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全民健保成人預防保健服務對於
疾病早期治療及降低全死因死亡的效果分析

The effectiveness of Adult Preventive Care Service under National Health Insurance on early disease treatment and reduction of all-cause mortality

研究生：林承昌 (R96846015)
Cheng-Chang Lin

指導教授： 季瑋珠 博士
李永淩 博士

Advisor : Wei-Chu Chie, Ph.D.
Yung-Ling Lee, Ph.D.

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等到要寫致謝這個部分，已經是 2009 年 7 月初了，當初想好一缸子要感謝的人，但是現在的我腦細胞已經凋亡了一大半，已寫不出心中無限的感激和悸動。但是最感恩的是在這裡遇到了很多好老師、好同學，讓資質駑鈍的我受益良多，兩年來各種報告、考試、資料處理、論文撰寫等一項項腦力、體力與壓力的考驗，若沒有老師的指導、同學的互相幫忙鼓勵及家人的支持，也無法有現在的成果。

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Abstract

Introduction：

Chronic diseases prevention became more important in the first decades of the 20th century, which stimulated the implementation of screening programs. The National Health Insurance (NHI) reimbursed the adult preventive care service package for beneficiaries aged 40 and older in Taiwan since 1996. About one-third of its target population utilized this service periodically. However, there has been little evidence for the effectiveness of the service, particular in clinical outcomes.

Purpose：

The purpose of this study is to assess effectiveness of the adult preventive service on early treatment of chronic disease and the reduction of mortality.

Material and methods：

A total of 32,039 subjects aged 40-100 years by the year 2000 were identified from the representative 200,000-person sample in the reimbursement database of the National Health Insurance in Taiwan. Uptakes of preventive service during 1998-2000 were retrieved, and subjects were followed from Jan 1, 2001 to Dec 31, 2007, information about ambulatory visits and inpatient care during this period was also collected.

Multiple logistic regression and Cox proportional hazard regression were applied to estimate the odds ratio and hazard ratio on newly treated

hypertension, diabetes, hyperlipidemia and all-cause mortality for those who ever utilize the service. Extended Cox model with counting process was implemented to treat the time-dependent covariate and assess the effectiveness of each uptake.

Results：

There were 16,080 male (50.2%) and 15,959 female(49.8%) in the study population and the average age of each group were 55.6±11.9 years and 56.0±11.9 years. During the seven years follow-up, 32.1%, 9.1% and 14.5% of each defined cohort developed newly treated hypertension, diabetes and hyperlipidemia.

The hazard ratios (HR) of each uptake on newly treated hypertension within one year were 1.80(95% confidence interval, CI: 1.64-1.97), 1.67(95%CI: 1.50-1.85) and 1.56 (95%CI: 1.43-1.72) among subjects aged 40-54, 55-64 and 65-100. For newly treated diabetes, the hazard ratios were 1.59(95%CI: 1.19-2.13), 2.21(95%CI: 1.87-2.61) and 1.76(95%CI: 1.50-2.05) among subjects aged 40-54, 55-64 and 65-100. For newly treated hyperlipidemia, the hazard ratios were 3.97(95%CI: 3.59-4.38), 3.21(2.85-3.63) and 2.82(95%CI: 2.49-3.20) among subjects aged 40-54, 55-64 and 65-100. All of these estimates were statistically significant ($p< 0.001$).

The hazard ratio of each uptake on all-cause mortality within one and within seven years were statistically significant only among subjects aged 65-100 (HR: 0.74, 95%CI: 0.67-0.84; HR: 0.80, 95% CI: 0.72-0.89, $p<0.001$).

Conclusion：

This study provides strong evidence for impact of adult preventive care service on major health outcomes. The results indicated the effectiveness of the service on early treatment of hypertension, diabetes and hyperlipidemia, and finally, reduction of all-cause mortality, especially in subjects aged 65-100.

Keywords：adult preventive care service, periodic health examination

中文摘要

背景：

疾病預防的觀念自二十世紀初期開始蓬勃發展，同時也促成了各類型週期性健康檢查計畫的實行。我國全民健康保險自從民國 85 年開始全面支付成人預防保健服務，服務內容包含生活型態及病史調查、物理檢查及實驗室檢查，其檢查項目涵蓋大部分我國國民主要死因的疾病篩檢，每年約有三成民眾接受此項服務。然而至今少有足夠之證據和文獻有效的評估成人預防保健服務的效用，尤其是在臨床上結果的分析。

目的：

本研究的目的在探討對於高血壓、糖尿病及高血脂疾病病程，接受成人預防保健服務可以達成早期治療和降低全死因死亡率的效果。

材料與方法：

本研究為回溯性世代研究，採用具有全國代表性的全民健康保險研究資料庫 20 萬人抽樣歸人檔進行次級資料分析，研究材料採用抽樣歸人檔資料中第一及第二組資料，以民國 89 年為基準，擷取年齡 40 到 100 歲的保險對象做為追蹤世代，追蹤時間自民國 90 年 1 月 1 日至 96 年 12 月 31 日。由次級資料庫中擷取目標族群於 87 至 89 年間接受預防保健服務的資料,及其追蹤期間所有門、住、急診及治療記錄。

本研究使用 multiple logistic regression 及 Cox proportional hazard regression 分析曾接受此項服務對於新發生高血壓、糖尿病、高血脂治療及全死因死亡事件的勝算比(odds ratio)及風險比(hazard ratio)，本研究亦採用時間相依 Cox 模型進行分析。

結果：

本研究世代樣本共包含 16,080 位男性 (50.2%) 及 15,959 位女性(49.8%) ，平均年齡分別是 55.6±11.9 歲和 56.0±11.9 歲。在 7 年追蹤期間，原先沒有高血壓、糖尿病及高血脂的族群，各有 32.1%, 9.1%和 14.5%的比例發生目標疾病的治療。

研究結果發現，每次接受成人預防保健服務後 1 年，在 40-54 歲、55-64 歲和 65-100 歲的族群，其發生高血壓治療之風險比(hazard ratio)為 1.80(95% confidence interval, CI: 1.64-1.97)、1.67(95%CI: 1.50-1.85) 和 1.56 (95%CI: 1.43-1.72)；發生糖尿病治療的風險比為 1.59(95%CI: 1.19-2.13)、2.21(95%CI: 1.87-2.61) 和 1.76(95%CI: 1.50-2.05) ；發生高血脂治療的風險比則是 3.97 (95%CI: 3.59-4.38)、3.21(2.85-3.63)和 2.82(95%CI: 2.49-3.20)。這些估計值都具統計上顯著意義 ($p< 0.001$)。

每次接受成人預防保健服務後 1 年內及 7 年內，其發生全死因死亡的風險比僅在 65 至 100 歲的族群達到統計上顯著($p<0.001$)，其風險比分別 0.74(95%CI: 0.67-0.84) 及 0.80(95% CI: 0.72-0.89)。

結論：

本研究有效證實成人預防保健服務對於健康結果的影響。研究結果顯示使用成人預防保健服務，對於高血壓、糖尿病和高血脂三種影響國人健康的主要慢性病，能達到早期治療的效果, 且在 65 至 100 歲的族群，有降低全死因死亡風險的保護效果。

關鍵詞：成人預防保健服務、週期性健康檢查

Table of contents

List of Tables

List of Figure

Figure Page

List of appendices

Content Page

Chapter 1. Introduction

1.1 Background

Disease prevention became more prominent in the first decades of the 20th century, which stimulated the growth of clinical preventive medicine as a professional discipline, and the implementation of screening programs. While considerable attentions had been paid in the past to benefits of periodic health examination (PHE), the results were inconclusive and opinions regarding PHE were conflicting.

Application of health examination is increasing in many domains and for different purposes today, the most well-known is the role of secondary prevention, but the precise origin of health examination could be traced back to the middle of the nineteenth century [1, 2].

In the early 1900s, incentives for assessing and enhancing individuals' health through PHE were financial and economical. In private corporate industry, PHE was applied to insure the health of workers, and could contribute to productivity or morale; similarly, the life insurance industry used medical histories and scheduled physical exams for risk stratification. Physical exams were also utilized in school attending, military forces enrollment and gaining employment for similar objects.

Regarding medical history, Dobell (1861) advocated PHE as a way to identify earliest evasive periods of defect in the physiological state, Gould (1900) claimed that PHE was a method for gaining scientific knowledge of the early natural history of disease, after that, National Tuberculosis Association promoted PHE as a tool for early diagnosis of disease. In 1918, PHE was also advocated for early detection of cancer and hoped that would increase the probability of cure. The guiding concerns of early proponents were scientific and humanitarian, and PHE was meant to advance knowledge and prevent diseases that had yet to be fully understood or effectively treated.

Even the American Medical Association (AMA) had advocated" annual physical examination" and the rise of preventive medicine in 1920s, PHE did not become popular and enthusiastic during 1930s and the Great Depression. PHE regained attention in the mid-1940s with the development of medical technology. The term "Multiphasic health screening (MHC)" represented a mass screening, which involved physicians only minimally and was done by using technology that could be applied economically and efficiently. In 1950s, clinics devoted to executive physical examinations, and PHE became prominent administrative concerns in prepaid health care, the most influential experience was that of the Kaiser Permanente Health Plan in the San Francisco area. The PHE thus came to serve the purposes of satisfying patient demand for health care and improving the efficiency of the health care delivery system.

The emergence of evidence-based medicine in the 1960s raised serious questions concerning the value of PHE, and this trend provoked several large randomized controlled trials, including multiphasic screening trial at Kaiser (1964) and South-East London screening trail in the U.K. (1967), each had more than 6 years follow-up. Both two studies were costly and demonstrated minimal improvement in clinical outcomes. These frustrated results challenged the employment of PHE, and ultimately influenced British public policy against multiphasic screening at that time.

The preventive services moved toward individualized in the 1970s. PHE evolved into visits with the primary emphasis of evaluation and offering preventive health services based on patients' age, gender and risk status for recognizable and treatable conditions. Frame and Carlson (1975) evaluated the impact of screening measures on altering disease progression and outcomes with regard to 36 major medical conditions. After that, Canadian Task Force (CTF) and U.S. Preventive Services Task Force (USPSTF) began to assess specific preventive cares and their clinical impact in several medical conditions. These efforts endorsed the evidence-based approaching of PHE in later decades [3].

Through these historical changes, Han (1997) provided an extensive and objective summary in historical changes of PHE, he proposed eight objectives of it, listed as follows: (a) the goal of early disease detection and the reduction of morbidity and mortality, (b) scientific knowledge, (c) economic savings, (d) professional empowerment, (e) physician-patient relationship, (f) data collection, (g) satisfaction of patient demand, (h) administrative efficiency. While most available evidence contributed to the first and third objectives, other objectives are equally important [2].

Although available evidence only endorsed some preventive services among asymptomatic subjects, PHE still had its place in many public health domains. With the growing of geriatric population and prevalence of chronic disorders, many efforts were made, some preventive services such as annual health examination were applied, which included physical exams, screenings of essential disorders, health promotion, immunization or reminder system differently.

In the U.S., Medicare provided coverage for annual preventive visits and some preventive services in elderly. “Medicare demonstration project” was launched in the 1990s, several trials regarding Medicare preventive services package were conducted. In Japan, the project of “Health services for the elderly” was launched since 1983. Nakanishi et al. (1995, 1996) conducted surveys to assess the efficacy and cost-effectiveness of policy on health care for the elderly, these studies reported some benefits of PHE [4].

In Taiwan, the preventive services were included in the National Health Insurance (NHI) Program. NHI Program was implemented since 1995, which was a comprehensive, unified, universal health insurance program for all citizens of Taiwan. The coverage rate achieved 96% since 1996, and the government made some preventive services free for gender, children, adults aged 40-year-old and older, these services included screening of child’s development, prenatal check-up, screening for some cancer and periodic health examination for adults and elderly residents.

1.2 Specific objectives

The purpose of this study is to demonstrate effectiveness of the adult preventive service on chronic disease treatment and the reduction of mortality.

Chapter 2. Literature review

2.1 Randomized controlled trials for effectiveness of PHE

Kaiser Multiphasic Health Check-up(MHC) Study was a large trial included 10,713 subjects aged 35-54 years in 1964, Study group was encouraged to undergo an annual MHC, control group received usual care. In this study, the MHC consisted of a series of laboratory and radiologic tests, self-report history, and follow up physical exam by an internist. Exams included electrocardiogram (ECG), measurement of blood pressure, anthropometry, chest X-rays, mammography, visual acuity, tonometry, audiometry, spirometry, urine test and serum chemistry panel. The report of MHC would be sent to the patient's regular physician. Outcomes assessed included self-reported disability, costs, and mortality. Mortality outcomes were followed up to 16 years. Collen (1973) and Friedman (1986) published the results of Kaiser MHC study [3, 5-10], main results revealed that study group experienced a significant 30% reduction in deaths from pre- specified "potentially postponable" causes, largely associated with lower death rates from colorectal cancer and hypertension. This reduction was most pronounced in the early years of the study. The major limitations of this study included self-administrated questionnaire, potential inadequate adjustment for confounders, such as baseline differences, interactions with other health care systems or services. Study design and results were summarized in Table 2-1.

The South‐East London screening study group (1967) performed a large randomized controlled trial (RCT), which enrolled 7,229 community dwelling persons in South London who attended two large group practices. Study group received a general practice-based screening service for persons aged 40-64 and followed up for nine years. Main outcomes were disease detection, habitual changes, self- reported major disability, hospitalization and mortality rate. Screening consisted of symptoms questionnaire, physical examination, anthropometry, laboratory tests and image studies, study design and results were summarized in Table 2-2. Results were passed to the general practitioners for advanced management. Nine years after the initial screening, no significant differences were found between the two groups in any of the outcome measures. The major limitations were similar to Kaiser MHC study, especially for potential inadequate adjustment for confounders, for example, subjects may exposed to other health services, and undetermined durable effects of PHE many years later. These two large RCTs had highlighted the major restriction in this kind of study design, that is, the assumption of comparability between groups was difficult to fulfill in long-term follow-ups. Besides, the approach of blindness was limited in these RCTs [11].

Imperial Cancer Research Fund OXCHECK Study Group (1989) conducted a RCT in five urban and suburban general practices in Bedfordshire, England. This RCT was designed to assess the effectiveness of health checks delivered by nurses in primary care, and outcomes were changes of risk factors for cardiovascular disease and cancer. Over 4,500 subjects aged 35-64 years were enrolled, study group received dietary and behavioral assessment, health check-up, laboratory and image study in year one, both study and control group underwent terminal health check-ups in year four. Study design and results were summarized in Table 2-3. Main outcomes included serum cholesterol, blood pressure, adiposity and proportion of morbidity. Results indicated that health check-up could reduce risk dietary habits, and lower the cholesterol. In this study, intention-to-treat analysis was applied [12, 13].

Four studies were conducted regarding effectiveness of Medicare demonstration project during 1989-93, two attributed to one series study. All of them were RCTs, which consisted of different services, the basic components were preventive service package, health promotion and counseling. Medicare enrolled participants aged 65 or older. Study designs and results were discussed as follows and summarized in Table 2-4 [14-17].

Morrissey et al. (1995) assessed the impact of reimbursement for Medicare preventive service package, in which subjects received annual preventive check-up and health promotion visits. Reminding system, office setting and charting form were supported in primary care. 1,914 elderly subjects were included, and followed 2 years. Main outcomes included performance of immunization and screenings, costs, hospitalization and self-administrated health related quality of life (HR-QOL). This study found that Medicare preventive service package could enhance performance dramatically, and had minimal increasing in HR-QOL.

Burton et al. (1995) conducted two studies regarding demonstration project, the first study enrolled 4,295 community-dwelling Medicare recipients. Study group underwent annual preventive visit, which consisted of preventive care and health risk counseling. In preventive care, physical examination, blood pressure, functional status, depression and incontinence tests, anthropometry, immunization and laboratory tests were used. Costs, ambulatory visits and hospitalization were set as outcomes. The results demonstrated that preventive package may reduce use of ambulatory visits without cost impact. Mixed model was implemented in this study, the author wanted to assess the directions and significance of impacts on outcomes. Burton followed another two years after prior endpoint, there was no advanced intervention. He applied Quality of Well-Being score (QWB) and assessed the risk attitude and lifestyle, performance of health care provider and costs were also evaluated. Significant differences were only found on performance of Papanicolaou smear and stool occult blood. The author concluded that benefits demonstrated in first two years regarding costs and health status couldn't be sustained.

Patrick et al. (1999) conducted another study in Seattle, 2,558 subjects were included and followed for two years. The Service package consisted of health risk assessment, a health promotion visit, disease prevention visit, counseling on exercise and diet with educational classes. Study outcomes contained immunization (influenza vaccine), changes of health habits and attitudes, weight status, mortality and health status (QWB). In line with previous studies, significant differences could be found in immunization and change in exercise habit. In research of Medicare demonstration project, it was not clear whether the improvement of a part or all of intervention.

Theobald et al. (1998) used registry database to explore impacts of PHE on mortality outcomes. The study enrolled over 30,000 Stockholm residents in Sweden, who aged 18-65 years and were randomized to 12 subgroups according to age and health need. Study group was invited to receive general health examination with a referral and follow-up system (Table 2-5). Outcomes included all cause and specific cause mortality 20 years later and were obtained from national death registry. The results were inconclusive and could not support the effectiveness of PHE. This study had similar limitations of other large RCTs discussed above [18].

Another interesting study was conducted by Fletcher et al. (1977), he implemented multiphasic screening and try to demonstrate its benefit on early detection of important medical problems. Only 112 subjects who aged 45-60 years were enrolled (Table 2-5). As a matter of course, immediate effect of MHC brought on significant finding in study group, however, early management of disorder may be more suitable as an outcome than early diagnosis of that [19].

2.2 Observational studies for effectiveness of PHE

Most of studies conducted since 1900 have an observational design, which may attributed to the fact that randomized trials of PHE are by nature large and very expensive. Here we reviewed six observational studies regarding effectiveness of PHE, the study designs and detail results were summarized in Table 2-6.

Hama et al. (2001) reported a retrospective study which analyzed 240 subjects, the study group had received pre-assignment health check-up in the last year. Contents of health check-up including physical examination, laboratory tests, and image studies. Outcomes included disease detection, change of blood pressure, serum cholesterol and adiposity. The results showed fewer hyperlipidemia and hypertension among study group. The author applied logistic regression and proposed pre-assignment medical examination may contribute to predicting the health status. We should interpret this conclusion cautiously, due to limitation of observational study, that is, lessen inferences that can be drawn from their results [20].

Another retrospective study came from occupational field, Burton et al. (2002) assessed the effect of executive physical examination in Bank One medical database. 1,773 subjects aged 40 or older were selected. Study group underwent at least one physical examination during past six years. Outcomes were costs from medical claims and days of disability three years later. The results revealed more costs and less disability were found among study group.

This study had other limitations not mentioned above, such as baseline differences were not described, only age and sex were adjusted in statistics. Besides, this result could not be applied in general population [21].

Chiou et al. (2002) reported an excellent finding regarding PHE in Taiwan. This retrospective cohort study enrolled 1,193 elderly subjects resided in Kaohsiung City randomly. The study initiated in 1993, subjects received baseline interviews and were provided of free annual physical examination. The physical examination consisted of similar items in adult preventive service, image study was also provided. The author used extended Cox regression model and adjusted covariates such as age, gender, education, co-morbidity status and living area. The relative risk (RR) of mortality for each annual health examination service was 0.71 (P=0.136). This result could only generalize to urban elderly population. Although this finding came from observational study, and we didn't know by what component the PHE contributing to outcome, we still could conclude cautiously, that is, lower risk of mortality did have positive relationship of utilization of PHE [22].

In the field of cross-sectional studies, Nakanishi et al. (1995) evaluated the correlation between the use of preventive health services under the Japanese Health Services for the Elderly Act and the demands for in-patient and out-patient care by insured residents aged 40 or older who were covered by the National Health Insurance. The author used claim data of 9 cities located in northern part of Osaka in 1993. Results showed positive correlation between utilization rate of PHE and out-patient utilization (r=0.664, p=0.026), and inverse correlation of total medical costs (r=-0.779, p=0.07) and in-patient utilization (r=-0.89, p=0.001). This study reported correlation coefficient only on population level [23, 24].

Finkelstein et al. (2002) investigated the correlation between receiving PHE and receiving some preventive services. 19,600 female subjects from each household received in-depth interviews and collected data of socioeconomic status, education level, living area and utilization of health care. Individual information of receiving Papanicolaou smear, mammography, bone mineral density and cholesterol screening was retrieved from administrative data. The results indicated two messages, first was that having an annual health check-up was associated with age, income, education level and living area, the other message was the positive correlation between receiving PHE and Papanicolaou smear (OR: 6.7, 95%CI: 4.6-9.7), mammography (OR: 3.7, 95%CI: 2.3-5.9), bone mineral density(BMD) (OR: 3.7, 95%CI: 1.3-10.5) , cholesterol screening (OR: 3.0, 95%CI: 2.0- 4.5) [25].

Somkin et al. (2004) conducted similar study and included 463 women. The results showed that subjects who having check-up in last 12 months was associated with utilization of Papanicolaou smear(OR: 2.28, 95%CI: 1.68-3.0) and mammography(OR: 4.38, 95% CI: 2.95-6.5) [26].

2.3 Systematic review for effectiveness of PHE

The Agency for Healthcare Research and Quality (AHRQ) conducted technology assessment and want to establish evidence regarding effectiveness of PHE in 2006, Boulware et al. (2006) developed conceptual framework and classified outcomes into five groups, list as follows: (a)patient attitudes, such as trust, satisfaction, or worry, (b)behavioral change, such as smoking, risk diet and lifestyle, (c)clinical outcomes, such as morbidity, mortality, early detection of disorder, (d)resources use and costs, such as hospitalization and out-patient utilization, (e)public health domain. This concept did enhance the process of literature review and study design. As review above, different definition and contents of PHE did cause difficulty in the process of review. Finally, 50 articles represented 33 studies were enrolled, they also established tool for quality evaluation. The best available evidence assessing benefits or harms of PHE consisted of 21 studies published from 1973 to 2004. In these studies, the author concluded that PHE had a consistently beneficial association only with patient receipt of Papanicolaou smears, cholesterol screening, and fecal occult blood testing. Limitations of this study included heterogeneous definitions of PHE and some trials were performed before USPSTF guidelines. PHE effects on mortality, resources utilization were inconclusive [3, 4]. Since most of the PHE studies were inconclusive, we can't contradict the effectiveness of PHE.

2.4 Summary of the effectiveness of PHE

In the past several decades, many efforts were done to assess the effectiveness and impacts of PHE, even historical changes brought about different objectives of it. RCTs provide the only study design capable of minimizing bias due to unmeasured confounding. However, it is difficult to follow long-term outcomes in RCTs. In Kaiser and South London RCTs, no significant positive effect was available, which may attribute to uselessness of PHE or potential inadequate adjustment of confounders. In studies of Medicare demonstration project, the benefits of the preventive service package were inconclusive and may not be sustained, these studies had similar limitations.

Despite of these frustrating results, some observational studies provided prominent evidence of association between PHE and benefits, like studies of Nakanishi and Chiou. Through these observational studies, we could obtain less inference of causality, and we didn't know by what component PHE contributing to outcome. As summarized above, retrospective cohort study was considered more suitable in PHE outcome evaluation, we can obtain detailed information of demographic, educational level, socioeconomic status and health care behavior.

Little research had been done on the effect of early disease detection and early intervention, which were primary purpose of screening.

2.5 Factors related to PHE utilization

In recent years, we have found mounting evidence of the influenced factors regarding health service utilization of preventive service. Health belief model and behavior model were the most frequently applied. Belcher (1990) conducted RCT in 1,224 male outpatients, this study indicated that only physician and clinic-oriented health promotion could keep patient's preventive activities [27]. Ho (1997) proposed some factors which may influence the use of adult preventive service, including married, having heard of this service, subjects without regular medical provider, sedentary lifestyle and taking vitamin pills habitually [28]. Another research conducted by Yang (2001) also evaluate the factors of utilization, this study indicated some significant factors, including low-income, low education level, without habits of cigarette and betel nuts use, having heard of this service [29].

In the same field, Hung (2004) demonstrated the correlation between chronic diseases and utilization of preventive service, including hypertension, heart disorder, pulmonary disorder and cancer, etc [30].

Living alone, well family support, belief of the service, and resident place were also mentioned in other observational studies (Lin, 2005; Cherrington, 2007; Tsai, 2007) [31-33].

In summary, consistent results supported that age, gender, socioeconomic status, morbidity and regular visit, attitude and belief toward the service, do have a correlation of PHE utilization.

2.6 Adult preventive care service program in Taiwan

The Bureau of National Health Insurance in Taiwan initiated the adult preventive care services since April 1996, which also named health examination or check-up for adults. This service is free for adults aged 40 and older and consists of two visits with laboratory tests and health care providers to assess subjects' overall health and risk factors, a referral system was also provided.

