6.5	130.3	1.6

linear assumption of logit of $W(t)$ may be more easily fulfilled.

The QoL adjusted survival functions may provide more detailed information for different choices of diagnoses and/or treatments, because different patients may have different preferences in different facets and domains. Both patients and doctors or nurses can look at the figures and numerical values of score-time for different facets or domains of their future QoL adjusted lives at any time point from the $Q(t)$ score functions, which can be used to facilitate decision-making. The measure of life-long cumulative QoL score can also be applied to the general population to calculate a nation's psychometric health life expectancy.

The results of this breast cancer study show that expected quality-adjusted survival time calculated from the utility measurement was generally higher than the rescaled psychometric score-adjusted survival time. This may indicate HRQoL measure in terms of utility is really higher than the 0–1 scaled psychometric scores for the breast cancer patients. However, it is also possibly caused by the scale construction difference. The simple 5 points ordinal scale representing increasing or decreasing severity may be enough for patients to mark their perception. But the descriptors for the lowest and highest scale points are often too extreme so that patients tend not to mark these points even when their health conditions are close to these ends. Moreover, most psychometric scores coming from the Likert scale may not be directly transformed into a ratio scale of between 0 and 1. These problems need to be resolved before the rescaled scores can be used to compare with other utility measures. Hence, the interpretation on direct comparison between expected quality-adjusted survival times using different measures must be cautious. Further refinement of psychometric instruments such as conducting a more detailed descriptor study before use will probably improve the accuracy and feasibility of our method.

Acknowledgements

We are greatly indebted to Drs C. Chantawong, S. Sumitsawan, A. Podhipak, S. Suksiriserekul, for kindly sharing the cohort and QOL data of breast cancer for this study. We are also grateful to Dr D. L. Fairclough and two anonymous peer reviewers for constructive comments. This paper is supported by a grant from the National Science Council of the Executive Yuan of the Republic of China. (grant no. NSC 89-2314-B-002-433-M56).

References

1. Berzon RA. Understanding and using health-related quality of life instruments within clinical research studies. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press; 1998, 3–15.
2. The WHOQOL Group. The World Health Organization Quality of Life assessment (WHOQOL): Position paper from the World Health Organization. Soc Sci Med 1995; 41: 1403–1409.
3. Tengs TO, Wallace A. One thousand health-related quality of life estimates. Med Care 2000; 38(6): 583–637.
4. Bowing A. Measuring Disease. Buckingham: Open University Press, 1995.
5. McDowell I, Newell C. Measuring Health: A Guide to Rating Scales and Questionnaires. New York: Oxford University Press, 1996.
6. Drummond MF, O'Brien B, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes. 2nd ed. New York: Oxford University Press, 1997.
7. Gold MR, Siegel JE, Russel LB, Weinstein MC. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press, 1996.
8. Patrick DL, Ericson P. Health Status and Health Policy: Allocating Resources to Health Care. New York: Oxford University Press, 1993.
9. Kaplan RM. Profile versus utility based measures of outcome for clinical trials. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998; 69–90.
10. Fairclough D. Methods of analysis for longitudinal studies of health-related quality of life. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998; 227–247.
11. Hays RD, Alonso J, Coons SJ. Possibilities summarizing health-related quality of life when using a profile instrument. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998; 143–153.
12. Hwang JS, Tsauo JY, Wang JD. Estimation of expected quality-adjusted survival by cross-sectional survey. Stat Med 1996; 15: 93–102.
13. Hwang JS, Wang JD. Monte Carlo estimation of extrapolation of quality-adjusted survival for follow-up studies. Stat Med 1999; 18: 1627–1640.
14. Chantawong C. Estimation of quality-adjusted survival of breast cancer patients in Chiangmai, Thailand. (Ph.D. dis-

sertation) Bangkok. Thailand: Mahidol University Faculty of Public Health, 1997.
15. Efron B, Tibshirani RJ. An Introduction to the Bootstrap. New York: Chapman and Hall, 1993.
16. MC-QAS software for estimating expected quality-adjusted survival time adjusted for psychometric scores and utilities for health related quality of life assessment. Available from URL: http://www.stat.sinica.edu.tw/jshwang.
17. Martin NC, Sriskho S, eds. Statistical Report of the Registry Unit, Chiangmai. Thailand: Faculty of Medicine, Chiangmai University, 1993, 16p.
18. The WHOQOL Group: Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med 1998; 28: 551–558.
19. Cox DR, Fitzpatrick R, Fletcher AE, Gore SM, Spiegelhalter DJ, Jones DR. Quality-of-life assessment: Can we keep it simple? J R Stat Soc A 1992; 155: 353–393.
20. Schwartz CE, Laitin EA. Using decision theory in clinical research: Applications of quality-adjusted life-years. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998; 119–141.
21. Wang JD. Basic Principles and Practical Application of Epidemiological Research. Singapore: World Scientific, 2002; 161–195.

Address for correspondence: Jung-Der Wang, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public health, No. 1, Section 1, Jen-Ai Road, Taipei, 10018, Taiwan
Phone : +886-2-2356-2224/2312-3456; Fax: +886-2-2322-4660
E-mail: jdwang@ha.mc.ntu.edu.tw

118

Journal of Toxicology and Environmental Health, Part A, 65:219–235, 2002

1528-7394/02 $12.00 + .00

Taylor & Francis
healthsciences

HEALTH RISK ASSESSMENT ON RESIDENTS EXPOSED TO CHLORINATED HYDROCARBONS CONTAMINATED IN GROUNDWATER OF A HAZARDOUS WASTE SITE

Lukas Jyuhn-Hsiarn Lee, Chang-Chuan Chan, Chih-Wen Chung

Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Taipei, Taiwan

Yee-Chung Ma, Gan-Shuh Wang

Institute of Environmental Health, College of Public Health, National Taiwan University, Taipei, Taiwan

Jung-Der Wang

Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, and Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

We conducted this study to estimate residents' chronic hazard and carcinogenic risk in a groundwater-contaminated community after on-site remediation in Taiwan during 1999–2000. We followed guidelines for assessing hazardous waste sites of the U.S. Environmental Protection Agency (EPA) and used empirically measured contaminant levels and exposure parameters to perform health risk assessment on seven chlorinated hydrocarbons. We measured groundwater concentrations of vinyl chloride, tetrachloroethylene, trichloroethylene, 1,1-dichloroethylene, 1,1,1-trichloroethane, cis-1,2-dichloroethylene, and 1,1-dichloroethane in 49 off-site residential wells by gas chromatography/mass spectrometry. Exposure parameters were mainly derived from our field survey of 382 residents, and partially from U.S. EPA default values. Total exposure dose estimation included routes of inhalation during showering and dermal absorption of showers and other activities involved with hand–water contacts. The ingestion route of water was not included because most residents drank boiled water with negligible contaminants. We calculated a hazard index (HI) for all seven chlorinated hydrocarbons and carcinogenic risks for known human carcinogen of vinyl chloride and probable human carcinogens of tetrachloroethylene and trichloroethylene, which had the same target organ, the liver. The HI values for reasonable maximal exposure (RME) and average exposure were 14.3 and 0.2, respectively. The cancer risks based on RME and average exposure (in parentheses) for vinyl chloride, tetrachloroethylene, and trichloroethylene were 8.4×10^{-6} (7.3×10^{-9}), 1.9×10^{-4} (1.3×10^{-7}), and 1.4×10^{-4} (1.2×10^{-6}), respectively. We applied Monte Carlo simulations to the sensitivity analysis, which showed that the contaminant levels, exposure duration, and time for showers were major determinants of health risks. We concluded that the contaminated groundwater was still unsafe for use even after the contaminated site underwent remediation by extraction and treatment in 1997.

Lukas J.-H. Lee was a recipient of an NHRI MD-PhD and DDS-PhD predoctoral fellowship (RE89M003). This study was supported in part by the Taoyuan Environmental Protection Bureau, Taiwan (TYEPB-1999-3-RCA-1), and the National Science Council of the Executive Yuan, Republic of China (NSC90–2320–B–002–127–M56).

Address correspondence to Professor Jung-Der Wang, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health, No. 1, Section 1, Jen-Ai Road, Taipei, Taiwan 100. E-mail: jdwang@ha.mc.ntu.edu.tw

95

Uncontrolled hazardous waste sites have emerged as a major environmental and public health concern in many countries. The Taiwan Environmental Protection Administration (EPA) has identified more than 160 hazardous waste sites (Taiwan EPA, 1999). In 1994, a hazardous waste site contaminated by a former factory involved in the manufacturing of electronic appliances was found in Taoyuan City, Taiwan (designated as the R factory). The factory was built and in operation between 1970 and 1992. Previous site investigations revealed that on-site soils and groundwater in the factory were contaminated by about 12 different chlorinated hydrocarbons for more than 10 yr (Bechtel, 1995; Target, 1995). Eight of them were also found in the off-site groundwater of the downstream area, namely, 1,1-dichloroethane (1,1-DCA), 1,2-dichloroethane (1,2-DCA), 1,1-dichloroethylene (1,1-DCE), *cis*-1,2-dichloroethylene (*cis*-1,2-DCE), 1,1,1-trichloroethane (1,1,1-TCA), tetrachloroethylene (PCE), trichloroethylene (TCE), and vinyl chloride (VC) (ITRI, 1994; Geomatrix, 1995). The highest contaminant level in an off-site residential well was 4800 μg/L for PCE, which was adjacent to the factory's source area with soil concentration up to 1100 mg/kg of PCE (Geomatrix, 1995; Bechtel, 1995). The Taiwan EPA declared the R factory a hazardous waste site in 1994 and requested remediation action on the contaminated soils and groundwater within the factory during 1996–1998 (Taiwan EPA, 1994–1997).

An extraction and treatment system for restoring contaminated groundwater had been operated for 6 mo in 1997 and failed to meet the requirements of World Health Organization (WHO) drinking-water guidelines (Geomatrix, 1998). There are about 10,000 residents currently living in the village downstream of the R factory. Many residents living in the vicinity of the factory relied mainly on locally extracted groundwater from residential wells as their primary source of domestic water supply until 1994. Some of them still continued to use these wells for showering, washing vegetables and dishes, or other cleaning activities, even though tap water was supplied. Concerned about these residents' potential health risks from chronic exposures to the contaminated groundwater, we initiated a comprehensive study entitled "Epidemiological Study and Health Risk Assessment for Residents Living Near a Contaminated Site Polluted by Volatile Chlorinated Compounds" during 1999–2000. This study included measurements of well waters, toxicological studies with animal models, epidemiological investigations, and health risk assessment for chlorinated hydrocarbons. We present here only part of the risk assessment. We demonstrate that a well-planned and carefully carried-out risk assessment can help evaluate potential health problems for a contaminated site and identify important exposure parameters for risk management.

METHODS

We conducted this site-specific risk assessment by following the detailed guidance for developing risk information at hazardous waste sites published

by the U.S. Environmental Protection Agency (U.S. EPA, 1989, 1998a), which included the following processes.

Hazard Identification of Contaminants in Groundwater

The hazard identification was mainly based on the considerations of contaminants' toxicity, environmental persistence, and concentrations. Chlorinated hydrocarbons with the characteristics of more toxic, persistent, mobile, or higher concentrations were our top choices of target chemicals of concern. In addition, we also considered degradation products from the chemicals used in the R factory as our target pollutants because many contaminants had been present for more than 10 yr (Bechtel, 1995). For example, PCE can lead to the production of seven chlorinated hydrocarbons, including TCE, *cis/trans*-1,2-DCE, 1,2-DCA, 1,1-DCE, 1,1-DCA, and VC. And 1,1,1-TCA can form 1,1-DCA, 1,1-DCE, and subsequently VC through anaerobic reductive dehalogenation (Sims et al., 1991). Although all of these chemicals can be determined by our analytical methods, described later, we only conducted quantitative risk assessment on the chemicals that exceeded the maximum contaminant levels (MCLs) of the U.S. EPA (1999). This practice was in line with the U.S. EPA's recommendations in the Risk Assessment Guidance for Superfund (RAGS) (U.S. EPA, 1989). Moreover, these chemicals' toxicological endpoints and target organs were obtained by reviewing epidemiologic studies and animal bioassays on these chlorinated solvents from the literature, such as the TOMES database (Micromedex, 1998), the Agency for Toxic Substances and Disease Registry Toxicological Profiles (ATSDR, 2000), Medline databases, etc. In order to perform quantitative risk assessments on noncarcinogenic health effects, we reviewed systemic toxicities, including hepatotoxicity, nephrotoxicity, and central nervous system depression, which resulted from chronic exposure to these chlorinated solvents. For conducting quantitative carcinogenic risk assessment, we selected only chemicals classified by the International Agency for Research on Cancer (IARC) as Group 1 or 2A (IARC, 1995). We summarized carcinogenic risks across chemicals that affected the liver as their major target organ based on animal studies (U.S. EPA, 2001a; Rhomberg, 2000).

Exposure Assessment

Groundwater Sampling and Analysis We conducted groundwater sampling from off-site residential wells that were still in use for domestic purposes. According to the local groundwater hydrogeology, the off-site groundwater flow direction was generally toward the north and northeast in the first aquifer (Geomatrix, 1998). Residential wells in the nearby communities were identified by a door-to-door survey. The wells were located from about 50 m up to 1 km away from the factory. For the downstream wells to the north of the factory, we collected a total of 69 samples from 44 wells with 1 sample per well for 32 wells and 2 to 3 samples per well for the other 12 wells. For the upstream community, we collected two groundwater samples of water from two wells to the south of the factory and

another three samples from three wells to the west of the factory. In total, we had 74 groundwater samples to describe environmental concentrations of chlorinated hydrocarbons surrounding the hazardous site.

We followed the standard procedures of sampling groundwater. In brief, water in the wells was drawn directly from the wells with a bailer and then stored in 30-ml brown bottles containing 30 mg preadded ascorbic acid. The bailer was washed with the well water twice before each collection. Each sampling bottle was filled completely and sealed immediately to ensure water samples without bubbles. All water samples were stored at 4°C before analysis, and the analytical work was completed within 2 wk after sampling.

Nineteen chlorinated volatile organic compounds (VOCs) were measured in this study, including VC, PCE, TCE, 1,1-DCE, *cis/trans*-1,2-DCE, 1,1,1-TCA, 1,1-DCA, 1,2-DCA, chloroethane, trichlorofluoromethane, methylene chloride, chloroform, benzene, bromodichloromethane, toluene, 1,1,2-trichloroethane, chlorobenzene, and 1,1,1,2-tetrachloroethane. The VOC concentrations were determined by using a method modified from U.S. EPA Method 524.2 (U.S. EPA, 1992a). Briefly, a purge and trap device (Tekmar 3000) was used to collect the analytes, which were subsequently analyzed by a gas chromatograph/mass spectrometer (HP6890 and HP5972, Hewlett Packard, USA) equipped with an RTX-Volatiles capillary column (60 m × 0.32 mm × 1.5 μm). Calibration was performed by the internal standard method using 50 μg/L fluorobenzene and 4-bromofluorobenzene in each sample for quantification. The detection limit of each VOC was calculated by 7 different analyses of the VOC standards at 0.4 μg/L. Based on threefold the standard deviation of the mean standard concentration, the detection limits for these 19 VOCs ranged from 0.01 to 0.1 μg/L. Nondetected (ND) values were replaced by half of their detection limits when calculating the geometric and arithmetic mean of concentrations. The reproducibility was evaluated with nine sets of groundwater samples containing VOCs and was calculated from two duplicate analyses. The relative mean deviation of these duplicates was within 20% for most of the target VOCs.

Water Exposure Parameters We used empirical data from our field survey to obtain exposure parameters for a more realistic risk prediction. Residents in the nearby communities were invited to participate in a complete physical examination including a detailed structured questionnaire. We collected data on body weight, height, exposure-related activities such as drinking water, showering, food and cloth washing, etc., as well as exposure duration and time. However, for ventilation rate, chemical-specific permeability coefficient, and average time, which were not collected in our study, the default values recommended by the U.S. EPA were adopted (U.S. EPA, 1992b, 1997a).

We considered all the potential exposure routes, including ingestion, inhalation, and dermal absorption, in the exposure assessment. First, we conducted an experiment to measure VOCs in boiling water to examine

whether ingestion of boiled water was a potential exposure pathway because the survey showed that 99% of the residents drank boiled water. Second, the inhalation exposure from volatilization in showers was estimated by using the model developed by Little (1992) and the physical characteristics of shower system in Taiwan reported by Kuo et al. (1998). The parameters of such shower rooms were 1.2 m^3 of air in the shower, water flow rate of 5 L/min, air flow rate of 50 L/min, air exchange rate of 2.5 times/h, water temperature of 44°C, and shower-head height of 1.8 m. Based on two-resistance theory, we can obtain overall mass-transfer coefficients with a liquid-phase basis ($K_{OL}A$) for PCE and TCE that were 7.2 L/min, and 9.2 L/min, respectively (Little, 1992). The values of $K_{OL}A$ for the other 5 chlorinated hydrocarbons were assumed to be 9.2 L/min because experimental data were not available. The values of absorption efficiency of chlorinated hydrocarbons in the alveoli were assumed around 50%, because TCE and 1,1,1-TCA were estimated to have inhalation absorption efficiency in the range of 30–78% (Pleil et al., 1998; Byard, 1989). Third, the dose from dermal absorption was estimated for showering and hand exposure-related activities, such as washing vegetables, washing dishes, and doing laundry by hand. The fractions of skin in contact with water were assumed to be 80% for showering, and 8% for washing activities involved with hand exposure, respectively. The chemical-specific permeability coefficients were derived from a report of dermal exposure assessment of the U.S. EPA (1992b).

The site-specific exposure parameters used in our study were obtained as follows: The exposure duration was defined as the period in years between the year of initial exposures after 1970 and the year at the end of exposures. The exposure time during showering was defined as the minutes per day that an individual spent for a shower using groundwater. A default value of 20 min/d was assumed for the exposure time of hand exposure-related activities. The skin surface area was estimated by using a formula (surface area = $0.0239H^{0.417}W^{0.517}$) proposed by the U.S. EPA (1997a) and the heights (H) and weights (W) of 382 individuals measured by the registered nurses.

Our risk assessments were based on two exposure scenarios: the reasonable maximum exposure (RME) as a precautionary estimate, and the average exposure proposed by the U.S. EPA (1989, 1998a, 2001b). For RME, we used the upper-bound estimate of each input variable, which were the 95% upper confidence limit of the arithmetic mean for chemical concentrations and the 95th percentiles of exposure parameters for their corresponding distributions. For average exposure, we used the geometric means of contaminant concentrations and the arithmetic means of exposure parameters to estimate health risks.

Chronic daily intakes were calculated both for inhalation while showering and for dermal absorption from showers and hand exposure-related activities. Lifetime intake was defined as the exposure dose per unit body

weight and per unit time, averaged over an assumed lifetime of 70 yr. The equations for calculating chronic daily intakes are displayed as follows:

Dermal contact:

$$\text{Chronic daily intake (mg/kg-d)} = \frac{C \times SA \times F \times PC \times ET \times EF \times ED \times CF}{BW \times AT}$$

(U.S. EPA, 1989, 1997a), where C is chemical concentration in groundwater (mg/L), SA skin surface area (m^2), F fraction of skin in contact with water (unitless), PC Permeability coefficient (cm/h), ET exposure time (h/d), EF exposure frequency (d/yr), ED exposure duration (yr), and AT average time (d) using lifetime intake for carcinogen = 70 × 365 and chronic intake for noncarcinogen = ED × 365, BW body weight (kg), and CF conversion factor (10^{-1} L/m^3).

Inhalation:

$$\text{Chronic daily intake (mg/kg-d)} = \frac{C_{air} \times VR \times AE \times ET \times EF \times ED \times CF}{BW \times AT}$$

(Kuo et al., 1998; U.S. EPA, 1989, 1997a), where C_{air} is concentration in air (mg/L), VR ventilation rate (m^3/h), AE absorption efficiency in alveoli (unitless) = 50%, ET exposure time (h/d), EF exposure frequency (d/yr), ED exposure duration (yr), AT average time (d) using lifetime intake for carcinogen = 70 × 365 and chronic intake for noncarcinogen = ED × 365, BW body weight (kg), and CF conversion factor (10^3 L/m^3).

Dose Response/Risk Characterization

Chronic hazards and carcinogenic risks were characterized by incorporating exposure assessment and toxicity values. Hazard index (HI) was used as an indicator of noncarcinogenic risk, which summarized the ratios of the chronic exposure doses to the chemical-specific reference dose (RfD) values. Carcinogenic risk was incremental probability of getting cancer over a lifetime, which was calculated from lifetime intake multiplied by slope factor for individual chemical carcinogen. The primary sources of the toxicity values, including RfD and slope factors, were from the U.S. EPA databases. We followed a hierarchy of preferred sources, namely, Integrated Risk Information System (IRIS), Health Effects Assessment Summary Tables (HEAST), and other provisional values that were available in the online database of the Risk Assessment Information System (ORNL, 2001). As weighting evidence of carcinogenic potential (U.S. EPA, 1996), we assessed carcinogenic risk for human carcinogen of VC and probable human carcinogens of PCE and TCE. The total organ HI was calculated by summarizing over all chlorinated hydrocarbons assuming additive effects of multiple chemicals (U.S. EPA, 1989).

