科技部補助專題研究計畫報告

台灣婦女更年期心血管疾病危險因子之變化：一個長期追蹤研究（L03）

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本研究具有政策應用參考價值：■否 □是，建議提供機關
（勾選「是」者，請列舉建議可提供施政參考之業務主管機關）
本研究具影響公共利益之重大發現：□否 □是

中 華 民 國 109 年 08 月 27 日

中 文 摘 要 ： 本計劃案先完成婦女停經年齡與死因別死亡率的解析。目的：過去的研究認為停經年齡與全死因、心血管、癌症、糖尿病等死因別死亡率有關，然而研究結果在不同的族群並不一致。本研究欲在台灣人群檢驗這些關係是否存在。研究設計：我們使用美兆人體生物資料庫的資料納入了36931位已停經的婦女(健康檢查在1999-2016年間進行)。停經年齡與共變項的資訊由健康問卷與體檢獲得。停經年齡分組為<40-44歲、45-49歲、50-54歲(對照組)、55-60歲。分析方法採用Cox比例風險迴歸模型。主要指標：死亡原因(死因檔2018年7月前之登錄)。結果：平均的停經年齡為50.2歲(標準差4.0)並且在14.6年的追蹤期間發生了5316個死亡事件。在調整出生世代、教育、抽菸、身體質量指數與共病之後，結果顯示婦女停經年齡為<40-44歲者相較於對照組糖尿病死亡的風險為1.44倍(HR=1.44, 1.03-2.02)。婦女停經年齡為45-49歲者相較於對照組的全死因死亡風險為1.07倍(HR=1.07, 1.01-1.14)且心血管死亡的風險為1.22倍(HR=1.22, 1.07-1.40)。結論：在台灣過早的停經(<40-44歲)與糖尿病死亡有關，較早的停經(45-49歲)與全死因和心血管的死亡有關。停經年齡可視為是心血管代謝相關的因子之一，與婦女的壽命有明確的關係。

中 文 關 鍵 詞 ： 停經年齡；全死亡率；糖尿病死亡率；心血管死亡率；癌症死亡率

英 文 摘 要 ： Objective: Previous research suggested age at menopause may predict risk of all-cause, cardiovascular disease (CVD) and cancer mortality; however, findings were inconsistent across populations. We aimed to investigate this association in a cohort of Taiwanese postmenopausal women.
Study design: We used data from the MJ Health Database in Taiwan and included a cohort of 36,931 postmenopausal women who entered health check-up programs during 1999 to 2016. Information on age at menopause and covariates were collected from health survey and medical examination at baseline. Age at menopause was categorized into <40-44, 45-49, 50-54 (reference) and 55-60 years. We used Cox proportional hazards regression for analysis.
Main outcome measures: Causes of death (obtained from the National Register of Death as of July, 2018).
Results: Average follow-up time was 14.6 years and 5,316 deaths were identified. After adjustment for birth cohort, education, smoking and comorbidities, results showed significant higher all-cause mortality in women having menopause at 45-49 years (Hazard Ratio [HR] = 1.07, 95% CI: 1.01, 1.14) than the reference category. These women were also associated with increased CVD mortality (HR = 1.22; 1.07, 1.40), while CVD risk declined in the 55-60 years category (HR = 0.84; 0.70, 1.02). We noted women having menopause at <40-44, 45-49 and 55-60 years may have higher cancer mortality, but results were not significant.
Conclusions: Earlier age at menopause is associated with

increased all-cause and CVD mortality in Taiwanese women. Age at menopause could be deemed an important disease marker for women at midlife that indicates future mortality risk.

