# 行政院國家科學委員會專題研究計畫 成果報告

## 荷爾蒙替代療法於停經婦女之使用型態與心血管風險評估研究（GM7）

## 研究成果報告(完整版)

計 畫 類 別 ：個別型
計 畫 編 號 ：NSC 100-2629-B-006-001-
執 行 期 間 ：100 年 08 月 01 日至 101 年 07 月 31 日
執 行 單 位 ：國立成功大學臨床藥學研究所

計 畫 主 持 人：高雅慧
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計畫參與人員：學士級-專任助理人員：趙子揚

報 告 附 件 ：出席國際會議研究心得報告及發表論文

公 開 資 訊 ：本計畫涉及專利或其他智慧財產權，2 年後可公開查詢

中 華 民 國 102 年 01 月 10 日

中文摘要：

研究背景

有關亞洲人發生深層靜脈栓塞的大規模流行病學資料相當缺乏，在亞洲人深層靜脈栓塞的發病率一般比白人低，由於過去這些研究都不是直接在亞洲國家所作的研究，所以無法真正反應真實亞洲人臨床狀況。西方人的研究發現女性賀爾蒙激素治療是一個明確的深層靜脈栓塞的危險因素。然而，亞洲人在停經後婦女接受口服賀爾蒙激素治療之深層靜脈栓塞的發病率和其危險因子，在亞洲的研究是相當缺少的。

研究目的

我們的目的是研究台灣停經後婦女在有無使用口服賀爾蒙激素治療發生深層靜脈栓塞的發生率。並評估停經後婦女接受口服賀爾蒙激素治療是否是發生靜脈血栓栓塞的危險因子。

研究方法

首先,我們要從台灣的全民健康資料庫，進行回溯性研究。自1998年至2008年年齡≧50歲的婦女。利用重疊病例對照研究，定義病例組為研究期間發生的深層靜脈栓塞的個案，以年齡、納入時間及追蹤時間配對出1:10的對照組，利用條件邏輯性回歸估計深層靜脈栓塞和不使用、現在和過去使用口服賀爾蒙激素治療之相關危險性。同時進行敏感性分析史本研究更具可信度。

研究結果

這個世代研究的1942064名婦女，其中8321位病例組並且配對出83141位控制組。和沒有使用過口服賀爾蒙激素相比，目前使用的口服賀爾蒙激素的患者具有較高發生深層靜脈栓塞的風險(OR 4.46，95%CI 4.04至4.92）、最近使用具有較高的風險（OR 2.26，95%CI 1.98-2.58）以及過去使用具有較高的風險（OR 1.63，95%CI 1.45-1.84）。此外，和沒有使用過口服賀爾蒙激素相比，目前使用口服雌激素具有較高發生深層靜脈栓塞的風險（OR 2.30，95%CI 1.92-2.75），口服雌激素/孕激素也有較高的風險（OR 5.24，95%CI 4.56-6.02）以及孕激素也有較高的風險（OR 3.65，95%CI 2.18-6.11）。

研究結論

深層靜脈栓塞的發生率在台灣遠比白人低。台灣的深層靜脈栓塞發生率雖低，停經後婦女如口服女性賀爾蒙激素治療仍會增加深層靜脈栓塞的風險。

中文關鍵詞：靜脈栓塞；深層靜脈栓塞；肺動脈栓塞；停經後症候群；女性賀爾蒙治療

英文摘要：Background: Little information is available on the

epidemiology of venous thromboembolism (VTE) in Asian populations. The incidence of VTE in Asians was generally lower compared to Caucasians. Hormone therapy (HT) is a definite risk factor of VTE in Western studies. However, information on the incidence and risk factors of VTE in postmenopausal women receiving HT in Asia is scarce.
Objective: We aimed to calculate the incidence of VTE in HT users and non-HT users, respectively. We also wanted to investigate the risk of VTE in postmenopausal women receiving HT.
Methods: We used the Taiwanese National Health Insurance claims databases to conduct a retrospective longitudinal cohort. The cohort identified all women aged ≧50 years between 1 January 1998 and 31 December 2008. Using a nested case–control approach, all incident cases of VTE occurring during the study period were identified and matched with up to 10 controls selected from the cohort members. Adjusted odds ratios (OR) of VTE with non-use, current and past use of oral HRT were estimated using conditional logistic regression.
Results: The cohort of 1,942,064 women included 8321 cases of VTE matched with 83141 controls. The adjusted odds ratios of VTE associated with current use of oral HT was 4.46 (95% CI 4.04 to 4.92) relative to no use. The risk of VTE was also increased with recent use of oral HT (ORs 2.26； 95% CI, 1.98–2.58) and remote use (ORs 1.63； 95% CI, 1.45–1.84) relative to no use. The risk was increased with current use of oral estrogen (ORs 2.30； 95% CI, 1.92–2.75), oral estrogen-progestogen (RR 5.24； 95% CI, 4.56–6.02), and progestogen (ORs 3.65； 95% CI, 2.18–6.11).
Conclusion: Although the incidence of VTE was low in Taiwanese population, oral HT was still associated with an increased risk of VTE in postmenopausal women. Women should take oral HT as short as possible if indicated. Oral estrogen only and estrogen-progestogen combination both contributed to the increased risk of new VTE event.

英文關鍵詞： Venous thromboembolism； deep vein thrombosis；
pulmonary embolism； postmenopausal syndrome；
hormone therapy

附件一

# 行政院國家科學委員會補助專題研究計畫

□期中進度報告
■期末報告

## 探討臺灣停經後婦女使用女性賀爾蒙和心肌梗塞、缺血性腦阻塞和靜脈栓塞發生之相關性

計畫類別：■個別型計畫　□整合型計畫
計畫編號： NSC 100-2629-B-006-001-
執行期間：2011 年 8 月 01 日至 2012 年 10 月 31 日

執行機構及系所：國立成功大學醫學系內科學科

計畫主持人：高雅慧
共同主持人：李政翰
計畫參與人員：鄭靜蘭

本計畫除繳交成果報告外，另含下列出國報告，共 1 份：
□移地研究心得報告
■出席國際學術會議心得報告
□國際合作研究計畫國外研究報告

處理方式：除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

中　華　民　國 101 年 12 月 31 日

# 中文摘要

**研究背景**

有關亞洲人發生深層靜脈栓塞的大規模流行病學資料相當缺乏，在亞洲人深層靜脈栓塞的發病率一般比白人低，由於過去這些研究都不是直接在亞洲國家所作的研究，所以無法真正反應真實亞洲人臨床狀況。西方人的研究發現女性賀爾蒙激素治療是一個明確的深層靜脈栓塞的危險因素。然而，亞洲人在停經後婦女接受口服賀爾蒙激素治療之深層靜脈栓塞的發病率和其危險因子，在亞洲的研究是相當缺少的。