Uncertainty/Sensitivity Analysis

Monte Carlo analysis was used with the risk calculations to incorporate individual input distributions of exposure variables to produce probability distributions of the health risk estimates and to assess uncertainties in the risk assessment (U.S. EPA, 1997b). The simulations were performed with Crystal Ball (Decisioneering, 2000) in conjunction with the spreadsheet program Microsoft Excel 2000. Health risk was calculated through 5000 iterations using randomly selected values derived from individual probability distributions of the corresponding exposure model parameters. The simulation model was also used for sensitivity analysis in which the relative importance of each input variable was assessed by calculating its contribution to variance.

RESULTS

The hazard identification step identified seven chlorinated hydrocarbons, which met our selection criteria, as target pollutants for health risk assessment. Table 1 summarizes the toxicological characteristics, health concerns, and groundwater concentrations of VC, PCE, TCE, 1,1-DCE, 1,1,1-TCA, *cis*-1,2-DCE, and 1,1-DCA. Hepatic effects were their common noncarcinogenic chronic hazards. The three chemicals with carcinogenic effects, VC, PCE, and TCE, had the liver as their major target organ. There were wide ranges of groundwater concentrations among these seven chlorinated hydrocarbons. Geometric mean (GM) concentrations ranged from 0.03 μg/L for VC to 15.26 μg/L for TCE. The 95% upper-bound concentrations ranged from 7.61 μg/L for VC to 889.65 μg/L for PCE. There was also significant spatial variation in groundwater concentrations as shown by an example result for TCE in Figure 1. High levels of TCE above the MCL (5 μg/L) were found in 29 out of 44 wells (66%) in the downstream community. The highest concentrations of contaminants were found in the wells closest to the R factory. An excessively high TCE concentration of 192 μg/L was found even in the well located about 1 km northerly from the factory. In contrast, all 19 VOCs were either at trace or nondetected (ND) levels in the 2 upstream wells to the south of the factory.

A total of 529 adult residents aged above 15 yr participated in our field survey, including 382 persons in the downstream community and 147 from the upstream community. The exposure-related characteristics of the 382 downstream residents are summarized in Table 2. The prevalence of hepatitis B virus (HBV) carriers was 13.6%. The average body weight and skin surface area used in this study were 61 kg and 1.66 m^2, respectively, which were less than the U.S. EPA anthropometrical default values for assessing risks on adults. The average durations of key water exposure parameters were 13.7 yr of taking showers and 13.0 yr of involving hand exposure-related activities. The average time for each shower was about 13.9 min, which was less than the U.S. EPA default value. The results of residuals in water at temperatures of 4, 45, 65, 85, and 100°C and at 1 min after 100°C

TABLE 1. Concentrations and Frequency Distribution of Chemicals of Potential Concern in the 44 Downstream Residential Wells

Chemicals of potential concern	Major target organ[a]			Percentage above MCL/PRG[b]	Geometric mean (range) (μg/L)	Arithmetic mean (95% UCL)[c] (μg/L)
	IARC cancer group	Carcinogenic effect (slope factor)	Noncarcinogenic effect (RfD)			
Vinyl chloride	1	Liver	Hepatic	29.5%/31.8%	0.03 (ND[d]–72.3)	3.75 (7.61)
Tetrachloroethylene	2A	Liver	Hepatic	45.5%/45.5%	2.63 (ND–5228.3)	519.57 (889.65)
Trichloroethylene	2A	Liver/lung	Hepatic/renal	65.9%/77.3%	15.26 (ND–1790.7)	253.41 (404.68)
1,1-Dichloroethylene	3	—	Hepatic	27.3%/72.7%	1.01 (ND–1240.4)	111.41 (200.79)
1,1,1-Trichloroethane	3	—	Hepatic	11.4%/0%	0.57 (ND–1504.4)	82.68 (163.23)
cis-1,2-Dichloroethylene	—[e]	—	Hepatic/blood	15.9%/15.9%	1.16 (ND–1376.0)	92.25 (181.06)
1,1-Dichloroethane	—	—	Renal	—/0	0.61 (ND–227.9)	16.60 (31.42)

[a]Toxicity values are derived from animal bioassays based on which target organ is primarily affected.
[b]Maximum contaminant level (MCL) is the water quality standard set by U.S. EPA (1999). Region 9 Preliminary Remediation Goal (PRG) is the risk-based contaminant level in residential tap water from inhalation exposure (U.S. EPA, 2000).
[c]95% Upper confidence limit (UCL) is the upper-bound estimate of the contaminant distribution, which is the input for conservative estimation of health risk under reasonable maximal exposure (RME) assumptions.
[d]ND (nondetected) value was replaced by (½ × detection limit) as calculating the geometric/arithmetic mean.
[e]—, Not available.

for PCE, TCE, 1,1-DCE, and 1,1-DCA are shown in Figure 2. The concentrations decreased significantly as water temperatures increased. There were negligible concentrations in the water after boiling for 1 min. Based on this finding, we excluded water ingestion exposure to VOCs from our risk estimation.

Table 3 presents the results of chronic exposure doses and health risk estimates for the routes of dermal absorption and inhalation based on the RME scenarios. The overall HI values calculated from inhalation exposure were about 10-fold higher than those from dermal absorption. Inhalation exposure from showering accounted for 61% of total cancer risks. There were 4 contaminants with HI greater than 1.0, which were PCE, TCE, 1,1-DCE, and *cis*-1,2-DCE. The summation of HI over 7 contaminants was 14.3, which was around an order of magnitude greater than the acceptable level. The carcinogenic risks for VC, PCE, and TCE were 8.4×10^{-6}, 1.9×10^{-4}, and 1.4×10^{-4}, respectively. The latter two IARC Group 2A car-

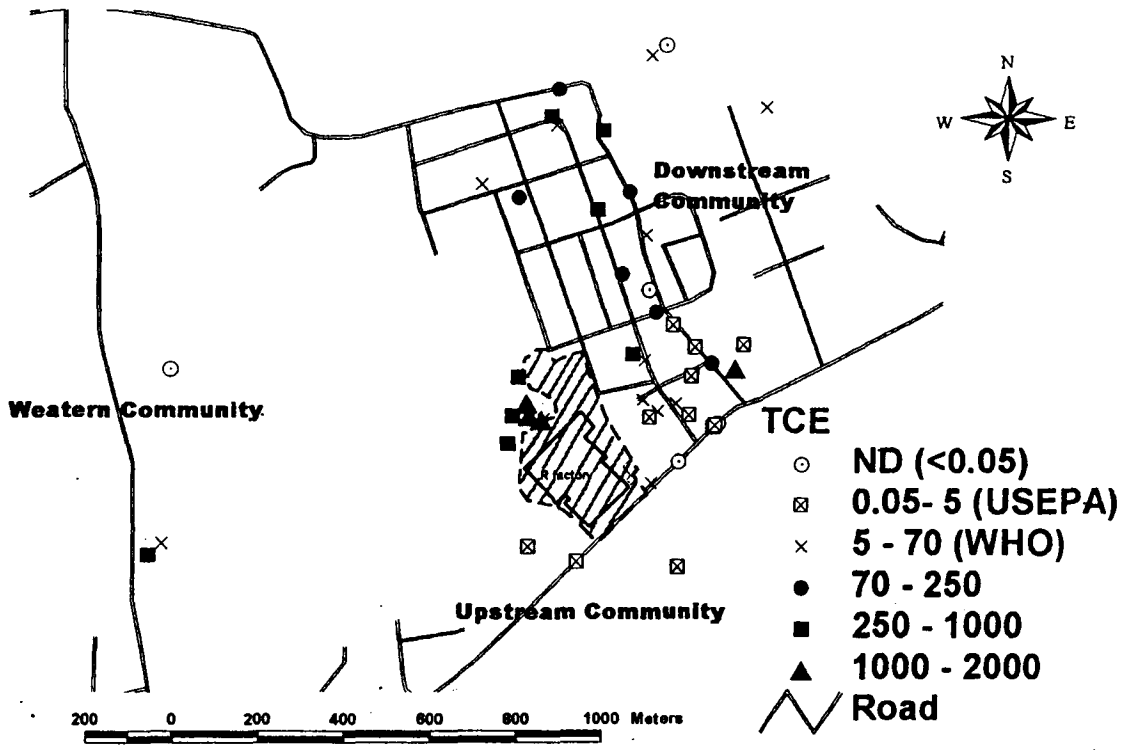


FIGURE 1. Geographic distribution of 49 residential wells near the R factory and levels of tricholoroethylene (TCE, μg/L), one of the major contaminants in the groundwater.

TABLE 2. Summary of Exposure-Related Characteristics of 382 Residents Aged Over 15 yr in the Downstream Community

Exposure-related characteristics[a]	Number	Downstream community
Gender		
Male	181	47.4%
Female	201	52.6%
Age group (yr)	382	
15–29	85	22.3%
30–49	163	42.7%
≥50	134	35.1%
Hepatitis B surface antigen positive	52	13.6%
Body weight (kg)	382	61.0 (± 10.7)
Body height (cm)	382	160.1 (± 8.6)
Skin surface area (m^2)	382	1.66 (± 0.17)
Exposure duration[b] (yr)		
For showers	336	13.7 (± 9.2)
For hand exposure-related activities	330	13.0 (± 8.8)
Exposure time during showering (min)	349	13.9 (± 6.9)

[a]Characteristics are presented in percentage for nominal variables and arithmetic mean (± standard deviation) for continuous variables.

[b]Exposure duration was defined as the period in years between the year of initial exposures after 1970 and the year at the end of exposures.

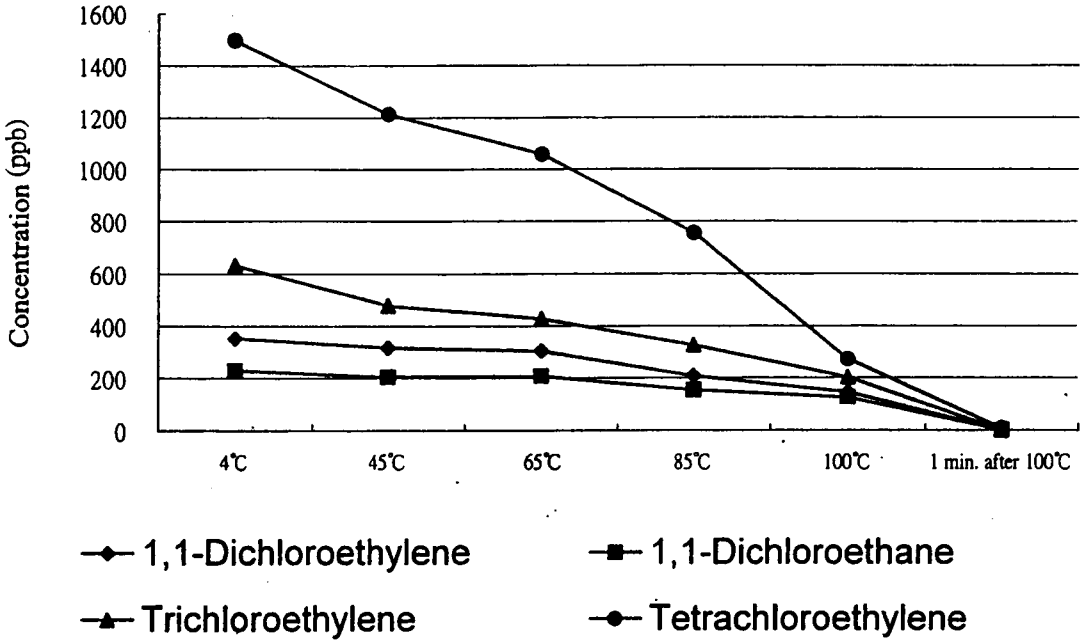


FIGURE 2. Concentrations of chlorinated hydrocarbons during the process of boiling, in an experiment on a water sample from a downstream contaminated well.

cinogens might pose cancer risks exceeding the upper limit of the acceptable range between 10^{-6} and 10^{-4} (U.S. EPA, 1990). The point estimates of health risks based on average exposure showed that HI was 0.2, and cancer risks of VC, PCE, and TCE were 7.3×10^{-9}, 1.3×10^{-7}, and 1.2×10^{-6}, respectively.

The input distributions of exposure-related variables, as well as assumed default values during Monte Carlo simulations, are summarized in Table 4. Figure 3 displays the cumulative probability distributions of simulated results and their associated sensitivity analyses for cancer risk (A) and HI (B). We found the simulated results were lognormal distributions. For cancer risk, the 95% upper-bound estimate was 7.3×10^{-5}, while the GM estimate was 2.2×10^{-6}. The sensitivity analysis showed that TCE and PCE contributed most to the variance of cancer risk estimates, while the exposure duration and time for showers accounted for another 9.9% and 8.1% of variance, respectively. For noncarcinogenic risk, the 95% upper-bound estimate was 8.9 and the GM estimate was 0.5. The variance of noncarcinogenic risk estimates was explained by TCE alone for 57.5% and exposure time of shower for 15.8%.

DISCUSSION

This is the first site-specific quantitative health risk assessment among more than 160 suspected hazardous waste sites throughout Taiwan. Based on the RME scenarios, we found that the community residents exposed to chlorinated hydrocarbons in the contaminated groundwater had an un-

TABLE 3. Calculated Health Risks, Both Noncarcinogenic and Carcinogenic, Based on Reasonable Maximal Exposure (RME)

Exposure route	Chemicals of potential concern	Noncarcinogenic effects: Chronic intake (mg/kg-d)	Reference dose (RfD) (mg/kg-d)	Source[a]	Hazard quotient	Carcinogenic effects: Lifetime intake (mg/kg-d)	Slope factor (mg/kg-d)	Source[a]	Cancer risk
Dermal absorption[b]	Vinyl chloride	6.46E–06	3.00E–03	IRIS (2000)	0.00	2.67E–06	7.20E–01	IRIS (2000)	1.92E–06
	Tetrachloroethylene	4.97E–03	1.00E–02	IRIS (1995)	0.50	2.05E–03	5.20E–02	NCEA (1995)	1.07E–04
	Trichloroethylene	7.53E–04	9.00E–04	RAP	0.84	3.11E–04	7.33E–02	NCEA (1995)	2.28E–05
	1,1-Dichloroethylene	3.74E–04	9.00E–03	IRIS (1994)	0.04				
	1,1,1-Trichloroethane	3.23E–04	1.80E–01	RAP	0.00				
	cis-1,2-Dichloroethylene	2.11E–04	1.00E–02	HEAST (1994)	0.02				
	1,1-Dichloroethane	3.25E–05	1.00E–01	HEAST (1994)	0.00				
Inhalation[c]	Vinyl chloride	1.01E–03	2.86E–02	IRIS (2000)	0.04	4.19E–04	1.54E–02	IRIS (2000)	6.45E–06
	Tetrachloroethylene	1.03E–01	1.71E–01	RAP	0.60	4.25E–02	2.00E–03	NCEA (1995)	8.50E–05
	Trichloroethylene	4.65E–02	6.00E–03	RAP[d]	7.75	1.93E–02	6.00E–03	NCEA (1995)	1.16E–04
	1,1-Dichloroethylene	2.64E–02	9.00E–03	IRIS (1994)[d]	2.93				
	1,1,1-Trichloroethane	2.06E–02	6.29E–01	RAP	0.03				
	cis-1,2-Dichloroethylene	1.54E–02	1.00E–02	HEAST (1994)[d]	1.54				
	1,1-Dichloroethane	3.11E–03	1.43E–01	HEAST (1994)	0.02				
Health risk				Hazard index	14.3			VC (IARC 1)	8.4E–06
								PCE (IARC 2A)	1.9E–04
								TCE (IARC 2A)	1.4E–04

[a]Hierarchy of toxicity data sources was listed in the preferred order as follows:

1. U.S. EPA Integrated Risk Information System (IRIS) online database.
2. U.S. EPA Health Effects Assessment Summary Tables (HEAST).
3. National Center for Environmental Assessment (NCEA)—provisional toxicity values developed by NCEA (U.S. EPA, 1995a, 1995b).
4. The Risk Assessment Program (RAP) has contacted Superfund and has been given provisional values that should be used for DOE-ORR projects. This value should be clearly documented as provisional. For other projects, the Superfund Health Risk Technical Support Center should be contacted directly at (513)569-7300 (ORNL, 2001).

[b]The dermal chronic RfD and dermal slope factor are derived using the methods provided in U.S. EPA (1989).

[c]The inhalation chronic RfDs are derived from the inhalation chronic RfCs. The RfDs are calculated as shown in the following equation: [RfC (mg/m^3) × 20 m^3/d]/70 kg = RfD (mg/kg-d). The inhalation slope factors are derived from the inhalation unit risks. The inhalation slope factors are calculated as shown in the following equation taken from *Supplemental Guidance to RAGS: Region 4 Bulletins Human Health Risk Assessment,* November 1995: unit risk $(\mu g/m^3)^{-1}$ × 70 kg × (20 $m^3/d)^{-1}$ × 1000 μg/mg = SFi $(mg/kg\text{-}d)^{-1}$.

[d]Route extrapolation: provisional values of inhalation RfDs for TCE, 1,1-DCE, and *cis*-1,2-DCE are assumed equal to their respective oral RfDs.

TABLE 4. Input Variables and Their Corresponding Distributions Used in the Probability Risk Calculations with Monte Carlo Simulations

Input variable	Unit	RME parameter	Best-fitted distribution	Mean	SD	Minimum	Maximum	Likeliest	
Site-specific parameter									
Body weight	kg	60.9	Lognormal	60.9	10.5	40.0	95.0		
Skin surface area	m^2	1.66	Lognormal	1.66	0.17	1.30	2.14		
Exposure time (shower)	min/d	30	Triangular			1.1	41.7	10.0	
Exposure duration (shower)	yr	29	Lognormal	14.69	15.25	1.0	29.0		
Exposure duration (hand exposure)	yr	27	Lognormal	13.87	13.93	0	29		
Default assumption									
Ventilation rate	m^3/h	0.84	0.7						(Layton, 1993)
Fraction of skin in contact with water	unitless	80% (Showering) 8% (Hand exposure)							(Assumed)
Exposure time (hand exposure)	min/d	20							(Assumed)
Permeability coefficient	cm/h	Chemical-specific value							U.S. EPA (1992b)
Average time	d	70 × 365 (carcinogen) ED × 365 (noncarcinogen)	70 × 365 (carcinogen) ED × 365 (noncarcinogen)						U.S. EPA (1989)

acceptable cancer risk. The total organ HI also indicated a potential health hazard. These RME risk levels were considered the high-end values on which remedial decision would be based, and provided the basis for developing protective exposure levels for future use as recommended by the U.S. EPA (2001b). Moreover, average risk estimates indicated a marginally significant cancer risk. Therefore, we must examine carefully the uncertainties involved in the processes of risk assessment before making any recommendation.

From our risk assessment, individual contaminants, including PCE, TCE, 1,1-DCE, and *cis*-1,2-DCE, posed an unacceptable chronic hazard to the liver, and PCE and TCE were probable human carcinogens involving the liver as the most sensitive tumor site. The potential health risks associated with the complex mixtures of chlorinated hydrocarbons might be greater than those of a single chemical because synergistic interactions may occur when mixtures are encountered (Seed et al., 1995). Moreover, a high HBV carrier rate of 15–20% was reported in the general population of Taiwan

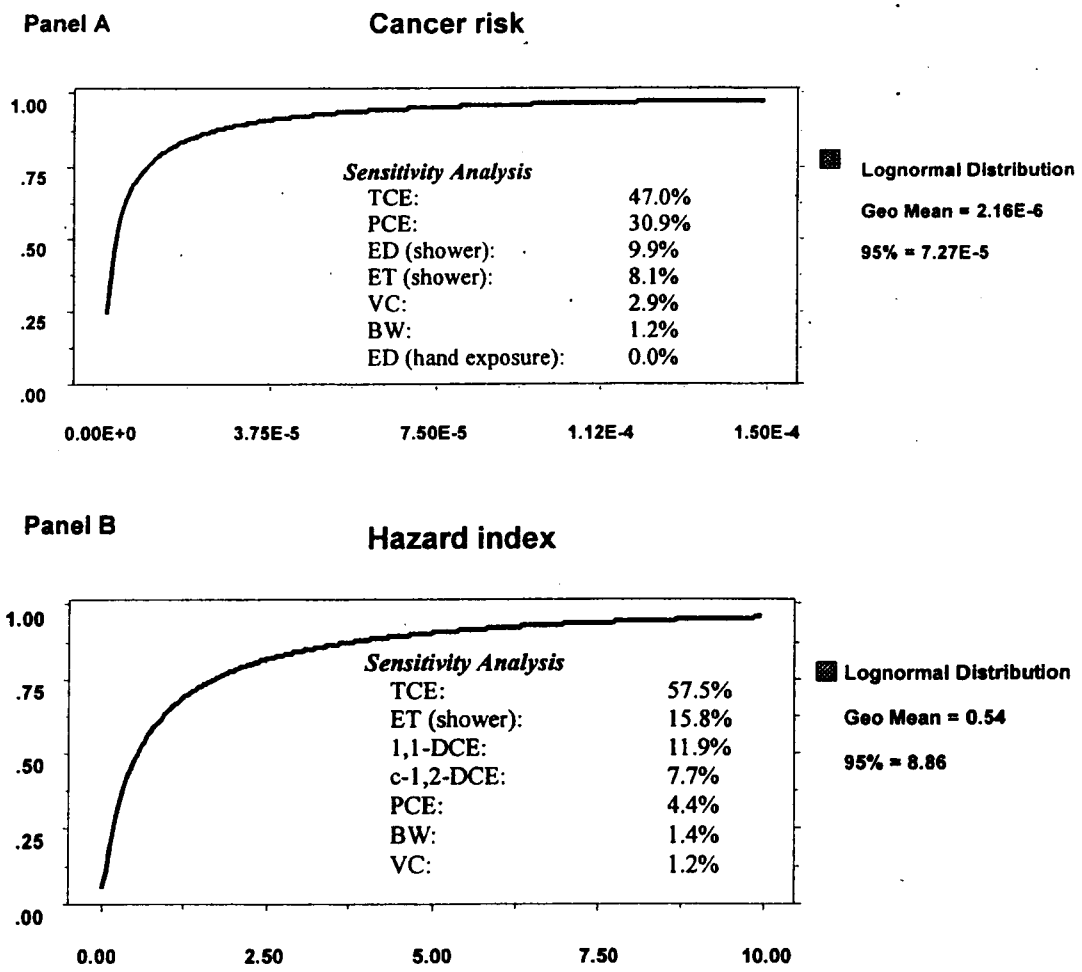


FIGURE 3. Cumulative probability distributions of health risks and associated sensitivity analysis using Monte Carlo simulations and assuming additive effects.