英文關鍵詞：Age at menopause; all-cause mortality; cardiovascular disease mortality; cancer mortality

1. INTRODUCTION

Menopause is the cessation of ovulation and marks the declining of sex hormones (e.g., estrogen) produced by the ovaries. A decline in estrogen in the body affects many organs and systems, including cardiovascular and bone systems, and increases disease risks, such as for metabolic syndrome[1], diabetes[2], cardiovascular diseases[3], osteoporosis and fractures[4-7]. Timing of onset of menopause matters to women's health as well. Age at menopause is not only a biological marker of starting reproductive aging but also indicates somatic aging. In epidemiological studies, early onset of menopause was found to be associated with more chronic diseases and death[8]. Findings from meta-analysis suggested that premature menopause (menopause under age 40) or early menopause (menopause between age 40 and 45) is linked to a higher risk of all-cause, cardiovascular disease and coronary heart disease mortality[9].

However, research findings regarding age at menopause and cancer mortality are less consistent. Because late onset of menopause indicates longer lifetime exposure to sex hormones, late menopause (menopause after age 55) is associated with more breast, uterine, and ovarian cancers[10,11,12]. Earlier studies such as Mondul et al. found that cancer mortality rates were lower in American women who experienced menopause at a younger age[10]. Recently, Roman Lay and colleagues from Brazil showed that women having menopause at 41-44 or 45-49 had twice the risk of cancer death than women having menopause at 50-54, and they did not find an increased risk in women having menopause after 55[13]. Research communities are still unsure about the association of age at menopause and cancer mortality given the heterogeneous study results.

To our best knowledge, there have been no published studies examining the association of age at menopause and cause-specific mortality in Taiwanese women. Women in Taiwan, as

those in other East Asian countries, may have different reproductive patterns and lifestyles than Caucasian women or women in other parts of the world. Racial and ethnic differences in reproductive health are important to study since they represent some underlying determinants of health, such as environmental, sociocultural and genetic factors[14]. Besides, the increasing life expectancy in Taiwanese women[15] has made research into the risk factors for cardiovascular diseases and cancers more and more important. We therefore carried out a cohort analysis to investigate the relation between age at menopause and risk of all-cause death, death from cardiovascular disease and death from cancers among Taiwanese women.

2. METHODS

2.1 Data source

We obtained participant data for the current analysis from the MJ Health Database built by the MJ Health Management Institution (http://www.mjhrf.org/main/index/en). In brief, the MJ Health Management Institution is a private healthcare facility in Taipei, Taiwan that provides health examination services and has been collecting the health survey and medical examination data since 1994. The health survey questionnaire asked participants questions regarding sociodemographic, lifestyles, medical history, and reproductive history, etc. The health examination included physical exams, blood analysis, urine analysis and image tests, etc. During health examination, participants were queried about the use of their data for research purposes and the MJ Health Database included only those who gave proper consent. Many participants had multiple visits for health examination over the years and the database has included over 1.5 million participant's visits. Researchers in Taiwan and across the world have used this database and published many important epidemiologic studies[16].

Questions on menopausal status were added into the questionnaire in 1999; hence, we included female participants who came to MJ Health Examination Centers from 1999 up to 2016. We further restricted our inclusion criteria to women who had reached menopause and who aged 49 years or older when doing health examination. When a women had multiple visits in the database, we only kept data from their first visit after menopause. As a result, we set up a study cohort consisting of 36,931 postmenopausal women who, on average, aged 61 years at baseline. The protocol for this study was approved by the Ethics Committee at the National Cheng Kung University in Taiwan.

2.2 Study outcome: mortality

The main outcome of the study was death from all causes, death from cardiovascular diseases and death from all cancers, identified from January 1999 through July 2018. We linked our participant data to the data file of the National Register of Death using a unique citizen identifying number. The underlying cause of death was classified by International Classification of Diseases, 9th or 10th Revision (ICD-9-CM or ICD-10-CM). Death from cardiovascular diseases included death from coronary heart disease (ICD-9=410-414 and 420-429; ICD-10= I20-I25), stroke (ICD-9=430-438; ICD-10= I60-I69) and other circulatory diseases (ICD-9=390-392, 393-398, 401-405 and 440; ICD-10= I10-I15, I01-I02.0, I05-I09, I27, I30-I52, I70 and I71). For cancer deaths, we used codes of ICD-9=140-208 or ICD-10=C00-C97.

