SUNLIGHT AND LUNG CANCER SURVIVAL IN PATIENTS DIAGNOSED AND REFERRED TO THE BC CANCER AGENCY BETWEEN 1980 AND 1989

by

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Abstract

Background

Lung cancer is the deadliest form of cancer in the world. Recent reports indicate that patients who are diagnosed and treated, especially with surgery, during sunny periods have better survival.

Research questions (objectives)

1) Is there an association between a lung cancer patient's survival and the amount of sunshine around the time of their diagnosis?

2) Is there an association between a lung cancer patient's survival and the amount of sunshine around the time of their treatment?

Design

A population based retrospective study

Materials and methods

We examined BC patients diagnosed with lung cancer during 1980-1989 and referred to the BCCA for treatment. Data from BCCA computerized medical charts were linked with observations from the BC weather service. Survival analyses were adjusted for patient factors (i.e., age and gender), disease characteristics (i.e., stage and cell histology) and treatment information (i.e., surgery, radiation therapy and chemotherapy use).Each analysis consisted of a univariate and multivariate test of the sunshine variable's association with the patients' survival. The univariate analysis was a Kaplan-Meier plot with log-rank test. The multivariate analysis

was the hazard ratio from a Cox proportional-hazards model adjusting for patient age, disease stage, treatment, tumor laterality and tumor presenting site.

Results

This study considered 9302 patient records. Our results indicate that the monthly mean vitamin D sunshine (UV) index might be a prognostic indicator for this disease, especially among patients with non-small cell lung cancer. It showed that sun exposure and subsequent vitamin D production increase the survival of some of the patient who diagnosed with lung cancer between the period of 1980 and 1989 in BC.

Conclusions

90% of active vitamin D in our body is triggered by UV exposure. Different studies have shown that vitamin D has inhibitory effects in the development of cancers such as colon, breast and pancreas. Although the monthly mean vitamin D sunshine (UV) index is an indirect measure of vitamin D exposure, it might affect the prognosis for some lung cancer patients.

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List of Abbreviations

Apr	April
Aug	August
BC	British Columbia
BCCA	British Columbia Cancer Agency
BCCR	British Columbia Cancer Registry
CCS	Canadian Cancer Statistics
CI	Confidence interval
CMC	Computerized medical charts
CT	Computerized tomography (scan)
Dec	December
Feb	February
HR	Hazard ratio
Jan	January
Jul	July
Jun	June
lat	Latitude
lon	Longitude
Mar	March
MMVDSI	Monthly mean vitamin D sunshine index
MnDph	Mean hourly dose of vitamin D action spectrum

n	Total number of cases
Nov	November
NSCLC	Non-small cell lung cancer
NS	Not significant
Oct	October
PET	Positron Emission Tomography
RSR	Relative survival ratio
SCC	Squamous cell carcinoma
SCLC	Small cell lung cancer
Sep	September
Tis	Tumor in situ
TNM	Tumor size, Node (lymph node) involvement, Metastasis
UV	Ultraviolet
WHO	World Health Organization

Acknowledgments

First of all, I would like to dedicate my thesis to Dr. Chris Bajdik, my supervisor. He was not only my supervisor, but also my mentor. He has taught me a lot and I am sure I will use all of them throughout my life.

I also want to thank my thesis committee members, Dr. Tim Lee and Dr. Sam Wiseman. Their advices were very constructive and helpful during doing my project.

Dedication

I also like to thank my lovely wife, Yalda Mahmoudi. Her motivations and positive energy has had a great impact on me. Additionally, I am thankful for my family, specially my mom and dad who have always supported and encouraged me in my life. Last but not least my gratitude goes to my friend, Ehsan Bayaki. Since I have moved to Vancouver, he has helped me in every way possible without any hesitation. I have valued his friendship for the last fifteen years and I am looking forwards to many more years.

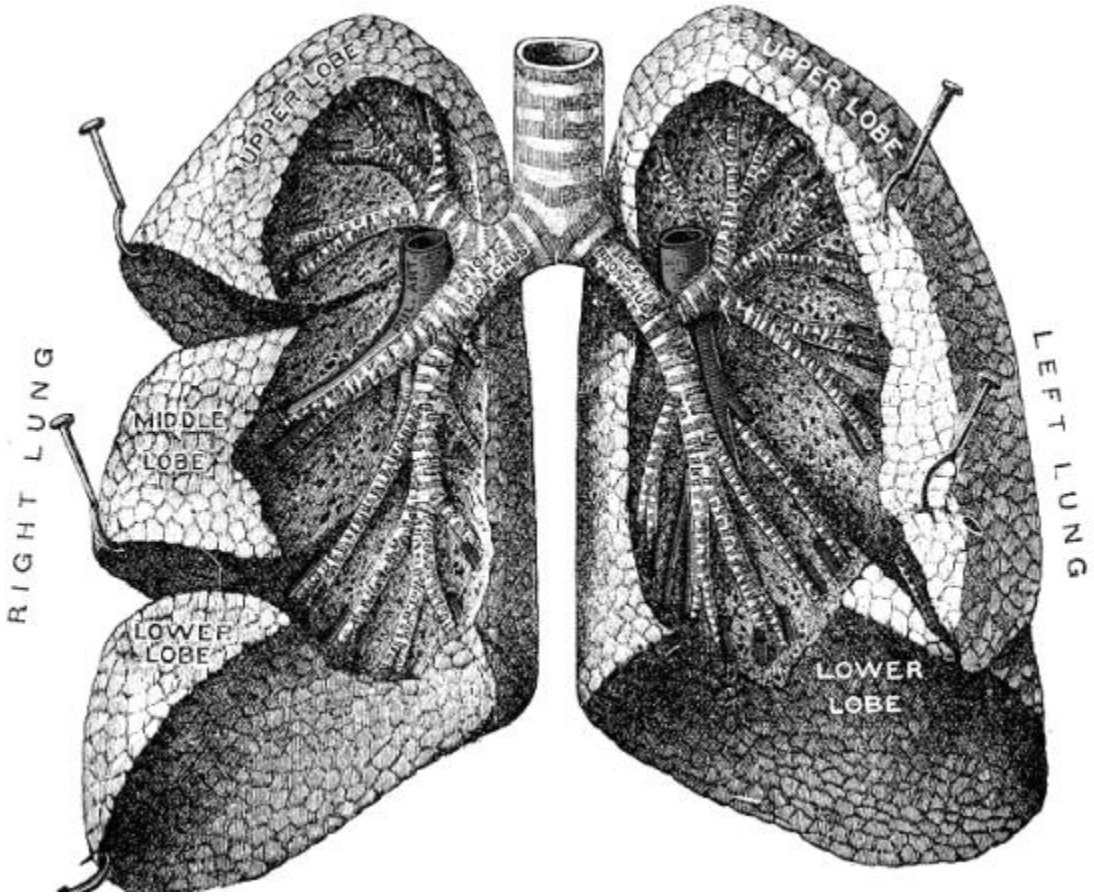
1. Introduction

1.1 Thesis overview

This thesis is about lung cancer survival and sunlight exposure. My study is explained in four chapters. Chapter one is about lung cancer, sunlight and how sunlight exposure might affect a lung cancer patient's survival. The study methods are discussed in chapter two and the results are presented in chapter three. Finally, chapter four is a discussion in which I explain the implications of this study in cancer research.

Figure 1.1 is an illustration from a standard medical text of human lung anatomy.

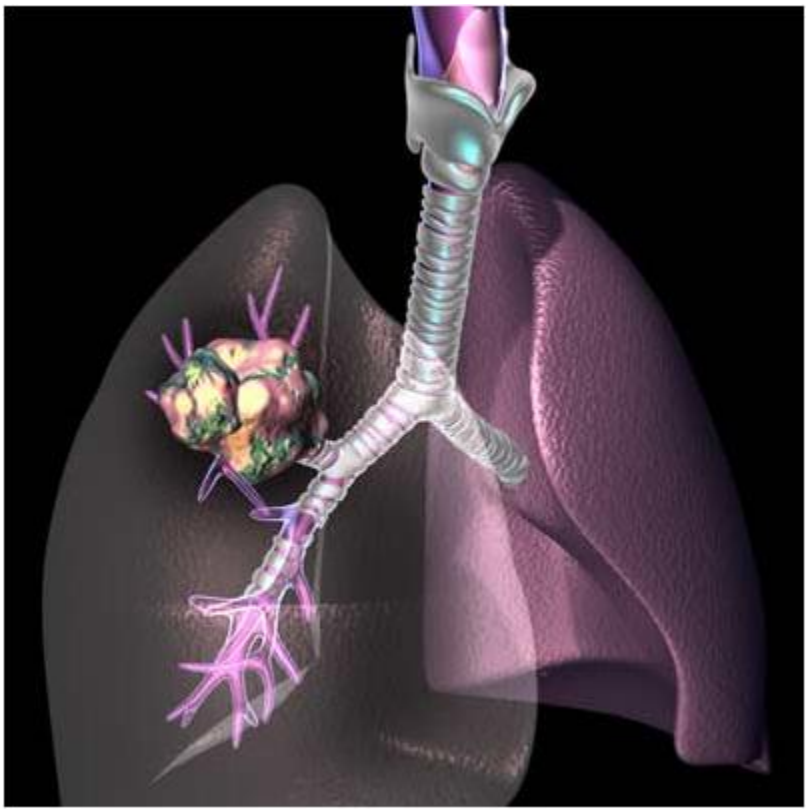
Figure 1.1- Lung anatomy (Gray's Anatomy of the Human Body, 20th ed. 1918)



1.2 Lung cancer

Lung cancer, like other types of cancer, is the result of an imbalance in cell growth. Uncontrolled division and proliferation of lung tissue cells eventually forms a mass known as a lung tumor. Figure 1.2 illustrates human lung cancer.

Figure 1.2-Lung cancer (Copyright of Cleveland clinic organization.)



1.2.1 Descriptive epidemiology

Lung cancer is the most common cause of death due to cancer worldwide[1]. According to the World Health Organization (WHO), it is the most common newly-diagnosed cancer in men worldwide, and ranks second after prostate cancer in the western world[1]. Further, it is the second most common cancer in women worldwide. Canadian Cancer Statistics (CCS) in 2010 reports that lung cancer is the most common cause of death due to cancer in the last decade nationally

and the second-most-incident cancer[2]. Based on this report, mortality and incidence rates are the highest in Quebec and the lowest in British Columbia among men[3]. And Nova Scotia is predicted to have the highest rate of lung cancer among women[3].

1.2.2 Risk factors

One of the most established risk factors for lung cancer is tobacco smoking[4] and almost 18 of every 20 lung cancer deaths in developed countries are caused by it[5]. In the United States, smoking is the cause of about 87% of lung cancer cases[6] (90% of male cases and 85% of female cases). In Canada, about 85% of new lung cancer cases are related to smoking[7].

There is less evidence about other factors associated with lung cancer. Radon exposure is the second major risk factor for the disease[8]. Asbestos has a synergistic effect with tobacco smoking in lung cancer formation[9]**.** Heavy metals such as chromium, nickel and arsenic are also believed to be associated with this cancer[10]. There is evidence that a 1% airborne particulate matter concentration increases lung cancer risk by as much as 14%[11-12].

Lung cancer is initiated by oncogene activation or tumor suppressor gene inactivation[13]. For example, K-ras proto-oncogene mutations are responsible for 10-13% of lung adenocarcinoma[14-15]. The oncogene epidermal growth factor receptor (*EGFR*) regulates cell proliferation, apoptosis, angiogenesis and tumor invasion – all of which are amplified in non-small cell lung cancer[14]. Chromosomal damage also can cause inactivation of tumor suppressor genes on 3p, 5q, 13q, and 17p – which is common in small cell lung cancer[14]. Other genes such as *c-MET*, *NKX2-1*, *LKB1*, *PIK3CA*, and *BRAF* also may be amplified or mutated in lung cancer patients[14]. Mutations also might occur when someone develops lung cancer. Examples are variations in the genes coding interleukin-1[16], cytochrome P450[17], apoptosis[18] and DNA repair molecules[19].

1.2.3 Pathology

Most lung cancers arise from epithelial cells and are carcinomas[20]. These are mainly categorized as small cell lung cancer (SCLC) or non-small cell lung carcinoma (NSCLC). This is based on a cooperative effort by the WHO and International Association for Study of Lung Cancer. The categorization is summarized in Table 1.1.

Table 1.1: Histopathological and epidemiological characteristics of lung cancer

Lung cancer type		**Incidence**	**Smoking**	**Location in the lung**	**Cell histology**	**Metastasis**
Small Cell Lung Cancer (SCLC)		~17%	strong	central	Oat cell, neuroendocrine origin in endobronchial cells	Disseminated at presentation
Non-Small Cell Lung Cancer (NSCLC)	Adenocarcinoma	39-43%	weak	peripheral	Glandular, mucin producing	Early, distant
	Squamous cellcarcinoma (SCC)	~30%	strong	Central	Keratin, intracellular bridges	Slow, local invasion, may cavitate
	Large cell carcinoma	9%	yes	peripheral	Anaplastic, undifferentiated	Early, distant

(Incidence rates are summarized from Travis et all: Cancer 75:191,1995)

Lung cancers are remarkably heterogeneous tumors that may contain more than one histological subtype[21]. There are other types of lung cancer than SCLC and NSCLC. For example, carcinoid tumors, carcinoma of salivary glands and adenosquamous carcinoma are those who are least frequent cancers with epithelial origin. These types of lung cancer were not present in the data for this thesis.

1.2.4 Diagnosis (signs and symptoms)

A summary of lung cancer patients' signs and symptoms is given in Tables 1.2 and 1.3. Many of these can be expressed based on the tumor location[22], but paraneoplastic phenomena are better classified by clinical characteristics. These phenomena are mediated by humoral factors (by hormones or cytokines) or an immune response against the tumor[23]. Other features are the result of metastasis[24].

Table 1.2: Clinical signs and symptoms in lung cancer based on the extent of disease spread

Disease spread	**Signs and symptoms (% of patients that are affected)**
Locoregional	Cough (75%), shortness of breath (60%), Chest pain (45%), spitting of blood (35%), Wheezing, Difficulty swallowing, Hoarseness, Sputum (salty suggests bronchoalveolar)
Metastatic	Bone pain, Jaundice, Seizures, Headaches, Adrenal lesions, Skin lesions

Table 1.3: Paraneoplastic syndromes in lung cancer

System	Clinical presentation	Type of lung cancer
Skeletal	Clubbing	Not SCLC
Dermatologic	Acanthosis nigricance, dermatomyositis	Carcinoma
Endocrine	Hypercalcemia, hypophosphatemia	SCC (Squamous cell carcinoma)
	Cushing syndrome, syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH)	SCLC
Neuromyopathic	Eaton-Lambert Syndrome, polymyositis, subacute cerebellar degeneration, spinocerebellar degeneration, peripheral neuropathy	SCLC
Vascular/Hematologic	Nonbacterial endocarditis, Trousseau's syndrome, disseminated intravascular coagulation (DIC)	Carcinoma
Renal	Nephrotic syndrome	

1.2.5 Staging

Staging a tumor is a process to assess the extent of its spread. Based on the type of tumor the staging systems differ. A well-known staging method for lung cancer is the TNM system which is mostly used for NSCLC. In this system, a tumor is staged based on its size (T), the lymph node involvement (N) and the presence of metastasis to distant organs (M). There are different clinical investigations for staging lung cancer using imaging methods (e.g., ultrasound) and surgical methods (e.g., diagnostic thoracotomy). Using the TNM system, lung cancer is categorized in 4 stages, as described in Table 1.4-1.6.

Table 1.4: TNM staging in lung cancer (The contents is obtained from different sources)

		Description
Primary tumor size (T)	Tis	Carcinoma in situ
	T1	Tumor <= 3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus* (i.e., not in the main bronchus)
	T2	Tumor with any of the following features of size or extent: > 3 cm in greatest dimension, involves main bronchus, >= 2 cm distal to the carina, invades the visceral pleura, associated with atelectasis or obstructive pneumontitis that extends to the hilar region but does not involve the entire lung
	T3	Tumor of any size that directly invades any of the following: chest wall (including superior sulcus tumors), diaphragm, mediastinal pleura, parietal pericardium, or tumor in the main bronchus < 2 cm distal to the carina, but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung
	T4	Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea,esophagus, vertebral body, carina; or tumor with a malignant pleural or pericardial effusion, or with satellite tumor nodule(s) within the ipsilateral primary-tumor lobe of the lung
Regional lymph nodes involvement (N)	N0	No regional lymph node metastasis
	N1	Metastasis to ipsilateral peribronchial and/or ipsilateral hilar lymph nodes, and intra-pulmonary nodes involved by direct extension of the primary tumor
	N2	Metastasis to ipsilateral mediastinal and/or subcarinal lymph node(s)
	N3	Metastasis to contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)
Distant metastasis (M)	M0	No distant metastasis
	M1	Distant metastasis present

Table 1.5: Usual staging of lung cancer for NSCLC

Stage	TNM Subset	Stage	TNM Subset
0	Carcinoma in situ	IIIA	T3N1M0, T1N2M0, T2N2M0, T3N2M0
IA	T1N0M0		
IB	T2N0M0	IIIB	T4N0M0, T4N1M0, T4N2M0 T1N3M0, T2N3M0, T3N3M0 T4N3M0
IIA	T1N1M0		
IIB	T2N1M0, T3N0M0	IV	Any T, Any N, M1

Table 1.6: Usual staging of lung cancer for SCLC

Limited disease	Primary tumor confined to hemithorax, ipsilateral hilar nodes, ipsilateral and contralateral, supraclavicular nodes, ipsilateral and contralateral, mediastinal nodes, pleural effusion
Extensive disease	More advanced than limited disease, metastases to contralateral lung, or distant metastases

1.2.6 Treatment

Treatment for lung cancer patients is based on the tumor's cell type, the tumor's degree of invasion and the patient's comorbidity status. There are 3 major types of treatments: surgery, chemotherapy and radiotherapy[25-26]. Table 1.7 shows how lung cancer patients are treated based on their tumor stage.

Surgery

Physicians do imaging investigations such as CT and PET scans to determine whether the cancer is surgically resectable[27]. The appropriateness of surgery is also determined by a patient's comorbidity status, using blood tests and spirometry. Surgery only is usually an option for stage IA or earlier unilateral NCSLC only. Surgical procedures in lung cancer include wedge resection, lobectomy and pneumonectomy.

Chemotherapy

The most common chemotherapeutic medications for SCLC patients are cisplatin and etoposide[28]. NSCLC patients are often treated with cisplatin or carboplatin, in combination with gemcitabine, paclitaxel, docetaxel, etoposide, or vinorelbine[29]. Depending on a patient's age and other characteristics, various molecules also can be used for treating advanced lung cancer. For example, Gefitinib targets the EGFR gene and is useful for some patient types[30-31].

Radiotherapy

If surgery is not used, physicians usually administer radical radiotherapy with chemotherapy for NSCLC patients[32]. For SCLC, chest radiotherapy would accompany chemotherapy[33]. Based on a tumor's location and type, other types of radiation therapy might be used such as brachytherapy or prophylactic cranial irradiation[34-35].

Table 1.7: Lung cancer treatment

Stage		Treatment
Non-Small Cell Lung Cancer (NSCLC)	IA	Lobectomy/Pneumonectomy
	IB	Lobectomy/Pneumonectomy ± adjuvant chemotherapy if high risk features (e.g. large tumor, high grade
	II	Lobectomy/Pneumonectomy ± adjuvant chemotherapy
	IIIA (T1N2M0)	Concurrent chemoradiation followed either by lobectomy/pneumonectomy or radiation boost
	IIIA (Unresectable) and IIIB	Concurrent chemoradiation with potential chance of cure, and possible sequential chemoradiation
	IIIB (with malignant pleural effusion) and IV	Radiation, palliative chemotherapy, resection if solitary central nervous system (CNS) metastasis, and possible targeted therapy
Small Cell Lung Cancer (SCLC)	Limited stage	Radiation, concurrent chemotherapy, and prophylactic cranial (head) irradiation (PCI)
	Extensive stage	Palliative chemotherapy, and possible targeted therapy

1.2.7 Prognosis

In general, SCLC has the poorest prognosis of all lung cancer types, and NSCLC patients have a better prognosis if they are diagnosed at an early disease stage. Table 1.8 summarizes 5-year survival in lung cancer patients. The prognosis of NSCLC patients depends on their pulmonary symptoms, tumor size, tumor histology, disease stage, disease metastasis to lymph nodes and vascular invasion of the disease[36]. The prognosis for SCLC patients depends on patient's status, patient gender, disease stage, and CNS or liver involvement at the time of diagnosis[37].

Table 1.8: Lung cancer prognosis

Cell type	Stage	Prognosis
Non-Small Cell Lung Cancer (NSCLC)	IA	70% 5-year survival rate
	IB	60% 5-year survival rate
	IIA	50% 5-year survival rate
	IIB	40% 5-year survival rate
	IIIA	30% 5-year survival rate
	IIIB	15% 5-year survival rate
	IV	5-10% 5-year survival rate
Small Cell Lung Cancer (SCLC)	Limited stage	15-20% 5-year survival rate
	Extensive stage	<5% 5-year survival rate

In Canada, the 5-year lung cancer relative survival ratio (RSR) in 2002-2004 was 13% for men and 17% for women. The relative survival rate (RSR) is the chance that a patient will survive a set time period after diagnosis divided by the percentage of the corresponding age-and-sex-specific general population. For example, the five-year relative survival rate for lung cancer describes the percentage of patients with that disease that are alive five years after diagnosis, divided by the percentage of the corresponding Age-and-sex-specific general population that are alive after five years. The RSR is calculated to adjust for the chance of death due to conditions other than the cancer. Canadian Cancer Statistics (CCS) in 2009 reports that lung cancer value is among the RSR values for the least favorable cancer types. (RSR=6% for pancreatic cancer and RSR=14% for esophageal cancer) [38]. Based on this report, lung cancer relative survival was highest among young patients (20-39 y) [39]. Further, the age-standardized RSR during 2002-2004 was highest in Manitoba (19%) [40] and lowest in Prince Edward Island (11%) [40]. The age-standardized 5-year RSR in British Columbia was 12-14%[40].

1.3 Sunlight and vitamin D

Vitamin D belongs to the group of fat-soluble vitamins (i.e., vitamins K, A, D and E). It has two physiologically relevant forms: 25(OH) D (calcidiol) and 1,25(OH)D (calcitriol). The most important physiologic effect of vitamin D is regulating the concentration of calcium and phosphate in the bloodstream, promoting the healthy mineralization, growth and remodeling of bone. Vitamin D is carried in the blood stream to the liver where it is converted to 25(OH) D. The immune system or kidneys convert the circulating 25(OH) D to 1, 25(OH) D, which is the biologically active form of vitamin D. In humans, having an optimal vitamin D level is related to sun exposure or artificial UV-B (280-320 nm) sources[41]. It's also related to consumption of

vitamin D enriched foods such as eggs, margarine, oily fish and vitamin supplements[42]. Sun-induced vitamin D is usually the main source of this vitamin, but vitamin D status changes seasonally for people in Canada[43].

1.4 Sunlight, vitamin D and cancer prognosis

Recent studies have shown the effects of vitamin D in survival of patients with prostate, breast, ovarian, pancreatic, and colorectal cancer as well as Hodgkin disease [44-50]. Those studies were motivated by the idea that active forms of vitamin D (D3) affect proliferation, differentiation and apoptosis in different kinds of cells[51-53]. (This effect is likely to be an immunomodulatory one.) The effects are probably the results of interactions between active vitamin D derivatives and/or membrane targets[51, 54]. In vitro studies performed with lung cancer cell-lines showed that vitamin D derivatives have an inhibitory effect on cell-growth and proliferation[55]. Animal investigations have demonstrated the ability of vitamin D derivatives to suppress angiogenesis, metastasis and invasion[56-58]

Recently it has been hypothesized that seasonal variation of vitamin D might affect the prognosis of patients with colon cancer, breast cancer, prostate cancer as well as Hodgkin's disease[59-60]. In a separate study, the same researchers found that sun-induced vitamin D improves lung cancer prognosis specifically in males under age 50 years[61]. In a separate US study, scientists found a positive effect for season of surgery and recent vitamin D intake on lung cancer survival[62]. A comprehensive UK study has produced similar results[63].

1.5 Hypothesis

Lung cancer is one of the most important and deadliest cancers in Canada and BC. There are lots of researches that have been done in this field but a few ones have addressed the significance of vitamin D in lung cancer prognosis. In addition, there is only some published research in which sun exposure used as an indicator of vitamin D effects in lung cancer prognosis. Based on this background, my research questions are:

1) Is there an association between a lung cancer patient's survival and the amount of sunshine during their diagnosis?
2) Is there an association between a lung cancer patient's survival and the amount of sunshine during their treatment?

Based on these questions and the possible adjusting factors, my formal hypothesis is:

Primary Hypothesis: Sunlight at the time of diagnosis and first treatment affects the length of lung cancer patients' survival in BC. The effect of sunlight depends on (1) a patient's age, (2) a patient's gender, (3) the lung cancer's stage, (4) the lung cancer's histology, (5) types of treatment, (6) the primary tumor's location in the lung and (7) the tumor's laterality.

This study attempts to provide evidence about whether sunlight improves the effectiveness of lung cancer treatment in BC. It might lead to interventions that involve vitamin D supplementation for lung cancer patients during their treatment.

2. Materials and methods

2.1 Proposed variables and methods

2.1.1 Lung cancer patient information

Based on our hypothesis, our study population was those who were diagnosed because of lung cancer in British Columbia. In addition, we needed some information for each patient regarding on date of birth and death, sex, age, place of residence, primary tumour site and stage of disease at diagnosis, pathology of tumour, cause of death and method of treatment. Since we assumed that sunshine variables would be available, we decided to do a pilot study for the period of 2000 to 2005. The study period of the full analysis is from 1980 to 1989.

2.1.2 Sunshine measures

The production of active vitamin D in our body depends on sun exposure. Vitamin D has shown to have inhibitory effects in development and progression of different cancers. It has been proven that vitamin D varies monthly because of the sun exposure in those months. In fact, we can use the weather data as an indirect measure of population's active vitamin D level.

2.1.3 Methods

We proposed to separately analyze data based on the histological types of tumor (small-cell lung cancer and non-small cell lung cancer), kinds of patient death (lung-cancer reasons or non-lung-cancer reasons), and type of treatment received by the patient (surgery, chemotherapy, radiation). Each analysis was to consist of a univariate and multivariate test of the variables. The univariate analysis was a Kaplan-Meier plot with log-rank test. The multivariate analysis used

the Hazard Ratio estimate from a Cox proportional-hazards regression model adjusting for patient age, disease stage, other treatment modalities received by the patient (i.e., chemo=yes/no; radiation=yes/no), tumor laterality (being in the right or left side of the lung) and tumor anatomic site in lower respiratory tract.

2.2 Pilot study

2.2.1 Study

At the beginning of a project, the first thing that should be considered is evaluating the available data. To get this, I decided to do a pilot study to find how I can gather the data for my project and what would be the available ones.

Lung cancer population

When a patient in BC is diagnosed with a cancer, he or she is often referred to a BCCA centre. The centre records the patient's information and stores it in the BC Cancer Registry (BCCR) and computerized medical charts (CMC).

From the BCCR, I requested a sample of information for lung cancer patients who were referred to BCCA between 2000 and 2005. Each patient had a unique ID which had information regarding of date of birth, date of death, sex, age at the diagnosis, place of residence, BCCA referred centre, type of tumor and its location in the lung, treatment received and its date, stage of the tumor. In addition, it had the name of physicians who were involved in diagnosing, managing and treating of a patient.

Sunshine measures

After this, I discussed my project with different meteorologists to find a reliable sunshine measure. I also reviewed previous publications in this field again to find what they used in their studies. Based on my findings, I considered five potential sunshine measures.

A- Season of diagnosis

Some previous studies used this variable because of seasonal variation of vitamin D production in their area. They found that the level of production was higher in studies conducted in sunny seasons. I discussed this with an expert meteorologist, and found that there is seasonal variation in vitamin D production in British Columbia.

B- Season of first treatment

According to the sample data, I found that it usually takes a month for a patient to receive any treatment after diagnosis in BC. In many cases, the season changed between diagnosis and treatment. This change could substantially affect the level of vitamin D in patients because the new season could be more or less sunnier.

C- Bright sunshine

This is the total hours of sunshine for each day. It was measured in different centres across BC but recording stopped after 2000. Another problem is that there is lots of missing information in some centers.

D- Total cloud amount

This the total amount of cloud recorded hourly, which is an indirect measure of sunshine. If we calculate the period between sunrise and sunset, then it is necessary to subtract the total cloudy hours for each day. This might not be accurate because people can still be exposed to UV during cloudy periods.

E: MnDph (Monthly mean hourly dose of vitamin D action spectrum)

This is one of the most accurate measures of UV that was available. There are different subdivisions of UV, but wavelength 315-280 nm is related to vitamin D production. This information was recorded during 1980-1989 for various values of latitude (lat) and longitude (lon) across Canada. The 10-year average of this measure was calculated, and there were no significant year-to-year variability for a significant month of the year in the values for each lon and lat. Accordingly, the measure has not been recorded in any subsequent year because month-to-month changes can be determined from the existing years of data. (Please see the MMVDSI generation diagram in A1 in appendix section)

F- Month of diagnosis and month of treatment

As discussed earlier, vitamin D production in our body has a direct association with sun exposure. Further, there was at least one month period between the diagnosis and treatment for lung cancer patients in BC. Therefore, *Month of diagnosis and month of treatment is* an indirect measure of sunshine exposure.

2.2.2 Lessons learned from the pilot study

In terms of the lung cancer population, I found that the BCCR and CMC have comprehensive information regarding the patients, their tumors and their treatments. In the case of sunshine measures, I decided that some measures couldn't be used because of substantial missing information. I decided to perform analyses using month of diagnosis, month of first treatment, season of diagnosis, and season of first treatment.

The most useful sunshine measure was *MnDph* but it was recorded based on *lat* and *lon* values. Patients' addresses were recorded using postal codes. If we wanted to use this data, we had to find a way to convert postal codes to *lat* and *lon.*

2.3 Final variables and methods

2.3.1 Lung cancer population

MnDph hasn't been used in previous studies, but offers the best available measure of sunshine in BC. The variable is only available for the period of 1980-1989. Therefore, I decided to base the study on lung cancer patients referred to BCCA between 1980 and 1989. I excluded lung cancer diagnoses where: a patient has been diagnosed previously with another type of cancer, a patient lived less than 30 days after diagnosis (Because usually it took a 1-month period for patients to receive treatment. Therefore, those who died in less than a month could not be used in the analyses since we wanted to adjust our analyses for treatment options.), and any non-bronchogenic carcinomas (i.e., diagnoses that were mesothelioma or carcinoid). For *MnDph,* we excluded 1432 additional cases because there was another 781 cases whose postal code was

missing. The final study population for *MnDph* analysis was 8521 cases and 9302 cases for the other sunshine measures' analyses. (Please see the A2 in appendix)

2.3.2 Sunshine measures

My final choices of sunshine measurement were *month of diagnosis, month of first treatment, season of diagnosis, season of first treatment,* and *MnDph.* Season was categorized as Spring (March-April-May), Summer (June-July-August), Fall (September-October-November) and Winter (December-January-February). As mentioned earlier, *MnDph* was calculated as the 10-year average for each hour for each *lat* and *lon*. I calculated the mean value of each month based on the mean of each day for each *lat* and *lon*, and then I converted postal codes (I used the online system from www.postalcodedownload.com) to *lat* and *lon,* and linked the monthly values to the patient data. The result was that each patient has a sunshine measure (based on new *MnDph* data set). I named the value "the monthly mean vitamin D sunshine index (MMVDSI)".

2.3.3 Methods

I separately fitted a model to the data for histological types of tumor (small-cell lung cancer and non-small cell lung cancer), patient cause of death (lung-cancer reasons or non-lung-cancer reasons), and type of treatment received by the patient (surgery, chemotherapy, radiation). Each analysis consisted of a univariate and multivariate test of the variables.

The univariate analysis was a Kaplan-Meier plot with log-rank test. The multivariate analysis was a Hazard Ratio estimate from a Cox proportional-hazards regression model adjusting for patient age (less than 50, 50-60, 60-70 and more than 70), disease stage (below or equal to stage II or above stage II for NSCLC; extended and limited for SCLC), other treatment modalities received by the patient (surgery, chemo, or radiation), tumor laterality (being in the

right or left side of the lung) and tumor anatomic site in lower respiratory tract. The last date of follow-up was May 30th 2007 for all cases.

We used SPSS software for all the analyses. All p-values <0.05 were considered statistically significant, and all p-values <0.1 are reported as "not significant" or NS.

3. Results

This chapter begins with a descriptive summary of the study's main variables. Detailed results of the analysis are given for small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC) in section 3.2 and 3.3. There is a summary and overview of the results in section 3.4. Some simple variations of the main analyses are presented in section 3.5. All the graphs and tables are at the end of this chapter in section 3.6.

3.1 Patient characteristics, disease factors and treatment

Figures 3.1-3.7 show demographic characteristics of patients in the study and characteristics of their disease. Table 1 shows the main form of treatment that study patients received.

Figure 3.1- Patient age at diagnosis

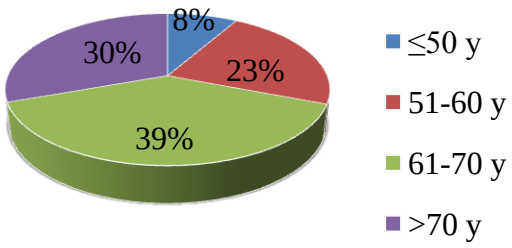


Figure 3.2- Cancer laterality (Tumor location)

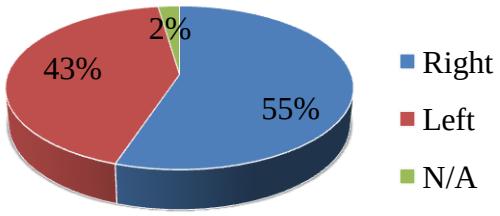


Figure 3.3- Patient sex

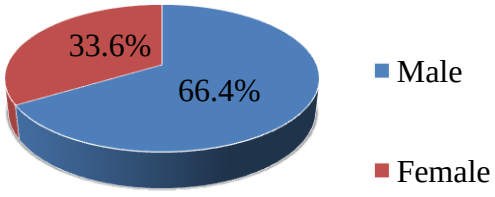


Figure 3.4- Patient cause of death

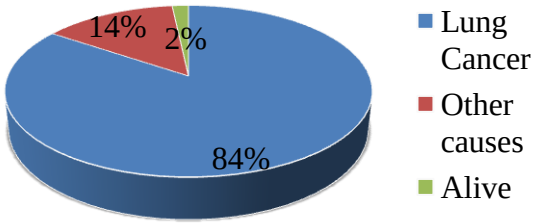


Figure 3.5- Disease stage (at time of diagnosis)

(N/A: not available based on the BBCA registry data set)

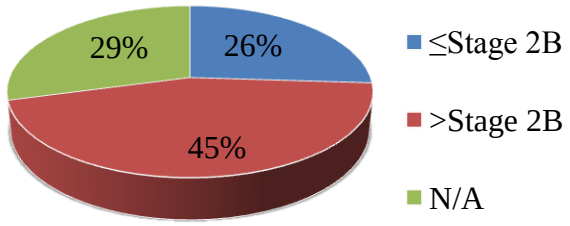


Figure 3.6- Disease histology classification

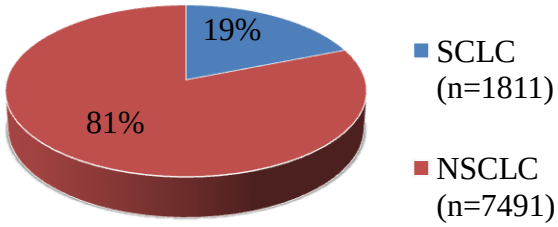


Figure 3.7- Disease site **(**Location of tumor in lower respiratory tract**)**

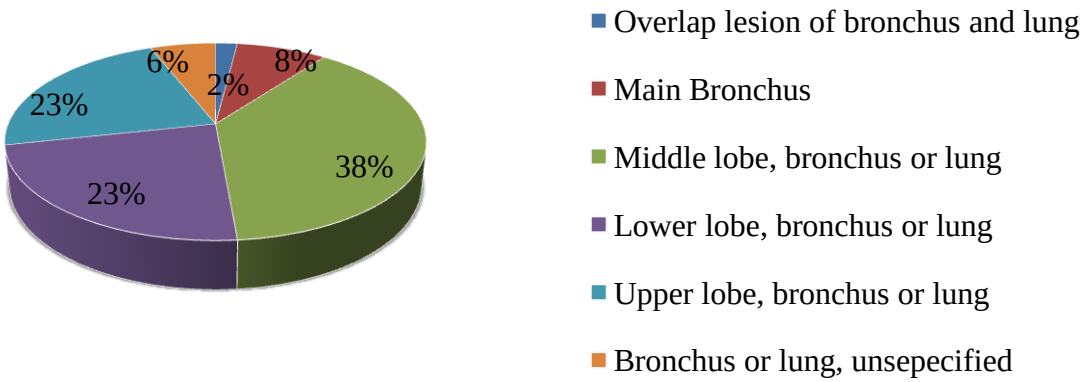


Table 3.1- Treatment summary for study patients

	Yes	No	N/A	Only	Total
Chemotherapy	999	3538	4765	167	9302
Radiotherapy	5048	846	3408	2059	9302
Surgery	1373	3165	4764	319	9302

N/A: not available based on the BCCA registry data set (They might have been treated somewhere else for example)

3.2 Small-cell lung cancer (SCLC)

In this part, there are references to 90 graphs (Graph 3.1 – Graph 3.90) and 45 tables (Table 3.5 – Table 3.49). Results are presented for 3 different subgroups of patients according to the type of therapy that they received as part of their treatment: those who received surgery, those who received radiotherapy, and those who received chemotherapy. In each subgroup, results are presented for the variables:

- season of diagnosis and season of first treatment
- month of diagnosis and month of first treatment
- monthly mean vitamin D sunshine index (MMVDSI)

Results are presented for men and women separately, and for men and women together.

3.2.1 Patients who received surgery with or without other treatments

There are 30 graphs (Graph 3.1 – Graph 3.30) and 15 tables (Table 3.5 – Table 3.16) for patients who received surgery as part of their treatment.

3.2.1.1Men

The survival curves associated with season of diagnosis are shown in Graphs 3.1 and 3.2; the survival curves associated with season of first treatment are shown in Graphs 3.3 and 3.4. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.5 and 3.6. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.5 and 3.6; the survival curves associated with month of first treatment are shown in Graphs 3.7 and 3.8. The log-rank tests only were significant for those patients who died because of non-lung-cancer

reasons. The corresponding multivariate tests and HRs are shown in Tables 3.7 and 3.8. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.9 and 3.10. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.9. None of the associations were significant.

3.2.1.2 Women

The survival curves associated with season of diagnosis are shown in Graphs 3.11 and 3.12; the survival curves associated with season of first treatment are shown in Graphs 3.13 and 3.14. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.10 and 3.11. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.15 and 3.16; the survival curves associated with month of first treatment are shown in Graphs 3.17 and 3.18. The log-rank test only was significant for month of first treatment in those patients who died because of lung cancer. The corresponding multivariate tests and HRs are shown in Tables 3.12 and 3.13. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.19 and 3.20. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.14. The association only was significant in those patients who died because of lung cancer.

3.2.1.3 Men and women together

The survival curves associated with season of diagnosis are shown in Graphs 3.21 and 3.22; the survival curves associated with season of first treatment are shown in Graphs 3.23 and

3.24. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.15 and 3.16. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.25 and 3.26; the survival curves associated with month of first treatment are shown in Graphs 3.27 and 3.28. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.17 and 3.18. The association was only significant for month of diagnosis in those patients who died because of lung cancer.

The survival curves associated with MMVDSI are shown in Graphs 3.29 and 3.30. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.19. None of the associations were significant.

3.2.2 Patients who received radiotherapy with or without other treatments

There are 30 graphs (Graph 3.31 – Graph 3.60) and 15 tables (Table 3.20 – Table 3.44) for patients who received radiotherapy as part of their treatment.

3.2.2.1Men

The survival curves associated with season of diagnosis are shown in Graphs 3.31 and 3.32; the survival curves associated with season of first treatment are shown in Graphs 3.33 and 3.34. The association was only significant for month of first treatment in those patients who died because of lung cancer. The corresponding multivariate tests and HRs are shown in Tables 3.20 and 3.21. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.35 and 3.36; the survival curves associated with month of first treatment are shown in Graphs 3.37 and

3.38. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.22 and 3.223. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.39 and 3.40. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.24. None of the associations were significant.

3.2.2.2 Women

The survival curves associated with season of diagnosis are shown in Graphs 3.41 and 3.42; the survival curves associated with season of first treatment are shown in Graphs 3.43 and 3.44. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.25 and 3.26. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.45 and 3.46; the survival curves associated with month of first treatment are shown in Graphs 3.47 and 3.48. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.27 and 3.28. The test only was significant for month of first treatment in those patients who died because of lung cancer.

The survival curves associated with MMVDSI are shown in Graphs 3.49 and 3.50. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.29. None of the associations were significant.

3.2.2.3 Men and women together

The survival curves associated with season of diagnosis are shown in Graphs 3.51 and 3.52; the survival curves associated with season of first treatment are shown in Graphs 3.53 and 3.54. None of the associations were significant. The corresponding multivariate tests and HRs

are shown in Tables 3.30 and 3.31. The test only was significant in those patients who died because of lung cancer.

The survival curves associated with month of diagnosis are shown in Graphs 3.55 and 3.56; the survival curves associated with month of first treatment are shown in Graphs 3.57 and 3.58. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.32 and 3.33. The association only was significant in those patients who died because of lung cancer.

The survival curves associated with MMVDSI are shown in Graphs 3.59 and 3.60. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.34. None of the associations were significant.

3.2.3 Patients who received chemotherapy with or without other treatments

There are 30 graphs (Graph 3.61 – Graph 3.90) and 15 tables (Table 3.35 – Table 3.49) for patients who received chemotherapy as part of their treatment.

3.2.3.1 Men

The survival curves associated with season of diagnosis are shown in Graphs 3.61 and 3.62; the survival curves associated with season of first treatment are shown in Graphs 3.63 and 3.64. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.35 and 3.36. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.65 and 3.66; the survival curves associated with month of first treatment are shown in Graphs 3.67 and 3.68. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.37 and 3.38. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.69 and 3.70. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.39. None of the associations were significant.

3.2.3.2 Women

The survival curves associated with season of diagnosis are shown in Graphs 3.71 and 3.72; the survival curves associated with season of first treatment are shown in Graphs 3.73 and 3.74. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.40 and 3.41. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.75 and 3.76; the survival curves associated with month of first treatment are shown in Graphs 3.77 and 3.78. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.42 and 3.43. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.79 and 3.80. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.44. None of the associations were significant.

3.2.3.3 Men and women together

The survival curves associated with season of diagnosis are shown in Graphs 3.81 and 3.82; the survival curves associated with season of first treatment are shown in Graphs 3.83 and 3.84. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.45 and 3.46. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.85 and 3.86; the survival curves associated with month of first treatment are shown in Graphs 3.87 and

3.88. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.47 and 3.48. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.89 and 3.90. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.49. None of the associations were significant.

3.3 Non-small-cell lung cancer (NSCLC)

In this part, there are references to 90 graphs (Graph 3.91 – Graph 3.180) and 45 tables (Table 3.50 – Table 3.94). Results are presented for 3 different subgroups of patients according to the type of therapy that they received as part of their treatment: those who received surgery, those who received radiotherapy, and those who received chemotherapy. In each subgroup, results are presented for the variables:

- season of diagnosis and season of first treatment
- month of diagnosis and month of first treatment
- monthly mean vitamin D sunshine index (MMVDSI)

Results are presented for men and women separately, and for men and women together.

3.3.1 Patients who received surgery with or without other treatments

There are 30 graphs (Graph 3.91 – Graph 3.120) and 15 tables (Table 3.50 – Table 3.64) for patients who received surgery as part of their treatment.

3.3.1.1 Men

The survival curves associated with season of diagnosis are shown in Graphs 3.91 and 3.92; the survival curves associated with season of first treatment are shown in Graphs 3.93 and 3.94. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.50 and 3.51. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.95 and 3.96; the survival curves associated with month of first treatment are shown in Graphs 3.97 and 3.98. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.52 and 3.53. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.99 and 3.100. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.54. None of the associations were significant.

3.3.1.2 Women

The survival curves associated with season of diagnosis are shown in Graphs 3.101 and 3.102; the survival curves associated with season of first treatment are shown in Graphs 3.103 and 3.104. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.55 and 3.56. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.105 and 3.106; the survival curves associated with month of first treatment are shown in Graphs 3.107 and 3.108. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.57 and 3.58. The association was only significant for month of first treatment in those patients who died because of non-lung-cancer reasons.

The survival curves associated with MMVDSI are shown in Graphs 3.109 and 3.110. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.59. The association only was significant in those patients who died because of lung cancer.

3.3.1.3 Men and women together

The survival curves associated with season of diagnosis are shown in Graphs 3.111 and 3.112; the survival curves associated with season of first treatment are shown in Graphs 3.113 and 3.114. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.60 and 3.61. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.115 and 3.116; the survival curves associated with month of first treatment are shown in Graphs 3.117 and 3.118. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.62 and 3.63. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.119 and 3.120. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.64. None of the associations were significant.

3.3.2 Patients who received radiotherapy with or without other treatments

There are 30 graphs (Graph 3.121 – Graph 3.150) and 15 tables (Table 3.65 – Table 3.78) for patients who received radiotherapy as part of their treatment.

3.3.2.1Men

The survival curves associated with season of diagnosis are shown in Graphs 3.121 and 3.122; the survival curves associated with season of first treatment are shown in Graphs 3.123 and 3.124. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.65 and 3.66. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.125 and 3.126; the survival curves associated with month of first treatment are shown in Graphs 3.127 and 3.128. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.67 and 3.68. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.129 and 3.130. The log-rank test only was significant in those patients who died because of lung cancer. The corresponding multivariate tests are shown in Table 3.69. The association only was significant in those patients who died because of lung cancer.

3.3.2.2 Women

The survival curves associated with season of diagnosis are shown in Graphs 3.131 and 3.132; the survival curves associated with season of first treatment are shown in Graphs 3.133 and 3.134. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.70 and 3.71. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.135 and 3.136; the survival curves associated with month of first treatment are shown in Graphs 3.137 and 3.138. The association only was significant for month of first treatment in those patients who died because of non-lung-cancer reasons. The corresponding multivariate tests and HRs are

shown in Tables 3.72 and 3.73. The test only was significant for month of first treatment in those patients who died because of lung cancer.

The survival curves associated with MMVDSI are shown in Graphs 3.139 and 3.140. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.74. None of the associations were significant.

3.3.2.3 Men and women together

The survival curves associated with season of diagnosis are shown in Graphs 3.141 and 3.142; the survival curves associated with season of first treatment are shown in Graphs 3.143 and 3.144. The association only was significant for season of first treatment in those patients who died because of lung cancer. The corresponding multivariate tests and HRs are shown in Tables 3.75 and 3.76. The association only was significant for season of first treatment in those patients who died because of lung cancer.

The survival curves associated with month of diagnosis are shown in Graphs 3.145 and 3.146; the survival curves associated with month of first treatment are shown in Graphs 3.147 and 3.148. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.77 and 3.78. The association only was significant for month of diagnosis in those patients who died because of lung cancer.

The survival curves associated with MMVDSI are shown in Graphs 3.149 and 3.150. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.79. The association only was significant in those patients who died because of lung cancer.

3.3.3 Patients who received chemotherapy with or without other treatments

There are 30 graphs (Graph 3.151 – Graph 3.180) and 15 tables (Table 3.80 – Table 3.94) for patients who received chemotherapy as part of their treatment.