**研究目的**

我們的目的是研究台灣停經後婦女在有無使用口服賀爾蒙激素治療發生深層靜脈栓塞的發生率。並評估停經後婦女接受口服賀爾蒙激素治療是否是發生靜脈血栓栓塞的危險因子。

**研究方法**

首先,我們要從台灣的全民健康資料庫，進行回溯性研究。自1998年至2008年年齡≧50歲的婦女。利用重疊病例對照研究，定義病例組為研究期間發生的深層靜脈栓塞的個案，以年齡、納入時間及追蹤時間配對出1:10的對照組，利用條件邏輯性回歸估計深層靜脈栓塞和不使用、現在和過去使用口服賀爾蒙激素治療之相關危險性。同時進行敏感性分析史本研究更具可信度。

**研究結果**

這個世代研究的1942064名婦女，其中8321位病例組並且配對出83141位控制組。和沒有使用過口服賀爾蒙激素相比，目前使用的口服賀爾蒙激素的患者具有較高發生深層靜脈栓塞的風險(OR 4.46，95％CI 4.04至4.92)、最近使用具有較高的風險（OR 2.26，95％CI 1.98-2.58）以及過去使用具有較高的風險（OR 1.63，95％CI 1.45-1.84）。此外，和沒有使用過口服賀爾蒙激素相比，目前使用口服雌激素具有較高發生深層靜脈栓塞的風險（OR 2.30，95％CI 1.92-2.75），口服雌激素/孕激素也有較高的風險（OR 5.24，95％CI 4.56-6.02）以及孕激素也有較高的風險（OR 3.65，95％CI 2.18-6.11）。

**研究結論**

深層靜脈栓塞的發生率在台灣遠比白人低。台灣的深層靜脈栓塞發生率雖低，停經後婦女如口服女性賀爾蒙激素治療仍會增加深層靜脈栓塞的風險。

**關鍵字：** 靜脈栓塞；深層靜脈栓塞；肺動脈栓塞；停經後症候群；女性賀爾蒙治療

# Abstract

**Background:** Little information is available on the epidemiology of venous thromboembolism (VTE) in Asian populations. The incidence of VTE in Asians was generally lower compared to Caucasians. Hormone therapy (HT) is a definite risk factor of VTE in Western studies. However, information on the incidence and risk factors of VTE in postmenopausal women receiving HT in Asia is scarce.

**Objective:** We aimed to calculate the incidence of VTE in HT users and non-HT users, respectively. We also wanted to investigate the risk of VTE in postmenopausal women receiving HT.

**Methods:** We used the Taiwanese National Health Insurance claims databases to conduct a retrospective longitudinal cohort. The cohort identified all women aged ≧50 years between 1 January 1998 and 31 December 2008. Using a nested case–control approach, all incident cases of VTE occurring during the study period were identified and matched with up to 10 controls selected from the cohort members. Adjusted odds ratios (OR) of VTE with non-use, current and past use of oral HRT were estimated using conditional logistic regression.

**Results:** The cohort of 1,942,064 women included 8321 cases of VTE matched with 83141 controls. The adjusted odds ratios of VTE associated with current use of oral HT was 4.46 (95% CI 4.04 to 4.92) relative to no use. The risk of VTE was also increased with recent use of oral HT (ORs 2.26; 95% CI, 1.98–2.58) and remote use (ORs 1.63; 95% CI, 1.45–1.84) relative to no use. The risk was increased with current use of oral estrogen (ORs 2.30; 95% CI, 1.92–2.75), oral estrogen–progestogen (RR 5.24; 95% CI, 4.56–6.02), and progestogen (ORs 3.65; 95% CI, 2.18–6.11).

**Conclusion:** Although the incidence of VTE was low in Taiwanese population, oral HT was still associated with an increased risk of VTE in postmenopausal women. Women should take oral HT as short as possible if indicated. Oral estrogen only and estrogen- progestogen combination both contributed to the increased risk of new VTE event.



***Keywords:*** Venous thromboembolism; deep vein thrombosis; pulmonary embolism; postmenopausal syndrome; hormone therapy

## INTRODUCTION

About 50 to 80 percent of women report menopause-related symptoms such as hot flushes, night sweats, vaginal dryness, insomnia, mood swings, and depression.[58-60] There is strong evidence, including data from randomized clinical trials, that estrogen therapy is a highly effective approach to controlling vasomotor and genitourinary symptoms.[61-63] Therefore, HT can improve the quality of life for women with hypo-estrogenic symptoms.[1] Many women are still prescribed estrogen therapy to treat postmenopausal symptoms despite recent data showing that overall health risks may exceed benefits of long term HT.[2] Estrogen inhibits the age-related loss of bone that occurs in most women after menopause. Observational studies have indicated that the use of estrogen reduces the risk of vertebral fracture by approximately 50 percent and the risk of hip fracture by 25 to 30 percent.[2,3] In contrast, harmful effects of HT include endometrial cancer and breast cancer.[4]

Estrogens have many different effects on the coagulation system.[64-68] These include increases in the levels of procoagulant factors VII, X, XII, and XIII and reductions in the anticoagulant factors protein S and antithrombin. These changes predict a change toward a more procoagulant state (which is confirmed in studies examining global tests, such as APC resistance or thrombin generation),[69-72] which is not counterbalanced by an increased fibrinolytic activity.[73] Randomized trials have shown that estrogen therapy reduces plasma levels of low density lipoprotein by 10 to 14 percent and increases plasma levels of high-density lipoprotein by 7 to 8 percent, changes known to be associated with a reduced risk of cardiovascular disease.[74,75] Estrogen has also been shown to reduce levels of Lp(a) lipoprotein, inhibit oxidation of low-density lipoprotein, improve endothelial vascular function, and reverse postmenopausal increases in fibrinogen and plasminogen-activator inhibitor type 1 — changes that should also reduce the risk of cardiovascular disease.[76] At the same time, however, estrogen therapy may have potentially detrimental effects on cardiovascular biomarkers, such as increasing triglyceride levels; activating coagulation as a result of increases in factor VII, prothrom- bin fragments 1 and 2, and fibrinopeptide A 10; and increasing levels of C-reactive protein, a marker of inflammation associated with an increased risk of cardiovascular events. The estrogens in hormonal replacement therapy have hemostatic effects similar to those in oral contraceptives. It is currently unclear how these effects are brought about at the molecular level of the estrogen receptor. It is likely that these effects at the cellular level are also under genetic control, because the hemostatic system of some women appears to be more sensitive to the effect of estrogens than that of other women.[77] It is also unclear how estrogens and progestins interact in their effect on thrombosis, for instance, in the higher risk of oral contraceptives containing a third generation progestin. It appears that estrogens are prothrombotic rather than proatherogenic, which explains the absence of an increased risk in former users.[78]

Furthermore, randomized controlled trials showed that HT might increase the risk of coronary heart disease and stroke.[2,5] Since the publication of the Women Health Initiative (WHI) results,[2] medical practices of HT have been dramatically altered.[8] Cardiovascular disease, including VTE, is an important determinant of the benefit-to-risk profile of HT.[9] Both observational studies[10-13] and clinical trials[2,14] have shown a significant increase in VTE risk among postmenopausal women using HT. Observational studies indicate that the postmenopausal use of estrogen increases the risk of DVT by a factor of 2 to 3.5. The finding in HERS that the risk of thromboembolic events was increased by a factor of 2.7 among women assigned to receive estrogen–progestin therapy is consistent with this estimate.[14] The development of a rational strategy for prescribing postmenopausal HT requires careful analysis of the potential benefits and risks. As previously mentioned, the VTE incidence in Asia populations is possibly lower than that in Western populations;

therefore, the safety issue of HT in postmenopausal women in Taiwan needs to be determined.