2.3 Study exposure: age at menopause

Age at menopause was obtained from participants' responses to the health survey questionnaire. We asked participants "Have you reached menopause (having gone 12 months in a row without a period)? If yes, what was your age at menopause?" Age at menopause was further categorized into <40-44, 45-49, 50-54, and 55-60 years. Other gynecology-related

questions included (1) “Have you been using hormone therapy (HT)?”, (2) “Have you been taking contraceptive pills?” and (3) “Have you had any gynecological surgery?”

2.4 Covariates

Covariates were derived based on information gained from health survey or medical examination at baseline. Sociodemographic variables included birth year (categorized into five groups: ≤1930, 1931-1935, 1936-1940, 1941-1945 and 1946-1950), age at time of survey, educational level attained (illiterate, elementary school, junior high school, senior high school and college or above) and marital status (married, never married, divorced and widowed). Lifestyle variables included smoking (current or former smoker vs. non-smoker) and drinking (current or former drinker vs. non-drinker). Clinical variables included history of diabetes mellitus, hypertension and hyperlipidemia and body mass index (BMI) in kg/m^2.

2.5 Data analysis

We compared baseline characteristics across categories of age at menopause by χ^2 test or analysis of variance. We used survival analysis (Cox proportional hazards model) to investigate the association between age at menopause and all-cause, cardiovascular or cancer mortality. We defined the time origin as date of birth, and age in years was used as the time scale. We computed the follow-up time in years (from age at entry to the event of interest, i.e., all-cause death, cardiovascular death or all-cancer death). To adjust for the age differences at baseline, our survival model allowed for delayed entry[17]. The participants were at risk after they entered our study, for example, at age 50 or 60 years, depending on their age at first health check-up survey.

We further constructed multivariable Cox regression models that adjusted for potential confounders for the association of age at menopause with mortality, including birth year,

education, smoking and comorbidities. These covariates were chosen according to our previous research[18]. Moreover, we stratified the analysis by the attained age (<80 years and ≥80 years) of our participants. Missing data on covariates were imputed through multiple imputations when doing the analysis[19].

Given that hysterectomy, oophorectomy, and use of HT and contraceptive pills can mask the true age at natural menopause of our participants, we also conducted sensitivity analysis where we excluded those who had any gynecological surgery or had been using HT or contraceptive pills. To graphically display the association of age at menopause and mortality, we computed the hazard ratios using the restricted cubic splines model and plotted the estimates and 95% confidence intervals. All analyses were conducted using the STATA software version 15 (Stata Corp, College Station, TX), and the restricted cubic splines plots were generated using the R software 3.5.3 (codes provided by Woodward et al.[20]).

3. RESULTS

Our analysis included 36,931 Taiwanese women. **Table 1** shows the baseline characteristics across four categories of age at menopause. The mean age at survey was 61.2 $\pm$ 6.9 (standard deviation) years and the baseline age was older (62.3 $\pm$ 6.2) in women who were 55-60 years old at menopause. There were also significant between-category differences in birth cohort, educational level, body mass index, smoking status and history of hypertension and diabetes. There were no significant differences in marital status, history of hyperlipidemia or drinking status among women in different categories of age at menopause.

The total follow-up time for all participants in this study were 538,459 person-years. There were 5,316 deaths identified during the follow-up period; 1,141 deaths (21%) were due to

cardiovascular diseases, and 2,011 (38%) were due to cancers (see **Table 2**). The unadjusted results showed a higher risk of all-cause death in women who had menopause at <40-44 (hazard ratio [HR] = 1.10, 95% CI: 1.00, 1.21) and 45-49 years (HR = 1.08, 95% CI: 1.01, 1.15) than the reference group (women who had menopause at 50-54 years).

Table 2 also shows women who had menopause at 45-49 years had 21% higher risk (95% CI: 1.06-1.39) of cardiovascular death, relative to the reference group. Women who were 55-60 years old at menopause had a lower risk of cardiovascular death than the reference group, but the effect was not significant (HR = 0.88, 95% CI: 0.73, 1.06). The association between age at menopause and cancer mortality did not reach statistical significance but higher risks are noted in women who had menopause at <40-44, 45-49 and 55-60 years, as compared to the reference group.