Contents of the adult preventive care list as follows: (a) records of self-reported medical history, dietary habits and lifestyle, (b) physical examination, including anthropometry, blood pressure, visual acuity, hearing function test, oral hygiene, (c) laboratory tests, included complete blood count, urine analysis, serum chemistry panels (plasma sugar, liver, renal and lipid profile), (d) Counseling for morbidity, risk behavior and psychological support. This service package provided two times of visit, first visit was for collection of data and for retrieving report and counseling in secondary visit. The NHI reimbursed this service package every three year for adults aged between 40 and 65, and annually, for 65 and above. In general, the adult preventive care service was similar to Medicare preventive services package, and was some form of opportunistic screening. Tsai (2007) analyzed the utilization of this preventive service under NHI, the utilization rate was 31.6% in 1999, and reached 35.4% in 2005 [33].

Although some items in adult preventive care service, such as blood routine, urine analysis, albumin, liver and renal profile, and its frequency were not recommended according to guide of clinical preventive services published by USPSTF, there is no empirical evidence regarding Chinese ethnicity to omit them.

In Taiwan, a growing number of research regarding the adult preventive service are now available, most of current studies focused on the satisfaction survey, influenced factors of utilization and descriptive results of morbidity. Yang (2001) described the distribution of abnormal finding on 572 subjects. Tsai (2007) applied bivariate analysis between newly diagnosed diseases and covariates on 10,141 subjects, these results were outlines in table 2-7. However, there have been few attempts to estimate the effectiveness of the service, particular in clinical outcomes.

2.7 Hypothesis proposed

Participants in NHI who had received or attended at the adult preventive care service would obtain more effectiveness than those didn't receive or attend at the service in following aspects:

(a) Recent effect：Achieving earlier management of chronic disease.

(Hypertension, Diabetes, and Hyperlipidemia).

(b) Long-term effect：Lower risk of mortality.

Table 2-1. Literature review of RCTs – Kaiser MHC study

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
Collen (Prev med,1973)	Randomized control trial	**<u>Source population</u>** : 46,000 Kaiser Foundation Health Plan members served by the Oakland & San Francisco facilities. **<u>Inclusion criteria</u>** : Age 35-54 at entry (birth year 1910 -1929), at least 2 yrs attended at the plan **<u>Exclusion criteria</u>** : 1. Subjects selected had moved far from the MHC clinics 2. Few uncovered identification errors **<u>Sample size</u>** Int.(5156) Ctrl(5557)	**<u>Intervention</u>** : Annual multiphasic health checkup (MHC) 1. History / Symptoms 2. U/R, CBC, SMA 3. BP, VA, tonometry, audiometry, anthropometry 4. ECG, CxR, MMG, Spirometry 5. Biennial question-naire 6. Follow-up and physical examination by an internist **<u>Control</u>** : Kaiser Health Plan members aged 35-54 who received usual care.(was not urged to take MHC) **<u>F/U length</u>** : 7 yrs **<u>Attendance</u>** : Int.- 78.1%(3326) Ctrl- 76.4%(3544)	**<u>Item</u>** : 1. OPD visits 2. Newly diagnosis 3. Hosp.(days/ 1000subjects) 4. Self-report disability(%) 5. Self-report chr. morbidity (%) 6. Overall mortality (Cumulative%) 7. Death rates for potentially post-ponable causes 8. Cost benefit anallysis **<u>Statistics</u>** : Chi-square test **<u>Adjustment</u>** : Implicit *<u>Postponable causes</u>: - Cancers ~ colorectal	**<u>Result</u>** : 1.No significant difference 2. Significant higher newly-recorded diagnoses per subject 3. 45-50 y/o men had lower utilization 4. Baseline 10.9% v.s. 14.6% 7 yrs later(*) 21.1% v.s.24.6% 5. Baseline 47% v.s. 45% 7 yrs later(*) 61% v.s. 54% 6. Overall mort. 35.6‰ v.s. 39.2‰ 7. Postponable causes mort.(*) 3.7‰ v.s. 7.4‰ Colorectal ca.	1. No report on baseline difference. (study group tends to be fairly healthy, higher SES) 2. No report on re liability & validity of questionnaire. 3. Prominent self-selection PHE in control group, leading to incomparablility. 4. Inadequate adjustment for residual confound-ding. 5. No information of drop out group. 7. Lack of subgroup analysis on some results.

Table 2-1. Literature review of RCTs – Kaiser MHC study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
			Uptake : Int.- mean 3.5 PHEs Ctrl- mean 1.3 PHEs	~ breast/cervix/ endometrium ~ prostate ~ kidney - HTN,-HCVD - CVA	0.4‰ v.s. 1.8‰ (*) 8. A net saving more than $800 per subject (* p<0.05)	
Friedman (J Chron Dis,1986)	Randomized Control Trial	**Source population** : 46,000 Kaiser Foundation Health Plan members served by the Oakland & San Francisco facilities. **Inclusion criteria** : Age 35-54 at entry (birth year 1910 -1929) , at least 2 yrs attended at the plan **Exclusion criteria** : 1. Subjects selected had moved far from the MHC clinics 2. Few uncovered identification errors **Sample size** Int.(5156) Ctrl(5557)	**Intervention** : Annual multiphasic health checkup (MHC) 1. History / Symptoms 2. U/R, CBC, SMA 3. BP, VA, tonometry, audiometry, anthropometry 4. ECG, CxR, MMG, Spirometry 5.Biennial question-naire 6. Follow-up and physical examination by an internist **Control** : Kaiser Health Plan members aged 35-54 who received usual care.(was not urged to	**Item** : 1. Hosp. (Times/Days) 2. Self-report disability(%) 3. Overall mortality (Cumulative%) 4. Death rates for potentially post-ponable causes (Cancers, HTN, HCVD, CVA) **Statistics :** 1. Wilcoxon ran sum test 2. Chi-square test 3. Chi-square test **Adjustment :** No report	**Result** : 1. Int.:53510 days Ctrl.: 55585 days Int.:10.38 times Ctrl.: 10 times 2.significant diff-erence of disab-ility at 5 & 7yrs among men aged 45-54 3. Overall mort. 113.9‰ v.s. 116.1 ‰ 4. Post-ponable causes mort.(*) 15‰ v.s. 21.5‰ Colorectal ca. 2.3‰ v.s. 5.2‰ (*) (*p<0.05) **Key finding** :	1. No report on baseline diff-erence. (study group tends to be fairly healthy, higher SES) 2. No report on re-liability & validity of questionnaire. 3. Prominant self-selection PHE in control group, leading to incom-parablility. 4. Inadequate adjustment for residual confoundding. 5. No information of drop out group.

Table 2-1. Literature review of RCTs – Kaiser MHC study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
			take MHC) **F/U length** : 16 yrs **Attendance** : Int.- 64.5%(3326) Ctrl- 63.8%(3544) **Uptake** : Int.- mean 6.8 PHEs Ctrl- mean 2.8 PHEs		Study group have lowered rate of mortality over 16 years from the potentially post-ponable causes of death.	6. Lack of subgroup analysis on some results.

Table 2-2. Literature review of RCTs – South-East London study

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
The South-East London screening study group (Int J Epidemiol, 2001) (Original 1977, republished, 2001)	Randomized control trial	**Source pop** : Patients of 2 large group practices in South London. **Inclusion criteria** : 1. 40~64 y/o in 1967 **Exclusion criteria** : No report **Sample size** Int.(3876) Ctrl.(3353) *Random allocation by family	**Intervention** : 1. In 1967 & 1970, multiphasic screening was done 2. Multiphasic screening contents: - Self-report symptoms questionnaire interview - BP and anthropometry - Visual testing - Audiometry - CxR, 12-leads EKG - Spirometry - Hb, PVC, blood urea, random blood sugar, protein-bound iodine, serum cholesterol, serum uric acid - Basic physician examination 3. Results were passed to the general practitioner for advanced management **Control** : received usual care **F/U length** :	**Items** : 1. Disease detect (self-report) - Angina - high DBP - ECG ischemic change - bronchitis symptoms 2. Health habits (self-report) - percentage still smoking 3. Major disability (%) self-report 4. Hospitalization - admissions/ 1000 person years at risk 5. Mortality rate (per 1000 person-years at risk) - All cause death - Neoplasm - CNS - CVD - Respiratory - All other causes **Statistics** :	**Result** : (int. v.s. ctrl) 1.Disease detection Angina 21.9% v.s. 22.4% High DBP 2.8% v.s.3.1% ECG change 17.9% v.s.16.6% Bronchitis symp. 29.0% v.s.30.6% 2. Health habits: smoking 51.5% v.s.50.8% 3. Major disability: 2.5% v.s. 1.8% (no significant difference) 4. Hospitalization: 73.4‰ v.s.70.7‰ (no significant difference) 5. Mortality rate: All casue death 10‰ v.s.9.2‰ Neoplasm 2.5‰ v.s.2.6‰ CNS	1. No detail reports on baseline difference 2. Incomplete presentation of significance 3. Potential inadequate adjustment of residual confounding

Table 2-2. Literature review of RCTs – South-East London study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
			1967-1972 (6yrs) In conclusion, 9 yrs result also revealed no statistical difference in any outcomes. **Attendance** : 73% participated in first year, 65.5% at second screening	1. Multifactor analy sis in item1 2. Bivariate analysis **Adjust** : Adjust Age, sex, smoking, lipids, BP, diabetes, social class, practice group in item1	0.9‰ v.s.0.7‰ CVD 4.3‰ v.s.2.8‰ Respiratory 1.4‰ v.s.2.9‰ Allother cause 0.9‰ v.s.1.1‰ (Authors reported there were no statis-tically significant differences,) **Key finding** : Failed to demon-strate any benefiit on either mortality or morbidity.	

Table 2-3. Literature review of RCTs –OXCHECK study

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
Oxcheck study group (BMJ, 1995)	Randomized control trial	**Source pop** : Five urban general practices in Bedfordshire (mixed urban & sub-urban),subjects was invited to participate **Inclusion criteria** : Age 35-64, Will to participate **Exclusion criteria** : No respond to invitation Inaccuracy of registration **Sample size** Int.(2776) Ctrl(2783)	**Intervention** : 1. History / Symptoms 2. Serum cholesterole 3. BP, anthropometry 4. ECG, CxR, MMG, Spirometry 5.Lifestyle question-naire (self-report) 6. Post-visit counseling by **nurses** **Control** : Received no health check at baseline but received a health check in year 4. **F/U length** : 3 years **Attendance** : Int.- 81.7%(1660) Ctrl- 81.3%(1916)	**Items** : 1. Total cholesterol 2. BP 3. BMI 4. Risk behavior(%) - smoking(≧1/D) - alcohol use - exercise< 1/mon - full cream milk - use butter/hard margarine 5. Proportion of morbidity - TC≧8mmol/l - DBP≧100 mmHg - BMI ≧30kg/m^2 6. Cumulative frequemcy of T.C. **Statistics** : 1. t test for contin-uous variable 2. Chi-square test for proportion 3. Analysis by	**Result** : (Ctrl.-int.) 1. 0.19(0.12~0.26)* 2. SBP: 2.5(1.3~3.7)* DBP: 0 .5 (0.8~2.2)* 3. 0.38(0.12~0.64) 4. Smoking: 1.4%(-1.3~4.1) Alcohol use: 0.6%(-1.3~2.5) Few exercise: 3.3%(0.5~6.1)* Full cream milk: 7.5%(4.8~10.3)* Butter/margarine: 8.7%(6.0~11.4)* 5.High cholesterol: 3.9%(2.4~5.3)* Abnormal DBP: 1.1%(-0.1~2.3) Obesity: 1.6%(-0.6~3.8) *:p<0.05 **Key finding** :	1. Use intention-to-treat analysis, maybe under-estimate. 2.Inacurracy of anthropometry and self-report questionnaire 3.No report on reliability & validity on questionnaire 4. Some reports on p value were not detail 5.Potential inade-quate adjustment of residual con-founding

Table 2-3. Literature review of RCTs –OXCHECK study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
				intention to treat 4. Subgroup analysis by sex **Adjust** : No report	1. PHE promote dietary change 2.Reduce cholesterol concentration 3. Small difference in blood pressure	

Table 2-4. Literature review of RCTs – Medicare demonstration project study

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
Morrissey (Med care, 1995)	Randomized control trial	**Source pop** : 1. 10 primary-care medical practices in central North Carolina. 2.Medicare demons-tration project (sponsored by the Health Care Financing Administration, HCFA) **Inclusion criteria** : 1. Age≧65 y/o 2. Received care in past 2 yrs 3. Will to participate **Exclusion criteria** : Subjects were enrolled in HMO **Sample size** Int.(954) Ctrl(960)	**Intervention** : Reimbursement for Medicare preventive services package: 1. Preventive care - History / Symptoms - BP, VA, audiometry, anthropometry - Glycosuria, Stool OB - CBE, Pap smear, DRE - Function/Depression/In-continence screen -Pneumococcal/Influenza vaccine -Hct, cholesterol 2. Health promotion -Physical activity, nutrition, Stress mange, Fall, Smoking, Alcohol 3. Reminding system 4. Office system for Nr. 5. Standard form for charting preventive care *Done by care team, annually **Control** :	**Items** : 1. Performance: - Pap smear - Influenza vaccine -cholesterole screen -Stool OB screen 2. Costs: - 3 yrs post-Intervene-tion cumulative Medicare charges 3. Hospitalization: - days per enrollee -admission per enroll-ee 4. Quality of Life: -HR-QOL **Statistics** : 1. Descriptive 2. Log linear model 3. Descriprive 4. t-test (mean post- score difference), adjust baseline value **Adjust** : Log lineer model	**Result** : (int. v.s. Ctrl.) 1. Pap: 85% v.s.31% Influenza vaccine: 72% v.s.52% Cholesterol screen: 60% v.s.50% Stool OB: 91% v.s.43% Mammography: 43% v.s.28% 2. Charges: waiver services $294 per subject 3. Days per enrollee: 7.27 v.s.8.55 Admission per enrollee: 0.73 v.s. 0.79 4. Quality of well being: 0.01($p<0.05$) Perceived quality of life:	1. Results potent-ially not general-izable beyond elderly Medicare recipient 2. No report on baseline morbid-ity status or treating method 3. No report on p value or confi-dence interval in some items 4.Inadequate statistic method on performance & utilization 5. It is not clear whether the improvement was a result of a part or all of intervention 6. Relative short follow up period

Table 2-4. Literature review of RCTs – Medicare demonstration project study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
			The comparison group received usual care. (receive preventive services as customarily offered by physician's practive) **F/U length** : 1. Costs- 2ys intervenetion, 1 yr F/U 2. Other-2 years **Attendance** : 1. 82% completed 2. Report on drop out **Uptake** : 88% received at least one clinical screening; 87% received at least one health promotion service	adjust for demographic varbiables & baseline reimbursed costs	1.59($p<0.01$) Perceived health status: 0.14($p<0.01$) **Key finding** : 1.Increased performance dramatically 2. Minimal increase HR-QOL	
Burton (Am J Public Health, 1995)	Randomized control trial	**Source pop** : Community-dwelling Medicare recipients in Baltimore.Medicare demonstration project. **Inclusion criteria** : 1. Age≧65 y/o	**Intervention** : Coverage for an annual preventive visit and tests : 1. Preventive care - physical examination - History / Symptoms - BP, VA, audiometry,	**Items** : 1. Costs: - Total health care charges - Mean monthly Medicare Part A & B charges 2. Hospitalization:	**Result** : (intervention effect) Total charges: $-8.19($p=0.841$) Ambulatory visit: -0.034(pp=-0.028) Hospitalization: -0.01($p=0.689$)	1. Results potentially not generalizable beyond elderly Medicare recipient 2. It is not clear whether the

Table 2-4. Literature review of RCTs – Medicare demonstration project study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
		2. Received care in past 2 yrs 3. Will to participate **Exclusion criteria** : 1. Participate before 2. Subjects were enrolled in other HMO **Sample size** Int.(2105) Ctrl(2090) (Demonstrate similarity in baseline health status, SES, health habits between groups, except lower physical activity & large portion of Black in control group)	anthropometry - Stool OB - CBE, Pap smear, DRE - Function/Depression/In-continence screen -Pneumococcal/Influenza vaccine -Cholesterol 2.Counseling -health risk **Control** : Receive usual care. (receive preventive services as customarily offered by physician's practive) **F/U length** : 2 years **Attendance** : Int.- 74.7%(1573) Ctrl- 72.9%(1524) **Uptake** : 63% received at least Intervention for once	- mean inpatient days per year 3. Ambulatory visit: - visit times per year **Statistics** : Mix model **Adjust** : Only time effect	**Key finding** : 1. There appears to be a modest health benefit with no negative cost impact. 2.Intervention may reduce use of ambulatory visit	improvement was a result of a part or all of inter-vention 3. Relative short follow up period 4. Baseline incom-parablility may lead to difficulty in interpretation
Burton (Med care, 1997)	Randomized control trial	Set as study in 1995	**Intervention & control** : Set as study in 1995, No advanced intervene-	**Items** : 1. Quality of Well-Being scores (QWB)	**Result** : (Int v.s. ctrl) 1. t-test: baseline to 2 yrs:	1. Results potent-ially not general-izable beyond elderly Medicare

Table 2-4. Literature review of RCTs – Medicare demonstration project study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
			tion **F/U length** : 2 years after end of intervention **Attendance** : Int.- 71.6%(1382) Ctrl- 74.2%(1380)	[Cut-off score:5, 10, classify as no problem, moderate, severe] (structured telephon interview) 2. Health behavior -Physical activity -Smoking -Alcohol drinking -overweight -attempt to reduce weight -attempt to reduce cholesterol -attempt to reduce salt 3.Use of preventive services -Pap smear -Stool OB -Mammography 4. Costs -charges **Statistics** : 1. Subgroup analysis and t-test, multi-variate regression 2. Chi-square to test proportion	-0.063 v.s. -0.083 (no significant) 2yr to 4 yr: -0.091 v.s. -0.84 (no significant) Regression (β): baseline to 2 yrs: 0.0694($p<0.001$) 2yr to 4 yr: 0.0298($p=0.273$) 2. No significant change in first or later 2 yrs F/U 3. Pap smear: baseline to 2 yrs: 16.5% v.s. 13.1% ($p<0.001$) Stool OB: baseline to 2 yrs: 23.4% v.s. 13.5% ($p<0.001$) 4. No significant difference for total charge, Part A & B claim	recipient 2. Baseline incom-parablility may lead to difficulty in interpretation

Table 2-4. Literature review of RCTs – Medicare demonstration project study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
				3. Mix model with adjustment of time effect **Adjust** : In regression model, adjust significant different variables at base-line (age, sex, marriage, living alone, SES, QWB score-baseline)	**Key finding** : Modest benefits found in first 2 years cannot be sustained to obtain long- term benefit.	
Patrick (Health Care Financ Rev, 1999)	Randomized control trial	**Source pop** : Medicare recipients in 4 GHC medical center in Seattle. Medicare demo-nstration project. **Inclusion criteria** : 1. Age≧65 y/o 2. Received care in past 2 yrs 3. Will to participate **Exclusion criteria** : 1. Severely cognitive im-paired 2. Having terminal illness	**Intervention** : 1. Health risk assess-ment - telephone interview 2. Health promotion visit (90 minute nurse visit) -health risk appraisals -positive behavior rein-forcement -referral for intervention 3. Disease prevention visit(Physician & Nr.) - history and physical examination - reviewed pts' health	**Items** : 1. Performance: - Influenza vaccine within last 24 months 2. Health habits change: - physical activity - dietary fat and fiber - BSE - smoking, alcohol, seat belt use 3. Patient attitude: - mean score health worry 4. BMI 5. Costs:	**Result** : 1. Influenza vaccine (change from baseline): -Int.: 62% v.s. 79% ($p<0.05$) -Ctrl.: 66% v.s. 78% 2. Habits change (int. v.s. ctrl.): physical activity 27% v.s. 21% ($p<0.05$) Healthy Diet 19% v.s. 17% ($p>0.05$)	1. Description of outcomes not detailed 2. Potentially inad-equate adjust-ment for residual confounding 3. No report on treating baseline difference 4. Implicit calcula-tion of costs (not include cost of intervention)

Table 2-4. Literature review of RCTs – Medicare demonstration project study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
		Sample size Int.(1282) Ctrl.(1276) *Baseline difference was significant at: -Self-rated health (Int. < ctrl.) -Stress past year (Int. > ctrl.) -Immunization rate (Int. > ctrl.) -Hypertension rate (Int. > ctrl.)	risks 4. Followup classes 5. Counseling - exercise - high fiber/low fat diet - advance directives **Control** : Medicare enrollees receiving usual care. **F/U length** : 2 years after intervention(24 & 48 months) **Uptake** : Year1 health promotion & disease prevention visits: 90% Year 2 Both health promotion and disease prevention visits: 83% *Attended none in any year: 9%	- average total cost per participant 6. Mortality: - at 24months - at 48months 4. Health status: -Quality of Well-Being score **Statistics** : t-test Chi-square test **Adjust** : No report	Breast self exam. 21% v.s. 17% (p>0.05) Smoking 2% v.s. 3% (p>0.05) Alcohol sue 6% v.s. 7% (p>0.05) Seat belt sue 10% v.s. 12% (p>0.05) 3. Mean score health worry: 0.42 v.s 0.69 (p=0.047) 4. Health status change (int. v.s. ctrl): -0.01 v.s 0.00 (p>0.05) 5. BMI change: (int. v.s. ctrl) -3% v.s. -4% (p>0.05) 6. Costs: (int. v.s. ctrl) 24 months $3564 v.s. 3300 (p>0.05) 48 months $3998 v.s. $4010	5. Results potentially not generalizable beyond elderly Medicare recipient

Table 2-4. Literature review of RCTs – Medicare demonstration project study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
					(p<0.05) 7. Mortality(<75y/o) 24months 2.8% v.s. 2.4% (p=0.267) 48 months 5.9% v.s. 5.6% (p=0.528) Mortality (>75y/o) 24months 7.5% v.s. 5.0% (p=0.005) 48 months 16.0% v.s. 13.5% (p=0.05) **<u>Key finding</u>** : 1. Improving vaccination, physical activity 2.Reduction of “worry”. 3.Mixed results of costs and other items	

Table 2-5. Literature review of RCTs –others

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
Fletcher (JAMA, 1977)	Randomized control trial	**Source population** : Pts of medical polyclinic of the Royal Victoria Hospital **Inclusion criteria** : Age 40-65, at least 2 visits per year (for each 112 physicians, a pt was assigned to one of three group) **Exclusion criteria** : Pt received other medical care **Sample size** Int.(36) Ctrl-abstract(40) Ctrl-review(36) (Demonstrate similarity in age,sex, maritus, language and physician specialist between groups)	Physicians write down problem list before and after giving information **Intervention** : Multiphasic screening group, at visit : 1. CBC, SMA, syphilis 2. BP, VA, tonometry, audiometry, anthro-pometry 3. ECG, CxR, Spirometry 4. CBE, Pap smear 5. Health questionnaire **Control** : 1. Chart abstract group Provide abstract of results of same itmes within the past year, at visit 2. Chart review group No further aid or intervention	**Items** : 1.Identify new medical problems (all & important) after intervention (items per subject) **Statistics** : Chi-square test	**Result** : Significant higher detected cases(all & important medi-cal problems) in intervention group (2.13 v.s.0.35 v.s. 0.11, $p<0.005$) **Key finding** : The physicians identify more new medical problems and important new medical problems with the help of MHC	1.No data of other outcomes, like mortality and disability 2.Subjects were not healthy or asymptomatic 3. No report on Pt's baseline morbidi-ty 4.Small sample size

Table 2-5. Literature review of RCTs –others (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
Theobald (Int J Epidemio, 1998)	Randomized control trial	**Source pop** : Stockholm residents (Sweden), 1969-70 **Inclusion criteria** : Age 18-65 **Exclusion criteria** : **Sampling**: Population was divided by “age group” & “health need” into 12 subgroups, and random sampling with intervention was done. **Sample size** Int.(3064) Ctrl.(29122)	**Intervention** : General health examination: 1. Bio-psyco-social interview 2. Physical and dental examinations 3. Exercise tests 4. Psychological tests 5. ECG 6.Blood tests With a referral to GP or hospital if indicated **Control** : Stockholm residents aged 18-65 who received usual care. **F/U length** : 20 years(1970~1990) **Uptake** : 2578/3064 (84%) of intervention group	**Items** : Outcome was linked through national death registry 1. All cause mortality 2. Cardiovascular disease mortality 3. Cancer mortality 4. Accidents and Intoxication mortality **Statistics** : Cox regression model **Adjust** : Age, sex, need for service.	**Result** : All cause mortality RR(rate ratio): 1.03(0.94~1.14) CVD mortality RR: 1.06 (0.91~1.23) Cancer mortality RR: 1.06(0.88~1.23) Accident & intoxication mortality RR: 0.97(0.73~1.30) *Subgroup analysis by sex also revealed negative finding **Key finding** : 1.Results are inconclusive 2.Absent benefit of PHE	1.No report on baseline difference 2. No treat of possible historical effect 3. Negative finding may due to inadequate adjustment of residual confounding 4. No intermediate data