3.3.3.1 Men

The survival curves associated with season of diagnosis are shown in Graphs 3.151 and 3.152; the survival curves associated with season of first treatment are shown in Graphs 3.153 and 3.154. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.80 and 3.81. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.155 and 3.156; the survival curves associated with month of first treatment are shown in Graphs 3.157 and 3.158. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.82 and 3.83. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.159 and 3.160. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.84. None of the associations were significant.

3.3.3.2 Women

The survival curves associated with season of diagnosis are shown in Graphs 3.161 and 3.162; the survival curves associated with season of first treatment are shown in Graphs 3.163 and 3.164. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.85 and 3.86. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.165 and 3.166; the survival curves associated with month of first treatment are shown in Graphs 3.167

and 3.168. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.87 and 3.88. The association only was significant for month of first treatment in those patients who died because of lung cancer.

The survival curves associated with MMVDSI index are shown in Graphs 3.169 and 3.170. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.89. None of the associations were significant.

3.3.3.3 Men and women together

The survival curves associated with season of diagnosis are shown in Graphs 3.171 and 3.172; the survival curves associated with season of first treatment are shown in Graphs 3.173 and 3.174. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.90 and 3.91. None of the associations were significant.

The survival curves associated with month of diagnosis are shown in Graphs 3.175 and 3.176; the survival curves associated with month of first treatment are shown in Graphs 3.177 and 3.178. None of the associations were significant. The corresponding multivariate tests and HRs are shown in Tables 3.92 and 3.93. None of the associations were significant.

The survival curves associated with MMVDSI are shown in Graphs 3.179 and 3.180. None of the associations were significant. The corresponding multivariate tests are shown in Table 3.94. None of the associations were significant.

3.4 Summary

We reviewed the results, focusing on relationships for which there was a significant multivariate association between survival and monthly mean vitamin D sunshine index for patients who died because of lung cancer. We chose this focus because the vitamin D index is the best sunshine measure in our study, and the multivariate tests adjusted for other prognostic variables. Based on this focus, we found three groups for which there was a significant relationship between survival and sunshine:

1- Female SCLC patients

2- Female NSCLC patients

3- Male NSCLC patients

Tables 3.2 – 3.4 summarize the results for each group.

In Table 3.2, I present the multivariate results for different treatment groups in female SCLC patients. Patients who received surgery are not very informative because there are few of them (i.e., n<30). For patients who received radiotherapy, multivariate estimates for month of first treatment, season of diagnosis and season of first treatment were significant. For patients who received chemotherapy, none of the sunshine measures were significantly associated with survival in multivariate tests.

In Table 3.3, I present the multivariate results for different treatment groups in female NSCLC patients. For patients who received surgery, MMVDSI was significantly associated with survival in multivariate tests. The HR values for this variable increased for each level of exposure except for the highest category. For patients who received radiotherapy, none of the sunshine measures were significantly associated with survival in multivariate tests. For patients

who received chemotherapy, only the sunshine measure month of diagnosis was significantly associated with survival in multivariate tests.

In Table 3.4, I present the multivariate results for different treatment groups in male NSCLC patients. For patients who received surgery, none of the sunshine measures was significantly associated with survival in multivariate tests. For patients who received radiotherapy, MMVDSI was significantly associated with survival in multivariate tests. The HR values for this variable increased for the first three categories of exposure, but not thereafter. For patients who received chemotherapy, none of the sunshine variables were significantly associated with survival in multivariate tests.

Table 3.2- Female patients with SCLC who died because of lung cancer: HR estimates and multivariate P-values for each treatment group.

Treatment	HR (95% CI) for MMVDSI					Multivariate P				
	A	B	C	D	E	MMVDSI	Month of Diagnosis	Month of first Treatment	Season of Diagnosis	Season of first Treatment
Surgery (n=25)	1	N/A	0.07 <0.01-1.1	N/A	N/A	0.05	NS	NS	NS	NS
Radiotherapy (n=157)	1	1.14 0.6-2.0	2.02 1.0 -3.9	1.44 0.8-2.5	1.33 0.7-2.3	NS	0.062	0.045	0.043	0.038
Chemotherapy (n=310)	1	1.13 0.7-1.6	0.99 0.6 -1.4	0.78 0.5-1.1	1.04 0.6-1.5	NS	NS	0.096	NS	NS

A: ≤0.406 **B:** 0.406-0.812 **C:** 0.812-1.218 D: 1.218-1.624 **E:** ≥1.624

HR is hazard ratio; MMVDSI is monthly mean vitamin D sunshine index;

CI is confidence interval; N/A is not available; NS is not significant with p>0.1

Table 3.3- Female patients with NSCLC who died because of lung cancer: HR estimates and multivariate P-values for each treatment group.

Treatment	HR (95% CI) for MMVDSI					Multivariate P				
	A	B	C	D	E	MMVDSI	Month of Diagnosis	Month of first Treatment	Season of Diagnosis	Season of first Treatment
Surgery (n=431)	1	1.03 0.7-1.4	1.14 0.8-1.5	1.43 1.0-1.9	0.79 0.5-1.1	0.050	NS	NS	NS	NS
Radiotherapy (n=1377)	1	1.09 0.9-1.3	1.21 1.0-1.4	1.12 0.9-1.3	1.01 0.8-1.2	NS	NS	NS	0.072	NS
Chemotherapy (n=81)	1	0.70 0.3-1.4	1.82 0.8-4.0	2.77 1.0-7.6	0.66 0.2-2.0	NS	0.025	NS	NS	NS

A: ≤0.406 **B:** 0.406-0.812 **C:** 0.812-1.218 D: 1.218-1.624 **E:** ≥1.624

HR is hazard ratio; MMVDSI is monthly mean vitamin D sunshine index;

CI is confidence interval; N/A is not available; NS is not significant with p>0.1

Table 3.4- Male patients with NSCLC who died because of lung cancer: HR estimates and multivariate P-values for each treatment group.

Treatment	HR (95% CI) for MMVDSI					Multivariate P				
	A	B	C	D	E	MMVDSI	Month of Diagnosis	Month of first Treatment	Season of Diagnosis	Season of first Treatment
Surgery (n=847)	1	1.08 0.8-1.3	1.26 1.0-1.5	1.08 0.8-1.3	1.00 0.7-1.3	NS	NS	NS	NS	NS
Radiotherapy (n=2687)	1	1.07 0.9-1.2	1.22 1.0-1.3	0.92 0.8-1.0	1.03 0.9-1.1	<0.01	0.060	NS	NS	NS
Chemotherapy (n=157)	1	1.14 0.6-2.0	2.02 1.0-3.9	1.44 0.8-2.5	1.33 0.7-2.3	NS	0.057	NS	NS	NS

A: ≤0.406 **B:** 0.406-0.812 **C:** 0.812-1.218 D: 1.218-1.624 **E:** ≥1.624

HR is hazard ratio; MMVDSI is monthly mean vitamin D sunshine index; CI is confidence interval; N/A is not available; NS is not significant with p>0.1

3.5 Additional analyses

Having completed the main analyses, we fitted some extra models to investigate alternative patient groups, treatment groups and variable categories. In particular, I was interested in separately considering patients age <50 years and age $\geq$ 50 years. I was also interested is considering patients who received monotherapy (i.e., only chemotherapy, only radiotherapy or only surgery). Those results are summarized in sections 3.5.1 and 3.5.2. A final analysis re-evaluated the test outcomes using a correction for multiple testing. That analysis is presented in section 3.5.3.

3.5.1 Small-cell lung cancer

3.5.1.1 Patients age <50 years who received monotherapy

Patients who received only surgery

There were no significant results in any of the univariate or multivariate analyses.

Patients who received only radiotherapy

The univariate and multivariate analyses showed a significant association for season of diagnosis among females who died because of lung cancer. MMVDSI was also significantly associated with survival in univariate analysis for females who died because of lung cancer. We also performed the analyses for females and males together. The univariate and multivariate analyses for month of diagnosis and season of first treatment were significant in patients who died because of lung cancer. The multivariate analyses for month of diagnosis and season of diagnosis were significant in patients who died because of lung cancer.

Patients who received only chemotherapy

The multivariate analyses for season of diagnosis and MMVDSI were significant among males who died because of lung cancer. The univariate and multivariate analyses for season of first treatment were significant in males who died because of lung cancer. We also performed the analyses for both females and males together. The univariate analyses for month of first treatment were significant in patients who died because of lung cancer. The multivariate analysis was significant for season of diagnosis in patients who died because of lung cancer. The univariate and multivariate analyses for season of first treatment were significant in patients who died because of lung cancer.

3.5.1.2- Patients age ≥50 years who received monotherapy

Patients who received only surgery

The multivariate analysis for month of diagnosis was significant in men and women combined for patients who died because of lung cancer.

Patients who received only radiotherapy

The multivariate analysis for season of first treatment was significant separately in males and females who died because of lung cancer. In analyses that considered males and females together, only the multivariate analysis for season of first treatment was significant.

Patients who received only chemotherapy

There were no significant results in any of the univariate or multivariate analyses.

3.5.1.3- Monotherapy without age categorization

Patients who received only surgery

There were no significant results in any of the univariate or multivariate analyses.

Patients who received only radiotherapy

The univariate analysis for month of diagnosis and the multivariate analysis for month of first treatment were significant in females who died because of lung cancer. The univariate and multivariate analyses were significant for month of first treatment for males who died because of lung cancer. And. The univariate and multivariate analyses were significant for season of diagnosis for males who died because of lung cancer. The univariate and multivariate analyses were significant for season of first treatment for males and females separately who died because of lung cancer.

We also performed the analyses for males and females together. The univariate and multivariate analyses were significant for all of the sunshine variables in patients who died because of lung cancer.

Patients who received only chemotherapy

The univariate analysis for month of first treatment was significant for males who died because of lung cancer.

3.5.2 Non-small-cell lung cancer

3.5.2.1 Patients age <50 years who received monotherapy

Patients who received only surgery

The univariate analysis showed a significant association with survival for season of diagnosis in females who died because of lung cancer. We also performed the analyses for males and females together. The univariate analyses for season of diagnosis and season of first treatment were significant in those patients who died because of lung cancer. The multivariate analysis was also significant for month of first treatment in patients who died because of lung

cancer. The univariate and multivariate analyses for month of diagnosis was significant in patients who died because of lung cancer.

Patients who received only radiotherapy

The univariate and multivariate analyses for season of first treatment were significant for patients who died because of lung cancer.

Patients who received only chemotherapy

There were no significant results in either univariate or multivariate analyses.

3.5.2.2 Patients age ≥50 years who received monotherapy

Patients who received only surgery

The only significant result was in multivariate analyses of the association of survival with MMVDSI for males and females together who died because of lung cancer.

Patients who received only radiotherapy

The multivariate analyses for season of first treatment were significant separately in males and females who died because of lung cancer. The multivariate analysis for MMVDSI was significant in males who died because of lung cancer. Also, the univariate analysis for month of diagnosis was significant in males who died because of lung cancer. We also performed the analyses for both females and males. The univariate and multivariate analyses for season of first treatment were significant in patients who died because of lung cancer. The multivariate analysis for MMVDSI was significant in patients who died because of lung cancer.

Patients who received only chemotherapy

The multiivariate analyses for month of first treatment and MMVDSI were significant in males who died because of lung cancer.

3.5.2.3- Monotherapy without age categorization

Patients who received only surgery

There were no significant results in either univariate or multivariate analyses.

Patients who received only radiotherapy

The univariate and multivariate analyses for season of first treatment were significant separately in females and males who died because of lung cancer. The univariate and multivariate analyses for MMVDSI were significant in males who died because of lung cancer. We also performed the analyses for females and males together. The univariate and multivariate analyses for season of first treatment were significant in patients who died because of lung cancer. The multivariate analysis for MMVDSI was significant in patients who died because of lung cancer.

Patients who received only chemotherapy

The multivariate analysis for season of diagnosis was significant in males who died because of lung cancer. We also performed the analyses for females and males together. The univariate and multivariate analyses for month of first treatment were significant in patients who died because of lung cancer. The multivariate analysis for month of diagnosis was significant in those patients who died because of lung cancer. (Please see A3 in appendix)

3.5.3 Multiple testing analysis

I re-evaluated the statistical results adjusting for the multiple tests. I used an informal Bonferroni method for this re-evaluation, in which I multiplied the original test P-values by the number of tests performed in the main analysis. (The main analysis is the 180 tests involving

MMVDSI.) The only test in which the P-value remained significant after the Bonferroni re-analysis was that for males with NSCLC who received radiotherapy.

3.6 Main results' graphs and tables

Table 3.5- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for males with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	45	8	NS	NS	3.07 0.5-18.1	3.28 0.5-18.6	1	2.44 0.4-13.5
Other causes	45	37	NS	NS	N<5	N<5	1	N<5

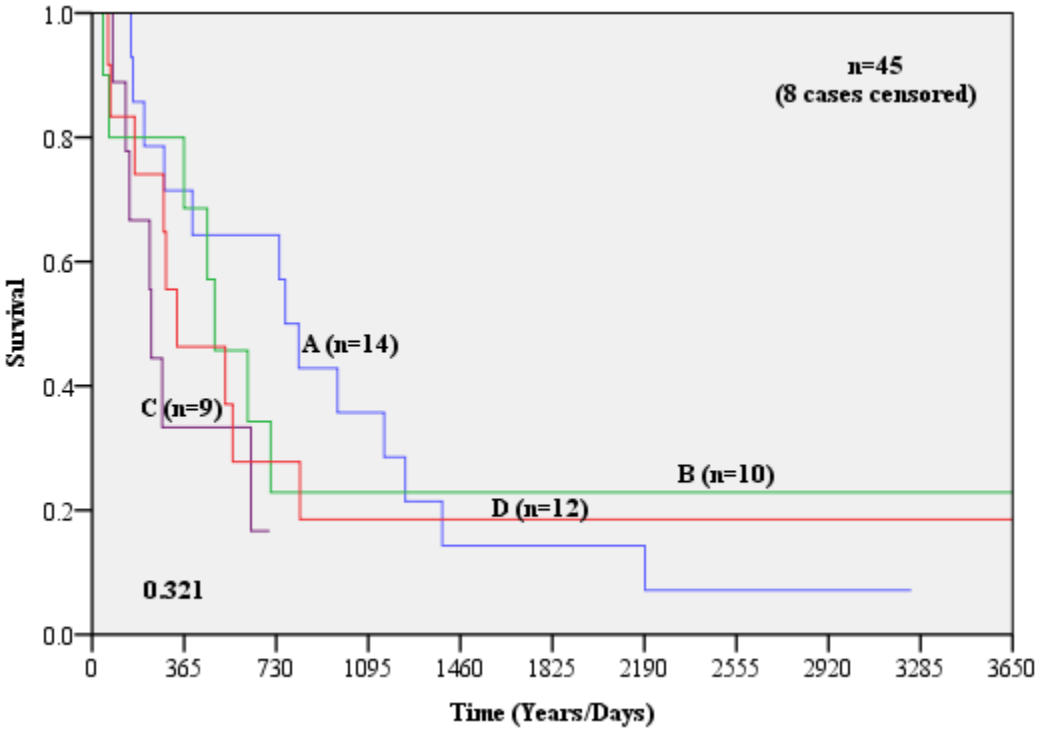
- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- N is number of uncensored cases.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.1- Survival according to season of diagnosis for males with SCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.2- Survival according to season of diagnosis for males with SCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

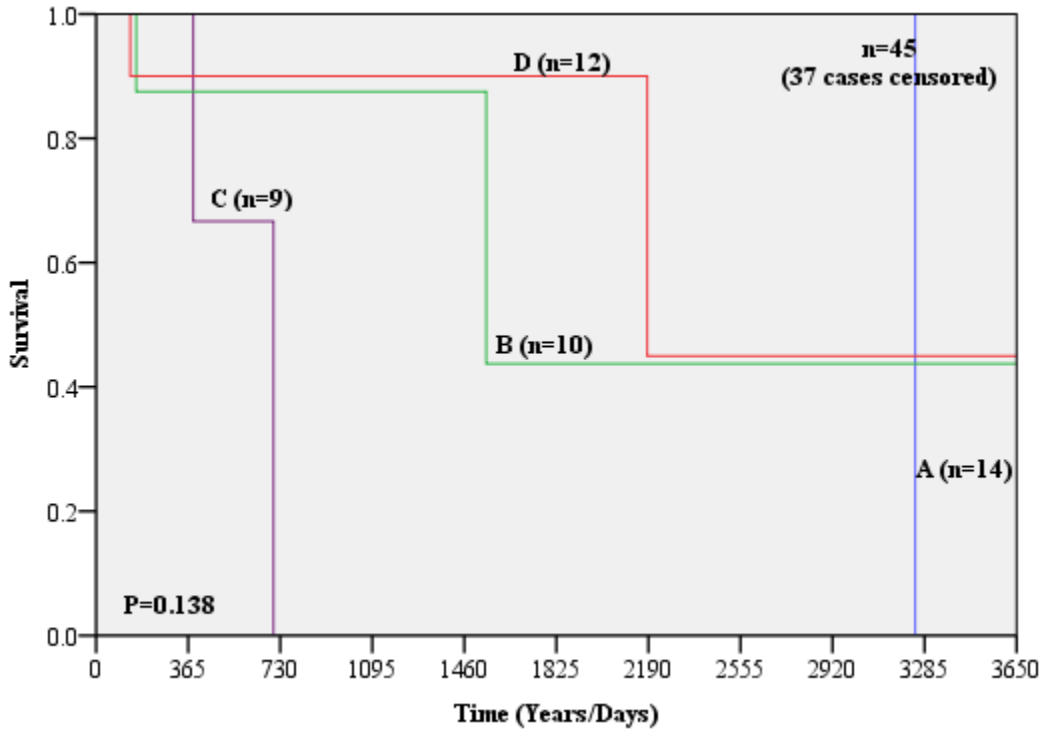


Table 3.6- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for males with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	45	8	NS	NS	1	N<5	N<5	N<5
Other causes	45	37	NS	NS	1	6.56 0.1->100	2.97 0.1-74.4	0.38 <0.01-25.2

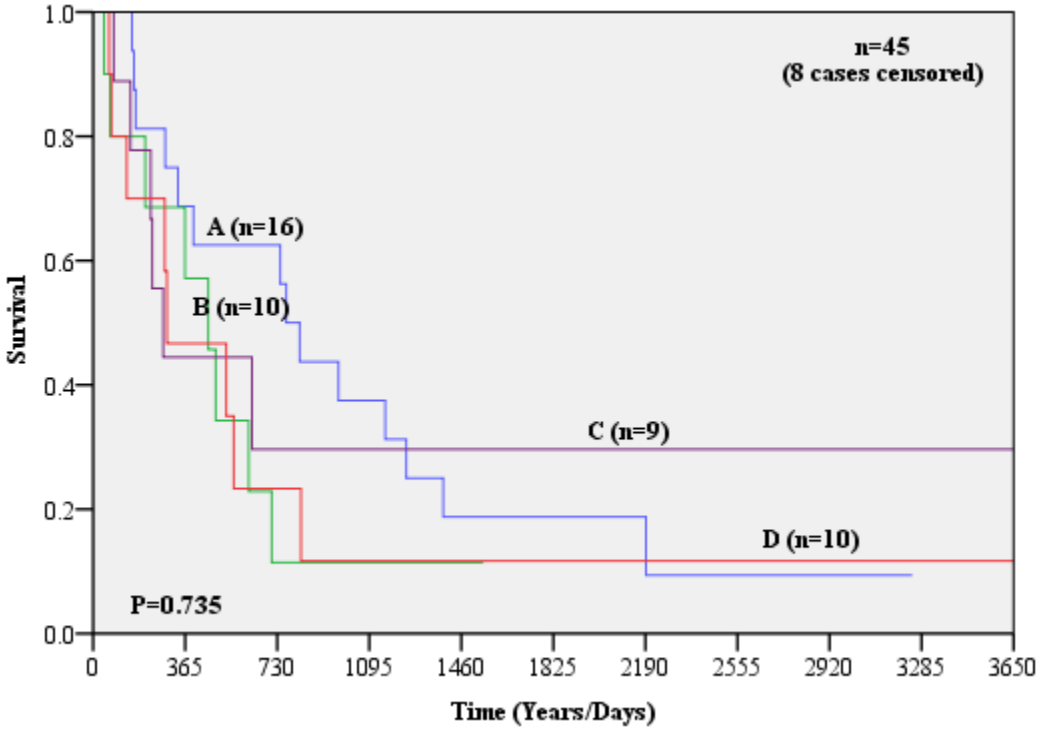
●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and season of first treatment.

●NS is not significant; A is spring, B is summer, C is fall and D is winter.

●N is number of uncensored cases.

●Number of caes is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.3- Survival according to season of first treatment for males with SCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.4- Survival according to season of first treatment for males with SCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

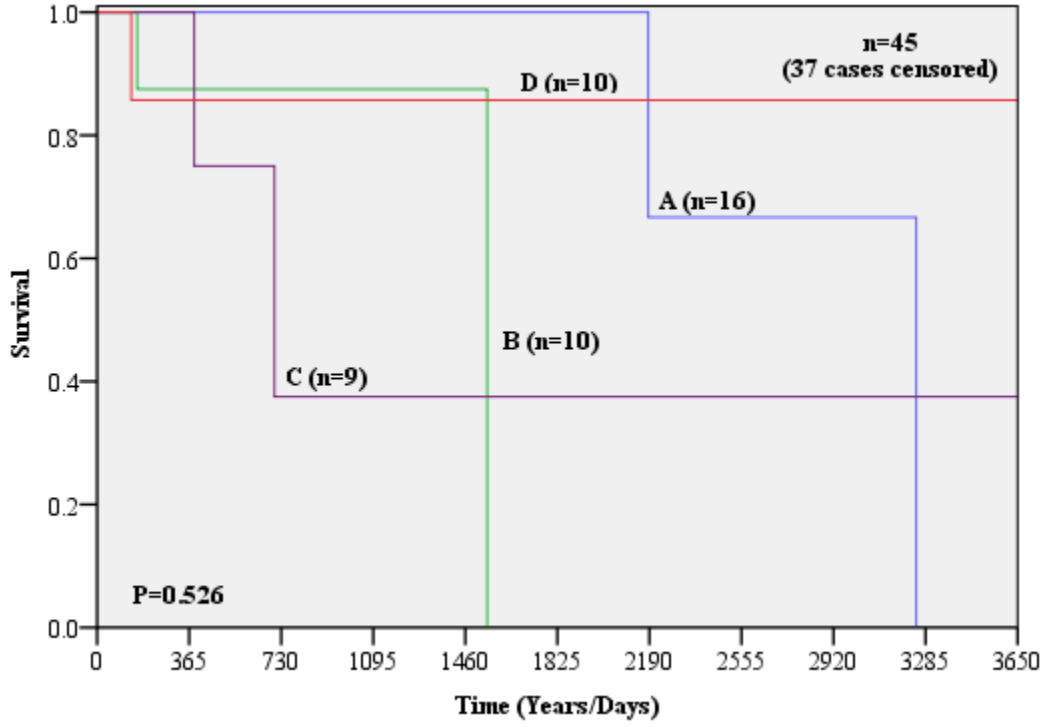


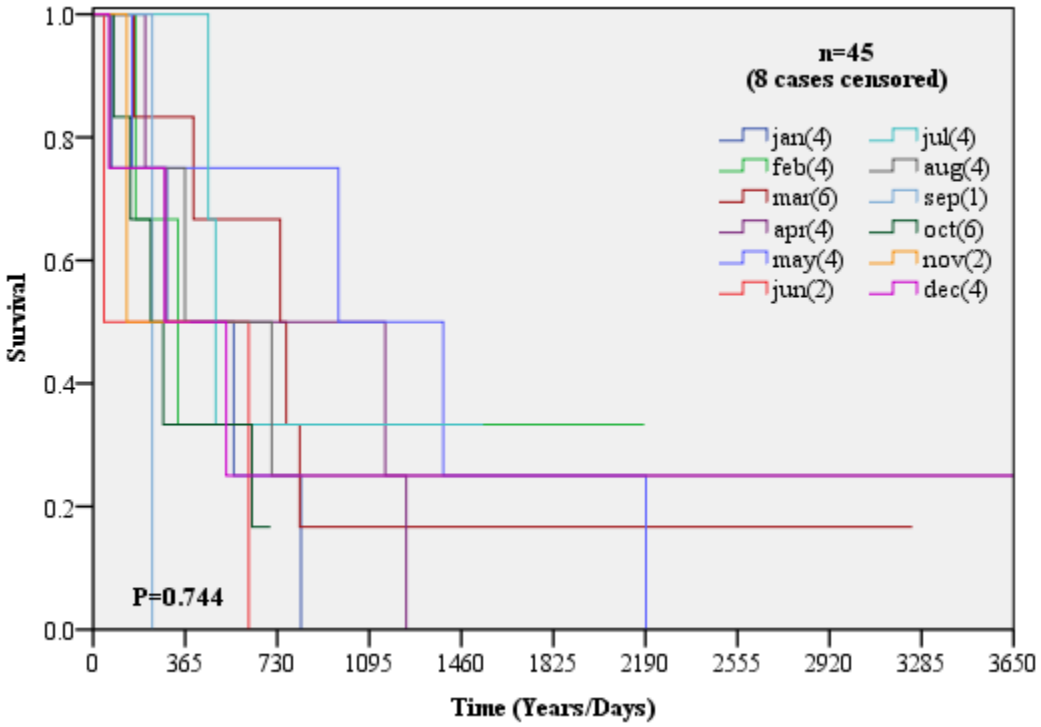
Table 3.7- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for males with SCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	0.030
Multivariate P value		NS	NS
Number of cases		45	45
Number of censored cases		8	37
HR (95% CI)	Jan	1	1
	Feb	n<5	N<5
	Mar	n<5	N<5
	Apr	n<5	N<5
	May	n<5	N<5
	Jun	n<5	N<5
	Jul	n<5	N<5
	Aug	n<5	N<5
	Sep	n<5	N<5
	Oct	n<5	N<5
	Nov	n<5	N<5
	Dec	n<5	N<5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and month of diagnosis.

●NS is not significant ●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.5- Survival according to month of diagnosis for males with SCLC who received surgery: lung cancer deaths



Graph 3.6- Survival according to month of diagnosis for males with SCLC who received surgery: non-lung-cancer death

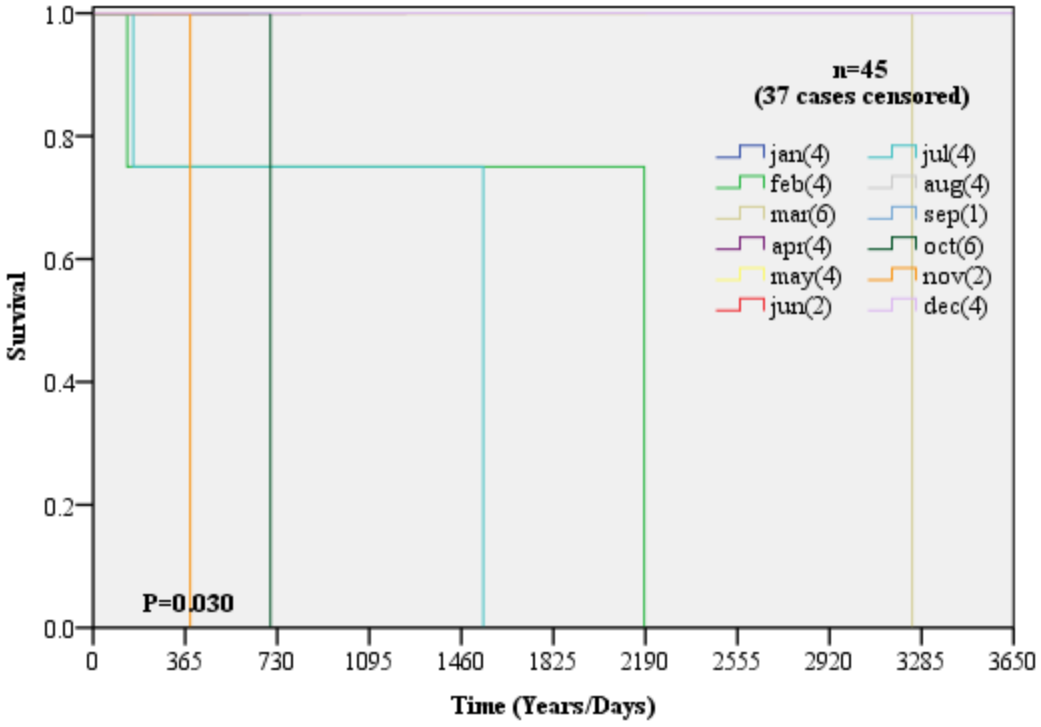


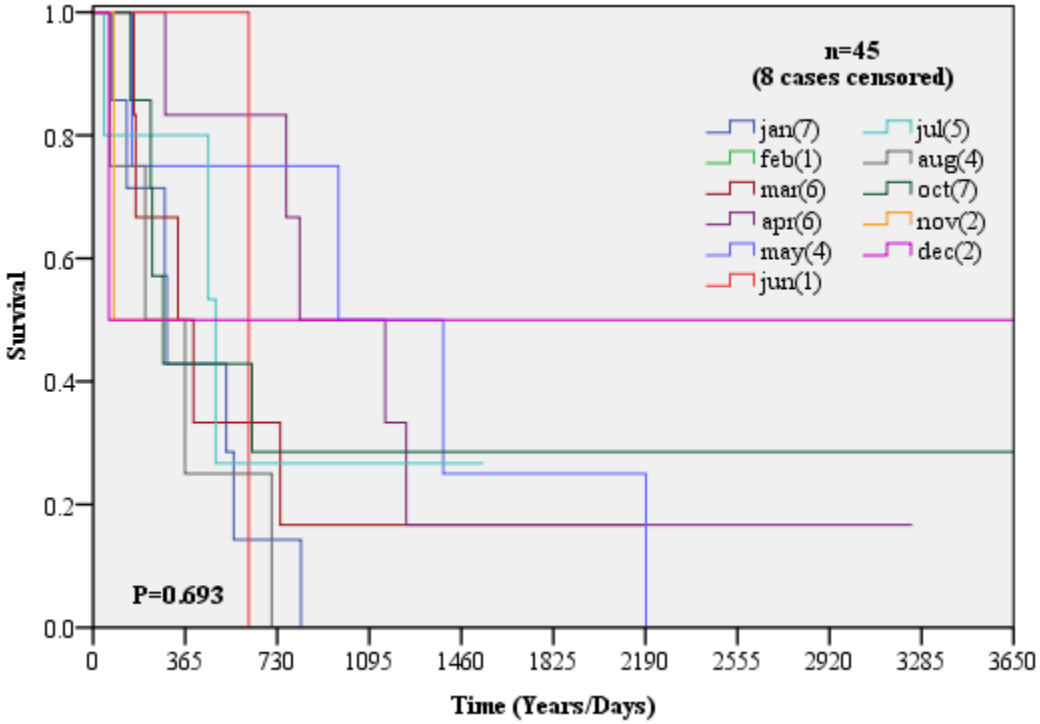
Table 3.8- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for males with SCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	<0.01
Multivariate P value		NS	NS
Number of cases		45	45
Number of censored cases		8	37
HR (95% CI)	Jan	1	1
	Feb	N<5	N<5
	Mar	N<5	N<5
	Apr	N<5	N<5
	May	N<5	N<5
	Jun	N<5	N<5
	Jul	N<5	N<5
	Aug	N<5	N<5
	Sep	N<5	N<5
	Oct	N<5	N<5
	Nov	N<5	N<5
	Dec	N<5	N<5

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and month of first treatment.

•NS is not significant•N is number of uncensored cases•Number of caes is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.7- Survival according to month of first treatment for males with SCLC who received surgery: lung cancer deaths



Graph 3.8- Survival according to month of first treatment for males with SCLC who received surgery: non-lung-cancer deaths

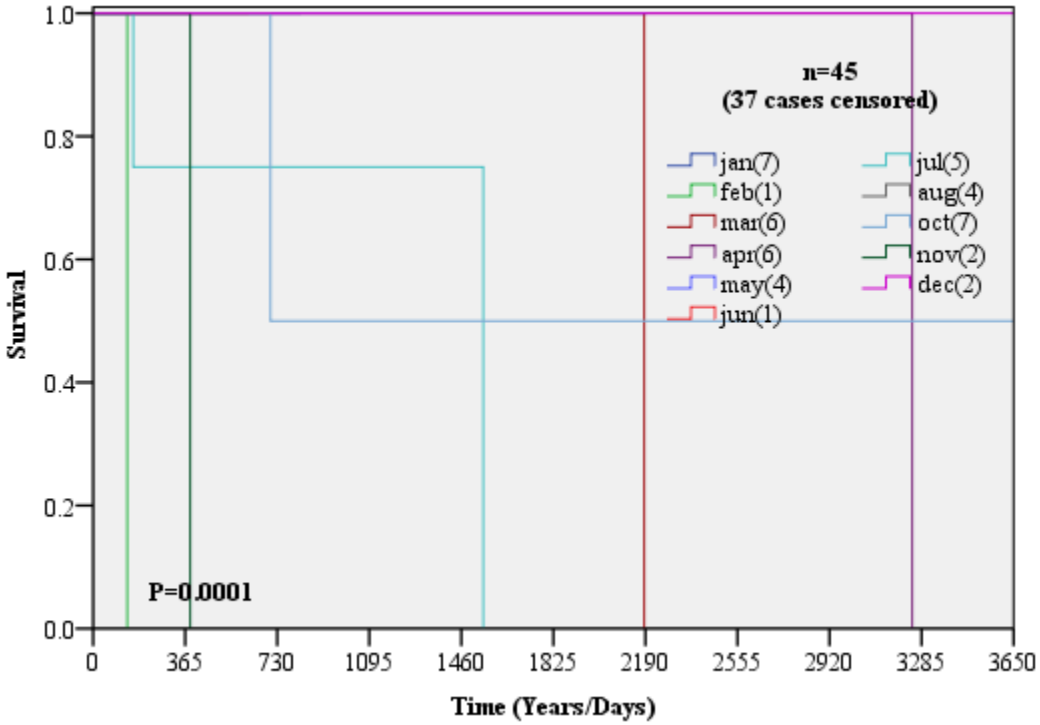


Table 3.9- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for males with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	45	8	NS	NS	1	0.48 0.1-2.1	4.79 0.7-29.2	2.27 0.6- 8.0	n<5
Other causes	45	37	NS	NS	1	N<5	N <5	N <5	N <5

(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

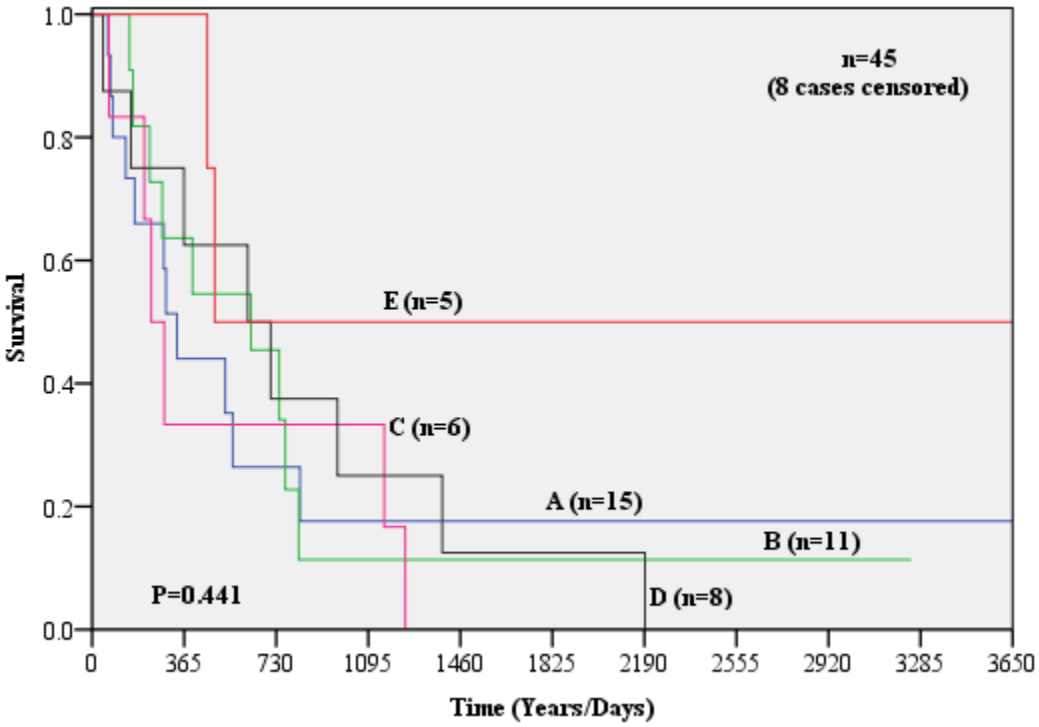
- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and monthly mean vitamin D sunshine index.

- NS is not significant;

- N is number of uncensored cases

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.9- Survival according to MMVDSI for males with SCLC who received surgery: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.10- Survival according to MMVDSI for males with SCLC who received surgery: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

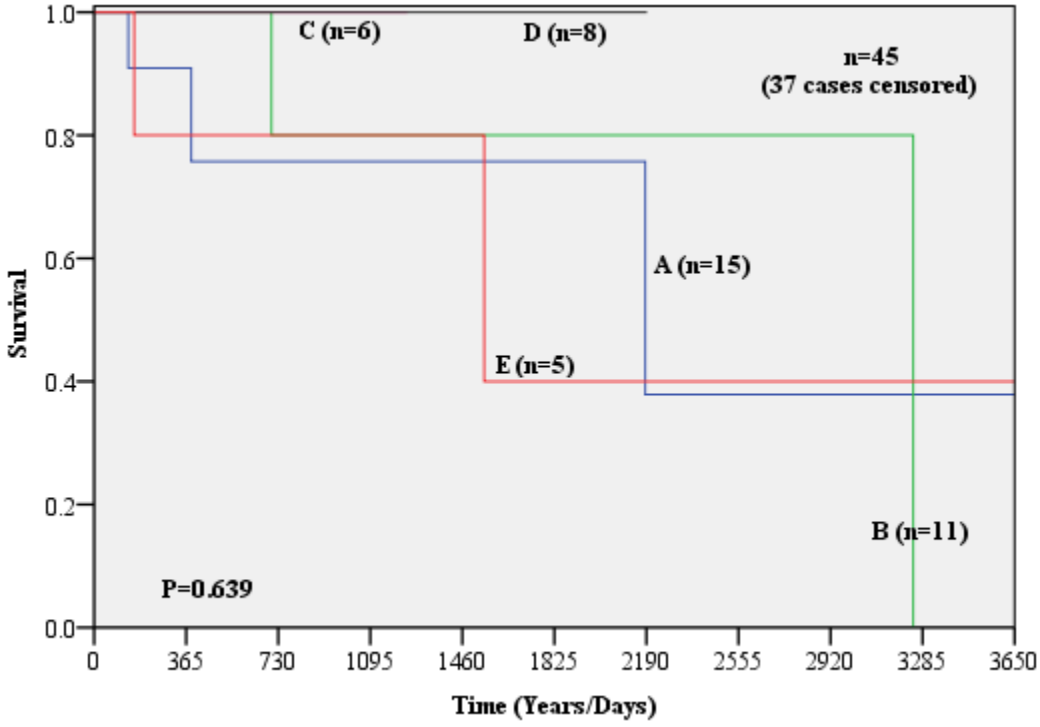


Table 3.10- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for females with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	25	9	NS	NS	N<5	N<5	1	6.0 0.2-<100
Other causes	25	16	NS	NS	N<5	N<5	1	1 0.0-30.0

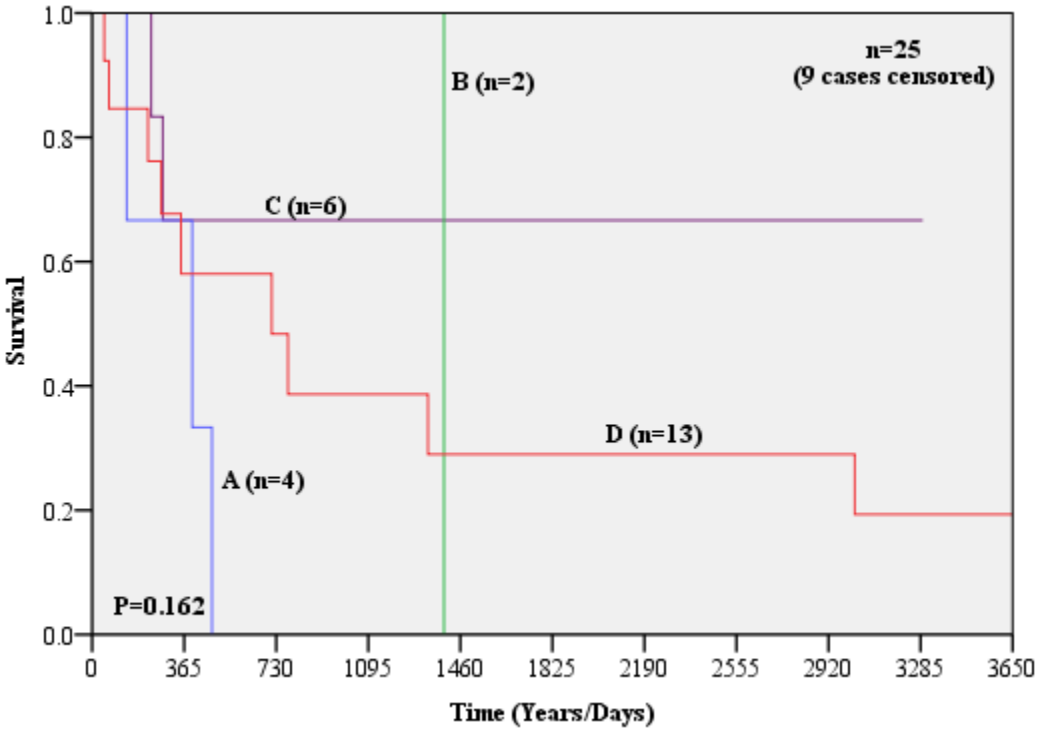
- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- N is number of uncensored cases

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.11- Survival according to season of diagnosis for females with SCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.12- Survival according to season of diagnosis for females with SCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

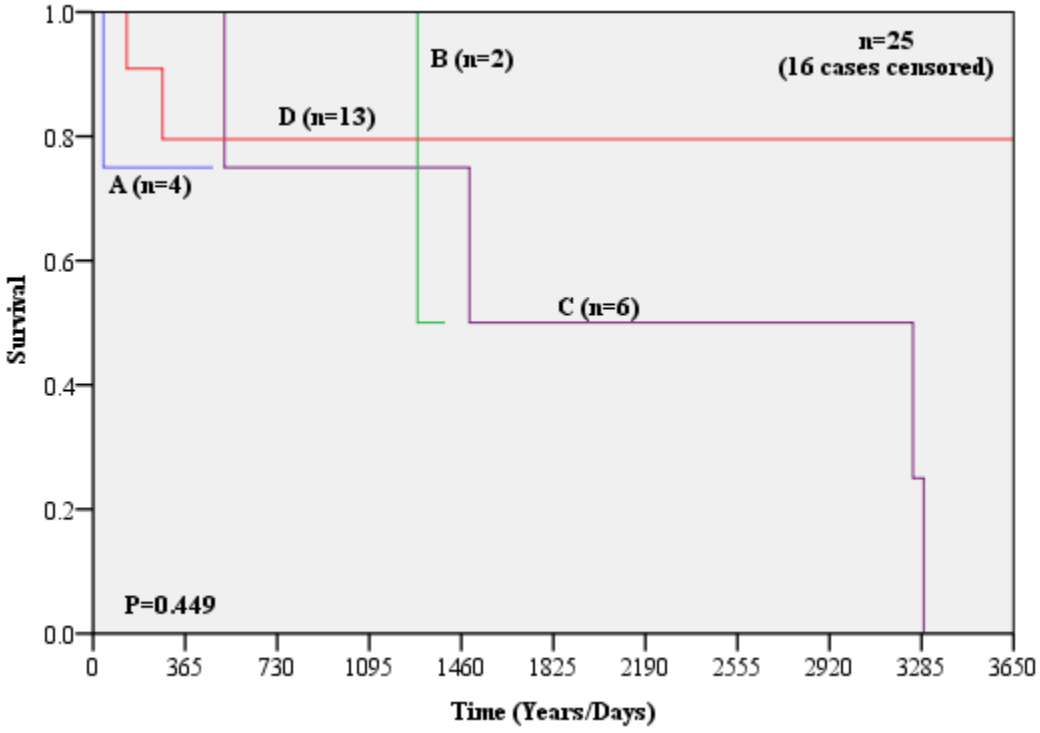


Table 3.11- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for females with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	25	9	NS	NS	1	N<5	N<5	1.71 0.1-20.4)
Other causes	25	16	NS	NS	1	N<5	N<5	1 0.0-18.1

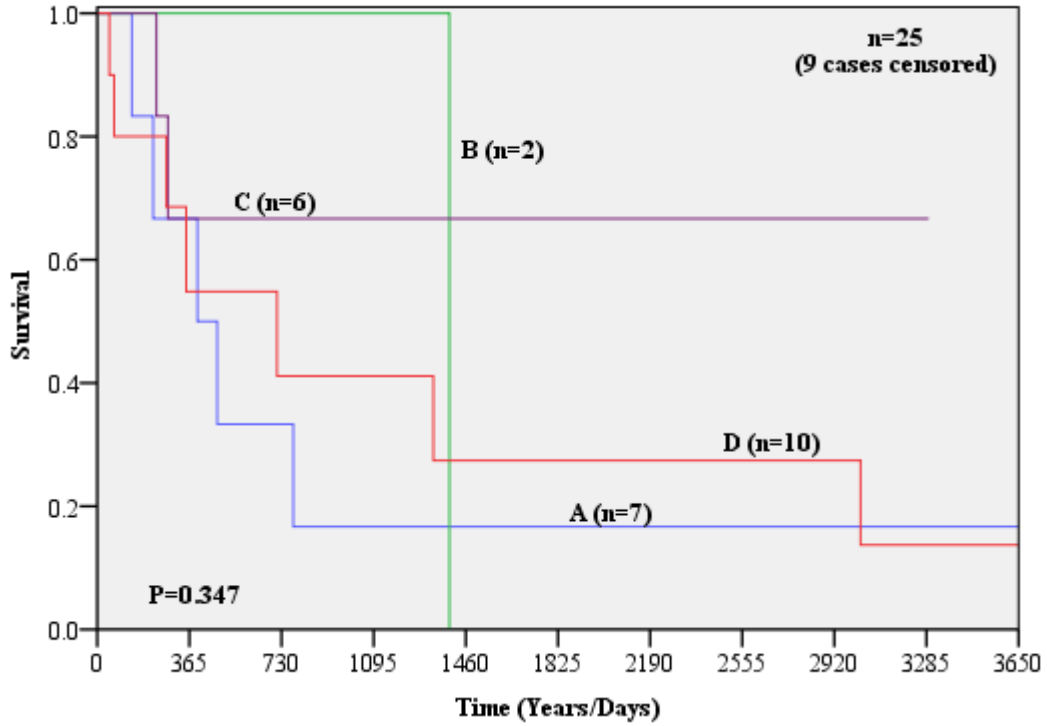
- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- N is number of uncensored cases

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.13- Survival according to season of first treatment for females with SCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.14- Survival according to season of first treatment for females with SCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

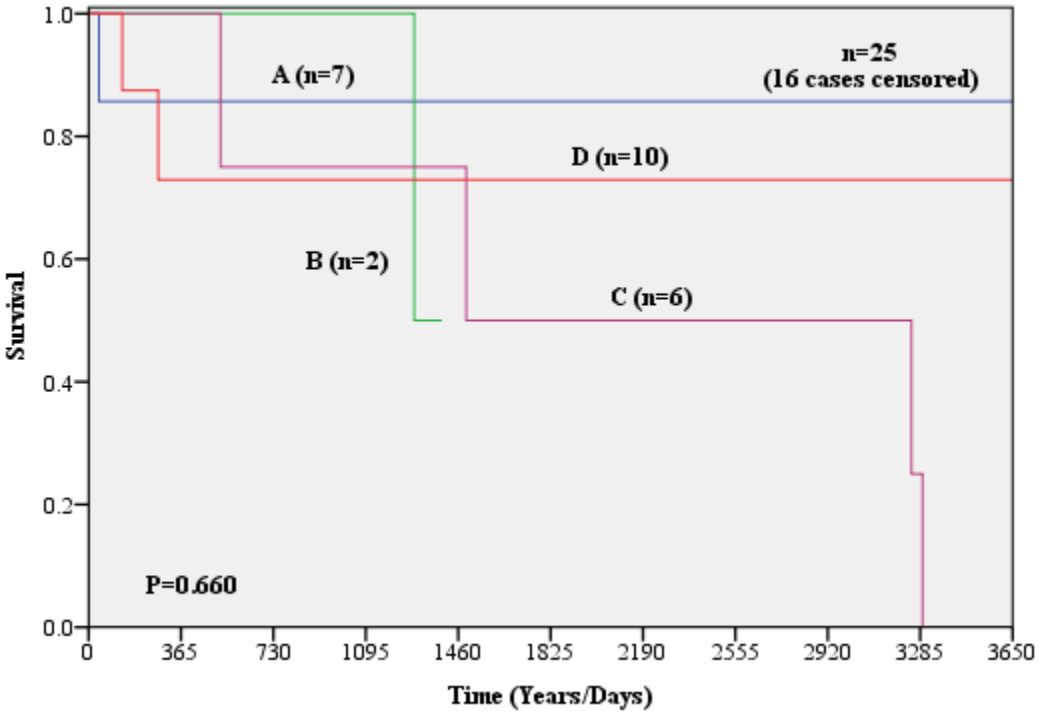


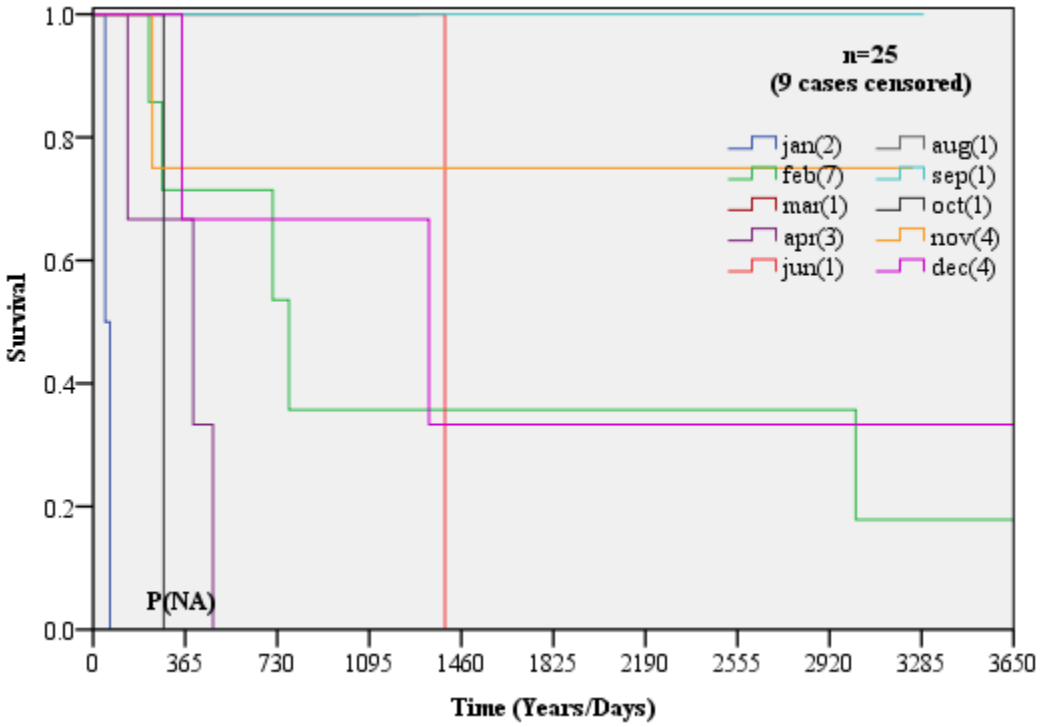
Table 3.12- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for females with SCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		<0.01	NS
Multivariate P value		NS	NS
Number of cases		25	25
Number of censored cases		9	16
HR (95% CI)	Jan	1	1
	Feb	N<5	N<5
	Mar	N<5	N<5
	Apr	N<5	N<5
	May	N<5	N<5
	Jun	N<5	N<5
	Jul	N<5	N<5
	Aug	N<5	N<5
	Sep	N<5	N<5
	Oct	N<5	N<5
	Nov	N<5	N<5
	Dec	N<5	N<5

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and month of diagnosis.