Results from the multivariable models, with adjustment for birth cohort, educational attainment, smoking status and comorbidities (history of hypertension, diabetes and hyperlipidemia), can be found in **Table 2** as well. These effects (HRs) did not change much from the effects in unadjusted models. Results of the sensitivity analysis (n=21,621), where we excluded those who had any gynecological surgery or had been using HT or contraceptive pills, can be found in the **Supplementary Table**. Although the effect estimates (HRs) for mortalities were slightly different from our main analysis findings (**Table 2**), the overall pattern seemed to be similar.

The **Figure** graphed the adjusted hazard ratios from the restricted cubic splines models for the association of age at menopause and mortalities, with 50 years as the reference age. We found that for all-cause death the shape of the curve was smooth, with lowest risk of all-cause mortality at around 52 years of age at menopause. For cardiovascular death, we observed a

curve with inverted U shape. Women who had menopause at around 45 years had the highest risk of cardiovascular mortality and the risk was decreasing for women who had menopause at a later age. For all-cancer mortality, the risk was slightly higher at an earlier age at menopause but the risk started getting increased again for women who had a later age at menopause.

We stratified the association of age at menopause with risk of mortality by attained age (<80 years and ≥80 years). The results can be found in **Table 3**. When comparing the results from women with attained age <80 years versus ≥80 years, we observed that some effect estimates were attenuated in women with attained age ≥80 years. For example, women with attained age <80 years and who had menopause at <40-44 years had 1.15 (adjusted HR, 95% CI: 1.02-1.30) times risk of all-cause mortality than the reference group; the effect was 1.09 (95% CI: 0.93-1.28) in women with attained age ≥80 years. Women with attained age <80 years and who had menopause at 55-60 years had 0.76 (adjusted HR, 95% CI: 0.58-0.99) times risk of cardiovascular mortality than the reference group; the effect was 0.95 (95% CI: 0.73-1.24) in women with attained age ≥80 years.

4. Discussion

Based on a large cohort of postmenopausal women in Taiwan, we found that early (40-44) and earlier (45-49) age at menopause were associated with higher risk of all-cause mortality. In further cause-specific analysis, earlier age at menopause was significantly associated with higher risk of CVD mortality while later (55-60) age at menopause was assocaited with lower risk. The results on cancer mortality were not statistically significant, but the risk may be higher both in women having earlier menopause and in women having later menopause. Our study

highlights that age at menopause is an important disease marker for postmenopausal women and that sex hormone plays a crucial role in women's health.

The results suggested a 22% increase in the risk of CVD mortality in women having menopause at 45-49 years and a 16% decrease in risk in women having menopause at 55-60 years, as compared to women having menopause at 50-54 years. Sex hormone such as estrogen is known to have cardioprotective effects. For example, estrogen reduces fibrosis and oxidative stress, stimulates angiogenesis and vasodilation and improves mitochondrial function[21]. Less lifetime exposure to estrogen, using earlier age at menopause as a surrogate, is therefore likely to increase the risk of CVD and CVD mortality.

However, we noted in our study that women who had their menopause the earlest (<40-44 years) did not have a significant higher risk of CVD death, which may be due to the following reasons. For one thing, women with early menopause or premature menopause may die of causes other than CVD. The impact of hormone deficiency is universal and involes multiple organs and systems. Some studies have shown in women with early menopause the causes of death may be a consequence of osteoporosis or fractures[6]. Modul and colleagues[10] reported that women who had earlier menopause had higher risk of mortality that can be attributed to respiraptry disease, genitourinary disease and external causes, which reflected the complications of fractures. For another, our sample of women were surveyed at a relatively old age (mean: 61.2 years). The women who had premature menopause or early menopause would have a lower chance of entering our sample because they might be more likely to die prematurely. This leads to the issue of left truncation in survival analysis[22] and we tried to address it by computing the survival time that adjusted for delayed entry.