## METHODS

### Study Setting and Design

First of all, we conducted a nationwide population-based cohort study that was analyzed using a nested case-control study to evaluate HT and risk of VTE. The NHI databases used in this study include all inpatient and outpatient medical claims in Jan 1, 1997 and Dec 31, 2008. From the databases, we could extract medical information of disease diagnosis, prescription drugs, procedures, and surgery incurred during a hospitalization or at an outpatient visit. For electronic processing by the National Health Insurance in Taiwan, all the health care service providers are requested to submit the diagnosis information using the International Classification of Disease-Clinical Modification, ninth revision (ICD-9-CM) together with service claims.

The cohort consists of all women aged ≧50 between 1 January 1998 and 31 Dec. 2008. We excluded all subjects with a diagnosis of VTE prior to age 50, history of HRT use before age 50. The remaining women were followed until the date of the first VTE, death, end of registration with the practice, or end of the study period (31 Dec. 2008), whichever occurred first. (Figure 1) In the nested case-control study, all incident cases of VTE within the cohort, occurring during the study period were identified from the inpatient claims database by an ICD9-CM code of 451.1x; 451.2; 451.83; 453.1; 453.2; 453.4; 453.8; 453.9; 415.1x. To avoid misdiagnoses, we selected patients who met the following criteria: (1) the discharge diagnosis was DVT or PE; (2) the patient must have received a course of subcutaneous or intravenous anticoagulation therapy with unfractioned heparin or surgical thrombectomy during hospitalization and continued oral warfarin therapy after discharge; and (3) a length of stay of at least 3 days, unless they died. For each case, we randomly selected up to 10 controls among the cohort members in the risk sets defined by the case. Each case was matched with controls on age (± 2 years) and the year of start in the practice (± 2 years). Controls had to be alive, contributing data to the practice and be free of VTE on the event date of their corresponding case. The event date of the case was assigned to the matched controls and defined their index date.

### Definition of Venous Thromboembolism

In our study, VTE included deep vein thrombosis and pulmonary embolism. VTE admissions were identified from the inpatient claims database by an ICD9-CM code of 453.1; 453.2, 453.3; 453.8; 453.9; 415.1x. For fear of misdiagnoses, we carefully selected patients who met the following criteria: (1) the principal or secondary discharge diagnosis was deep vein thrombosis or pulmonary thromboembolism; (2) the patient must have received a course of anticoagulation therapy with warfarin, heparin, or surgical thrombectomy during hospitalization and continued oral warfarin therapy after discharge; (3) patient had VTE and died during the hospitalization period. During follow-up, a recurrence of VTE was defined as hospitalization with a principal diagnosis of deep vein thrombosis or pulmonary thromboembolism plus the above-mentioned criteria.

### Co-morbid Diseases and Potential Risk Factors

For each patient, the co-morbidities for VTE were retrieved from both the inpatient and outpatient claims database for 180 days before and after the date of the index event. Several proven diseases predisposing patients to VTE were selected based on ICD-9-CM codes (Appendix). History of VTE was defined as being hospitalized due to VTE before the index event in 2001. Hormone therapy included estrogen and progesterone therapy. Chronic lung disease included emphysema, chronic bronchitis, bronchiectasis, other obstructive pulmonary disease, and chronic respiratory failure. We recorded only serious neurologic diseases including stroke or other central and peripheral nervous disease with associated extremity paresis or paralysis. The

potential risk factors such as pregnancy, surgery, extremity trauma, and hormone therapy were recorded as present only if documented within 3 months preceding the VTE event. Operations were classified as major neurologic, thoracic, abdominal, urogenital, or orthopedic.

**Hormone therapy exposure**

A list of all medications containing estrogens and /or progestogens recommended for HT and available in Taiwan during the study period was extracted from the database. In Taiwan, we did not find any prescriptions of transdermal HT, tibolone, and estradiol implant during these years. For each matched set of case and controls, we could identify all prescriptions for oral HRT from the databases in the year before the index date. HT prescriptions are categorized into the following exposure groups: estrogens only, estrogens combined with progestogens, and progestogens only. For each women, the date of the last issued HT prescription before the index date was documented. The exposure period of interest is the year before the index date. Individuals are considered current users if their last HT prescription in this 1-year period lasted at least one month until the index date. Past users are defined by at least one prescription issued in the year before the index date but stopped therapy more than 1 month before the index date. We further separated past users into recent and remote users. Recent users are defined by at least prescription issued in the year before the index date but the last prescription was beyond 30 days of index date and within 121 days of index date. Remote users are defined by at least prescription issued in the year before the index date but the last prescription was beyond 120 days of index date and within one year of index date. Non-users are those who have not received any prescription of HT in the year preceding the index date. The duration of each prescription was calculated from the number of tablets prescribed.

**Statistical analysis**

During the study period, the population of Taiwan was about 22.4 million (16.8 million adults). Demographic data were expressed as means (±SD) or percentages. In general, differences in proportions were tested with the chi-square test or Fisher's exact test, and differences in location parameters of continuous variables were tested with a Student *t* test. Non-users are those who have not received any prescription of HT in the year preceding the index date. This constitutes the reference group. We estimate unadjusted and adjusted rate ratios (RR) with 95% confidence intervals of the association between HT use and VTE using conditional logistic regression for matched case–control data. Along with the matching of age, enrolled year, and duration of follow-up, potential confounders included in the analyses are history of varicose veins, inherited hypercoagulable diseases, diagnosed cancer in the year before the index date, major surgery in the month prior to the index date, hypertension, chronic lung disease, renal insufficiency, cardiovascular and cerebrovascular diseases. We conducted several additional analyses to test the robustness of our findings. First, we altered the definition of "current use" to include their last HT prescription in this 1-year period lasted at least 7 days until the index date. To test the specificity of our findings, we replicated our analysis in patients without switching of HT prescriptions during the observed period. We also assessed the effect of potential misclassification of current exposure on the estimated odds ratios by adding 30 days to the calculated duration of use for all cases and controls exposed. Thus, some persons who were not classified as currently exposed at the index date based on the calculated duration of use in our main analysis became exposed. Finally, the analyses are restricted to cases and controls without major risk factors for VTE (i.e.cancer, cardiovascular diseases, renal insufficiency, chronic lung disease, inherited coagulopathy, peripheral nervous disease associated with extremity paresis or paralysis, major surgery in the month before the index date). All computations are performed using the SAS software version 9.1.3 (SAS Institute Inc., Cary, NC, USA).