•NS is not significant•N is number of uncensored cases•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.15- Survival according to month of diagnosis for females with SCLC who received surgery: lung cancer deaths



Graph 3.16- Survival according to month of diagnosis for females with SCLC who received surgery: non-lung-cancer deaths

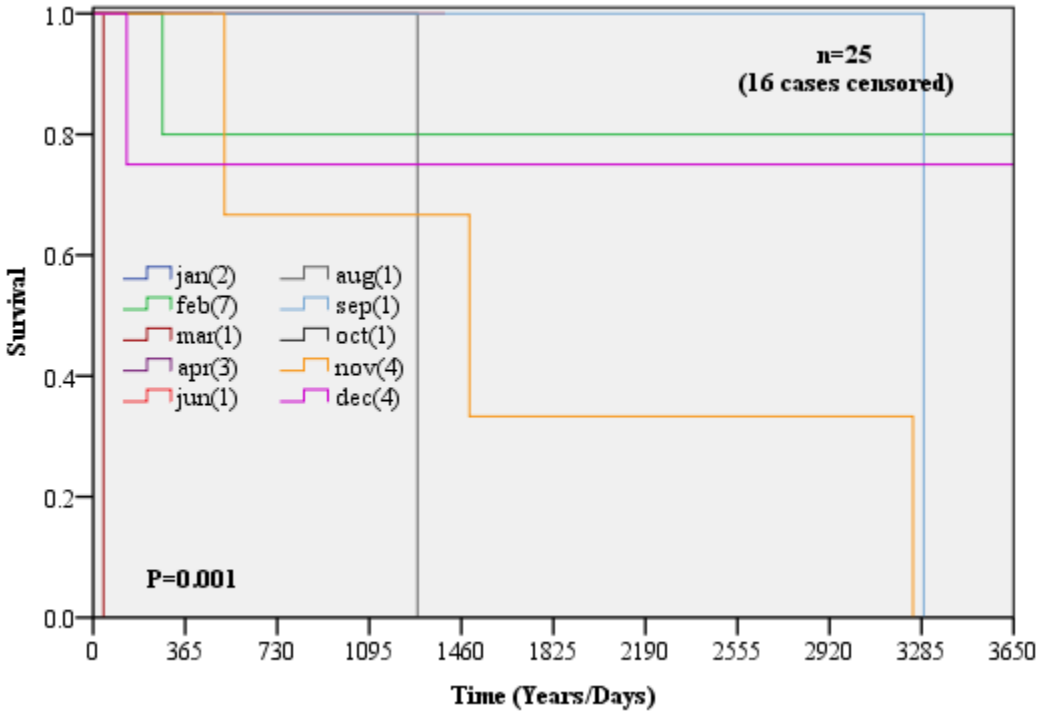


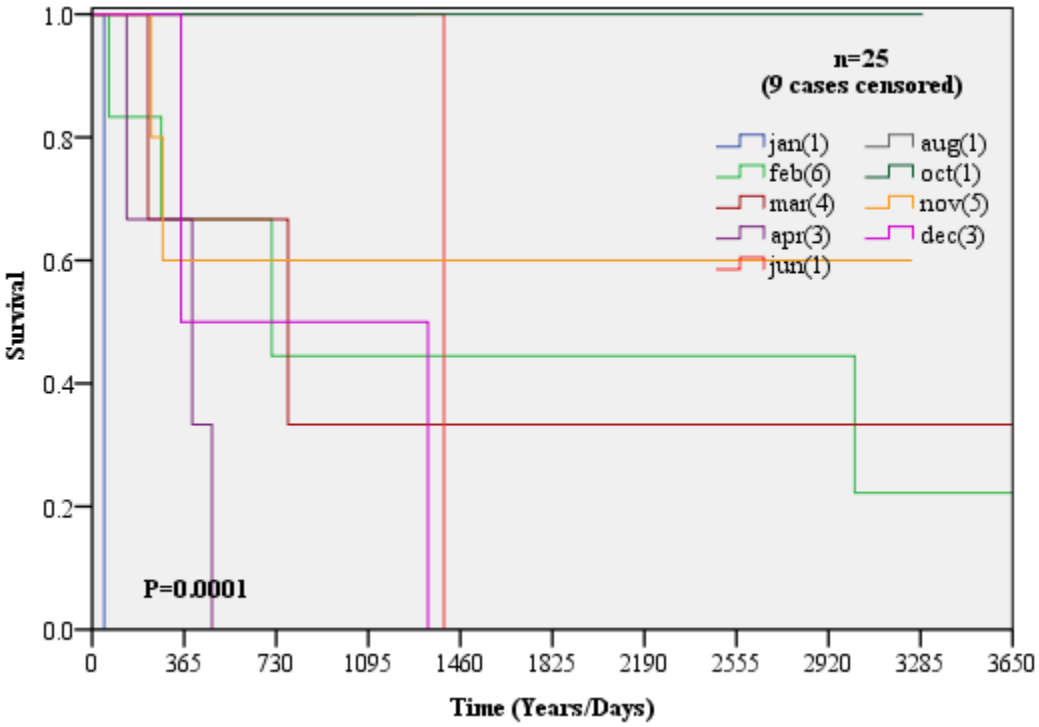
Table 3.13- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for females with SCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		<0.01	NS
Multivariate P value		NS	NS
Number of cases		25	25
Number of censored cases		9	16
HR (95% CI)	Jan	1	1
	Feb	N<5	N<5
	Mar	N<5	N<5
	Apr	N<5	N<5
	May	N<5	N<5
	Jun	N<5	N<5
	Jul	N<5	N<5
	Aug	N<5	N<5
	Sep	N<5	N<5
	Oct	N<5	N<5
	Nov	N<5	N<5
	Dec	N<5	N<5

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and month of first treatment.

•NS is not significant•N is number of uncensored cases•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.17- Survival according to month of first treatment for females with SCLC who received surgery: lung cancer deaths



Graph 3.18- Survival according to month of first treatment for females with SCLC who received surgery: non-lung-cancer deaths

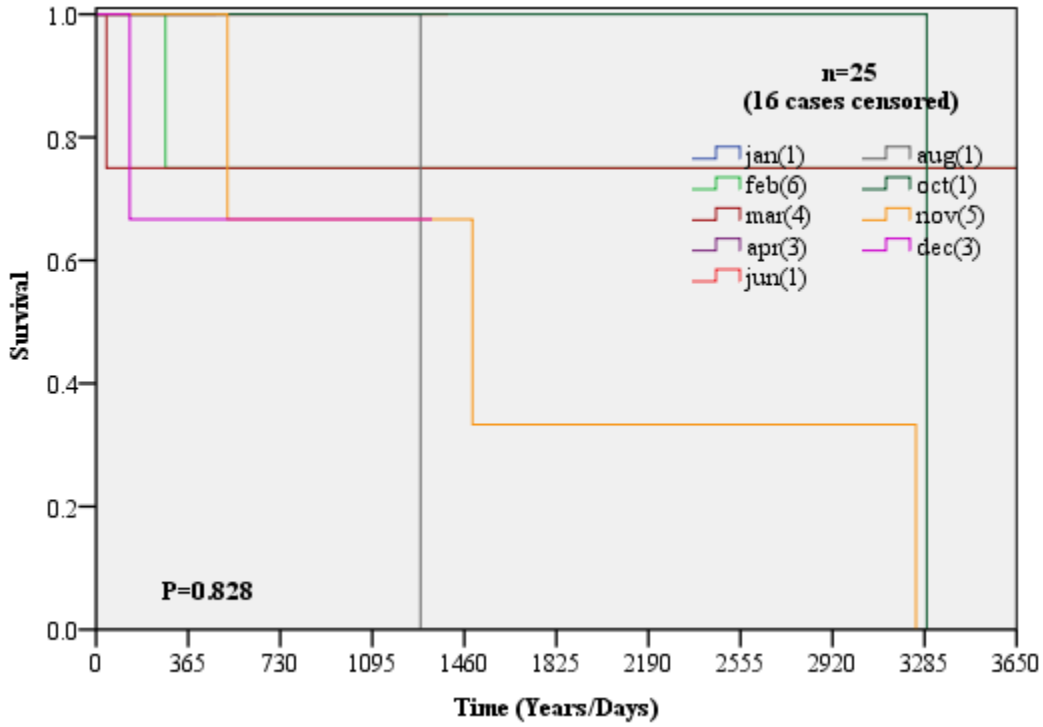


Table 3.14- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for females with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	25	9	NS	0.05	1	N<5	N<5	N<5	N<5
Other causes	25	16	NS	NS	1	N<5	N<5	N<5	N<5

(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

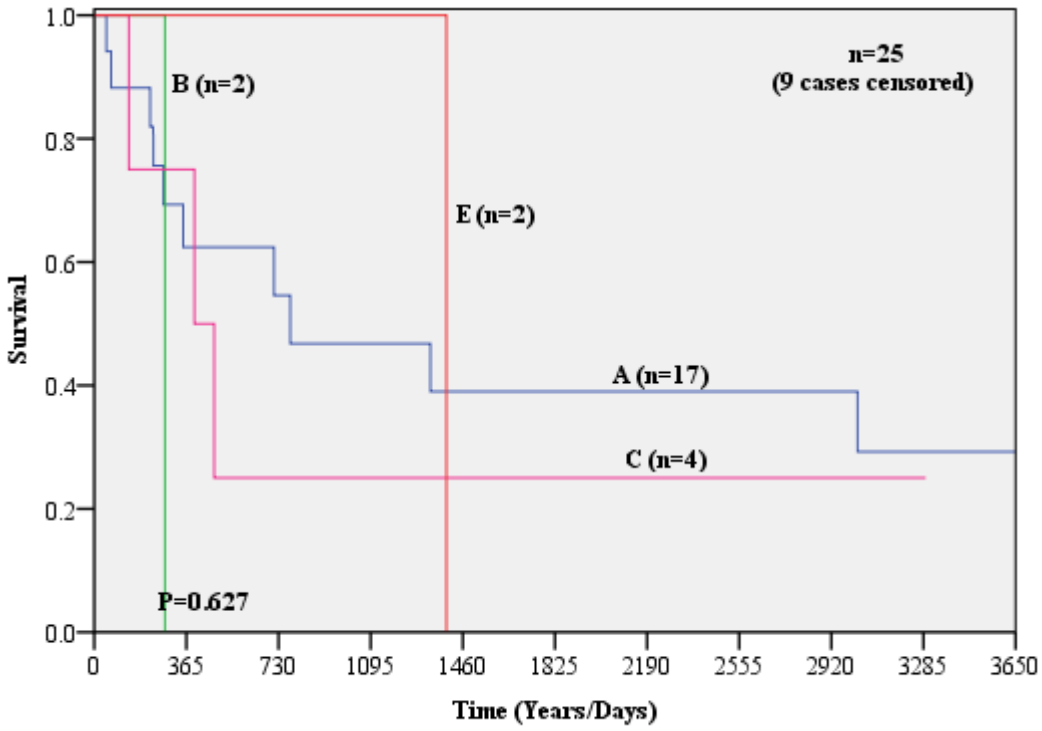
●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and monthly mean vitamin D sunshine index.

●NS is not significant

●N is number of uncensored cases

●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.19- Survival according to MMVDSI for females with SCLC who received surgery: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.20- Survival according to MMVDSI for females with SCLC who received surgery: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

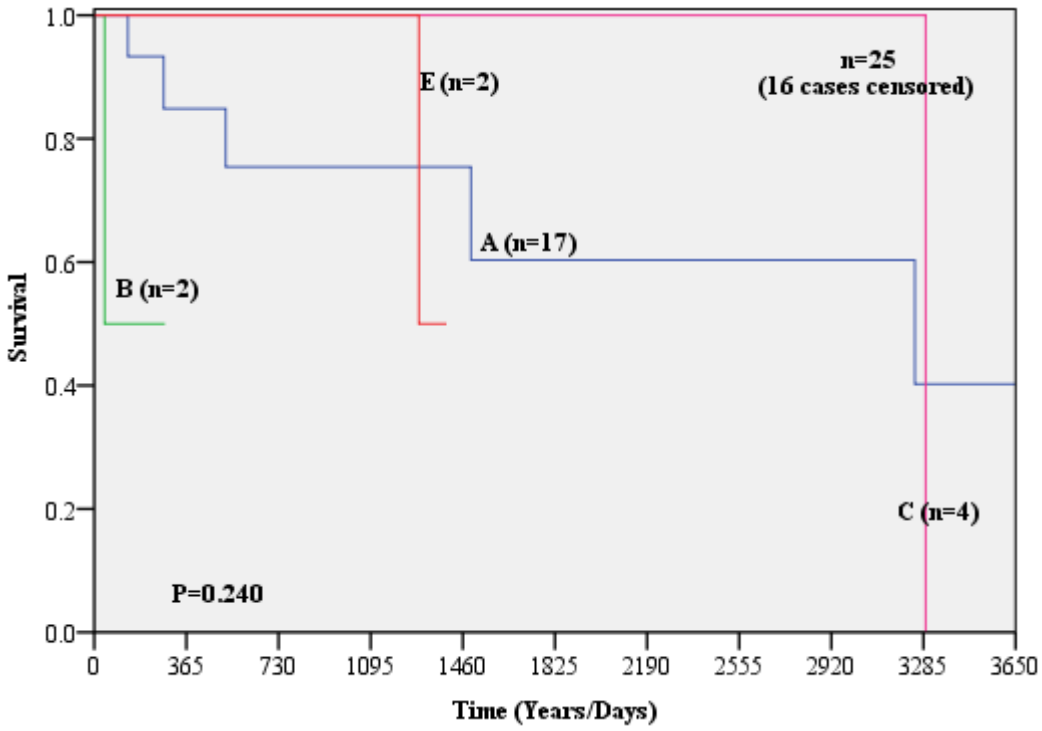


Table 3.15- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for male and female patients with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	70	17	NS	NS	1.39 (0.4-4.1)	1.72 (0.5-5.1)	1	1.16 (0.4-3.0)
Other causes	70	53	NS	NS	N<5	N<5	1	10.33 (0.0-1.8)

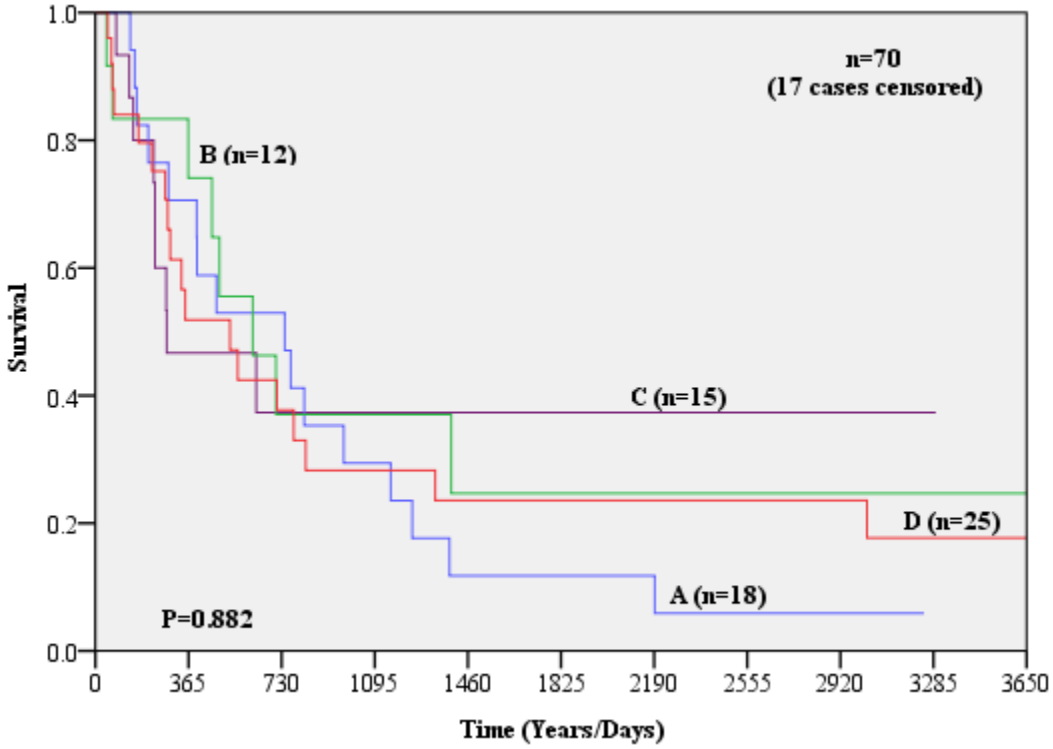
- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- N is number of uncensored cases

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.21- Survival according to season of diagnosis for male and female patients with SCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.22- Survival according to season of diagnosis for male and female patients with SCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

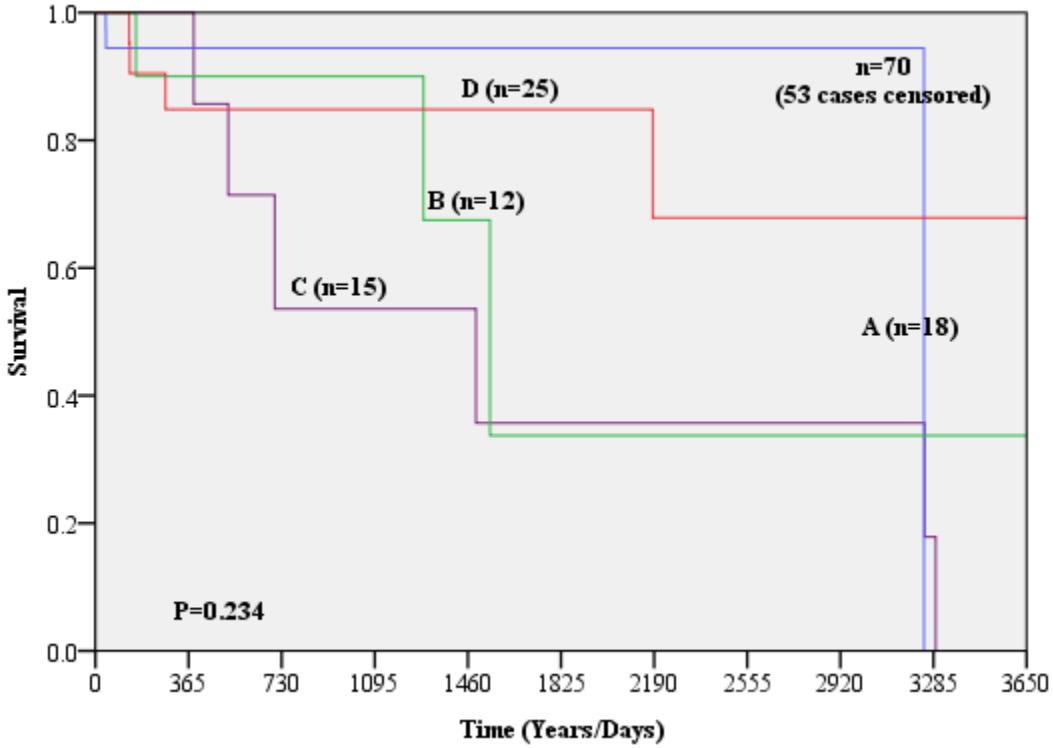


Table 3.16- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for male and female patients with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	70	17	NS	NS	1	1.95 0.6-5.7	0.81 0.2-2.2	1.22 0.5-2.7
Other causes	70	53	NS	NS	1	N<5	N<5	4.68 0.4-45.6

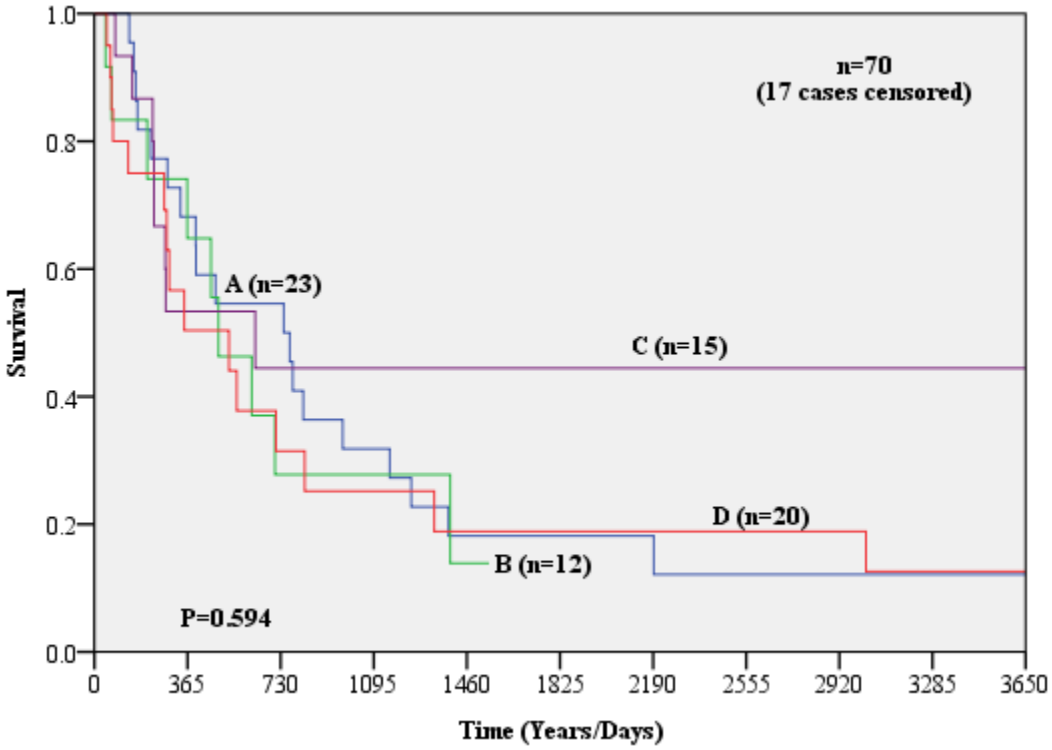
●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and season of first treatment.

●NS is not significant; A is spring, B is summer, C is fall and D is winter.

●N is number of uncensored cases

●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.23- Survival according to season of first treatment for male and female patients with SCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.24- Survival according to season of first treatment for male and female patients with SCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

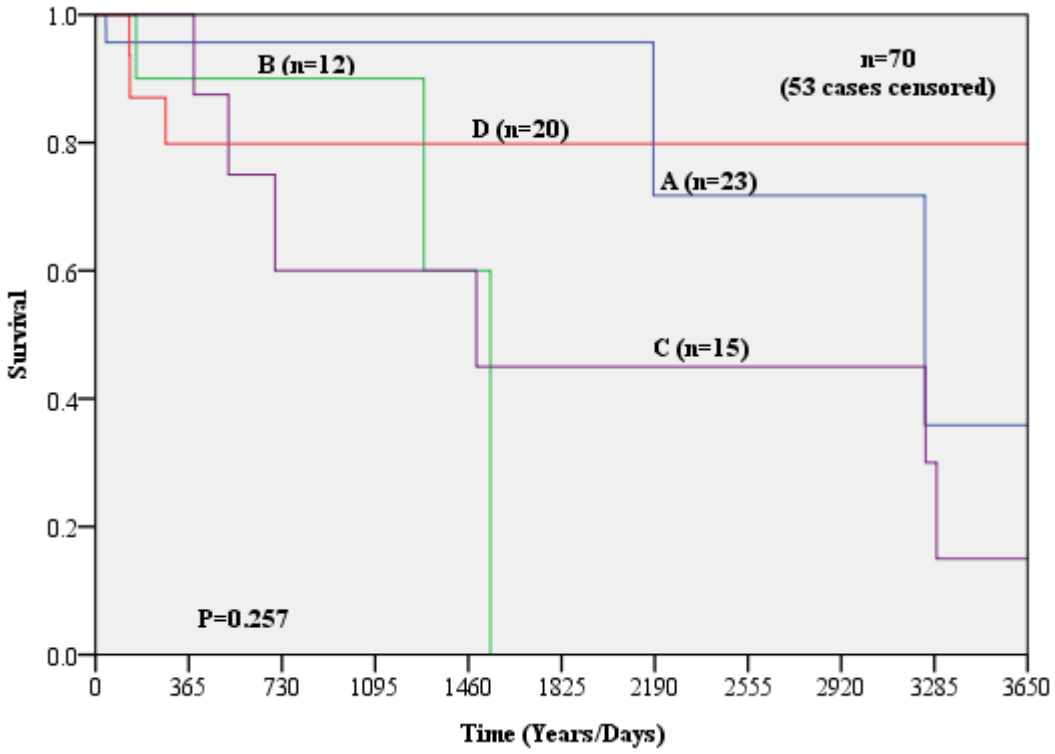


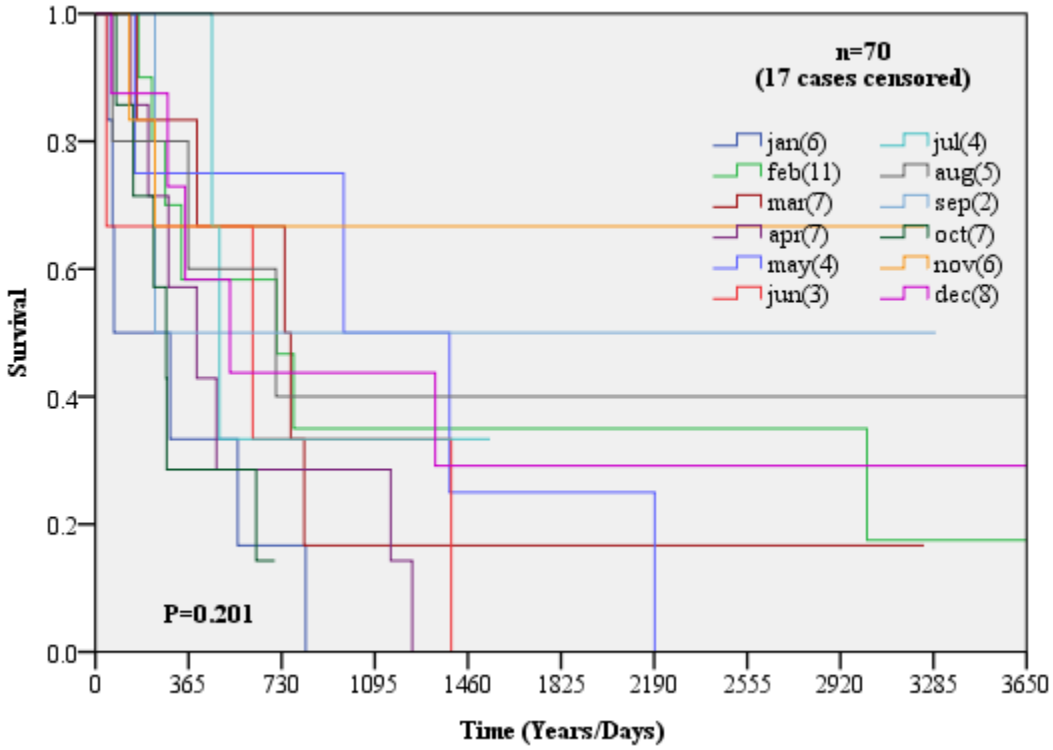
Table 3.17- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for male and female patients with SCLC who received surgery

Treatment		Surgery	
Cause of death		Lung cancer	Other causes
Univariate P value		NS	NS
Multivariate P value		0.010	NS
Number of cases		70	70
Number of censored cases		17	53
HR (95% CI)	Jan	1	1
	Feb	0.37 0.0-1.6	N<5
	Mar	0.07 0.0-0.4	N<5
	Apr	0.38 0.0-2.4	N<5
	May	N<5	N<5
	Jun	N<5	N<5
	Jul	N<5	N<5
	Aug	N<5	N<5
	Sep	N<5	N<5
	Oct	0.30 0.0-1.7	N<5
	Nov	N<5	N<5
	Dec	0.02 0.0-0.1	N<5

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and month of diagnosis.

•NS is not significant•N is number of uncensored cases•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.25- Survival according to month of diagnosis for male and female patients with SCLC who received surgery: lung cancer deaths



Graph 3.26- Survival according to month of diagnosis for male and female patients with SCLC who received surgery: non-lung-cancer deaths

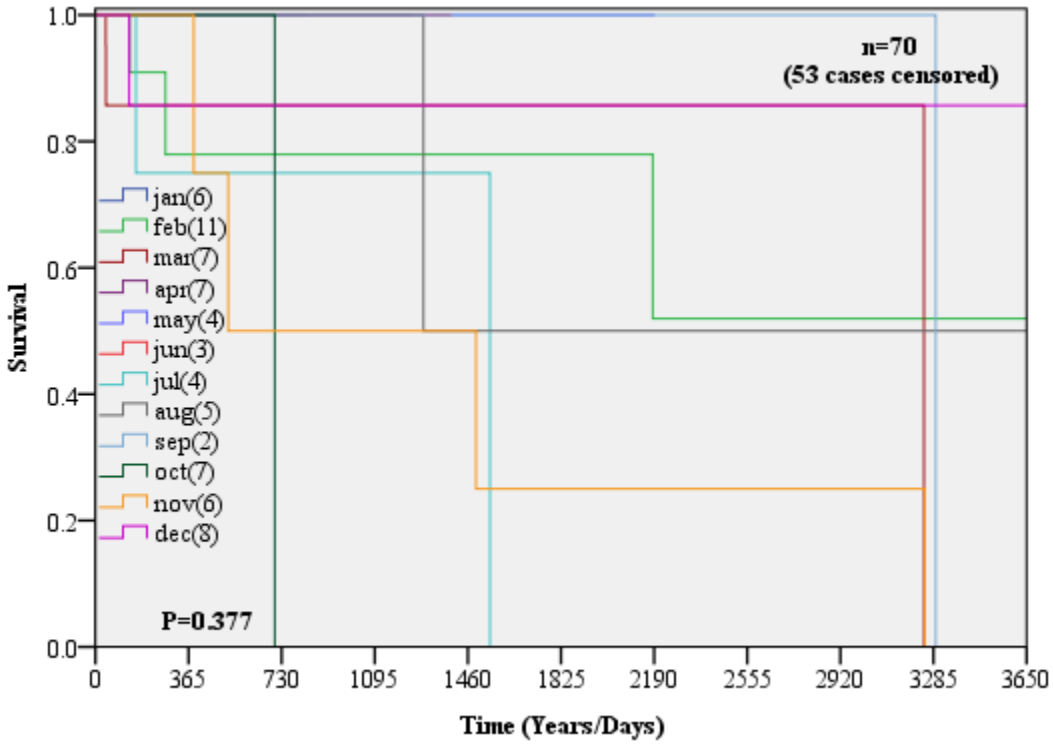


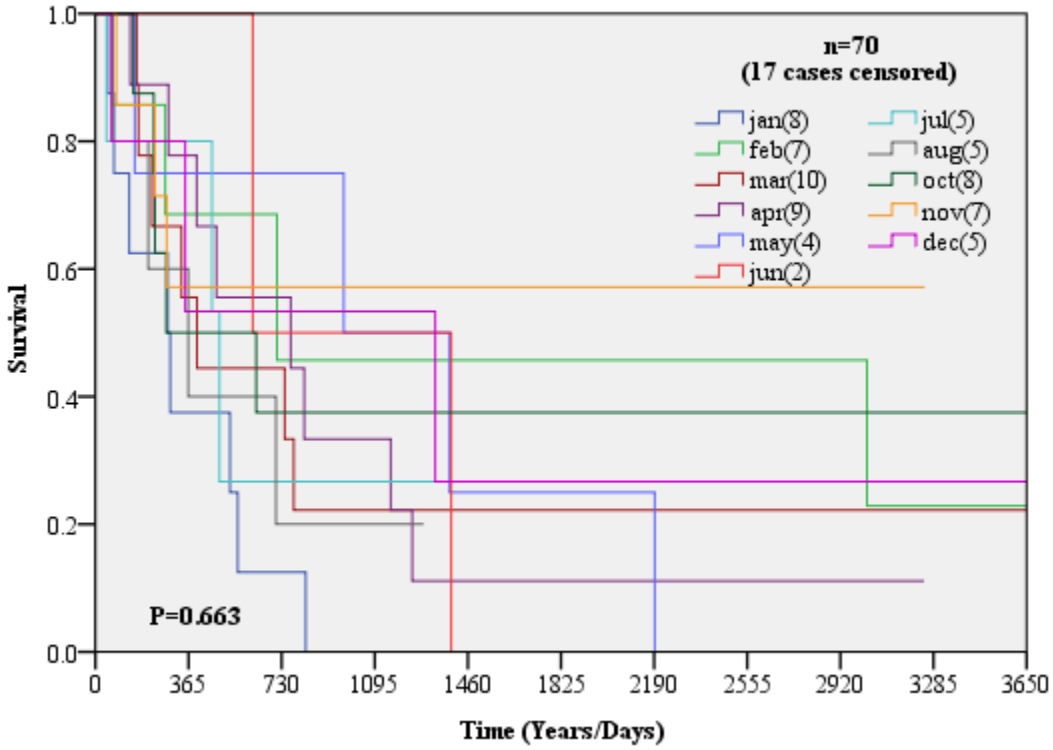
Table 3.18- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for male and female patients with SCLC who received surgery

Treatment		Surgery	
Cause of death		Lung cancer	Other causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		70	70
Number of censored cases		17	53
HR (95% CI)	Jan	1	1
	Feb	1.26 0.1-8.1	N<5
	Mar	0.44 0.1-1.7	N<5
	Apr	0.32 0.0-1.4	N<5
	May	N<5	N<5
	Jun	N<5	N<5
	Jul	N<5	N<5
	Aug	N<5	N<5
	Sep	N<5	N<5
	Oct	0.48 0.1-2.2	N<5
	Nov	N<5	N<5
	Dec	0.10 0.0-0.6	N<5

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and month of first •NS is not significant

•N is number of uncensored cases•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.27- Survival according to month of first treatment for male and female patients with SCLC who received surgery: lung cancer deaths



Graph 3.28- Survival according to month of first treatment for male and female patients with SCLC who received surgery: non-lung-cancer deaths

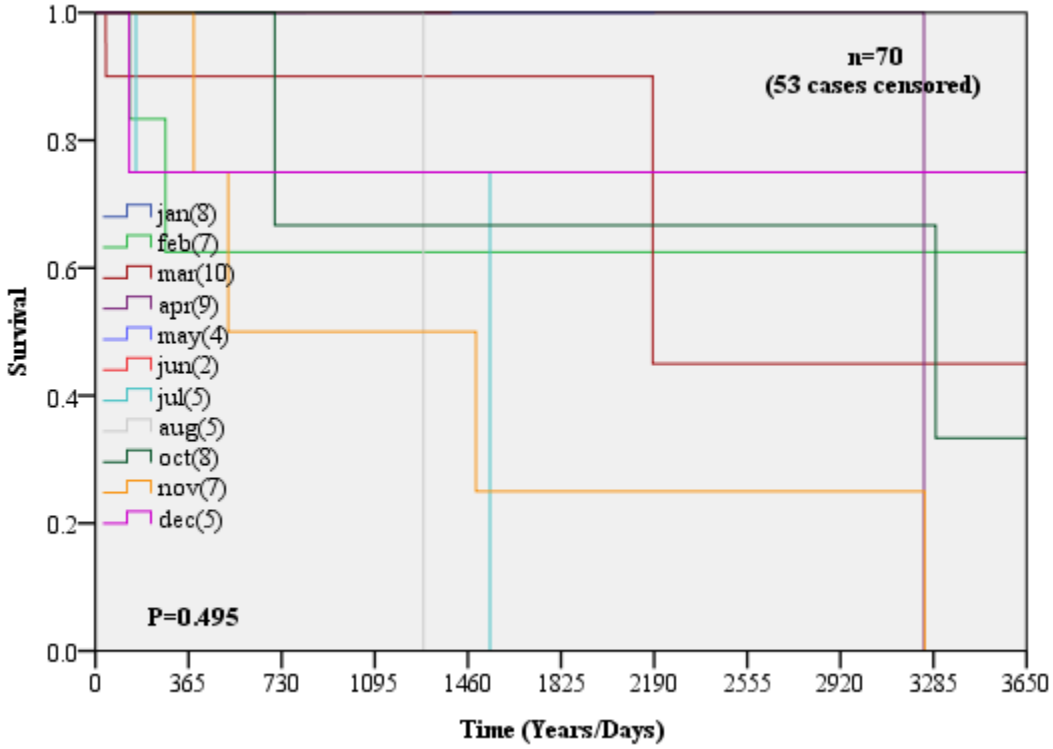


Table 3.19- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for male and female patients with SCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	70	17	NS	NS	1	0.81 0.2-2.2	2.33 0.8-6.7	2.43 0.8-6.7	N<5
Other causes	70	53	NS	NS	1	N<5	N<5	N<5	N<5

(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

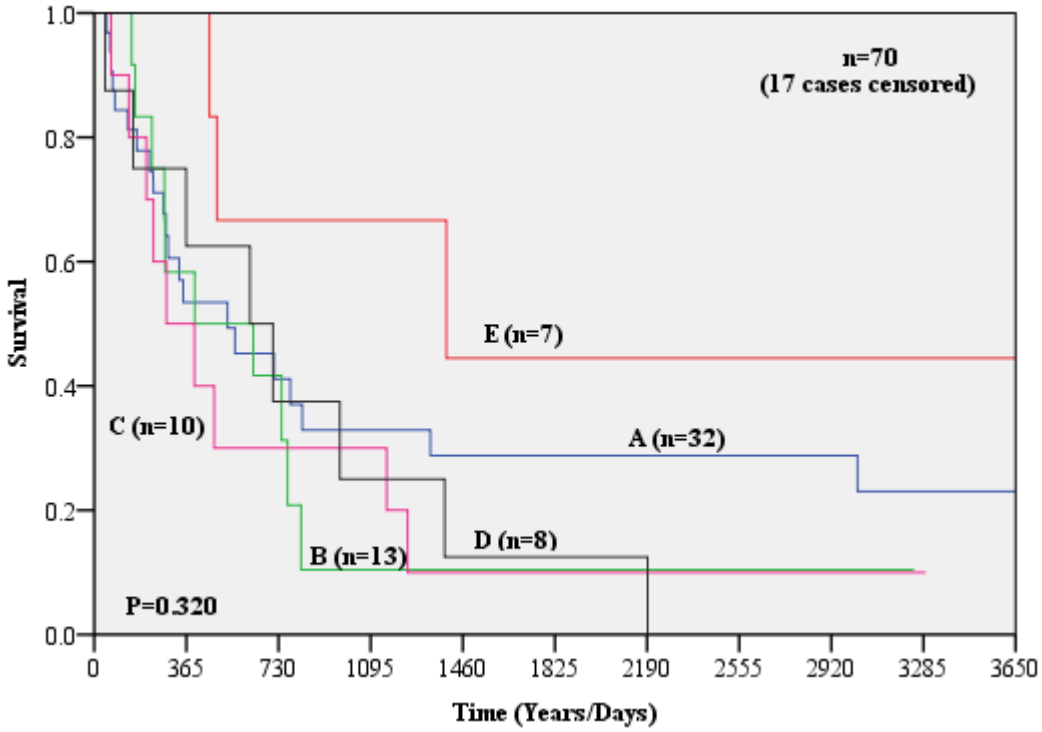
●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and chemotherapy), disease site and monthly mean vitamin D sunshine index.