As for cancer mortality, their relationship with age at menopause is less clear given that we noted slightly higher cancer deaths in women having earlier menopause and also later menopause, but the results were not statistically significant. Because we were not able to differentiate different types of cancer in our study, the type of cancer associated with earlier menopause may be different from the type of cancer associated with later menopause. For instances, previous research has shown that women exposed to longer time of sex hormones have an increased risk for breast cancer and ovarian cancer[12,23,24,25]. At the same time, we also learned from clinical trials that use of HT was associated with a lower risk for colorectal cancer, stomach cancer and lung cancer[26-29]. The relationship between age at menopause and cancer incidence or cancer mortality is rather complicated since the effects may vary greatly depending on the type of cancer. Hence, we think that systematic research synthesis may be needed in order to exmaine these associations carefully and identify the current evidence gap.

In the analysis that was stratified by attained age (≤80 versus >80 years), there were differences in the associations between age at menopause and cause-specific mortality. The magnitude of effect for all-cause mortality and CVD mortality seemed to be stronger in women with an attained age ≤80, while the effect for cancer mortality seemed to be stronger in women with an attained age >80. We do not fully understand the reasons; perhaps some of the conditions related to early menopause such as CVD and stroke may develop and progress rather quickly in the women's life course. In contrast, the development and progression of some breast cancer may be relatively slow. But due to the small proportion of deaths and potentially a lack of power after we made the stratification, we cannot really conclude with the current data.

The present study is not free from limitations. In the questionnaire, these women were not asked if they had received hysterectomy or bilateral oophorectomy, which leads to surgical menopause prior to natural menopause. The only relevant question we could use was if they

had received gynecological surgery, so in the sensitivity analysis we excluded those women who had received any gynecological surgery from our sample. Also, in the sensitivity analysis we excluded women who reported having used HT and oral contraceptives to minimize the confounding influences, and the results overall were not so different from the primary analysis. Moreover, there were concerns with regard to the misclassification of age at menopause, since age at reaching menopause was based on women's recall, and some of them were surveyed at relatively old age. But previous research has shown that recall of age at menopause is oftentimes reliable[30], so we did not expect that misclassification of age at menopause would bias the true association seriously.

The major strength of this study is the large sample size (n = 36,931) of postmenopausal women and the prospective long-term follow-up (up to almost 20 years). Through linking our health examination data and the National Register of Death in Taiwan, we were able to track the vital status of our study participants. Besides, because we had data on the categories of causes of death, analysis of the cause-specific mortality was hence made possible. To conclude, our study demonstrated the association between women's age at menopause and risk of all-cause, CVD and cancer mortality in an East Asian population. The findings suggest that age at menopause is an important disease marker for midlife women that is indicative of future longevity. The study sheds lights on the physiological mechanisms for chronic diseases in women after menopause and may inform clinicians about future development of management strategies or interventions.