**Results**

The study population consisted of 2271065 post-menopausal women. Within this population, we excluded women with previous history of VTE and HT use before they were 50 year-old. During the follow-up period, 8321 cases of new VTE were identified. The final analysis included 8321 cases of VTE, matched to 83141 controls. (Figure 1)

Table 1 describes the characteristics of cases of VTE and their matched controls. As expected, cases were more likely to have varicose veins, to have experienced immobilization, surgery in the month before the index date, and to have been diagnosed with cancer and other cardiovascular diseases in the previous year. In the year preceding the index date, 18.0% of the cases and 6.9% of the controls had received at least one HRT prescription, of which 8.8% and 2.3%, respectively, were current users at the time of the index date.

The risk of VTE was increased with current use of oral HT (adjusted OR 4.46; 95% CI, 4.04–4.92) relative to nonusers. (Table 2) Similarly, the risk was increased with recent use of oral HT (OR 2.26; 95% CI, 1.98–2.58) or remote use of oral HT (RR 1.63; 95% CI, 1.45–1.84). On the other hand, the risk was increased with current use of oral estrogen (RR 1.49; 95%CI, 1.37–1.63) and oral estrogen–progestogen (RR 1.54; 95% CI, 1.44–1.65). (Table 3) Considering the duration of oral HT, the risk of VTE was both increased either with shorter duration (<90 days) of current use or with longer duration (≧90 days) of current use. We repeated several kinds of sensitivity analysis. Table 4 showed past use of oral HT and the risk of VTE. The risk was increased with past use of oral estrogen (RR 1.58; 95%CI, 1.27–1.98) and oral estrogen–progestogen (RR 3.53; 95% CI, 2.90–4.29), but not progestogen only. We excluded unhealthy women with potential VTE risk factors such as cancer, heart failure, varicose veins, and receiving major surgery. The result appeared similarly in Table 5. Current, recent, and remote users of oral HT all had a higher risk of VTE than that in non-users. Extending the duration of HT exposure by adding 30 days to the prescription (Table 6) or restricting the analyses to patients without HT switching did not change the results. (Table 7)

## Discussion

In my previous study, [34] the overall crude incidence of VTE was 14.4 events per 100,000 person-years in men and 17.4 events per 100,000 person-years in women. In women, the incidence drastically increased from 2.0 events per 100,000 person-years in those younger than 30 years to 118.2 events per 100,000 person-years in those over 80 years. For women, the overall VTE recurrent rate was 10.1% vs 11.4% (p=0.41) in hormone group and other women, respectively. Meanwhile, there was no difference in the prevalence of HT including estrogen or (and) progesterone use (14.8% versus 12.8%, p=0.25) between cases and controls. Although the use of HT, pregnancy, and puerperium have been associated with VTE in women, we did not identify a significant gender difference in VTE incidence in the range of 20 to 60 years of age. We neither observed lower recurrent VTE rate in hormone-related subgroup.

In my another study,[35] the overall incidence of VTE following major knee arthroplasties was 0.47% in men and 0.45% in women. The gender was not associated with procedure-related VTE. For women, there was no difference in the prevalence of HT including estrogen and/or progesterone use (6.1% versus 6.0%, p=0.926) between VTE and non-VTE groups. Therefore, I assume that oral HT may not be a risk factor of VTE in healthy postmenopausal women, but should be avoided in high-risk postmenopausal women such as active cancer, varicose veins, et al.

The present nationwide population-based cohort and nested case-control study showed that current use of oral HT increases the risk of VTE by twofold to fifthfold. This increased risk was also observed, but declining in recent and remote users. Although we also identified other VTE risk factors in postmenopausal women, HT

use was still the independent risk factor. In five epidemiologic studies involving 592 cases of VTE of which 130 (22.0%) were current HT users, the risk of VTE was increased approximately twofold (OR 2.3; 95% CI, 1.7–3.0).[10,12,13,98,99] VTE is not confined to the first year of HT use, but the increased risk declines from approximately four-fold in the first year to less than two-fold after the third year of use.[10,12,99,100]

The best currently available data for postmenopausal HT do not support a cardiovascular benefit. The risks for VTE may vary with the route of administration of HT because oral estrogens have greater impact on coagulation factors than do transdermal routes of administration.[10,99,101,102] A meta-analysis of observational studies found that oral estrogen, but not transdermal estrogen, was associated with an increased risk for VTE.[103] The odds ratios (95% CI) for first-time VTE were 2.5 (1.9, 3.4) in current users of oral estrogen and 1.2 (95% CI, 0.9–1.7) in current users of transdermal estrogen, compared with nonusers. In our study, we could not compare the effect of oral and transdermal route of HT on VTE because transdermal HT is not available and reimbursed in Taiwan. HT should not be prescribed for the prevention of cardiovascular disease, and short-term prescription for relief of menopausal symptoms should be the main indication. A recent statement from the American Heart Association also urges caution in the prescription of postmenopausal HT.[104] HT should be avoided in women with a personal or family history of venous thrombosis.

Our findings have several clinical implications for Asian populations. Although our previous studies showed that the incidence of VTE in Taiwan was obviously lower than that in Western countries, the current use of oral HT in postmenopausal women increases the risk of VTE by twofold to fifthfold. In this specific women population, they also had some comorbid diseases such as heart failure, coronary heart disease, varicose veins, and renal disease which were also VTE risk factors. Therefore, physicians should take care of prescribing oral HT to postmenopausal women with other potential VTE risk factors. We also observed that the risk of VTE in longer-duration (>3 moths) current users seemed to be higher than that in short-duration current users. This suggests that women should take oral HT as short as possible if indicated. Oral estrogen only, estrogen- progestogen, and progestogen only all contributed to the increased risk of new VTE event.

There are several limitations in the present investigation. First, the healthcare claims data could not provide the body mass index and smoking status. Previous studies disclosed that obesity possibly contributed to VTE risk among the postmenopausal women. Because the information on body mass index from all patients including VTE and non-VTE patients was unavailable, we thought that the selection bias would not happen in this study. Second, transdermal HT was not available in Taiwan during the study period so we could not evaluate if transdermal HT would make a difference from oral HT. Third, we did not take into account that some women might seek non-western medicine treatment for menopausal-related symptoms. Since our data source was obtained from the NHI inpatient and outpatient visit records, no information on over-the counter herbal products or nutritional supplements for menopausal symptoms was included.