●NS is not significant

●N is number of uncensored cases

●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.29- Survival according to MMVDSIfor male and female patients with SCLC who received surgery: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.30- Survival according to MMVDSIfor male and female patients with SCLC who received surgery: non-lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

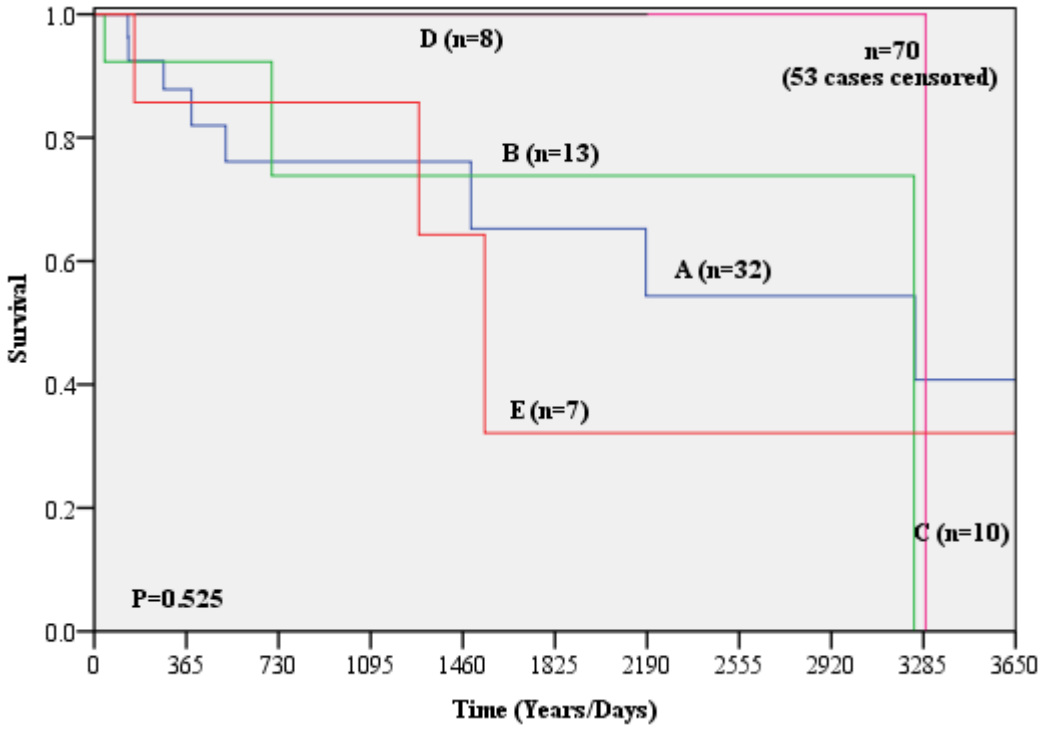


Table 3.20- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for males with SCLC who received radiotherapy

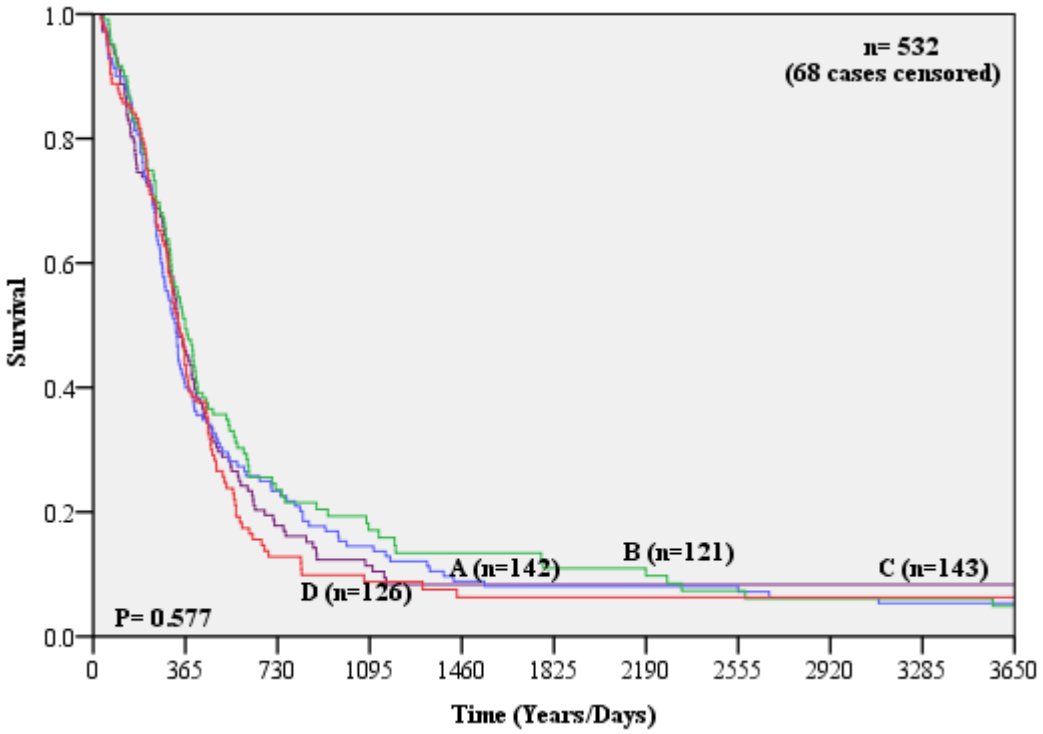
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	532	68	NS	0.043	1.04 0.8-1.3	0.88 0.7-1.1	1	1.13 0.8-1.4
Other causes	532	469	NS	NS	0.52 0.2-1.1	0.582 0.2-1.2	1	0.86 0.4-1.8

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.31- Survival according to season of diagnosis for males with SCLC who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.32- Survival according to season of diagnosis for males with SCLC who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

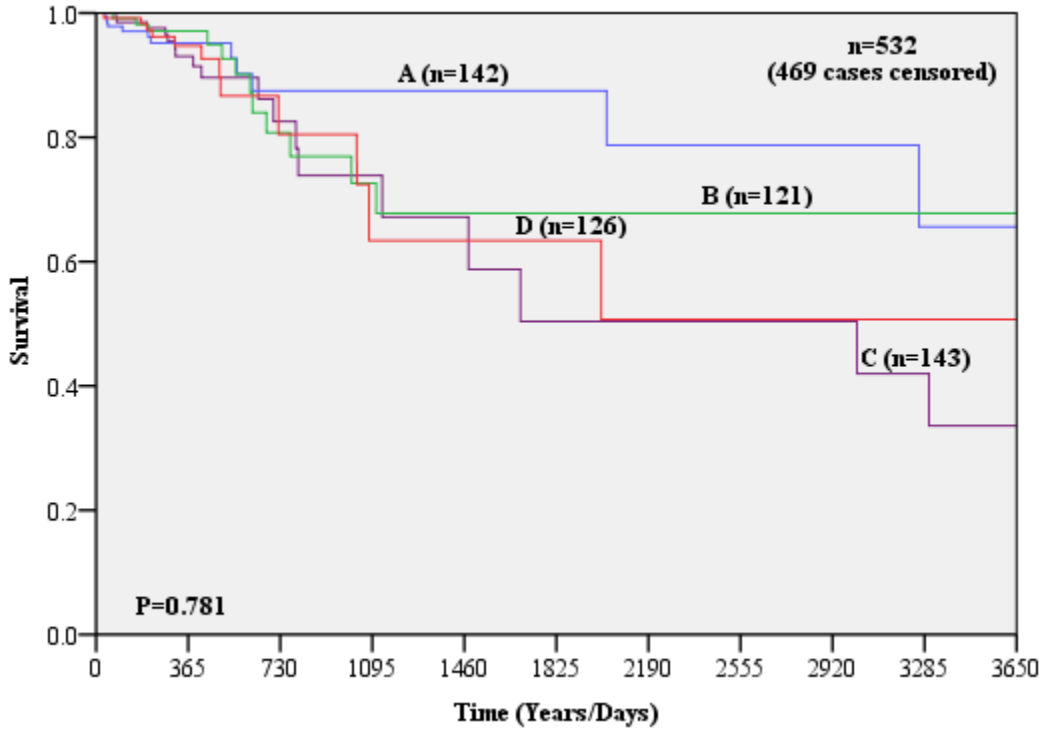


Table 3.21- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for males with SCLC who received radiotherapy

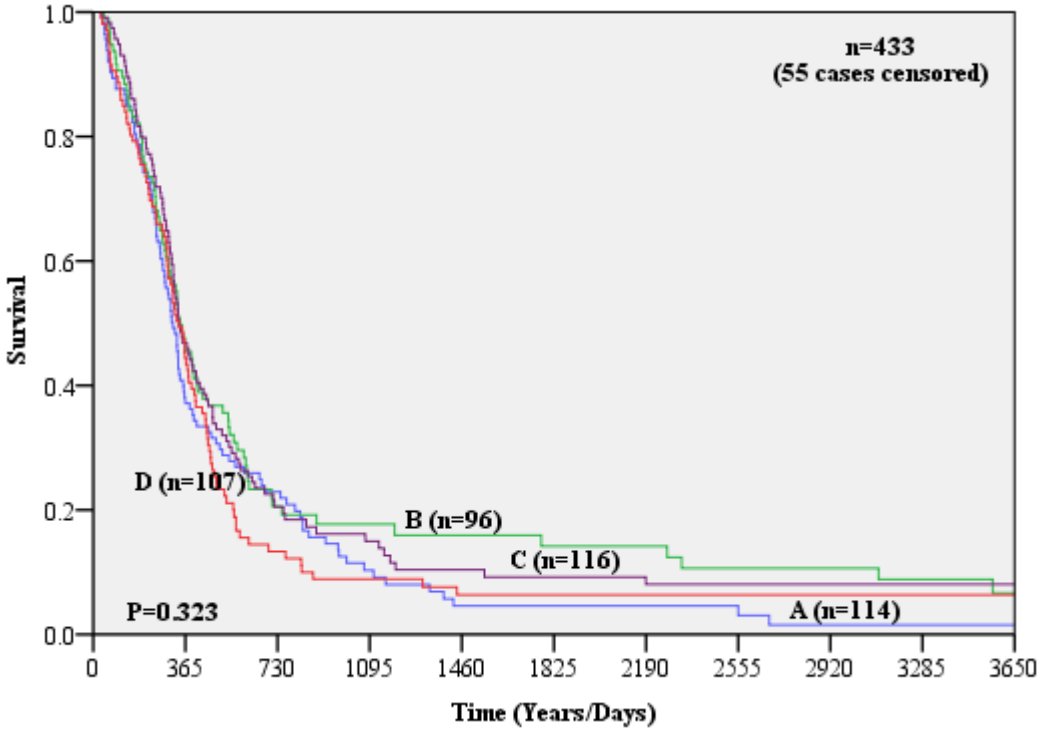
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	433	55	NS	0.038	1	0.78 0.5-1.0	0.76 0.5-1.0	0.96 0.7-1.2
Other causes	433	381	NS	NS	1	1.28 0.5-2.9	0.75 0.3-1.7	1.08 0.4-2.6

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death.

Graph 3.33- Survival according to season of first treatment for males with SCLC who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.34- Survival according to season of first treatment for males with SCLC who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

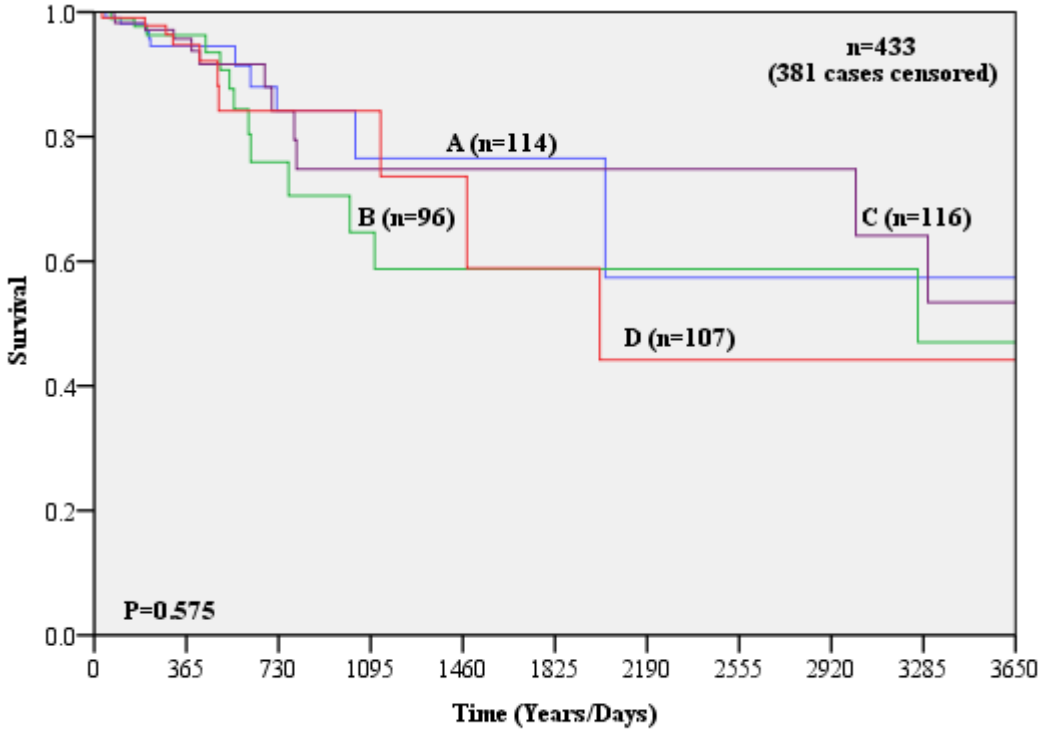


Table 3.22- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for males with SCLC who received radiotherapy

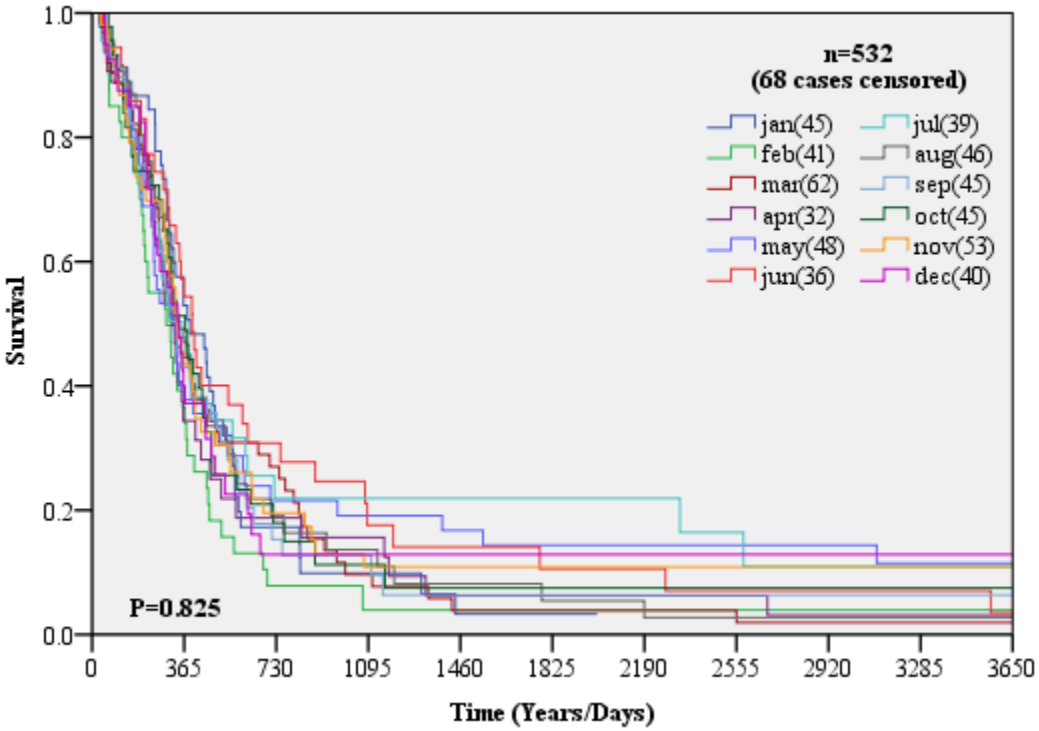
Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		532	532
Number of censored cases		68	469
HR (95% CI)	Jan	1	1
	Feb	1.35 0.8-2.1	N<5
	Mar	1.01 0.6-1.5	N<5
	Apr	1.02 0.6-1.6	N<5
	May	0.88 0.5-1.3	1.11 0.3-3.8
	Jun	0.74 0.4-1.1	N<5
	Jul	0.76 0.4-1.2	1.06 0.2-3.9
	Aug	0.93 0.6-1.4	N<5
	Sep	0.95 0.6-1.4	1.52 0.4-5.5
	Oct	0.91 0.5-1.4	1.10 0.2-4.4
	Nov	0.92 0.5-1.4	1.44 0.4-5.1
	Dec	0.89 0.5-1.4	1.46 0.3-5.5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and month of diagnosis.

●NS is not significant ●N is number of uncensored cases

●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.35- Survival according to month of diagnosis for males with SCLC who received radiotherapy: lung cancer deaths



Graph 3.36- Survival according to month of diagnosis for males with SCLC who received radiotherapy: non-lung-cancer deaths

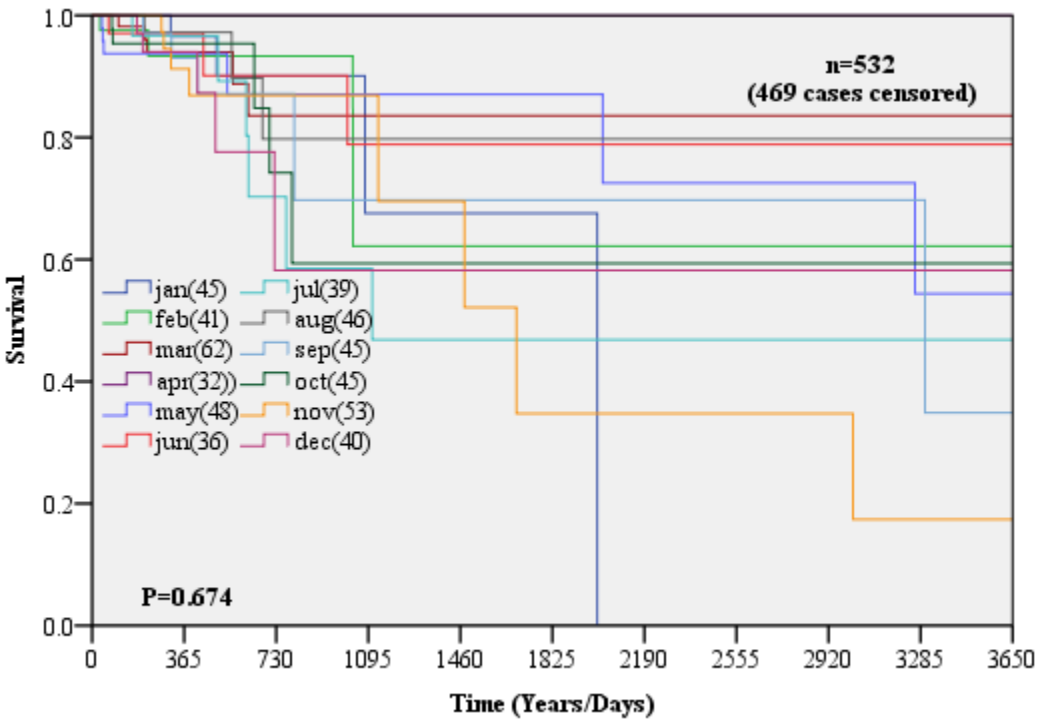


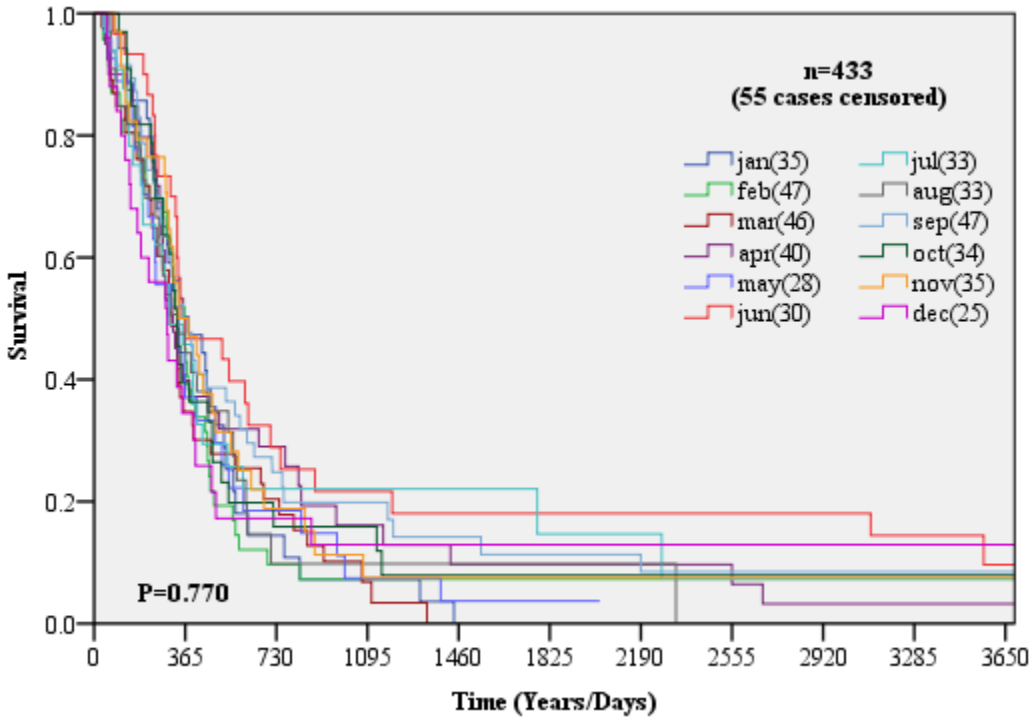
Table 3.23- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for males with SCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		433	433
Number of censored cases		55	381
HR (95% CI)	Jan	1	1
	Feb	1.05 0.6-1.7	0.80 0.1-3.9
	Mar	1.28 0.7-2.0	N<5
	Apr	0.89 0.5-1.46	0.77 0.1-3.6
	May	1.15 0.6-1.9	N<5
	Jun	0.71 0.4-1.2	N<5
	Jul	0.95 0.5-1.6	1.73 0.4-7.2
	Aug	1.05 0.6-1.7	1.92 0.4-8.4
	Sep	0.67 0.4-1.0	0.51 0.1-2.3
	Oct	0.79 0.4-1.3	N<5
	Nov	0.92 0.5-1.5	N<5
	Dec	1.12 0.6-1.9	N<5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and month of first treatment.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.37- Survival according to month of first treatment for males with SCLC who received radiotherapy: lung cancer deaths



Graph 3.38- Survival according to month of first treatment for males with SCLC who received radiotherapy: non-lung-cancer deaths

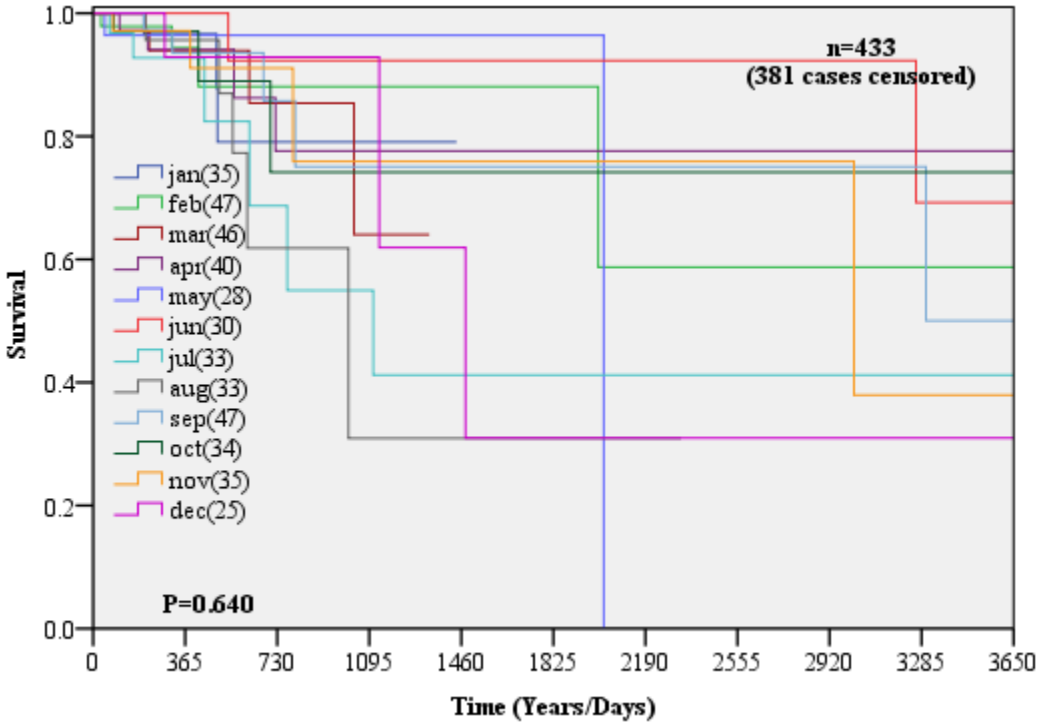


Table 3.24- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for males with SCLC who received radiotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	531	68	NS	NS	1	0.93 0.7-1.2	1.01 0.7-1.3	0.85 0.6-1.1	0.75 0.5-1.0
Other causes	531	468	NS	NS	1	0.70 0.3-1.5	0.57 0.2-1.4	0.69 0.3-1.4	0.81 0.3-1.8

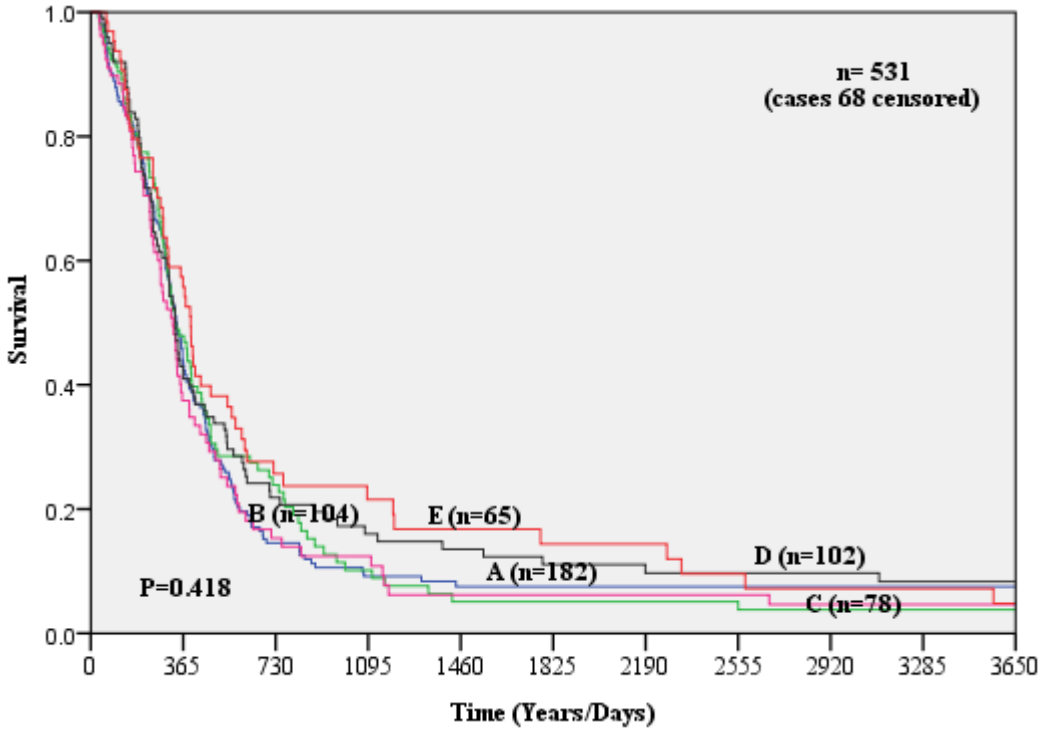
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.39- Survival according to MMVDSI for males with SCLC who received radiotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.40- Survival according to monthly MMVDSI for males with SCLC who received radiotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

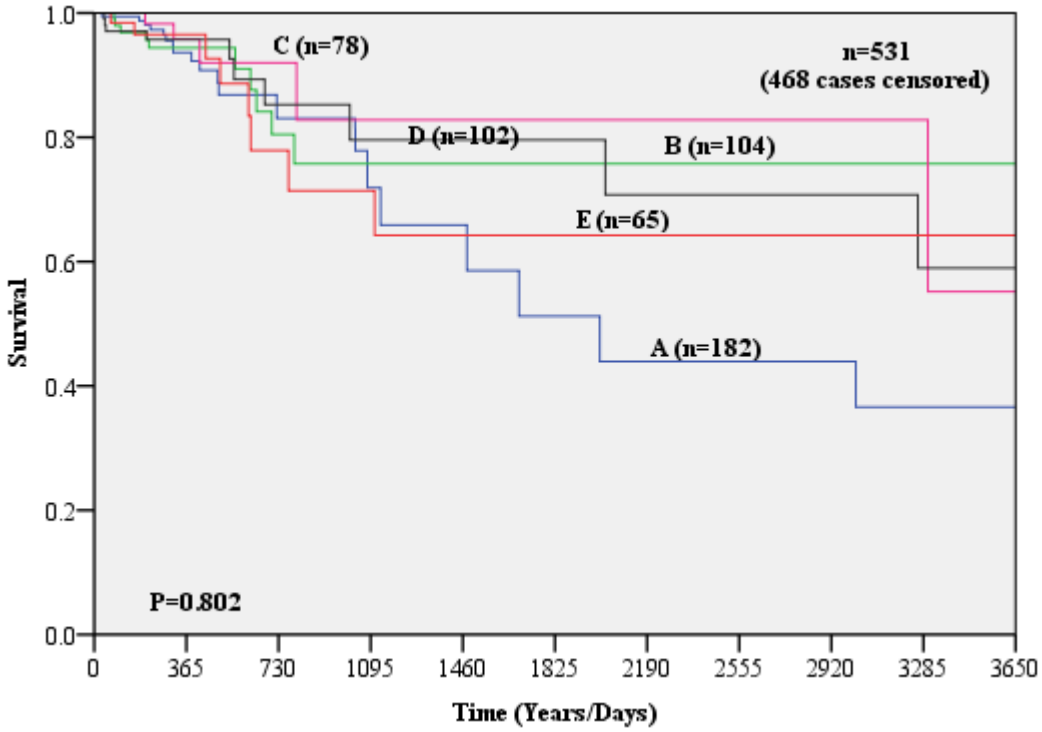
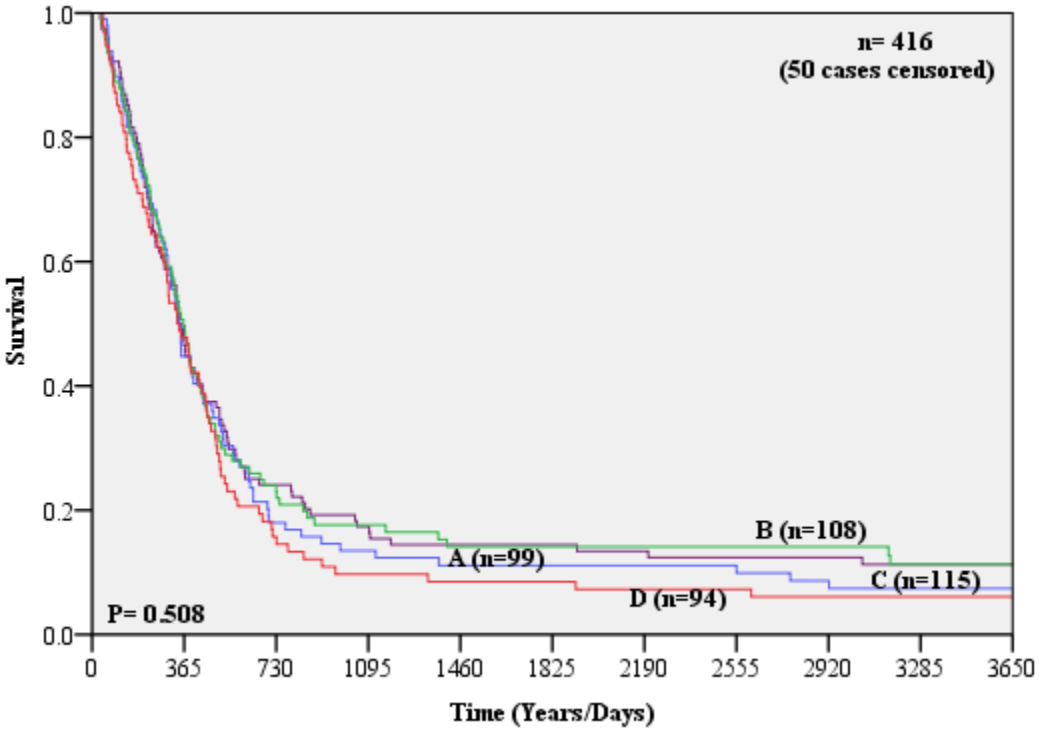


Table 3.25- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for females with SCLC who received radiotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	416	50	0.043	NS	1.19 0.8-1.6	0.86 0.6-1.1	1	1.32 0.9-1.7
Other causes	416	374	NS	NS	1.02 0.3-2.7	1.41 0.5-3.3	1	1.05 0.3-2.8

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and season of diagnosis.
- NS is not significant; A is spring, B is summer, C is fall and D is winter.
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.41- Survival according to season of diagnosis for females with SCLC who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.42- Survival according to season of diagnosis for females with SCLC who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

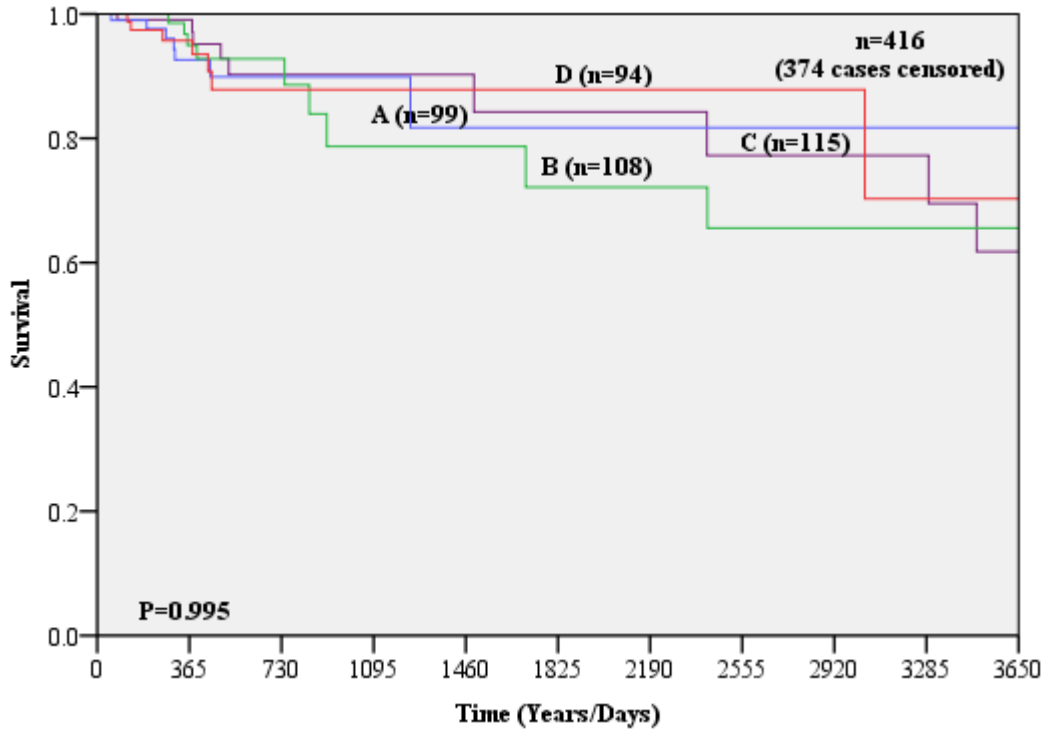


Table 3.26- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for females with SCLC who received radiotherapy

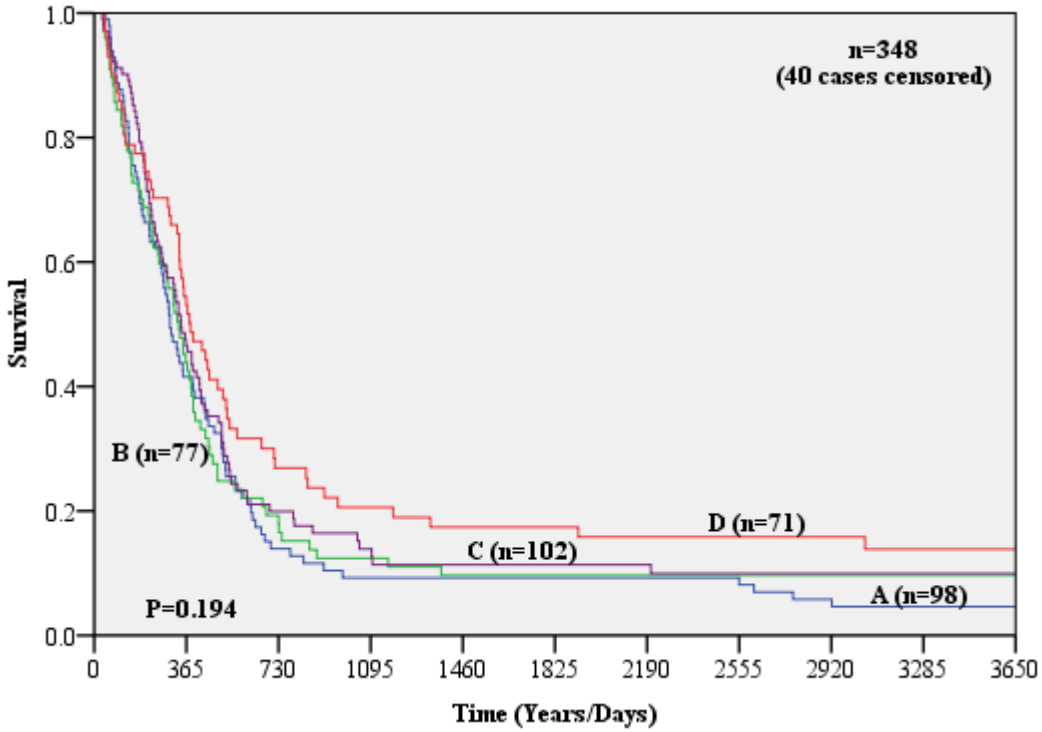
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	348	40	NS	NS	1	0.67 0.48-9.4	0.68 0.5-0.9	0.69 0.5-0.9
Other causes	348	314	NS	NS	1	1.12 0.31-3.9	1.31 0.4-3.6	1.40 0.4-4.0

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.43- Survival according to season of first treatment for females with SCLC who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.44- Survival according to season of first treatment for females with SCLC who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

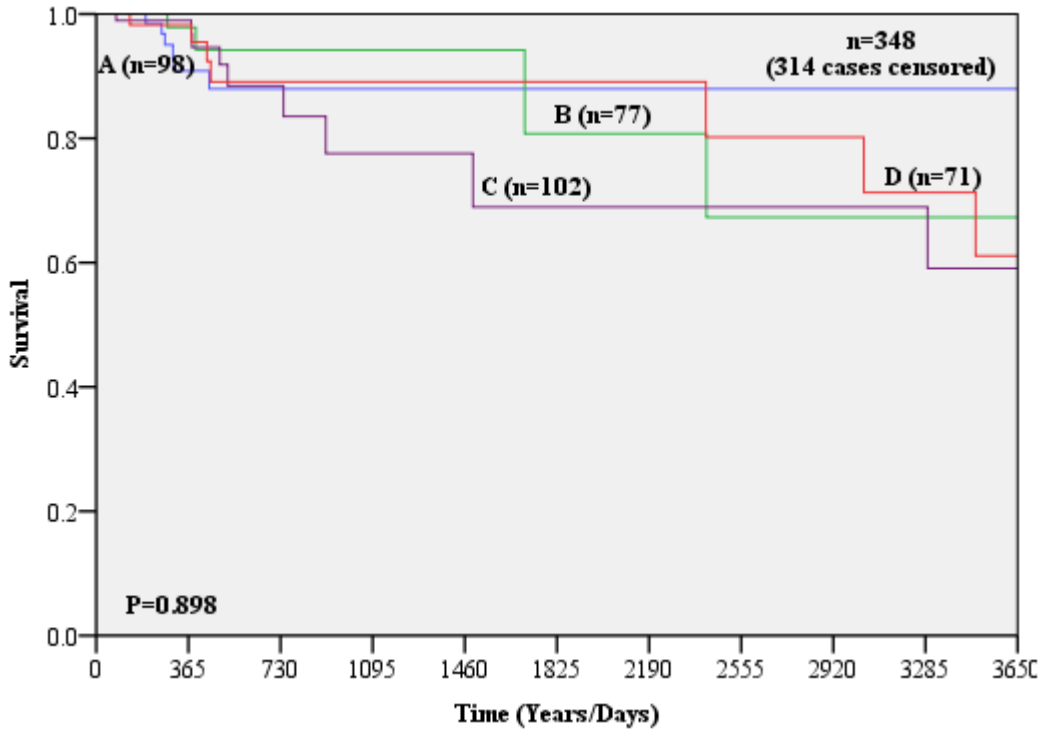


Table 3.27- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for females with SCLC who received radiotherapy

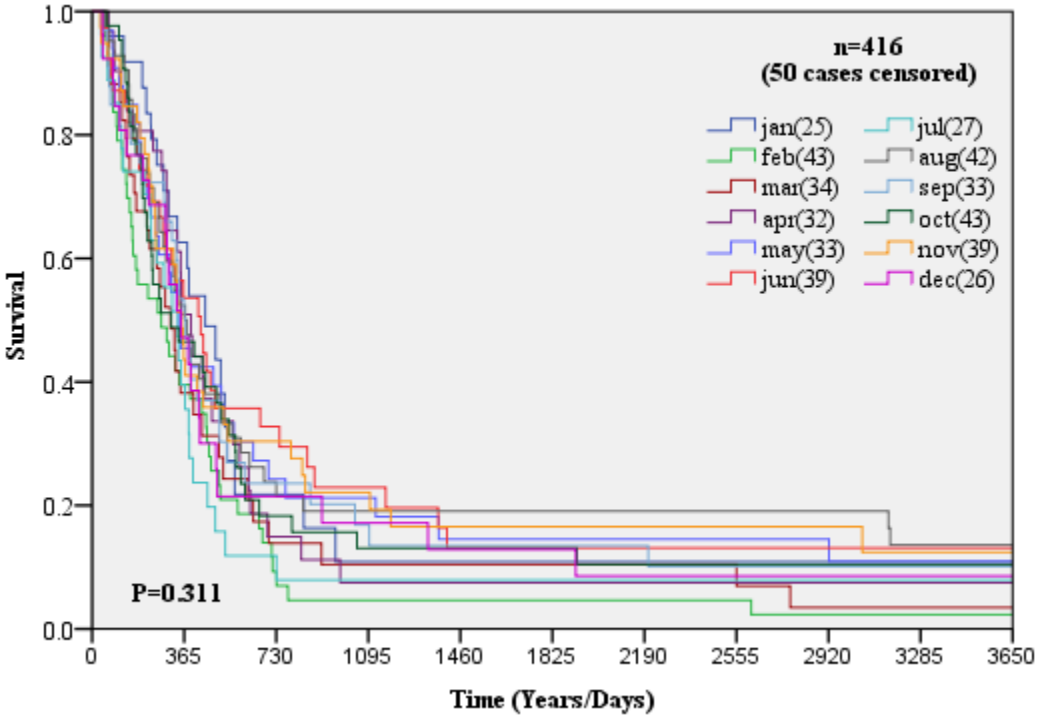
Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.062	NS
Number of of cases		416	416
Number of censored cases		50	374
HR (95% CI)	Jan	1	1
	Feb	1.85 1.0-3.2	N<5
	Mar	1.63 0.9-2.9	N<5
	Apr	1.23 0.6-2.2	N<5
	May	1.14 0.6-2.0	N<5
	Jun	0.84 0.4-1.5	0.71 0.2-2.4
	Jul	1.35 0.7-2.5	n<5
	Aug	0.89 0.5-1.6	n<5
	Sep	1.27 0.7-2.3	n<5
	Oct	1.00 0.5-1.7	n<5
	Nov	1.09 0.6-1.9	n<5
	Dec	1.44 0.7-2.7	n<5

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and month of diagnosis.

•NS is not significant•N is number of uncensored cases

•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.45- Survival according to month of diagnosis for females with SCLC who received radiotherapy: lung cancer deaths



Graph 3.46- Survival according to month of diagnosis for females with SCLC who received radiotherapy: non-lung-cancer deaths

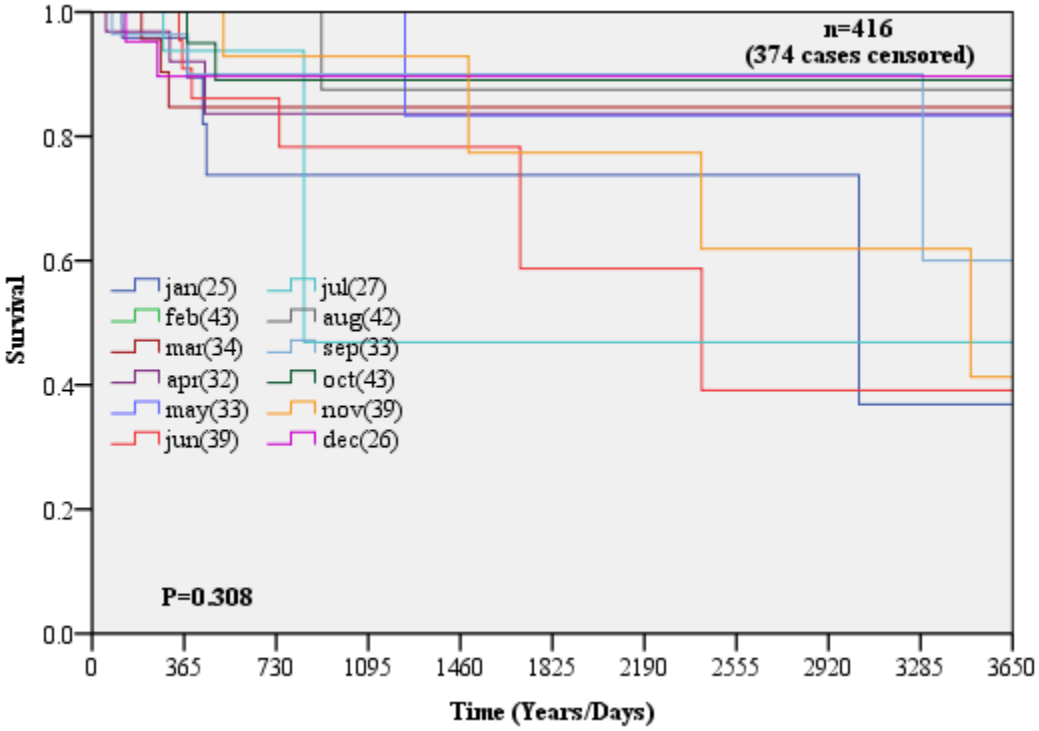


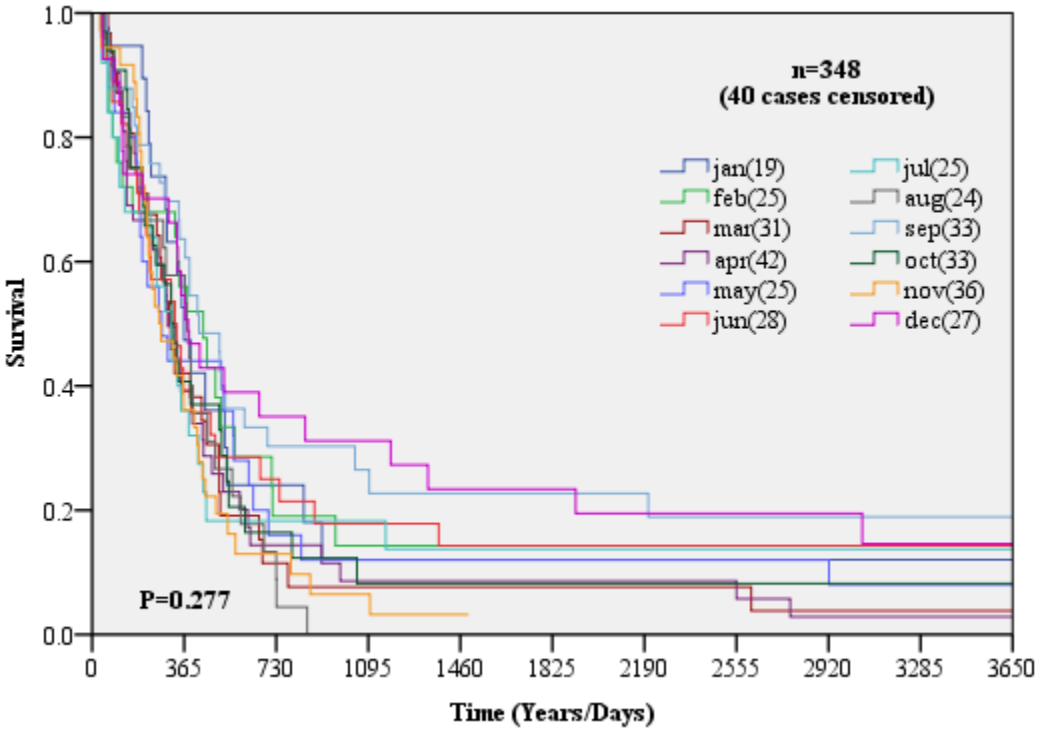
Table 3.28- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for females with SCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.045	NS
Number of cases		348	348
Number of censored cases		40	314
HR (95% CI)	Jan	1	1
	Feb	1.05 0.5-2.0	N<5
	Mar	1.61 0.8-3.0	N<5
	Apr	1.51 0.8-2.7	N<5
	May	0.97 0.6-1.8	N<5
	Jun	0.91 0.4-1.7	1.31 0.0-17.9
	Jul	0.83 0.4-1.6	n<5
	Aug	1.06 0.5-2.0	N<5
	Sep	0.63 0.3-1.2	N<5
	Oct	1.02 0.5-1.9	N<5
	Nov	1.29 0.6-2.4	N<5
	Dec	0.74 0.3-1.4	N<5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and month of first treatment.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.47- Survival according to month of first treatment for females with SCLC who received radiotherapy: lung cancer deaths



Graph 3.48- Survival according to month of first treatment for females with SCLC who received radiotherapy: non-lung-cancer deaths

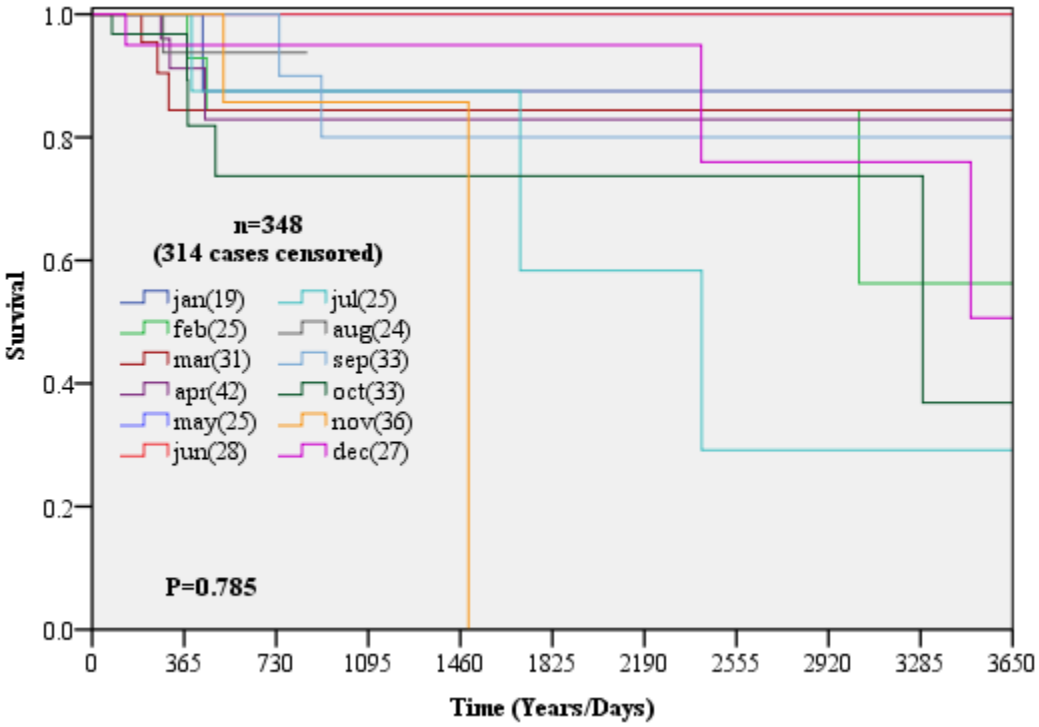


Table 3.29- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for females with SCLC who received radiotherapy

Cause of Death	Total number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	414	49	NS	NS	1	0.98 0.7-1.3	0.95 0.6-1.3	0.75 0.5-1.0	0.80 0.5-1.1
Other causes	414	373	NS	NS	1	1.14 0.4-3.1	1.42 0.5-3.6	0.96 0.3-2.6	1.40 0.4-4.3

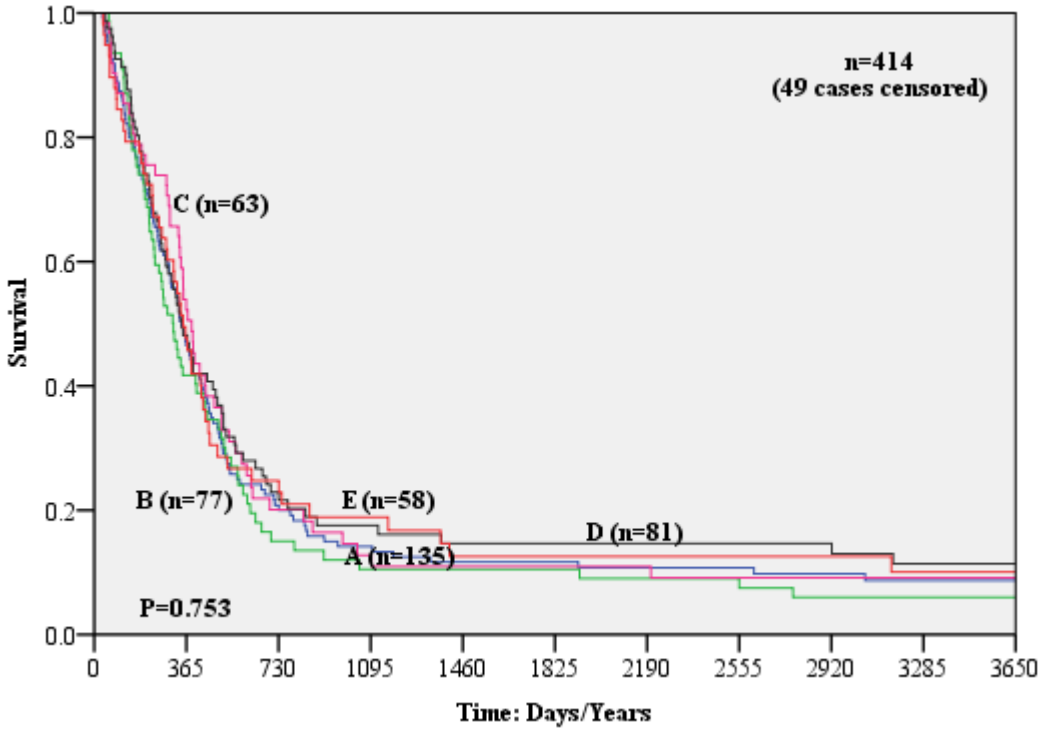
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and monthly mean vitamin D sunshine index.