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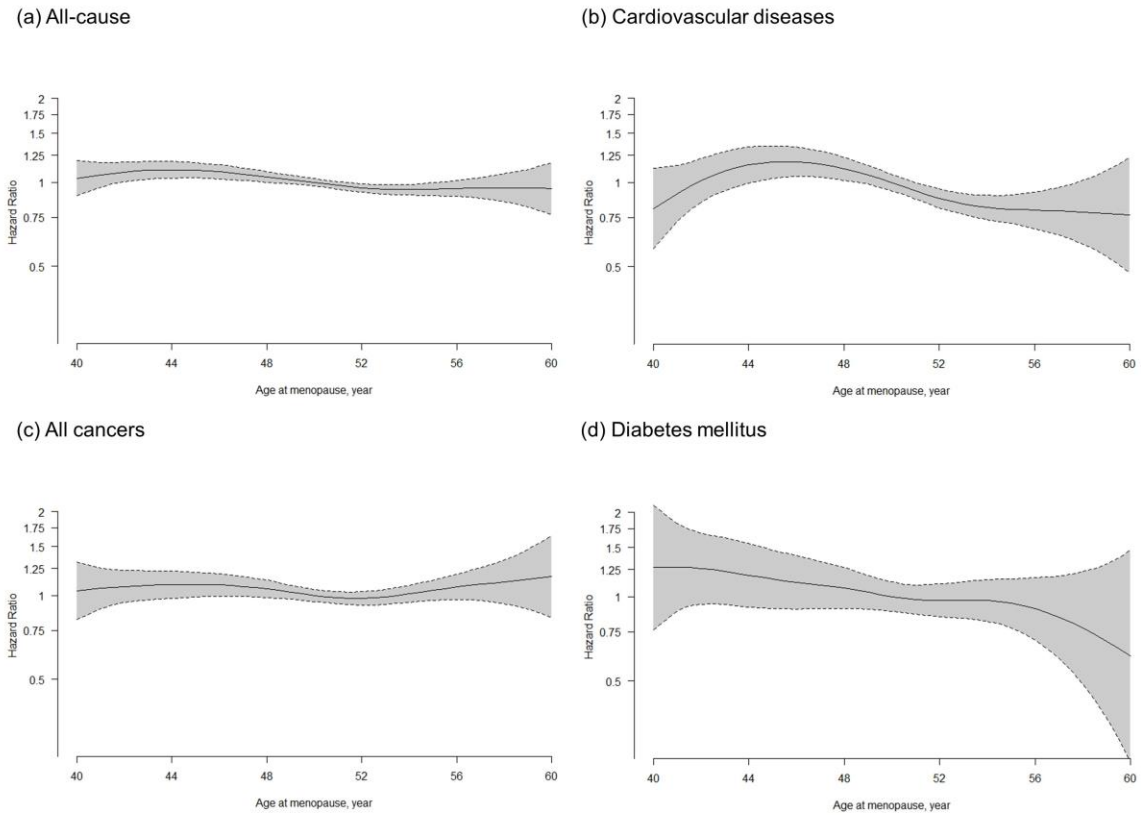

Figure legend

Restricted cubic spline plots with adjusted hazard ratios (95% CI) for all-cause (a), cardiovascular (b) and all-cancer (c) mortality associated with women's age at menopause. We adjusted for birth cohort, education, smoking status, hypertension, diabetes and high blood cholesterol in analysis.

Table 1.

Baseline characteristics stratified by age at menopause (N=36,931)

	Age at menopause (years)					
Characteristics	**Total n=36,931**	**<40-44 n=3,384**	**45-49 n=9,155**	**50-54 n=19,265**	**55-60 n=5,127**	***P*-value**
Age at baseline in years, mean ± SD	61.2±6.9	61.1±7.1	61.1±7.2	61.0±6.9	62.3±6.2	<0.001
Birth cohort, %						<0.001
1930 or before	7.8	7.6	8.6	7.7	7.2	
1931-1935	10.8	10.6	11.3	10.5	11.2	
1936-1940	20.3	18.9	20.7	19.7	23.2	
1941-1945	27.0	27.0	25.5	27.0	29.9	
1946-1950	34.0	35.9	34.0	35.2	28.5	
Marital status, %						0.071
Never married	0.7	0.8	0.9	0.7	0.5	
Married	70.8	69.3	70.6	71.1	71.5	
Divorced	2.9	3.4	3.0	2.8	2.7	
Widowed	25.5	26.5	25.5	25.4	25.3	
Education, %						<0.001
Illiterate	21.9	22.3	24.0	20.7	22.1	
Elementary	44.2	43.0	43.2	44.4	45.9	
Junior high	11.9	11.8	11.1	12.2	12.2	
Senior high	12.2	12.2	11.6	12.7	11.3	
College or above	9.9	10.7	10.1	10.0	8.6	
Body mass index (kg/m^2), mean ± SD	24.3±3.5	24.4±3.6	24.3±3.5	24.2±3.4	24.6±3.4	<0.001
Hypertension, %[a]						<0.001
Yes	46.9	45.7	45.8	46.5	51.5	
No	53.1	54.3	54.2	53.5	48.5	
Diabetes, %[b]						<0.001
Yes	14.1	15.9	14.2	13.3	15.9	
No	85.9	84.1	85.8	86.7	84.1	
High blood cholesterol, %[c]						0.303
Yes	25.8	24.9	26.1	25.6	26.5	
No	74.2	75.1	74.0	74.4	73.5	
Smoking, %						0.016
Current or former smoker	9.7	10.6	10.3	9.3	9.8	
Never smoker	90.3	89.4	89.7	90.8	90.2	