Although the incidence of VTE is low in Taiwanese population, oral HTs including estrogen only, estrogen- progestogen, and progestogen only are all associated with an increased risk of VTE in postmenopausal women.

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**Conflicts of interest statement**

No conflict of interest was declared.

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**Appendix. World Health Organization International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] used for present analysis.**

| Disease category | ICD-9-CM |
|---|---|
| Embolism and thrombosis of vena cava | 453.2 |
| Embolism and thrombosis of other specified veins | 453.8 |
| Embolism and thrombosis of unspecified site | 453.9 |
| Pulmonary embolism | 415.1-9 |
| Malignant neoplasm of lip, oral cavity and pharynx | 140-149 |
| Malignant neoplasm of digestive organs and peritoneum | 150-159 |
| Malignant neoplasm of respiratory and intrathoracic organs | 160-165 |
| Malignant neoplasm of connective tissues | 170-176 |
| Malignant neoplasm of genitourinary organs | 179-189 |
| Malignant neoplasm of brain and other nervous system | 191-192 |
| Malignant neoplasm of endocrine glands | 193-194 |
| Hematology malignancy (lymphoma and leukemia) | 200-208 |
| Hypertension (malignant, benign, unspecified) | 401.0-405.9 |
| Heart failure (unspecified, left heart, systolic, diastolic) | 428.0-428.9 |
| Ischemic heart disease | 410-414 |
| Renal insufficiency | 580-589 |
| Chronic lung disease | 490-496 |
| Diabetes mellitus | 250.00-250.90 |
| Ischemic stroke and intracerebral hemorrhage | 434.0-434.9, 436, 430-432.9 |
| Degenerative and paralytic neurologic disease | 438.X, 330-337, 340-349 |
| Varicose veins of lower extremities | 454.0-9 |
| Pregnancy | 640.0-677.9 |
| Spine fracture | 805.0-806.9 |
| Extremity fracture and dislocation | 808.0-828.9, 830.0-839.9 |
| Hypercoagulable status | 289.81 |
| Major central nervous and spine surgery | 01.0-05.9 |
| Major thorax surgery | 29.0-39.9 |
| Major abdomen surgery | 42.0-59.9 |
| Major orthopedic surgery | 78.0-84.9 |
| Major urogenital surgery | 60.0-71.9 |

**Table 1 Characteristics of nested case-control study patients among postmenopausal women**

| characteristics | Cases (n=8321) | Controls (n=83141) |
|---|---|---|
| Age | 64.3 (±9.0) | 64.3 (±9.0) |
| Cancer | 1960 (23.6) | 9530 (11.5) |
| Hypertension | 5224 (62.8) | 47184 (56.8) |
| Heart failure | 1842 (22.1) | 8113 (9.8) |
| Coronary heart disease | 2916 (35.0) | 18093 (21.8) |
| Renal insufficiency | 1533 (18.4) | 8715 (10.5) |
| Chronic lung disease | 2292 (27.5) | 16637 (20.0) |
| Diabetes mellitus | 2652 (31.9) | 22911 (27.6) |
| Stroke | 1118 (13.4) | 8674 (10.7) |
| Serious neurologic disease | 1725 (20.7) | 13533 (16.3) |
| Varicose veins | 368 (4.4) | 375 (0.5) |
| History of hysterectomy | 76 (0.9) | 54 (0.1) |
| Major surgery | | |
| Neurologic surgery | 224 (2.7) | 667 (0.8) |
| Thoracic surgery | 1218 (14.6) | 2895 (3.5) |
| Abdominal surgery | 1159 (13.9) | 3680 (4.4) |
| Urogenital surgery | 282 (3.4) | 720 (0.9) |
| Orthopedic surgery | 451 (5.4) | 463 (0.66) |

**Table 2 Conditional logistic regression to estimate the odds ratios for the association between hormone therapy and venous thromboembolism**

| HT exposure | Cases (n=4140) | Controls (n=82800) | Adjusted OR (95% CI) |
|---|---|---|---|
| No use | 3653 (88.2) | 77338 (93.4) | 1.00 (reference) |
| HT use | | | |
| Current (<=30 days) | 208 (5.0) | 1507 (1.8) | 2.36 (1.99-2.80) |
| Recent (31-90 days) | 87 (2.1) | 953 (1.2) | 1.43 (1.12-1.83) |
| Remote (>90 days) | 192 (4.7) | 3002 (3.6) | 1.06 (0.90-1.25) |
| Varicose veins | 213 (5.1) | 617 (0.8) | 5.07 (4.20-6.10) |
| Heart failure | 2006 (48.5) | 20869 (25.2) | 1.98 (1.81-2.15) |
| Hypertension | 2819 (68.1) | 41611 (50.3) | 1.11 (1.01-1.22) |
| Osteoarthritis | 2095 (50.6) | 25582 (30.9) | 1.45 (1.35-1.56) |
| Neurologic surgery | 100 (2.4) | 736 (0.9) | 1.39 (1.09-1.78) |
| Thoracic surgery | 620 (15.0) | 4507 (5.4) | 1.76 (1.58-1.97) |
| Abdominal surgery | 619 (15.0) | 5633 (6.8) | 1.67 (1.50-1.86) |
| Urogenital surgery | 138 (3.3) | 1007 (1.2) | 1.84 (1.50-2.27) |
| Orthopedic surgery | 233 (5.6) | 358 (0.4) | 8.17 (6.72-9.94) |

**Table 3 Current use of hormone therapy and the risk of venous thromboembolism**

| HT exposure | Cases (n=7413) | Controls (n=79142) | Adjusted OR (95%CI) |
|---|---|---|---|
| No use | 6829 (92.1) | 77276 (97.6) | 1.00 (reference) |
| HT use | | | |
| Estrogen | 188 (2.5) | 861 (1.1) | 2.30 (1.9-2.8) |
| Estrogen- progestogen | 369 (5.0) | 944 (0.1) | 5.24 (4.6-6.0) |
| Progestogen | 27 (0.4) | 61 (1.2) | 3.65 (2.2-6.1) |
| Duration <90 days | | | |
| Estrogen | 78 (1.1) | 444 (0.6) | 1.73 (1.32-2.26) |
| Estrogen- progestogen | 118 (1.7) | 364 (0.5) | 4.44 (3.52-5.62) |
| Progestogen | 20 (0.3) | 44 (0.1) | 3.34 (1.82-6.12) |
| Duration >=90 days | | | |
| Estrogen | 110 (1.5) | 463 (0.6) | 2.67 (2.11-3.38) |
| Estrogen- progestogen | 251 (3.5) | 624 (0.8) | 5.43 (4.58-6.43) |
| Progestogen | 8 (0.1) | 20 (0.03) | 4.81 (1.88-12.31) |