(Chen & Sung, 1978; Sung et al., 1984). The physical examination also disclosed a similar prevalence (13.6%) of HBV carriers among the downstream residents, who might be more susceptible to hepatic carcinogens such as aflatoxin (Wang et al., 1996). Therefore, the lack of a proper synergistic assessment model between these chlorinated solvents and chronic hepatitis B infection (Du & Wang, 1998) might further aggravate the magnitude of underestimation of risk.

Inhalation exposure from showering contributed most to health risk estimates in our study. Traditionally, ingestion of drinking water was considered a primary route of exposure to contaminated water (McKone, 1989). However, our empirical data indicated that the route of water ingestion was negligible. Moreover, research has shown that VOCs inhaled from tap water may exceed exposure via direct ingestion (McKone & Knezovich, 1991). Since we did not exhaustively include all the pathways of other indoor air exposure, such as boiling water, cooking, dishwashing, toilets, etc., the calculated health risk might be likely to be an underestimate.

As the sensitivity analysis revealed, the environmental concentrations and exposure duration for showers were the two key contributors to the total variances in the exposure modeling. It also indicated that TCE was the most important pollutant in determining health risk at this site, which could be used as an indicator for remediation. However, uncertainties associated with assumptions and scientific knowledge in our risk characterization must also be addressed. One limitation in our estimation of inhalation doses was that the $K_{OL}A$ values for TCE and PCE were obtained from experimental data (Little, 1992), but those for the other five chemicals were assumed. We performed sensitivity analysis to assess the degree of impact from the assumption of $K_{OL}A$ values. The results showed that the estimates of cancer risk and HI increased by less than 0.4%, and 5%, respectively, as the $K_{OL}A$ values for the other five chemicals were all increased up to 10-fold. Therefore, the magnitude of impact from $K_{OL}As$ of these chemicals on health risk estimates was relatively small and it would not influence our conclusion. For dermal exposure, the exposure duration of doing laundry by hand was difficult to define because most residents could not recall exactly how much time they spent on doing laundry by hand. By performing sensitivity analysis, we found that dermal absorption from hand exposure-related activities accounted for less than 5% of cancer risk estimates even if an assumed 40-min exposure time was used. Moreover, this exposure duration contributed less than 0.1% of the total variance of cancer risk, as shown in Figure 3A. Thus, the assumed 20 min did not significantly bias the risk estimates. Due to the scope of this study, the target organ doses were not estimated in our study using physiologically based pharmacokinetic (PBPK) models (Roy et al., 1996; Bogen & Gold, 1997). The results of this study must be interpreted with some caution. Further studies are warranted to provide toxicity values based on PBPK models for any refined risk assessment.

Our results indicated that chlorinated hydrocarbons in groundwater may tend to be persistent pollution for decades due to their physical characteristics of dense nonaqueous-phase liquids (DNAPLs) (Huling & Weaver, 1991), and vinyl chloride, a more toxic and persistent chemical under anaerobic conditions, may be produced from degradation of PCE and TCE. The current levels of contaminants, especially PCE and TCE, were shown to be much higher than the water quality standards set by the U.S. EPA (1999). However, most people in the downstream community were still unaware of potential health effects of the groundwater contamination. Some of them had consistently used the contaminated groundwater for domestic water supply until 2000 because of economic incentives. Therefore, risk management is urgently needed to educate the residents, based on our risk assessment.

CONCLUSION

According to our risk assessment, increased chronic and carcinogenic risks on the liver may still be a potential public health concern for people living downstream, especially for sensitive subpopulations, such as HBV carriers. We recommend that all the community people should discontinue using the contaminated groundwater for any purpose. The environmental health advisories have to continue the medical surveillance and follow-up on the community residents. Further research will be needed to address the actual health impact on the residential population.

REFERENCES

Agency for Toxic Substances and Disease Registry. 2000. *Hazardous Substance Release and Health Effects Database* (HazDat Database). http://www.atsdr.cdc.gov/hazdat.html, cited 13 July.

Bechtel Environmental, Inc. 1995. *1990 Preliminary site investigation report. Taoyuan Site, Taiwan, Republic of China.* San Francisco, CA: Bechtel Environmental, Inc.

Bogen, K. T., and Gold, L. S. 1997. Trichloroethylene cancer risk: Simplified calculation of PBPK-Based MCLs for cytotoxic end points. *Regul. Toxicol. Pharmacol.* 25:26–42.

Byard, J. L. 1989. Hazard assessment of 1, 1, 1 -trichloroethane in groundwater. In *Risk assessment of environmental and human health hazards: a textbook of case studies,* ed. D. J. Paustenbach, pp. 331–344. New York: John Wiley & Sons.

Chen, D. S., and Sung, J. L. 1978. Hepatitis B virus infection and chronic liver diseases in Taiwan. *Acta Hepatogastroenterol.* 25:423–430.

Decisioneering, Inc. 2000. *Crystal Ball 2000 user manual.* Denver, CO: Decisioneering, Inc.

Du, C. L., and Wang, J. D. 1998. Increased morbidity odds ratio of primary liver cancer and cirrhosis of the liver among vinyl chloride monomer workers. *Occup. Environ. Med.* 55:528–532.

Geomatrix Consultants, Inc. 1995. *Revised health assessment. Taoyuan and Chupei sites, Taiwan, Republic of China.* San Francisco, CA: Geomatrix Consultants, Inc.

Geomatrix Consultants, Inc. 1998. *Groundwater remediation technical practicability evaluation report, Taoyuan site, Taiwan.* San Francisco, CA: Geomatrix Consultants, Inc.

Huling, S. G., and Weaver, J. W. 1991. *Dense nonaqueous phase liquids.* EPA/540/4-91/002. Ada, OK: Robert S. Kerr Environmental Research Laboratory, U.S. EPA.

International Agency for Research on Cancer. 1995. Dry cleaning, some chlorinated solvents and other industrial chemicals. *IARC Monogr. Eval. Carcinogen. Risks Hum.* 63.

Industrial Technology Research Institute (Taiwan). 1994. *Project report of sampling and analysis of residential wells near the Taoyuan site* [in Chinese]. Hsinchu, Taiwan: Union Chemical Laboratory, ITRI.

Kuo, H. W., Chiang, T. F., Lo, I. I., Lai, J. S., Chan, C. C., and Wang, J. D. 1998. Estimates of cancer risk from chloroform exposure during showering in Taiwan. *Sci. Total Environ.* 218:1–7.

Layton, D. W. 1993. Metabolically consistent breathing rates for use in dose assessments. *Health Phys.* 64:23–36.

Little, J. C. 1992. Applying the two-resistance to contaminant volatilization in shower. *Environ. Sci. Technol.* 26:1341–1349.

McKone, T. E. 1989. Household exposure models. *Toxicol. Lett.* 49:321–339.

McKone, T. E., and Knezovich, J. P. 1991. The transfer of trichloroethylene (TCE) from a shower to indoor air: Experimental measurements and their implications. *J. Air Waste Manage. Assoc.* 41: 832–837.

Micromedex, Inc. 1998. *Toxicology, Occupational Medicine & Environmental Series (TOMES Plus System) CD-ROM database.* Greenwood, CO: Micromedex, Inc.

Oak Ridge National Laboratory. 2001. *Risk assessment toxicity values in the Risk Assessment Information System (RAIS) database.* http://risk.lsd.ornl.gov/tox/tox_values.shtml, cited 23 July.

Pleil, J. D., Fisher, J. W., and Lindstrom, A. B. 1998. Trichloroethylene level in human blood and exhaled breath from controlled inhalation exposure. *Environ. Health Perspect.* 106:573–580.

Rhomberg, L. R. 2000. Dose-response analyses of the carcinogenic effects of trichloroethylene in experimental animals. *Environ. Health Perspect.* 108(suppl. 2):343–358.

Roy, A., Weisel, C. P., Lioy, P. J., and Geogopoulos, P. G. 1996. A distribution parameter physiologically-based pharmacokinetic model for dermal and inhalation exposure to volatile organic compounds. *Risk Anal.* 16:147–160.

Seed, J., Brown, R. P., Olin, S. S., and Foran, J. A. 1995. Chemical mixtures: Current risk assessment methodologies and future directions. *Regul. Toxicol. Pharmacol.* 22:76–94.

Sims, J. L., Suflita, J. M., and Russell, H. H. 1991. *Reductive dehalogenation of organic contaminants in soil and ground water.* EPA/540/4-90/054. Ada, OK: Robert S. Kerr Environmental Research Laboratory, U.S. Environmental Protection Agency (EPA).

Sung, J. L., Chen, D. S., Lai, M. Y., Yu, J. Y., Wang, T. H., Wang, C. Y., Lee, C. Y., Chen, S. H., and Ko, T. M. 1984. Epidemiological study on hepatitis B virus infection in Taiwan. *Chin. J. Gastroenterol.* 1:1–9.

Taiwan Environmental Protection Administration. 1994–1997. *The 1st–10th meeting reports of the investigation committee on groundwater pollution* [in Chinese]. Taipei, Taiwan: Environmental Protection Administration, Executive Yuan, Republic of China.

Taiwan Environmental Protection Administration. 1999. *Environmental Policy Monthly* II(11). May http://www.epa.gov.tw/english/epm/issue9905.htm, cited 21 August 2001.

Target Environmental Services, Inc. 1995. *Soil gas/perched groundwater/soil survey, Taoyuan site, Taiwan.* Columbia, MD: Target Environmental Services, Inc.

U.S. Environmental Protection Agency. 1989. *Risk assessment guidance for Superfund (RAGS), Vol. I, Human health evaluation manual (Part A)—Interim final.* EPA/540/1-89/002. Washington, DC: U.S. EPA.

U.S. Environmental Protection Agency. 1990. National oil and hazardous substances pollution contingency plan. Final rule. *Fed Reg.* 8:8670–8852.

U.S. Environmental Protection Agency. 1992a. *Measurement of purgeable organic compounds in water by capillary column gas chromatography/mass spectrometry.* Revision 4.0, Method 524. Cincinnati: Environmental Monitoring System Laboratory.

U.S. Environmental Protection Agency. 1992b. *Dermal exposure assessment: principles and applications—Interim report.* EPA/600/8-91/011B. Washington, DC: U.S. EPA.

U.S. Environmental Protection Agency. 1995a. *Risk assessment issue paper for: Carcinogenicity information for trichloroethylene (TCE)* (CASRN 79-01-6). Cincinnati, OH: Superfund Technical Support Center, National Center for Environmental Assessment.

U.S. Environmental Protection Agency. 1995b. *Risk assessment issue paper for: Carcinogenicity information for tetrachloroethylene (perchloroethylene, PERC)* (CASRN 127-18-4). Cincinnati, OH: Superfund Technical Support Center, National Center for Environmental Assessment.

U.S. Environmental Protection Agency. 1996. *Proposed guidelines for carcinogen risk assessment.* EPA/600/P-92/003C. Washington, DC: U.S. EPA. http://www.epa.gov/ORD/WebPubs/carcinogen, cited 5 June 1999.

U.S. Environmental Protection Agency. 1997a. *Exposure factor handbook, Vol. I, General factors.* EPA/600/P-95/002Fa. Washington, DC: U.S. EPA.

U.S. Environmental Protection Agency. 1997b. *Guiding principles for Monte Carlo analysis.* EPA/630/R-97/001. Washington, DC: U.S. EPA. http://www.epa.gov/ncea/monteabs.htm, cited 6 July 2000.

U.S. Environmental Protection Agency. 1998a. *Risk assessment guidance for Superfund (RAGS), Vol. I, Human health evaluation manual (Part D, Standardized planning, reporting, and review of superfund risk assessments)—Interim.* Publication 9285.7-01D. Washington, DC: U.S. EPA. http://www.epa.gov/superfund/programs/risk/ragsd/index.htm, cited 5 August 2000.

U.S. Environmental Protection Agency. 1999. *National primary drinking water regulations.* EPA/810/F-94/001. http://www.epa.gov/safewater/consumer/mcl:pdf, cited 15 February.

U.S. Environmental Protection Agency. 2000. *Region 9 preliminary remediation goals (PRGs) tables.* http://www.epa.gov/region09/waste/sfund/prg/files/PRG2000.xlw, cited 23 July 2001.

U.S. Environmental Protection Agency. 2001a. *Integrated risk information system (IRIS) online database.* http://www.epa.gov/iris, cited 19 July.

U.S. Environmental Protection Agency. 2001b. *Region 4 human health risk assessment bulletins—supplement to RAGS.* http://www.epa.gov/region04/waste/ots/healtbul.htm, cited 26 July.

Wang, L. Y., Hatch, M., Chen, C. J., Levin, B., You, S. L., Lu, S. N., Wu, M. H., Wu, W. P., Wang, L. W., Wang, Q., Huang, G. T., Yang, P. M., Lee, H. S., and Santella, R. M. 1996. Aflatoxin exposure and risk of hepatocellular carcinoma in Taiwan. *Int. J. Cancer* 67:620–625.

原 著

公元1980至1997年本國衛生署死因資料庫準確性之確認與補正

謝功毅[1] 陳保中[1,2,3] 王榮德[1,2,3,*]

GONG-YIH HSIEH[1], PAU-CHUNG CHEN[1,2,3], JUNG-DER WANG[1,2,3,*]

[1] 國立台灣大學公共衛生學院職業醫學與工業衛生研究所，台北市仁愛路一段一號
Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University. No. 1, Jen-Ai Rd., Sec. 1, Taipei, Taiwan, R.O.C.

[2] 國立台灣大學公共衛生學院職業病防治示範中心
Center for Research of Environmental and Occupational Diseases (CREOD), College of Public Health, National Taiwan University .

[3] 國立台灣大學醫學院附設醫院內科部
Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan.

*通訊作者Correspondence author. E-mail: jdwang@ha.mc.ntu.edu.tw

目標：目前國內將死亡診斷書建立成死因資料庫有衛生署及內政部兩個單位。本研究之目的係使用內政部死因資料檔中正確及完整部份來補正衛生署自公元1985至1997年死亡之身分證字號及户政資料，同時填補衛生署自公元1980至1997年教育及村里兩變項及衛生署自公元1980至1984年之身分證字號，以作爲未來相關研究之參考與應用。**方法**：首先將兩死因資料庫內身分證字號及户政資料皆相同之個案，先填補衛生署死因資料庫之教育及村里之資料，然後把不可連結之部分以身分證字號或户政資料各做連結碼，來補正衛生署死因資料庫內缺漏或錯誤之户政資料或身分證字號，及填補教育及村里之資料。同時建立兩資料庫間互相無法連結之個案資料庫。**結果**：第一部分，自公元1980至1997年以身分證字號與户政資料爲連結碼，經由兩資料庫互連，可連結出1,259,600個個案。連結不上之個案利用身分證字號與户政資料分別比對後，可補正衛生署之户政資料有3,168個個案，身分證字號有33,036個個案。另外，兩資料庫可連結之部分，教育及村里變項補正百分比都達98%以上。第二部分，公元1980至1984年，主要填補衛生署身分證字號。以户政資料包括出生年月日、死亡年月日、縣市代碼、鄉鎮代碼全部變項爲連結碼可以填補身分證字號達88.83%。公元1980至1997年，兩資料庫未連結上之個案未作補正者，共有衛生署46,305個個案及內政部63,157個個案，可能是失去追蹤及延遲申報個案。**結論**：本研究結果可使世代研究及存活分析在使用衛生署的死因資料檔案範圍往前推至公元1980年；研究族群之區域分層只能切割到最小單位鄉鎮，但補正後可使之細分到村里。另外衛生署及內政部未連結上之個案可建立檔案作爲延遲申報個案及失蹤建檔個案之參考，以便作爲將來研究追蹤死亡個案之依據。(台灣衛誌 2002；**21(5)**：329-338)

關鍵詞：死亡登記、資料庫、衛生署、內政部。

Verification and correction of error for death registration data of the Department of Health R.O.C. between 1980 and 1997

Objective: Both the Department of Health (DOH) and Ministry of Interior (MOI) of Taiwan have established a computerized death registry based on the death certificates of the dead in Taiwan during the past two decades. The purpose of this study is to verify the accuracy of the dataset of death registration for the DOH with the dataset from the MOI. Because the data of the DOH during 1980-84 lacked the identification number (ID no.), our second objective is to establish guidelines for replacing the missing ID no.. **Method:** Firstly, decedents in the two datasets linked by same ID no. and demography including dates of birth, death, and places of living between 1985 and 1997 were identified and codes of education and village taken from the MOI were filed in those of the DOH. Decedents that could only be linked by ID no. or demography between 1985 and 1997, were refiled the demography or ID no. after making sure of the correction in the MOI. Secondly, due to the lack of information of ID no. in the DOH for decedents between 1980 and 1984, we linked the two decedents with social demography including dates of birth and death, area codes of detailed address, and then imputed ID no. into dataset of the DOH based on dataset of the MOI. **Result:** There were 1,259,600 decedents identified from 1985-97 with completely the same ID no. and demographic data. After verification of the data, we refiled the missing demographic data for 3,168 subjects and the missing ID no. for 33,036 subjects into the dataset of the DOH. According to the study results, there were 0.0512% of total subjects with complete overlapping demographic data. Thus, after linking the two datasets with the same complete demographic data, we were able to refile 88.83% of the missing IDs for all the death certificate data of the DOH during 1980-84. There were 46,305 cases in the dataset of the DOH and 63,157 cases in that of the MOI during 1980-97, that were unlinkable. This was probably because they were lost track of or there was a delay in registration. **Conclusion:** This study corrected many errors, filled in ID no. for 1980-84, and imputed information of education and village into the death registration dataset of the DOH. This can be useful for future studies. Beside, the unlinkable cases in the datasets of the DOH and MOI were identified and a separate dataset files for future usage was built up. *(Taiwan J Public Health. 2002;21(5):329-338)*

Key words: death registration, dataset, Department of Health, Ministry of Interior.