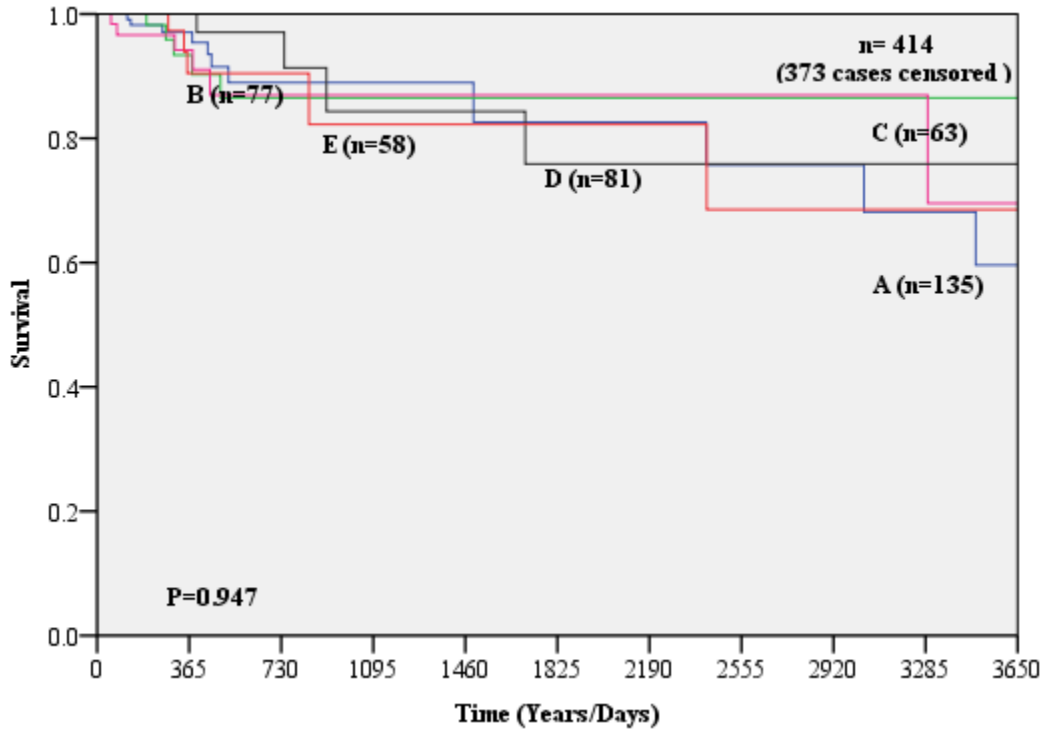
- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.49- Survival according to MMVDSI for females with SCLC who received radiotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.50- Survival according to MMVDSI for females with SCLC who received radiotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



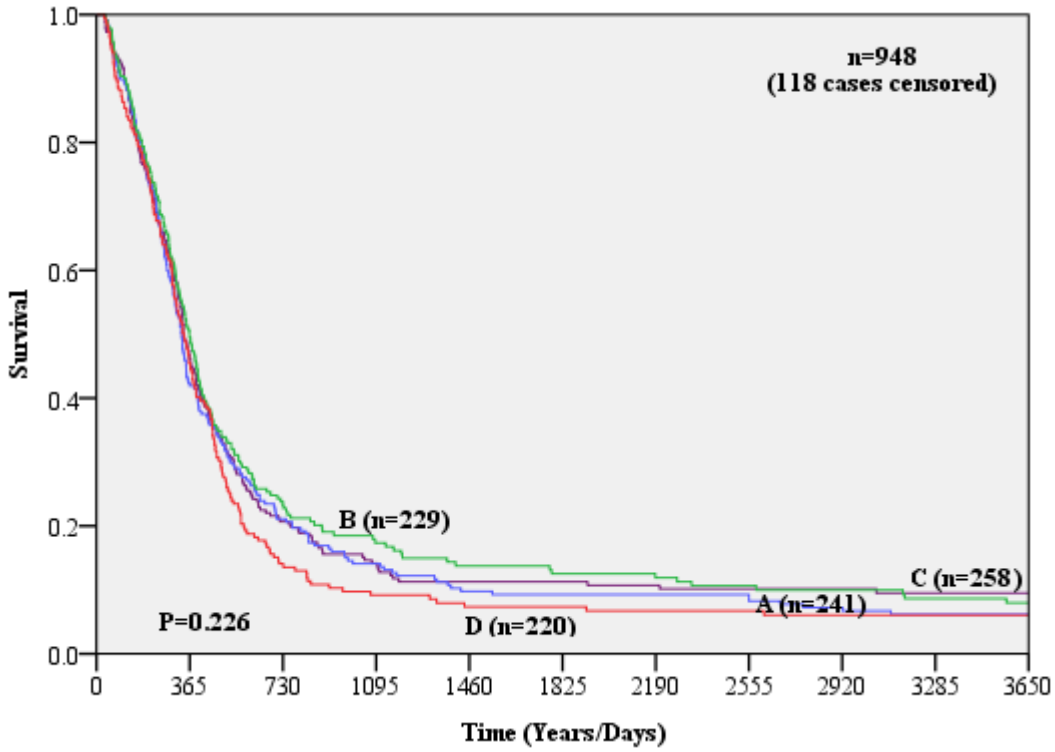
Table

3.30- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for male and female patients with SCLC who received radiotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	948	118	NS	0.041	1.07 0.8-1.2	0.89 0.7-1.0	1	1.19 0.9-1.4
Other causes	948	843	NS	NS	0.84 0.4-1.4	0.85 0.5-1.4	1	1.03 0.5-1.8

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and season of diagnosis.
- NS is not significant; A is spring, B is summer, C is fall and D is winter.
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.51- Survival according to season of diagnosis for male and female SCLC patients who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.52- Survival according to season of diagnosis for male and female SCLC patients who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

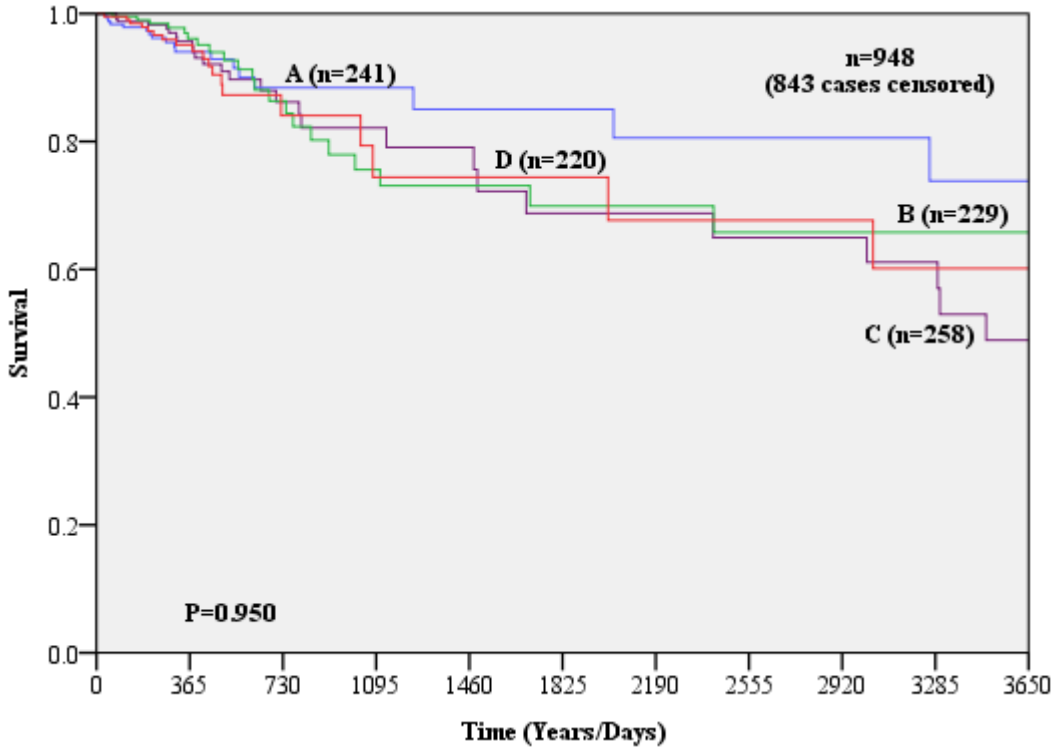


Table 3.31- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for male and female patients with SCLC who received radiotherapy

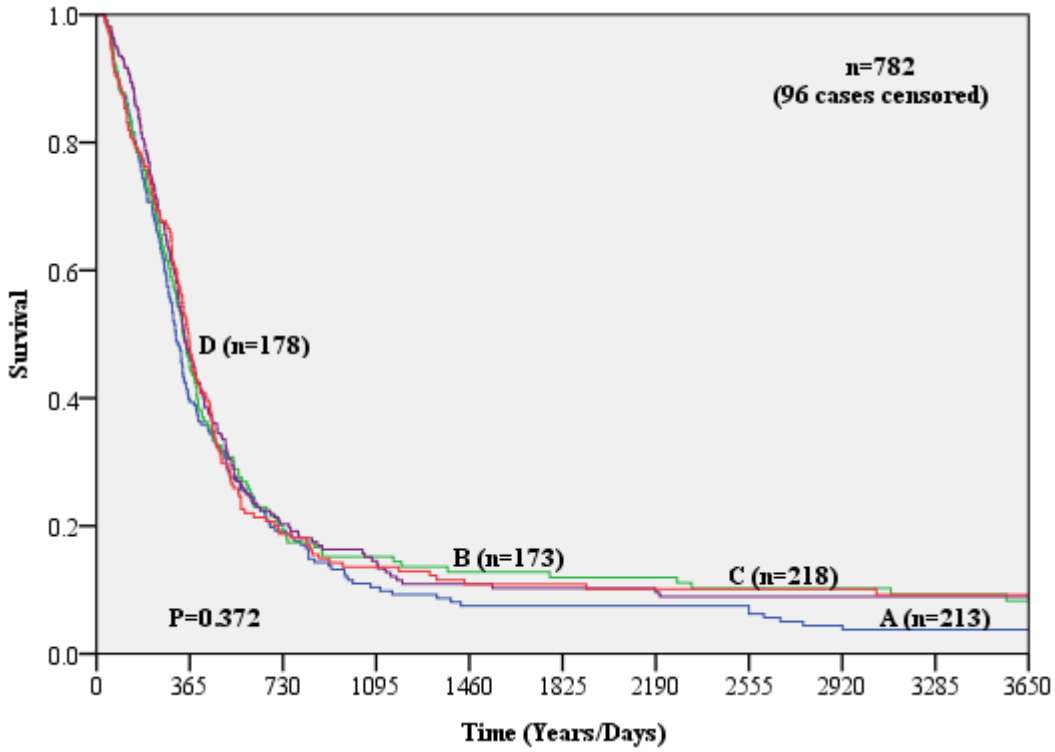
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	782	96	NS	<0.01	1	0.78 0.6-0.9	0.73 0.6-0.9	0.85 0.6-1.0
Other causes	782	696	NS	NS	1	1.28 0.6-2.4	1.06 0.5-1.9	1.12 0.5-2.1

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.53- Survival according to season of first treatment for male and female SCLC patients who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.54- Survival according to season of first treatment for male and female SCLC patients who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

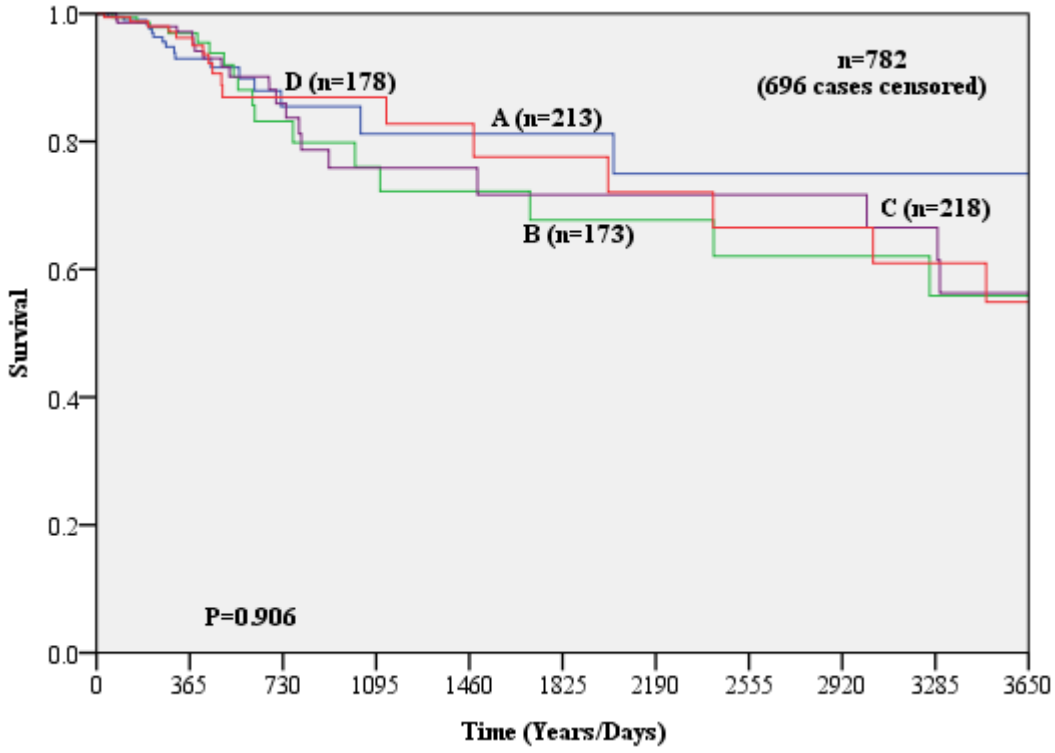


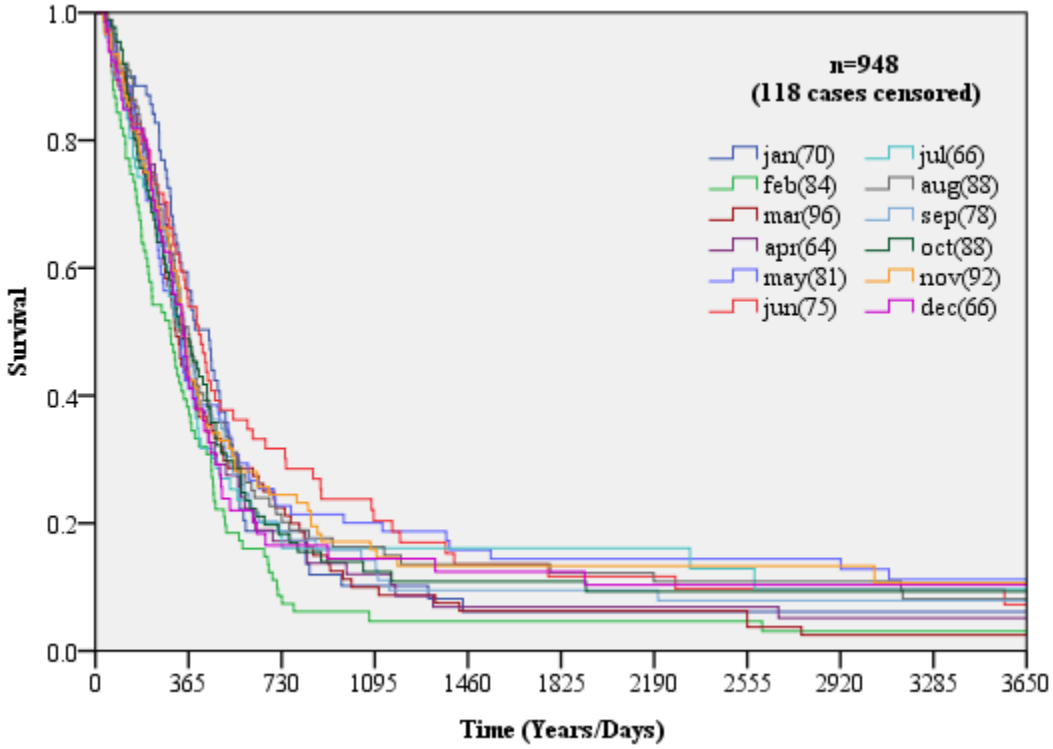
Table 3.32- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for male and female patients with SCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.033	NS
Number of cases		948	948
Number of censored cases		118	843
HR (95% CI)	Jan	1	1
	Feb	1.53 0.1-2.1	N<5
	Mar	1.20 0.8-1.6	0.64 0.2-1.6
	Apr	1.08 0.7-1.5	N<5
	May	0.91 0.6-1.3	0.67 0.2-1.6
	Jun	0.78 0.5-1.1	0.74 0.3-1.8
	Jul	0.99 0.6-1.4	0.72 0.2-1.8
	Aug	0.92 0.6-1.2	0.33 0.1-0.9
	Sep	1.02 0.7-1.4	0.84 0.3-2.0
	Oct	0.97 0.6-1.3	0.45 0.1-1.1
	Nov	1.00 0.7-1.4	0.84 0.3-2.0
	Dec	1.07 0.7-1.5	0.68 0.2-1.8

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and month of diagnosis.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.55- Survival according to month of diagnosis for male and female SCLC patients who received radiotherapy: lung cancer deaths



Graph 3.56- Survival according to month of diagnosis for male and female SCLC patients who received radiotherapy: non-lung-cancer deaths

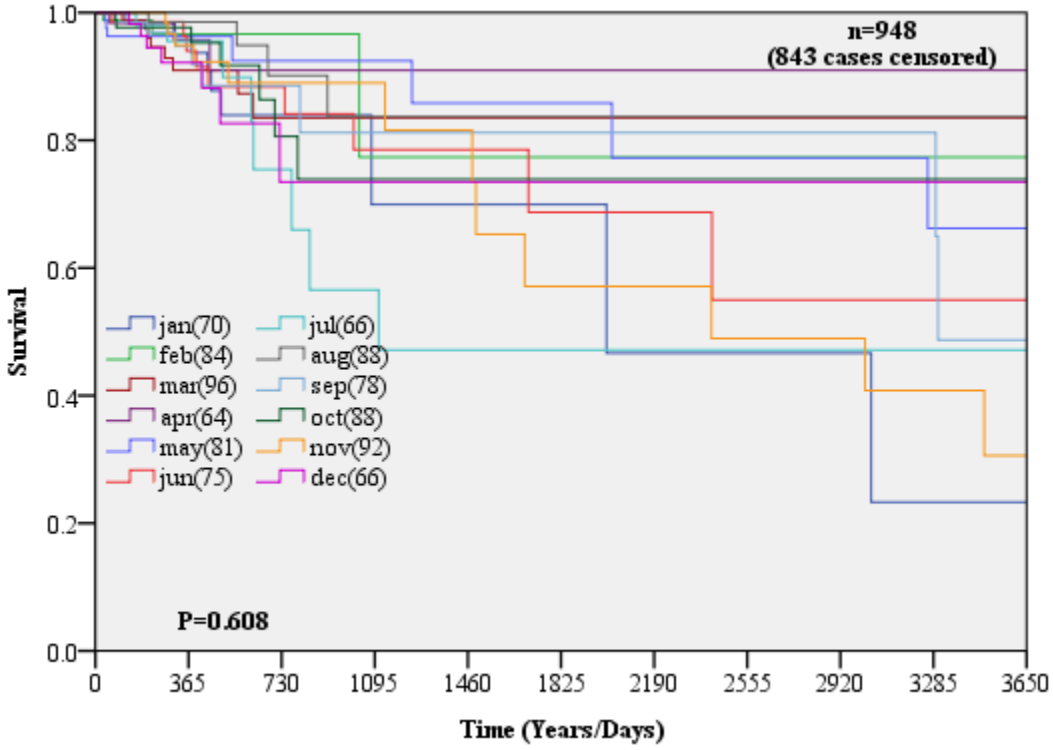


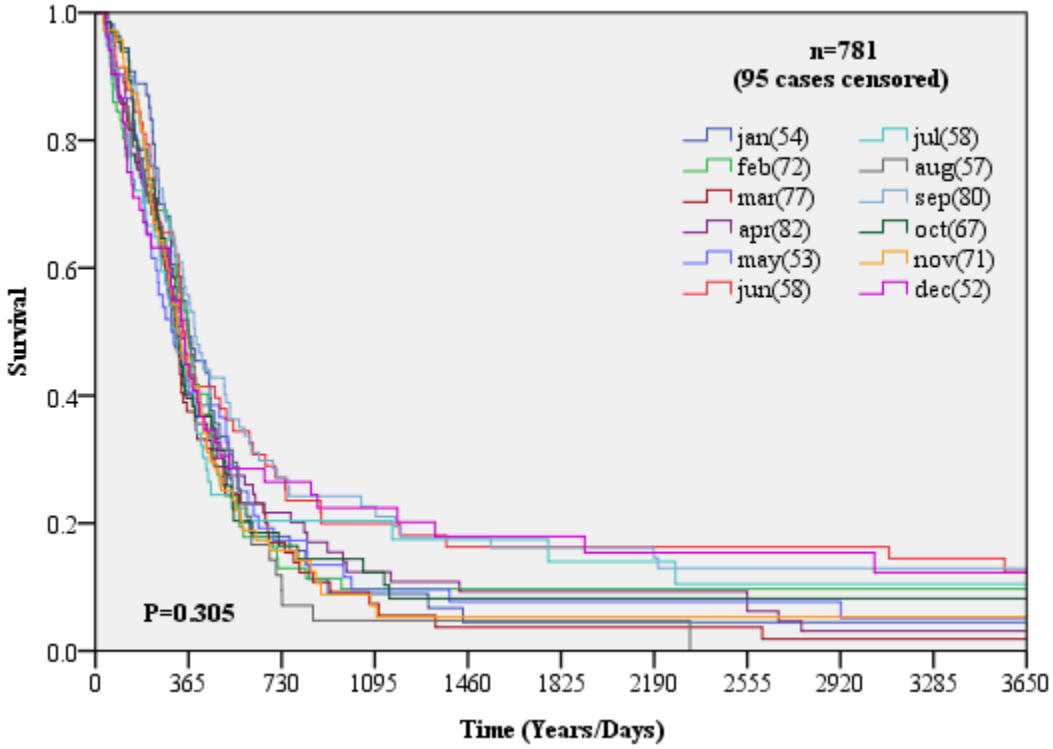
Table 3.33- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for male and female patients with SCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.017	NS
Number of cases		781	781
Number of censored cases		95	695
HR (95% CI)	Jan	1	1
	Feb	1.12 0.7-1.6	1.87 0.5-6.5
	Mar	1.41 0.9-2.0	2.16 0.5-7.8
	Apr	1.21 0.8-1.7	1.75 0.4-6.2
	May	1.05 0.7-1.5	N<5
	Jun	0.80 0.5-1.2	1.02 0.2-3.9
	Jul	0.96 0.6-1.4	2.92 0.8-10.1
	Aug	1.13 0.7-1.6	2.63 0.6-10.0
	Sep	0.69 0.4-1.0	1.22 0.3-4.1
	Oct	0.92 0.6-1.3	1.62 0.4-6.0
	Nov	1.15 0.7-1.6	2.05 0.5-7.7
	Dec	0.96 0.6-1.4	1.80 0.5-6.5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and month of first treatment.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.57- Survival according to month of first treatment for male and female SCLC patients who received radiotherapy: lung cancer deaths



Graph 3.58- Survival according to month of first treatment for male and female SCLC patients who received radiotherapy: non-lung-cancer deaths

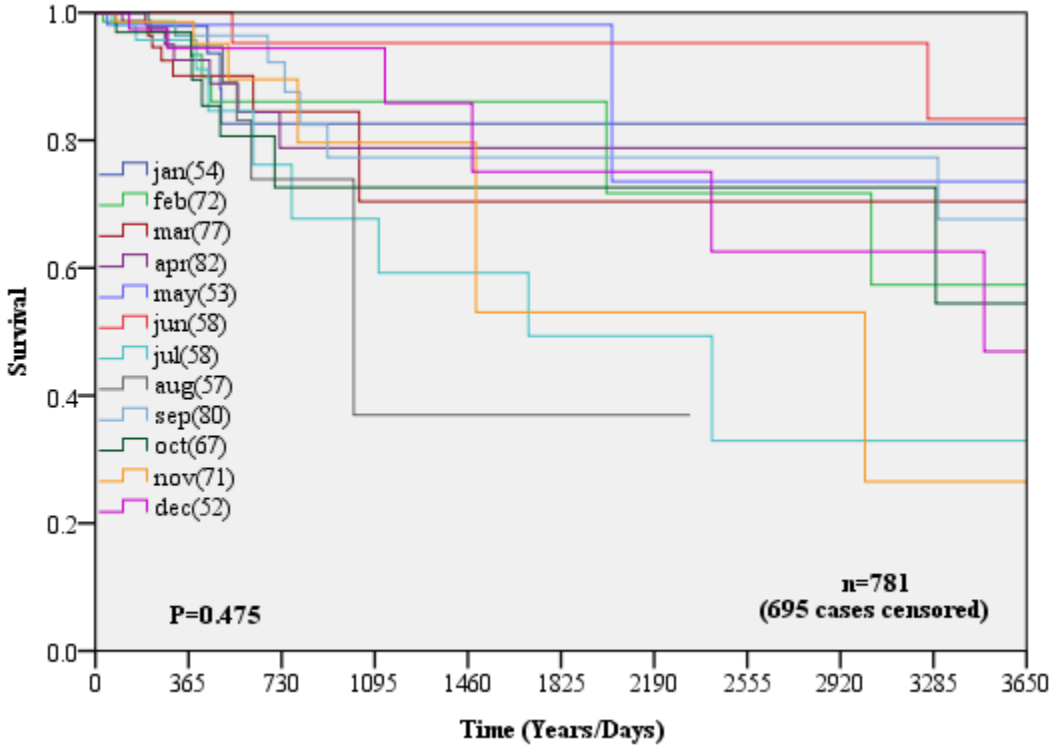


Table 3.34- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for male and female patients with SCLC who received radiotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	945	117	NS	0.097	1	0.97 0.7-1.1	0.95 0.7-1.1	0.80 0.6-0.9	0.77 0.6-0.9
Other causes	945	841	NS	NS	1	0.87 0.4-1.5	0.86 0.4-1.6	0.86 0.4-1.5	0.91 0.4-1.7

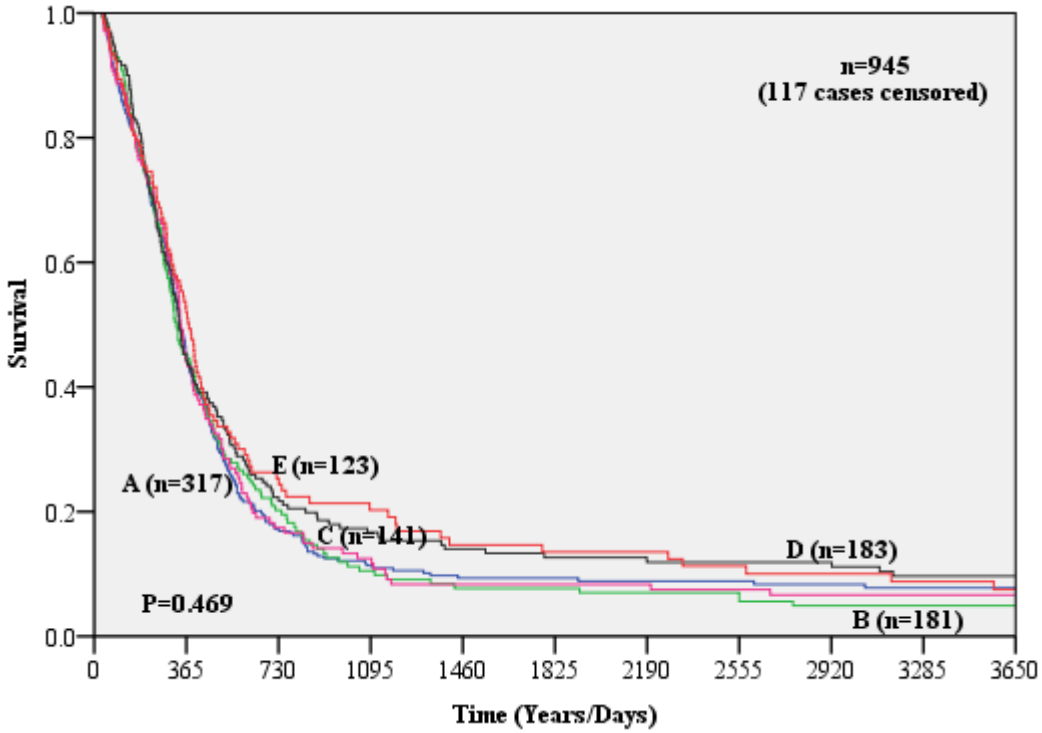
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and chemotherapy), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.59- Survival according to MMVDSI for male and female SCLC patients who received radiotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.60- Survival according to MMVDSI for male and female SCLC patients who received radiotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

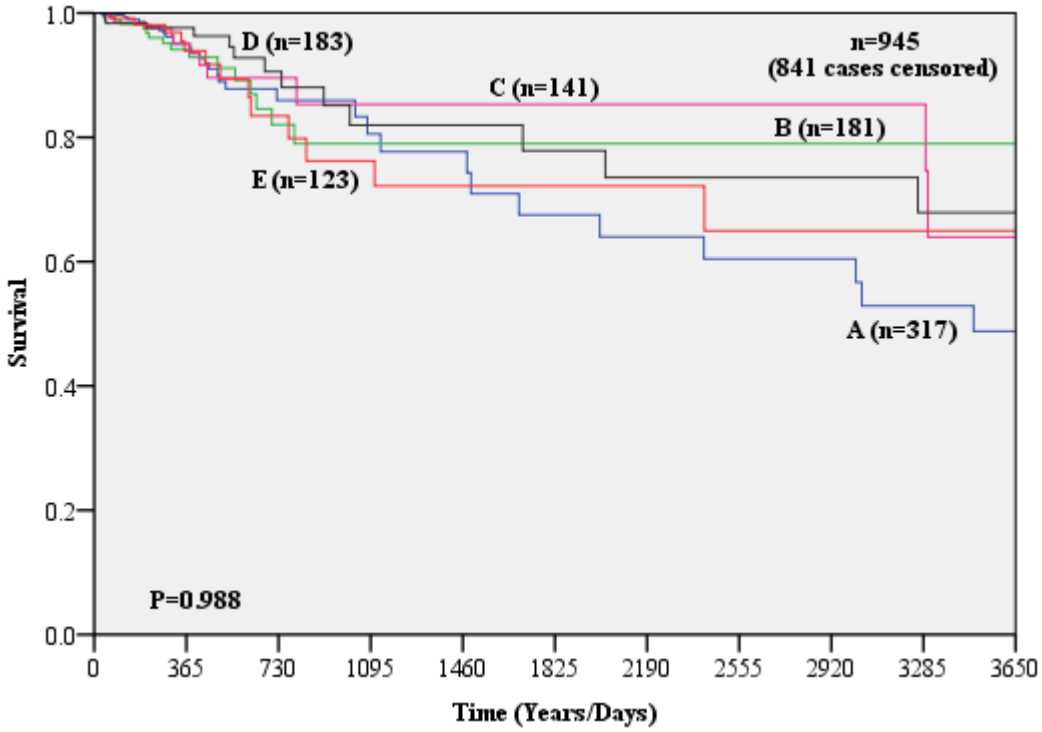


Table 3.35- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for males with SCLC who received chemotherapy

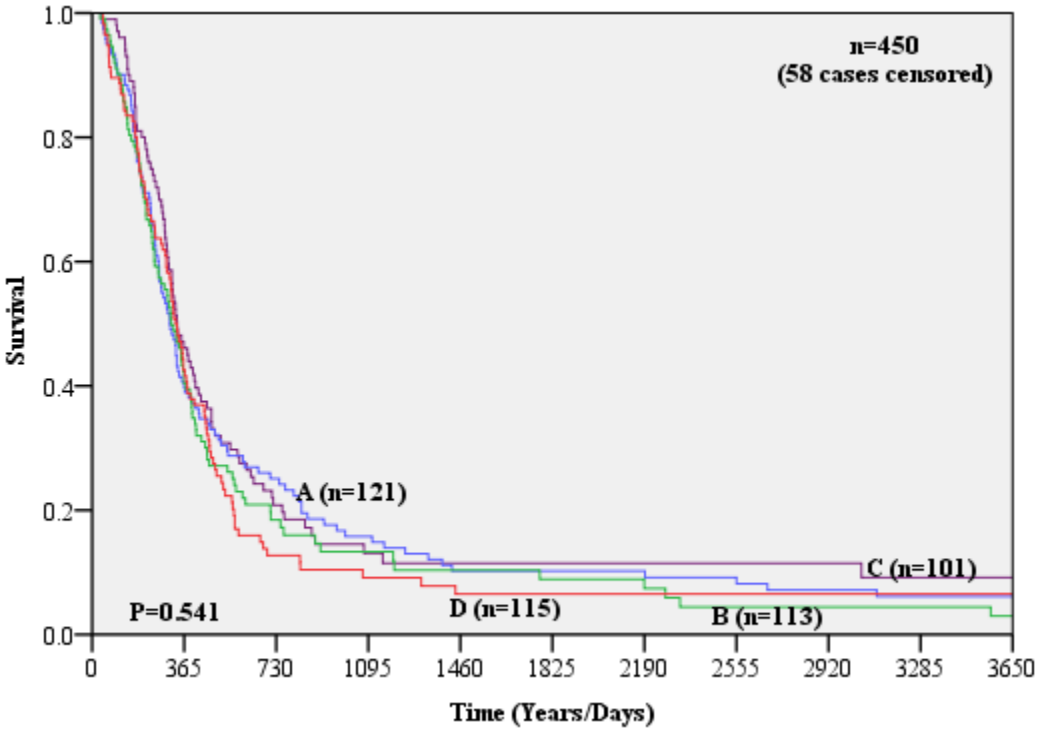
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	450	58	NS	NS	1.17 0.8-1.5	1.24 0.9-1.7	1	1.25 0.9-1.7
Other causes	450	398	NS	NS	0.62 0.2-1.5	1.40 0.6-3.2	1	1.19 0.4-2.8

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.61- Survival according to season of diagnosis for males with SCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.62- Survival according to season of diagnosis for males with SCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

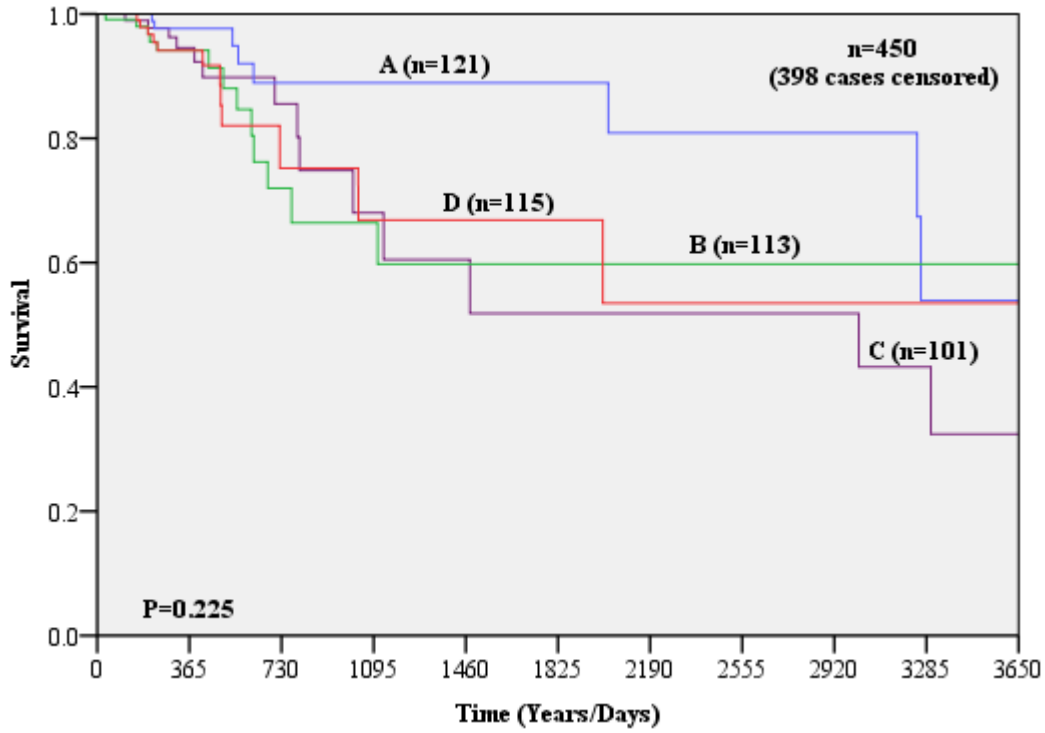
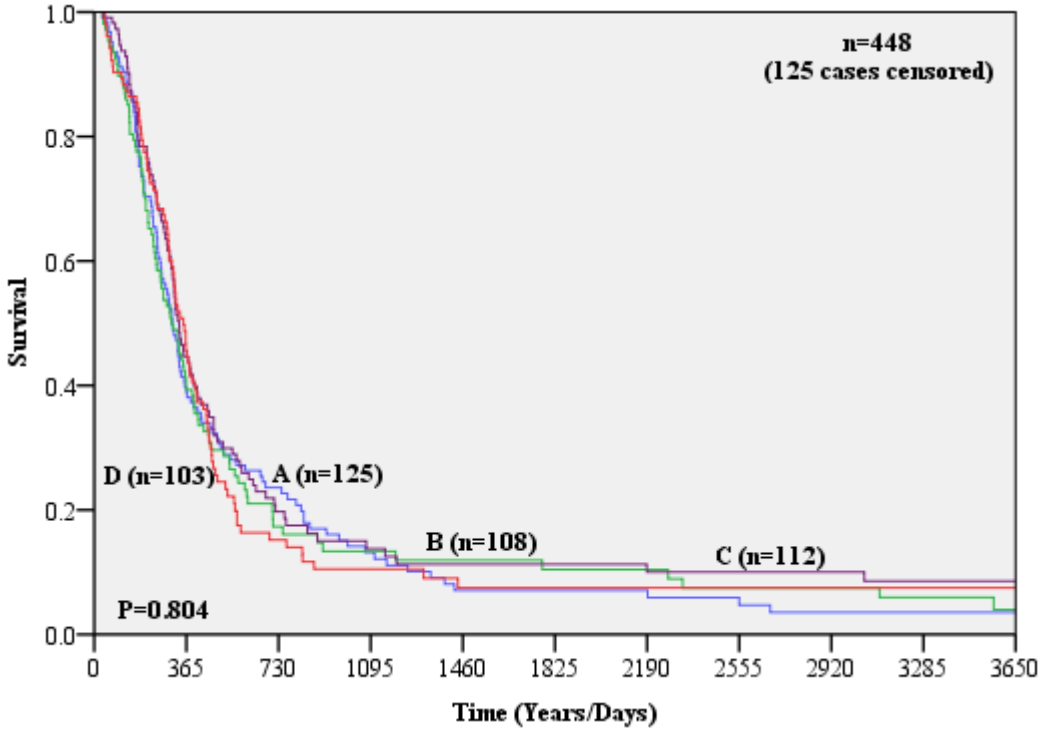


Table 3.36- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for males with SCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	448	57	NS	NS	1	0.95 0.7-1.2	0.92 0.69-1.12	1.03 0.77-1.37
Other causes	448	396	NS	NS	1	1.9 0.7-4.6	1.51 0.6-3.6	1.98 0.8-4.8

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and season of first treatment.
- NS is not significant; A is spring, B is summer, C is fall and D is winter.
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.63- Survival according to season of first treatment for males with SCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.64- Survival according to season of first treatment for males with SCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

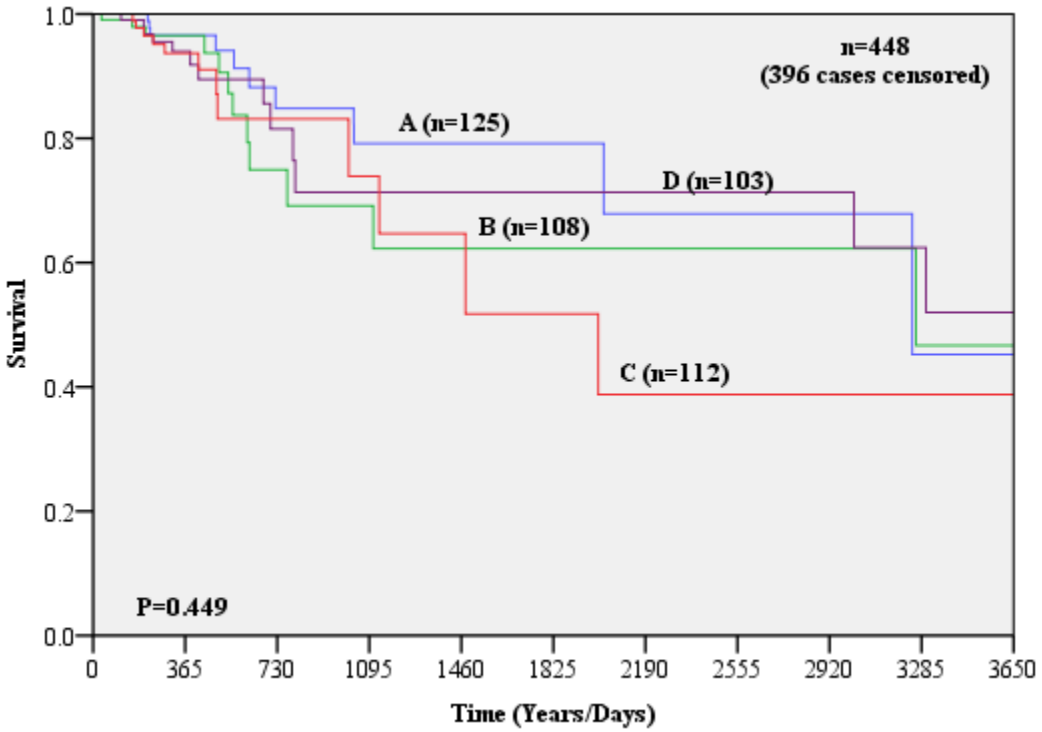


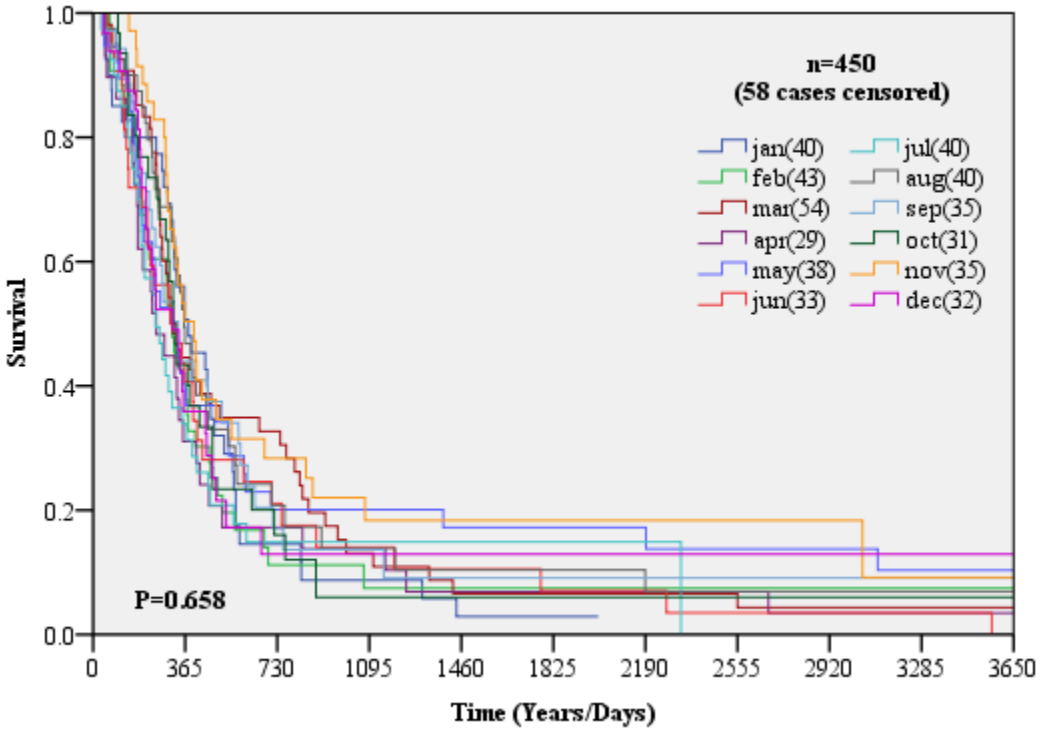
Table 3.37- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for males with SCLC who received chemotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		450	450
Number of censored cases		58	398
HR (95% CI)	Jan	1	1
	Feb	0.83 0.5-1.3	N<5
	Mar	0.79 0.5-1.2	0.47 0.1-1.9
	Apr	1.09 0.6-1.8	N<5
	May	0.77 0.4-1.2	0.66 0.1-2.6
	Jun	0.92 0.5-1.5	N<5
	Jul	1.08 0.6->100	1.73 0.4-6.3
	Aug	0.73 0.4-1.2	1.04 0.2-3.7
	Sep	0.77 0.4-1.2	0.78 0.1-3.1
	Oct	0.97 0.5-1.6	N<5
	Nov	0.53 0.3-0.9	0.62 0.1-2.7
	Dec	0.88 0.5-1.4	1.27 0.2-5.5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and month of diagnosis.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.65- Survival according to month of diagnosis for males with SCLC who received chemotherapy: lung cancer deaths