**Table 4 Past use of hormone therapy and the risk of venous thromboembolism**

| HT exposure | Cases (n=7125) | Controls (n=78526) | Adjusted OR (95% CI) |
|---|---|---|---|
| No use | 6829 (95.9) | 77276 (98.4) | 1.00 (reference) |
| Past HT use | | | |
| Estrogen | 118 (1.7) | 661 (0.8) | 1.58 (1.27-1.98) |
| Estrogen- progestogen | 171 (2.4) | 534 (0.7) | 3.53 (2.90-4.29) |
| Progestogen | 7 (0.1) | 55 (0.1) | 0.69 (0.28-1.70) |

**Table 5 The association between hormone therapy and venous thromboembolism in healthy postmenopausal women**

| HT exposure | Cases (n=2306) | Controls (n=51744) | Adjusted OR (95% CI) |
|---|---|---|---|
| No use | 1823 (79.1) | 48394 (93.5) | 1.00 (reference) |
| HT use | | | |
| Current (<=30 days) | 281 (12.2) | 1237 (2.4) | 6.34 (5.32-7.56) |
| Recent (31-120 days) | 95 (4.1) | 815 (1.6) | 3.38 (2.62-4.36) |
| Remote (>120 days) | 107 (4.6) | 1298 (2.5) | 1.97 (1.57-2.48) |

**Table 6 The association between hormone therapy and venous thromboembolism in postmenopausal women (we extended the duration of HT exposure by adding 30 days to the prescription)**

| HT exposure | Cases (n=8321) | Controls (n=83141) | Adjusted OR (95%CI) |
|---|---|---|---|
| No use | 6829 (82.1) | 77369 (93.1) | 1.00 (reference) |
| HT use | | | |
| Current (<=30 days) | 877 (10.5) | 2501 (3.0) | 3.93 (3.59-4.30) |
| Recent (31-120 days) | 265 (3.2) | 1249 (1.5) | 2.08 (1.80-2.42) |
| Remote (>120 days) | 349 (4.2) | 2022 (2.43) | 1.58 (1.39-1.80) |

**Table 7 The association between hormone therapy and venous thromboembolism in postmenopausal women after excluding HR switchers**

| HT exposure | Cases (n=8104) | Controls (n=82663) | Adjusted OR (95% CI) |
|---|---|---|---|
| No use | 6829 (84.3) | 77276 (93.5) | 1.00 (reference) |
| HT use | | | |
| Current (<=30 days) | 584 (7.2) | 1866 (2.3) | 3.74 (3.36-4.16) |
| Recent (31-120 days) | 296 (3.7) | 1250 (1.5) | 2.30 (1.99-2.65) |
| Remote (>120 days) | 395 (4.9) | 2271 (2.8) | 1.60 (1.42-1.81) |

附件二

# 國科會補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現或其他有關價值等，作一綜合評估。

| |
|---|
| 1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估<br>■ 達成目標<br>□ 未達成目標（請說明，以 100 字為限）<br>□ 實驗失敗<br>□ 因故實驗中斷<br>□ 其他原因<br>說明： |
| 2. 研究成果在學術期刊發表或申請專利等情形：<br>論文：□已發表 □未發表之文稿 ■撰寫中 □無<br>專利：□已獲得 □申請中 □無<br>技轉：□已技轉 □洽談中 □無<br>其他：（以 100 字為限） |

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）（以500字為限）

目前十分強調實證醫學，臨床醫師不能只憑著自己的經驗治療病人，雖然在臨床上，東方人似乎比較少會發生靜脈栓塞，但是苦於缺少大規模流行病學的統計資料，這將是東方人第一個有如此大規模全國性有關停經後婦女有無使用賀爾蒙發生靜脈栓塞的流行病學的研究。本研究團隊已查過過去的文獻，發現截至目前為止，亞洲國家只有以小規模某家醫院或數家醫院表的文章並沒有像西方國家有以社區或全國性發表有關停經後婦女發生靜脈栓塞的大規模流行病學文章。而目前台灣醫師在2002年之後因為WHI這篇研究的結果，越來越少給予停經症候群婦女女性賀爾蒙治療，因為在白種人婦女使用女性賀爾蒙治療會明顯增加靜脈栓塞。因此我們全面性探討停經後婦女發生靜脈栓塞的流行病學，大約得知台灣的深層靜脈栓塞發生率雖低，停經後婦女如口服女性賀爾蒙激素治療仍會增加深層靜脈栓塞的風險，尤其是同時存在一些可能增加深層靜脈栓塞的危險因子。但是如果在停止使用口服女性賀爾蒙激素之後，會隨時間增長而逐漸降低深層靜脈栓塞的風險，但是在台灣並無使用經皮女性賀爾蒙激素治療，所以無法得知經由不同路徑給予女性賀爾蒙激素治療是否會有不同深層靜脈栓塞的風險。希望在本疾病的流行病學特性詳加了解情況下，可提供未來國內醫師在給予口服女性賀爾蒙激素治療時，必須考慮病患是否存在發生深層靜脈栓塞的風險，如給予口服女性賀爾蒙激素治療時應盡量縮短療程既能改善停經後症狀也能降低深層靜脈栓塞的風險。

附件四

# 國科會補助專題研究計畫項下出席國際學術會議心得報告

日期：100 年 9 月 4 日

| | | | |
|---|---|---|---|
| 計畫編號 | NSC 100-2629-B-006-001- | | |
| 計畫名稱 | 荷爾蒙替代療法於停經婦女之使用型態與心血管風險評估研究（GM7） | | |
| 出國人員姓名 | 鄭靜蘭 | 服務機構及職稱 | 國立成功大學/助理教授 |
| 會議時間 | 101 年 08 月 22 日<br>至<br>101 年 08 月 26 日 | 會議地點 | 巴塞隆納、西班牙 |
| 會議名稱 | (中文)第二十八屆國際藥物流行病學與風險管理研討會<br>(英文) 28th International Conference on Pharmacoepidemiology & Therapeutic Risk Management | | |
| 發表論文題目 | (中文)以病例對照研究分析 Allopurinol 引起史帝文強森症候群之相關危險因子<br>(英文)Risk factors associated with allopurinol related Stevens-Johnsons Syndrome- a case control study in Taiwan | | |

## 一、參加會議經過

1. 8/22 及 8/23 是會議的教育訓練課程(pre-conference educational sessions)，課程內容以介紹藥物流行病學及風險管理為主，由歐美國家之專家學者講述基本的理論及方法，包含(1) pharmacogenomics：from basics to high dimensionality data analysis: concurrent, introductory and advanced topics in the field of pharmacogenetic epidemiology (2) medical device epidemiology (3)introduction to pharmcogentics (4) medical device epidemiology (5) introduction to pharmacoepidemiology (6)registries/prospective cohort studies (7) propensity scores (8) comparative effectiveness research (9) intermediate pharmacoepidemiolog-2012 theme: dealing with unmeasured covariates (10) regulatory pharmacoepidemiology/health care decision-making (11) introduction to drug utilization research (12) advanced topics in pharmacoepidemiology (13) introduction to therapeutic risk management and evaluation-focus on implementation in the EU (14) advanced drug utilization research (15) healthcare databases