	Age at menopause (years)					
Characteristics	**Total n=36,931**	**<40-44 n=3,384**	**45-49 n=9,155**	**50-54 n=19,265**	**55-60 n=5,127**	***P*-value**
Drinking, %						
Current or former drinker	6.0	6.0	5.9	5.9	6.6	0.402
Never drinker	94.0	94.0	94.1	94.1	93.4	

[a] Hypertension was defined as using antihypertensives, self-reported having hypertension or that systolic blood pressure was ≥140 mmHg or diastolic blood pressure was ≥90 mmHg.

[b] Diabetes was defined as using diabetes medications, self-reported having diabetes or that fasting blood glucose was ≥126 mg/dl.

[c] High blood cholesterol was defined as using cholesterol-lowering medications or that total cholesterol was ≥240 mg/dl.

Abbreviation: SD=standard deviation

Table 2.
Hazard ratios of age at menopause and mortality

			Unadjusted		Adjusted[a]	
Age at menopause	**Person-years**	**No. of deaths**	**Hazard ratio**	**95% CI**	**Hazard ratio**	**95% CI**
All-causes						
<40-44	48853	498	1.10	1.00-1.21	1.09	0.99-1.20
45-49	135469	1424	1.08[b]	1.01-1.15	1.07[b]	1.01-1.14
50-54	282783	2667	1.00	-	1.00	-
55-60	71354	727	1.00	0.92-1.09	0.98	0.90-1.06
Cardiovascular diseases (ICD9=390-392, 393-398, 401-405, 410-414, 420-429, 430-438, 440; ICD10=I10-I15, I01-I02.0, I05-I09, I20-I25, I27, I30-I52, I60-I69, I70, I71)						
<40-44	48853	101	1.06	0.85-1.31	1.05	0.85-1.30
45-49	135469	342	1.21[b]	1.06-1.39	1.22[b]	1.07-1.40
50-54	282783	563	1.00	-	1.00	-
55-60	71354	135	0.88	0.73-1.06	0.84	0.70-1.02
All cancers (ICD9=140-208; ICD10=C00-C97)						
<40-44	48853	182	1.07	0.92-1.26	1.07	0.91-1.25
45-49	135469	534	1.10	0.99-1.23	1.10	0.99-1.22
50-54	282783	991	1.00	-	1.00	-
55-60	71354	304	1.13	0.99-1.29	1.12	0.99-1.28
Diabetes mellitus (ICD9=250; ICD10=E10-E14)						
<40-44	48853	43	1.52[b]	1.09-2.13	1.44[b]	1.03-2.02
45-49	135469	99	1.20	0.94-1.54	1.19	0.93-1.53
50-54	282783	166	1.00	-	1.00	-
55-60	71354	47	1.03	0.74-1.42	0.91	0.66-1.26

[a] Adjusted for birth cohort, education, smoking status, body mass index, hypertension, diabetes, and high blood cholesterol

[b] $p<0.05$

Abbreviations: CI=Confidence Interval; ICD=International Classification of Diseases