Graph 3.66- Survival according to month of diagnosis for males with SCLC who received chemotherapy: non-lung-cancer deaths

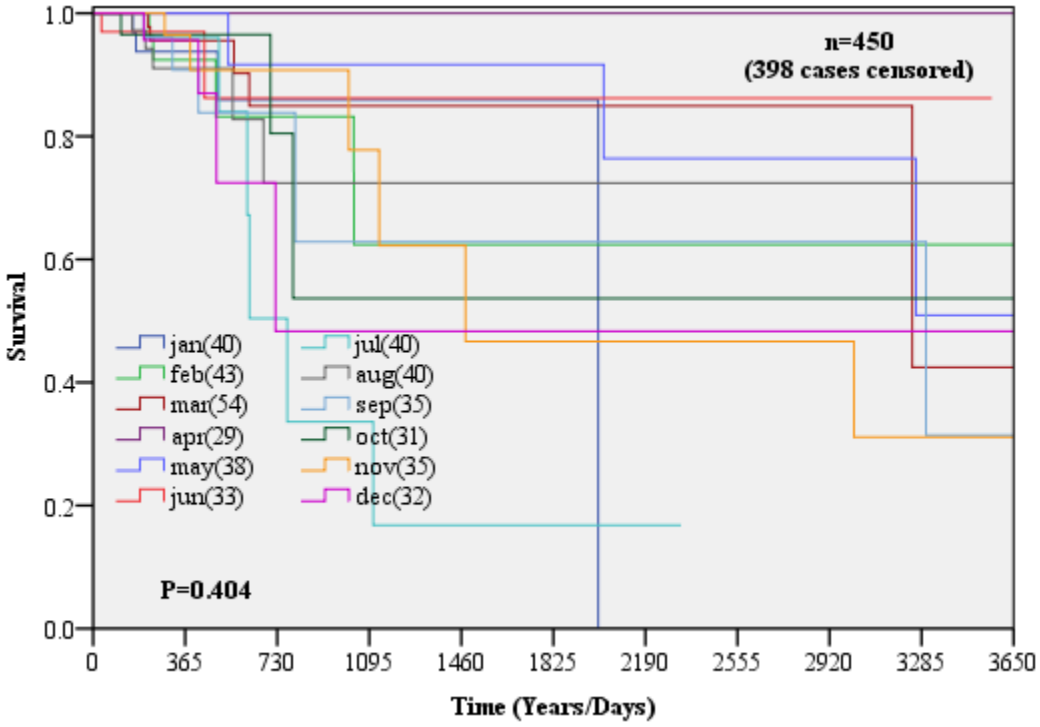


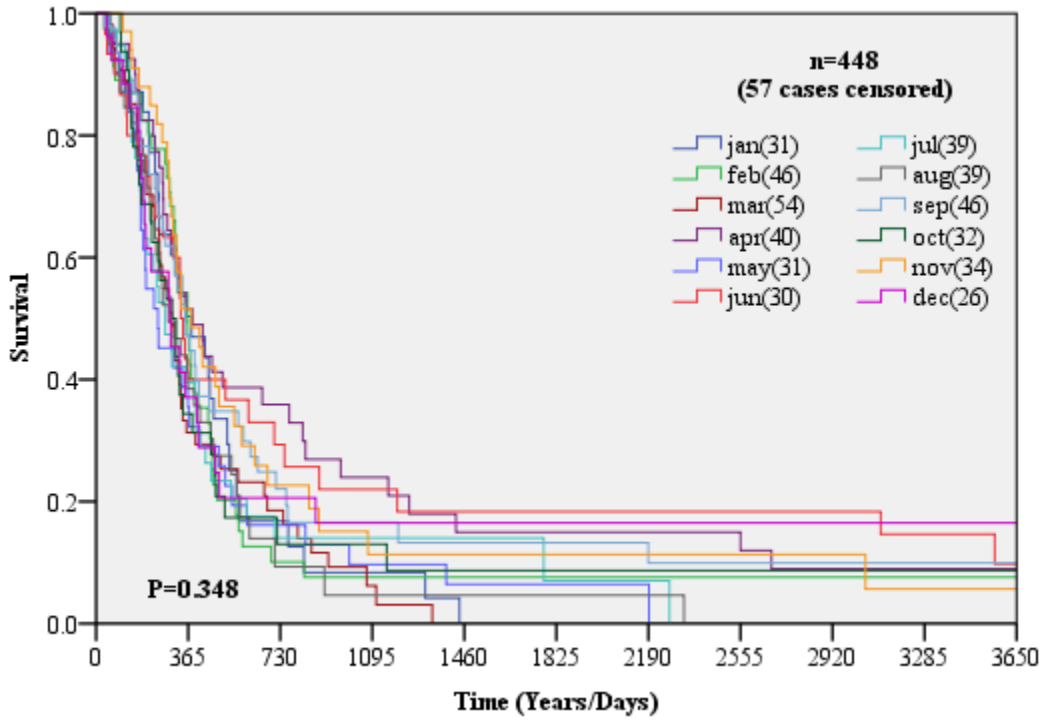
Table 3.38- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for males with SCLC who received chemotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		448	448
Number of censored cases		57	396
HR (95% CI)	Jan	1	1
	Feb	0.79 0.4-1.3	N<5
	Mar	1.00 0.6-1.6	0.93 0.2-4.0
	Apr	0.58 0.3-1.0	N<5
	May	1.05 0.6-1.7	0.26 0.0-2.6
	Jun	0.67 0.3-1.1	0.52 0.1-2.5
	Jul	0.92 0.5-1.5	1.21 0.2-5.3
	Aug	0.86 0.5-1.4	1.16 0.2-5.2
	Sep	0.69 0.4-1.1	0.82 0.2-3.4
	Oct	1.04 0.6-1.8	N<5
	Nov	0.65 0.3-1.1	0.51 0.0-52.7
	Dec	0.75 0.4-1.3	0.98 0.2-4.8

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and month of first treatment.

•NS is not significant•N is number of uncensored cases•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.67- Survival according to month of first treatment for males with SCLC who received chemotherapy: lung cancer deaths



Graph 3.68- Survival according to month of first treatment for males with SCLC who received chemotherapy: non-lung-cancer deaths

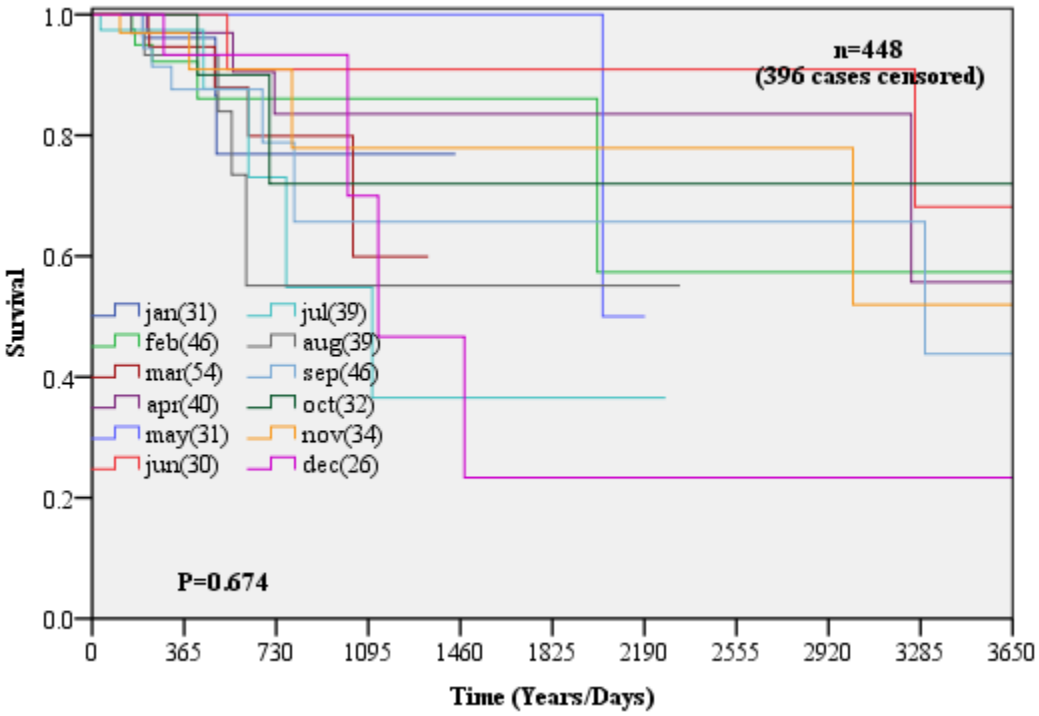


Table 3.39- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for males with SCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	450	58	NS	NS	1	0.70 0.7-1.4	0.38 0.8-1.5	0.69 0.7-1.4	0.65 0.7-1.4
Other causes	450	398	NS	NS	1	0.67 0.2-1.6	0.59 0.2-1.6	0.99 0.4-2.2	1.21 0.5-2.8

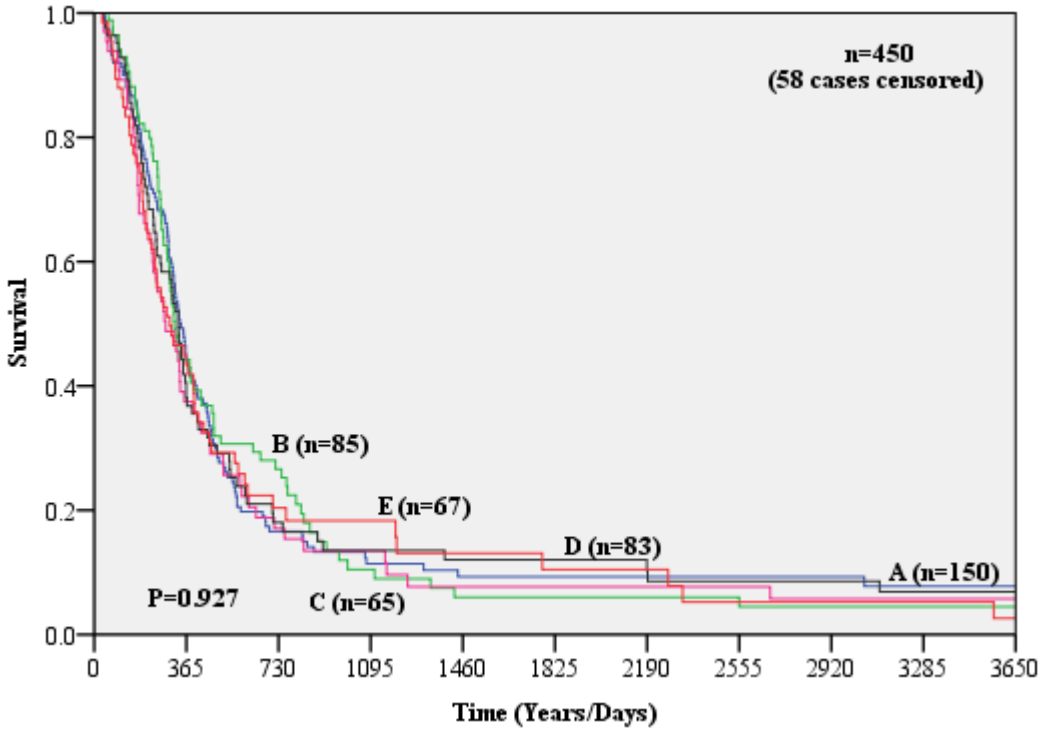
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.69- Survival according to MMVDSI for males with SCLC who received chemotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.70- Survival according to MMVDSI for males with SCLC who received chemotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

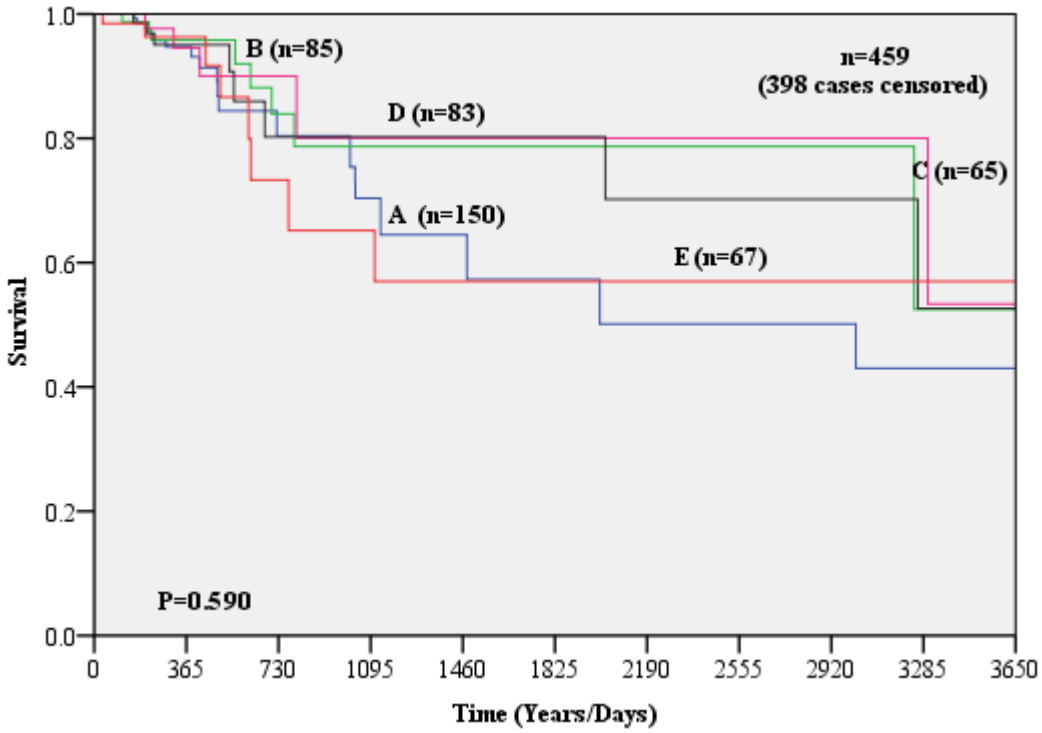


Table 3.40- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for females with SCLC who received chemotherapy

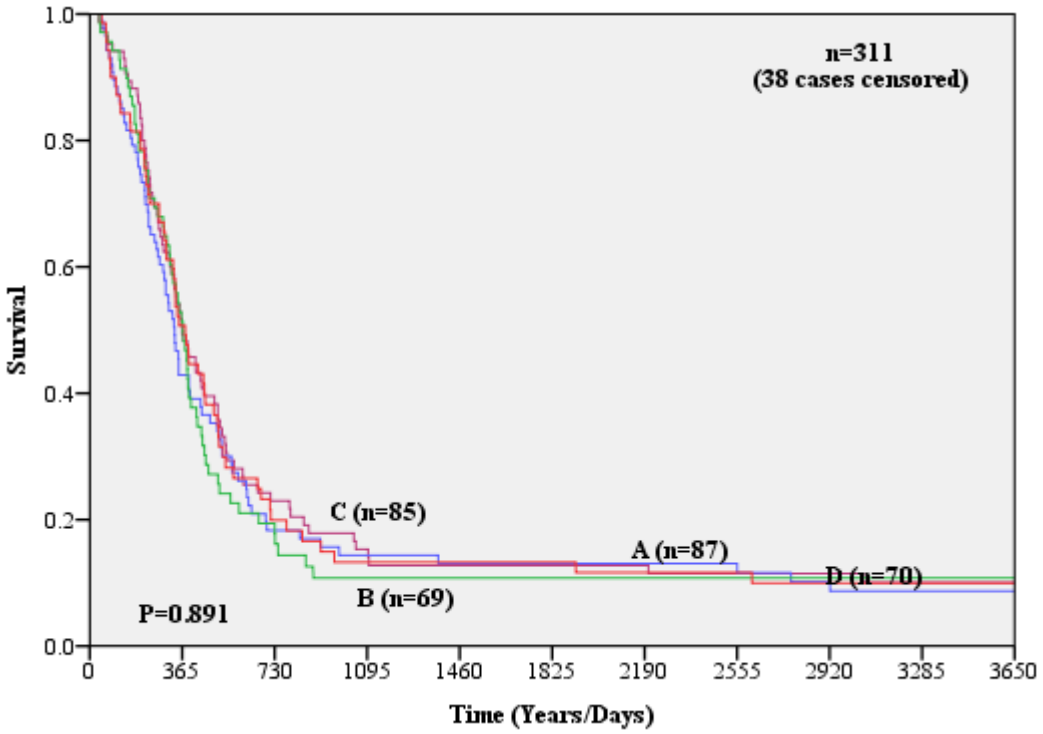
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	311	38	NS	NS	1.01 0.7-1.4	0.91 0.6-1.2	1	1.01 0.7-1.4
Other causes	311	278	NS	NS	0.92 0.2-2.8	1.42 0.4-4.4	1	0.88 02-2.8

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.71- Survival according to season of diagnosis for females with SCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.72- Survival according to season of diagnosis for females with SCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

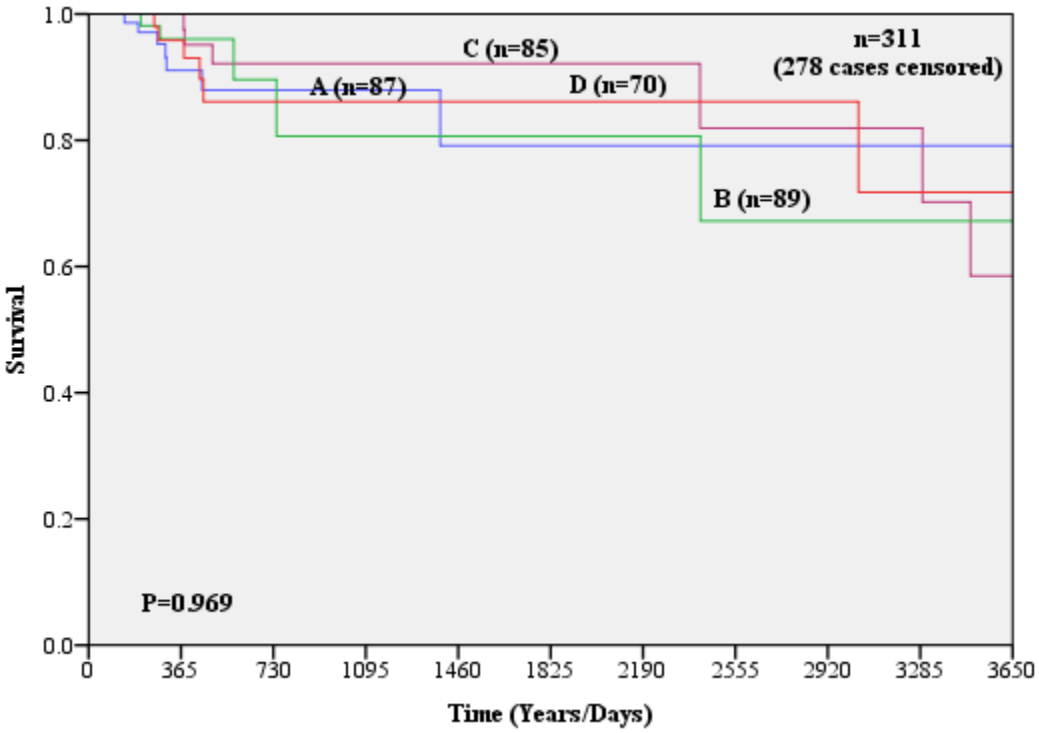


Table 3.41- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for females who received chemotherapy

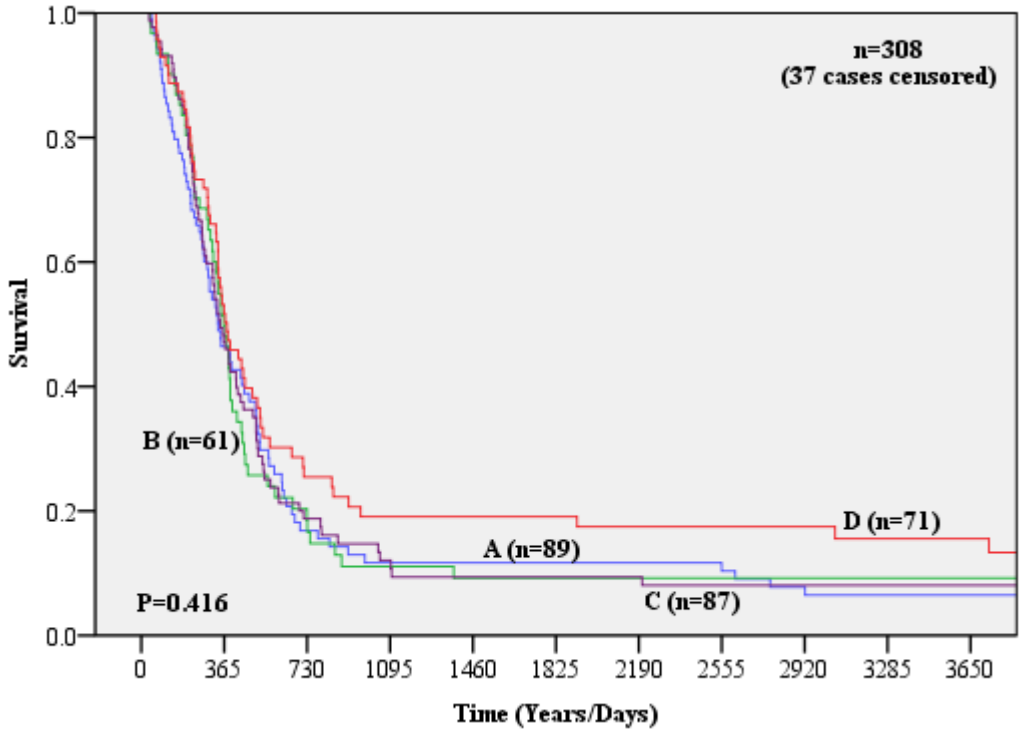
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring	Summer	Fall	Winter
Lung cancer	308	37	NS	NS	1	0.84 0.5-1.2	0.86 0.6-1.1	0.73 0.5-1.0
Other causes	308	276	NS	NS	1	1.37 0.4-4.2	0.85 0.2-2.4	1.17 0.4-3.1

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.73- Survival according to season of first treatment for females with SCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.74- Survival according to season of first treatment for females with SCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

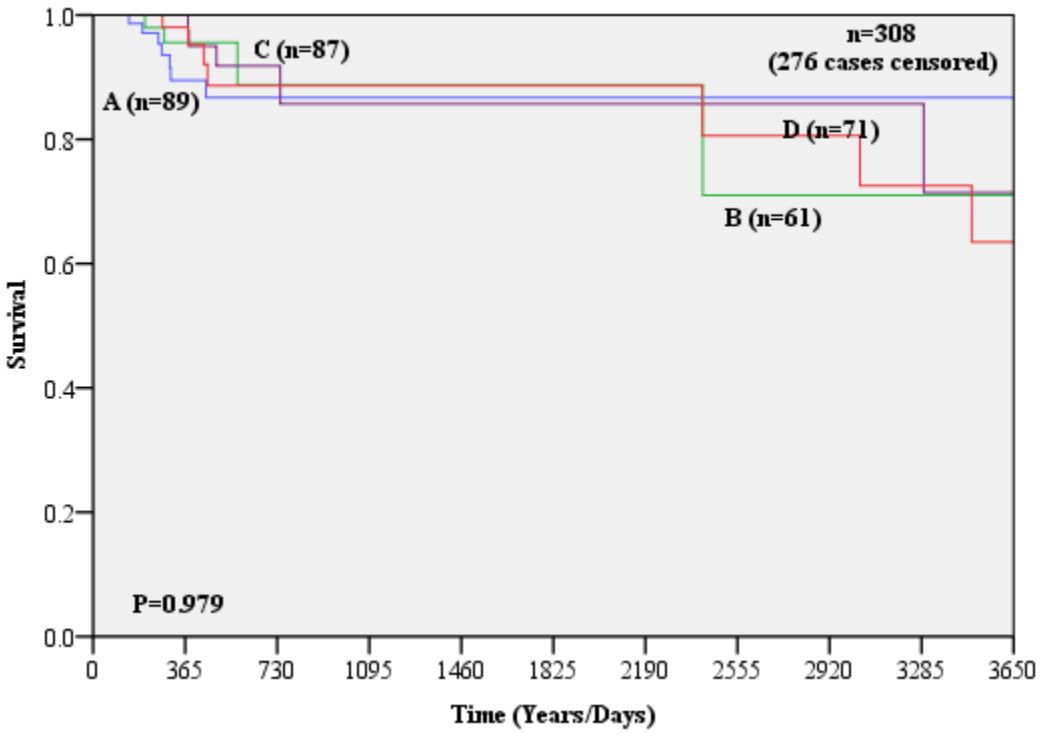


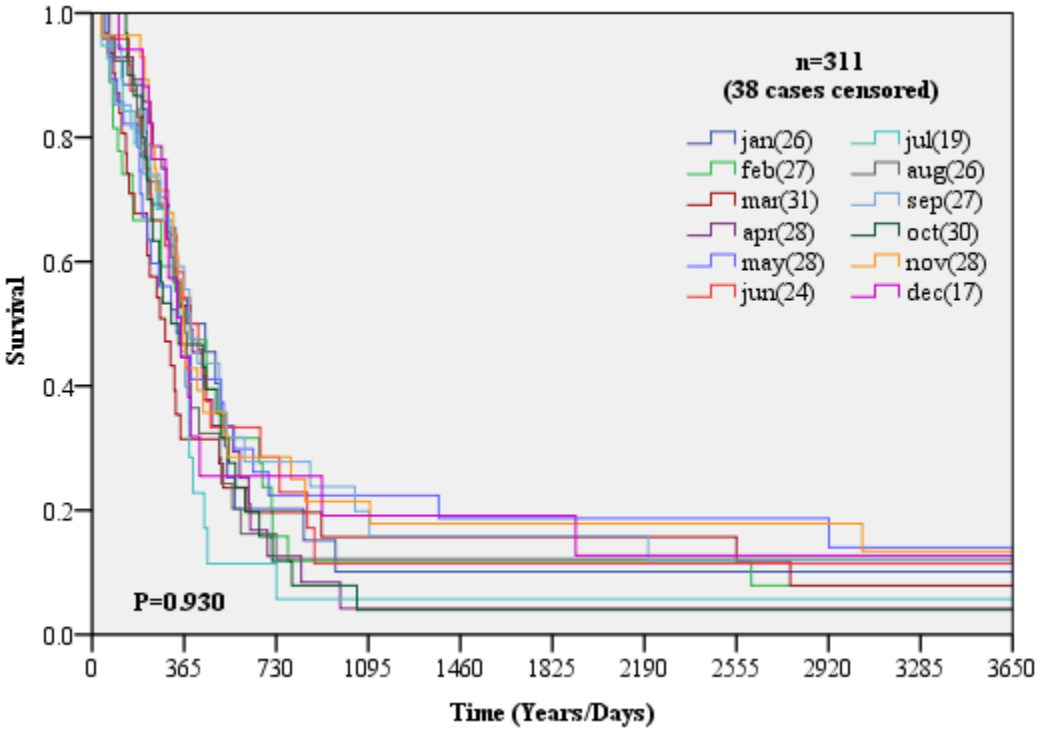
Table 3.42- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for females with SCLC who received chemotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		311	311
Number of censored cases		38	278
HR (95% CI)	Jan	1	1
	Feb	1.89 1.0-3.5	N<5
	Mar	1.71 0.9-3.1	N<5
	Apr	1.35 0.7-2.4	N<5
	May	1.01 0.5-1.8	N<5
	Jun	1.02 0.5-1.9	N<5
	Jul	1.51 0.7-2.9	N<5
	Aug	1.27 0.6-2.3	N<5
	Sep	1.39 0.7-2.6	N<5
	Oct	1.34 0.7-2.4	N<5
	Nov	1.34 0.7-2.4	N<5
	Dec	1.40 0.7-2-8	N<5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and month of diagnosis

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.75- Survival according to month of diagnosis for females with SCLC who received chemotherapy: lung cancer deaths



Graph 3.76- Survival according to month of diagnosis for females with SCLC who received chemotherapy: non-lung-cancer deaths

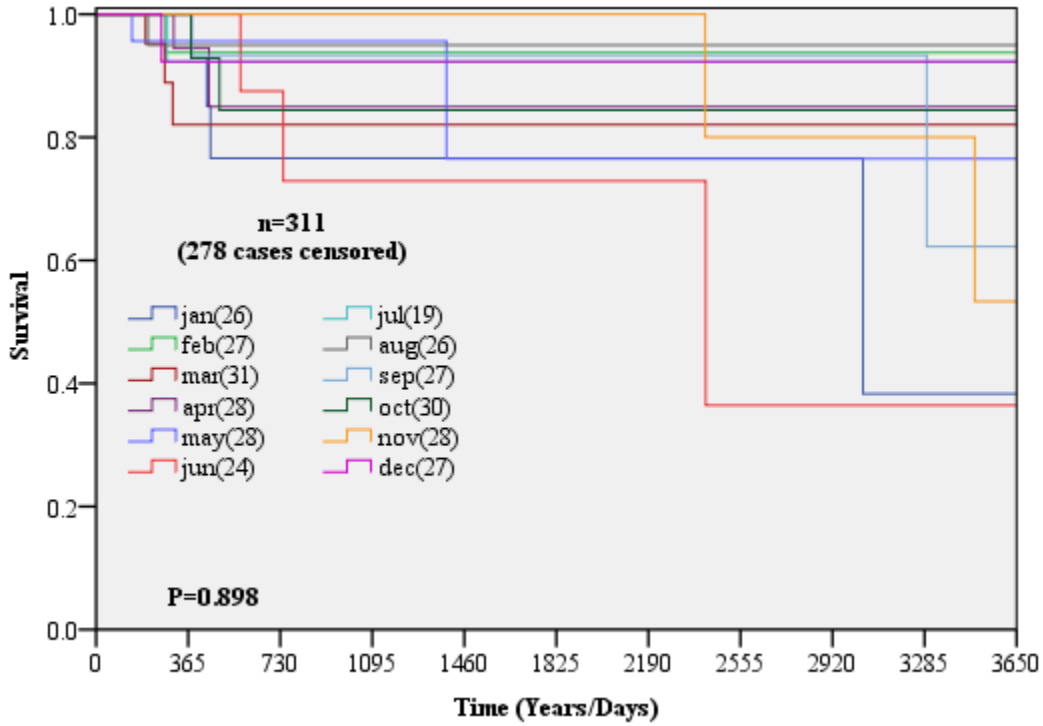


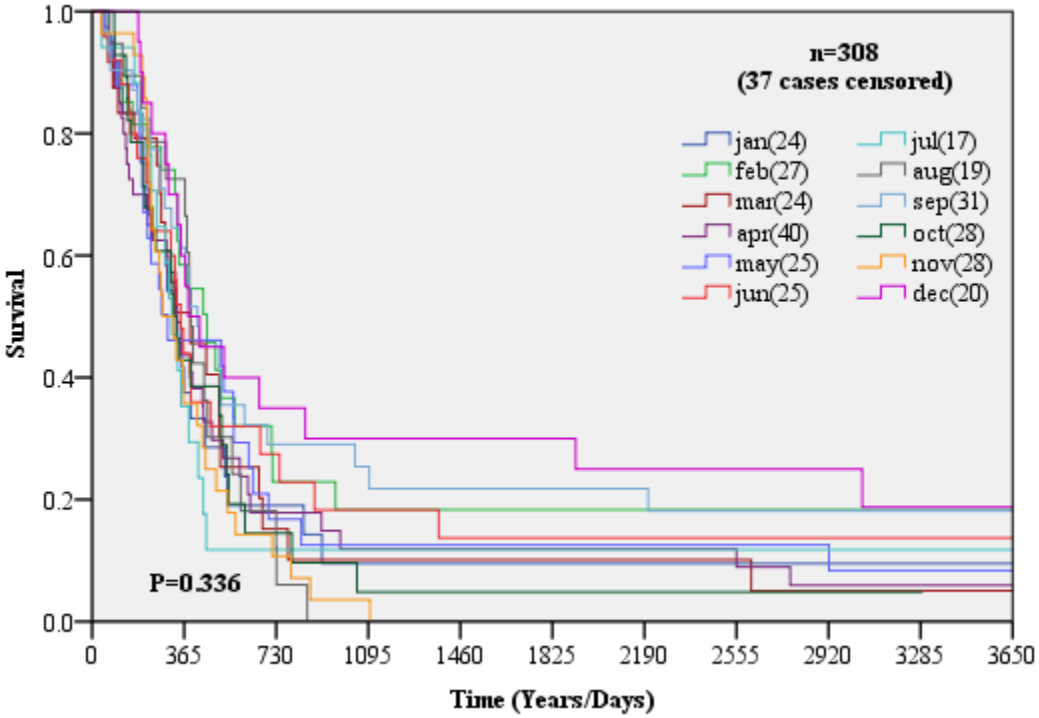
Table 3.43- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for females with SCLC who received chemotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.096	NS
Number of cases		308	308
Number of censored cases		37	276
HR (95% CI)	Jan	1	1
	Feb	0.70 0.3-1.3	N<5
	Mar	1.46 0.7-2.7	N<5
	Apr	1.11 0.6-1.9	N<5
	May	0.74 0.4-1.3	N<5
	Jun	0.74 0.3-1.4	N<5
	Jul	1.10 0.5-2.2	N<5
	Aug	0.97 0.5-1.8	N<5
	Sep	0.64 0.3-1.1	N<5
	Oct	1.37 0.7-2.5	N<5
	Nov	1.11 0.6-2.0	N<5
	Dec	0.65 0.3-1.2	N<5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and month of first treatment.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.77- Survival according to month of first treatment for females with SCLC who received chemotherapy: lung cancer deaths



Graph 3.78- Survival according to month of first treatment for females with SCLC who received chemotherapy: non-lung-cancer deaths

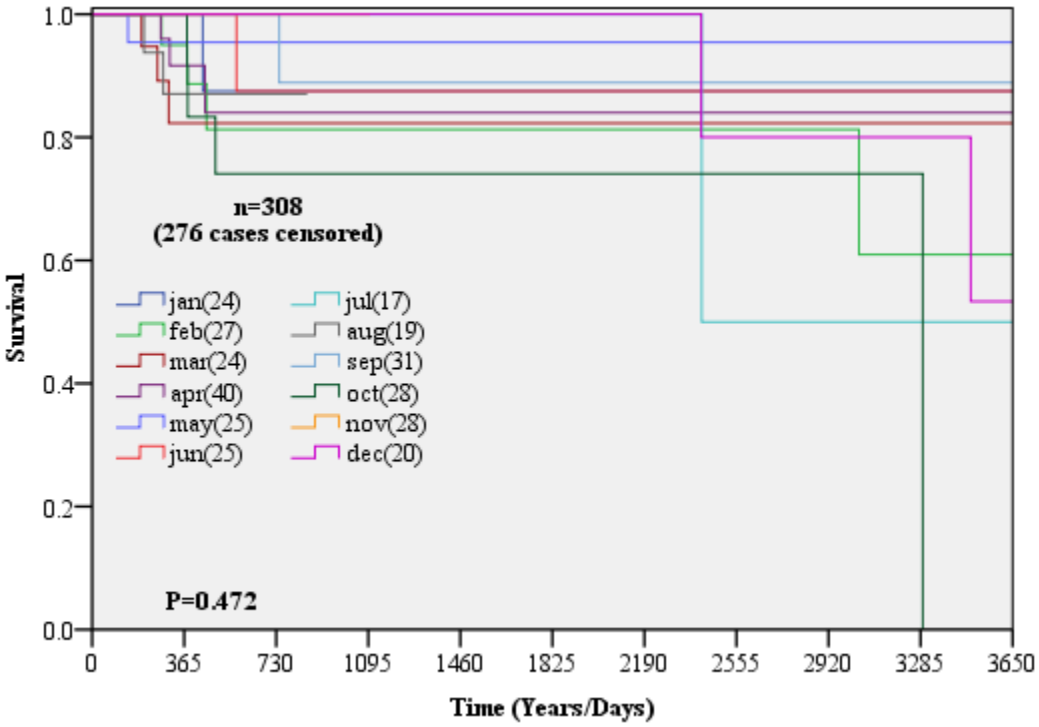


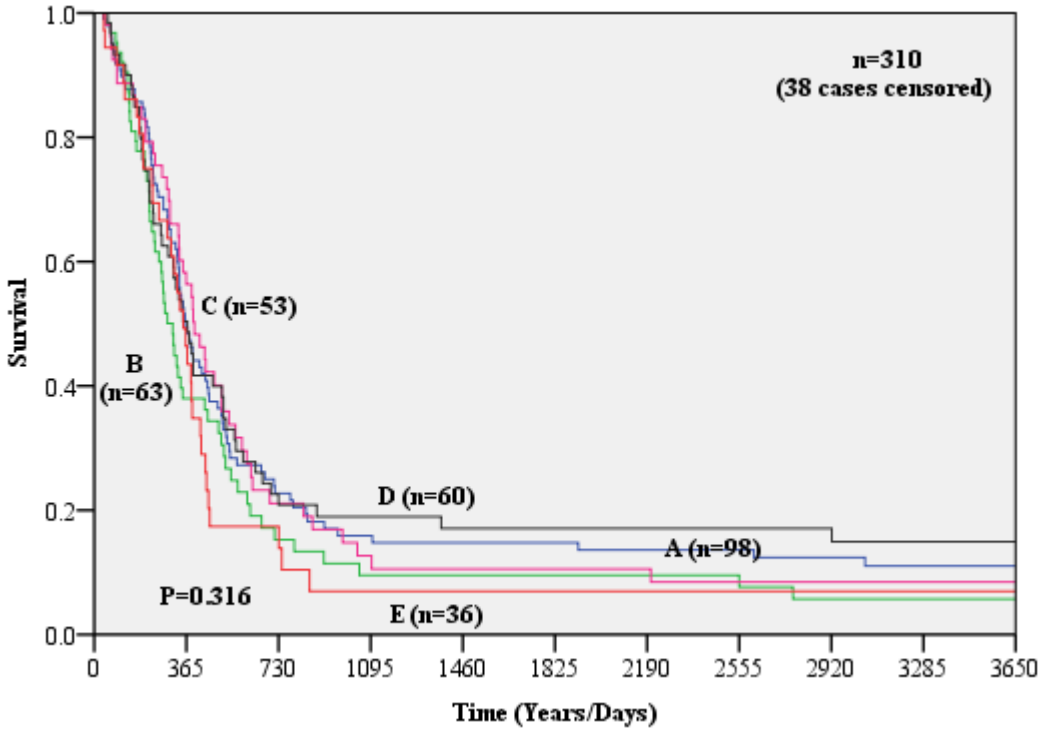
Table 3.44- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for females with SCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	310	38	NS	NS	1	1.13 0.7-1.6	0.99 0.6-1.4	0.78 0.5-1.1	1.04 0.6-1.5
Other causes	310	277	NS	NS	1	1.32 0.3-4.6	1.10 0.3-3.3	1.30 0.4-3.9	N<5

(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and monthly mean vitamin D sunshine index.
- NS is not significant
- N is number of uncensored cases
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.79- Survival according to MMVDSI for females with SCLC who received chemotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.80- Survival according to MMVDSI for females with SCLC who received chemotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

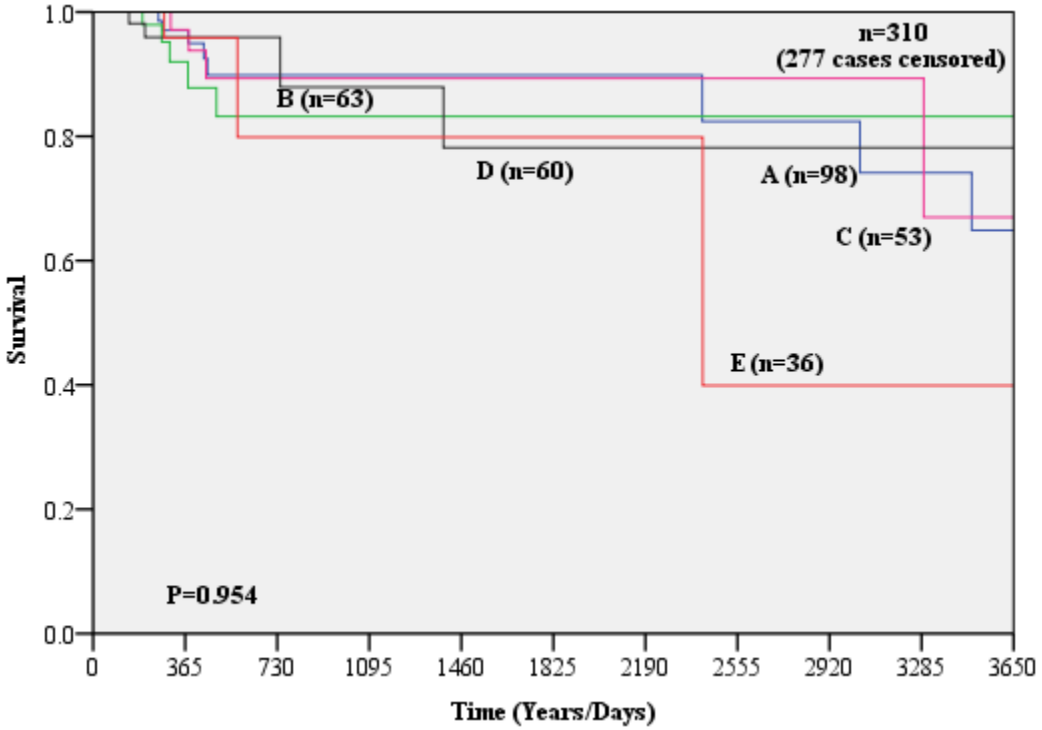


Table 3.45- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for male and female patients with SCLC who received chemotherapy

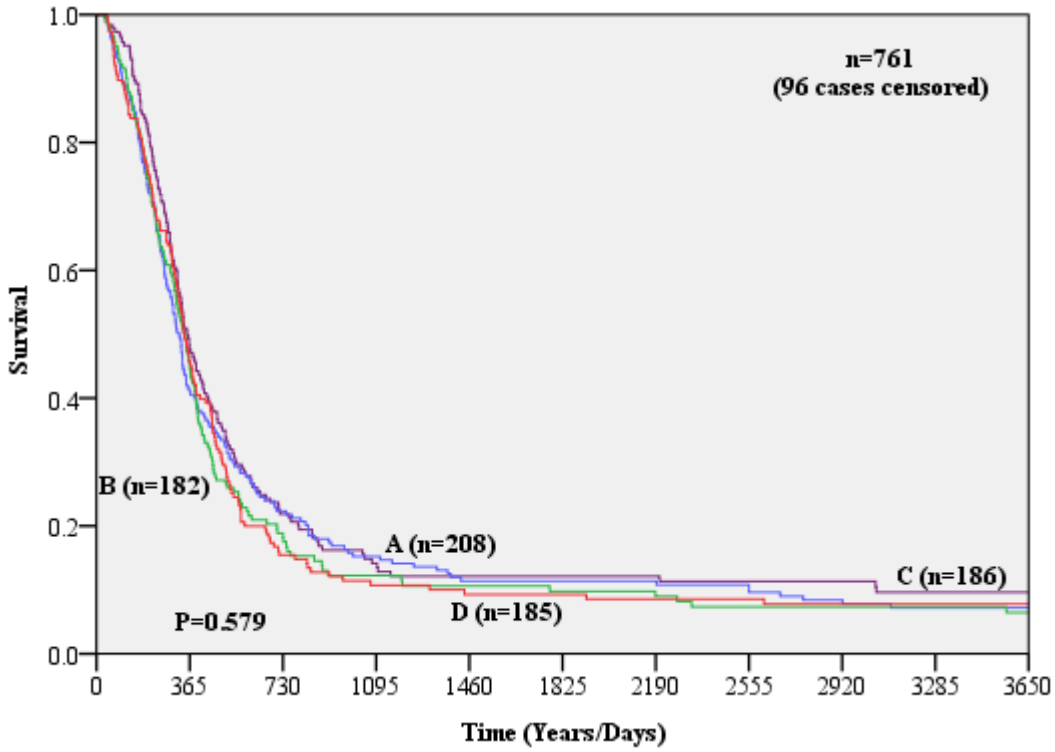
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	761	96	NS	NS	1.07 0.8-1.3	1.08 0.8-1.3	1	1.15 0.9-1.4
Other causes	761	676	NS	NS	0.83 0.4-1.5	1.36 0.7-2.5	1	1.10 0.5-2.0

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.81- Survival according to season of diagnosis for male and female patients with SCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.82- Survival according to season of diagnosis for male and female patients with SCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