前　言

資料庫對於流行病學之研究佔有相當重要的地位，尤其資料庫完整性及正確性對於研究之結果有重大的影響性。目前國內建立許多資料庫如死因資料檔、新生兒出生檔、勞保資料檔、公保資料檔等等。所有的世代研究[1,2]及存活分析[3,4]多必須依賴正確的死亡診斷書。

目前國內將死亡診斷書建立成死因資料庫的有衛生署及內政部戶政司兩個單位，而其兩者之內容有所差異；此點可由其形成之歷史來解釋：衛生署死因資料檔自公元1952年起由台灣省政府衛生處負責收集，資料收集方式由鄉鎮市區公所於每月初至當地戶政事務所影印前一個月之死亡證明書，經註記後送各衛生局初核，核定原死因及填註各欄代號[5,6]，自公元1971年起開始利用電腦集中處理，但是沒有輸入死亡者姓名、戶籍地址、職業別及住址，且公元1971至1984年間亦未輸入身分證字號。在美國，財稅資料中對一個人之存活與死亡資料保存極爲完整，本國亦然。內政部戶政司公元1978至1997年死因資料電子檔是委託財稅資料中心建立，但是公元1979年該年電子檔遺失，自公元1998之後才由內政部戶政司自力建立；除了輸入身分證字號外，尚有教育程度及村里代碼，但未記載死因代碼及性別。(下文『內政部戶政司』以『內政部』簡稱之)

回顧過去有關使用台灣死亡資料檔案之研究，有理論性的研究[7,8]、死亡原因的驗證[9]及探討社會[10,11]、經濟[12]、疾病[13]等因子究，但肇因於資料庫完整性的缺乏，每每使資料在應用上有所限制。鑒於衛生署從公元1985年後才建立身分證字號，因此在職業世代暴露追蹤研究中，往往無法探討1985年之前的死亡情形，而導致較早建廠之公司的職業死因研究無法有一個完整之時間趨勢解釋。在環境污染評估方面，暴露分層如果只能細分到鄉鎮爲單位，則其精確度實在大有問題。另外，在應用死因資料檔案之研究，其人數之準確相當重要，而在衛生署延遲申報之部分卻只從公元1996年開始，因此如能加以追溯俾可以減少死亡率之低估，使研究更加準確。

基於上述之各種理由，死因資料庫之補正實在是目前研究相當重要之議題，本研究收集內政部及衛生署的資料來做比對，用較正確的檔案來補正不正確的檔案。因此，本研究的目的如下：1.比較兩個死因資料檔案之不同與其完整性，並加以補正。2.衛生署延遲申報檔案只從公元1996年開始建立，而內政部每年死因資料檔是有建立延遲申報檔，所以用內政部死因資料檔來填補衛生署延遲申報檔案。3.衛生署死因資料中自公元1980至1984年並無建立死亡個案之身分證字號，所以用內政部死因資料檔來填補衛生署之身分證字號。4.用內政部死因資料檔中教育及村里變項來填補衛生署此二種變項。

投稿日期：91年6月20日
接受日期：91年12月25日

材料與方法

資料庫所含之變項

本研究範圍爲公元1980至1997年，資料來源取自衛生署死因資料檔案(不包含延遲申報個案)計有1,815,134個個案，及內政部死因資料檔案計有1,829,924個個案。衛生署資料含有變項：死亡者身分證字號、性別、縣市代碼、鄉鎮代碼、出生年民國前後、死亡者出生日期、死亡者死亡日期、死亡地點、死亡場所代碼、死亡種類代碼、職業代碼、婚姻狀況代碼、國際詳細死因分類號碼、「800」以後損傷及中毒之國際詳細死因分類、診斷者代碼、國際基本死因分類號碼、國際簡略死因分類號碼。內政部資料變項與衛生署資料不同之處，在於具有衛生署沒有建立之死亡者教育程度、死亡申請登記日期、村里代號；但沒有建立國際詳細死因分類號碼、「800」以後損傷及中毒之國際詳細死因分類、診斷者代碼。

身分證字號之規則(內政部戶政司公佈的規則)

身分證字號之錯誤是指根據內政部戶政司公佈的身分證檢查碼檢查辦法來檢查不符

合者。身分證字號之檢查號碼檢查方法是依據中華民國五十九年十二月十八日臺內戶字第三五五六六四號令所公佈；其檢查方法如下：首先照附表所列數字將英文字母代號換爲數字，再按照十位數字，第一位乘一，第二位乘九，第三位乘八，第四位乘七，……，最後一位乘一，將各位相對數字所乘之積相加，然後前項所得之和除以十，求得其餘數，最後以十減去前項所得之餘數即爲檢查號碼。但由於此數碼仍爲0到9中之任一數，故在隨機之假設下，此數錯誤機率爲0.1。身分證字號其正確範圍第1碼26個英文字母A～Z；第2碼爲性別碼男女以1～2爲代表號；第3～9碼爲阿拉伯數字0～9共10個代表號；第10碼爲身分證字號檢查碼共10個代表號0～9。

戶政資料之範圍及準確性

戶政資料是指出生年月日、死亡年月日、縣市代碼及鄉鎮代碼之綜合資訊；其中偶而有一項以上缺漏無填寫者，視爲戶政資料之缺漏。戶政資料錯誤是指出生年月日、死亡年月日、縣市代碼及鄉鎮代碼任何一個變項不符合其正確範圍者。其正確範圍如下，出生年：民國1年至86年(公元1912至1997年)、出生月：1至12月、出生日：1至31日；死亡年：民國69年至86年(公元1980至1997年)、死亡月：1至12月、死亡日：1至31日；縣市代碼：A至Z、鄉鎮代碼：01～33。假定錯誤完全是隨機發生時，任何一個變項有錯誤之機率，各爲其正確範圍之倒數；例如身分證字號第1碼26個爲英文字母；第2碼爲性別2個代表號；第3～9碼爲阿拉伯數字10個代表號；第10碼爲身分證字號檢查碼共10個代表號。身分證字號可能排列出之最多組數爲$26\times2\times10\times10\times10\times10\times10\times10\times10\times10=5,200,000,000$，因此其隨機錯誤之機率爲1.92E-10，同理戶政資料錯誤機率爲5.76E-12。但是登錄與輸入牽涉到人爲疏失，因此這些計算數字爲此資料錯誤機率之下限。

補正方法

本研究擬以衛生署死因資料檔爲主體，而以內政部死因資料檔之身分證字號及戶政資料來補正。連結比對之方法綜述如下：首先篩檢在個別資料庫內身分證字號及戶政資料皆相同的個案；以便找出同一個案重複輸入之機率，其次比對身分證字號與戶政資料之有無缺漏、錯誤及重複。之後，倘兩資料庫間以身分證字號及戶政資料皆爲連結碼互相連結，完全相同之個案則表示兩邊爲同一個案，這些個案可利用內政部資料來補正衛生署之村里及教育變項。未連上之部分，先以戶政資料爲連結碼，在兩資料庫間互相連結，可連結上之部分補正衛生署之村里及教育變項及身分證字號錯誤部分。其次，再以身分證字號爲連結碼，在兩資料庫間互相連結，可連結上之部分補正衛生署戶政資料錯誤部分；而有關村里及教育變項補正部分，除了戶政資料可補正外，另外還有戶政資料個案正確時，則比對內政部出生及死亡年月日如有4個以上變項相同則爲可補正之個案。內政部用身分證字號或戶政資料與衛生署無法連結上之部分，可作爲補充衛生署死因資料庫內因延遲申報或不明原因未建檔之個案，另外開列加入其中，以備有存活追蹤研究之參考。

補正原則

本研究補正有缺漏，或數字超出正常範圍，或檢查碼有錯誤者，其原則如下：1.衛生署死因資料庫之被補正變項(身分證字號、戶政資料)是缺漏或錯誤，意即戶政資料有任何一個變項缺漏或不在正確範圍，且身分證字號缺漏或檢查碼錯誤才納入可補正之個案。2.內政部死因資料庫之補正變項(身分證字號，戶政資料)必須是完全正確，才納入可補正之個案。

連結原則

當連結碼(身分證字號、戶政資料)連結成功，但如有重複連結或其他因素無法判定是否連結成功，則以其他資訊(戶政資料、身分證字號)來做比對。其戶政資料比對優先順序如下：死亡年月日、出生年月日、縣市代碼及鄉鎮代碼。此時，另一戶政資料不同之

個案，即被判定爲連結失敗。當使用戶政資料爲連結碼，比較衛生署與內政部間之兩個身分證字號，必須確認兩者間之身分證字號內十碼必須超過8個相同，才可被判定爲連結成功之個案。補正個案與被補正個案兩者間之身分證字號比較優先順序依第1碼、第2碼、第10碼、第3～9碼。

連結碼選取原則

當以戶政資料爲連結碼時，必須先檢視及比對哪些戶政資料特異性最高。以衛生署及內政部公元1985至1997年死因資料檔爲基準，建立戶政資料(出生年月日、出生年月、死亡年月日、死亡年月、縣市代碼、鄉鎮代碼)各種組合爲連結碼，比對出其重複連結比率，依此原則來決定各種組合爲連結碼之優先順序，本研究以重複連結個案比率最少者爲連結碼之標準，作填補之依據。

結　果

公元1980至1997年兩資料庫基本特徵比較

首先針對公元1985至1997年間兩資料庫均有身分證字號及戶政資料者相比，當身分證字號且戶政資料一樣視爲相同個案時，衛生署之死因資料庫重複輸入率較內政部高出約七倍(見表一)；在身分證字號缺漏及身分證字號檢查碼錯誤方面衛生署都有較高的百分率，可以大致推論內政部死因資料在個案數目及身分證字號較衛生署爲準確。因此本研究使用內政部死因資料中之身分證字號及戶政資料，來補正衛生署的缺漏與錯誤可能是較合理且減少錯誤之作法。

補正公元1980至1997年衛生署死因資料身分證字號、戶政資料、教育及村里變項

兩資料庫因爲身分證字號且戶政資料完全相同被剔除之個案數，衛生署有2,410個及內政部361個(見圖一)。然後，以身分證字號且戶政資料爲連結碼兩資料庫互連可連結出1,259,600個個案，而連結不上之個案衛生署計有118,437個個案及內政部計有132,134個個案。再單獨用身分證字號或戶政資料分別比對兩資料庫，身分證字號相同者有65,810個個案，其中有296個個案身分證檢查碼不正確，補正衛生署戶政資料有3,168個個案，即可補正教育及村里變項，而戶政資料缺漏且錯誤有1個個案無法補正，其他有62,641個個案的戶政資料是在正確範圍內，比對內政部出生及死亡年月日4個以上變項相同者達60,260個個案，可補正教育及村里變項。另一方面戶政資料相同者有43,124個個案，補正衛生署身分證字號有33,036個個案，但有4個個案身分證字號缺漏與352個個案身分證字號檢查碼錯誤無法補正。另外，教育變項補正1,368,313個個案及村里補正1,343,999個個案；兩資料庫可連結之部分，兩個變項補正百分比都達98%以上(見表二)。兩資料庫以身分證字號或戶政資料爲連結碼未連結上之個案來補正，共有衛生署9,503個個案及內政部23,213個個案，可能是失去追蹤或延遲申報個案。

戶政資料特異性

公元1980至1984年衛生署資料庫中並無建立身分證字號，因此爲了使兩資料庫連結有規則遵循，其建立規則方法如下：從公元1985至1997年，共取得衛生署1,380,447個個案及內政部1,392,095個個案爲比對其重複比率之對象。兩資料庫內先篩選出身分證字號正確且唯一的個案，再以身分證字號且死亡年份爲連結碼使兩資料庫互相連結，可以連結上有1,320,787個個案；以這些個案爲基準。建立戶政資料(出生年月日、出生年月、死亡年月日、死亡年月、縣市代碼、鄉鎮代碼)各種組合爲連結碼使兩資料庫互相連結後之重複比率；結果發現以戶政資料全部變項爲連結碼時，其重複個案連結率爲0.0512%，是各種組合中爲重複連結比率最少者(見表三)，定其爲連結碼之標準。

補正公元1980至1984年衛生署死因資料身分證字號、教育及村里變項

接著進行衛生署身分證字號補正，從公元1980至1984年，主要填補衛生署身分證字

表一　公元1985年至1997年衛生署與內政部死因資料庫身分證字號及户政資料之重複或缺漏率

特徵	內政部 N (%)	衛生署 N (%)
身分證字號且戶政資料*重複[1]	720 (0.052)	4,812 (0.35)
身分證字號缺漏一碼以上[2]	0 (0)	350 (0.03)
身分證字號重複(戶政資料不同人)[2]	12 (0.001)	537 (0.04)
身分證字號檢查碼錯誤[2]	3,769 (0.27)	36,461 (2.64)
戶政資料*有一項以上缺漏[2]	376 (0.03)	3,226 (0.23)
戶政資料*重複(身分證字號不同人)[2]	26 (0.002)	68 (0.05)
總計	1,392,095	1,380,447

* 戶政資料是指是指出生年月日、死亡年月日、縣市代碼及鄉鎮代碼之綜合資訊。

[1] 衛生署死因資料檔案計有1,380,447個個案，及內政部死因資料檔案計有1,392,095個個案。

[2] 身分證字號且戶政資料爲連結碼兩資料庫互連，而連結不上之個案衛生署計有118,437個個案及內政部計有132,134個個案。

號。以戶政資料全部變項爲連結碼可連結上內政部91.53%，只挑內政部資料中身分證字號無誤者，則可以填補身分證字號達88.83%(見表四)。且檢查其縣市、鄉鎮代碼都合乎邏輯，進行村里及教育補正，結果教育變項補正388,141個個案及村里補正364,498個個案；兩個變項補正百分比都達83%以上。兩資料庫未連結上之個案，共有衛生署36,802個個案及內政部39,944個個案，可能是失去追蹤及延遲申報個案。至於連結碼放寬標準之得失，在本文之討論部分多加了一個議題『不同戶政資料組合之特異性』中有詳加討論。

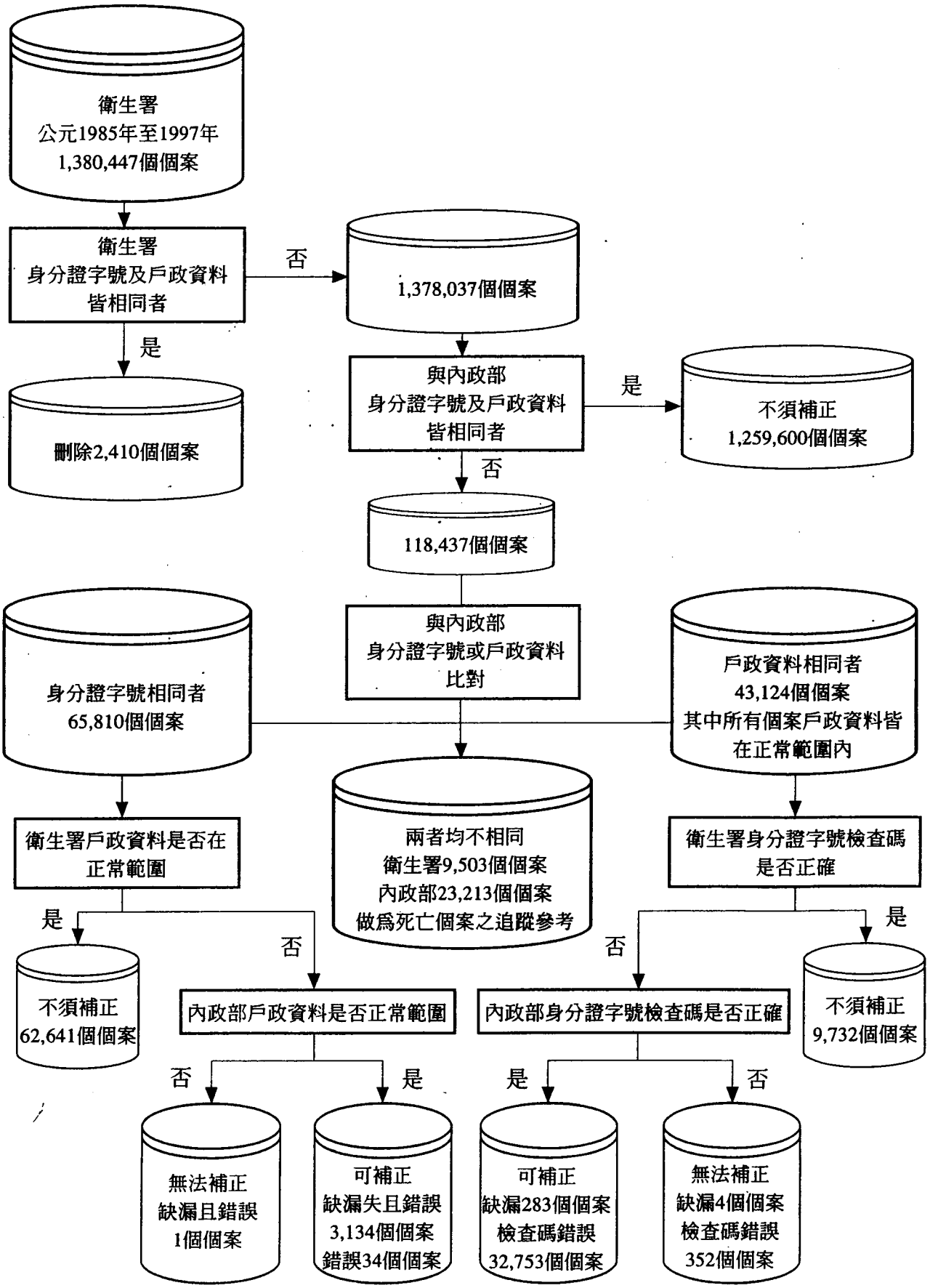
討　論

本研究以衛生署死因資料檔爲主體，使用內政部死因資料檔正確資訊來補正，重新整理出一個死因資料檔案，可提供未來研究之參考。以下針對戶政資料及身分證字號之準確性、連結策略之檢討、不同戶政資料組合之特異性、補正後資料庫之運用與限制等進行討論，並對未來應用死因資料建檔與校正提出建議。

戶政資料及身分證字號之準確性

各行政機關建立檔案，是以其本身之目的及用途爲導向，因此其所關注的焦點也不同。以死因資料檔而言，衛生署之目的是提供本國生命統計資料，因此對死亡相關資料如死亡種類代碼等可能較爲重視，但個案之基本資料與少數失蹤的個案可能就未建檔。然而，內政部與其立場可能較不相同，其建檔的目的是爲了追蹤報稅與各種行政用途，剛好可能與衛生署有互補性。本研究即利用此特性，來進行補正之工作。兩資料庫共有變項部分之完整性，綜合在表一上。就個案數而言，衛生署死因資料建檔是從公元1971年開始，但其延遲申報案檔只從公元1996年才建立；而內政部死因資料檔和延遲申報案檔都是從公元1978年建立，但公元1979年當年資料卻已經毀損。在個人資料方面，身分證字號衛生署在公元1984年之前是未建檔的，而內政部從建檔開始即有建立；比較公元1985年至1997年兩資料庫之身分證字號，發現衛生署有缺漏而內政部均完整。衛生署死因資料之身分證字號重複率及檢查碼錯誤較內政部爲高；另外戶政資料方面，衛生署有一項缺漏者個案及重複率都較內政部偏高。但是出生日期在民國前後之變項分析結果，因內政部有3%缺漏個案而衛生署無缺漏個案，爲兩資料庫比對方便起見，此項不列入戶政資料庫之比對項目。在性別碼方面只有衛生署才有建立，且比較其性別碼與身分

圖一　公元1985年至1997年衛生署死因資料檔案補正身分證字號及户政資料之流程



表二　公元1985年至1997年衛生署死因資料檔案補充教育及村里資料代碼

		與內政部身分證字號且戶政資料相同者	與內政部戶政資料相同者	與內政部身分證字號相同者
	校對結果			
可連結個案		1,259,600	43,124	65,810
教育資料*	正確	1,259,406	43,115	65,792
	錯誤	141	4	14
	缺漏	53	5	4
村里資料**	正確	1,238,267	42,554	63,178
	錯誤	15,146	391	711
	缺漏	6,187	179	1,921

* 教育資料：依據教育程度查記作業要點附件一(中華民國86年11月10日內政部台(86)戶字號及教育部(86)統86127441號會銜函訂定)，如符合其教育程度代碼爲正確；不符合者爲錯誤；未填寫者爲缺漏。

** 村里資料：依據中華民國台閩地區各市鎮鄉村里代碼(行政院主計處公告)，如符合其村里代碼爲正確；不符合者爲錯誤；未填寫者爲缺漏。

表三　公元1985年至1997年內政部與衛生署死因資料庫，以身分證字號且死亡年份爲連結碼對連，內政部與衛生署死因資料庫所連結上之個案有1,320,787人，在以出生年月日、死亡年月日、縣市代碼、鄉鎮代碼作各種組合之連結碼所產生之連結率。

連結碼	連結產生重複個案數 N(%)	假定完全隨機情況重複機率*
出生年月日＋死亡年月日＋縣市代碼＋鄉鎮代碼	676 (0.0512)	7.53E-12
出生年月日＋死亡年月日＋縣市代碼	3,290 (0.2491)	2.49E-10
出生年月＋死亡年月日＋縣市代碼＋鄉鎮代碼	6,939 (0.5254)	2.34E-10
出生年月日＋死亡年月＋縣市代碼＋鄉鎮代碼	8,133 (0.6158)	2.34E-10
出生年月日＋死亡年月日	47,739 (3.6144)	6.46E-09
出生年月＋死亡年月日＋縣市代碼	76,205 (5.7697)	7.71E-09
出生年月日＋死亡年月＋縣市代碼	83,819 (6.3461)	7.71E-09
出生年月＋死亡年月＋縣市代碼＋鄉鎮代碼	191,318 (14.4852)	7.24E-09
出生年月＋死亡年月日	1,183,146 (89.5789)	2.00E-07
出生年月日＋死亡年月	1,270,964 (96.2278)	2.00E-07

* 假設各變項均爲獨立，理論上可能產生重複之機率。

表四　公元1980年至1984年衛生署死因資料庫以出生年月日、死亡年月日、縣市代碼及鄉鎮代碼做各種組合之連結碼，連結內政部死因資料庫可補正身分證字號、教育及村里百分率。

變項名稱		連結上之個案數	連結上之百分比	可補正身分證字號之個案數	可補正身分證字號之百分比	可補正教育之個案數	可補正教育之百分比	可補正村里之個案數	可補正村里之百分比
出生年月日+死亡年月日+縣市代碼+鄉鎮代碼		397,885	91.53	386,134	88.83	388,141	89.29	364,498	83.85
出生年月日+死亡年月日+縣市代碼(再增連上之個案)		2,848	0.66	2,779	0.64	2,785	0.64	2,429	0.56
出生年月+死亡年月日+縣市代碼+鄉鎮代碼(再增連上之個案)		8,683	2.00	8,417	1.94	8,440	1.94	8,022	1.85
出生年月日+死亡年月+縣市代碼+鄉鎮代碼(再增連上之個案)		7,155	1.65	6,947	1.60	6,943	1.60	6,650	1.53
連結上之個案		416,571	95.83	404,277	93.00	406,309	93.47	381,599	87.79
未連結上之個案	衛生署	18,116	4.17						
	內政部	21,258	4.86						
未補正之個案				30,410	7.00	28,378	6.53	53,088	12.21
總和	衛生署	434,687	100.00	434,687	100.00	434,687	100.00	434,687	100.00
	內政部	437,829	100.00						

證字號第二碼亦有差異性0.6%存在，因此本研究不把出生日期民國前後及性別碼納入連結碼。內政部有建立個案之村里變項代碼是補正的一個重要資訊，對未來研究環境流行病學可能有相當大的幫助，故在本研究中特別把它填補到衛生署資料中。基於上述內政部資料除了死因資料未能鍵入之外，大致上準確性比衛生署好，因此本研究用內政部死因資料檔來補正衛生署之死因資料，以便未來在世代研究及存活分析使用。