Table 3.
Hazard ratios of age at menopause and mortality by attained age

	Attained age <80					Attained age ≥80				
		Unadjusted		Adjusted[a]			Unadjusted		Adjusted[a]	
Age at menopause	No. of Deaths	Hazard ratio	95% CI	Hazard ratio	95% CI	No. of Deaths	Hazard ratio	95% CI	Hazard ratio	95% CI
All-causes										
<40-44	316	1.11	0.99-1.25	1.15[b]	1.02-1.30	182	1.09	0.93-1.28	1.09	0.93-1.28
45-49	904	1.11[b]	1.02-1.20	1.06	0.98-1.15	520	1.01	0.91-1.12	1.02	0.92-1.13
50-54	1675	1.00	-	1.00	-	992	1.00	-	1.00	-
55-60	448	0.94	0.84-1.04	0.95	0.86-1.06	279	1.06	0.93-1.21	1.05	0.92-1.20
Cardiovascular diseases (ICD9=390-392, 393-398, 401-405, 410-414, 420-429, 430-438, 440; ICD10=I10-I15, I01-I02.0, I05-I09, I20-I25, I27, I30-I52, I60-I69, I70, I71)										
<40-44	56	1.11	0.83-1.47	1.15	0.86-1.53	45	1.01	0.74-1.39	1.01	0.73-1.38
45-49	183	1.23[b]	1.02-1.48	1.18	0.98-1.42	159	1.16	0.95-1.41	1.17	0.96-1.43
50-54	299	1.00	-	1.00	-	264	1.00	-	1.00	-
55-60	67	0.76[b]	0.58- 0.99	0.76[b]	0.58-1.00	68	0.97	0.74- 1.27	0.95	0.73-1.24
All cancers (ICD9=140-208; ICD10=C00-C97)										
<40-44	135	1.03	0.86-1.23	1.07	0.89-1.28	47	1.25	0.91-1.72	1.25	0.91-1.72
45-49	413	1.12	0.99-1.26	1.08	0.96-1.22	121	1.06	0.85-1.32	1.06	0.85-1.32
50-54	772	1.00	-	1.00	-	219	1.00	-	1.00	-
55-60	233	1.08	0.93-1.25	1.10	0.95-1.28	71	1.22	0.93-1.59	1.23	0.94-1.61
Diabetes mellitus (ICD9=250; ICD10=E10-E14)										
<40-44	30	1.80[b]	1.20-2.71	1.73[b]	1.14-2.61	13	1.15	0.63-2.08	1.14	0.63-2.07
45-49	64	1.32	0.97-1.81	1.18	0.86-1.61	35	1.01	0.67-1.52	1.07	0.71-1.61
50-54	99	1.00	-	1.00	-	67	1.00	-	1.00	-
55-60	26	0.89	0.58-1.38	0.89	0.57-1.37	21	1.18	0.72-1.93	1.09	0.66-1.78

[a] Adjusted for birth cohort, education, smoking status, body mass index, hypertension, diabetes, and high blood cholesterol

[b] $p<0.05$

Abbreviations: CI=Confidence Interval; ICD=International Classification of Diseases

108年度專題研究計畫成果彙整表

計畫主持人：余聰	**計畫編號：**108-2629-B-006-001-
計畫名稱：台灣婦女更年期心血管疾病危險因子之變化：一個長期追蹤研究（L03）	

成果項目			量化	單位	質化 （說明：各成果項目請附佐證資料或細項說明，如期刊名稱、年份、卷期、起訖頁數、證號...等）
國內	學術性論文	期刊論文	0	篇	
		研討會論文	0		
		專書	0	本	
		專書論文	0	章	
		技術報告	0	篇	
		其他	0	篇	
國外	學術性論文	期刊論文	1	篇	Age at menopause and mortality in Taiwan: A cohort analysis Maturitas. 2020 Jun;136:42-48.
		研討會論文	0		
		專書	0	本	
		專書論文	0	章	
		技術報告	0	篇	
		其他	0	篇	
參與計畫人力	本國籍	大專生	0	人次	
		碩士生	0		
		博士生	0		
		博士級研究人員	0		
		專任人員	0		
	非本國籍	大專生	0		
		碩士生	0		
		博士生	0		
		博士級研究人員	0		
		專任人員	0		
其他成果 （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。）					