2. 8/24 大會正式開始，主要與會者仍以歐美國家居多，但在論文發表上臺灣是亞洲地區之冠，比日本、韓國、印度、澳洲的投稿篇數還多，並且有 4 篇是口頭發表。keynote speech 是邀請英國 NICE(National Institute for Health and Clinical Excellence)的 chairman，Dr. Sir Michael Rawlins 針對如何藉由藥物流行病學之研究成果應用於制定藥品使用規範。
3. 8/24 至 8/26 大會期間參加了以下 concurrent session
   (1) Method tapas: 以方法學為主，由不同國家的研究者報告利用不同的研究方法於藥物流行病學之應用①the impact of unmeasured confounders in cardiovascular studies performed in administrative databases②comparison of five diagnosis based comorbidity measures in predicting health-related quality of life in multiple sclerosis patients ③combining data in multi-country studies: mega-analysis versus meta-analysis④design aspects of pharmacoepidemiological two-phase studies⑤use of claims data to predict dependence in older adults⑥automated identification of asthma patients within an electronical medical record database using machine learning
   (2) Drug utilization in cardiovascular disease: ①time trends in antihypertensive drug use and blood pressures in Swedish primary health care 2001-2008②predictors of first-step antihypertensive treatment among older adults at high risk for cardiovascular outcome③oral hypoglycemic agent adherence and hospitalization among patients with type 2 diabetes: a call for enhanced guidelines④drug treatment after transient ischaemic attack or ischaemic stroke: are we doing enough to reduce secondary risk?⑤potentially inappropriate drugs in elderly hypertensive patients with impaired renal function⑥prevalence of potentially inappropriate medication prescribing among older US adults
   (3) Advanced methods and measures for studying complex drug utilization patterns with patient-level databases
   (4) CV meds: what would you do? ①the effect of statin use on acute kidney injury risk following coronary artery bypass graft surgery②statin use and risk of atrial fibrillation or flutter: a population-based case-control study③the assessment of statin-associated severe muscle toxicity in Japan-by using claims database with laboratory information(此篇是台灣與日本的交換學生利用日本的資料所進行的研究)④cardiovascular risk of olmesartan compared with other angiotensin-II receptor blockers⑤angioedema events and use of drugs that act on the renin-angiotensin-aldosterone system (RAAS)⑥risk of acute renal failure likely due to concurrent use of ACE-inhibitors, angiotensin receptors blockers, diuretics and anti-inflammatory drugs
   (5) Tapas: junk drawer ①orlistat and the risk of acute liver injury: a self-controlled

case-series study in united kingdom general practice research database②comparative effectiveness of linezolid and vancomycin among a national cohort of veterans affairs patients with methicillin-resistant staphylococcus aureus③risk of venous thromboembolism among Taiwan osteoporosis populations: alenderonate vs raloxifene users(此篇是台灣成功大學博士班學生利用台灣全民健保資料庫分析台灣骨質疏鬆症婦女使用之藥品是否會產生靜脈血管栓塞之不良反應)④quantifying staphylococcus aureus disease burden with clinical microbiology culture data: attributable time trends in a regional healthcare system⑤the prevalence of X-linked hypohidrotic ectodermal dysplasia in Denmark from 1995-2010⑥risk of incident cardiovascular disease events in patients with psoriasis: a retrospective cohort study using the general practice research database

(6) Cross-national or multi-database research networks: a new initiative in Asia-Pacific region and ongoing initiatives in Europe and US 在 2009 年由日本、韓國、臺灣、澳洲、美國的學者發起跨國的研究，結合各國的資料針對同一主題進行藥物流行病學研究，目前已有初步的成果，因此於大會中分享在亞洲地區的經驗。

(7) Drug utilization research: adherence and persistence ①The effect of copayment on antiretroviral medications adherence for newly treated HIV-positive adults with commercial insurance②patient-reported reasons for discontinuation of commonly used treatments for moderate to severe psoriasis③difference in persistence rates between responders and non-responders to mailed questionnaires④real-life treatment persistence with golimumab, etanercept and aimumab in patients with rheumatoid arthritis in canada⑤determinants, pattern, and outcomes of non-adherence to HARRT in a Portuguese cohort of HIVE-1 infected subjects⑥twelve-year trend in treatment seeking for buprenorphine, heroin and amphetamine abuse in finland

(8) Globalisation of utilization research: current challenges and triumphs

(9) Methods: the real deal①primary non-compliance and its determinants: implications for implications for misclassification of drug exposure②a comparison of methods for estimating exposure-time trends in case-case-time-control designs③utility of nested case control design for risk assessment in the presence of an important risk modifier in pharmacoepidemiological studies: evidence from simulated data④calendar time as an instrumental variable in nonexperimental comparative effectiveness research of dynamic therapies⑤cox's proportional hazards regression using instrumental variables⑥statistical methods for comparing the effectiveness of treatment regimens in long-term observational comparative effectiveness research studies with time-varying tretments

4. 8/26 大會結束前的熱門話題的主題為"evaluating cancer risk with diabetes treatment: methodological challenges"，由 5 位學者分別報告如何應用藥物流行病學方法學於

觀察性研究評估糖尿病用藥與癌症之風險，包含如果控制 selection bias、adherence 的測量、控制組的選擇等議題進行討論。

5. 8/26 發表論文，許多國外的學者對於臺灣健保資料庫表示興趣，另外有英國、韓國及丹麥的學者對藥品引起 stevens-johnson syndrome 主題有興趣，因此進行了討論。

## 二、與會心得

1. 國際藥物流行病學與風險管理研討會是由國際藥物流行病學會統籌主辦每年的大會，而國際藥物流行病學會是一個由各國專家學者組成的非營利組織，學會的成員包含醫師、藥師、政府官員、統計學家等，其研究方向係利用流行病學之理論基礎，以病患安全為主軸，進行藥品療效及安全性之相關研究。因此在每年大會開始前會安排的教育訓練課程，不但讓新的會員有基本的認識，也可以讓舊的成員複習。
2. 參加的 concurrent session，可以了解各國在藥品使用評估研究上的現況，以及研究主題，並且可以學習不同研究結果的呈現方式。
3. 藥物使用評估研究成果若要與其他國家進行比較，必須按照目前公認之藥物分類系統 WHO/ATC 進行編碼，在大會中也到 WHO/ATC 的攤位請教相關事宜，因此對此編碼系統有更清楚的了解。
4. 在大會上發表論文，與不同國家的學者討論研究成果，不但可以吸取他人的經驗，更可以向他們介紹臺灣的健保資料庫。
5. 今年度雖然臺灣是亞洲地區參與人數最多的國家，但大部分是來自學術單位，而藥物流行病學研究的成果可作為用藥安全決策參考依據之一，因此許多國家之醫療決策單位也共同參與本會。