連結策略之檢討：未來使用身分證字號或戶政資料比對流行病學研究個案是否死亡之準確性推估

本研究發現公元1985年至1997年身分證字號相同之個案戶政資料仍連結不上者超過6萬筆以上；而戶政資料相同之個案身分證字號仍連結不上者超過4萬筆以上(見圖一)。是否連結策略上有誤造成此種現象？仔細探討這些個案，發現衛生署62,641個個案中，比較兩資料庫出生及死亡年月日六個變項中，五個以上變項相同者共有56,018個個案。同樣的方法在兩資料庫戶政資料均相同的43,124個個案中，有9,732個個案身分證字號檢查碼錯誤，比較兩資料庫身分證字號十個號碼中，八個以上號碼相同者共有8,288個個案。根據表3之各碼相同重複機率很低上來想，檢測是否兩資料庫無法相連結之這些個案仍是同一人，可能在人為輸入時誤差造成無法相連結。可見我們以上連結策略並未造成誤差使未來連上之個案假性增加。同時可以大致推論，將來使用此校正後資料庫，以身分證字

號來比對作流行病學追蹤是否死亡準確性可達98.58%(=(1,259,600+65,810+32,753+283)/1,378,037)；反之，如果以戶政資料爲連結碼作追蹤是否死亡，約可達94.76%(=(1,259,600+43,124+3,134+34)/1,378,037)。

不同戶政資料組合之特異性

公元1980至1984年間兩資料庫間檢視及比對哪些戶政資料特異性最高，在本研究中爲了補正嚴謹度之考量，因此以重複連結個案比率最少者爲連結碼之標準，作填補身分證字號之依據。我們發現當出生及死亡年月日、縣市與鄉鎮代碼均相同時，重複比率爲0.0512%以下。如果欲使用本資料庫者，有其他研究目標欲放寬連結碼標準，定重複連結比率到小於1%之組合時(見表三)，可放寬至缺鄉鎮代碼、或缺出生日、或缺死亡日3種組合爲連結碼，可以再增加填補身分證字號4.18%，教育變項4.18%案及村里3.94%(見表四)。由上可知，把連結碼條件放寬雖然可以增加填補百分率，但是其重複連結比率相對的增加，如何取得最佳條件可依照研究本身之特性來決定。不過本研究已先將所有戶政資料均拿來比對且相同者，補上了身分證字號供大家方便使用。(目前已做好光碟，有意者請向衛生署統計室申請死因資料庫通過，轉給作者且附上工本費即可提供。)

補正後資料庫之運用與限制

此補正過之檔案，在年代方面使用身分證爲連結碼時，以往研究範圍只能從公元1985年之後的，本研究結果可使研究範圍往前推至公元1980年；先前研究族群之區域分層只能切割到最小單位鄉鎮，但補正後可使之細分到村里。另外連結後內政部未連結上衛生署之個案，可建立衛生署公元1986年之前未建檔之延遲申報個案及失蹤建檔個案，作爲將來研究追蹤死亡個案之依據。

補正後重新整理之死因資料檔案，仍然有部限制存在。在衛生署死因資料檔中應補正而不能補正之個案有兩類，1.未連結上之個案，2.連結上，但內政部無正確資訊來補正之個案。經過補正後的死因資料庫，不管是以身分證字號或戶政資料爲連結碼都仍然還有機會產生重複連結之個案。此時必須再佐以其他相關資訊加以比對來判定正確連結之個案。對於本研究無法補正個案，在未來應該更進一步找出原始書面資料加以校對訂正，以力求資料之完整及正確。

對未來死因資料建檔與校正提出建議

比對兩資料庫公元1985年至1997年資料補正之結果，衛生署身分證字號每年補正率約有2～3%；而戶政資料約在0.01%以下，其補正率未因年代改變而有所減少，因此建議衛生署對死因資料在未來應定期進行補正工作。除了建檔時考慮與內政部連線將村里、教育變項納入之外，對延遲申報個案須補建檔，且對失去追蹤個案可每年定期(例如1～2次)配合戶口普查或校正、失蹤人口、刑事案件、出入境資料來加以比對更新。另外如果可將現有未建立電子檔案之死亡證明書書面資料建爲電子檔案，將可能更方便查詢與校正以增進其準確性。

誌　謝

本研究係由國科會計畫(NSC 90-2320-B-002-127-M56)補助部份研究經費。感謝衛生署及內政部提供死因資料。

參考文獻

1. Chen CC, Kuo CJ, Tsai SY. Causes of death of patients with substance dependence: a record-linkage study in a psychiatric hospital in Taiwan. Addiction 2001;**96**:729-36.
2. Manjer J, Andersson I, Berglund G, Bondesson L, Garne JP, Janzon L et al. Survival of women with breast cancer in relation to smoking. Eur J Surg 2000;**166**:852-8.
3. Martikainen P, Valkonen T, Martelin T. Change in male and female life expectancy by social class: decomposition by age and

cause of death in Finland 1971-95. J Epidemiol Community Health 2001;**55**:494-9.
4. Svartbo B, Olov BL, Gunnarsson T, Steen L, Ribe M. Survival during and after hospitalization: a medical record linkage. Int J Health Care Qual Assur Inc Leadersh Health Serv 1999;**12**:13-7.
5. 台灣省政府衛生處：國際疾病、傷害及死因分類表。台灣省政府衛生處，1995。
6. 行政院衛生署：國際疾病傷害及死因分類表(1975 Revision)。台北：行政院衛生署，1981。
7. Lee WC. Characterising life-span variability in a population using the life-table-based Lorenz-curve analysis. J Epidemiol Biostat 2000;**5**:315-20.
8. Lee WC. The meaning and use of the cumulative rate of potential life lost. Int J Epidemiol 1998;**27**:1053-6.
9. Lu TH, Lee MC, Chou MC. Accuracy of cause-of-death coding in Taiwan: types of miscoding and effects on mortality statistics. Int J Epidemiol 2000;**29**:336-43.
10. Liang J, Bennett JM, Krause NM, Chang MC, Lin HS, Chuang YL et al. Stress, social relations, and old age mortality in Taiwan. J Clin Epidemiol 1999;**52**:983-95.
11. Liu X, Hermalin AI, Chuang YL. The effect of education on mortality among older Taiwanese and its pathways. J Gerontol B Psychol Soc Sci 1998;**53**:S71-82.
12. Chiang T. Economic transition and changing relation between income inequality and mortality in Taiwan: regression analysis. Br Med J 1999;**319**:1162-5.
13. Chen CJ, You SL. Epidemiology of cervical cancer in Taiwan. Gynecol Oncol 1997; **67**:115-6.

附表

縣市別	代號	數字換算	縣市別	代號	數字換算	縣市別	代號	數字換算
台北市	A	10	苗栗縣	K	19	花蓮縣	U	28
台中市	B	11	台中縣	L	20	台東縣	V	29
基隆市	C	12	南投縣	M	21	澎湖縣	X	30
台南市	D	13	彰化縣	N	22	陽明山	Y	31
高雄市	E	14	雲林縣	P	23	金門縣	W	32
台北縣	F	15	嘉義縣	Q	24	連江縣	Z	33
宜蘭縣	G	16	台南縣	R	25	嘉義市	I	34
桃園縣	H	17	高雄縣	S	26	新竹市	O	35
新竹縣	J	18	屏東縣	T	27			

Assessing Health-Related Quality of Life in Patients with Hepatocellular Carcinoma

Shortened title: Quality of life in HCC Patients

Lukas Jyuhn-Hsiarn Lee [a], Chien-Hung Chen [b], Grace Yao [c], Chih-Wen Chung [d], Jin-Chuan Sheu [b], Po-Huang Lee [e], Yih-Jian Tsai [a], Jung-Der Wang [b, d]

[a] Bureau of Health Promotion, Department of Health, Taiwan.

[b] Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taiwan.

[c] Department of Psychology, College of Science, National Taiwan University, Taiwan.

[d] Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Taiwan.

[e] Department of Surgery, National Taiwan University Hospital and National Taiwan University College of Medicine, Taiwan.

Address correspondence to: Professor Jung-Der Wang, National Taiwan University, College of Public Health, Taipei 100, Taiwan.

Telephone: 886-2-2351 6561 Fax: 886-2-2391 1308

E-mail: jdwang@ha.mc.ntu.edu.tw

Abstract

We assessed health-related quality of life in patients with hepatocellular carcinoma (HCC) using Taiwan versions of WHOQOL-BREF, EORTC QLQ-C30 and utility measures. A total of 172 subjects were consecutively enrolled from patients with HCC who followed up regularly at a university hospital from February to April 2002. The internal consistency (Cronbach's alpha) coefficients ranged from 0.67 to 0.82 for the four domains of WHOQOL-BREF. Each domain score of WHOQOL-BREF correlated significantly with utility measured by visual-analogue scale and standard gamble (Pearson's correlation range, 0.40 to 0.59, and 0.17 to 0.38, respectively), and also positively associated with self-evaluated health status and happiness. Moderate to high correlations were found between WHOQOL-BREF and EORTC QLQ-C30 in the aspects of physical, psychological, and general health. These QOL scores were compared with data from 213 healthy persons using general linear model. The patients with HCC were found to have significantly lower scores on physical, psychological domains and general health. The WHOQOL-BREF can have wide coverage of items for differentiating surgery and non-surgical treatment, which may be useful to estimate QOL difference between different treatments among the HCC patients.

Key words: **Hepatocellular carcinoma, Quality of life, Utility, WHOQOL**

Introduction

Liver cancer, primarily hepatocellular carcinoma (HCC), is one of the most common malignant neoplasms worldwide [1], especially in Southeastern Asia including Taiwan [2]. Even though HCC is not a common cancer in most developed countries, a trend of increasing incidence of HCC has been disclosed in the Western world, which may be associated with chronic hepatitis infections [3]. As the prognosis for HCC patients is poor, with a median survival generally less than 5 years [4], the quality of life (QOL) is becoming more important on the outcome assessment for clinical services.

QOL is an important dimension of health, and it has been defined by the World Health Organization as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns." [5] There has been a rapid growth in the assessment of health-related quality of life (HRQOL) as a technique for clinical research since 1970s [6]. Up to 2000, there were at least one thousand HRQOL estimates reviewed by Tammy et al. (2000) [7], and a comprehensive table was compiled to provide quality weights for many diseases. A large proportion of these QOL weights, however, were based on the viewpoints of authors and experts. Patients' preference was the main concern in about 39% of all respondents. Empirical studies using patient-centered QOL are warranted for quantifying effectiveness in clinical research [8]. While a generic instrument may be suitable for comparison between diseases, clinical decision-making may require

disease-specific questionnaire to differentiate minute differences in QOL between treatments. The objective of this study was to compare and validate generic and condition-specific measurements of HRQOL in patients with HCC, using both health profiles and utility measures.

Subjects and Methods

Subjects

One hundred and seventy-two patients with HCC were recruited consecutively at the National Taiwan University Hospital (NTUH) from February to April 2002. These subjects selected for QOL measurement included (1) the HCC cohort diagnosed during 1996-2000 who have been followed up regularly at the outpatient clinics, and (2) newly diagnosed HCC patients who were hospitalized during the study period. The diagnosis of HCC was confirmed by histological evidence or clinical diagnosis mainly based on AFP levels higher than 400 ng/ml with positive findings of image studies. The institutional review board approved this study and informed consent was obtained from every participant prior to the survey.

Instruments

The participants were requested to evaluate their quality of life over the past two weeks with a self-administrated questionnaire. The instruments for measuring QOL in our study were briefed as follows:

(1) The short-form version of WHOQOL questionnaire, i.e., WHOQOL-BREF, has been developed in Taiwan, and good reliability and validity of the Taiwan version were also reported [9, 10]. The Taiwan version of the WHOQOL-BREF contains the 26 original items, plus two additional items of national importance. The first two questions concern the global QOL and general health, and the remaining 24 items can be grouped into four domains, as follows: physical, psychological, social, and environment. Two national items, "Being respected" and "Eating" were included in the Taiwan version, each from a culture-specific facet that constitutes Social (TW), and Environment (TW) domains, respectively [9]. The score of each domain range from 4 to 20. The Taiwan version of WHOQOL-BREF with a 5-point Likert scale was used to assess QOL of HCC patients regarding personal subjective experiences.

(2) The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC QLQ-C30, version 3.0) is a cancer-specific QOL instrument originally designed for use in cancer clinical trials. The questionnaire includes five functional scales (physical, role, social, emotional and cognitive), global QOL/general health, and symptoms frequently reported by cancer patients (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea) as well as an item on the financial impact [11]. It consists of 30 items, uses a 4-point scale for 28 items and a 7-point scale for two overall measures. The Taiwanese version of QLQ-C30 has been developed

through formal processes and field test and verified by EORTC [12]. This cancer-specific instrument was used to examine the convergent validity with the Taiwan version of WHOQOL-BREF in the patients with HCC.

(3) Utility were measured with the visual-analogue scale (*VAS*) and standard gamble (*SG*) method. To assess utility by means of *VAS*, the participants were asked to rate their overall health-related QOL in the recent two weeks from 0 ("worst" condition) to 100 ("best" condition). With a flow diagram of making choices of taking a hypothetical curative therapy in the *SG*, the quality weight of HCC was assessed by comparing his/her health state to a gamble with a probability (p) of achieving full health and a complementary probability (1-p) of death. The probability of full health was titrated from 99% down to 5% until the HCC patient was indifferent between the alternatives, and the quality weight of this HCC patient would be equal to the probability p [13].

Instrument validation with statistical analyses

Reliability and Validity

The internal consistency reliability of an instrument was evaluated using Cronbach's alpha coefficient. We expected the alpha coefficient to exceed 0.7 in four domains and the general health/QOL item. Content validity, which indicates consistency between items and corresponding domains, was assessed with Pearson's correlation coefficients. Generally two instruments measuring similar constructs should be highly correlated. We performed the convergent validity analysis by assessing the correlation between WHOQOL-BREF domain scores and related health status measures. The health status measures used in this study included: (1) global QOL/general health measured with WHOQOL-BREF and EORTC QLQ-C30; (2) the self-evaluated health status and self-evaluated happiness, both measured by a 5-point response scales; (2) utility measures using VAS and SG. With testing a hypothesis that WHOQOL-BREF accurately assessed QOL in patients with HCC, we expected the domain scores to demonstrate moderate correlations with global QOL/general health, self-evaluated health status/happiness, and utility measures.

The discriminant validity was assessed through comparing QOL measures between HCC patients and healthy people, between the patients who underwent surgery and non-surgical treatment, as well as inpatients and outpatients. The QOL data of 213 healthy persons, who were hospital volunteers or employees, were obtained as the healthy controls from the prior field survey [10]. Each item and domain score of the WHOQOL-BREF were compared between HCC patients and healthy subjects using Student's t test. Taking gender and age into account, the difference of each aspect of QOL between surgery and non-surgical treatment, inpatients and outpatients using the general linear model approach [14].

Exploratory factor analysis was conducted to assess construct validity using squared multiple correlation for communality estimates, extracting factors by principal factor method; and followed by Promax rotation. Data analyses were performed using SAS (Statistical

Analysis System) software Version 8.1. Two-tailed p values of less than 0.05 were considered to be statistically significant.

Results

Characteristics of participants

Table 1 summarizes the demographic characteristics of the 172 patients with HCC. 76% of the patients were males, with a mean age of 61.7 years, ranged from 21 to 90 years. Surgery was the major (73%) treatment modality among the patients. 79% of the participants were from outpatient clinics.

Internal consistency

The Cronbach's alpha coefficients for the four domains of WHOQOL-BREF ranged from 0.67 to 0.82. It suggested that items within domains of WHOQOL-BREF were moderately internally consistent. The alphas obtained for the entire WHOQOL-BREF, EORTC QLQ-C30 instruments were 0.91, and 0.89, respectively.

Convergent validity

Correlations between the corresponding subscales of WHOQOL-BREF and EORTC QLQ-C30 ranged from r =0.16 for the social domain (very poor agreement) to r =0.65 for the physical domain (good agreement), as shown in Table 2. Some symptom subscales of EORTC QLQ-C30, including pain, fatigue, insomnia, and financial problems, were significantly correlated with the corresponding items of WHOQOL-BREF, ranging from r =0.45 for pain to r = 0.76 for insomnia. In addition, the four domain scores of WHOQOL-BREF were all correlated significantly with patients' self-rated health status/happiness (Spearman's r range, 0.26 to 0.61 and 0.34 to 0.66 across domains, respectively, all $P < 0.01$), and also moderately correlated with utility measures using *VAS* (Table 3).

Significantly moderate correlations were found between *SG* utility and physical, psychological and environment domains of WHOQOL-BREF. The items in the WHOQOL-BREF that were significantly correlated with SG utility included physical safe (r = 0.32), self-esteem (r = 0.30), sleep (r = 0.29), sexual life (r = 0.28), positive feeling (r = 0.27), energy (r = 0.27), pain, spirit, thinking, body image, information, morbidity, activities of daily living (ADL), work, personal relationship, social care, negative feeling, and eating. But medical dependence, financial, social support, home environment, transportation, and being respected were not associated with SG utility.

Content/Construct validity

The four domain scores were significantly correlated with the global QOL (ranging from 0.36 for physical domain to 0.48 for psychological domain, all $P < 0.01$) and the general health (ranging from 0.25 for environment domain to 0.45 for physical domain, all $P < 0.01$).

Item-domain correlations ranged from 0.56 for pain to 0.83 for activities of daily living (physical domain), from 0.49 for negative feeling to 0.75 for self-esteem (psychological domain), from 0.74 for sexual life to 0.79 for personal relationship (social domain), from 0.49 for social care to 0.66 for leisure (environment domain). The items with similar construct such as pain, fatigue, insomnia, and financial problems were moderately to highly correlated between WHOQOL-BREF and EORTC QLQ-C30 (r range, 0.45 to 0.76, all $P < 0.0001$). Exploratory factor analysis revealed similar four factors (physical, social environment, psychological, and other environment) that corresponded to the structure of WHOQOL-BREF domains.

Discriminant validity

Table 4 shows the comparison of mean QOL scores between patients with HCC and healthy controls, patients who received surgery and non-surgical treatment. The items of QOL significantly affected in the HCC patients compared with the healthy controls included energy, sleep, morbidity, medical dependence, work (physical domain), body image (psychological domain), sexual life, but showed better scores in social support, home environment, social care, information, physical environment, transportation and eating (environment domain).

The SG utility was higher in the patients who underwent surgery with significantly better condition in fatigue, appetite loss and constipation. Global health measured by the WHOQOL-BREF, altogether with items of medical dependence, positive feeling, body image, spirit and physical safe were significantly better in the surgery group. The items of WHOQOL-BREF are apparently more widely covered, and more sensitive in differentiating surgery and other treatment. But the EORTC QLQ-C30 was more specific in detecting difference in physical symptoms between surgery and non-surgical treatment, such as fatigue, appetite loss and constipation.

The outpatients had significantly higher scores than inpatients in the aspects of physical, environment, global QOL in WHOQOL-BREF (especially in terms of pain, positive feeling, leisure) after controlling for gender and age. With the EORTC QLQ-C30 instrument, the inpatients had poorer global health/QOL, physical function, role function, emotional function, social function, and more affected in fatigue, nausea/vomit, pain, insomnia, appetite loss, and financial problems after adjustment for gender and age.

Patients were classified into three groups according to disease duration: (1) those who had HCC less than one year, (2) between 1 and 3 years, and (3) more than three years. Significantly decreased HRQOL in aspects of *SG* utility, physical and environmental domains, and global QOL was observed in patients diagnosed within one year compared with the other duration groups and the results were consistent after adjustment with age and gender.

Discussion

This is the first study to validate QOL measurement of patients with HCC in Taiwan using multidimensional psychometric profiles and utility measures. Two HRQOL

instruments were used for measuring health profile of patients with HCC in our study: one is WHOQOL-BREF, a generic instrument; the other is EORTC QLQ-C30, a cancer-specific instrument. The latter was more sensitive to detect cancer-related symptoms, especially for inpatients, and therefore it may be more responsive to clinically important changes and more useful in assessing HRQOL in the clinical trial setting, but it may not allow comparison among different diseases other than cancer. Through cross-validation with EORTC QLQ-C30, we found that WHOQOL-BREF can be a valid QOL instrument with some items to differentiate between surgery and non-surgery, at the same time allowing a wider range of diseases and conditions to be compared. Cross-cultural comparison of various diseases worldwide may be a potential research topic using WHOQOL-BREF instruments [15].

The *SG* method involves making decision under uncertainty. Utility measured using the *SG* method can be linked to a theoretical foundation in the von Neumann-Morgenstern expected utility theory, and therefore is the preferred estimate for cost-effectiveness analysis under condition of uncertainties [16]. However, it was difficult for some elderly patients in our study, especially less educated, to have valid responses to hypothetical scenarios of medical conditions. Thus, we found that the correlations of *SG* utility with WHOQOL-BREF domain scores were lower compared with those of *VAS*.

The subjective utilities measured by *VAS* and *SG* methods for patient with HCC were around 0.6 and 0.8, respectively, while the objective QOL weights from the viewpoints of experts ranged from 0.2-0.49 [7]. Our data suggested that patients would feel much better than experts' judgment. However, the discrepancy may also come partially from different degree of disease severity and patient selection.