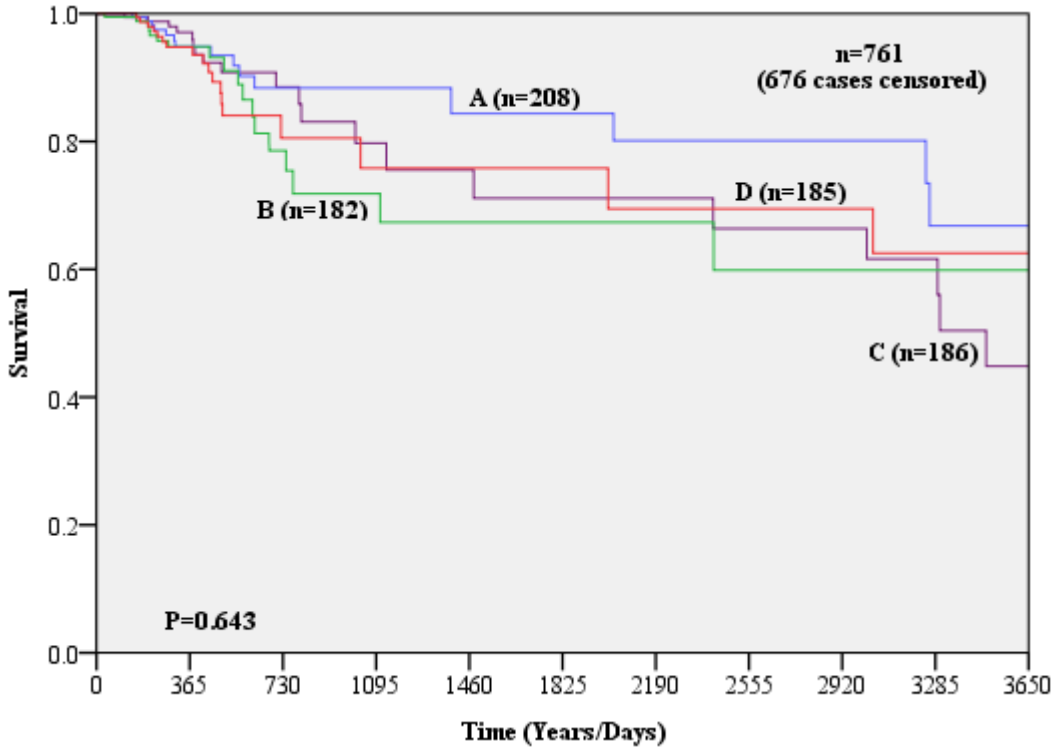
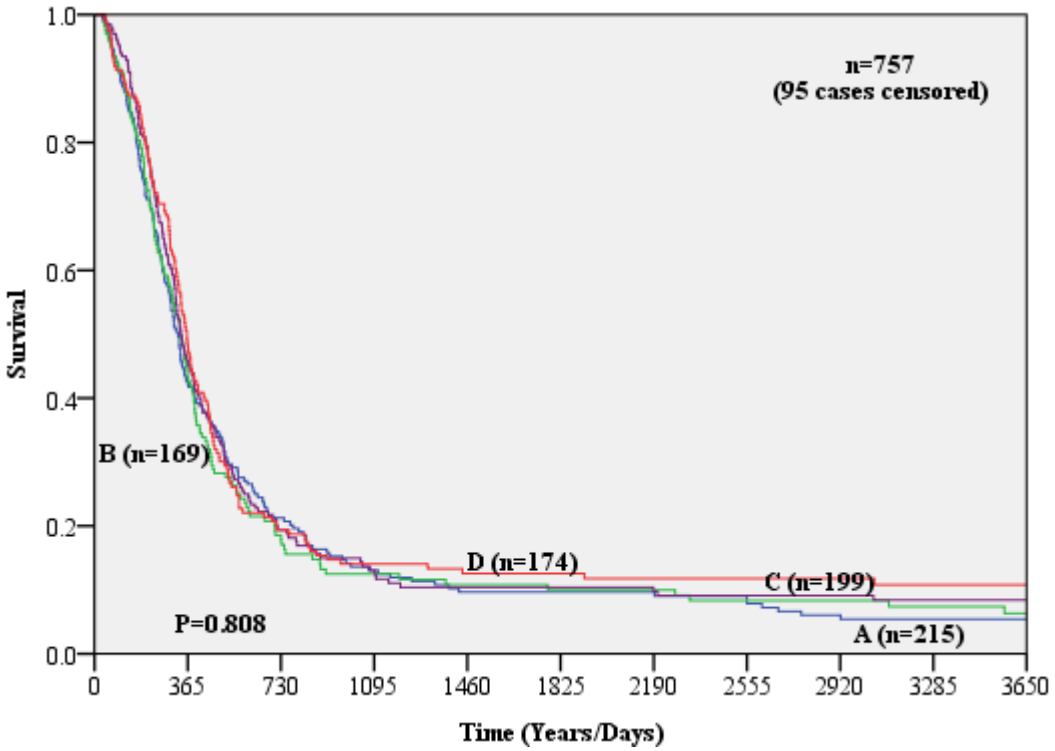


Table 3.46- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for male and female patients with SCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	757	95	NS	NS	1	0.94 0.7-1.1	0.94 0.7-1.1	0.92 0.7-1.1
Other causes	757	673	NS	NS	1	1.89 0.9-3.7	1.29 0.6-2.3	1.56 0.8-2.9

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and season of first treatment.
- NS is not significant; A is spring, B is summer, C is fall and D is winter.
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.83- Survival according to season of first treatment for male and female patients with SCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.84- Survival according to season of first treatment for male and female patients with SCLC who received chemotherapy: non-lung-cancer death (A is spring, B is summer, C is fall and D is winter)

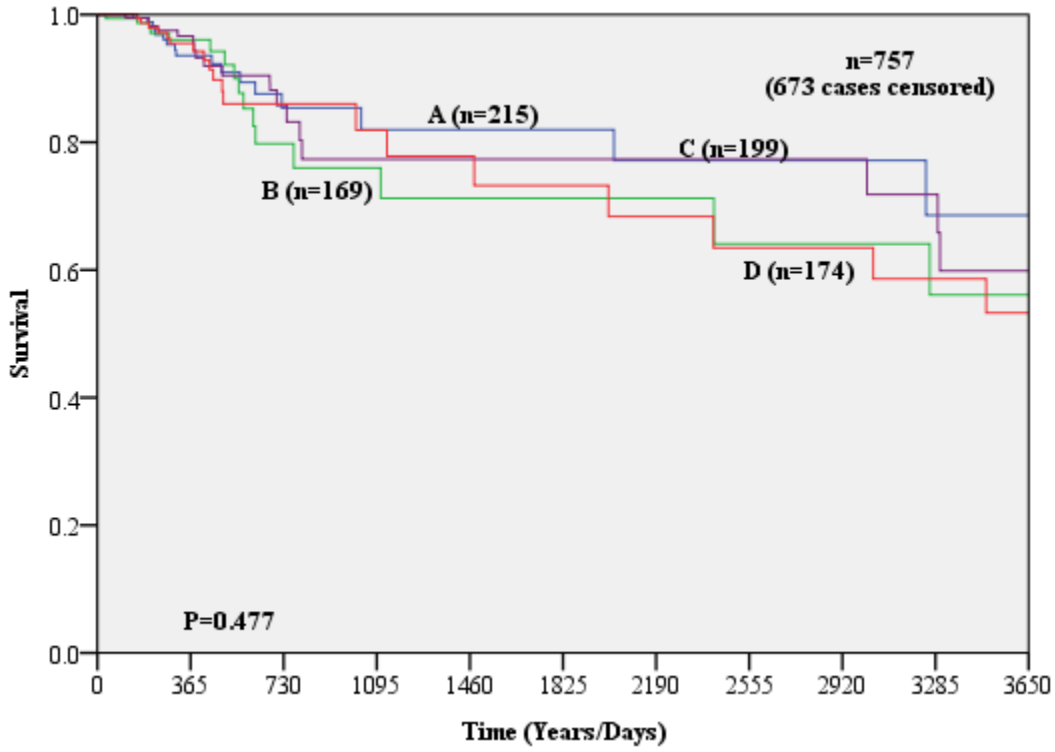


Table 3.47- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for male and female patients with SCLC who received chemotherapy

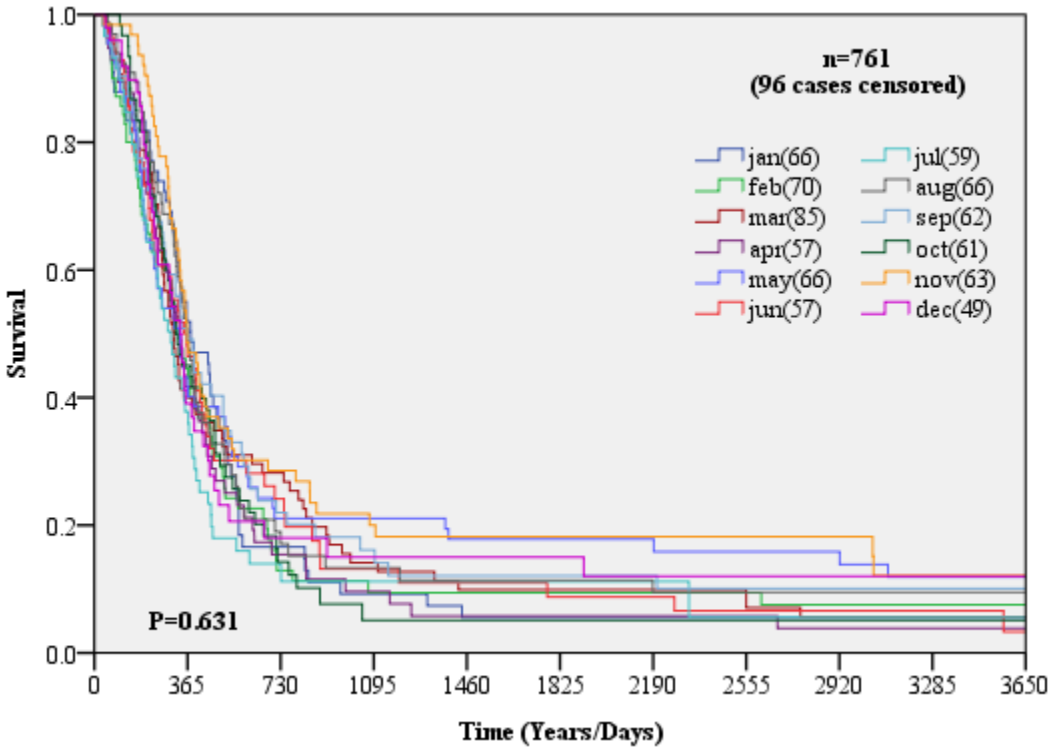
Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		761	761
Number of censored cases		96	676
HR (95% CI)	Jan	1	1
	Feb	1.15 0.7-1.6	0.54 0.1-1.7
	Mar	1.03 0.7-1.4	0.55 0.1-1.5
	Apr	1.16 0.7-1.7	N<5
	May	0.87 0.6-1.2	0.78 0.2-2.0
	Jun	0.97 0.6-1.4	0.74 0.2-2.0
	Jul	1.25 0.8-1.8	1.62 0.5-4.6
	Aug	0.90 0.6-1.3	0.86 0.3-2.2
	Sep	0.95 0.6-1.4	0.68 0.2-1.8
	Oct	1.12 0.7-1.6	0.84 0.2-2.5
	Nov	0.80 0.5-1.1	0.70 0.2-1.9
	Dec	1.16 0.7-1.7	0.88 0.2-2.7

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and month of diagnosis.

●NS is not significant ●N is number of uncensored cases

●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.85- Survival according to month of diagnosis for male and female patients with SCLC who received chemotherapy: lung cancer deaths



Graph 3.86- Survival according to month of diagnosis for male and female patients with SCLC who received chemotherapy: non-lung-cancer deaths

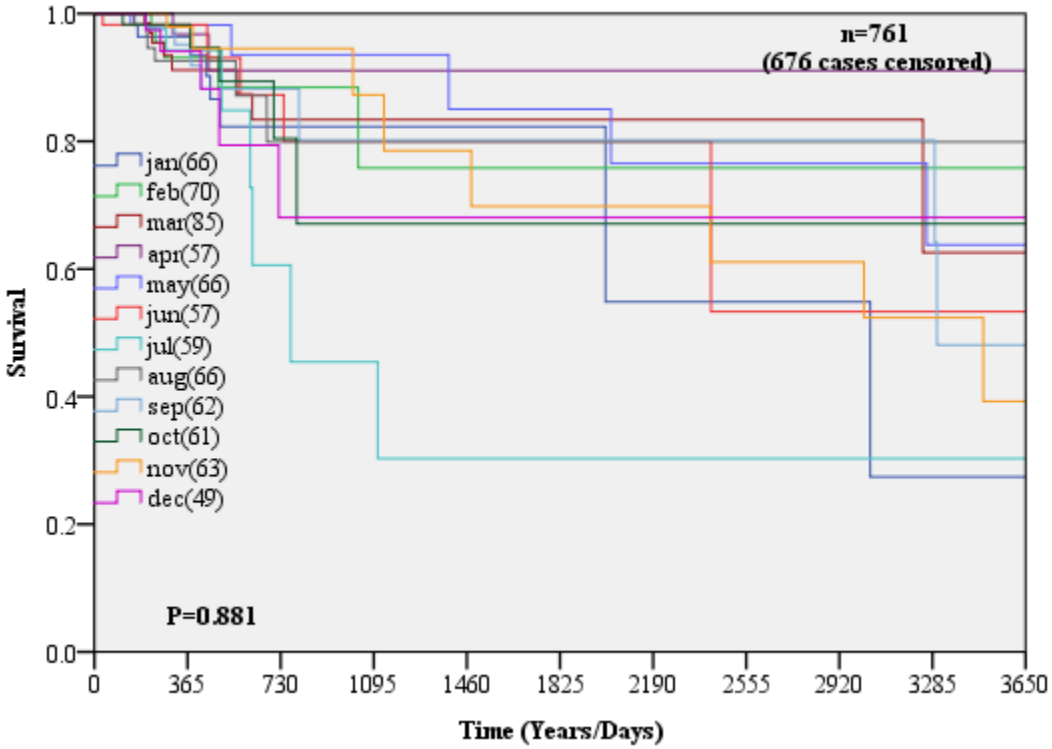


Table 3.48- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for male and female patients with SCLC who received chemotherapy

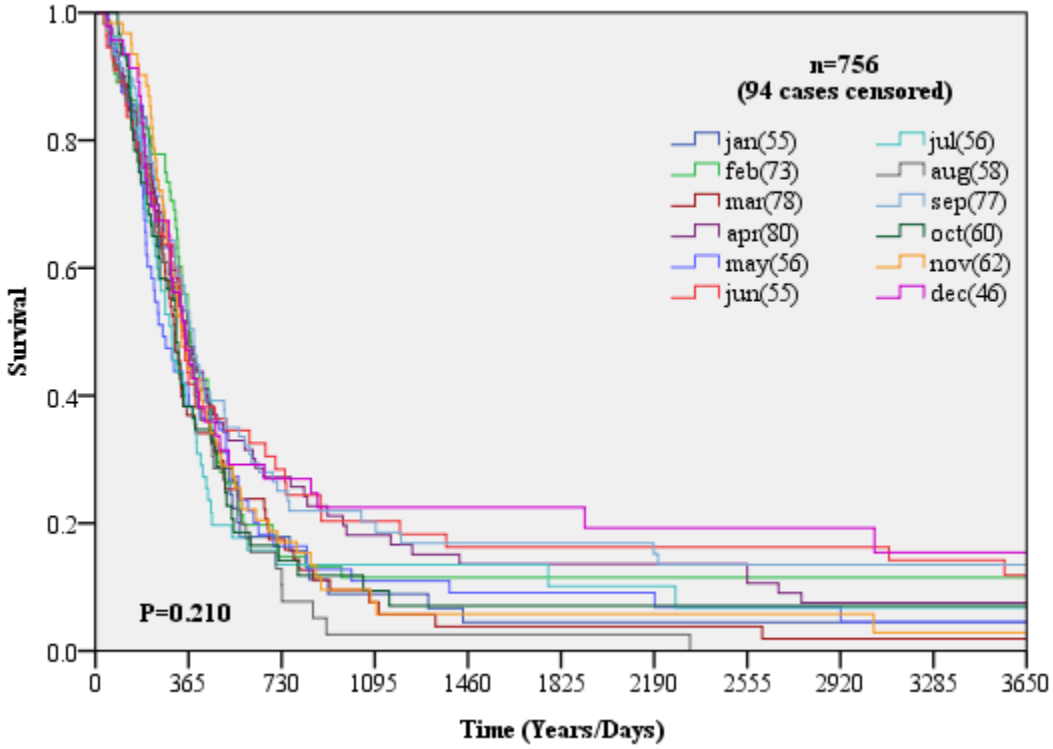
Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		756	756
Number of censored cases		94	672
HR (95% CI)	Jan	1	1
	Feb	0.82 0.5-1.2	1.50 0.4-5.0
	Mar	1.12 0.7-1.6	1.95 0.5-6.8
	Apr	0.78 0.5-1.1	0.63 0.1-2.4
	May	0.94 0.6-1.4	N<5
	Jun	0.73 0.4-1.1	1.22 0.3-4.4
	Jul	1.00 0.6-1.5	1.94 0.5-7.3
	Aug	0.89 0.6-1.3	2.28 0.6-8.3
	Sep	0.70 0.4-1.0	1.12 0.3-3.7
	Oct	1.17 0.7-1.7	1.75 0.4-6.5
	Nov	0.89 0.6-1.3	N<5
	Dec	0.75 0.4-1.1	1.59 0.4-5.7

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and month of first treatment.

●NS is not significant ●N is number of uncensored cases

●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.87- Survival according to month of first treatment for male and female patients with SCLC who received chemotherapy: lung cancer deaths



Graph 3.88- Survival according to month of first treatment for male and female patients with SCLC who received chemotherapy: non-lung-cancer deaths

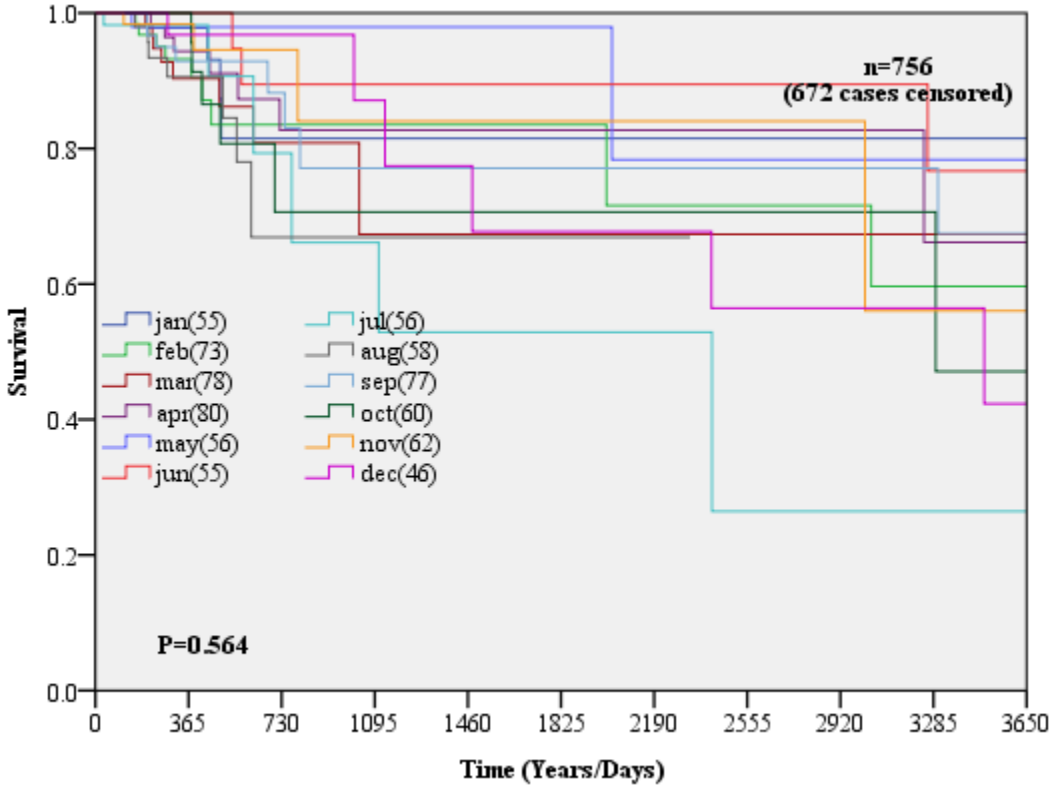


Table 3.49- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for male and female patients with SCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	760	96	NS	NS	1	1.09 0.8-1.3	1.05 0.8-1.3	0.93 0.7-1.1	1.11 0.8-1.4
Other causes	760	675	NS	NS	1	0.87 0.4-1.6	0.77 0.3-1.5	1.08 0.5-1.9	1.42 0.7-2.8

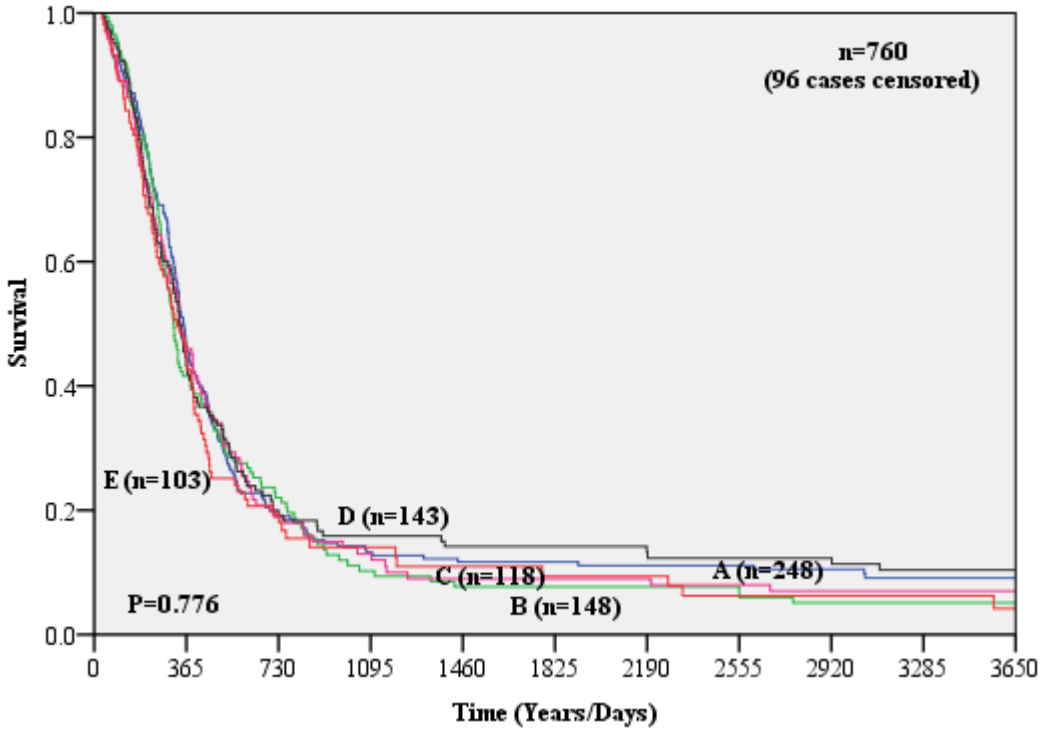
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (surgery and radiotherapy), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.89- Survival according to MMVDSIfor male and female patients with SCLC who received chemotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.90- Survival according to MMVDSI for male and female patients with SCLC who received chemotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

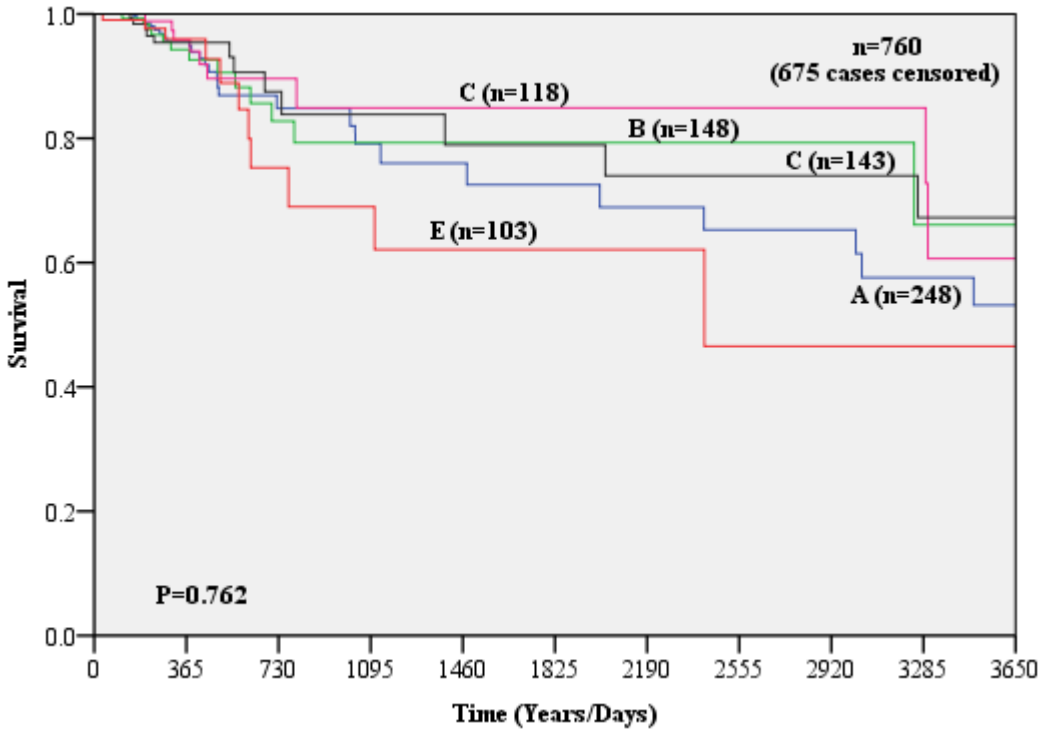


Table 3.50- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for males with NSCLC who received surgery

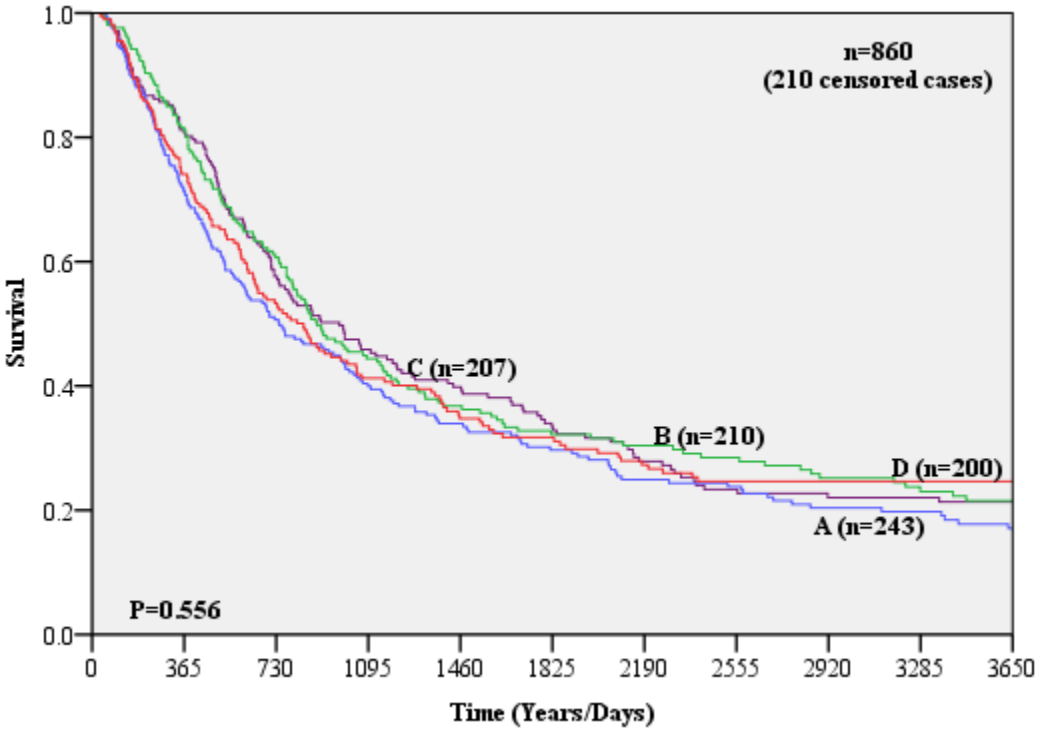
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	860	210	NS	NS	1.11 0.9-1.3	0.99 0.7-1.2	1	0.92 0.7-1.1
Other causes	860	690	NS	NS	0.90 0.5-1.4	1.05 0.6-1.6	1	1.05 0.6-1.6

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and season of diagnosis.

•NS is not significant; A is spring, B is summer, C is fall and D is winter.

•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.91- Survival according to season of diagnosis for males with NSCLC who received surgery: lung cancer deaths only (A is spring, B is summer, C is fall and D is winter)



Graph 3.92- Survival according to season of diagnosis for males with NSCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

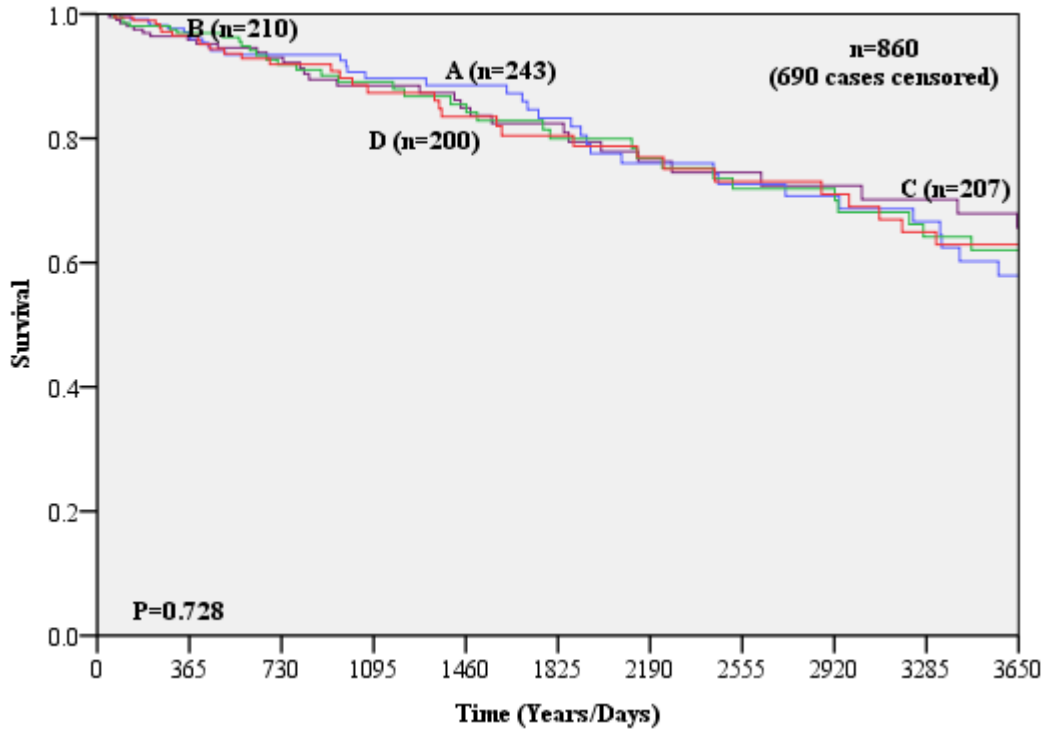


Table 3.51- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for males with NSCLC who received surgery

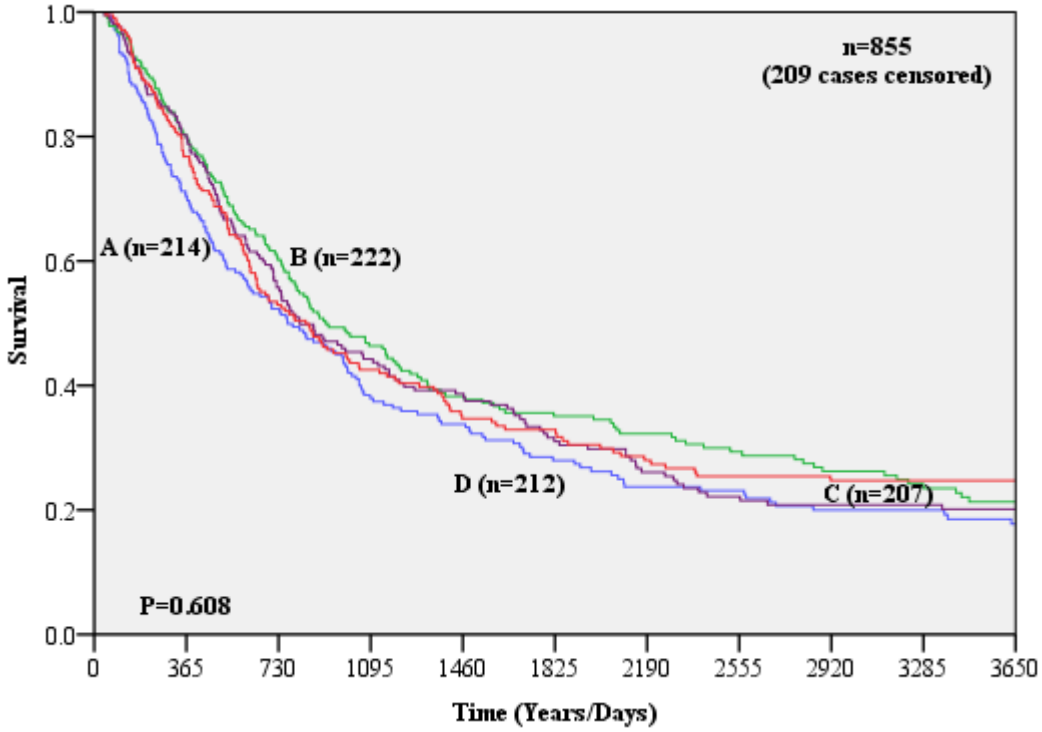
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	855	209	NS	NS	1	0.90 0.7-1.1	0.94 0.7-1.1	0.94 0.7-1.1
Other causes	855	690	NS	NS	1	1.2 0.7-1.9	1.32 0.8-2.1	1.57 1.0-2.4

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.93- Survival according to season of first treatment for males with NSCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.94- Survival according to season of first treatment for males with NSCLC who received surgery: non-lung-deaths (A is spring, B is summer, C is fall and D is winter)

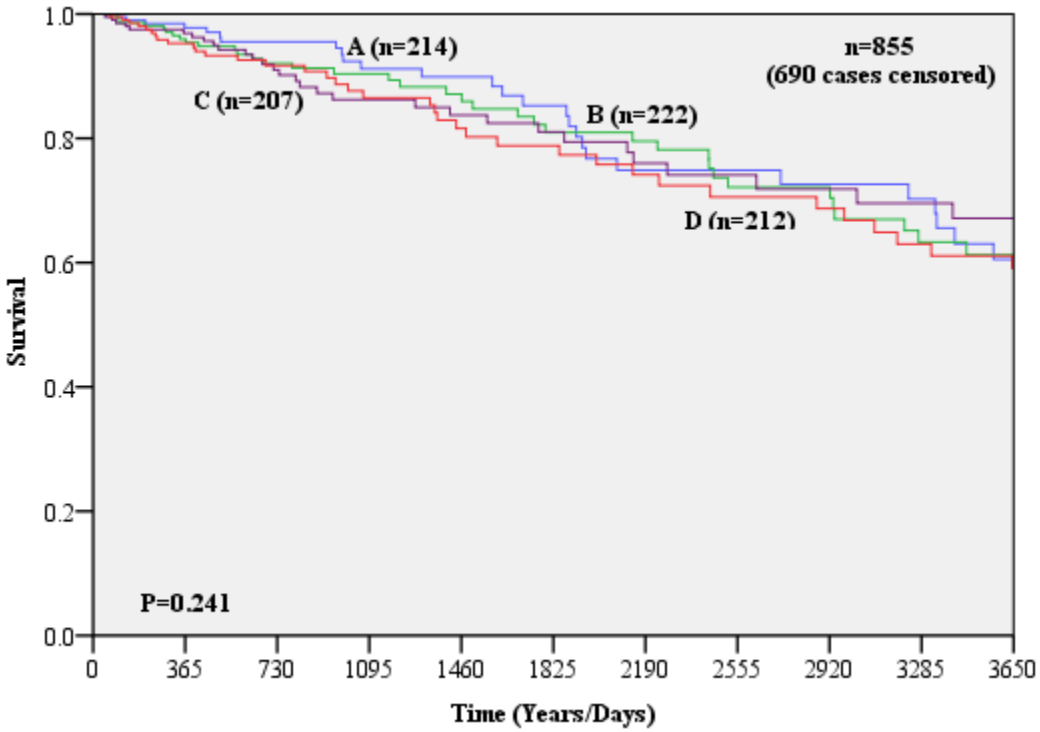


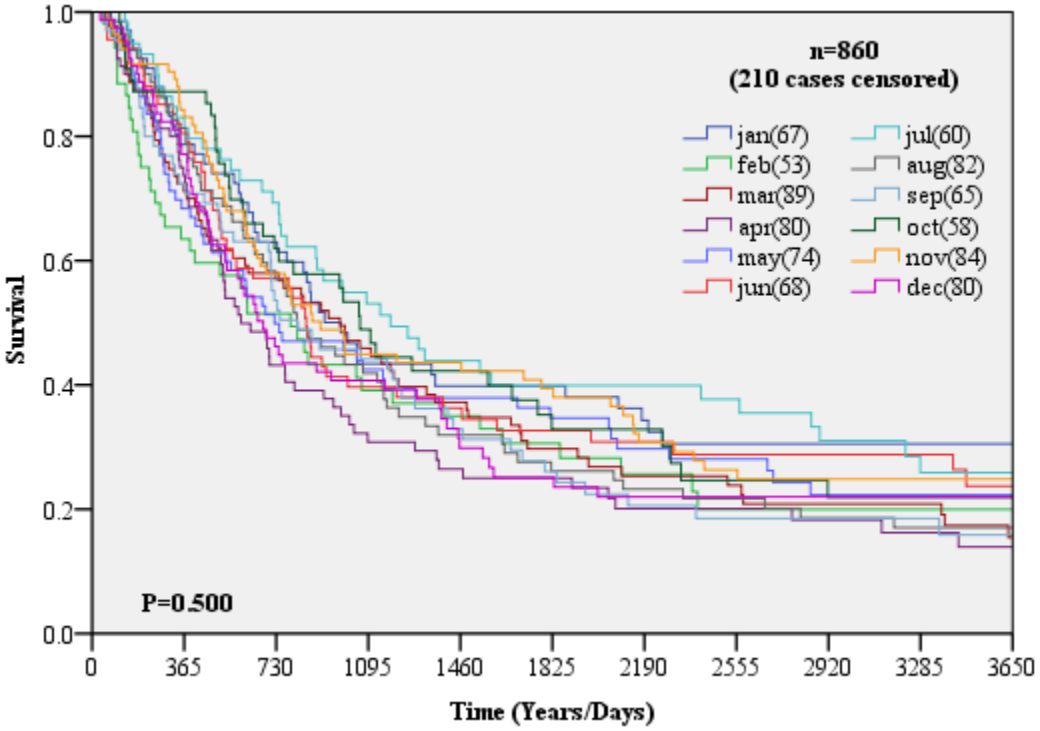
Table 3.52- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for males with NSCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		860	860
Number of censored cases		210	690
HR (95% CI)	Jan	1	1
	Feb	1.11 0.7-1.7	0.1.08 0.5-2.3
	Mar	1.26 0.8-1.8	0.72 0.3-1.4
	Apr	1.36 0.9-2.0	0.81 0.3-1.7
	May	1.17 0.7-1.7	0.92 0.4-1.8
	Jun	1.04 0.6-1.5	1.07 0.5-2.1
	Jul	1.02 0.6-1.5	0.81 0.3-1.7
	Aug	1.27 0.8-1.8	0.88 4.1-1.8
	Sep	1.32 0.8-1.9	0.62 0.2-1.4
	Oct	0.95 0.6-1.4	1.49 0.7-3.0
	Nov	1.10 0.7-1.6	0.69 0.3-1.4
	Dec	1.03 0.6-1.5	0.81 0.4-1.6

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and month of diagnosis.

●NS is not significant ●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.95- Survival according to month of diagnosis for males with NSCLC who received surgery: lung cancer deaths



Graph 3.96- Survival according to month of diagnosis for males with NSCLC who received surgery: non-lung-cancer deaths

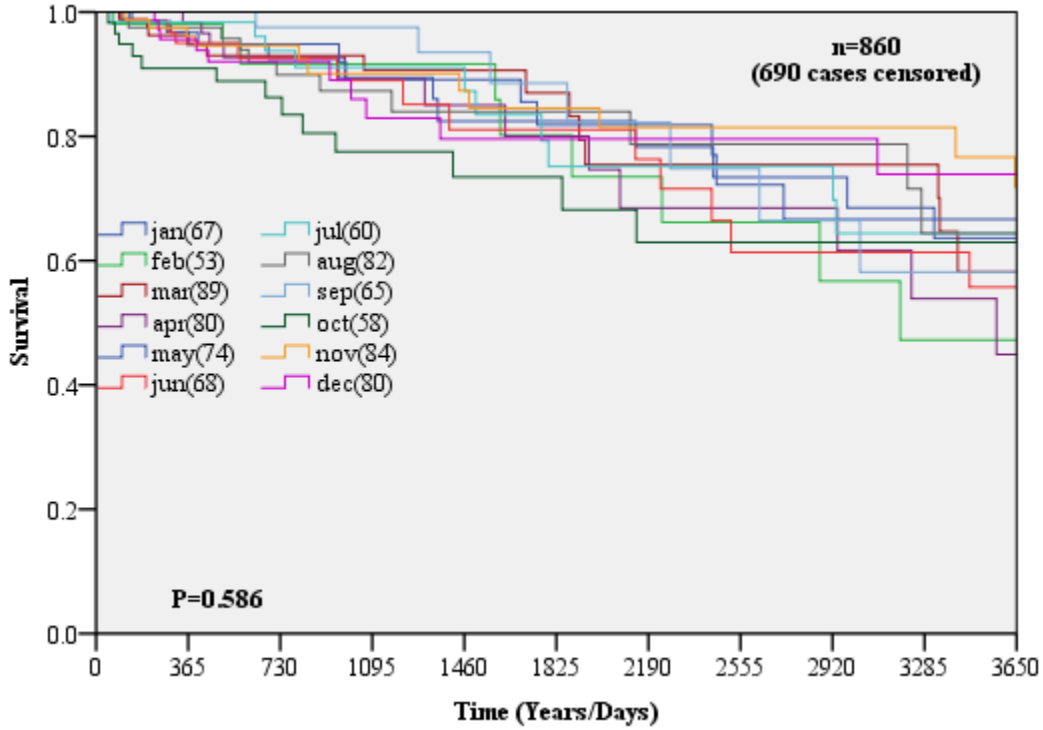


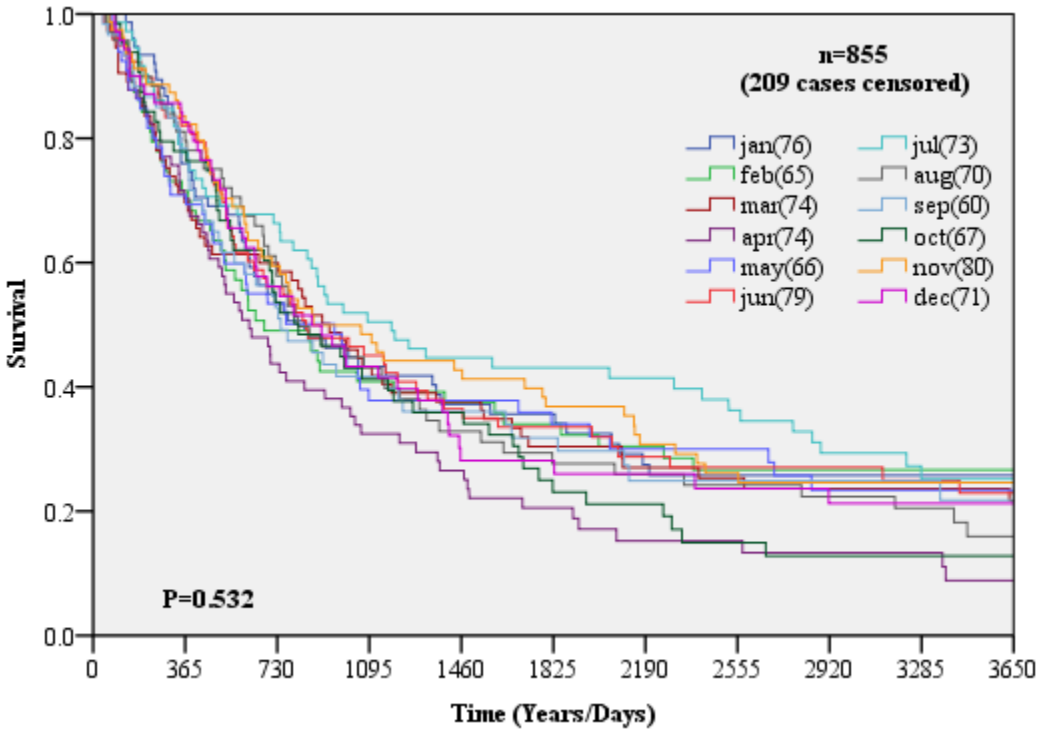
Table 3.53- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for males with NSCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		855	855
Number of censored cases		209	685
HR (95% CI)	Jan	1	1
	Feb	1.09 0.7-1.6	1.28 0.6-2.5
	Mar	1.02 0.7-1.5	0.59 0.2-1.2
	Apr	1.42 0.9-2.0	0.96 0.4-2.2
	May	1.08 0.7- 1.5	0.88 0.4-1.8
	Jun	1.10 0.7-1.6	1.11 0.5-2.2
	Jul	0.92 0.6-1.3	0.87 0.4-1.8
	Aug	1.16 0.7-1.7	1.05 0.5-2.2
	Sep	1.16 0.7-1.7	1.23 0.5-2.6
	Oct	1.06 0.7-1.5	1.10 0.5-2.3
	Nov	1.08 0.7-1.5	0.86 0.4-1.8
	Dec	1.12 0.7-1.6	1.36 0.6-0.2

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and month of first treatment.