Table 2-6. Literature review of observational study

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
Hama (Mil med, 2001)	Retrospective cohort study	**Source pop** : Employees of the Japan Maritime Self-Defense Force working on the Iwo Jima military defense base(Dec, 1999) **Inclusion criteria** : 1.Age≧35 y/o * Demonstrate similarity in baseline age, height, weight, BMI, SBP, DBP, vital capacity between groups **Sample size** Exposure(196) NonExp(44)	**Exposure** : Received preassignment health check-up in past 1 year Preassignment health check-up content: 1. Physical examination 2. S/R, U/R, SMA 3. BP, anthropometry 4. ECG, CxR, Spirometry 5. Screening for heaptitis B,C and syphilis **Non-exposure** : Didn't receive that **F/U length** : 1 year	**Items** : 1. Disease detect - arrhythmia - neurological problems - Hyperlipidemia -hyperuricemia -GI ulcer -Hypertension -BMI≧28.6kg/m^2 -proteinuria 2. Blood pressure - mean SBP(mmHg) - mean DBP - proportion of HTN 3. Cholesterol - mean TC(mg/dl) - mean TG -mean LDL - mean HDL - proportion of hyperlipidemia 4. BMI change - mean BMI(kg/m^2) - proportion of BMI ≧28.6kg/m^2 **Statistics** : T test Dichotomous out-	**Result** : 1. Disease detect Hyperuricemia OR:1.5(0.43~5.26) Hypertension OR:3.09(1.01~9.52) Hypelipidemia OR:5.86(1.94~17.74) Severe obesity OR:10.9(1.58~76.63) 2. Blood pressure (mean difference, ctrl.-exp.) Mean SBP 2.2 (p=0.914) Mean DBP 1.4 (p=0.468) Proportion of HTN (int. v.s. ctrl.) 4.1% v.s. 11.4% 3. Cholesterole (mean difference, ctrl.-exp.)	1. Potentially inadequate adjustment for residual confounding 2. Relative small sample size 3. No report on baseline morbidity distribution and previous medical treatment. 4. Possible inaccuracy and variation of laboratory study

Table 2-6. Literature review of observational study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
				comes were analyzed by logistic regression **Adjust** : Age, sex, smoking, lipids, BP, diabetes, social class, general practice group	Mean TC -17.1 (p=0.028) Mean TG -20.2 (p=0.416) Mean LDL -0.5 (p=0.944) Mean HDL -0.9 (p=0.799) Proportion of hyperlipidemia (int. v.s. ctrl.) 3.1% v.s. 15.9% (p<0.05) 4. BMI (mean difference, ctrl.-exp.) Mean BMI 1.0 (p=0.068) Proportion of severe obesity (int. v.s. ctrl.) 0.5% v.s. 4.5% (p>0.05) **Key finding** : May early detect	

Table 2-6. Literature review of observational study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
					hypertension, hyperlipidemia and obesity	
Burton (J Occup Environ Med, 2002)	Retrospective cohort study	**Source pop** : Bank One executives who were enrolled in the Bank Medical Plan **Inclusion criteria** : 1. Age≧40 y/o 2. Voluntary 3. Took at least one PE during the period 1989 to 1995. **Sample size** Exposure(1046) NonExp(727)	**Exposure** : Executive physical examination: 1. CBC, SMA, U/R 2. BP, VA, tonometry, spirometry, anthropometry 3. ECG, 4. Complete history and physical examination **Non-exposure** : Never had an examination during 1989~1995 **F/U length** : 3 years	**Items** : 1. Costs - average cost in medical claims paid per employee 2. Disability - average number of short-term disability (STD) days per employee - Total short-term disability days in 3 years - Any short-term disability days (%) **Statistics** : Multiple regression Chi-square test for proportion **Adjust** : Age and sex	**Result** :(Exp. V.s. Ctrl.) 1. Costs Average cost in medical claim $5361 v.s. $2426 (p=0.0263) 2. Disability Average STA days per enroll. 2.78 v.s. 4.03 (p<0.01) Total STD days 2134 v.s. 2707 (p<0.001) Any STD days% 6.2% v.s 11% (p>0.05) **Key finding** : Executive physical examination program is of value	1. No demonstration on baseline difference 2. Use of claim data not specified for research Purposes 3. Potential inadequate adjustment of residual confounding 4. Subjects was voluntary to join in

Table 2-6. Literature review of observational study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
Chiou (Prev Med, 2002)	Retrospective cohort study	**<u>Source pop</u>** : Residents of Kaohsiung City, Taiwan, 1993 **<u>Inclusion criteria</u>** : 1. age≧65y/o **<u>Sample size</u>** 1193 *A stratified random sample scheme was used in each of the 11 districts of Kaohsiung City.	**<u>Exposure</u>**: 1. Baseline interview (1993) 2. Annual physical examination: -Weight, height -BP,VA,hearing, oral hygiene -U/R, stool OB, lipid profile, fasting serum glucose 4. Complete history and physical examination 5. Referral for advanced management **<u>Non-exposure</u>**: Baseline interview only (1993) **<u>F/U length</u>** : 6 years	**<u>Items</u>** : 1. Mortality - Relative risk of mortality **<u>Statistics</u>** : Cox proportional hazard model **<u>Adjust</u>** : Age, sex, race, education, comorbities, living arrangements	**<u>Result</u>** : For those receiving check-up (RR) 1. At least once in past 6 year : 0.50(0.36~0.69) 2. At least 3 times in past 6 year: 0.25(0.12~0.51) **<u>Key finding</u>** : Elderly subjects who received PHE had lower mortality than those who did no.	1.Using only dichotomous variable for comorbidity 2. It is not clear whether the improvement was a result of a part or all of intervention 3. NHI adult health checkup start since 1996
Nakanishi (Soc Sci Med, 1996)	Cross section study	**<u>Source pop</u>** : 1. 9 cities located in northern part of Osaka, japan 2. Inpaitent and outpatient NHI claim	**<u>Exposure</u>** : 1. Health examinations - interview, physical tests - anthropometry -BP, U/R, SMA - screenings for stomach ca., uterus ca., lung ca., breast	**<u>Items</u>** : 1. Costs - Inpatient cost per Subject - Rate of high inpatient cost (600,000 yen or more) per	**<u>Result</u>** : 1. Inpatient cost: r:-0.724 (p=0.014) Rate of high inpatient cost:	1. Subjects may receive other health check-ups 2.Potential inadequate adjustment of residual

Table 2-6. Literature review of observational study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
		data of residents **Inclusion criteria** : aged 40 or older **Exclusion criteria** : Patient with mental health disorders **Sample size** 227,581 inpatient and outpatient claims	cancer, colon ca. 2. Issuance of a health Notebook - check-up results 3. Health education 4. Health counseling 5. Rehabilitation programs 6. Home-visit guidance **F/U length** : Claim data of May, 1993 **Uptake** : 23.1%~65.1% in 9 cities *NHI cover rate, 1991: 34.3%	1000subjects - Outpatient cost per Subject - Rate of high outpatient cost (600,000 yen or more) per 1000subjects 2. Hospitalizations - Hospital admission rate per 1000subject - Rate of long stay (180 days or more per Subject) 3. Outpatient utilization - Outpatient utilization Rate per 1000 subjects 4. Correlation between total medical cost per subject and cost for preventive services per subject **Statistics** : 1. Report on Simple correlation coefficients	r:-0.625 (p=0.036) Outpatient cost: r:-0.454 (p=0.11) Rate of high outpatient cost: r:-0.708 (p=0.016) 2. Admission rate: r:-0.89 (p=0.001) Rate of long stay: r:-0.584 (p=0.049) 3. Outpatient use rate: r:0.664 (p=0.026) 4. Total medical cost & preventive services cost (per subject): r:-0.779 (p=0.007) **Key finding** : 1.Reduction in inpatient utilization and cost 2.Increasing out-	confounding 3.Report correlation coefficient only on population level 4. Only 1 month claim data

Table 2-6. Literature review of observational study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
				2. Outcome corre-late with rate of use of health check-ups(city level) **Adjust** : Outcome value (days & yen) was adjusted with age group & sex	patient utilization 3.Reduction in total medical cost	
Finkelstein (Can Fam physic-ian, 2002)	Cross section study (secondary data analysis)	**Data Source** : Administrative data 1. National Population Health Survey (NPHS) of 1994-1995 2.Linked to Ontario He-alth Insurance Plan (OHIP) billing files **Sample size** A representative sample of 19,600 households	**Action** : In each household, one person was randomly selected for an in-depth interview. Information collected included age, educa-tion, and household income. **Attendance** : The national response rate to the survey was 88%.	**Items** : 1. Dependent variables : Receiving Pap smear, MMG, BMD and chol-sterol screen 2. Independent variable: - age - household income - education - urban/rural - having an annual health check-up - having regular phy-sician	**Result** : Women who had PHE were more likely to have(OR) : 1. Pap smears 6.7 (4.6 ~ 9.8) 2. Mammograms 3.7 (2.3 ~ 5.9) 3. Densitometry 3.7 (1.3~ 10.5) 4. Cholesterol test 3.0 (2.0~4.5) **Key finding** : 1. Having screening was associated with age, income,	1. Results potent-ially not general-izable beyond adult female. 2. Should interpret the OR carefully 3. Using billing data may overestimate prevalence of preventive ser-vices

Table 2-6. Literature review of observational study (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
				- numbers of visits to GPs **Statistics** : Logistic regression	education, and place of residence. 2. Positive correlation between receiving PHE and Pap smear, mammography, BMD, cholesterol screening	
Somkin (Med Care, 2004)	Cross section study	**Source pop** : Residents in Alameda County, California (urban area) **Inclusion criteria** : 1.women aged 40 to 74 2. respondents to a telephone survey **Exclusion criteria** : Women who had underwent hysterectomy **Sample size** 463	1.Interview : aim to investigate the relationship between race/ ethnicity, access, satisfaction, and regular MMG and Pap smear receipt. 2. Independent variable including that subjects had received a check-up in the last 12 months.	**Items** : Factors related to receipt of MMG and pap smear **Statistics** : Logistic regression **Adjust** : Age, race, insurance, education, language, years in U.S., annual household income.	**Result** : Checkup in last 12 months (OR) 1. MMG: 2.28 (1.68~3.0) 2. Pap smear: 4.38(2.95~6.50) **Key finding** : Having a check-up in the past year were associated with regular MMG and Pap smear.	1.Small sample size 2. Source population from urban region 3. Results potentially not generalizable beyond adult female.

Table 2-7. Studies of adult preventive care service in Taiwan

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
Yang (DOH88-NH-038, 1999)	Observation-al study	**Source pop** : Residents in Taiwan **Inclusion criteria** : Had received adult preventive health service in June, 1998 *Residents who didn't receive health check-up in the past 3 yrs , were selected randomly into control group. **Sample size** Exposure.(610) Non-exposure(750)	**Action** : 1. Computer assisted telephone interview 2. Analysis of check-up results	**Items** : 1.Factors related to receipt of adult preventive health checkup 2. Description and identification of abnormal finding 3. Investigate satis-faction **Statistics** : Bivariate analysis (Chi-suqare test) **Adjust** : No report	**Result** : 1. Related factors: - less educated - not working - less income - non-smoking - never use betal but - agree with "check-up was necessary" - habits of visiting physician - knew or heard about check-up before 2. Adult preventive health service possibly identify new disorder: Dermatological, ophthalmic disorder, dyslipidemia, liver disease, extremity disease, urologic disease, HTN,DM, UTI,	1. No report on health outcome and cost 2. Potential inadequate adjustment of confounding

Table 2-7. Studies of adult preventive care service in Taiwan (continued)

Author (Publication, year)	Study Design	Subjects	Intervention	Outcome/ Statistic	Result	Limitation
					and benign neoplasma 3.66% of examinee group were very satisfied or satisfied about the service	
Tsai (DOH96-HP-1103, 2007)	Observational study	**Source pop** : Clinic physicians and hospital physicians in Taiwan **Inclusion criteria** : Physicians who were registered in Taiwan Association of Family Medicine **Sample size** 1. Questionnaire(961) 2. Health check-up reports(10141)	**Action** : 1. Self-report questionnaire 2. Analysis of check-up results	**Items** : 1. Appropriate in target age group 2. Need for increasing frequency 3. Omit seat belt and helmet 4. Add waist circumstance 5. Omit CBE, DRE 6. Add MCV, LDL, HBsAg, Anti-HBC 7. Poor performance of DRE/CBE 8. Description and identification of abnormal finding **Statistics** : Descriptive	**Result** : 1. 60% 2. 69% 3. >50% 4. 58% 5. 20% / 31% 6. 65~80% 7. 57-64% 8. the dominant new diagnosis: dyslipidemia	No report on health outcome and cost

Chapter 3. Materials and methods

3.1 Data sources

In this research, we will apply the secondary data from "National health insurance research database (NHIRD)". Each year, Bureau of National Health Insurance (BNHI) collects data from the National Health Insurance program and sorts it into data files, including registration files and original claim data for reimbursement. These data files are de-identified by scrambling the identification codes of both patients and medical facilities. The encryption is consistent in the database.

One subset is the so-called "cohort dataset" which includes the claims data of 200,000 people from 1996 to 2001 (longitudinal health insurance dataset, LHID2000). These 200,000 people have been randomly sampled from 23,753,407 people (about 1%) who had ever been insured under the NHI from March 1, 1995 to December 31, 2000. According to the NHIRD, the sampled people are representative of all NHI beneficiaries in distributions of age, sex, and expenses. This cohort dataset released by BNHI was divided into 4 subsets, each contains 50,000 subjects, and was representative of the original cohort dataset. The purpose of such a cohort data set is to follow up a representative group of the population longitudinally [34-36].

3.2 Study Design

This study was an observational cohort design based on claim data of NHIRD. In the cohort dataset, beneficiaries who aged between 40 and 100 in 2000 were recruited. The major purpose of this research was to evaluate the probable benefit of adult preventive care service (Figure 3-1).

Baseline characteristics as demographic characteristics (age, gender, level of premium, insurance applicants), geographic characteristics (most frequently visited region), status of morbidity (Charlson comorbidity index, hypertension, diabetes, and hyperlipidemia) were collected in year 2000. Subjects were followed up for seven years (from Jan 1, 2001 to Dec 31, 2007).

Frequency of attending adult preventive care service was counted during 1998-2000, and uptake of this service before the endpoint during follow-up period was also collected.

As study hypothesis, we supposed that utilization of adult preventive care service may contribute to early detection and management of chronic disease, like hypertension, diabetes and hyperlipidemia. So subjects with target disease were excluded at baseline in such conditions.

Chen (2007) conducted a population-based longitudinal study through NHIRD to investigate factors associated with the diagnosis of neurodevelop-mental disorders, he used enrollee category(insurance applicants) as a proxy variable of socioeconomic status(SES) [37].

The present study employed “level of premium” and “insurance applicants” as proxy measures of SES. In Taiwan, some enterprises or corporations also provided their employee with periodic occupational health check-up, here we assumed that the later covariate was also used to adjust such condition.

As mentioned above, resident place was a significant factor related to utilization of health service; here we applied "most frequently visited region" as a representative variable of "accessibility and availability of medical resources".

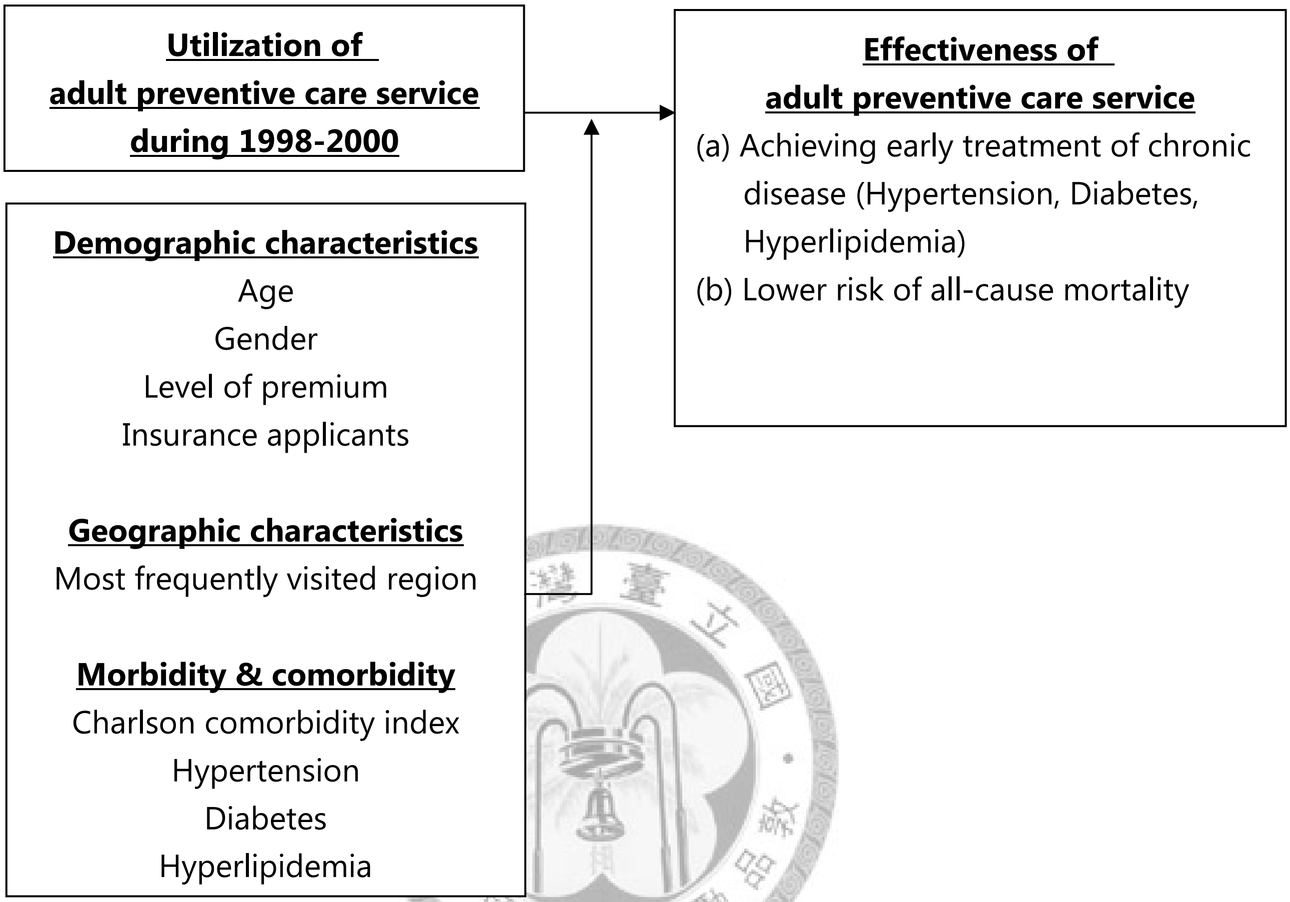
Charlson comorbidity index (CCI) was formed by weighting 19 comorbid conditions by one point to six points, which considered not only the number but the seriousness of comorbidity.

Several studies have demonstrated the rationale of use CCI in secondary data. CCI may be useful in exploratory data analysis and removal of residual confounding [38-41]. In current study, CCI was calculated as a baseline covariate through diagnosis codes in ambulatory and hospitalization datasets.

The NHI reimbursed this service package every three year for adults aged between 40 and 65, and annually, for over 65. Put differently, subjects received services on different time and in different place, this condition did raise difficulty evaluating the effect of adult preventive care service. Frequency of service uptake was collected and computed in different ways, such as frequency between 1998 and 2000, 2001 and 2007, and by dichotomous measure.

However, bias of "confounding by indication" may not be avoided, that is, some morbidity and baseline characteristics may influence the utilization of service and the outcomes of interest. Another problem was the "time-dependent covariate effect", the cohort was followed up from Jan 1, 2000 to Dec 31, 2007, utilization of preventive care service still occurred during the observational period , stated another way, there did exist interaction between time and the frequency of service uptake. These two questions warranted advanced management in data collection and analysis, for example, adjustment of confounding factors in multivariable regression model and extended Cox regression model [42].

Figure 3-1 Research framework



3.3 Study subjects

The target population contained adults older than 40- and younger than 100-year-old. Beneficiaries of the National Health Insurance represented the source population. The longitudinal dataset from origin of NHIRD would be the eligible population.

Following the hypothesis of this study, the inclusion and exclusion criteria for selection of eligible subjects were described as follows：

(a) Inclusion criteria：

Age between 40 and 100 years.

(b) Exclusion criteria：

Missing or erroneous coding of gender.

Participants drop NHI before Jan 1, 2000.

Participants with target disease(hypertension, or diabetes, or hyperlipidemia) at baseline(hypothesis 1)

3.4 Data retrieving and definition of variables

3.4.1 Data retrieving

As study design, the registry file for beneficiaries (ID file), ambulatory visit file (CD file), ambulatory prescription file (OO file), inpatient admission file (DD file), and registry file for contracted medical facilities (HOSB file) in the cohort datasets were employed, and useful items in each files were described below：

(a) Registry file for beneficiaries (ID file)：

Identification (ID), premium (INS_AMT), birthday (ID_birthday), sex (ID_SEX), insurance applicants (ID_INS_TYPE), date of join and drop from insurance (ID_IN_DATE, ID_OUT_DATE).

(b) Ambulatory visit file (CD file)：

Serial number and identification for each visit (FEE_YM, APPL_TYPE, APPL_ DATE, CASE_TYPE, SEQ_NO), contents of visit (FUNC_TYPE, FUNC_DATE, TREAT_END_DATE, CARD_ SEQ_NO, ACODE_ICD_9_X, DRUG_DAY). The diagnosis of each ambulatory visit was coded using the International Classification of Disease, 9th revision (ICD-9-CM).

(c) Ambulatory prescription file (OO file)：

Serial number and identification for each visit (FEE_YM, APPL_TYPE, APPL_ DATE, CASE_TYPE, SEQ_NO), contents of prescription (DRUG_NO).

(d) Inpatient admission file (DD file)：

Serial number and identification for each visit (FEE_YM, APPL_TYPE, HOSP_ID, APPL_ DATE, CASE_TYPE, SEQ_NO), contents of visit (, FUNC_TYPE,

IN_DATE, OUT_DATE, ICD9CM_CODE_X, TRAN_CODE). The diagnosis of each inpatient course was coded using the International Classification of Disease, 9th revision (ICD-9-CM).

(e) Inpatient prescription file (DO file)：

Serial number and identification for each visit (FEE_YM, APPL_TYPE, APPL_DATE, CASE_TYPE, SEQ_NO), contents of therapy (ORDER_CODE).

(f) Registry file for contracted medical facilities (HOSB file)：

Identification (HOSP_ID), information regarding the facility (HOSP_CONT_TYPE, CNT_S_DATE, CNT_E_DATE, HOSP_TYPE_ID,).

3.4.2 Data categorization and definition of variables

By the research framework, data collected from cohort datasets were categorized and computed. Definition and criteria of categorization were summarized in Table 3-1, 3-2.

(a) Independent variables：

Sex：

Sex was categorized into male and female.

Age：

Subjects' age was computed at baseline (by Jan 1, 2000), and was divided into three categories for subgroup analysis, including "age 40-54 years", "age 55-64 years", "age 65-100 years"

Level of premium：

There were six levels of premium according to the rule released by NHI in 1999. In current study, it was reclassified into three levels. (Level 1：NT$ 0-22,800；Level 2：NT$ 24,000-36,300；Level 3：NT$ 38,200-57,800).

Type of insurance applicants：

Type of insurance applicants was classified into 3 categories depend on its characteristic (Category 1 : civil servants, full-time or regularly paid personnel in governmental agencies and schools；Category 2 :employees of privately owned enterprises or institutions；Category 3 : substitute service draftees, members of low-income families, and veterans).

Existence of hypertension, diabetes and hyperlipidemia at baseline：

Dichotomous variable. Diagnosis codes of each ambulatory visit in 2000 were collected and counted. Morbidity status was positive when the definite ICD-9-CM codes appeared at least 3 times in 2000.

(Hypertension：first three digits of ICD-9-CM contained 401, 402, 403, 404, 405；Diabetes：first four digits of ICD-9-CM contained 2501, 2502, 2503, 2504, 2509；Hyperlipidemia：first three digits of ICD-9-CM contained 272.)

Charlson Comorbidity Index(CCI)：

Continuous variable. By the research design, CCI was applied as a proxy measure of the comorbidity severity. The ICD-9-CM codes of ambulatory and inpatient care in 2000 were retrieved and computed.