Caution should be taken in interpreting our results in that the available respondents may tend to over-estimate QOL of HCC. These 172 participants comprised a consecutive sample of all patients with HCC at the NTUH because a random sampling was not practical due to budget constraints and patient availability. Since these patients were recruited consecutively during the 2-month study period, they were a quasi-systematic probability sample from the HCC cohort assuming that most patients were eligible for QOL measurement. In fact, 79% of the respondents were collected at the outpatient clinics and they were very responsive to our survey. However, HCC patients currently with decompensated hepatic failure, hepatic encephalopathy, under hospice care in the terminal stage, or those suffering from other severe medical complications were hardly feasible for QOL measurement. Thus, our QOL data may represent HCC patients who were more stable and better QOL measures.

Acknowledgement

We are indebted to our colleagues in the Department of Medical Records for their excellent work in cancer registry system. We would like to thank Dr. Jing-Shiang Hwang for statistical consultation. We also thank Ms. Li-Chen Chen for her assistance in patients interviewing. Lukas J.-H. Lee was a recipient of an NHRI MD-PhD and DDS-PhD predoctoral fellowship (RE89M003) during January, 2001-July, 2002. This study was

supported in part by the National Science Council of the Executive Yuan (grant no. NSC91–2320–B–002–082–M56) and the National Health Research Institute (grant no. NHRI-EX92-9204PP).

References

1. Parkin DM, Whelan SL, Ferlay J,Raymond L, Young J. Cancer Incidence in Five Continents, Vol. VII. IARC Scientific publications No. 143. Lyon: IARC, 1997.
2. Chen CJ, Lee SS, Hsu KH, Tsai SF, You SL, Lin TM. Epidemiologic characteristics of malignant neoplasms in Taiwan. I. All cancer sites. J Natl Public Health Assoc (ROC) 1988; 8:59-71.
3. El-Serag HB, Mason AC. Rising incidence of hepatocellular carcinoma in the United States. N Engl J Med 1999;340:745-750.
4. Befeler AS, Di Bisceglie AM. Hepatocellular carcinoma: diagnosis and treatment. Gastroenterology. 2002;122:1609-1619.
5. WHOQOL Group. Development of the WHOQOL: Rationale and current status. Int J Mental Health 1994; 23: 24-56.
6. Testa MA, Simonson DC. Assessment of quality-of-life outcomes. N Engl J Med 1996;334:835-840.
7. Tammy O, Tengs TO, Wallace A. One thousand health-related quality of life estimates. Medical Care 2000;38:583-637.
8. Carr AJ, Higginson IJ. Are quality of life measures patient centred? BMJ 2001;322:1357-1360.
9. Yao G, Chung CW, Yu CF, Wang JD. Development and verification of validity and reliability of the WHOQOL-BREF Taiwan Version. J Formos Med Assoc 2002; 101:342-351.
10. WHOQOL-Taiwan Group. Introduction to the Development of the WHOQOL-Taiwan Version. Chi J Public Health (Taipei) 2000;19:315-324.
11. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JCJM, Kaasa S, Klee MC, Osoba D, Razavi D, Rofe PB, Schraub S, Sneeuw KCA, Sullivan M, Takeda F. European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993;85:365-376.
12. Chie WC, Yang CH, Hsu Chiun. Introduction of the EORTC disease-specific quality of life questionnaires for cancer patients (Chinese). Formosan J Med 2002;6:220-227.
13. Gold MR, Siegel JE, Russel LB, Weinstein MC. Cost-effectiveness in health and medicine. New York: Oxford University Press, 1996.
14. Littell RC, Freund RJ, Spector PC. SAS System for linear models. 3rd edition. Cary, NC: SAS Institute, 1991.
15. Saxena S, Carlson D, Billington R. WHO quality of life assessment instrument (WHOQOL-Bref): the importance of its items for cross-cultural research. Qual Life Res 2001;10:711-721.
16. Torrance GW. Designing and conducting cost-utility analyses. In: Quality of life and pharmacoeconomics in clinical trials, 2nd edition. Spilker B eds. Philadelphia: Lippincott-Raven Publishers ; New York, NY: Raven Press, 1996: 1105-1111.

Table 1. Demographic characteristics of 172 patients with HCC

Characteristics	n (% of patients)
Male Gender	130 (75.6)
Age (years)	
≥ 65	76 (41.2)
Range	21 – 90 yr
Mean ± SD	61.7 ± 12.3 yr
Education of high school or more	83 (48.3)
Married	146 (84.9)
Have current job	69 (40.1)
Personal income per month	
None	65 (38.5)
Less than NT$ 40000	54 (32.0)
More than NT$ 40000	50 (29.6)
Disease duration	
≤ 1yr	35 (20.4)
1-3 yr	78 (45.4)
≥ 3 yr	59 (34.3)
Outpatient	136 (79.1)
Treatment	
Surgical	126 (73.3)
Medical	42 (24.4)
Supportive	4 (2.3)
Diagnosis during 2001-2	35 (20.3)
Interview Method	
Self-Administ.	73 (42.4)
Interviewer-Assist.	93 (54.1)
Proxy-Administ.	6 (3.5)

Table 2. Pearson's correlations between WHOQOL-BREF domains, EORTC QLQ-C30 functional/symptom scales, and utility measures

	WHOQOL-BREF domains and global QOL/general health facet								Utility measurement	
EORTC QLQ-C30	Physical	Psychological	Social	Social (TW)	Environment	Environment (TW)	Global QOL	General Health	Utility (VAS)	Utility (SG)
Global health status / QoL	0.473**	0.396**	0.207*	0.257**	0.349**	0.379**	0.426**	0.355**	0.574**	0.307**
Physical functioning	0.651**	0.409**	0.160†	0.189†	0.301**	0.300**	0.169†	0.288**	0.476**	0.196†
Role functioning	0.402**	0.185†	0.033†	0.038†	0.161†	0.180†	0.243*	0.224*	0.294**	0.212*
Emotional functioning	0.463**	0.393**	0.232*	0.221*	0.390**	0.429**	0.270**	0.316**	0.413**	0.318**
Cognitive functioning	0.500**	0.437**	0.155†	0.157†	0.328**	0.357**	0.121†	0.218*	0.399**	0.263**
Social functioning	0.409**	0.267**	0.160†	0.215*	0.302**	0.359**	0.230*	0.253**	0.345**	0.205*
Fatigue	-0.639**	-0.401**	-0.166†	-0.210*	-0.313**	-0.364**	-0.183†	-0.322**	-0.401**	-0.238*
Nausea / Vomiting	-0.152†	-0.196*	-0.056†	-0.119†	-0.240*	-0.258**	-0.219*	-0.165*	-0.258**	-0.244*
Pain	-0.467**	-0.331**	-0.141†	-0.115†	-0.284**	-0.325**	-0.241*	-0.286**	-0.292**	-0.245*
Dyspnoea	-0.408**	-0.393**	-0.263**	-0.267**	-0.301**	-0.308**	-0.193†	-0.224*	-0.298**	-0.220*
Insomnia	-0.482**	-0.353**	-0.108†	-0.162†	-0.276**	-0.329**	-0.200*	-0.327**	-0.322**	-0.232*
Appetite loss	-0.372**	-0.182†	-0.048†	-0.103†	-0.270**	-0.288**	-0.215*	-0.145†	-0.221*	-0.218*
Constipation	-0.043†	-0.133†	-0.167†	-0.196†	-0.012†	-0.010†	-0.075†	0.015†	-0.142†	-0.005†
Diarrhea	-0.262**	-0.142†	-0.119†	-0.198*	-0.203*	-0.224*	-0.140†	-0.143†	-0.318**	0.002†
Financial Problems	-0.322**	-0.317**	-0.279**	-0.338**	-0.490**	-0.525**	-0.188†	-0.166†	-0.257**	-0.163†
Utility measurement										
Utility (VAS)	0.591**	0.554**	0.399**	0.477**	0.502**	0.499**	0.433**	0.479**	1	0.307**
Utility (SG)	0.276**	0.375**	0.211*	0.172†	0.273**	0.292**	0.364**	0.335**	0.307**	1

† $p<0.05$ * $p<0.01$ ** $p<0.001$

Table 3. Spearman's correlations between WHOQOL-BREF domains and self-rated health/happiness

	Self-rated heath	Self-rated happiness	Utility (VAS)	Utility (SG)
WHOQOL-BREF				
Global QOL	0.351**	0.436**	0.366**	0.392**
General health status	0.492**	0.522**	0.438**	0.383**
Domain scores				
Physical	0.613**	0.656**	0.536**	0.213*
Psychological	0.536**	0.594**	0.536**	0.271**
Social	0.264**	0.344**	0.432**	0.225*
Social (TW)	0.279**	0.364**	0.480**	0.152†
Environment	0.423**	0.460**	0.464**	0.258**
Environment (TW)	0.416**	0.458**	0.450**	0.272**
Utility measurement				
Utility (VAS)	0.547**	0.533**	1	0.306**
Utility (SG)	0.291**	0.320**	0.306**	1

† $p<0.05$ * $p<0.01$ ** $p<0.001$

Table 4. Comparison of mean Quality-of-life scores† between surgery and non-surgery, HCC patients and healthy controls

	Surgery	Non-surgery	Healthy Controls	HCC patients
No. of patients				
WHOQOL-BREF				
Global QOL	68.41	66.52	68.80	67.91
General health status	61.90*	50.43	70.61	58.84*
Physical	60.07	54.76	70.83	58.65*
Psychological	59.67	55.30	60.71	58.50
Social	62.65	63.72	63.66	62.94
Social (TW)	62.10	63.32	62.41	62.43
Environment	64.24	61.14	56.72	63.41*
Environment (TW)	64.14	61.55	56.43	63.44*
EORTC QLQ-C30				
Global health status / QoL	65.48	60.14		64.05
Physical functioning	78.73	73.77		77.40
Role functioning	87.30	79.71		85.27
Emotional functioning	76.72	73.01		75.73
Cognitive functioning	76.98	74.64		76.36
Social functioning	75.79	73.19		75.10
Fatigue	67.11*	58.21		64.73
Nausea / Vomiting	95.24	95.29		95.25
Pain	79.10	76.81		78.49
Dyspnoea	87.04	84.06		86.24
Insomnia	64.02	58.70		62.60
Appetite loss	88.62*	78.26		85.85
Constipation	90.48*	81.88		88.18
Diarrhea	83.86	84.78		84.11
Financial Problems	85.48	81.16		84.31
Utility measurement				
Utility (VAS)	66.15	62.83	--	65.26
Utility (SG)	83.56*	74.49	--	81.25

* $p<0.05$ (based on Student's t test)

† all scores were transformed to a 0-100 metric, using linear transformation

Table 4. Comparison of mean Quality-of-life scores† between healthy controls and HCC patients, surgery and non-surgery (Continue)

Domain	Facet	Healthy Controls	HCC patients	HCC Surgery	HCC Non-surgery
Physical	F1.Pain	75.61	76.16	77.46	72.61
Physical	F2.Energy	69.48	61.16*	62.22	58.26
Physical	F3.Sleep	70.05	59.53*	59.37	60.00
Physical	F9.Mobility	80.95	69.07*	70.16	66.09
Physical	F10.ADL	71.98	68.84	70.32	64.78
Physical	F11.Medication Dependent	95.33	66.40*	69.21*	58.70
Physical	F12.Work	74.11	67.72*	68.73	64.89
Psychological	F4.Positive Feeling	53.99	55.70	57.46*	50.87
Psychological	F5.Thinking	64.23	65.23	64.60	66.96
Psychological	F6.Self-Esteem	72.96	70.81	71.43	69.13
Psychological	F7.Body Image	80.66	72.67*	74.29*	68.26
Psychological	F8.Negative Feeling	67.55	64.65	64.76	64.35
Psychological	F24.Spirit	71.60	70.81	72.54*	66.09
Social	F13.Personal Relationship	70.71	71.63	71.90	70.87
Social	F14.Social Support	70.90	74.07*	73.49	75.65
Social	F15.Sex	71.37	64.56*	64.60	64.44
Social*	F25.Being Respected*	67.30	69.42	68.73	71.30
Environment	F16.Physical Safe	66.16	66.98	68.73*	62.17
Environment	F17.Home Environment	70.70	75.93*	76.03	75.65
Environment	F18.Financial	61.42	62.79	61.90	65.22
Environment	F19.Social Care	70.42	76.28*	77.30	73.48
Environment	F20.Information	66.79	70.17*	70.95	67.83
Environment	F21.Leisure	60.85	64.07	65.87	59.13
Environment	F22.Physical Environment	55.85	64.53*	64.76	63.91
Environment	F23.Transportation	61.80	75.47*	75.08	76.52
Environment*	F26.Eating*	74.15	79.53*	80.16	77.83

* $p<0.05$ (based on Student's t test)

† all scores were transformed to a 0-100 metric, using linear transformation

附錄三

出席國際會議心得報告及發表論文

加拿大出國報告〔91.08.09-91.08.26〕

王榮德

此次參加世界流行病學大會 The World Congress of Epidemiology 及國際環境流行病學協會年會 ISEE〔International Society of Environmental Epidemiology〕主要有以下幾個心得：

〔1〕AIDS 治療成本效性分析

在 The World Congress of Epidemiology 中，第一天開會典禮即是由一位專門在替 AIDS 找資源及經費的學者演講，他指出在 2010 年會有 2 千萬位孤兒因爲父母死於這個疾病，2020 年將再有 8 千萬人死於這個病。在幾個非洲國家中的一個波札那，差不多 39%的成人是 HIV 感染，預期壽命大概只有 30-40 歲；在沙哈拉沙漠以南的非洲國家約有 1500 萬位以上的得病婦女，因爲沒有錢而得不到醫療的支援。所以我認爲我們那篇和方啓泰醫師一起合作估算愛滋病患醫療費用使用及存活分析的論文應該早一點發表，其中第一篇可以先估算目前這樣的治療方式可以活多久；第二篇是方醫師的研究發現 1997 年 4 月雞尾酒療法以後疾病發生率(incidence rate)的增加，比 1997 年 4 月以前的發生率取對數後之斜率較爲平緩，顯示雞尾酒療法的療效；第三篇應該來估算多少百分比的帶原率以下的時候，就應該要全面在全世界可以治療此病的國家推動治療的方法。

有一位美國機構派在日內瓦聯絡工作的醫師，他收集了全世界的 AIDS 個案的情形，但台灣的資料只有到 1995 年，他希望我們可以提供更新的資訊以供分析。在台灣 AIDS 的增加情形並沒有很快，我想是因爲我們全面提供治療的藥物，所以我們的資料要趕快發表，可能會對世界上有貢獻。

〔2〕Surveillance of Risk Factors

世界衛生組織現在有一套針對非傳染病〔noncommunicable diseases〕risk factor 的 surveillance 方法，已經標準化訂定使用程序，這也是我們國民健康局應該要去做的方向，以後我們工廠的健康促進、社區的健康促進通通要參照其問卷方式收集這樣的資料。他們的 surveillance 分三個層次，第一步驟是只有問卷而已，來看健康促進做得好不好，如抽煙、喝酒、營養、身體活動的調查；第二步驟再加上物理測量〔physical

measurements〕，測量身高、體重、腰圍、血壓；第三步驟再加上血醣、膽固醇、三酸甘油脂。以後我們的問卷應該就是要加上這些資料以與世界衛生組織同步。WHO 現在的標準問法，也可以從網頁 http://www5.who.int/noncommunicable-diseases/main.cfm?p=0000000384 去看更詳細的資料。人家的研究已經進入行爲的領域，我可能還會再找個機會跟國民健康局翁瑞亨局長談這個問題，未來各個地方如果要做健康促進一定要收這套較有共識的監測資料。在做了上述三個層次資料後，再更深入則是要做結果之評估，也就是針對會發生什麼病，去計算此病之存活時間與生活品質〔quality of life〕以及計算不同的預防工作或醫療服務之成本效性〔cost-effectiveness〕看每個疾病會損失多少 QALY。例如用平均一個高血壓的病人會花多少錢，高血壓病人可以活多少年，生活品質變化如何；再把兩者跟醫療費用結合之後，即可作成本效性評估。我們目前的研究方法與發現在世界上大概有潛力可以領先。甚至我們從前面這些 risk factor，我們可能可以推估未來 psychometric score〔心理計量分數〕會損失多少。

健康促進有一個部分可以做的場合是在工廠裡面，未來政府一定要花錢在這個上面，才可以減少一部份健保財政上的負擔。去年到約克開健康經濟學的會議之後，我才發現台灣健保的工作其實已經是世界上做得數一數二的，但是立法委員爲了選票還是拼命阻止費率的調整。我到加拿大的時候發現很多華人都還保留台灣健保的身分，很多人是生了病之後就回到台灣治療，加拿大的制度是論人計酬，整個哥倫比亞大概 300 萬人口，但是電腦斷層儀卻只有四架，如果比較緊急的時候就必須坐飛機到美國去做，這樣的制度與設備對於民眾來說真的是很不方便。

健康促進不僅可以在社區做，在工廠也可以做，在工廠把員工的健康管理好之後，對於製程、經營的管理也會比較好。世界上好像極少有國家是像我們國家的部分半導體廠商一樣是 12 個小時的工作輪替，所以我們現在碩士班學生黃文昌的論文一定也要趕快想辦法可以發表，讓大家知道這樣的工作輪替對於健康的影響。

明年我們要想辦法在 UC Berkley 的 International Conference on Economics 把抽煙的影響做個估計，因爲全世界對這個領域都會有興趣，此次大會遇到有一部份流行病學家

也在想經濟學家會不會對這個問題也有興趣可以一起合作，事實上我覺得 outcome evaluation 當中如果存活情形了解之後，再結合計算每年這個疾病大概會花多少錢，就可以得到一個估計，馬上可以給政府對於煙稅、酒稅應該抽多少提供一個參考。

〔3〕健康衝擊評估 Health Impact Assessment

Health Impact Assessment 在歐洲的 WHO 已全面在推動了，我也跟本所的詹所長講好，要把我們原先預定成立的職業病與環境病中心改名爲 Center for Health Risk Assessment and Management，研究 Health Impact。原先歐盟的國家政策在分析時只有研究環境衝擊評估 Environmental Impact Assessment，但是環境衝擊評估裡面一定也要做健康衝擊評估；衝擊多大的測量，一個就是生命損失有多少，另一個就是 QALY 的損失有多少，例如台灣在 1998 有一個國家能源政策的會議，當時我就主張要有健康衝擊的評估，這樣才不會把台灣一直往後拖。我覺得以後就是要用健康風險評估與管理來吸引全亞洲其他國家的學生來這裡讀博士班。其實明年就會有一個泰國的護士要來這裡作博士後研究，她是我當初去泰國當客座教授的時候，就一同以她的名義向世界衛生組織申請一個有關乳癌的研究。此次去開會也遇到中山醫學院公衛系一位呂宗學老師，他說乳癌的篩檢現在也有很大的爭議，就像荷爾蒙療法一樣。他建議從這個角度做切入的時候，說不定之前的那篇乳癌研究的文章就可以得到發表。目前歐盟國家規定所有的國家政策都一定要有健康衝擊評估，這也是將來我覺得台灣應該走的方向。

〔4〕Precautionary Principle

這次有個展覽在談 DES〔diethylstilbestrol〕，這個藥物在 1937-1938 年被一位化學家發現，1941-1947 因爲哈佛大學有對婦產科教授覺得它可以安胎，陸續被 500 萬人使用，有些還是在懷孕期間吃了這個藥，結果有些生出來的女童在 12、3 歲就出現有陰道癌，男童會有小便上的困難或是夭折，加拿大有學者就把這些人的照片、家族史、所有的故事都以展示的方式發表出來，讓大家可以了解這件事的影響。這也讓我想到這次整個會議的重點之一在討論 precautionary principle，一定要事情未發生前預先就很小心。美國 WHI 的計劃預計針對 5 萬名婦女，進行 10 年有關荷爾蒙療法的研究，目前進行了 5 年多，他們把現有收集的資料拿出來分析，結果發現當中乳癌、心臟血管病的發生率

增加。

這次 ISEE 的演講裡面也有討論基因工程研究出來的那些食物吃了到底好不好，如果是基於 precautionary principle，我們就必須特別小心，因爲這是還沒有定論的。

Precautionary principle 是完全基於西方醫學倫理，他有四大根基，一個是 autonomy，尊重自主的原則；第二個是 non-maleficence，不加害人的原則，這就是 first do no harm，爲什麼藥物要很嚴格的評估，就是先要評估 safety 再評估 efficacy；第三個是 beneficence，對人有益的原則；第四個才是 justice，正義的原則。醫學倫理的傳統四個原則都是考慮 first do no harm 在 beneficence 之前，最近比較有一點爭論。但是傳統下來都是 first do no harm or evil，其次才是 reduce harm or evil，再其次是 prevent harm or evil，最後才是 do something beneficial to people。所以醫生的各種措施跟藥物都應該要先了解他的安全性才可以來做使用。同樣道理也應用到核能的事件上，核能的事情我覺得一開始他們就是沒有 precaution，像美國、蘇聯全世界核能最強的國家都還是有可能發生意外。Precautionary principle 另一方面也可以運用在 health promotion，preventive service 你也要用 Precautionary principle，先要不能對人有害。

〔5〕Climate Change

這次的會議的另一個主題在討論全球氣候變遷會對人體造成危害，像是會增加很多的洪水跟土石流；乾旱會增加；病媒造成的疾病會如瘧疾也會增加；目前台灣的登革熱也有可能會跨過大甲溪以北。這是本國要注意的。

Quality of Life Research 00: 000–000, 2003.