## 三、考察參觀活動（無是項活動者略）：

無

## 四、建議

1. 國際藥物流行病學與風險管理研討會大多是在歐美國家舉辦，對於國內參與此會議之學者給予相關補助。
2. 2014 年第三十屆國際藥物流行病學與風險管理研討會將在臺灣舉辦，臺灣的健保資料庫是一難得的研究資源，目前國內亦有許多研究成果發表，但在研究方法的應用上仍需參考國外的經驗，因此希望有更多學者以及醫療決策單位可參與此次會議。

## 五、攜回資料名稱及內容

1. 大會手冊: 內容為本次大會的行程表及摘要檢索
2. 會員手冊: 包含所有的會員基本資料，如姓名、機構、聯絡資訊等
3. 摘要集：本次大會所發表論文之摘要

## 六、其他:

無

# 國科會補助計畫衍生研發成果推廣資料表

日期:2013/01/09

| 國科會補助計畫 | 計畫名稱: 荷爾蒙替代療法於停經婦女之使用型態與心血管風險評估研究 (GM7) |
|---|---|
| | 計畫主持人: 高雅慧 |
| | 計畫編號: 100-2629-B-006-001- 學門領域: 性別主流科技計畫 |

無研發成果推廣資料

# 100 年度專題研究計畫研究成果彙整表

| 計畫主持人：高雅慧 | 計畫編號：100-2629-B-006-001- |
|---|---|
| 計畫名稱：荷爾蒙替代療法於停經婦女之使用型態與心血管風險評估研究（GM7） | |

| 成果項目 | | | 量化 | | | 單位 | 備註（質化說明：如數個計畫共同成果、成果列為該期刊之封面故事...等） |
|---|---|---|---|---|---|---|---|
| | | | 實際已達成數（被接受或已發表） | 預期總達成數(含實際已達成數) | 本計畫實際貢獻百分比 | | |
| 國內 | 論文著作 | 期刊論文 | 0 | 0 | 100% | 篇 | |
| | | 研究報告/技術報告 | 1 | 1 | 100% | | |
| | | 研討會論文 | 0 | 0 | 100% | | |
| | | 專書 | 0 | 0 | 100% | | |
| | 專利 | 申請中件數 | 0 | 0 | 100% | 件 | |
| | | 已獲得件數 | 0 | 0 | 100% | | |
| | 技術移轉 | 件數 | 0 | 0 | 100% | 件 | |
| | | 權利金 | 0 | 0 | 100% | 千元 | |
| | 參與計畫人力（本國籍） | 碩士生 | 0 | 0 | 100% | 人次 | |
| | | 博士生 | 1 | 1 | 100% | | |
| | | 博士後研究員 | 0 | 0 | 100% | | |
| | | 專任助理 | 1 | 1 | 100% | | |
| 國外 | 論文著作 | 期刊論文 | 0 | 0 | 100% | 篇 | |
| | | 研究報告/技術報告 | 0 | 0 | 100% | | |
| | | 研討會論文 | 0 | 0 | 100% | | |
| | | 專書 | 0 | 0 | 100% | 章/本 | |
| | 專利 | 申請中件數 | 0 | 0 | 100% | 件 | |
| | | 已獲得件數 | 0 | 0 | 100% | | |
| | 技術移轉 | 件數 | 0 | 0 | 100% | 件 | |
| | | 權利金 | 0 | 0 | 100% | 千元 | |
| | 參與計畫人力（外國籍） | 碩士生 | 0 | 0 | 100% | 人次 | |
| | | 博士生 | 0 | 0 | 100% | | |
| | | 博士後研究員 | 0 | 0 | 100% | | |
| | | 專任助理 | 0 | 0 | 100% | | |

| | |
|---|---|
| 其他成果<br>(無法以量化表達之成果如辦理學術活動、獲得獎項、重要國際合作、研究成果國際影響力及其他協助產業技術發展之具體效益事項等，請以文字敘述填列。) | 無 |

| | 成果項目 | 量化 | 名稱或內容性質簡述 |
|---|---|---|---|
| 科教處計畫加填項目 | 測驗工具(含質性與量性) | 0 | |
| | 課程/模組 | 0 | |
| | 電腦及網路系統或工具 | 0 | |
| | 教材 | 0 | |
| | 舉辦之活動/競賽 | 0 | |
| | 研討會/工作坊 | 0 | |
| | 電子報、網站 | 0 | |
| | 計畫成果推廣之參與（閱聽）人數 | 0 | |

# 國科會補助專題研究計畫成果報告自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現或其他有關價值等，作一綜合評估。

1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估

■達成目標

□未達成目標（請說明，以 100 字為限）

□實驗失敗

□因故實驗中斷

□其他原因

說明：

2. 研究成果在學術期刊發表或申請專利等情形：

論文：□已發表 □未發表之文稿 ■撰寫中 □無

專利：□已獲得 □申請中 ■無

技轉：□已技轉 □洽談中 ■無

其他：(以 100 字為限)

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）(以 500 字為限)

目前十分強調實證醫學，臨床醫師不能只憑著自己的經驗治療病人，雖然在臨床上，東方人似乎比較少會發生靜脈栓塞，但是苦於缺少大規模流行病學的統計資料，這將是東方人第一個有如此大規模全國性有關停經後婦女有無使用賀爾蒙發生靜脈栓塞的流行病學的研究。本研究團隊已查過過去的文獻，發現截至目前為止，亞洲國家只有以小規模某家醫院或數家醫院表的文章並沒有像西方國家有以社區或全國性發表有關停經後婦女發生靜脈栓塞的大規模流行病學文章。而目前台灣醫師在 2002 年之後因為 WHI 這篇研究的結果，越來越少給予停經症候群婦女女性賀爾蒙治療，因為在白種人婦女使用女性賀爾蒙治療會明顯增加靜脈栓塞。因此我們全面性探討停經後婦女發生靜脈栓塞的流行病學，大約得知台灣的深層靜脈栓塞發生率雖低，停經後婦女如口服女性賀爾蒙激素治療仍會增加深層靜脈栓塞的風險，尤其是同時存在一些可能增加深層靜脈栓塞的危險因子。但是如果在停止使用口服女性賀爾蒙激素之後，會隨時間增長而逐漸降低深層靜脈栓塞的風險，但是在台灣並無使用經皮女性賀爾蒙激素治療，所以無法得知經由不同路徑給予女性賀爾蒙激素治療是否會有不同深層靜脈栓塞的風險。希望在本疾病的流行病學特性詳加了解情況下，可提供未來國內醫師在給予口服女性賀爾蒙激素治療時，必須考慮病患是否存在發生深層靜脈栓塞的風險，如給予口服女性賀爾蒙激素治療時應盡量縮短療程既能改善停經後症狀也能降低深層靜脈栓塞的風險。