Most frequently visited area：

Based on recording of ambulatory visits and hospitalization in 2000, the most frequently visited area was divided into four regions, including Taipei area, Northern and central area, South area and Eastern area. Off-shore islands, Taipei and Yilan country were enrolled in Taipei area.

Uptake of preventive care services：

For subject aged 40-64 years, the item was divided into 'ever' and 'never' uptake during 1998-2000. For subject older than 65 years, was divided into 'never', 'once' and 'at least 2 times' uptake through dummy coding.

(a) Dependent variables：

First treated event of hypertension, diabetes and hyperlipidemia：

Dichotomous variable. Diagnosis codes of each ambulatory visit between 2001-2007 were collected and counted. Definite ICD-9-CM codes should appeared with corresponding prescription, and the time of prescription must be longer seven days.

(Hypertension：first three digits of ICD-9-CM contained 401, 402, 403, 404, 405；Diabetes：first four digits of ICD-9-CM contained 2501, 2502, 2503, 2504, 2509；Hyperlipidemia：first three digits of ICD-9-CM contained 272.)

Death：

Exact date and status of death were not recorded in datasets of NHIRD, a conservative criteria was developed to define a surrogate endpoint of death through records of emergency department (ED) visits and hospitalization：

(1) Discharge with TRAN_CODE was coded as '5'.

(2) Discharge against medical advice (AAD, TRAN_CODE coded as '4' and 'A') and drop NHI within 30 days.

(3) Emergency department visits with cardiopulmonary resuscitation (procedure code : 47029c) and drop NHI within 30 days.

Observation period：

The follow-up duration was calculated in days. Each subject was observed from Jan 1, 2001 to the date of event occurrence mentioned above or the censored event (e.g. drop NHI), others were followed to Dec 31, 2007.

T1, T2 in counting process：

T1 was recorded by date of starting observation, receiving service, or the date 365 days after receiving service. T2 was recorded by date of receiving service, the date 365 days after receiving service or the occurrence date of event or censoring.

Table 3-1. Definition and categorization of independent variables

Variable name	Type of variable	Definition of variable
Co-variate		
Sex	Categorical	M=male; F=female
Age	Continuous	(Jan 1, 2000-birthday)/ 365.25
Agecat	Categorical	1=age 40-54 years；2=55-64 years；3=65-100 years
Level of premium	Categorical	1 = NT$ 0-22,800；2 =NT$ 24,000-36,300 ； 3= NT$ 38,200-57,800
Type of insurance applicants	Categorical	1 =civil servants, full-time or regularly paid personnel in governmental agencies and schools；2 =employees of privately owned enterprises or institutions；3 =substitute service draftees, members of low-income families, and veterans.
Existing hyper-tension at baseline	Categorical	1 =yes; 0 =no. (based on ambulatory visit data in 2000, ICD-9-CM: first 3 digits contain 401-405, count over 3 times)
Existing diabetes at baseline	Categorical	1 =yes; 0 =no. (based on ambulatory visit data in 2000, ICD-9-CM: first 4 digits contain 2500-2509, count over 3 times)
Existing hyper-lipidemia at baseline	Categorical	1 =yes; 0 =no. (based on ambulatory visit data in 2000, ICD-9-CM: first 3 digits contain 272, count over 3 times)
Charlson comorbidity index, (Deyo CCI)	Continuous	Based on ambulatory visit data in 2000, counting ICD-9-CM by appendix A3-1

Table 3-1. Definition and categorization of independent variables (continued)

Variable name	Type of variable	Definition of variable
Present of chronic disease	Categorical	1 =yes; 0 =no. (Existing hypertension, or diabetes or hyperlipidemia at baseline)
Most frequently visited area	Categorical	1=Taipei area; 2=Northern and central area; 3=South area; 4=Eastern area (based on ambulatory and inpatient care in 2000).
Uptake of service	Categorical	For subjects aged 40-64 years, were divided into 'ever' and 'never' uptake between 1998 -2000. For those older than 65 years, were divided into 'never', 'once' and 'at least 2 times' uptake.
Uptake of service before endpoint	Categorical	1=ever; 0=never (ever uptake service before follow-up endpoint during 2001-2007)
Observation period	days	Period from Jan 1, 2001 to target events / censored events or to Dec 31, 2007
T1	date	Date of starting observation, receiving service, or the date 365 days after receiving service
T2	date	Date of receiving service, the date 365 days after receiving service or the occurrence date of event or censoring

Table 3-2. Definition and categorization of dependent variables

Variable name	Type of variable	Definition of variable
Dependent variable		
First treated hypertension	Categorical	1 =yes; 0 =no. (based on ambulatory visit data between 2001-2007, ICD-9-CM: first 3 digits contain 401-405, and treated with antihypertensive medication firstly)
First treated diabetes	Categorical	1 =yes; 0 =no. (based on ambulatory visit data between 2001-2007, ICD-9-CM: first 4 digits contain 2500-2509, and treated with oral hyperglycemic agents firstly)
First treated hyperlipidemia	Categorical	1 =yes; 0 =no. (based on ambulatory visit data between 2001-2007, ICD-9-CM: first 3 digits contain 272, and treated with anti-dyslipidemia medication firstly)
Death	Category	1 =yes; 0 =no. Conservative definition： (1)hospitalization with death coding; (2)hospitalization with general and critical AAD coding and drop NHI within 30 days; (3)cardiopulmonary resuscitation and drop NHI within 30 days;

3.5 Statistical analysis

Descriptive statistics：

Descriptive statistics of baseline characteristics were implemented for subjects who ever and never uptake of service. Results of continuous variables were reported as mean ± standard deviation (M ± SD), and categorical variables presented as counts and proportions.

The Student's t-test and Chi-square test was carried out to determine the statistical significance of the differences between those who ever utilized the adult preventive care service and who did not.

Analytic statistics：

Firstly, crude ratio of univariate was calculated and tested through logistic regression, and then multivariate logistic regression was performed to estimate the odds ratio (OR) of utilization of preventive care service on outcomes of interest. Covariates were stepwise put into the model. Age, sex and the covariate "uptake of service before endpoint during follow-up" were forced to stay in the model after stepwise selection for rational adjustment. Linear test for trend was applied in subject aged 65-100 years to estimate the trend of different uptakes of service. Kaplan-Meier curve was depicted to test the proportional hazard assumption. The proportional hazard assumption was tested graphically by the non-crossing of the survival curve of the variables and the log(-log(survival)) versus log of survival time graph.

Hazard ratio (HR) would be obtained through Cox proportional hazard regression if the assumption was not violated. Wald test was carried out to determine the significance of the HR estimated by Cox proportional hazard model.

"Time-dependent covariate effect" was treated through Cox regression model with counting process. In current study, subjects utilized at different time and different time points and with different intervals. This model can handle time-dependent covariates as well as left-truncation and right censoring with controlling the risk sets, however this model do not allow individual predictive time-to-event curves, which is different from the Cox model, with only fixed covariate values [43]. During 2001-2007, we collected and constructed time-dependent sets of each uptake of preventive care service, and the effective period was defined as 1 year, in this model, covariates as age, sex, CCI and existing morbidities at baseline were used. For each subject, observation period was separated into several measurements if the hazards vary due to uptake of preventive service.

All tests of significance were two-sided, and a 5% significance level was used throughout. Statistical analyses are performed using Statistical Analysis System (SAS) for Windows, version 9.1 (SAS Institute Inc., Cary, NC, USA). The SAS codes of extended Cox model was displayed in appendix A3-2.

3.6 Sample size calculation

The number of subjects required for this research was estimated by the software "Power and Sample size program" [44]. Method of sample size estimation for independent cohort studies with dichotomous outcome was chosen. According to the distribution of our dataset (first subset), the proportion of those subjects who never and ever used services was 1.76, the probability of death for subjects who never used services was 0.078, and for those who ever used was 0.068. An uncorrected chi-squared statistic to evaluate this null hypothesis was employed, the type I error probability associated with this test of this null hypothesis is 0.05, and the power was set as 0.8. The estimated result revealed that 8,387 subjects who ever used and 14,762 subjects who never used services were needed. Following this estimation, at least 2 subsets of cohort datasets were required.

Chapter 4. Results

4.1 Descriptive results

Two subsets of the four cohort datasets of NHIRD were analyzed, and a total of 32,039 eligible subjects aged 40-100 years by the start of year 2000 were recruited. There were 16,080 male (50.2%) and 15,959 female(49.8%) in the study population and the average age of each group were 55.6±11.9 years and 56.0±11.9 years. Most premium level of subjects was level 1(NT$ 0-22,800). 44.4% participants were civil servants, personnel in governmental agencies, and 41.5% were employees of privately owned enterprises or corporations. The most frequently visited region distributed similarly in the Taipei area, Northern & Central area, or South area. Demographic and geographic characteristics of subjects were summarized in Table 4-1.

Variables of morbidity and comorbidity were listed in Table 4-2. The prevalence of definite hypertension, diabetes and hyperlipidemia in year 2000 were 16.8%, 6.8% and 4.1%. The average score of CCI was 0.69±1.27.

Table 4-3 revealed that uptakes of service were significant different among age groups, gender, levels of premium, categories of insurance applicants and frequently visited regions. The elderly, female, subjects with low-income status, and who used medical resources in area other than Taipei area used more services.

Table 4-4 and 4-5 indicated that subjects with chronic diseases or higher score of comorbidity were more likely to use preventive service.

Table 4-6 showed the summary of frequent visited facilities and clinical section, most of the services were provided at clinics and family medicine section.

Table 4-7 listed the size and event rate of different subsets, the hypertension-free subsets included 26,661 subjects, the diabetes-free and hyperlipidemia-free subsets included 29,872 and 30,712 subjects. During the seven years follow-up, all-cause mortality rate was 7.4%, event rates of newly treated hypertension, diabetes and hyperlipidemia were 32.1%, 9.1%, and 14.5%.

The mean and median observational time of hypertension-free cohort were 1,973.9 and 2,555 days; for diabetes-free cohort were 2,303.0 and 2,555 days; for hyperlipidemia-free cohort were 2,227.4 and 2,555 days.

4.2.1 Effectiveness on new disease treatment in subjects aged 40-54 years

Results of multiple logistic regression with stepwise selection were summarized in Table 4-8~10, covariates as level of premium, category of insurance applicants and frequently visit region were selected into model by the statement of “selection=stepwise”, age, sex and the covariate “uptake of service before endpoint during follow-up” were forced to enter in the model if they were removed from selection.

Age, male gender, and increment of baseline CCI score were consistently associated with higher risk of newly treated hypertension, diabetes and hyperlipidemia in subjects aged 40-54, who were free of these disease at baseline. Also, other chronic diseases at baseline were also at risk developing newly treated target disorder.

Subjects who ever utilized service during 1998-2000 had higher risks to be diagnosed to have newly treated hypertension (OR: 1.51, 95%CI: 1.38-1.65) and hyperlipidemia (OR: 1.15, 95%CI: 1.05-1.27), however, for diabetes, the association was positive but not significant (OR: 1.14, 95%CI: 0.99-1.31, p=0.071).

In Table 4-11, multiple logistic regression without stepwise selection was applied, it demonstrated similar findings, OR sustained significant across stepwise adjustment of covariates in hypertension and hyperlipidemia events, for diabetes events, the OR was still positive after adjustment.

In order to perform the Cox model, the Kaplan-Meier curve and log(-log(survival)) versus log of survival time graph were depicted to test the assumption (A 4-1~4-6).

Although the proportional hazard assumption wasn't completely matched, there were no prominent crosses of the survival curves for these three subsets. So, Cox model was applied to evaluate the HR of "uptake of preventive care service" to newly treated disorders.

Results of Cox model were similar to the multivariate logistic model (Table 4-12), subjects who ever utilized service during 1998-2000 had higher risk to develop newly treated hypertension(HR: 1.48, 95%CI: 1.37-1.60) and hyperlipidemia (OR: 1.47, 95%CI: 1.33-1.62), the HR was positive but not significant for diabetes events(HR: 1.13, 95%CI: 0.99-1.29, p=0.073).

Table 4-13 estimated each uptake of service during 2001-2007 and obtained significant and robust findings for newly treated hypertension (HR: 1.80, 95%CI: 1.64-1.97), diabetes (HR: 1.59, 95%CI: 1.19-2.13) and hyperlipidemia (HR: 3.97, 95%CI: 3.59-4.38).

4.2.2 Effectiveness on new disease treatment in subjects aged 55-64 years

In subjects aged 55-64 years, subjects who ever attended the service during 1998-2000 had higher risk to develop newly treated hypertension (OR: 1.76, 95%CI: 1.55-1.99), diabetes (OR: 1.73, 95%CI: 1.45-2.05) and hyperlipidemia (OR: 1.90, 95%CI: 1.65-2.17). Aside from significant finding, for this age interval, male had less risk developing newly treated hypertension, diabetes and hyperlipidemia, but significant only for hyperlipidemia. Table 4-17 showed similar results through stepwise adjustment of covariates.

The proportional hazard assumption was not violated through non-crossing of the survival curves for these three subsets (A4-7~4-12).

Results of Cox model resembled the multivariate logistic model (Table 4-18), subjects who ever utilized service during 1998-2000 had higher risks to develop newly treated hypertension (HR: 1.71, 95%CI: 1.56-1.88), diabetes (OR: 1.66, 95%CI: 1.41-1.95) and for hyperlipidemia (HR: 1.78, 95%CI : 1.58-2.01).

Results of extended Cox model with counting process listed in Table 4-19, this model estimated each uptake of service during 2001-2007 and obtained significant and robust findings for newly treated hypertension (HR: 1.67, 95%CI: 1.50-1.85), diabetes (HR: 2.21, 95%CI: 1.87-2.61) and hyperlipidemia (HR: 3.24, 95%CI: 2.85-3.63).

4.2.3 Effectiveness on new disease treatment in subjects aged 65-100 years

In subjects aged 65-100, the service was provided free annually, the uptake of preventive service during 1998-2000 was dummy coded to estimate the effect of one uptake and at least two uptakes.

Both stepwise adjustment of covariate and selective logistic model revealed accordant estimation (Table 4-20~4-23), for three target events, subjects who utilized service more than two times had higher risk than those who uptake only one time, and results of linear test for trend were significant.

In Table 4-20, 4-21, 4-22, increment of age had significant lower risk association with newly treated hypertension, diabetes. Male aged 65-100 had lower risk developing treated hypertension and diabetes than female.

The proportional hazard assumption was not violated through non-crossing of the survival curves for these three subsets (A4-13~4-18).

Table 4-24 showed consistent estimations on uptake one time and more than two times to newly treated hypertension (HR: 1.57, 95%CI: 1.43-1.73; HR: 2.10, 95%CI: 1.89-2.34), diabetes (HR: 1.25, 95%CI: 1.04-1.51; HR: 1.56, 95%CI: 1.23-1.90) and hyperlipidemia (HR: 1.39, 95%CI: 1.19-1.61; HR: 1.73, 95%CI: 1.48-2.03).

Results of extended Cox model with counting process listed in Table 4-25, this model estimated each uptake of service during 2001-2007 and obtained significant and robust findings for newly treated hypertension (HR: 1.56, 95%CI: 1.43-1.72), diabetes (HR: 1.76, 95%CI: 1.50-2.05) and hyperlipidemia (HR: 2.82, 95%CI: 2.49-3.20).

4.3 Effectiveness on death prevention

The mean survival time of those subjects who ever and never used services were 2,409.6 and 2,398.1 days; the median survival time of both two groups was 2555 days.

In multiple logistic model with stepwise selection (Table 4-26~4-28), those who ever utilized service during 1998-2000 were not associated with reduction or increasing risk of death, except subjects aged 65-100 who used services more than two times (OR: 0.74, 95%CI: 0.62-0.87). Across these three age groups, age, male gender, increment of baseline CCI score, existing chronic disease at baseline and those who lived in the East region were consistently associated with higher risk of all-cause mortality.

Table 4-29 yielded compatible findings, protective effect was significant only in subjects aged 65-100 years.

The proportional hazard assumption was not violated through non-crossing of the survival curves for these three subsets (A4-19~4-24).

In Cox model (Table 4-30), consistent results indicated that protective effect of preventive care services only existed in subjects aged 65-100 and uptake more than two times (HR: 0.84, 95%CI: 0.73-0.97).

Both multiple logistic model and Cox model indicated that the protective effect attenuated and became non-significant after adjustment of uptake service during follow-up. As mentioned above, utilization of preventive care service was time-dependent.

Table 4-31, 4-32 estimated the protective effect of each uptake of preventive care service, we assumed the protective effect to be one year and persisted after utilization. Both two models revealed significant findings on subjects aged 65-100 years (one year, HR: 0.74, 95%CI: 0.66-0.84), and the protective effect attenuated in the persisted model (seven years, HR: 0.80, 95%CI: 0.72-0.89).

4.4 Brief summary of results

For those who ever utilized the adult preventive services, the estimates on target events obtained from multivariate logistic model, Cox proportional hazard model were similar and stayed in the same direction. The results assessed from extended Cox model were also not violated, except on early diabetes treatment in subjects aged 40-54. Subjects who ever utilized the adult preventive service were with higher risks to be diagnosed to have newly treated hypertension, diabetes and hyperlipidemia.

The hazard ratio (HR) of each uptake on newly treated hypertension were

1.80, 1.71 and 1.67 among subjects aged 40-54, 55-64 and 65-100. For newly treated diabetes, the HR were 1.59, 2.21 and 1.76 among subjects aged 40-54, 55-64 and 65-100. For newly treated hyperlipidemia, the HR were 3.97, 3.21 and 2.82 among subjects aged 40-54, 55-64 and 65-100. All of these estimates were statistically significant ($p < 0.001$).

The hazard ratio (HR) of each uptake on death within one year were 0.94, 1.14 and 0.74 among subjects aged 40-54, 55-64 and 65-100, only the last was statistically significant.

The hazard ratio (HR) of each uptake on death within seven year were 0.90, 0.89 and 0.80 among subjects aged 40-54, 55-64 and 65-100, only the last was statistically significant.

Table 4-1. Distribution of demographic and geographic characteristics at baseline

Variables	Item	N	%	Mean	SD
Sex	Male	16,080	50.2		
	Female	15,959	49.8		
Age	Male			55.6	11.9
	Female			56.0	11.9*
Age group (years)	40-44	6,154	19.2		
	45-49	6,897	21.5		
	50-54	4,454	13.9		
	55-59	3,398	10.6		
	60-64	3,220	10.1		
	65-69	2,729	8.5		
	70-74	2,376	7.4		
	75-79	1,572	4.9		
	80-84	780	2.4		
	85-89	350	1.1		
	90-100	109	0.3		
Level of premium (NT$)	0-22800	25,587	79.9		
	24000-36300	2,820	8.8		
	38200-57800	3,632	11.3		
Category of insurance applicant	Category 1	14,240	44.4		
	Category 2	13,295	41.5		
	Category 3	4,504	14.1		
Most frequent visit region	Taipei area	10,620	33.1		
	Northern & Central	10,290	32.1		
	South area	10,286	32.1		
	East area	843	2.6		

*p =0.006.

Table 4-2. Distribution of morbidity and comorbidity at baseline

Variables	Item	N	%	Mean	SD
Existing hypertension	Yes	5,378	16.8		
	No	26,661	83.2		
Existing diabetes	Yes	2,167	6.8		
	No	29,872	93.2		
Existing hyperlipidemia	Yes	1,327	4.1		
	no	30,712	95.9		
Charlson comorbidity index (CCI)				0.693	1.27

Table 4-3. Characteristics of the overall subjects with or without utilization of preventive care service

Variables	Item	Never use (n=20,948)		Ever use (n=11,091)		P value
		N	%	N	%	
Age group (years)	40-54	13,013	62.1	4,492	40.5	<0.001
	55-64	4,073	19.4	2,545	22.9	
	65-100	3,862	18.4	4,054	36.6	
Sex	Male	11,095	47.0	4,985	55.1	<0.001
	Female	9,853	53.0	6,106	44.9	
Level of premium (NT$)	0-22800	16,089	76.8	9,498	85.6	<0.001
	24000-36300	2,077	9.9	743	6.7	
	38200-57800	2,782	13.3	850	7.7	
Category of insurance applicants	Category 1	10,133	48.4	4,107	37.0	<0.001
	Category 2	7,981	38.1	5,314	47.9	
	Category 3	2,834	13.5	1,670	15.1	
Most frequent visited region	Taipei area	7,629	36.4	2,991	27.0	<0.001
	Northern & Central	6,591	31.5	3,699	33.4	
	South area	6,210	29.6	4,076	36.8	
	East area	518	2.5	325	2.9	

Table 4-4. Morbidity of the overall subjects with or without utilization of preventive care service

Variables	Item	Never use (n=20,948)		Ever use (n=11,091)		P value
		N	%	N	%	
Existing hypertension	Yes	2,670	12.7	2,708	24.4	<0.001
	No	18,278	87.3	8,383	75.6	
Existing diabetes	Yes	1,134	5.4	1,033	9.3	<0.001
	No	19,814	94.6	10,058	90.7	
Existing hyperlipidemia	Yes	679	3.2	648	5.8	<0.001
	no	20,269	96.8	10,443	94.2	

Table 4-5. Comorbidity of subjects with or without utilization of preventive care service

Variable	N	Mean	SD	P value
Ever use	11,091	0.946	1.39	<0.001
Never use	20,948	0.559	1.17	

Table 4-6. Distribution of the category of visited hospital and section

Variable	Item*	N	(%)
Category of hospital	Clinic	7,288	65.7
	UA	1,399	12.6
	District	1,219	11.0
	Others	905	8.2
	Regional	231	2.1
	Center	49	0.4
Category of section	FamMed	3,771	34.0
	GP	2,302	20.8
	Gyn/Obs	59	0.5
	IntMed	3,435	31.0
	Others	42	0.4
	Pediatric	14	0.1
	Surgeon	69	0.6
	UA	1,399	12.6
Total		11091	100

* FamMed: family medicine, OBS/GYN: obstetrics and gynecology, UA: unavailable, IntMed: internal medicine

Table 4-7. Sizes and event rates of different cohort subsets

Datasets	Cohort		Events	
	N	%	N	%
Main cohort*				
Ever use	11,091	34.6	896	37.9
Never use	20,948	65.4	1,471	62.1
Total	32,039	100	2,367	100
Hypertension-free cohort†				
Ever use	8,383	31.4	3,389	39.6
Never use	13,278	68.6	5,175	60.4
Total	26,661	100	8,564	100
Diabetes-free cohort†				
Ever use	10,058	33.7	1,095	40.1
Never use	19,814	66.3	1,635	59.9
Total	29,872	100	2,730	100
Hyperlipidemia-free cohort†				
Ever use	10,443	34.0	2,046	46.0
Never use	20,269	66.0	2,403	54.0
Total	30,712	100	4,449	100

* Event of main cohort was set as all-cause mortality.

† Subjects with the target chronic disorder at baseline were excluded.