Integrating health profile with survival for quality of life assessment

Jing-Shiang Hwang[1] & Jung-Der Wang[2,3]
[1]*Institute of Statistical Science, Academia Sinica;* [2]*Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University. College of Public Health, Taipei (E-mail: jdwang@ha.mc.ntu.edu.tw);* [3]*Department of Internal Medicine, National Taiwan University Hospital, Taiwan*

Accepted in revised form 10 January 2003

Abstract

In cohort studies or clinical trials, measurements of quality of life (QoL) were averaged across available individuals for each group at given points in time to produce single measures for comparisons. However, estimates of these single measures may be severely biased if substantial mortality occurs over time. The objective of this study is to develop a method that integrates QoL measurement and survival for long-term evaluation of health services. We defined a mean QoL score function over time for an index population as the average QoL score of all individuals both alive and dead at each time point in the population. While a living subject's QoL can be assessed by asking one's subjective preference, the score of a decedent can be assigned a fixed value depending on the specific facet on health profile. The mean QoL score function over time is reduced to a single measure of expected cumulative QoL score, which is the area under the curve of mean QoL score function over a given time interval and can be estimated by taking a random sample from a cross-sectional survey. For the QoL score function to be extrapolated to life-long, it requires the assumption that the disease causes premature death or a long-term moderate impairment of QoL. We provided methods and computer programs for estimating mean QoL score functions and the reduced single measures for use in comparisons. A cohort of 779 breast cancer patients from Chiangmai, Thailand were followed for 12 years to demonstrate the proposed methods. The data included the 12-year complete survival records and QoL scores on 233 patients collected from a cross-sectional survey using WHOQOL questionnaire and standard gamble method. The expected cumulative QoL scores using utility and psychometric scales were compared among patients in four groups of clinical stages in this cohort for time from onset up to 12 years and life-long. We conclude that such an integration of QoL measurement with survival can be useful for the evaluation of health service and clinical decision.

Key words: Health profile, Monte Carlo method, Quality-adjusted life year, Quality-adjusted survival

Introduction

Health-related quality of life (HRQoL) assessment is increasingly used in clinical trials and other health outcome evaluation [1]. HRQoL is generally defined as the individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [2]. It is a multidimensional concept incorporating both functional status and the individual's perception of health. Thus, many generic and condition-specific questionnaires have been proposed to assess these effects [3–5]. These QoL measures are similar in that each expresses the effects of medical care in terms that can be reported directly by a patient. However, the rationales for the methods differ considerably. Most of the available psychometric measures include multiple dimensions such as physical functioning, psychological status and social relationships in order to create a profile of patient outcomes. While utility-based methods

Journal : QURE SPS Article No. : 50001 | Dispatch : 1-8-2003 | Pages : 13
PIPS No. : 5118808 | ☐ LE | ☑ TYPESET
MS Code : QURE 50001 | ☑ CP | ☐ DISK

assign a value to a specific health state to reflect global impact of that state on the patient's overall QoL [6–9].

Since a patient's QoL continuously fluctuates or changes over time, many HRQoL studies have considered summarizing measurement and analysis from a time perspective. In clinical trials, HRQoL assessments were often conducted by administering profile questionnaires at multiple time points before, during, and after an intervention, with a focus on summarizing or showing the changes in QoL over time (or longitudinally) and across different individuals for group comparison [10]. In practice, the summary measures are often constructed to obtain population mean QoL score estimates at given time points using sampled data from each population. However, it has been a noteworthy problem that the estimates can be biased if there is a substantial proportion, say, 40%, of mortality in a study over time [11]. There is also argument regarding the assignment of scores to those who die in the study. Thus, so far there have been relatively few methods developed for summarizing health profile measures taking account of mortality or survival across time during longitudinal follow-up.

In this study, we first clarify the definition of mean QoL score function over time for an index population, which is a function of average score across all individuals both alive and dead at a given time in the index population. While a living subject's QoL can be assessed by asking one's subjective preference, the score of a decedent can be assigned a fixed value depending on the specific facet on health profile. We then show that the mean QoL score function can be presented in terms of survival function and average QoL score function of the sub population of living individuals. When the survival data are complete, the survival function can be estimated quite accurately using available techniques. The average QoL score function of the sub population of living individuals can be estimated by kernel-smoothing the data of a random sample from a cross-sectional survey of QoL on the living individuals, which was demonstrated in a previous simulation study by Hwang et al. [12]. When the data are not complete such as in follow-up studies with heavy censoring, the mean QoL score functions can be accurately estimated over time only up to the end of the follow-up. Then, the lifetime score for the whole population can also be extrapolated by a Monte Carlo method proposed by Hwang and Wang [13]. Therefore, we can obtain relatively accurate mean QoL score function estimates, which can be further plotted against the whole life span for specific QoL domain or item scales in different treatment groups. When the QoL score function is replaced by utility function, the area under the whole life span is the expected quality-adjusted life expectancy (QALE).

Data from a cohort of 779 cases of breast cancer from Chiangmai, Thailand followed for 12 years were used as an example to illustrate the proposed methods [14]. The cohort was stratified into four groups with different clinical stages. To the end of the follow-up, June 30, 1997, the survival and mortality of the 779 patients were well recorded. Measurements of QoL were obtained through a cross-sectional survey on 223 patients during 1996–1997 using utility measurement of standard gamble and the questionnaire of World Health Organization quality of life (WHOQOL). We computed and compared expected QALYs in utility and psychometric scores for the four groups of cancer patients for time up to 12 years and lifelong.

Methods

In this section, we first clarify the definition and interpretation of mean QoL function over time for an index population and then introduce methods for estimating the function. Let $q_i(t)$ be the unobserved QoL score at time t since the onset of a specific disease or health condition on the ith individual patient in an index population. The QoL score can be measured using the utility or health profile instrument. In most QoL measurement, we often can rescale the QoL score to a value between 0 and 1, in which 0 represents the worst health status and 1 represents the perfect health. If a patient dies during the study, a constant value between 0 and 1, denoted by δ, could also be assigned after that time point for the patient. The population mean QoL score at each time t is constructed straightforwardly by the population average, $Q(t) = \frac{1}{N}\sum_{i=1}^{N} q_i(t)$, where N is the size of the index population. Let $G(t)$ denote the set of

subjects in this index population who are still alive at time t. The size of $G(t)$ is denoted by $M(t)$. Note that in the beginning of time 0, $M(t) = N$. The mean QoL score function over time t for the index population can be rewritten as the sum of scores of those who are still alive plus those who die:

$$Q(t) = \frac{1}{N}\left(\sum_{i\in G(t)} q_i(t) + \sum_{i\notin G(t)} q_i(t)\right)$$
$$= \frac{M(t)}{N} \times \frac{1}{M(t)} \sum_{i\in G(t)} q_i(t) + \frac{N - M(t)}{N} \times \delta.$$

Note that $M(t)/N$ is the survival rate at time t for the index population, denoted by $S(t)$. We may denote $\frac{1}{M(t)}\sum_{i\in G(t)} q_i(t)$ by $Q_s(t)$ representing the average QoL score for the sub population of individuals still alive at time t. We then obtain the following simple equation

$$Q(t) = S(t) \times Q_s(t) + [1 - S(t)] \times \delta$$

which establishes the relationship between population mean QoL score function and survival function. Note that when QoL score is assigned with a constant value of 1 for all living individuals and $\delta = 0$, $Q(t)$ is the survival function for the index population. Therefore, we can interpret the mean QoL score function as quality-adjusted survival function when the QoL score is in the 0–1 scale. More importantly, this equation provides an alternative way of estimating $Q(t)$ by separately estimating the survival function and the mean QoL score function for the sub population of the living individuals. The area under the curve of the mean QoL score function $Q(t)$ plotted against time t over the period $[a, b]$, presented by

$$Q[a, b] = \int_a^b S(t)Q_s(t)\,dt + \delta\int_a^b [1 - S(t)]\,dt,$$

is a common single measure of QoL, with a unit of psychometric score-time, which is conceptually the same as quality-adjusted life year (QALY) for the time period except substituting the utility measurement with health profile scores. This useful measure $Q[a, b]$ is the expected cumulative QoL score, which can be also interpreted as expected quality-adjusted survival time adjusted for the specific score/utility for an index population over the time period $[a, b]$. If the QoL score is a utility measurement, then the measure $Q[0, \infty]$ is exactly the QALE with the unit of QALY. When the QoL is a score from psychometric measurement, then the unit is a score-time, say, score-month or score-year, etc. Namely, it is a psychometric score adjusted by survival function and should specify the time unit for comparative purpose. The proposed formula is a generalization from that derived by Hwang et al. using integration techniques in which δ is restricted to be 0 [12].

To estimate the expected cumulative QoL score $Q[a, b]$, we can conduct on discrete time by dividing the entire time period $[a, b]$ into K disjointed short intervals $[t_{k-1}, t_k)$, $k = 1, K, K$, where $t_0 = a$ and $t_K = b$. The estimate of survival at time t_k, denoted by $\hat{S}(t_k)$, can be easily obtained using common approaches such as Kaplan–Meier method when complete survival data are available. To obtain the estimate of mean QoL for the sub population, $\hat{Q}_s(t_k)$, we only need measurements from a cross-sectional survey on the living individuals, instead of the costly repeated measures, and using kernel smoothing techniques or fitting a non-linear curve to the interviewed scores. The estimate of population mean QoL at time t_k is $\hat{Q}(t_k) = \hat{S}(t_k) \times \hat{Q}_s(t_k) + [1 - \hat{S}(t_k)] \times \delta$. The expected quality-adjusted survival time over the period $[a, b]$ can be estimated using a trapezoidal approximation:

$$\hat{Q}[a, b] = \frac{1}{2}\sum_{k=1}^{K}(t_k - t_{k-1})[\hat{Q}(t_k) + \hat{Q}(t_{k-1})].$$

Extrapolation to lifetime with censored follow-up data

When the data are complete, simulation studies conducted by Hwang et al. showed the estimator is quite accurate [12]. However, especially for follow-up studies with heavy censoring, the mean QoL score function $Q(t)$ for the index population can be accurately estimated only over time up to the end of follow-up. Hwang and Wang have proposed a Monte Carlo extrapolation approach to provide estimate of $Q(t)$ for t beyond the close of follow-up [13]. The main idea of that approach is to borrow information of long-term survival from a reference population matched with the same age and gender

for every individual of the index population. In other words, we can generate a hypothetical reference population composed of exactly the same age and gender distribution through Monte Carlo simulation method from the vital statistics. Then, fit a simple linear regression to the logit of the ratio between $Q(t)$ of the index population and the simulated survival function of the reference population for a certain point in time to the end of the follow-up. Finally, use the predicted line to extrapolate $Q(t)$ beyond the follow-up. On this approach, one must assume that the mean QoL score function $Q(t)$ for the index population at time t should be no greater than that of the reference population [13], which only holds for any disease that results in premature death or affects QoL moderately on a long-term basis. A feedback plot to check the linearity assumption is also provided to assure the validity. Simulation studies have shown that this is a potential approach for estimating mean QoL score function and survival function beyond the follow-up with a certain degree of accuracy. The Bootstrap approach was also proposed to estimate standard errors of the estimates [15]. The authors have provided a free package of S-Plus functions for computing the estimates and standard errors of the estimates for $Q[a, b]$ and other applications [16]. Users only need to input files of survival data, cross-sectional survey data of QoL score, and sample of age and gender from the index population, in addition to a file of life table if extrapolation is needed.

Example of a breast cancer cohort

The detailed information of a cohort of 779 cases of breast cancer who were first diagnosed during 1985–1994 were followed regularly at Chiangmai cancer registry for 12 years was described elsewhere [14]. Briefly, the Chiangmai cancer registry is a population-based registry, co-sponsored by the Chiangmai University Faculty of Medicine and WHO, which actively collected data on cancer patients from one university hospital, 10 private hospitals, and 26 public hospitals in Chiangmai province, Thailand [17]. The cohort has been stratified into four groups with different clinical stages with group sizes 81, 330, 226 and 142, respectively. The average onset age of these 779 patients were 50.3 ± 13.0 years old with a range of 22–95. By the time of censoring, June 30, 1997, there were 75, 244, 106, and 28 patients still alive for stages I–IV, and the 12-year survival rates were 93, 74, 47, and 13%, accordingly. To establish the QoL function curve through time for each stage, we needed to obtain a random sample of 50 in size [12]. In addition, we added 15–25 patients whose duration-to-dates were less than 2 years, because the original cohort no longer collected patients by the end of 1994 and the QoL function was relatively unstable during the first 2 years after diagnosis. A cross-sectional survey was then implemented and the response rate was about 80%. In total, we collected 64, 72, 69 and 28 patients in stages I–IV for HRQoL interview during 1996–1997. Patients were asked to fill out the WHOQOL-100 questionnaire followed by standard gamble method conducted by an interviewer to elicit the utility value of her current health state [8].

The WHOQOL-100 was originally designed by the WHOQOL group, which intended to assess detailed health profile on four domains with 25 facets inquiring about physical/independent, psychological/spiritual, social relationship and environment [2, 18]. Each facet consists of 4 items in which a five point Likert scale (1–5 score) is used. The facet score, given by the sum of its four item scores, ranges from 4 to 20. The domain score is obtained by averaging the facet scores in that domain. In this study we rescaled the domain score by subtracting 4 and then dividing by 16 to a value between 0 and 1 corresponding to the worst and best health status of that domain, respectively. The rescaled score is still a preference measure. But it can be treated as a psychometric QoL score for comparison with the utility measurement obtained from standard gamble method, which also ranges between 0 and 1.

Results

Figure 1 shows the estimated survival, average scores of physical domain of WHOQOL obtained from living patients and the physical domain score-adjusted survival functions over the 12-year follow-up period for the four stages of breast cancer patients. The plots were produced from the free package in which the survival functions were

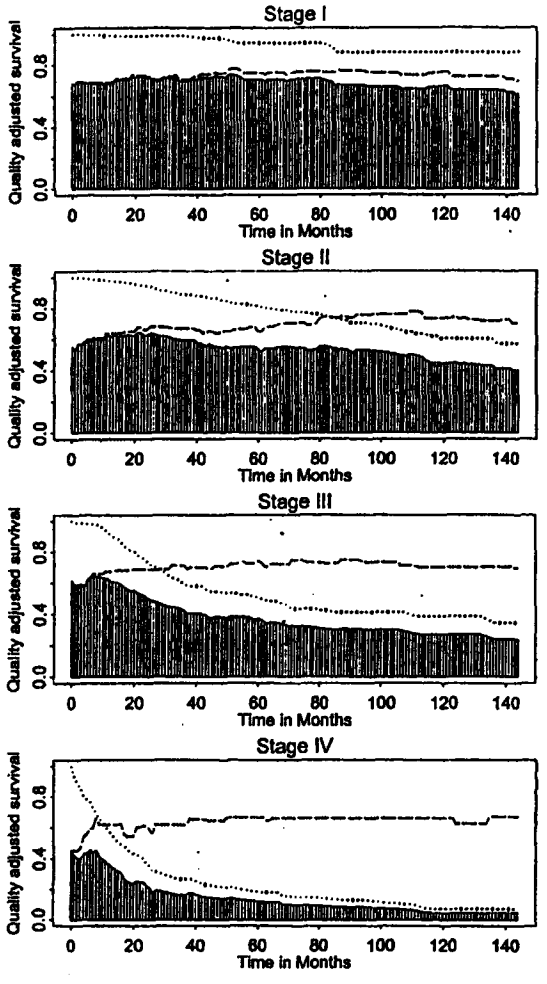


Figure 1. The estimated quality of life adjusted survival functions (solid curves) for stages I–IV breast cancer patients after 144 months of follow-up. Scores from the physical domain of WHOQOL were used for demonstration. The dotted curve is the estimated survival functions. The dashed curve is the estimated average quality of life score of living patients. The shaded area is the expected cumulative physical score-months over the 144 months of follow-up.

estimated using Kaplan–Meier method on the survival data of the breast cancer cohort. The estimated score function for physical domain of each subgroup of living individuals was obtained using kernel smoothing method on the sampled patients with different duration-to-dates. The shaded area under the estimated physical domain score-adjusted survival function in each plot was the expected cumulative physical domain score-time or physical domain adjusted survival time over the 12 years of follow-up. The average QoL scores of physical domain in living patients were usually lower in the first months of follow-up and then slowly increased to stable levels. Because only five stage IV patients survived for more than 5 years, the curve was over-smoothed after 5 years. However, the survival rates were very low for stage IV patients, and the estimated QoL adjusted survival function would not be greatly affected. Table 1 summarizes the results of estimated expected survival in months, expected quality-adjusted survival time adjusted for standard gamble utility, and for physical, psychological, social, and environmental domain scores, respectively, over the 12 years of follow-up and life-long. The estimated 12-year mean survival times are 134, 112, 77 and 33 months for the four stages, accordingly. The expected quality-adjusted survival time adjusted for utility, were higher than those adjusted with the psychometric scores in all the four stages. The 12-year cumulative psychometric adjusted survival for social domain seemed to be the worst domain compared with other QoL domains in WHOQOL, which indicates that social life is the most severely affected.

To extrapolate the mean QoL score function beyond the follow-up of 12 years, we have checked the linearity assumption for logit of the ratio between $Q(t)$ of the index population and the simulated reference population. As examples shown in Figure 2, the assumption seemed to be largely fulfilled for four stages for the last 60 months of 144-month follow-up. Figure 3 shows the estimated QoL adjusted survival functions up to 30 years for the stage I group. The curves against time beyond 144 months were extrapolated using the Monte Carlo approach on a reference group with age and gender matched for stage I group, which were generated from the general population using 1990 vital statistics of Thailand. The patterns of QoL adjusted survival functions over time were similar for utility measure, and psychometric scaling for physical and psychological domains, which shared a constant decreasing rate during this time period. The QoL adjusted survival functions for social and environmental domains behaved to have less decreasing rates. The lower half of Table 1 summarizes the results of estimated expected survival time, quality-adjusted survival

Table 1. The estimates of expected survival time (in months), quality-adjusted survival time (QAST) adjusted for standard gamble utility and psychometric scores obtained from physical, psychological, social and environmental domains during 144 months of follow-up and life-long for breast cancer patients in the four clinical stages.

QoL scale	Stage I		Stage II		Stage III		Stage IV	
	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
Over 144 months of follow-up								
Survival time	134.2	3.8	111.9	2.7	76.9	4.1	33.1	3.8
QAST adjusted for								
Standard gamble	117.7	3.6	92.4	2.9	62.1	3.5	26.7	3.3
Physical score	98.5	3.3	77.0	2.9	53.5	3.1	20.2	2.5
Psychological score	93.4	3.1	74.1	2.2	50.8	3.0	20.9	2.4
Social score	87.4	3.4	75.1	2.2	49.8	3.0	20.5	2.2
Environmental score	91.1	2.9	74.1	2.2	51.3	2.9	20.9	2.5
Extrapolated to life-long								
Survival time	277.5	59.8	166.2	15.3	118.6	17.1	36.9	6.1
QAST adjusted for								
Standard gamble	274.6	39.5	144.0	17.5	104.9	16.5	29.9	5.4
Physical score	215.5	33.2	122.3	16.0	84.0	13.3	22.8	4.1
Psychological score	203.5	30.6	111.9	12.0	74.6	10.4	23.5	4.3
Social score	213.5	42.4	122.9	14.2	82.7	12.3	23.2	3.9
Environmental score	221.8	31.7	118.7	12.9	77.6	12.1	23.5	4.3
Survival time for reference group	379.5	1.8	361.3	1.7	326.8	1.8	313.6	1.9

The standard errors were estimated using the Bootstrap approach. The reference group was created by matching onset ages of patients in each clinical stage group using female Thai vital statistics in 1990.

time adjusted for utility and for the four domain scores of WHOQOL after extrapolation to 50 years or life-long. The estimated life expectancies were 278, 166, 119 and 37 months for the four clinical stages of breast cancer patients. While the survival times for the four reference groups of people with perfect health (or QoL = 1) were 380, 361, 327 and 314 months, accordingly. The results revealed that psychological domain has the smallest life-long score-time for stages I–III, which implies that breast cancer patients need a long-term psychological care.

The results shown in Table 1 were based on the assumption of assigning the dead 0 score. To explore the sensitivity of assigning the death score, we calculated the expected psychological score-time adjusted survival time for the four stages with death score 0.1 and 0.2, respectively. We have chosen 0.2 because of the minimum psychological score of 0.22 found in the 233 sampled patients. The results are summarized in Table 2. The expected adjusted survival time increased as death scores increased. There were limited increased adjusted survival time for stage I patients because of a high survival rate. But the expected life-long adjusted survival time for psychological domain increased from 23.5 score-months with death score 0 to 130.3 score-months with death score 0.2 for the stage IV patients. The result indicates that expected quality-adjusted survival time was very sensitive to the assignment of death score for a disease with high mortality rate.