Table 4-8. Results of multiple logistic regression on newly treated hypertension in hypertension-free subjects aged 40-54 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.10	1.09-1.11	<0.001
Uptake of service (At least once vs. none)	1.51	1.38-1.65	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	0.48	0.44-0.52	<0.001
CCI (1 score increment)	1.12	1.07-1.17	<0.001
Existing diabetes at baseline (yes vs. no)	2.12	1.67-2.68	<0.001
Existing hyperlipidemia at baseline (yes vs. no)	1.52	1.15-2.01	0.003
Category of insurance applicants			
Category 1 vs. 3	1.01	0.88-1.16	0.155
Category 2 vs. 3	1.16	1.01-1.34	0.002
Most frequent visited region			
Taipei vs. East	0.78	0.60-0.99	<0.001
North/Central vs. East	0.94	0.73-1.21	0.298
South vs. East	0.91	0.70-1.16	0.938

*Multivariate logistic regression (stepwise selection, X^2=902.02, df=11)

*Covariates including : Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-9. Results of multiple logistic regression on newly treated diabetes in diabetes-free subjects aged 40-54 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.10	1.08-1.11	<0.001
Sex (Male vs. Female)	1.36	1.20-1.53	<0.001
Uptake of service At least once vs. none	1.14	0.99-1.31	0.071
Uptake of service before endpoint during follow-up (yes vs. no)	0.73	0.65-0.83	<0.001
CCI(1 score increment)	1.10	1.03-1.16	0.003
Existing hypertension at baseline	2.33	1.94-2.81	<0.001
Existing hyperlipidemia at baseline (yes vs. no)	1.74	1.27-2.38	<0.001
Level of premium			
Level 2 vs. 1	0.76	0.63-0.92	0.546
Level 3 vs. 1	0.66	0.55-0.78	0.003
Most frequent visited region			
Taipei vs. East	0.91	0.60-1.39	0.021
North/Central vs. East	1.13	0.75-1.71	0.409
South vs. East	1.27	0.84-1.92	0.011

*Multivariate logistic regression (stepwise selection and put variables of interest in, X^2=390.74, df=12)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-10. Results of multiple logistic regression on newly treated hyperlipidemia in hyperlipidemia-free subjects aged 40-54 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.06	1.05-1.08	<0.001
Sex (Male vs. Female)	1.15	1.05-1.27	0.004
Uptake of service At least once vs. none	1.53	1.38-1.71	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	1.11	1.00-1.23	0.044
CCI(1 score increment)	1.14	1.08-1.19	<0.001
Existing hypertension at baseline (yes vs. no)	2.23	1.91-2.60	<0.001
Existing diabetes at baseline (yes vs. no)	3.10	2.48-3.89	<0.001
Most frequent visited region			
Taipei vs. East	1.05	0.78-1.44	0.038
North/Central vs. East	0.80	0.58-1.09	0.001
South vs. East	0.97	0.71-1.35	0.743

*Multivariate logistic regression(stepwise selection and put variables of interest in, X^2=635.71, df=10)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-11. Crude and adjusted odds ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 40-54 years who ever vs. never uptake of preventive care service*

Variables	Adjusted for	Odds ratio(95% CI)	p value
Newly treated hypertension[†]	Crude	1.34(1.23-1.45)	<0.001
	Model 1	1.30(1.20-1.41)	<0.001
	Model 2	1.61(1.47-1.76)	<0.001
	Model 3	1.57(1.44-1.72)	<0.001
	Model 4	1.52(1.39-1.66)	<0.001
Newly treated diabetes[†]	Crude	1.17(1.02-1.33)	0.021
	Model 1	1.14(1.00-1.30)	0.055
	Model 2	1.11(1.09-1.13)	0.002
	Model 3	1.21(1.05-1.39)	0.007
	Model 4	1.13(0.98-1.30)	0.090
Newly treated hyperlipidemia[†]	Crude	1.72(1.56-1.90)	<0.001
	Model 1	1.68(1.52-1.85)	<0.001
	Model 2	1.64(1.48-1.82)	<0.001
	Model 3	1.65 (1.48-1.83)	<0.001
	Model 4	1.53(1.37-1.70)	<0.001

*Multivariate logistic regression
[†]Model 1 including covariate：Age, Sex.
Model 2 including covariate：model 1 + Uptake of service before endpoint during follow-up
Model 3 including covariate：model 2 + category of insurance applicant, Level of premium, Most frequent visited region
Model 4 including covariate：model 3 + CCI, Existing baseline morbidities

Table 4-12. Crude and adjusted hazard ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 40-54 years who ever and never uptake of preventive care service

Variables	Adjusted for	HR(95% CI)	p value
Newly treated hypertension†	Crude	1.27(1.19-1.37)	<0.001
	Model 1	1.24(1.15-1.33)	<0.001
	Model 2	1.58(1.46-1.70)	<0.001
	Model 3	1.54(1.43-1.66)	<0.001
	Model 4	1.48(1.37-1.60)	<0.001
Newly treated diabetes†	Crude	1.14(1.01-1.29)	0.037
	Model 1	1.12(0.99-1.27)	0.079
	Model 2	1.25(1.09-1.43)	0.001
	Model 3	1.22(1.06-1.39)	0.004
	Model 4	1.13(0.99-1.29)	0.073
Newly treated hyperlipidemia†	Crude	1.64(1.50-1.80)	<0.001
	Model 1	1.60(1.46-1.75)	<0.001
	Model 2	1.60(1.46-1.77)	<0.001
	Model 3	1.60(1.46-1.77)	<0.001
	Model 4	1.47(1.33-1.62)	<0.001

*Cox proportional hazard regression

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + Uptake of service before endpoint during follow-up

Model 3 including covariate：model 2 + category of insurance applicant, Level of premium, Most frequent visited region,

Model 4 including covariate：model 3 + CCI, Existing baseline morbidities

Table 4-13. Crude and adjusted hazard ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 40-54 years attending preventive service within 1 year*

Variables	Adjusted for	HR(95% CI)	p value
Newly treated hypertension†	Crude	1.86(1.70-2.04)	<0.001
	Model 1	1.83(1.67-2.01)	<0.001
	Model 2	1.80(1.64-1.97)	<0.001
Newly treated diabetes†	Crude	3.59(3.16-4.08)	<0.001
	Model 1	3.58(3.15-4.08)	<0.001
	Model 2	1.59(1.19-2.13)	0.002
Newly treated hyperlipidemia†	Crude	4.14(3.76-4.56)	<0.001
	Model 1	4.09(3.71-4.52)	<0.001
	Model 2	3.97(3.59-4.38)	<0.001

* Extended Cox proportional hazard regression-counting process for time-dependent covariate

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + CCI, Existing baseline morbidities

Table 4-14. Results of multiple logistic regression on newly treated hypertension in hypertension-free subjects aged 55-64 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.05	1.03-1.07	<0.001
Sex (Male vs. Female)	0.75	0.67-0.84	0.314
Uptake of service (At least once vs. none)	1.76	1.55-1.99	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	0.35	0.31-0.39	<0.001
Existing diabetes at baseline (yes vs. no)	1.57	1.21-2.02	0.001
Existing hyperlipidemia at baseline (yes vs. no)	1.71	1.22-2.38	0.002
Category of insurance applicant			
Category 1 vs. 3	1.07	0.88-1.30	0.672
Category 2 vs. 3	1.21	1.01-1.46	0.013

*Multivariate logistic regression (stepwise selection, X^2=402.91, df=8)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-15. Results of multiple logistic regression on newly treated diabetes in diabetes-free subjects aged 55-64 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.01	0.99-1.04	0.352
Sex (Male vs. Female)	0.92	0.79-1.08	0.314
Uptake of service At least once vs. none	1.73	1.45-2.05	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	0.45	0.38-0.53	<0.001
CCI(1 score increment)	1.09	1.03-1.16	0.005
Existing hypertension at baseline	1.40	1.16-1.69	0.001

*Multivariate logistic regression (stepwise selection and put variables of interest in, X^2=130.80, df=6)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-16. Results of multiple logistic regression on newly treated hyperlipidemia in hyperlipidemia-free subjects aged 55-64 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.01	0.99-1.03	0.517
Sex (Male vs. Female)	0.74	0.65-0.84	<0.001
Uptake of service At least once vs. none	1.90	1.65-2.17	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	0.87	0.76-1.00	0.056
CCI(1 score increment)	1.00	0.95-1.05	0.917
Existing hypertension at baseline (yes vs. no)	1.71	1.47-1.99	<0.001
Existing diabetes at baseline (yes vs. no)	2.30	1.84-2.88	<0.001
Most frequent visited region			
Taipei vs. East	1.06	0.73-1.54	0.004
North/Central vs. East	0.67	0.46-0.97	<0.001
South vs. East	0.82	0.56-1.19	0.346

*Multivariate logistic regression (stepwise selection and put variables of interest in, X^2=306.28, df=10)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-17. Crude and adjusted odds ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 55-64 years who ever and never uptake of preventive care service*

Variables	Adjusted for	Odds ratio(95% CI)	p value
Newly treated hypertension†	Crude	1.41(1.26-1.58)	<0.001
	Model 1	1.34(1.20-1.51)	<0.001
	Model 2	1.81(1.60-2.06)	<0.001
	Model 3	1.76(1.55-2.00)	<0.001
	Model 4	1.74(1.53-1.98)	<0.001
Newly treated diabetes†	Crude	1.38(1.18-1.61)	<0.001
	Model 1	1.37(1.17-1.60)	<0.001
	Model 2	1.82(1.54-2.16)	<0.001
	Model 3	1.79(1.51-2.13)	<0.001
	Model 4	1.69(1.42-2.01)	<0.001
Newly treated hyperlipidemia†	Crude	1.90(1.68-2.15)	<0.001
	Model 1	1.81(1.60-2.06)	<0.001
	Model 2	1.95(1.70-2.23)	<0.001
	Model 3	2.00(1.75-2.29)	<0.001
	Model 4	1.90(1.66-2.18)	<0.001

*Multivariate logistic regression

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + Uptake of service before endpoint during follow-up

Model 3 including covariate：model 2 + category of insurance applicant, Level of premium, Most frequent visited region

Model 4 including covariate：model 3 + CCI, Existing baseline morbidities

Table 4-18. Crude and adjusted hazard ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 55-64 years who ever and never uptake of preventive care service*

Variables	Adjusted for	HR(95% CI)	p value
Newly treated hypertension†	Crude	1.29(1.18-1.40)	<0.001
	Model 1	1.23(1.13-1.34)	<0.001
	Model 2	1.81(1.65-1.98)	<0.001
	Model 3	1.76(1.60-1.93)	<0.001
	Model 4	1.71(1.56-1.88)	<0.001
Newly treated diabetes†	Crude	1.31(1.14-1.52)	<0.001
	Model 1	1.31(1.13-1.51)	<0.001
	Model 2	1.81(1.54-2.12)	<0.001
	Model 3	1.78(1.51-2.09)	<0.001
	Model 4	1.66(1.41-1.95)	<0.001
Newly treated hyperlipidemia†	Crude	1.72(1.54-1.92)	<0.001
	Model 1	1.65(1.47-1.84)	<0.001
	Model 2	1.87(1.66-2.11)	<0.001
	Model 3	1.90(1.69-2.15)	<0.001
	Model 4	1.78(1.58-2.01)	<0.001

*Cox proportional hazard regression

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + Uptake of service before endpoint during follow-up

Model 3 including covariate：model 2 + category of insurance applicant, Level of premium, Most frequent visited region,

Model 4 including covariate：model 3 + CCI, Existing baseline morbidities

Table 4-19. Crude and adjusted hazard ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 55-64 years attending preventive service within 1 year*

Variables	Adjusted for	HR(95% CI)	p value
Newly treated hypertension†	Crude	1.76(1.58-1.95)	<0.001
	Model 1	1.68(1.51-1.86)	<0.001
	Model 2	1.67(1.50-1.85)	<0.001
Newly treated diabetes†	Crude	2.24(1.91-2.63)	<0.001
	Model 1	2.25(1.91-2.66)	<0.001
	Model 2	2.21(1.87-2.61)	<0.001
Newly treated hyperlipidemia†	Crude	3.30(2.95-3.70)	<0.001
	Model 1	3.24(2.87-3.65)	<0.001
	Model 2	3.21(2.85-3.63)	<0.001

* Extended Cox proportional hazard regression-counting process for time-dependent covariate

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + CCI, Existing baseline morbidities

Table 4-20. Results of multiple logistic regression on newly treated hypertension in hypertension-free subjects aged 65-100 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	0.97	0.96-0.98	<0.001
Sex (Male vs. Female)	0.76	0.67-0.846	<0.001
Uptake of service once vs. none	1.67	1.46-1.922	<0.001
At least 2 times vs. none	2.45	2.10-2.868	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	0.48	0.42-0.541	<0.001
CCI(1 score increment)	0.93	0.89-0.97	0.013
Existing diabetes at baseline (yes vs. no)	1.70	1.33-2.17	0.001
Existing hyperlipidemia at baseline (yes vs. no)	1.64	1.17-2.29	0.004
Most frequent visited region			
Taipei vs. East	0.68	0.49-0.95	0.005
North/Central vs. East	0.77	0.55-1.06	<0.345
South vs. East	0.81	0.59-1.13	0.900

*Multivariate logistic regression (stepwise selection and put variables of interest in, X^2=315.72, df=11)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-21. Results of multiple logistic regression on newly treated diabetes in diabetes-free subjects aged 65-100 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	0.94	0.93-0.95	<0.001
Sex (Male vs. Female)	0.84	0.72-0.98	0.025
Uptake of service once vs. none	1.22	1.00-1.48	<0.001
At least 2 times vs. none	1.59	1.29-1.94	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	0.55	0.46-0.65	<0.001
Existing hypertension at baseline (yes vs. no)	1.51	1.28-1.77	<0.001
Category of insurance applicant			
Category 1 vs. 3	1.05	0.85-1.31	0.459
Category 2 vs. 3	1.27	1.04-1.54	0.009

*Multivariate logistic regression (stepwise selection, X^2=158.13, df=8)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-22. Results of multiple logistic regression on newly treated hyperlipidemia in hyperlipidemia-free subjects aged 65-100 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	0.92	0.91-0.93	0.517
Sex (Male vs. Female)	0.61	0.53-0.69	<0.001
Uptake of service once vs. none	1.38	1.17-1.63	<0.001
At least 2 times vs. none	1.79	1.51-2.13	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	0.99	0.85-1.15	0.888
Existing hypertension at baseline (yes vs. no)	1.65	1.44-1.90	<0.001
Existing diabetes at baseline (yes vs. no)	1.39	1.15-1.68	0.001
Level of premium			
Level 2 vs. 1	0.84	0.39-1.81	0.187
Level 3 vs. 1	2.08	1.24-3.48	0.012
Most frequent visited region			
Taipei vs. East	1.15	0.79-1.66	0.001
North/Central vs. East	0.74	0.51-1.08	0.002
South vs. East	0.83	0.57-1.20	0.122

*Multivariate logistic regression (stepwise selection and put variables of interest in, X^2=417.72, df=12)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-23. Crude and adjusted odds ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 65-100 years with different uptake of preventive care service*

Variables	Adjusted for	Uptake once	Uptake >=2 times	P value[Δ]
		OR(95% CI)	OR(95% CI)	
Newly treated hypertension[†]	Crude	1.45(1.27-1.66)	1.85(1.60-2.13)	<0.001
	Model 1	1.41(1.24-1.61)	1.81(1.57-2.08)	<0.001
	Model 2	1.67(1.45-1.91)	2.46(2.10-2.87)	<0.001
	Model 3	1.66(1.45-1.91)	2.45(2.10-2.87)	<0.001
	Model 4	1.68(1.46-1.93)	2.46(2.10-2.88)	<0.001
Newly treated diabetes[†]	Crude	1.13(0.94-1.36)	1.33(1.11-1.59)	0.110
	Model 1	1.07(0.89-1.29)	1.29(1.08-1.55)	0.071
	Model 2	1.26(1.04-1.53)	1.70(1.39-2.07)	0.005
	Model 3	1.25(1.03-1.52)	1.70(1.39-2.07)	0.005
	Model 4	1.22(1.00-1.48)	1.57(1.28-1.93)	0.019
Newly treated hyperlipidemia[†]	Crude	1.46(1.25-1.70)	1.87(1.61-2.18)	0.003
	Model 1	1.37(1.17-1.61)	1.82(1.56-2.13)	0.001
	Model 2	1.41(1.19-1.66)	1.89(1.60-2.24)	0.001
	Model 3	1.44(1.22-1.70)	1.95 (1.64-2.31)	0.001
	Model 4	1.39(1.17-1.64)	1.80(1.52-2.14)	0.003

* Multivariate logistic regression

[†]Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + Uptake of service before endpoint during follow-up

Model 3 including covariate：model 2 + category of insurance applicant, Level of premium, Most frequent visited region

Model 4 including covariate：model 3 + CCI, Existing baseline morbidities

[Δ] p value of linear test for trend

Table 4-24. Crude and adjusted hazard ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 65-100 years who ever and never uptake of preventive care service*

Variables	Adjusted for	Uptake once	Uptake >=2 times
		HR(95% CI)	HR(95% CI)
Newly treated hypertension†	Crude	1.23(1.13-1.35)	1.37(1.25-1.51)
	Model 1	1.23(1.12-1.35)	1.37(1.25-1.51)
	Model 2	1.61(1.46-1.77)	2.19(1.97-2.43)
	Model 3	1.60(1.46-1.76)	2.18(1.96-2.41)
	Model 4	1.57(1.43-1.73)	2.10(1.89-2.34)
Newly treated diabetes†	Crude	1.05(0.88-1.25)	1.17(0.99-1.39)
	Model 1	1.02(0.86-1.22)	1.16(0.98-1.37)
	Model 2	1.32(1.10-1.58)	1.73(1.43-2.10)
	Model 3	1.31(1.09-1.57)	1.72(1.42-2.09)
	Model 4	1.25(1.04-1.51)	1.56(1.29-1.90)
Newly treated hyperlipidemia†	Crude	1.33(1.15-1.53)	1.60(1.39-1.84)
	Model 1	1.28(1.11-1.48)	1.58(1.38-1.82)
	Model 2	1.42(1.22-1.66)	1.86(1.59-2.17)
	Model 3	1.45(1.24-1.68)	1.90(1.63-2.22)
	Model 4	1.39(1.19-1.61)	1.73(1.48-2.03)

* Cox proportional hazard regression

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + Uptake of service before endpoint during follow-up

Model 3 including covariate：model 2 + category of insurance applicant, Level of premium, Most frequent visited region,

Model 4 including covariate：model 3 + CCI, Existing baseline morbidities

Table 4-25. Crude and adjusted hazard ratio for newly treated hypertension, diabetes, hyperlipidemia in disease-free subjects aged 65-100 years attending preventive service within 1 year*

Variables	Adjusted for	HR(95% CI)	p value
Newly treated hypertension[†]	Crude	1.59(1.45-1.74)	<0.001
	Model 1	1.59(1.45-1.74)	<0.001
	Model 2	1.56(1.43-1.72)	<0.001
Newly treated diabetes[†]	Crude	1.87(1.60-2.18)	<0.001
	Model 1	1.82(1.56-2.12)	<0.001
	Model 2	1.76(1.50-2.05)	<0.001
Newly treated hyperlipidemia[†]	Crude	3.01(2.66-3.42)	<0.001
	Model 1	2.90(2.56-3.29)	<0.001
	Model 2	2.82(2.49-3.20)	<0.001

* Extended Cox proportional hazard regression-counting process for time-dependent covariate
† Model 1 including covariate：Age, Sex.
Model 2 including covariate：model 1 + CCI, Existing baseline morbidities

Table 4-26. Results of multiple logistic regression on all-cause mortality in subjects aged 40-54 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.06	1.03-1.09	<0.001
Sex (Male vs. Female)	2.36	1.87-2.98	<0.001
Uptake of service (At least once vs. none)	0.91	0.70-1.20	0.520
Uptake of service before endpoint during follow-up (yes vs. no)	0.40	0.32-0.51	<0.001
Existing chronic disease at baseline (yes vs. no) (yes vs. no)	1.51	1.14-1.99	0.004
CCI(1 score increment)	1.58	1.49-1.68	
Level of premium			
Level 2 vs. 1	0.55	0.38-0.79	0.305
Level 3 vs. 1	0.45	0.32-0.63	0.008
Most frequent visited region			
Taipei vs. East	0.49	0.27-0.87	0.004
North/Central vs. East	0.61	0.34-1.10	0.446
South vs. East	0.65	0.36-1.16	0.859

*Multivariate logistic regression (stepwise selection and put variables of interest in, X^2=441.73, df=11)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-27. Results of multiple logistic regression on all-cause mortality in subjects aged 55-64 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.06	1.02-1.10	0.004
Sex (Male vs. Female)	2.14	1.70-2.70	<0.001
Uptake of service (At least once vs. none)	0.92	0.71-1.18	0.513
Uptake of service before endpoint during follow-up (yes vs. no)	0.38	0.30-0.49	<0.001
Existing chronic disease at baseline (yes vs. no)	1.19	0.93-1.51	0.169
CCI(1 score increment)	1.47	1.39-1.56	<0.001
Level of premium			
Level 2 vs. 1	0.89	0.59-1.35	0.124
Level 3 vs. 1	0.38	0.23-0.62	0.001

*Multivariate logistic regression (stepwise selection and put variables of interest in, X^2=367.53, df=9)

*Covariates including：Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-28. Results of multiple logistic regression on all-cause mortality in subjects aged 65-100 years*

Variables	Odds ratio(OR)	95% CI	p value
Age(1 year increment)	1.10	1.09-1.11	<0.001
Sex (Male vs. Female)	1.45	1.29-1.64	0.004
Uptake of service once vs. none	0.99	0.86-1.15	0.911
At least 2 times vs. none	0.74	0.62-0.87	<0.001
Uptake of service before endpoint during follow-up (yes vs. no)	0.47	0.41-0.53	<0.001
CCI(1 score increment)	1.27	1.23-1.32	<0.001
Existing chronic disease at baseline (yes vs. no)	1.22	1.07-1.38	0.003
Most frequent visited region			
Taipei vs. East	0.57	0.41-0.79	<0.001
North/Central vs. East	0.78	0.57-1.07	0.943
South vs. East	0.82	0.60-1.13	0.355

*Multivariate logistic regression (stepwise selection and put the variable of interest in, X^2=1005.34, df=10)

*Covariates including : Age, Sex, Uptake of service, CCI, Existing baseline morbidities, Category of insurance applicant, Level of premium, Most frequent visited region

Table 4-29. Crude and adjusted odds ratio for all-cause mortality in subjects with different uptake of preventive care service*

Variables	Adjusted for	Odds ratio(95% CI)	p value
Age 40-54 years†	Crude	0.78(0.61-1.00)	0.053
(At least once vs. none)	Model 1	0.82(0.64-1.05)	0.122
	Model 2	0.79(0.61-1.02)	0.065
	Model 3	0.68(0.52-0.88)	0.004
	Model 4	0.91(0.69-1.19)	0.488
Age 55-64 years†	Crude	0.73(0.59-0.91)	0.005
(At least once vs. none)	Model 1	0.75(0.60-0.94)	0.013
	Model 2	0.73(0.58-0.92)	0.007
	Model 3	0.64(0.50-0.81)	<0.001
	Model 4	0.89(0.69-1.15)	0.386
Age 65-100 years†	Crude	0.59(0.51-0.68)	<0.001
(At least 2 times vs. none)	Model 1	0.62(0.54-0.72)	<0.001
	Model 2	0.61(0.53-0.71)	<0.001
	Model 3	0.56(0.48-0.65)	<0.001
	Model 4	0.74(0.63-0.86)	<0.001

* Multivariate logistic regression

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + category of insurance applicant, Level of premium, Most frequent visited region

Model 3 including covariate：model 2 + CCI, Existing baseline morbidities

Model 4 including covariate：model 3 + Uptake of service before endpoint during follow-up

Table 4-30. Crude and adjusted hazard ratio for all-cause mortality in subjects who ever and never uptake of preventive care service*

Variables	Adjusted for	HR(95% CI)	p value
Age 40-54 years†	Crude	0.78(0.61-0.99)	0.045
(At least once vs. none)	Model 1	0.82(0.63-1.05)	0.109
	Model 2	0.79(0.61-1.01)	0.060
	Model 3	0.69(0.54-0.89)	0.004
	Model 4	0.94(0.73-1.23)	0.662
Age 55-64 years†	Crude	0.73(0.59-0.90)	0.003
(At least once vs. none)	Model 1	0.75(0.60-0.93)	0.008
	Model 2	0.73(0.58-0.90)	0.004
	Model 3	0.65(0.52-0.81)	<0.001
	Model 4	0.93(0.73-1.17)	0.525
Age 65-100 years†	Crude	0.59(0.52-0.67)	<0.001
(At least 2 times vs. none)	Model 1	0.64(0.56-0.73)	<0.001
	Model 2	0.63(0.55-0.72)	<0.001
	Model 3	0.59(0.52-0.67)	<0.001
	Model 4	0.84(0.73-0.97)	0.015

* Cox proportional hazard regression

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + category of insurance applicant, Level of premium, Most frequent visited region

Model 3 including covariate：model 2 + CCI, Existing baseline morbidities

Model 4 including covariate：model 3 + Uptake of service before endpoint during follow-up

Table 4-31. Crude and adjusted hazard ratio for all-cause mortality in subjects attending preventive service within 1 year*

Variables	Adjusted for	HR(95% CI)	p value
Age 40-54 years†	Crude	0.94(0.67-1.31)	0.700
	Model 1	0.99(0.71-1.39)	0.960
	Model 2	0.94(0.67-1.32)	0.705
Age 55-64 years†	Crude	0.75(0.58-0.98)	0.038
	Model 1	0.73(0.56-0.96)	0.025
	Model 2	1.14(0.91-1.43)	0.247
Age 65-100 years†	Crude	0.68(0.61-0.77)	<0.001
	Model 1	0.77(0.68-0.86)	<0.001
	Model 2	0.74(0.66-0.84)	<0.001

* Extended Cox proportional hazard regression-counting process for time-dependent covariate

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + CCI, Existing baseline morbidities

Table 4-32. Crude and adjusted hazard ratio for all-cause mortality in subjects ever uptake of preventive care service within 7 years*

Variables	Adjusted for	HR(95% CI)	p value
Age 40-54 years†	Crude	0.89(0.70-1.13)	0.891
	Model 1	0.96(0.75-1.23)	0.743
	Model 2	0.90(0.70-1.15)	0.384
Age 55-64 years†	Crude	0.90(0.73-1.12)	0.342
	Model 1	0.93(0.74-1.16)	0.506
	Model 2	0.89(0.71-1.12)	0.322
Age 65-100 years†	Crude	0.73(0.66-0.81)	<0.001
	Model 1	0.84(0.76-0.94)	0.002
	Model 2	0.80(0.72-0.89)	<0.001

* Extended Cox proportional hazard regression-counting process for time-dependent covariate

† Model 1 including covariate：Age, Sex.

Model 2 including covariate：model 1 + CCI, Existing baseline morbidities

Chapter 5. Discussion

5.1 Major findings and discussion

Clearly, we found the utilization of adult preventive care service had a significantly positive effect on early treatment of hypertension, diabetes and hyperlipidemia across all age groups. The research results also supported that uptake of this service may contribute to reduction in mortality, especially among the elderly.

The ten major causes of death in Taiwan have changed from infectious diseases in 1952 to chronic degenerative diseases in recent years, of which the prevalence of cardiovascular and cerebrovascular diseases increases the most significantly. In 2000, cerebrovascular diseases, heart disease, diabetes, nephritis, nephrotic syndrome, nephrosis and hypertensive diseases occupy 31.18% of total causes of death in Taiwan.

The adult preventive care service provided systematic approach to residents in Taiwan through medical history taking and lifestyle review, physical examination, laboratory tests (complete blood count, urine analysis, plasma sugar, liver, renal and lipid profile), and health counseling. These screening items were believed to cover for most of the major cardiovascular causes of death.

Frame and Carlso (1975) first proposed six criteria to evaluate the screening of a disease, list as follows: (a)the disease must has a significant effect on the quality or quantity of life, (b)acceptable methods of treatment must be available, (c) there must be an asymptomatic period during which detection and treatment significantly reduce morbidity and mortality, (d)treatment in the asymptomatic phase should yield outcome superior to that obtained by delaying treatment until symptoms appear, (e)tests must be available at a reasonable cost, (f) the incidence of the condition must justify the cost of the screening [45].

This study offered evidence for the effectiveness of adult preventive care service on early treatment of major chronic disease and reduction in mortality. In conceptual framework developed by Boulware et al. (2007), these findings prove benefits on clinical outcome and and could contribute to public health [4].

In this study, we also found that subjects with lower level of premium and low-income status didn't uptake the service less than others (Table 4-3). In Table 4-6, the result showed that subjects utilized the service mostly in clinics and section of family medicine. Both of these two findings provided evidence on the accessibility of the service.

Subjects aged 65-100 appeared to utilize more services (Table 4-3), this result may contribute to that NHI provided this free service package annually for them. Elderly subjects may have more underlying diseases and severity of comorbidity, these predisposed them to utilize the preventive care service.

According to the prevalence survey of hypertension, diabetes and hyperlipidemia in 2000 [46], the prevalence of these three diseases among those who aged 40 and older were 35%, 12.7% and 21.1%, however, Table 4-2 revealed only 16.8%, 6.8% and 4.1% of each disease. One explanation for this is our definition of these diseases, only those who ever visited more than three times in 2000 were considered positive.

It is worth noting that the association between age, gender and newly treated events. Increment of age had higher risk developing newly treated hypertension, diabetes and hyperlipidemia among subjects aged 40-64, this effect reversed among those who aged 65-100. This is because the subjects aged 65-100 were relatively healthier after excluding elderly with diseases at baseline (cohort subsets). Similar finding was found among different genders in subjects aged 65-100, male had lower risk developing target evens. One explanation for this is that female may with higher risk developing hyperlipidemia and cardiovascular disease after menopause [47].

In current study, protective effect of this service on death was significant only among those who aged 65-100. One explanation for this is that causes of death among subjects aged 40-64 were composed of more cancers, suicides and accident events than subjects aged 65-100. This study collected data of death only through claim data, those who died outside of the medical facilities couldn't be recruited in the research. Nevertheless, these estimates among subjects aged 40-64 still stayed in the same direction.

Through extended Cox model with counting process, rational estimate of each uptake could be obtained rather than that of ever receiving service, however, the results still should be interpreted cautiously, because that only covariate at baseline were adjusted in models.

For hypertension, diabetes and hyperlipidemia, receiving of preventive service may cause healthy attitude and lifestyle, in theory, which can lead to lower risk of disease occurrence or delay the medical intervention. But effects of these benefits were not showed, some explanation were listed below: (a) all subjects were older than 40 years, effect of those benefits were small, (b) sample sizes of each subset were large enough to demonstrate the achieving earlier disease treatment on those who in need.

The effectiveness of early disease treatment was less likely due to higher distribution of morbidity and comorbidity in those who ever used service, since morbidity and comorbidity were adjusted at baseline.

5.2 Comparison with previous studies

The main findings of this study are partially compatible with previous studies. Kaiser MHC study [3, 5-10] revealed a significant 30% reduction in deaths from pre-specified "potentially postponable" causes, largely associated with lower death rates from colorectal cancer and hypertension.

RCTs, such as South-East London study (1997), Patrick et al. (1999) revealed no significant effect on death prevention, in these studies, at least 2 years were follows, but only Chi-square test was used without advanced covariate adjustment. Theobald et al. (1998) applied Cox model but didn't adjust morbidity and comorbidity at baseline.

Chiou et al. (2002) conducted study among subjects aged older than 65 in Kaohsiung City, he used extended Cox regression model and adjusted covariates such as age, gender, education, co-morbidity status and living area. RR of all-cause mortality for those who ever utilized the health examination service was 0.71. The estimated RR of age, gender and existed chronic disease were similar to results of this study [22].

To our knowledge, few research regarding screening projects provided evidence on early treatment of hypertension, diabetes and hyperlipidemia, most studies set distribution of disease as an outcome. Fletcher et al. (1977), South-East London study (1997), Hama et al. (2001) proved the benefit on more disease detection of PHE [11, 20], Yang (2001) and Tsai (2007) described the effectiveness of disease detection of adult preventive care service in cross-section data [19, 29, 33].

In this study, claim data was applied; precise information about visit and treatment of each subject could be obtained, rather than data from cross – section investigation.

5.3 Possible mechanisms

According to the framework developed by Boulware (2006), the PHE may influence subject's health outcome through change in patient attitude, health behavior and diet, which may contribute to adequate disease management, improve clinical outcome, reduce resource use, and prevent from death[4].

The effectiveness of early treatment may be explained by considering the accessibility. Table 4-6 indicated that most of uptakes of the services occurred at clinics, where patients visited for their health problem most often. Reimbursement the service by NHI may enhance community clinics to detect and manage these chronic disease early.

The adult preventive care service contained self-report medical history and lifestyle, physical examination, laboratory tests and counseling, this items were believed to cover for most of the major causes of death. It was not clear whether the improvement of a part or all of intervention, however, this service did provide opportunity for early detection and management of disease, awareness of health, linkage between preventive service and primary care, satisfaction of patient demand [29, 33]

5.4 Strengths of this study

Current research had several methodological strengths. First, we applied NHI longitudinal datasets, which had large sample size and was nationally representative and allowed little room for selection or recall bias. Second, the claim data contained precise date of health visits. Third, for detecting newly treated events, the cohort datasets provide an adequate follow-up period. Fourth, we carried out extended Cox model to treat the time-dependent covariate, estimate of each uptake could be obtained through this model, and the results were consistent with those multivariate models in which uptake of service was only categorized into "ever" and "never". Fifth, using conservative definitions of covariates had less probability to overestimate the effectiveness of service. Sixth, estimates of age, gender, morbidity and CCI on target events were in accordance with current biomedical knowledge, which may support the validity of research model and accuracy of datasets.

5.5 Limitations of this study

There were several limitations in the study. First, exclusive reliance on claim data might result in potential disease misclassification bias. Second, the type of reimbursement of NHI could influence the assignment of coding in ambulatory visits or inpatient care record. Third, this NHI cohort datasets contained no information about actual residential area, socioeconomic status, function status, biomarker, etc. Fourth, diagnostic coding by ICD-9-CM in the ambulatory claims was not always precise. Fifth, subjects may utilize other type of health check-ups as well as changes in health behaviors, which may influence the estimates of interest variables. Sixth, this study used surrogate criteria for death, mortality was measured indirectly.

5.6 Conclusion and future perspectives

This study provides strong evidence for effectiveness of adult preventive care service on major health outcomes in early treatment of hypertension, diabetes and hyperlipidemia, as well as in reduction of all-cause mortality. Although recent systematic review revealed inconclusive effectiveness of PHE [4], nevertheless, this study demonstrate the associated benefit from implication and reimbursement of preventive care service in Taiwan.

Further study is needed to determine whether the higher survival rate of people who took advantage of the service was a direct result of the services or merely a reflection of better health concerns or health behaviors. Information of attitude and lifestyle should be collected concurrently at baseline.

Other aspects can be studied such as cost-effectiveness, the impact on medical resources utilization, improvement of physician-patient relationship, or enhancing performance of physician, estimate of competing risks model.

Adult preventive care service had implemented since 1996, modification of its contents is warranted, especially screening for cancers and related risk, which should be integrated effectively into the service in the future.

More efforts and resources should be devoted by the government to promote this preventive service and achieve a higher coverage rate among residents aged 40 years or older in Taiwan.

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Appendices

A3-1. Charlson Comorbidity Index and Corresponding ICD-9-CM Codes

Diagnosis description	Candidates of ICD-9-CM codes	Weights for diseases
Myocardial infarction	410-410.92; 412	1
Congestive heart failure	428-428.9	1
Peripheral vascular disease	441.0-441.9; 443.9; 785.4; V43.4	1
Cerebrovascular disease	430-438	1
Dementia	290-290.9	1
Chronic pulmonary disease	490-496; 500-505; 506.4	1
Rheumatologic disease	710.0; 710.1; 710.4; 714.0-714.2; 714.81; 725	1
Peptic ulcer disease	531-534.9	1
Mild liver disease	571.2; 571.4-571.49; 571.5; 571.6	1
Diabetes	250-250.3x; 250.7x; 250.8x; 250.9x	1
Diabetes with chronic complications	250.4x-250.6x	2
Hemiplegia or paraplegia	342-342.9; 344-344.9	2
Renal disease	581.81; 582-582.9; 583-583.81; 585; 586; 588-588.9	2
Any malignancy, including leukemia and lymphoma	140-195.8; 200-208.9	2
Moderate or severe liver disease	572-572.8; 456.0-456.21	3
Metastatic solid tumor	196-199.1	6
AIDS	042	6

A3-2 SAS codes of extended Cox model with counting process

/*Ttime-dependent covariate*/

proc tphreg data=appf.htntdset1yr covsandwich(aggregate) covm;

class expf(ref='0') sex(ref='F') dmb(ref='0') dyslipidb(ref='0');

model (T1,T2)*status(**0**)= expf age sex totalcci dmb dyslipidb /risklimits ;

where agecat2='01';

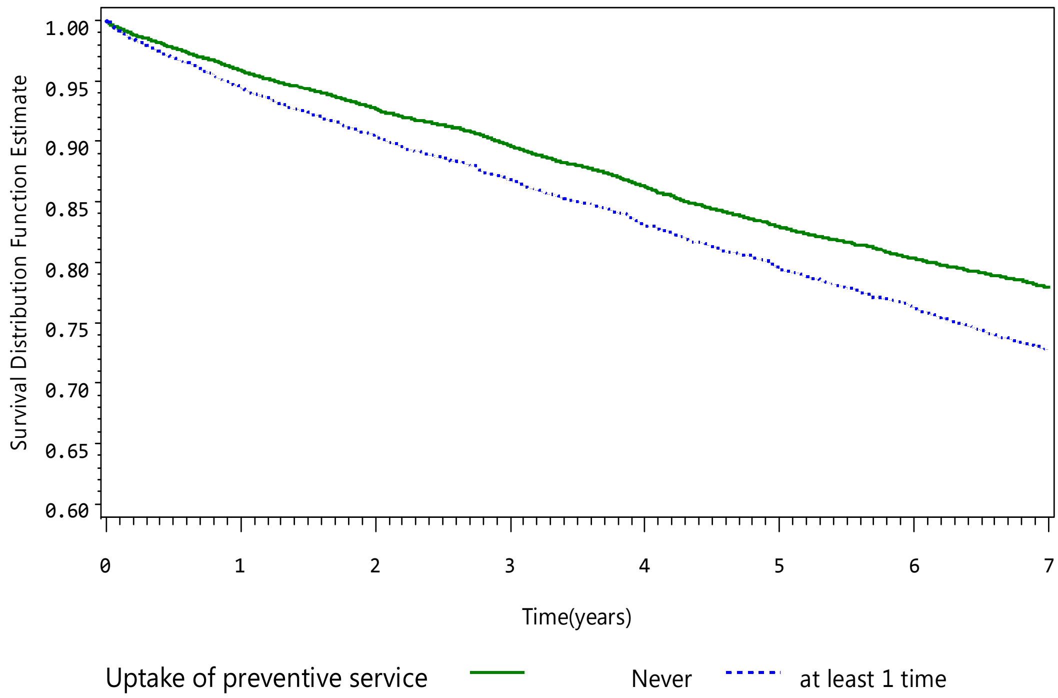
id perid;

run;

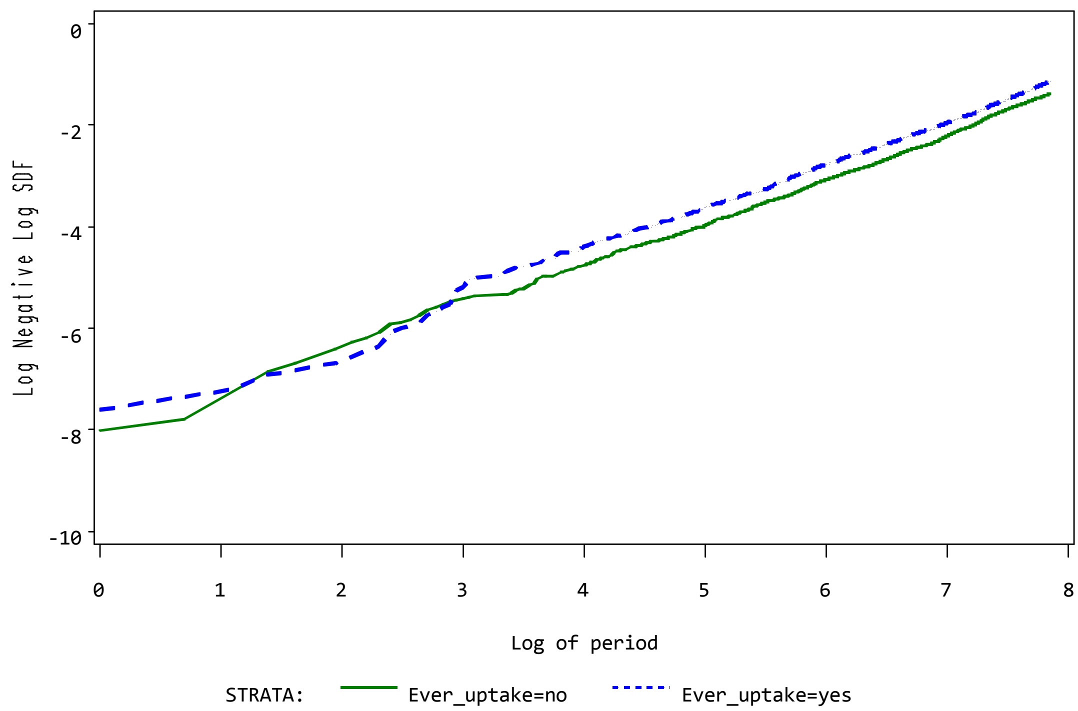
Example of data format :

	PerID	T1	t2	status	expf	age	sex	totalcci	DMb	Dyslipidb
1	0000b00c062337f484c42ceb1ca3dd32	01/01/2001	15/11/2004	0	0	49	F	0	0	0
2	0000b00c062337f484c42ceb1ca3dd32	15/11/2004	19/03/2005	0	1	49	F	0	0	0
3	0000b00c062337f484c42ceb1ca3dd32	19/03/2005	15/11/2005	0	1	49	F	0	0	0
4	0000b00c062337f484c42ceb1ca3dd32	15/11/2005	19/03/2006	0	1	49	F	0	0	0
5	0000b00c062337f484c42ceb1ca3dd32	19/03/2006	31/12/2007	0	0	49	F	0	0	0
6	0003bb6c5e5af514ac84cba16560d314	01/01/2001	31/12/2007	0	0	50	M	0	0	0
7	00045182106567f6f1253aa20f86aae9	01/01/2001	05/10/2005	0	0	41	F	1	0	0
8	00045182106567f6f1253aa20f86aae9	05/10/2005	05/10/2006	0	1	41	F	1	0	0
9	00045182106567f6f1253aa20f86aae9	05/10/2006	31/12/2007	0	0	41	F	1	0	0
10	0008aef04bb9f4ea199622f56cf2d658	01/01/2001	02/08/2001	0	0	77	M	3	0	0
11	0008aef04bb9f4ea199622f56cf2d658	02/08/2001	12/06/2002	0	1	77	M	3	0	0
12	0008aef04bb9f4ea199622f56cf2d658	12/06/2002	02/08/2002	0	1	77	M	3	0	0
13	0008aef04bb9f4ea199622f56cf2d658	02/08/2002	12/06/2003	0	1	77	M	3	0	0
14	0008aef04bb9f4ea199622f56cf2d658	12/06/2003	04/09/2003	0	0	77	M	3	0	0
15	0008aef04bb9f4ea199622f56cf2d658	04/09/2003	03/09/2004	0	1	77	M	3	0	0
16	0008aef04bb9f4ea199622f56cf2d658	03/09/2004	14/01/2005	0	0	77	M	3	0	0
17	0008aef04bb9f4ea199622f56cf2d658	14/01/2005	14/01/2006	0	1	77	M	3	0	0
18	0008aef04bb9f4ea199622f56cf2d658	14/01/2006	03/04/2006	1	0	77	M	3	0	0
19	000b087605f58b2e41be546d2864030c	01/01/2001	01/02/2001	1	0	44	M	0	0	0
20	000c5b4938161e461b5a599520a28581	01/01/2001	31/12/2007	0	0	41	M	0	0	0
21	000fe41503c937f657b286b2bc83479b	01/01/2001	21/06/2005	0	0	47	F	0	0	0
22	000fe41503c937f657b286b2bc83479b	21/06/2005	21/06/2006	0	1	47	F	0	0	0
23	000fe41503c937f657b286b2bc83479b	21/06/2006	31/12/2007	0	0	47	F	0	0	0
24	00102cbf1dbeea9a574f663eba796144	01/01/2001	09/01/2002	1	0	53	F	1	1	0
25	00144d413badd38b701bf5aeea5f8530	01/01/2001	31/12/2007	0	0	47	M	0	0	0

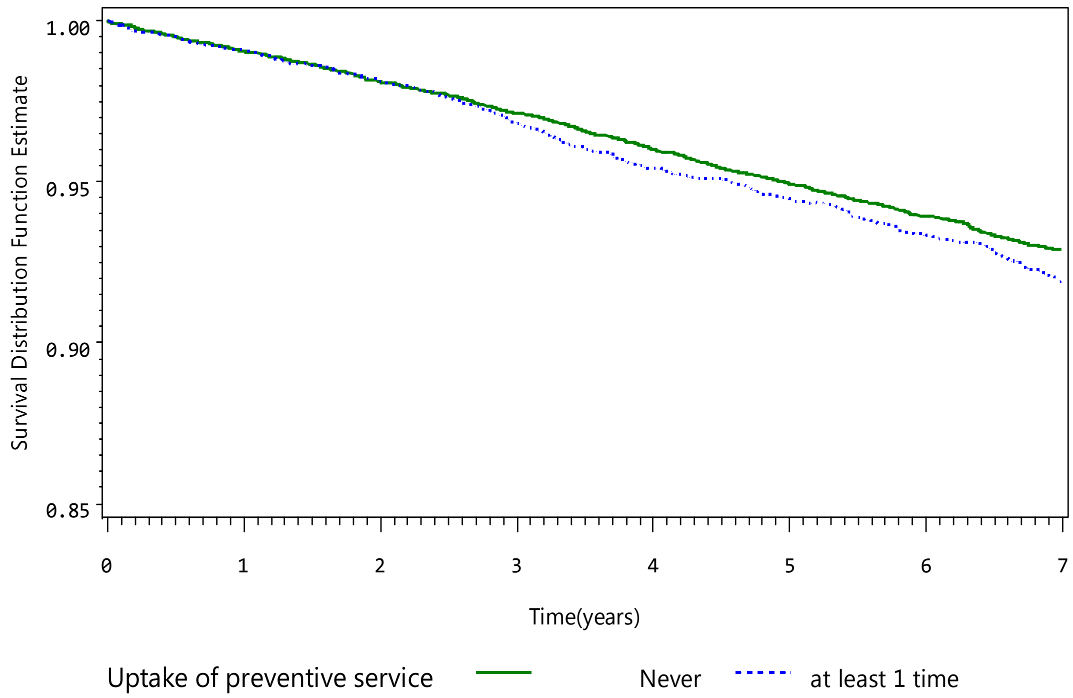
A4-1. Kaplan-Meier curve for newly treated hypertension in subjects aged 40-54 years who ever and never uptake of preventive care service



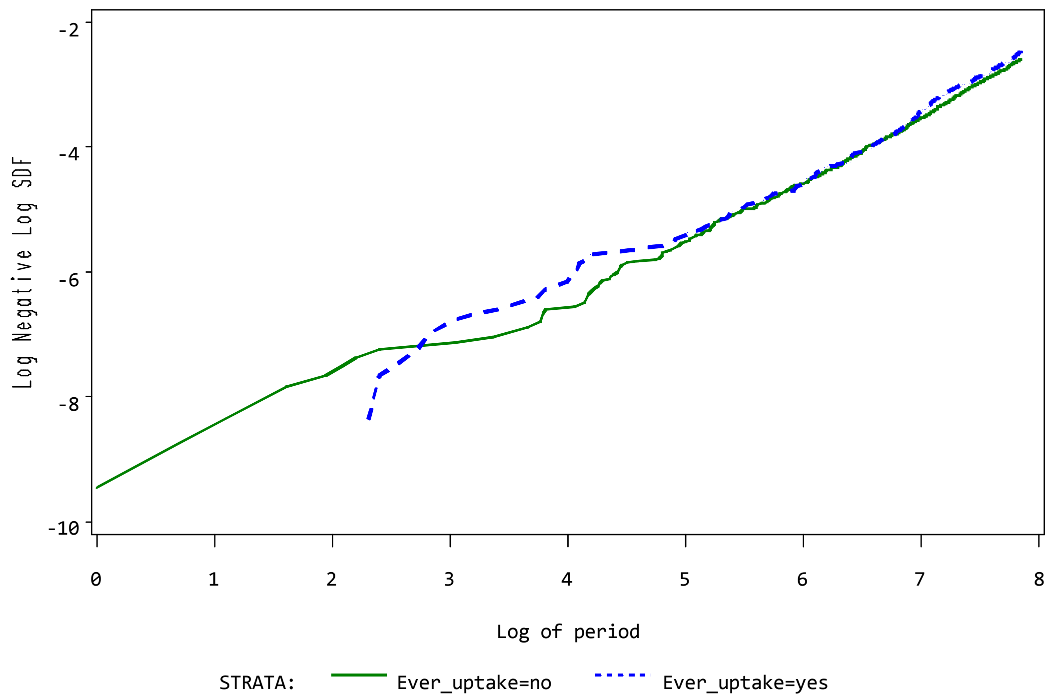
A4-2. Test of proportional assumption using for newly treated hypertension in subjects aged 40-54 years who ever and never uptake of preventive care service



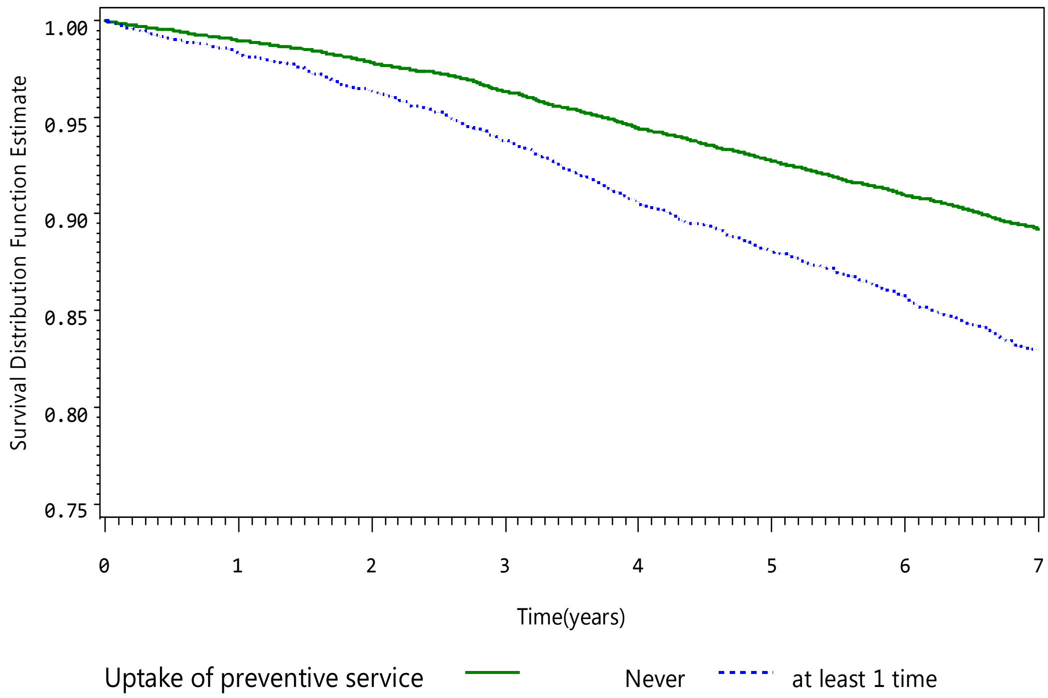
A4-3. Kaplan-Meier curve for newly treated diabetes in subjects aged 40-54 years who ever and never uptake of preventive care service