Discussions

In clinical trials, measured QoL scores using utility or psychometric health profile methods were usually compared for available patients at specific time points: before, during, and at the end of the trials. Summary measures over time were usually used for comparisons and reports. However, patient's survivorship is either ignored or considered separately from the observed QoL scores [19]. The ignorance of mortality has caused a serious problem of bias in the summarized QoL measures. In this study, we proposed a clear definition of mean QoL score function over time for an index population, which is the average score of all patients both alive and dead at a given time. Moreover, we

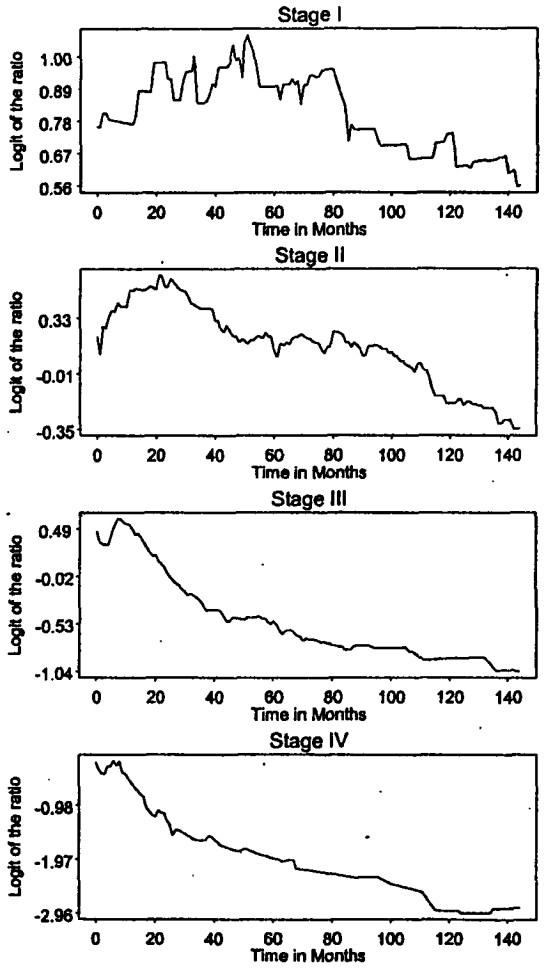


Figure 2. The logit of the ratio between the estimated mean physical QoL score function and survival function for reference population by clinical stages plotted against time over the 144 months of follow-up.

have also shown that the mean QoL score is the sum of following two products: the average score of surviving patients multiplied with population survival rate, and the mortality rate multiplied with the average score of decedents after assigning a fixed value. The survival of the population is then naturally integrated with QoL measure so that we can interpret the mean QoL score function as the QoL adjusted survival function. The QoL adjusted survival function is further extended to define the cumulative QoL score for an index population over a time duration, which can supplement the drawback of only comparing one or several specific time points. When the QoL score is rescaled to 0–1, life-long cumulative QoL score is equivalent to the commonly used expected quality-adjusted survival time in cost-effectiveness analysis [20]. We have provided a general form and procedures for calculating expected quality-adjusted survival time using both utility and health profile measures. Most HRQoL studies have assigned 0 score to the dead, although many people may disagree and there seems to have no consensus. Our proposed method allowed researchers to assign different constant values to the decedents according to different items or domains in health profile assessment. We propose that such a value had better be less than the lowest value of those alive during sensitivity analysis. Since the lowest possible score in our study for different domains was 0.22, we decided to assign scores of 0, 0.1 and 0.2 for sensitivity analysis of scoring the dead subjects, which therefore can be implemented to provide additional information for a more delicate clinical decision-making.

Although we have provided a clear interpretation of the combination of QoL with survival through the definition of population mean QoL, some practical problems are worth further clarification. The major critique on the combination of QoL and survival is the potential dependence of QoL on survival [19]. In general, patients who are about to die or to be lost to follow-up tend to have worse current scores, whereas those who survive longer tend to have somewhat better current scores [11, 20]. It indicates that the average scores obtained from a sample of the surviving patients might produce a positive bias because patients with worse scores may be less represented in the sample. Hence, a (stratified) random sample of currently surviving patients, which cover all different duration-to-dates or times-after-diagnosis, should be essential to an accurate measure for the combination of QoL measures and survival. In other words, our current approach of conducting a cross-sectional survey with kernel-smoothing the data to estimate the mean QoL function at different duration-to-dates may not be very accurate. It can be further improved by repeated measurements for the same cohort followed by constructing a mixed-effects model and adding more predictors of QoL as fixed factors.

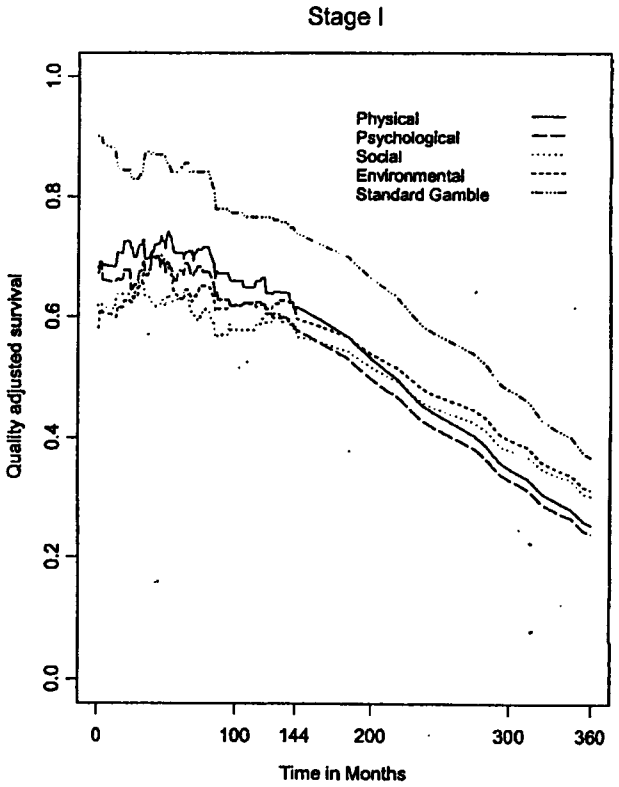


Figure 3. The estimated quality of life adjusted survival functions for stage I breast cancer patients using physical, psychological, social and environmental measures of WHOQOL and standard gamble utility.

By doing so, we can actually improve the estimates of QALE as well as lifetime psychometric scores.

Another concern is the choice of an appropriate reference population. While it is very convenient to use the life table of general population on vital statistics, one can only match with the index population on age and gender. A more accurate estimation may be achieved through a more deliberate selection of a reference population that are comparable with the index population on other determinants of outcome [21], because then the

Table 2. Results of sensitivity analysis for assigning scores of 0, 0.1 and 0.2 to the state of death on the estimates of expected cumulative psychometric score-months obtained from psychological score of four clinical stages of breast cancer for 144 months of follow-up and life-long

Time duration	Death Score	Stage I		Stage II		Stage III		Stage IV	
		Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
144 months	$\delta = 0$	93.4	3.1	74.1	2.2	50.8	3.0	20.9	2.4
	$\delta = 0.1$	94.4	3.0	77.3	2.0	57.5	2.6	32.0	2.2
	$\delta = 0.2$	95.4	2.5	80.6	1.8	64.2	2.2	43.1	1.7
Life-long	$\delta = 0$	203.5	30.6	111.9	12.0	74.6	10.4	23.5	4.3
	$\delta = 0.1$	213.3	27.4	135.2	11.0	111.3	8.4	76.9	2.7
	$\delta = 0.2$	216.1	29.1	156.5	8.6	148.1	6.5	130.3	1.6

linear assumption of logit of $W(t)$ may be more easily fulfilled.

The QoL adjusted survival functions may provide more detailed information for different choices of diagnoses and/or treatments, because different patients may have different preferences in different facets and domains. Both patients and doctors or nurses can look at the figures and numerical values of score-time for different facets or domains of their future QoL adjusted lives at any time point from the $Q(t)$ score functions, which can be used to facilitate decision-making. The measure of life-long cumulative QoL score can also be applied to the general population to calculate a nation's psychometric health life expectancy.

The results of this breast cancer study show that expected quality-adjusted survival time calculated from the utility measurement was generally higher than the rescaled psychometric score-adjusted survival time. This may indicate HRQoL measure in terms of utility is really higher than the 0–1 scaled psychometric scores for the breast cancer patients. However, it is also possibly caused by the scale construction difference. The simple 5 points ordinal scale representing increasing or decreasing severity may be enough for patients to mark their perception. But the descriptors for the lowest and highest scale points are often too extreme so that patients tend not to mark these points even when their health conditions are close to these ends. Moreover, most psychometric scores coming from the Likert scale may not be directly transformed into a ratio scale of between 0 and 1. These problems need to be resolved before the rescaled scores can be used to compare with other utility measures. Hence, the interpretation on direct comparison between expected quality-adjusted survival times using different measures must be cautious. Further refinement of psychometric instruments such as conducting a more detailed descriptor study before use will probably improve the accuracy and feasibility of our method.

Acknowledgements

We are greatly indebted to Drs C. Chantawong, S. Sumitsawan, A. Podhipak, S. Suksiriserekul, for kindly sharing the cohort and QOL data of breast cancer for this study. We are also grateful to Dr D. L. Fairclough and two anonymous peer reviewers for constructive comments. This paper is supported by a grant from the National Science Council of the Executive Yuan of the Republic of China. (grant no. NSC 89-2314-B-002-433-M56).

References

1. Berzon RA. Understanding and using health-related quality of life instruments within clinical research studies. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press; 1998, 3–15.
2. The WHOQOL Group. The World Health Organization Quality of Life assessment (WHOQOL): Position paper from the World Health Organization. Soc Sci Med 1995; 41: 1403–1409.
3. Tengs TO, Wallace A. One thousand health-related quality of life estimates. Med Care 2000; 38(6): 583–637.
4. Bowing A. Measuring Disease. Buckingham: Open University Press, 1995.
5. McDowell I, Newell C. Measuring Health: A Guide to Rating Scales and Questionnaires. New York: Oxford University Press, 1996.
6. Drummond MF, O'Brien B, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes. 2nd ed. New York: Oxford University Press, 1997.
7. Gold MR, Siegel JE, Russel LB, Weinstein MC. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press, 1996.
8. Patrick DL, Ericson P. Health Status and Health Policy: Allocating Resources to Health Care. New York: Oxford University Press, 1993.
9. Kaplan RM. Profile versus utility based measures of outcome for clinical trials. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998; 69–90.
10. Fairclough D. Methods of analysis for longitudinal studies of health-related quality of life. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998; 227–247.
11. Hays RD, Alonso J, Coons SJ. Possibilities summarizing health-related quality of life when using a profile instrument. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998; 143–153.
12. Hwang JS, Tsauo JY, Wang JD. Estimation of expected quality-adjusted survival by cross-sectional survey. Stat Med 1996; 15: 93–102.
13. Hwang JS, Wang JD. Monte Carlo estimation of extrapolation of quality-adjusted survival for follow-up studies. Stat Med 1999; 18: 1627–1640.
14. Chantawong C. Estimation of quality-adjusted survival of breast cancer patients in Chiangmai, Thailand. (Ph.D. dis-

sertation) Bangkok. Thailand: Mahidol University Faculty of Public Health, 1997.
15. Efron B, Tibshirani RJ. An Introduction to the Bootstrap. New York: Chapman and Hall, 1993.
16. MC-QAS software for estimating expected quality-adjusted survival time adjusted for psychometric scores and utilities for health related quality of life assessment. Available from URL: http://www.stat.sinica.edu.tw/jshwang.
17. Martin NC, Sriskho S, eds. Statistical Report of the Registry Unit, Chiangmai. Thailand: Faculty of Medicine, Chiangmai University, 1993, 16p.
18. The WHOQOL Group: Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med 1998; 28: 551–558.
19. Cox DR, Fitzpatrick R, Fletcher AE, Gore SM, Spiegelhalter DJ, Jones DR. Quality-of-life assessment: Can we keep it simple? J R Stat Soc A 1992; 155: 353–393.
20. Schwartz CE, Laitin EA. Using decision theory in clinical research: Applications of quality-adjusted life-years. In: Staquet MJ, Hays RD, Fayers PM (eds), Quality of Life Assessment in Clinical Trials: Methods and Practice. New York: Oxford University Press, 1998; 119–141.
21. Wang JD. Basic Principles and Practical Application of Epidemiological Research. Singapore: World Scientific, 2002; 161–195.

Address for correspondence: Jung-Der Wang, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public health, No. 1, Section 1, Jen-Ai Road, Taipei, 10018, Taiwan
Phone : +886-2-2356-2224/2312-3456; Fax: +886-2-2322-4660
E-mail: jdwang@ha.mc.ntu.edu.tw

COMMENTARY

As we attempt to evaluate the impact of changes in medical practice and public policy on the long-term health and well-being of populations, we are faced with the task of developing methods to integrate information on the quality and quantity of life. This is not a simple task and numerous approaches have been studied in the last decade [1–5]. The article by Hwang and Wang, based on two articles previously published in Statistics in Medicine in 1996 [6] and 1999 [7], is an attempt to apply their methods for the estimation of quality adjusted life years (QALYs) to a cohort of breast cancer survivors. The authors propose using a cross-sectional survey to estimate changes over time in the quality of life of breast cancer survivors over a 12-year period. These estimates are then combined with survival statistics to create an integrated measure. The authors then propose to use survival data from the general population and a parametric model extrapolating the relationship between the breast cancer population and the general population to estimate a lifetime quality-adjusted measure.

My first reservation about the methods proposed by Hwang and Wang is the use of data from a cross-sectional survey to estimate changes over time. While potentially more cost effective than a longitudinal study, this approach requires that there are no cohort effects for the survey to produce an unbiased estimate of the utility or health rating scores of the survivors. For example, survivors diagnosed 10 years ago are assumed to have the same trajectory of QOL scores as those diagnosed 2 years ago. This may not be generally true in medicine where new treatment and supportive care strategies are constantly being developed. Thus, subjects with longer follow-up are likely to have been treated initially with different strategies than subjects with shorter follow-up. In addition to this specific concern, there is the common concern about all surveys. It is critical that the survey be conducted in a manner that minimizes non-response bias and ensures that the respondents are truly a random sample of the intended population and not a convenient sub-sample of that population.

My greatest concern, shared by others [8], relates to the extrapolation to lifetime estimates with censored follow-up data. The assumption that a simple logistic regression function can model the relationship between $Q(t)$ in the index population and $S(t)$ in the reference populations is quite strong. I personally find it difficult to conceptualize this function of the quality of life in the index population and survival in both populations; thus, it is difficult to envision the settings where I would have some confidence in the assumptions. The condition cited by the authors is that the hazard of death in the index population is greater than that of the reference population (i.e., the disease results in premature death) or that the disease produces a negative effect on quality of life. This condition is necessary but not sufficient for the extrapolation to produce reasonable (unbiased) lifetime estimates. While examination of plots of the logit of the ratio of these two functions (Figure 2) may provide some assurance that this simple model is a reasonable approximation over the period during which scores and survival were observed, it is impossible to assure ourselves that the extrapolation is accurate without gathering additional follow-up data. In the breast cancer example presented by Hwang and Wang, the last 60 months of a 12-year study were used to estimate the relationship between the two populations. But if the study had been shorter, say 5 years, it is clear from Figure 2 that extrapolation of the Stage I and II curves from that shorter study would not have matched what was observed afterwards. Given that these are the patients with the longest survival, errors in the extrapolation would have the greatest impact on the resulting estimates of lifetime quality-adjusted survival.

My remaining concerns center on the use of preference (utility) versus health-rating scales and the interpretation of the results. The use of health-rating (psychometrically derived) scales to compute QALY measures is problematic. The interpretation and intended use of health-rating scales is different than for preference scales. As the preference scores are measured on a ratio scale, it is appropriate to interpret the product of the utility scores with time as quality adjusted life-years; a score of 0.6 over a 10-year period being equivalent to a score of 0.5 over a 12-year period. Further, the score for subjects who have died is generally accepted as zero by definition. The same is not true

for the health-rating scales. Individuals will often tolerate mild or moderate symptoms and inconvenience before they are willing to trade for increased risk of earlier death. This often results in a non-linear relationship between preference and health-rating scales [9–13]. The linear rescaling the WHOQOL (or any rating scale) to a range of 0–1 is unlikely to make it a valid preference measure that is interpretable on a ratio scale. Thus, it is dangerous to interpret the composite measure proposed by Hwang and Wang as an estimate of QALYs. It can, however, be interpreted as the area under the curve of $Q(t)$ vs. time given the assumed fixed value of d for individuals who have died.

While it is desirable for researchers to continue to develop new techniques, it is also important that we examine both the practical implementation of these methods and the underlying assumptions before putting them into general use. It is critical to use the right methods in the right setting; sophisticated techniques applied incorrectly generate confusion at best, inappropriate conclusions at worst.. Hopefully, this paper will engender thoughtful discussion and stimulate continued efforts to develop methods to integrate information on the quality and quantity of life.

References

1. Glasziou PP, Simes RJ, Gelber RD. Quality adjusted survival analysis. Stat Med 1990; 9: 1259–1276.
2. Zhao J, Tsiatis AA. A consistent estimator for the distribution of quality adjusted survival time. Biometrika 1997; 84: 339–348.
3. Glasziou PP, Cole BF, Gelber RD, Hilden J, Simes RJ. Quality-adjusted survival analysis with repeated quality-of-life measures. Stat Med 1998; 17: 1215–1219.
4. Shen LZ, Pulkstenis E, Hoseyni M. Estimation of mean quality adjusted survival time. Stat Med 1999; 18: 1541–1554.
5. Finkelstein DM, Schoenfeld DA. Combining mortality and longitudinal measures in clinical trials. Stat Med 1999; 18: 1341–1354.
6. Hwang JS, Tsauo JY, Wang JD. Estimation of expected quality-adjusted survival by cross-sectional survey. Stat Med 1996; 15: 93–102.
7. Hwang JS, Wang JD. Monte Carlo estimation of extrapolation of quality-adjusted survival for follow-up studies. Stat Med 1999; 18: 1627–1640.
8. Gelber RD, Goldhirsch A, Cole BF. Parametric extrapolation of survival estimates with applications to quality of life evaluation of treatments. Control Clin Trials 1993; 14: 485–499.
9. Torrance GW. Social preferences for health states: An empirical evaluation of three measurement techniques. Socio-Econ Plan Sci 1976; 10: 120–136.
10. Read JL, Quinn RJ, Berwich DM, Fineberg HV, Weinstein MC. Preferences for health outcomes: Comparison of assessment methods. Med Decis Making 1984; 4: 315–329.
11. Hornberger JC, Redeimeier DA, Peterson J. Variability among methods to assess patients well-being and consequent effect on a cost-effective analysis. J Clin Epidemiol 1992; 45: 505–512.
12. Tseval J, Goldman L, Soukup JR, et al. Functional status versus utilities in survivors of myocardial infarction. Med Care 1991; 29: 1153–1159.
13. O'Leary JF, Fairclough DL, Jankowski MK, Weeks JC. Comparison of time-tradeoff utilities and rating scale values if cancer patients and their relatives. Evidence for a possible plateau relationship. Med Decis Making 1995; 15: 132–137.

REJOINDER

Using a cross-sectional survey to estimate population mean quality of life (QoL) function, we estimated the mean QoL score at year t based only on the sampled patients who were diagnosed t years ago. Without input from patients who survived more than t years, the mean QoL score estimate at year t tends to be positively biased if the patient's QoL is improving during the study period due to newly developed medicine or health care. However, the current data may still be the best available information for policy decisions in health service, because no one can accurately predict the magnitude of improvement of QoL and survival as the progress of modern medicine is so fast. To improve the precision of estimates of the mean QoL score, quality-adjusted survival and extrapolation, we agree that more data from additional follow-up will be helpful. If cost and time are allowed, we would suggest implementing a new cross-sectional survey on randomly selected subjects from the follow-up population each year. A less biased estimate of the mean QoL function will be obtained using all the new and old interviewed QoL scores. With the additional QoL and survival data each year, we can also evaluate the precision of the estimated quality-adjusted survival and examine the performance of the extrapolation method.

The performance of the proposed extrapolation method is mainly determined by the behavior of quality-adjusted survival functions for the index population and reference population during the last few years of the follow-up. Since the reference population is often generated from the life table of a matched normal population, the survival function of the reference population is usually very stable. The instability in quality-adjusted survival function estimates for the index population is often caused by disease related factors, such as invasive diagnostic workup and/or vigorous intervention including surgery, radiotherapy, chemotherapy, etc., in the first 1–3 years after diagnosis. The estimate of the quality-adjusted survival function should be more stable after that time point. If the proposed plot of logistic transformation of the ratio of quality-adjusted survival of the index and reference populations does not show a satisfactory straight line, the accuracy of extrapolation is not guaranteed. In this case, we have to extend the follow-up to have more accurate long-term extrapolation.

The measure of quality-adjusted survival time is mainly used to adjust the survival time of each patient by his/her QoL scores. The idea of the method is related to averaging patients' QoL adjusted survival times [1, 2]. In this study, we obtained almost the same formula by first calculating population mean QoL scores in a given time interval and then summing up the scores across the time period. Because the inherent meaning and characteristics of psychometry is different from that of utility measurement, we must assign them with a different unit to differentiate the two.

Therefore, the integration of the product of survival function and QoL function has a unit of score-time such as score-month or score-year especially when psychometric scores are used for QoL measurements. It is best interpreted as the cumulative survival-weighted psychometric score for the specific domain, dimension, or facet, which is the area under the curve of $Q(t)$ versus time given the assumed fixed value of δ for decedents for the specific psychometric measurement. Namely, it is a psychometric score of a specific facet or domain adjusted by survival function and should specify the time unit for outcome assessment and comparison of effectiveness between two or more different health services. Although the results of quality-adjusted survival time adjusted for standard gamble utility and psychometric scores were tabulated together, we have noted that the units are different and the direct comparisons should be made with caution.

References

1. Hwang JS, Tsauo JY, Wang JD. Estimation of expected quality-adjusted survival by cross-sectional survey. Stat Med 1996; 15: 93–102.
2. Glasziou PP, Cole BF, Gelber RD, Hilden J, Simes RJ. Quality-adjusted survival analysis with repeated quality-of-life measures. Stat Med 1998; 17: 1215–1219.