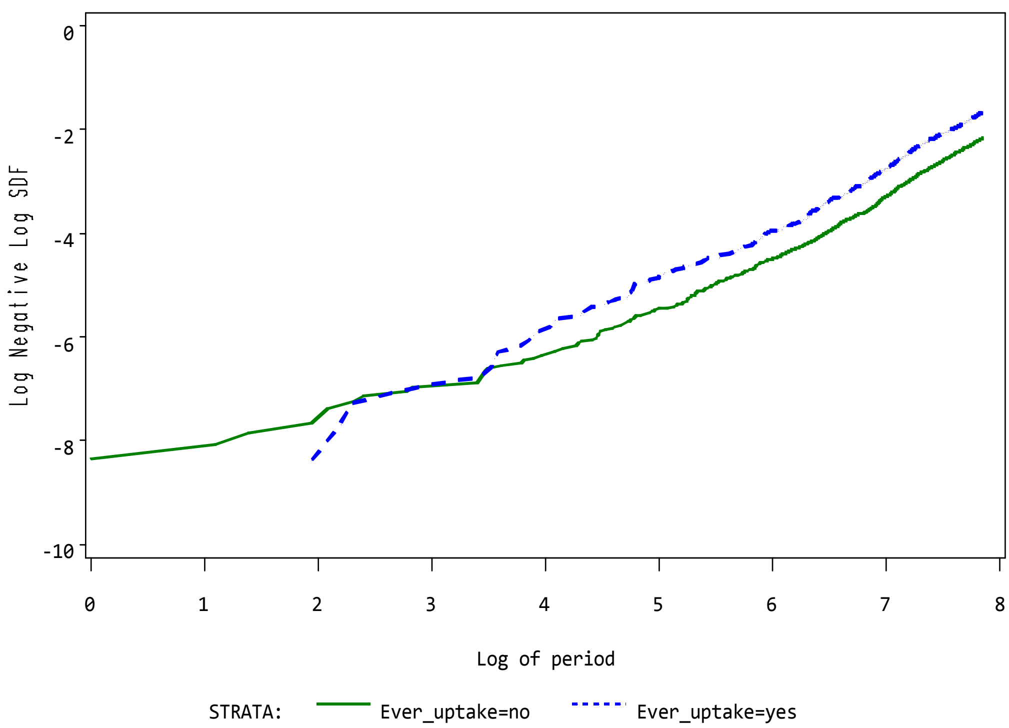
A4-4. Test of proportional assumption using for newly treated diabetes in subjects aged 40-54 years who ever and never uptake of preventive care service



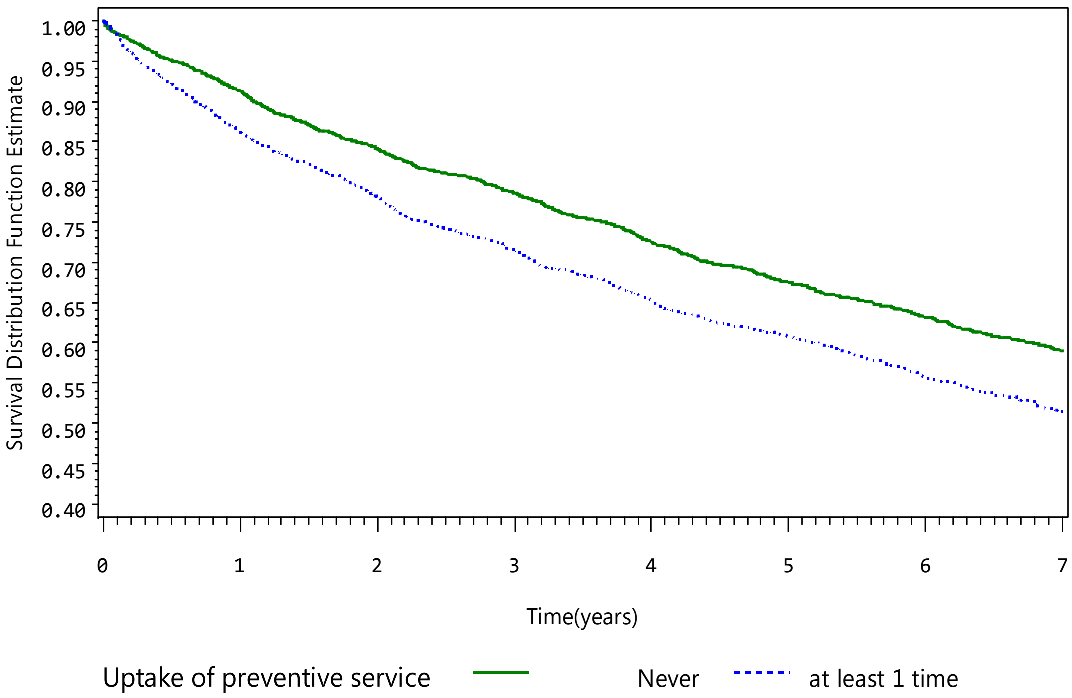
A4-5. Kaplan-Meier curve for newly treated hyperlipidemia in subjects aged 40-54 years who ever and never uptake of preventive care service



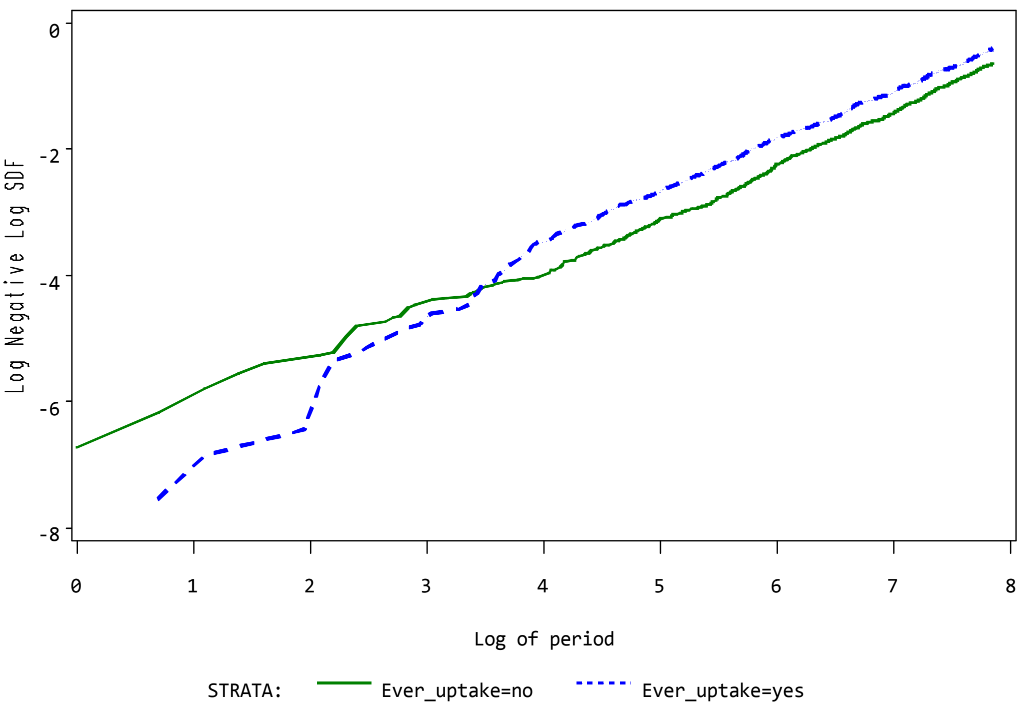
A4-6. Test of proportional assumption using for newly treated hyperlipidemia in subjects aged 40-54 years who ever and never uptake of preventive care service



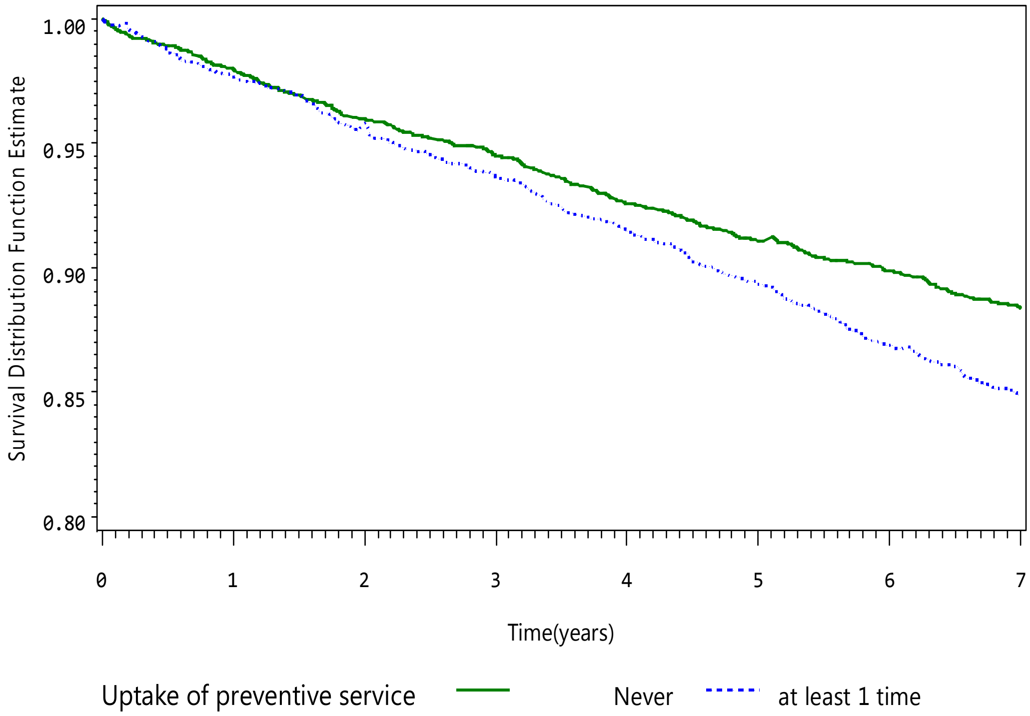
A4-7. Kaplan-Meier curve for newly treated hypertension in subjects aged 55-64 years who ever and never uptake of preventive care service



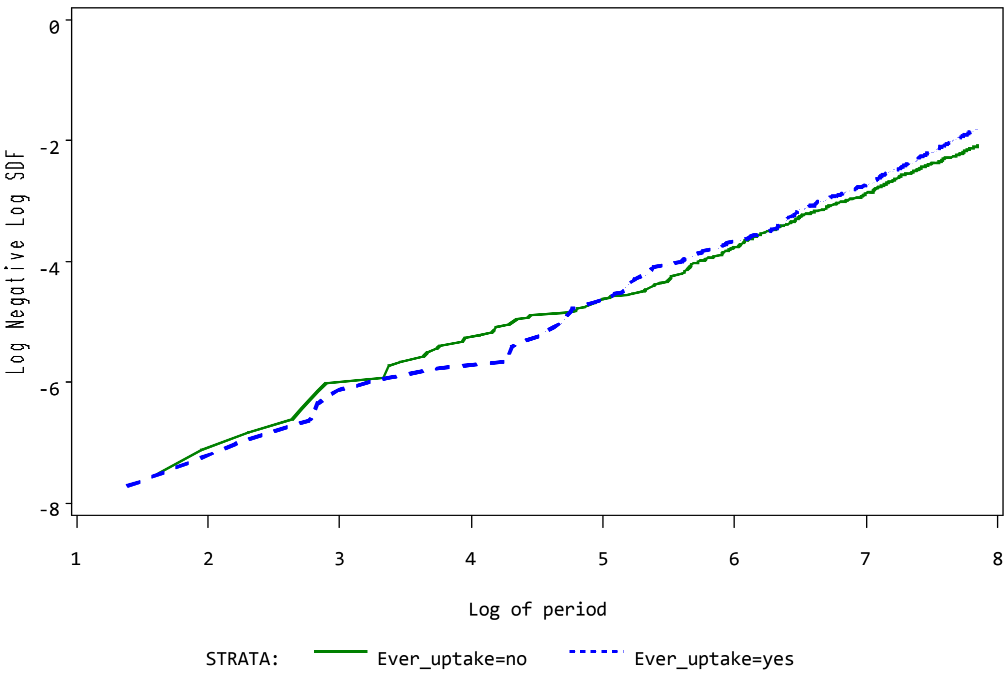
A4-8. Test of proportional assumption using for newly treated hypertension in subjects aged 55-64 years who ever and never uptake of preventive care service



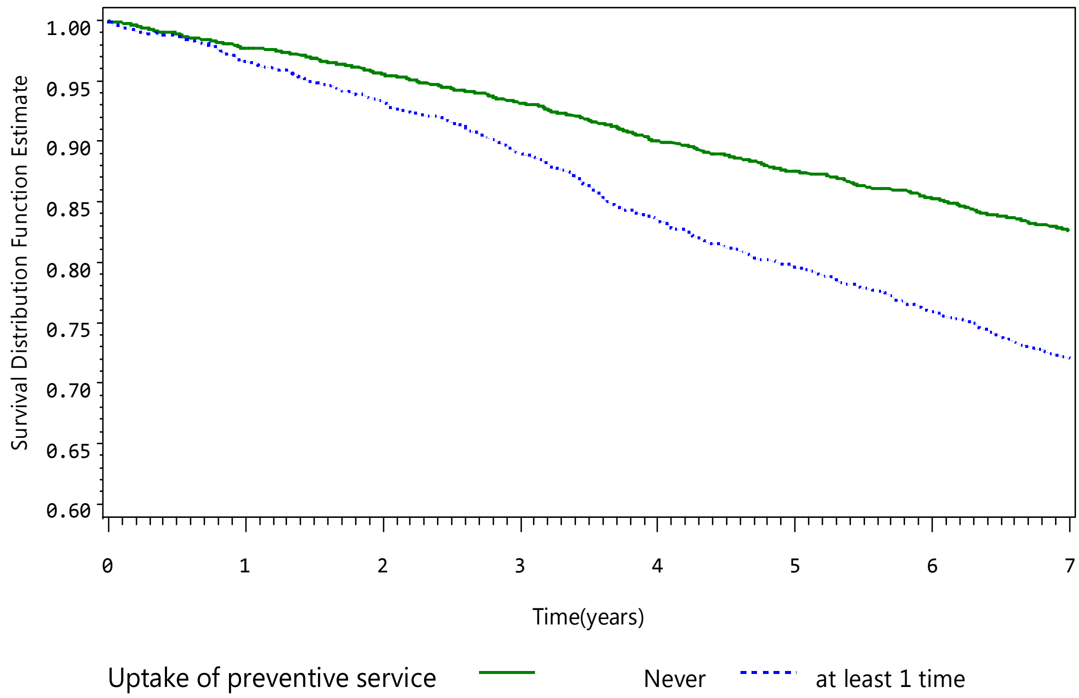
A4-9. Kaplan-Meier curve for newly treated diabetes in subjects aged 55-64 years who ever and never uptake of preventive care service



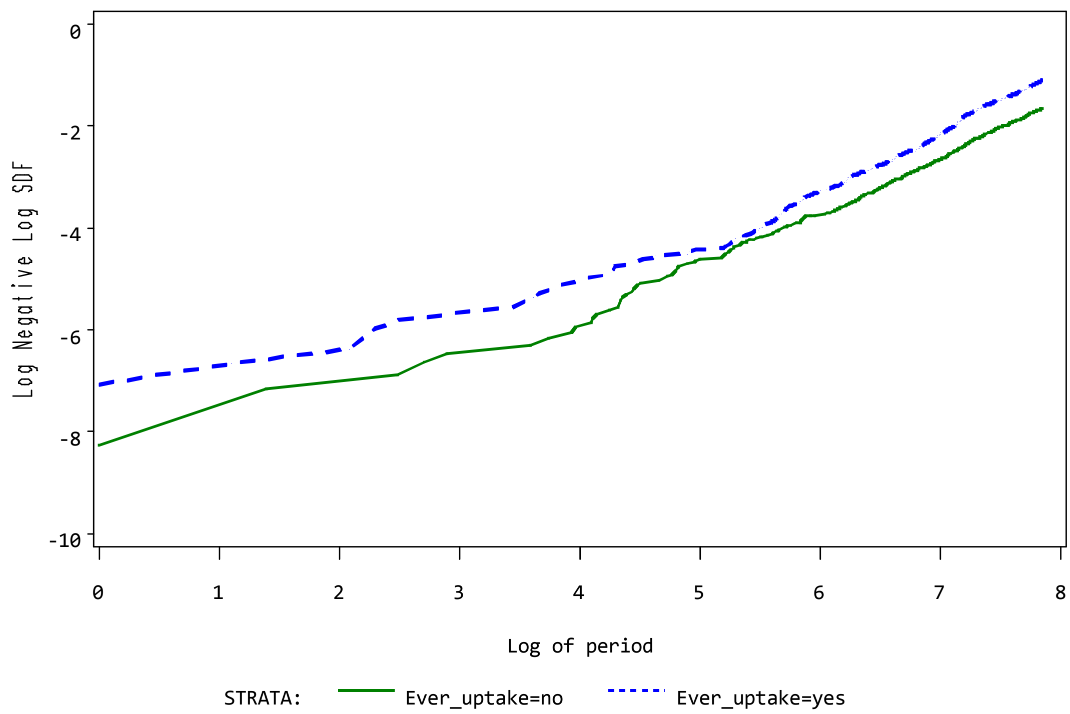
A4-10. Test of proportional assumption using for newly treated diabetes in subjects aged 55-64 years who ever and never uptake of preventive care service



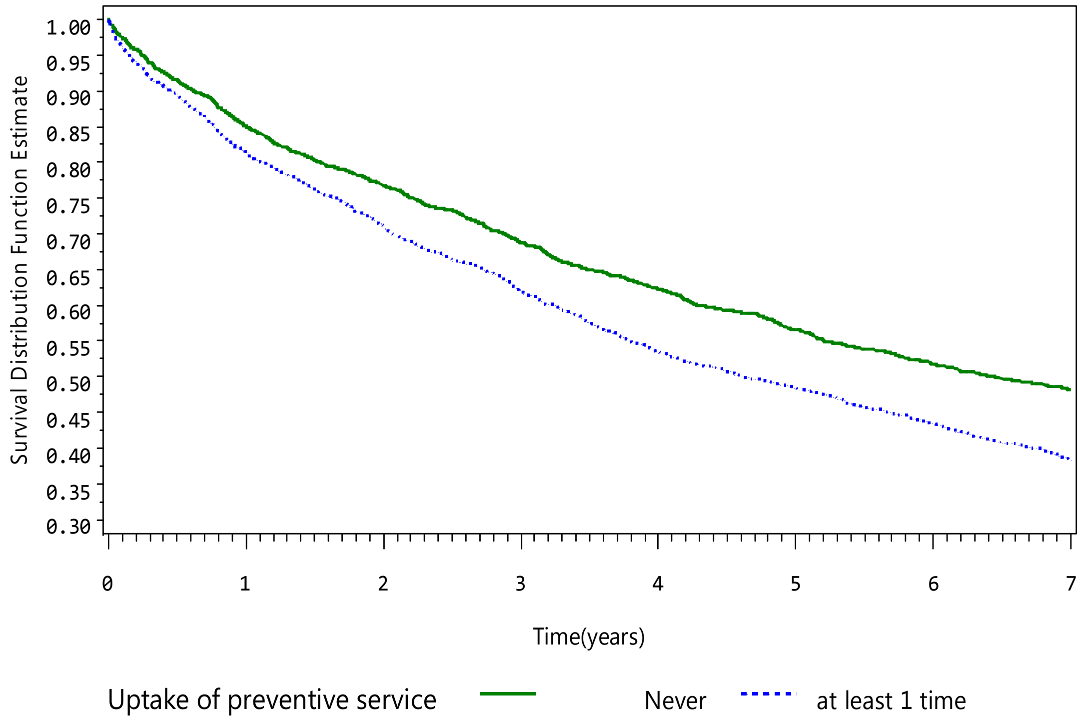
A4-11. Kaplan-Meier curve for newly treated hyperlipidemia in subjects aged 55-64 years who ever and never uptake of preventive care service



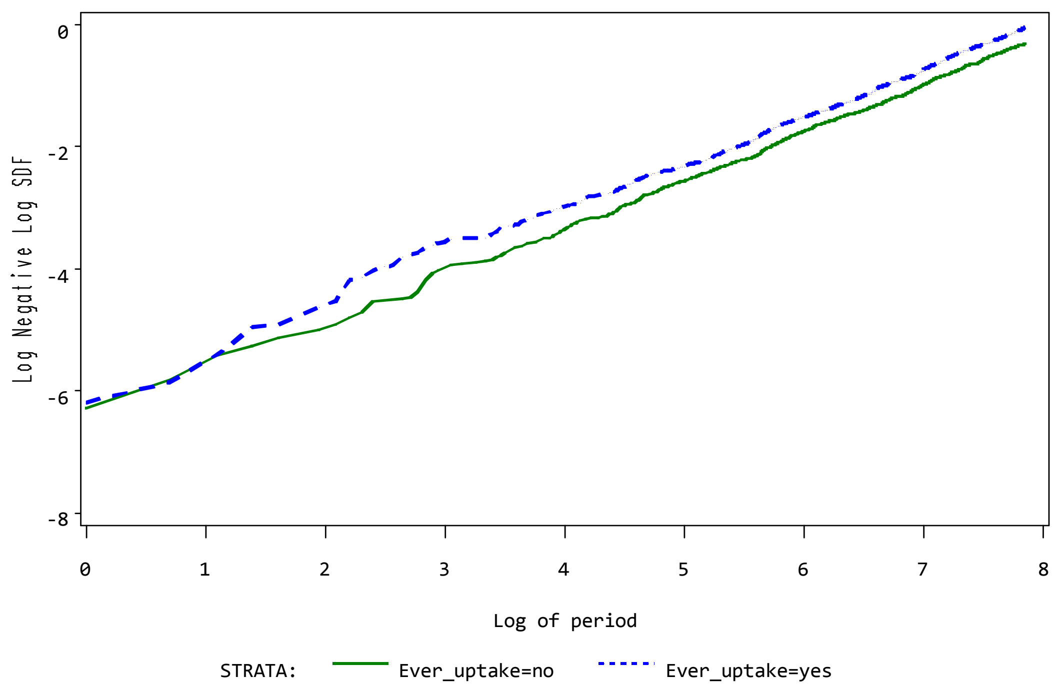
A4-12. Test of proportional assumption using for newly treated hyperlipidemia in subjects aged 55-64 years who ever and never uptake of preventive care service



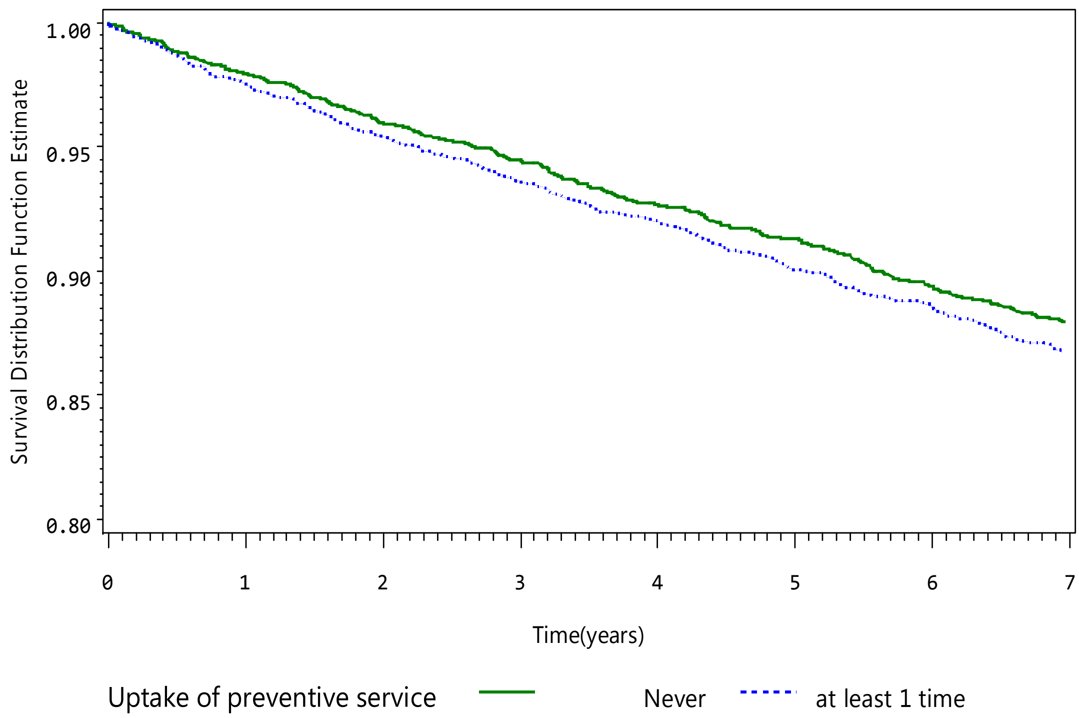
A4-13. Kaplan-Meier curve for newly treated hypertension in subjects aged 65-100 years who ever and never uptake of preventive care service



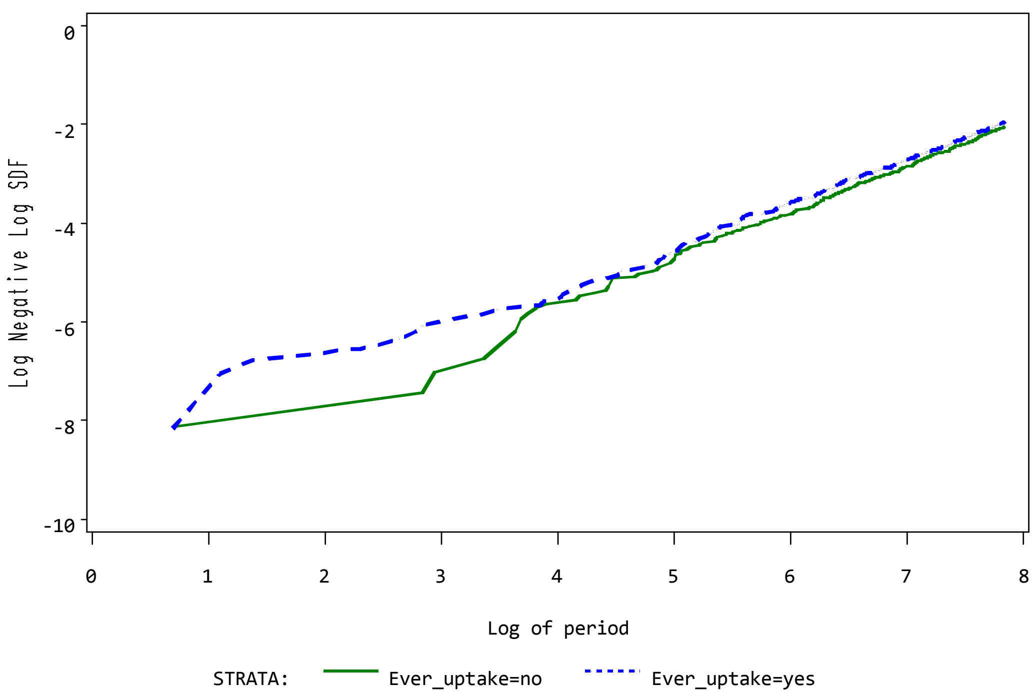
A4-14. Test of proportional assumption using for newly treated hypertension in subjects aged 65-100 years who ever and never uptake of preventive care service



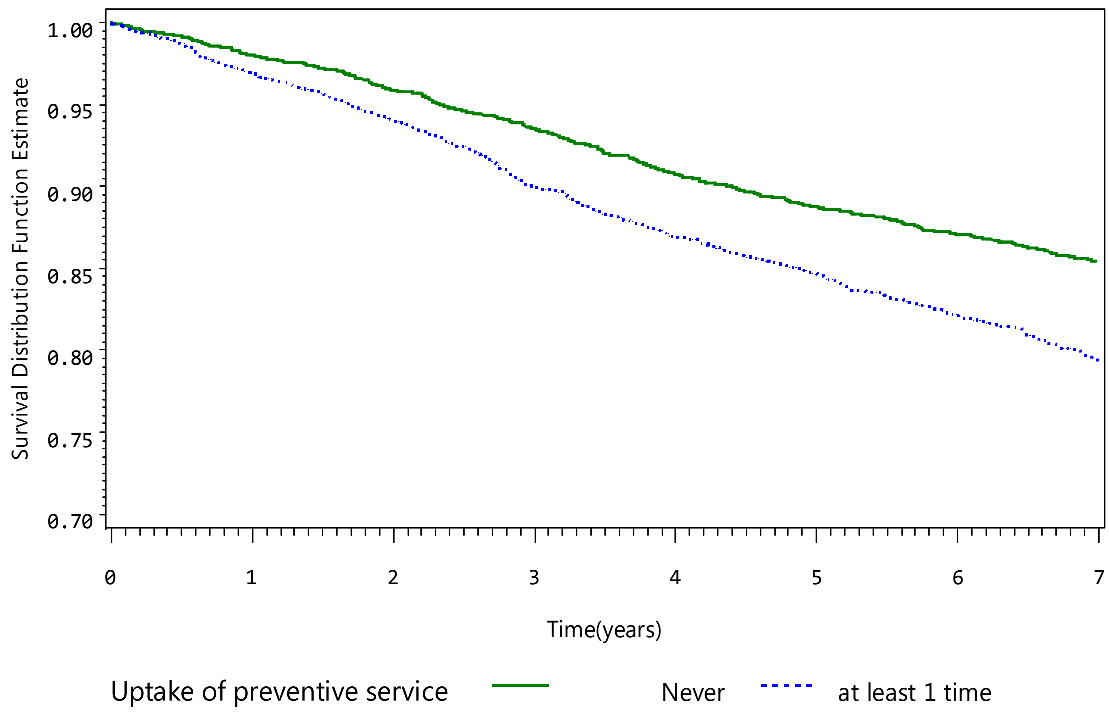
A4-15. Kaplan-Meier curve for newly treated diabetes in subjects aged 65-100 years who ever and never uptake of preventive care service



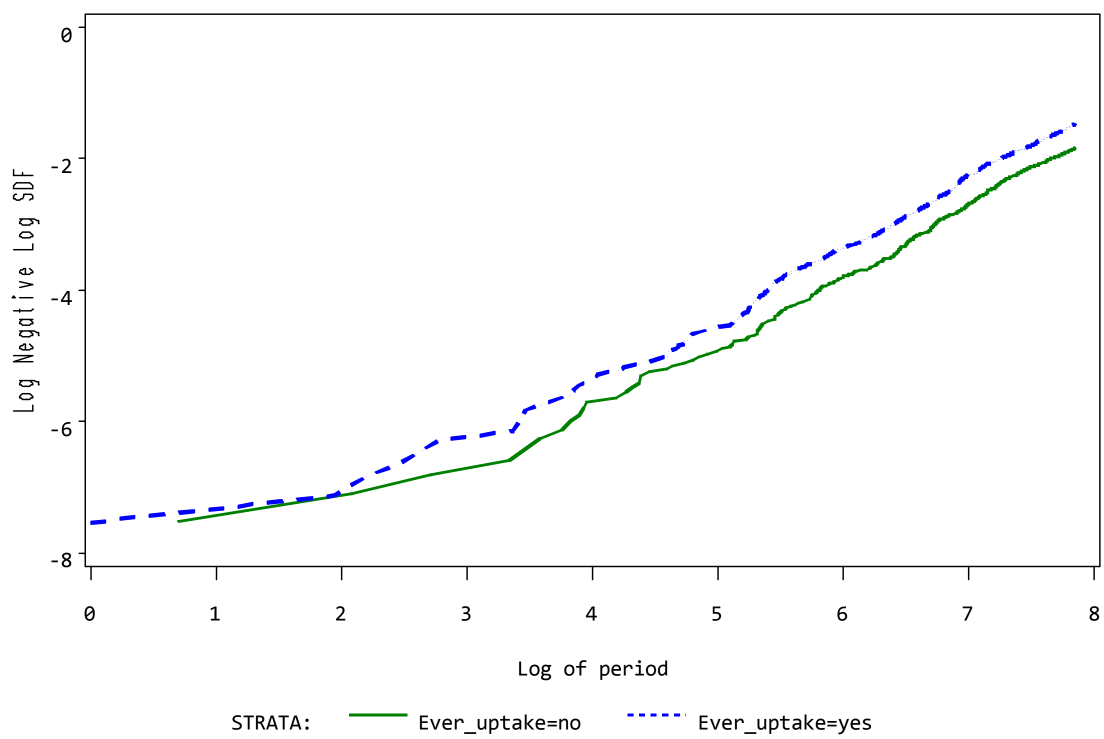
A4-16. Test of proportional assumption using for newly treated diabetes in subjects aged 65-100 years who ever and never uptake of preventive care service



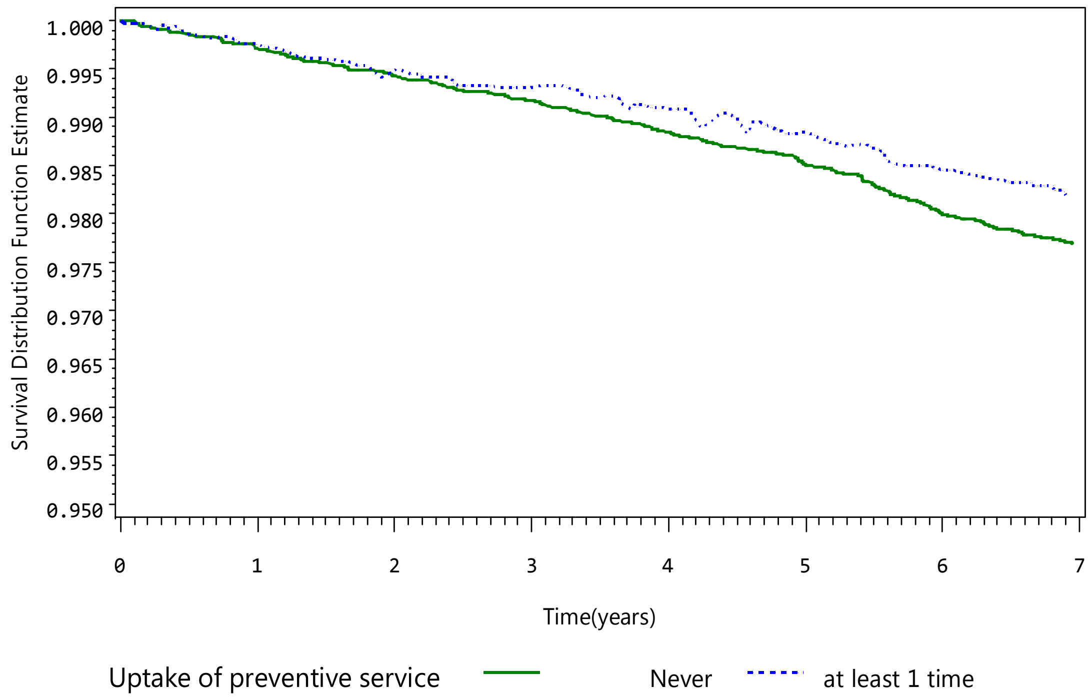
A4-17. Kaplan-Meier curve for newly treated hyperlipidemia in subjects aged 65-100 years who ever and never uptake of preventive care service



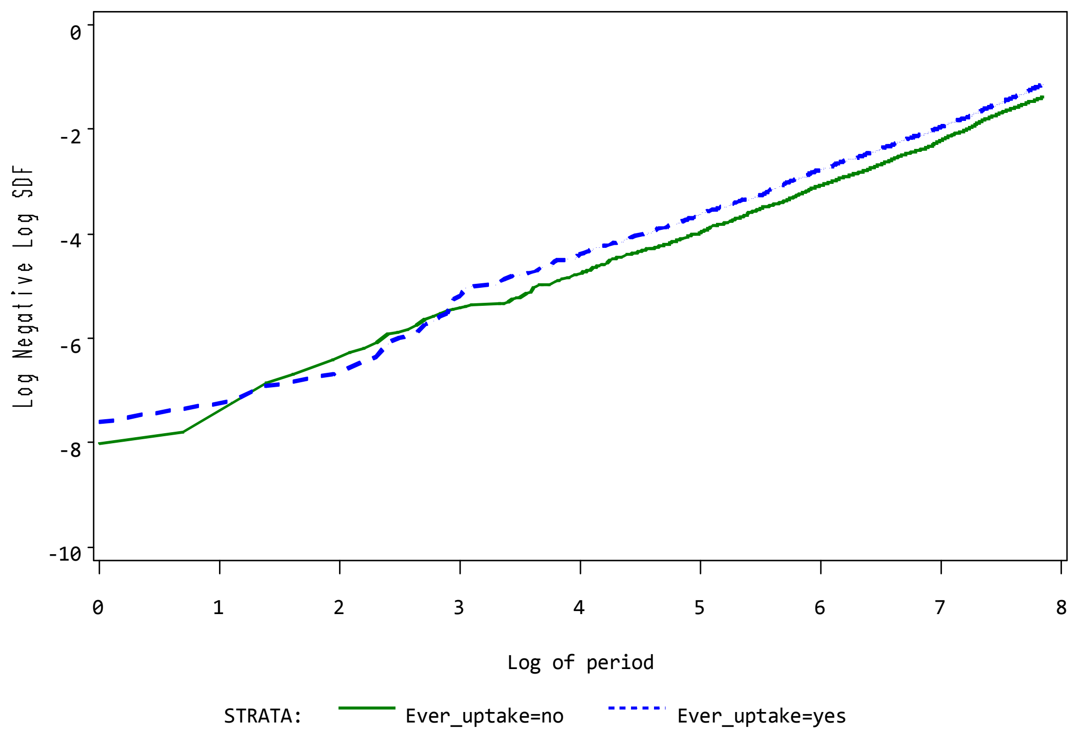
A4-18. Test of proportional assumption using for newly treated hyperlipidemia in subjects aged 65-100 years who ever and never uptake of preventive care service



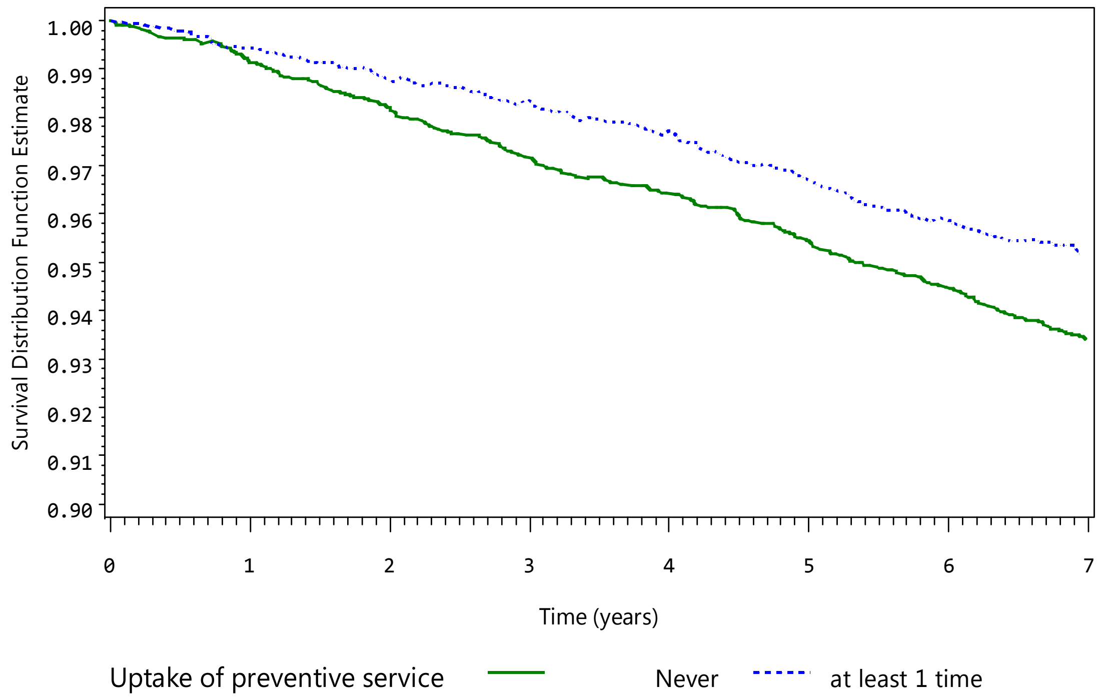
A4-19. Kaplan-Meier curve for all-cause mortality in subjects aged 40-54 years who ever and never uptake of preventive care service



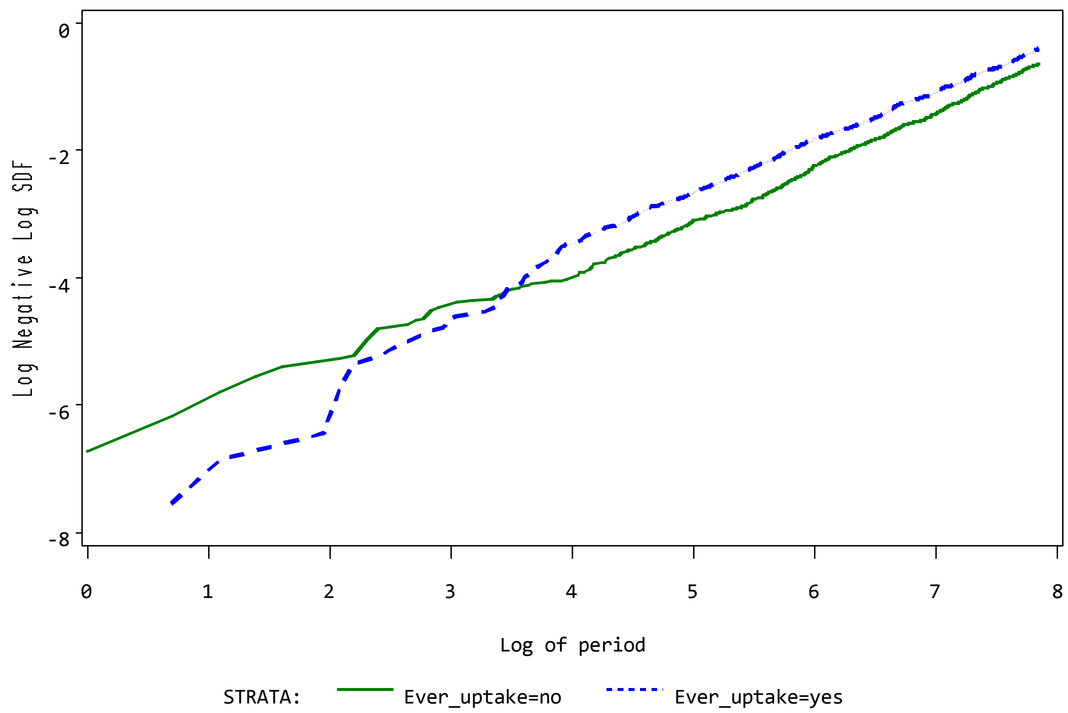
A4-20. Test of proportional assumption using for all-cause mortality in subjects aged 40-54 years who ever and never uptake of preventive care service



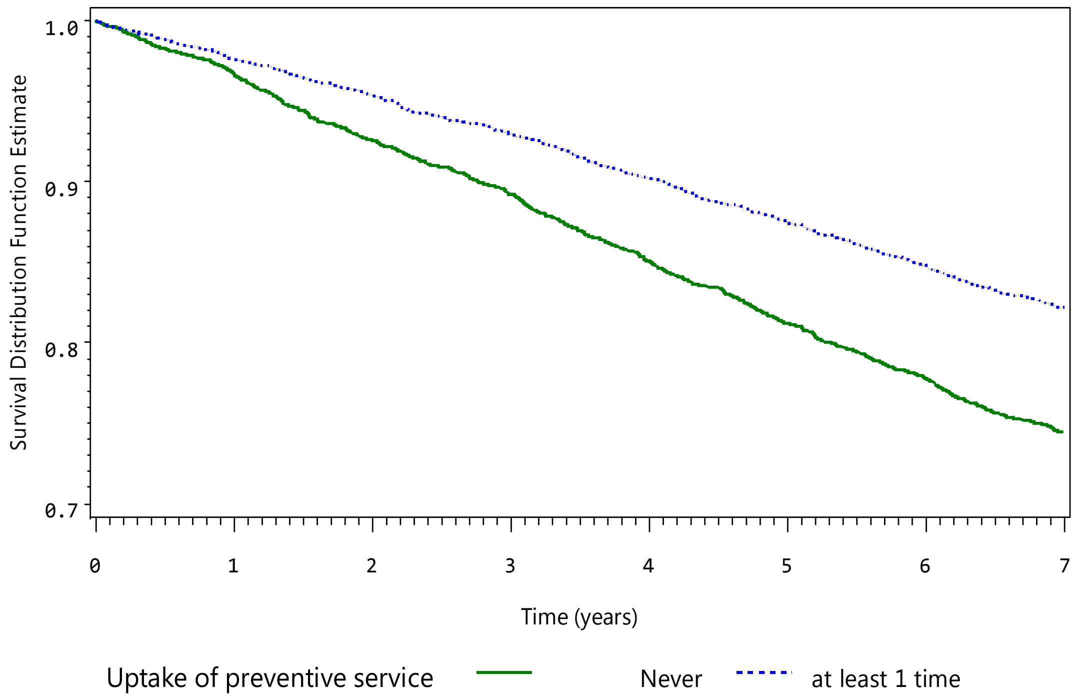
A4-21. Kaplan-Meier curve for all-cause mortality in subjects aged 55-64 years who ever and never uptake of preventive care service



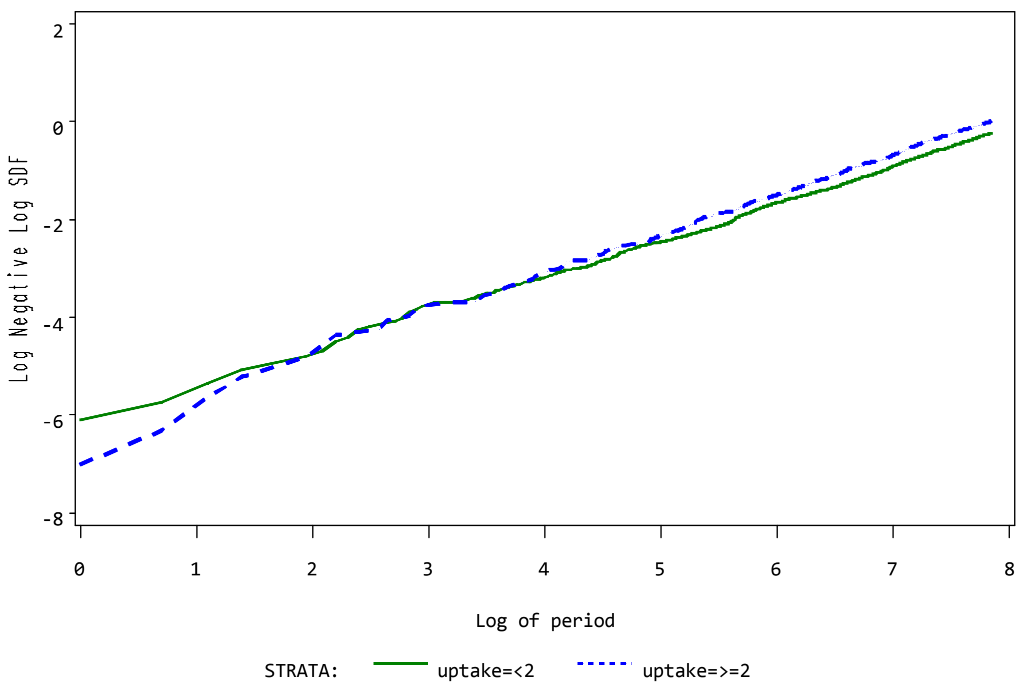
A4-22. Test of proportional assumption using for all-cause mortality in subjects aged 55-64 years who ever and never uptake of preventive care service



A4-23. Kaplan-Meier curve for all-cause mortality in subjects aged 65-100 years with different uptake of preventive care service



A4-24. Test of proportional assumption using Kaplan-Meier curve for all-cause mortality in subjects aged 65-100 years with different uptake of preventive care service



A5-1 Statement of the Bureau of National Health Insurance, Department of National Health Research Institutes

This study is based in part on data from the National Health Insurance Research Database provided by the Bureau of National Health Insurance, Department of Health and managed by National Health Research Institutes. The interpretation and conclusions contained herein do not represent those of Bureau of National Health Insurance, Department of Health or National Health Research Institutes.