•NS is not significant•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.97- Survival according to month of first treatment for males with NSCLC who received surgery: lung cancer deaths



Graph 3.98- Survival according to month of first treatment for males with NSCLC who received surgery: non-lung-cancer deaths

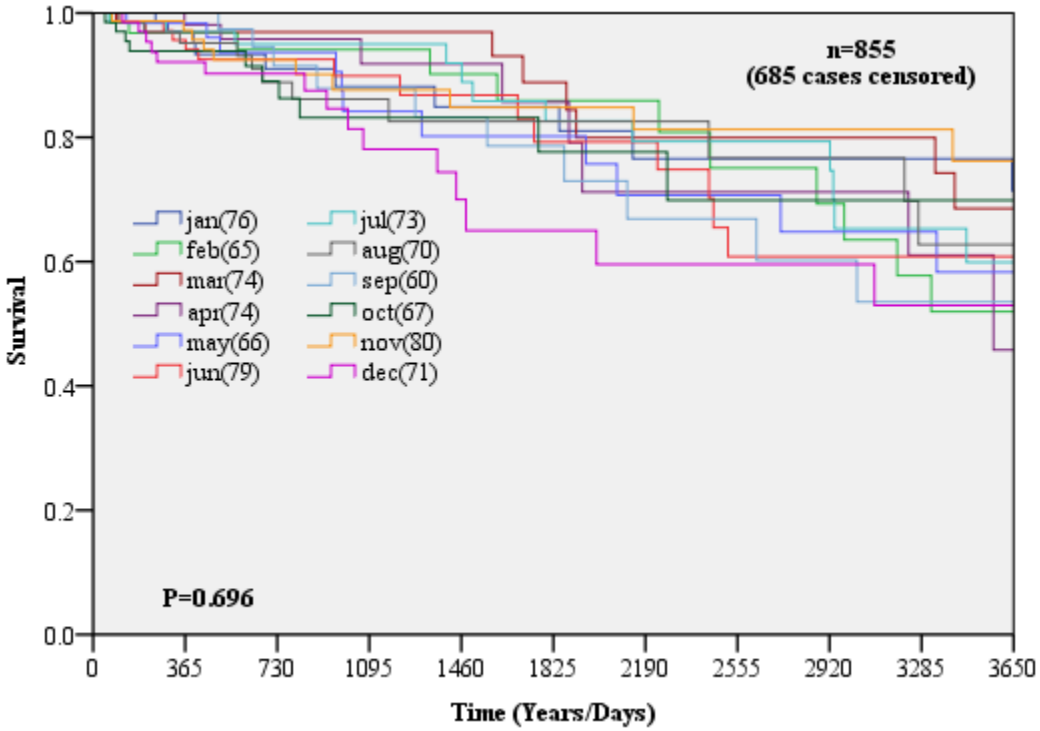


Table 3.54- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for males with NSCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	847	205	NS	NS	1	1.08 0.8-1.3	1.26 1.0-1.5	1.08 0.8-1.3	1.00 0.7-1.3
Other causes	847	678	NS	NS	1	1.12 0.7-1.7	0.79 0.4-1.3	1.04 0.6-1.6	0.99 0.6-1.6

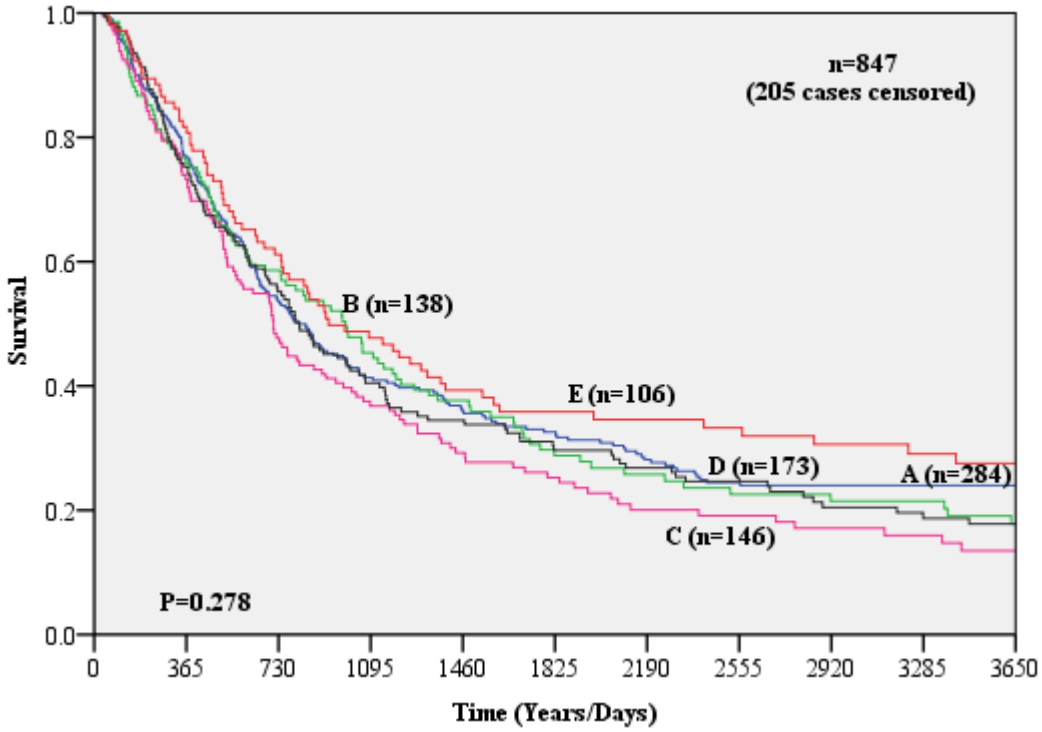
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.99- Survival according to MMVDSI for males with NSCLC who received surgery: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.100- Survival according to MMVDSI for males with NSCLC who received surgery: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

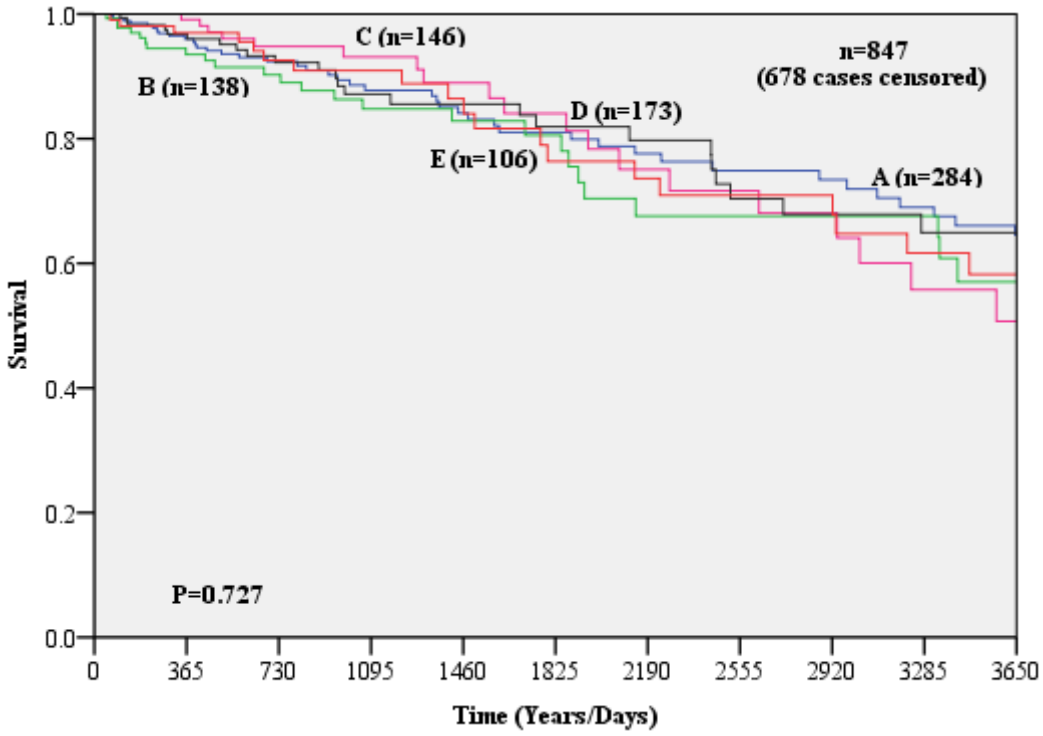


Table 3.55- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for females with NSCLC who received surgery

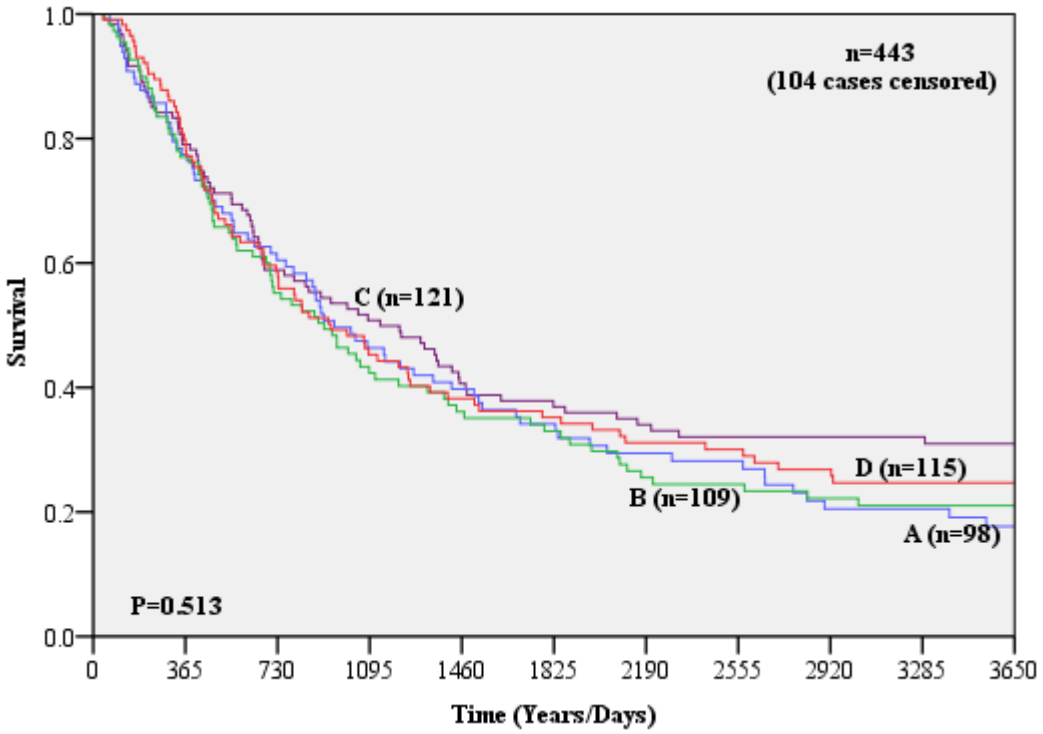
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	443	104	NS	NS	1.2 0.9-1.1	1.09 0.8-1.4	1	1.00 0.7-1.3
Other causes	443	372	NS	NS	0.91 0.4-1.8	1.10 0.5-2.0	1	0.63 0.3-1.2

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.101- Survival according to season of diagnosis for females with NSCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.102- Survival according to season of diagnosis for females with NSCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

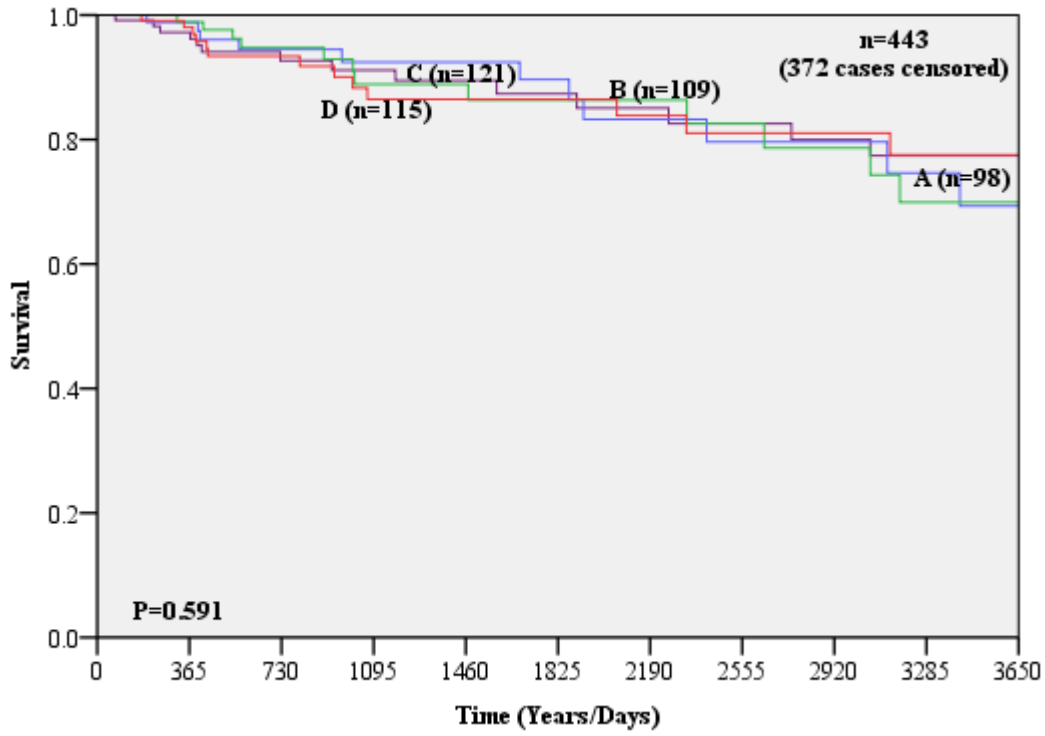


Table 3.56- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for females with NSCLC who received surgery

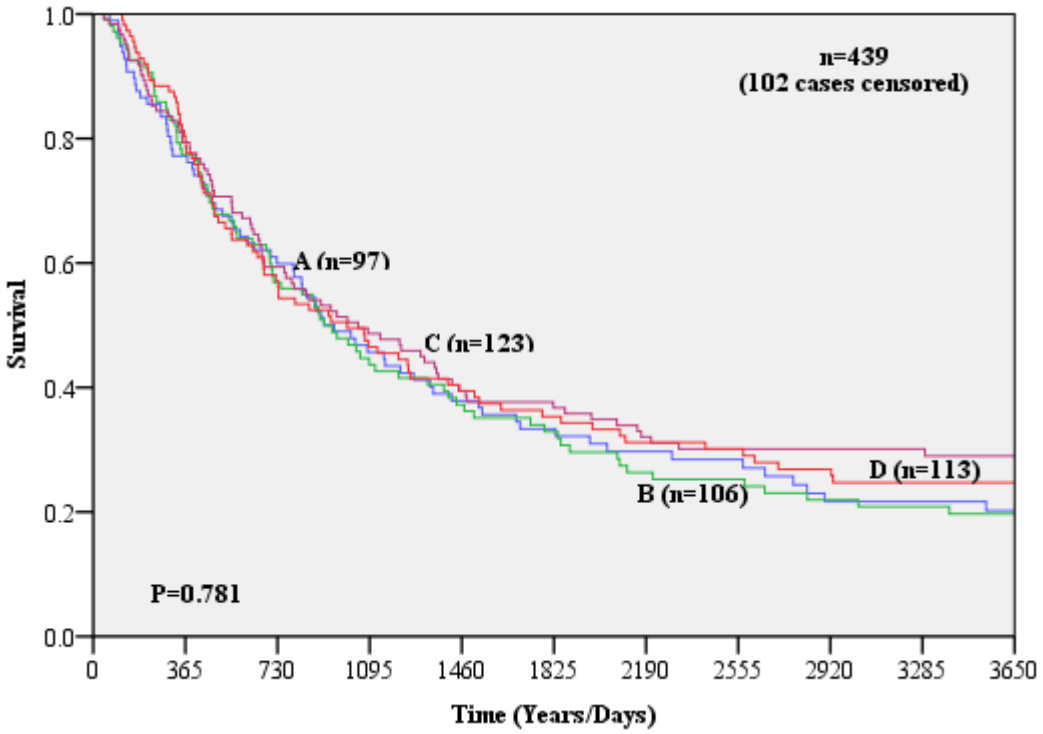
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	439	102	NS	NS	1	0.88 0.6-1.2	0.88 0.6-1.2	0.85 0.6-1.1
Other causes	439	372	NS	NS	1	0.96 0.4-2.0	1.26 0.6-2.6	0.66 0.2-1.4

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.103- Survival according to season of first treatment for females with NSCLC who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.104- Survival according to season of first treatment for females with NSCLC who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

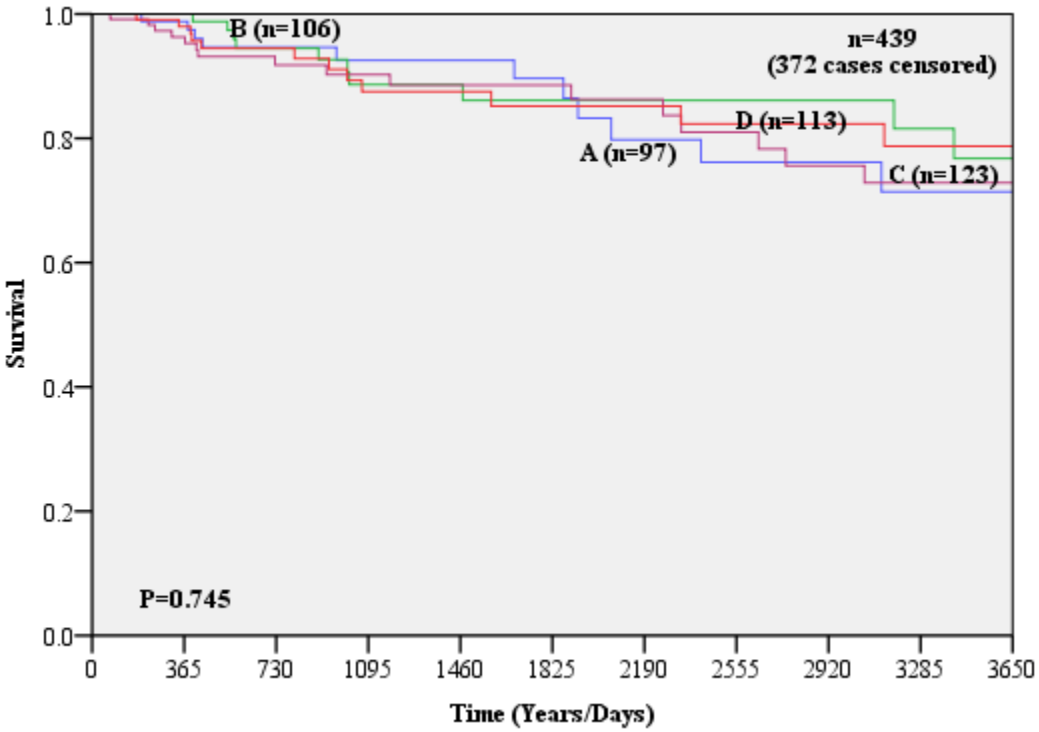


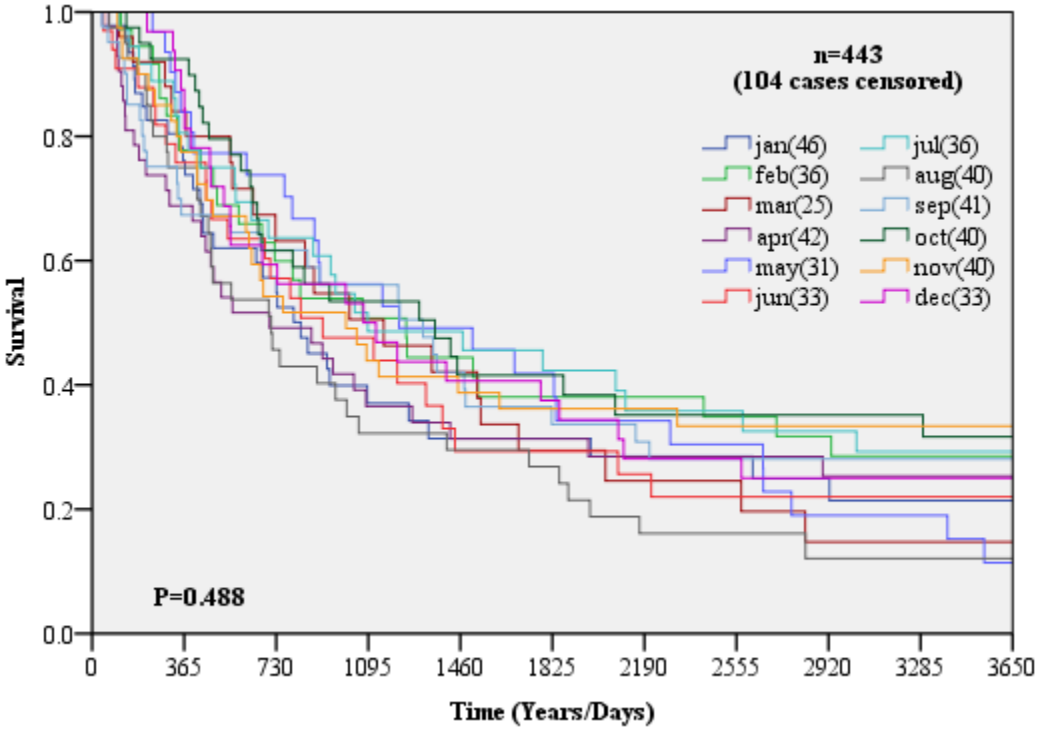
Table 3.57- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for females with NSCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		443	443
Number of censored cases		104	372
HR (95% CI)	Jan	1	1
	Feb	0.71 0.4-1.2	0.30 0.0-1.0
	Mar	1.22 0.7-2.1	N<5
	Apr	1.07 0.6-1.7	0.75 0.2-2.2
	May	0.96 0.5-1.6	N<5
	Jun	0.82 0.4-1.4	1.07 0.3-3.0
	Jul	0.66 0.3-1.1	0.96 0.3-2.6
	Aug	1.52 0.9-2.4	0.42 0.1-1.5
	Sep	0.96 0.5-1.5	1.21 0.4-3.2
	Oct	0.73 0.4-1.2	0.69 0.2-2.0
	Nov	0.91 0.5-1.5	0.42 0.1-1.5
	Dec	0.85 0.5-1.4	0.19 0.0-0.8

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and month of diagnosis.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.105- Survival according to month of diagnosis for females with NSCLC who received surgery: lung cancer deaths



Graph 3.106- Survival according to month of diagnosis for females with NSCLC who received surgery: non-lung-cancer deaths

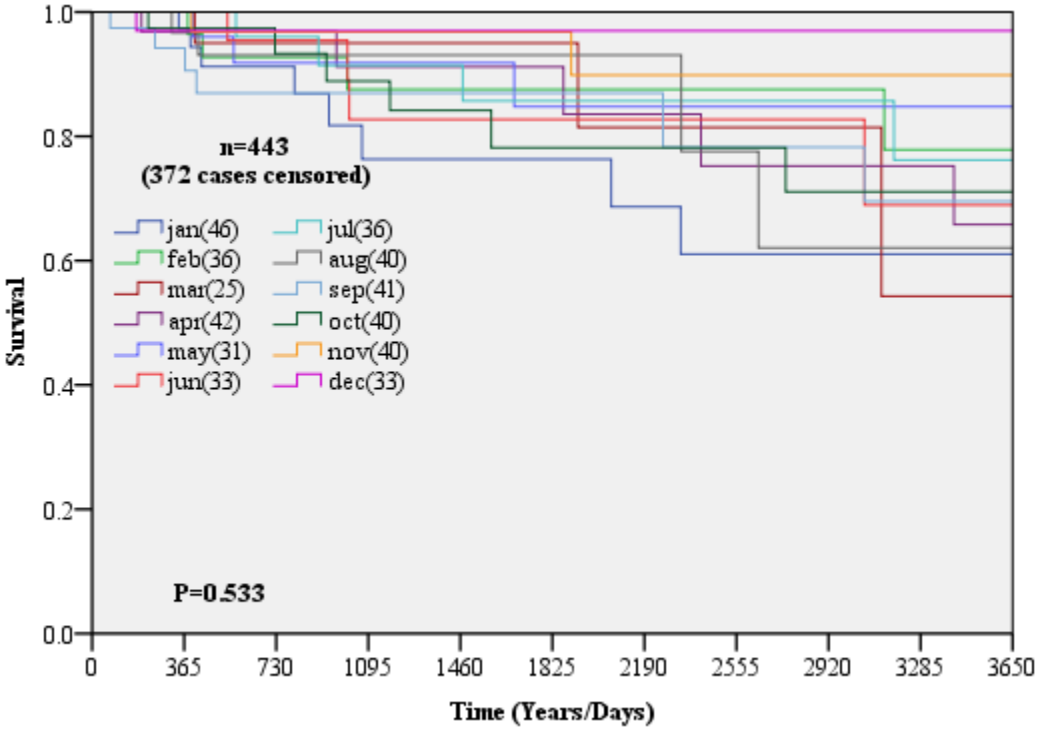


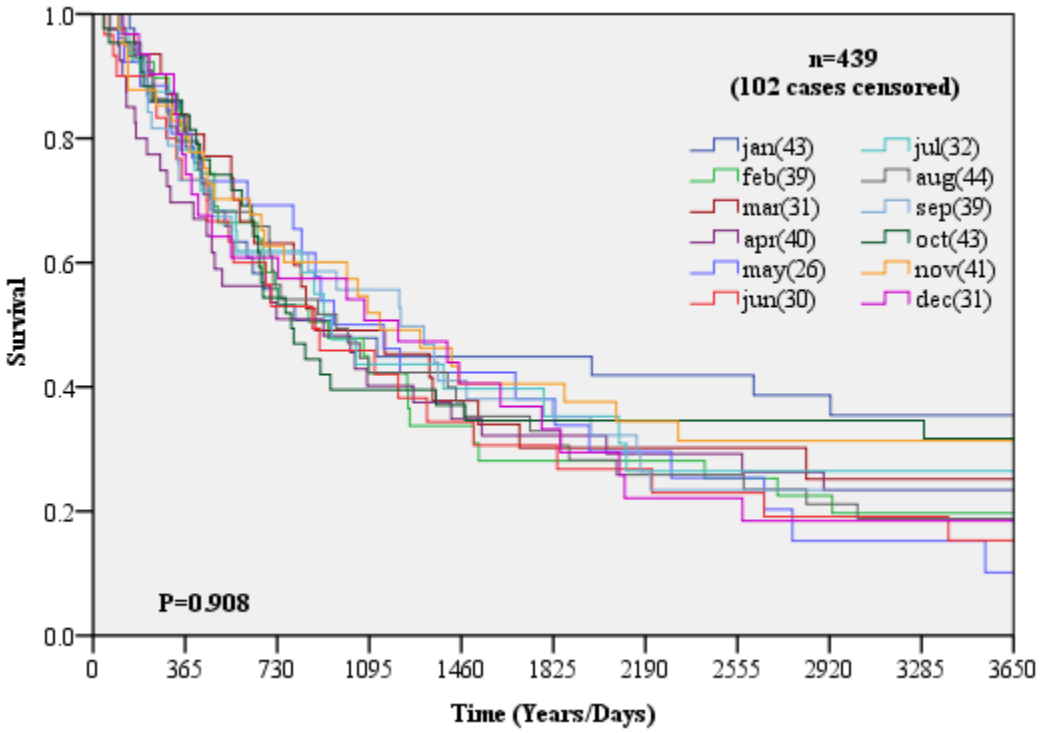
Table 3.58- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for females with NSCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	0.046
Number of cases		439	439
Number of censored cases		102	369
HR (95% CI)	Jan	1	1
	Feb	1.12 0.6-1.9	N<5
	Mar	1.03 0.5-1.8	1.73 0.5-5.3
	Apr	1.44 0.8-2.4	N<5
	May	1.24 0.6-2.2	N<5
	Jun	1.39 0.7-2.4	0.94 0.3-2.9
	Jul	0.82 0.4-1.4	1.59 0.5-4.4
	Aug	1.23 0.7-2.0	N<5
	Sep	1.43 0.8-2.4	2.59 0.9-6.7
	Oct	1.13 0.6-1.9	0.96 0.3-2.7
	Nov	0.96 0.5-1.6	0.78 0.2-2.2
	Dec	1.22 0.7-2.1	N<5

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and month of first treatment.

•NS is not significant•N is number of uncensored cases•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.107- Survival according to month of first treatment for females with NSCLC who received surgery: lung cancer deaths



Graph 3.108- Survival according to month of first treatment for females with NSCLC who received surgery: non-lung-cancer deaths

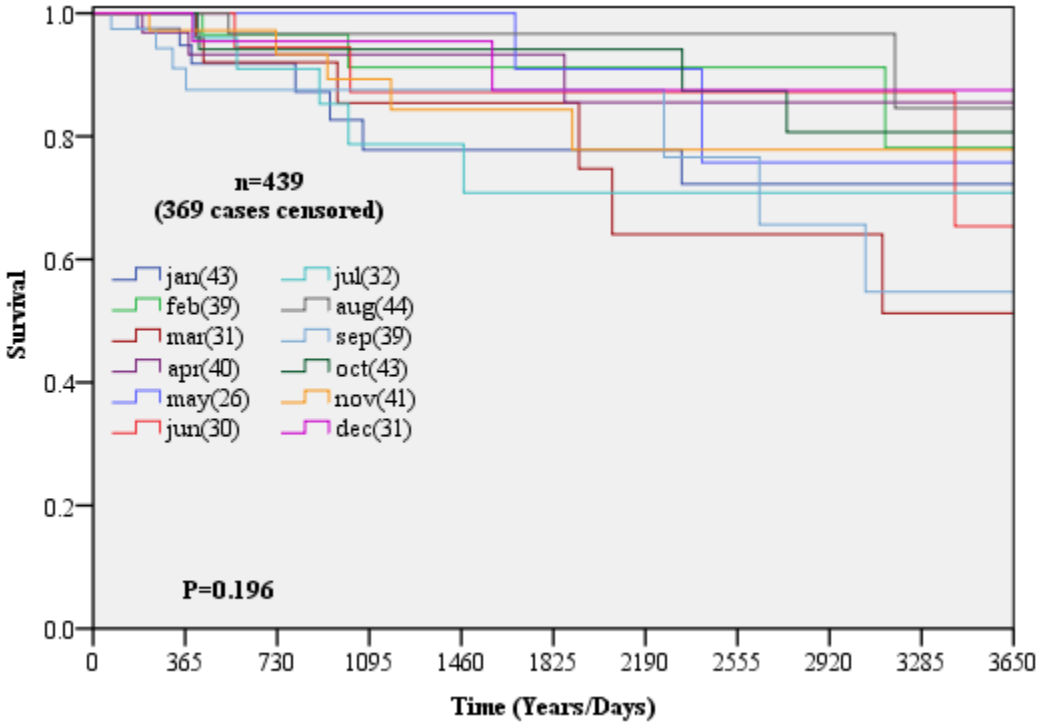


Table 3.59- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for females with NSCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	431	102	NS	0.050	1	1.03 0.7-1.4	1.14 0.8-1.5	1.43 1.0-1.9	0.79 0.5-1.1
Other causes	431	361	NS	NS	1	1.50 0.6-3.4	2.08 1.0-4.1	1.43 0.6-3.1	2.09 0.9-4.5

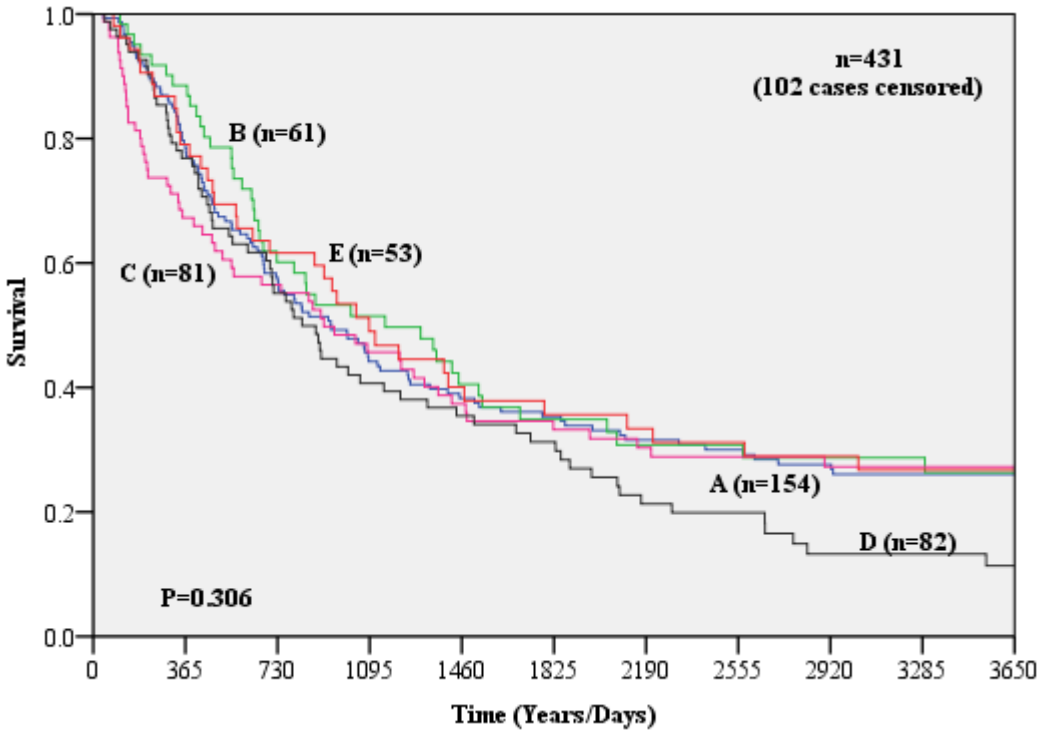
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.109- Survival according to MMVDSI for females with NSCLC who received surgery: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.110- Survival according MMVDSI for females with NSCLC who received surgery: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

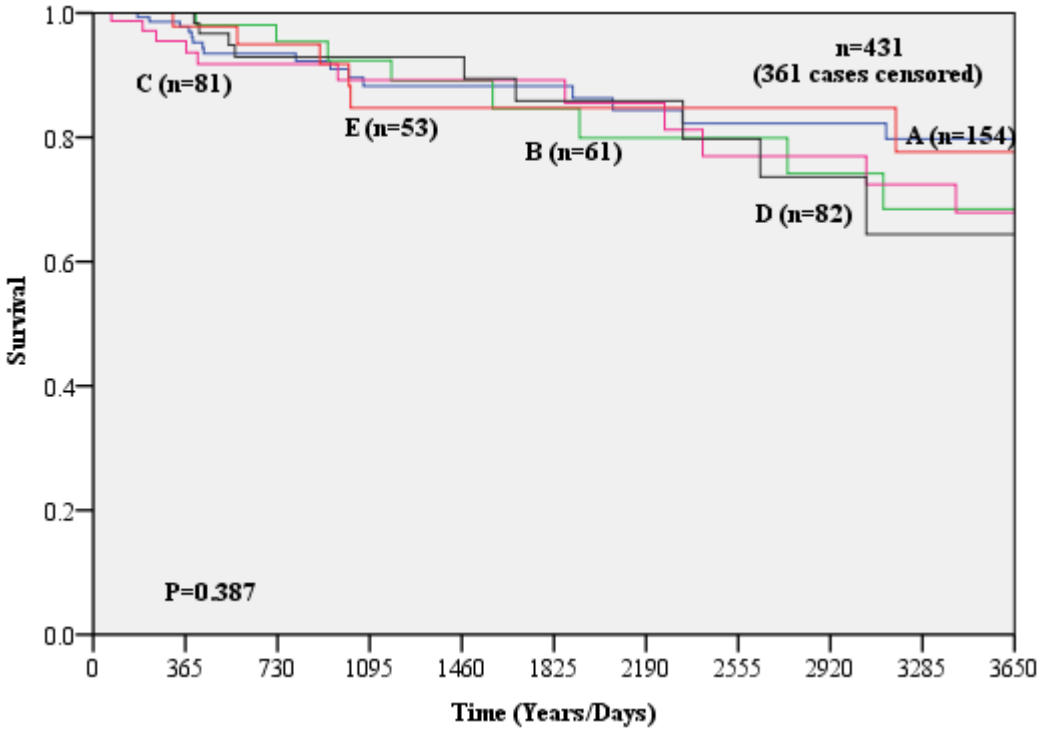


Table 3.60- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for male and female patients with NSCLC who received surgery

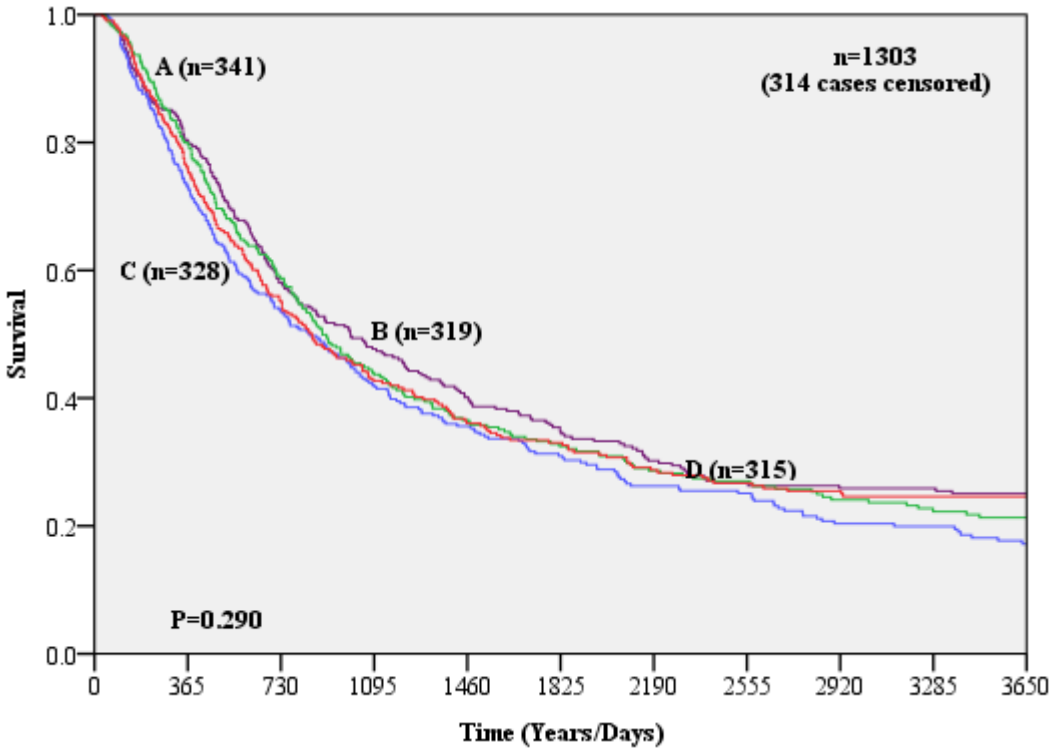
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring	Summer	Fall	Winter
Lung cancer	1303	314	NS	NS	1.15 0.9-1.3	1.02 0.8-1.2	1	0.94 0.7-1.1
Other causes	1303	1062	NS	NS	0.96 0.6-1.3	1.07 0.7-1.5	1	0.92 0.6-1.3

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.111- Survival according to season of diagnosis for male and female NSCLC patients who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.112- Survival according to season of diagnosis for male and female NSCLC patients who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

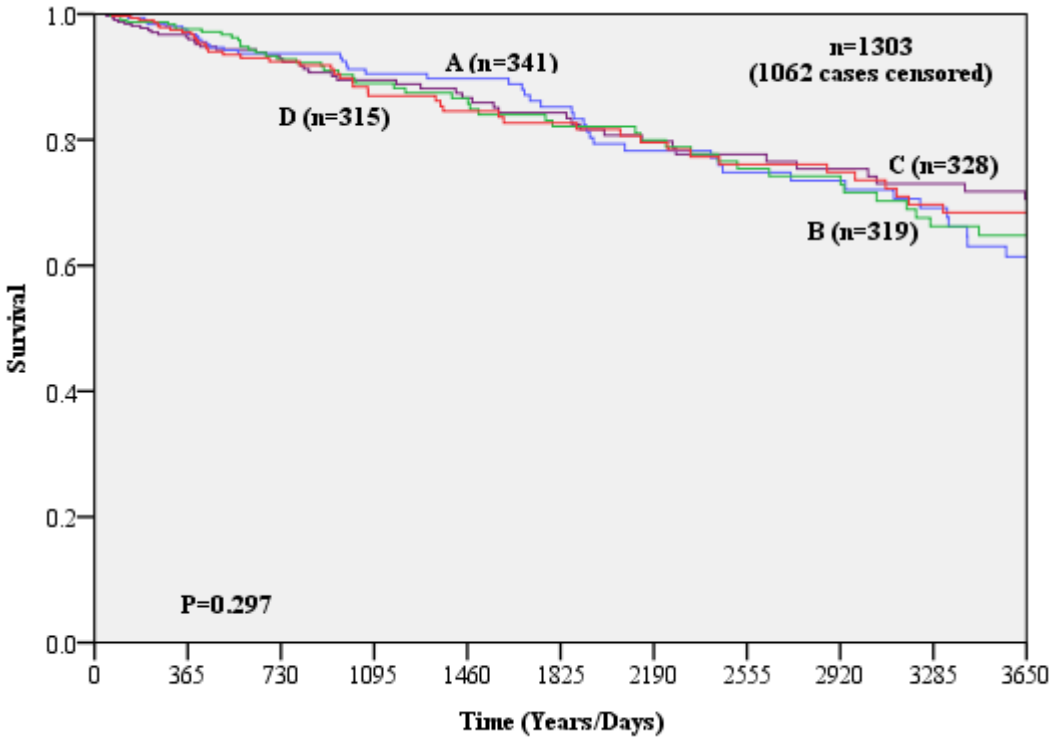


Table 3.61- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for male and female patients with NSCLC who received surgery

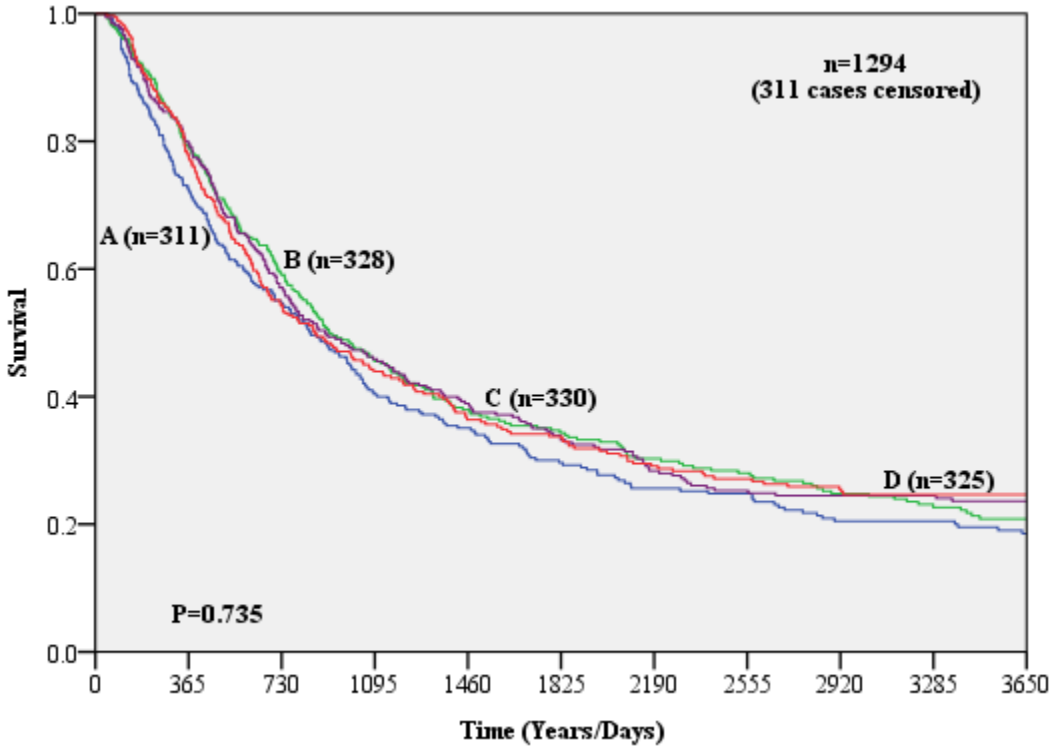
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	1294	311	NS	NS	1	0.90 0.7-1.0	0.95 0.7-1.1	0.90 0.7-1.0
Other causes	1294	1054	NS	NS	1	1.18 0.8-1.7	1.34 0.9-1.9	1.20 0.8-1.7

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.113- Survival according to season of first treatment for male and female NSCLC patients who received surgery: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.114- Survival according to season of first treatment diagnosis for male and female NSCLC patients who received surgery: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

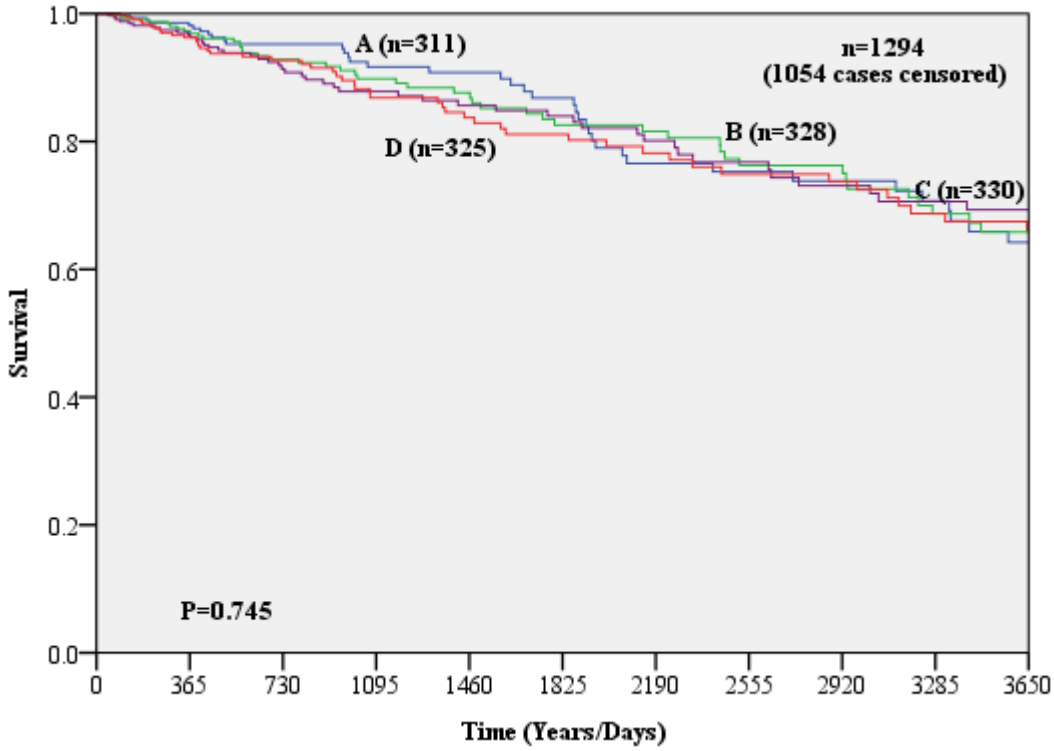


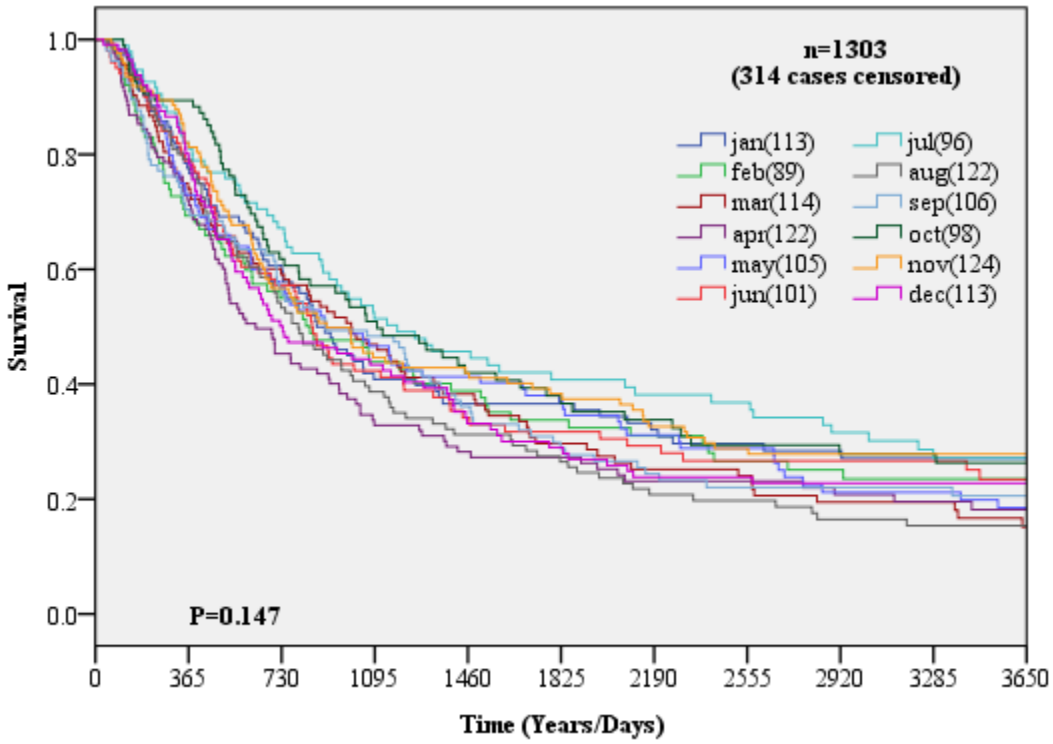
Table 3.62- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for male and female patients with NSCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.067	NS
Number of cases		1303	1303
Number of censored cases		314	1062
HR (95% CI)	Jan	1	1
	Feb	0.89 0.6-1.2	0.69 0.3-1.3
	Mar	1.20 0.8-1.6	0.79 0.4-1.4
	Apr	1.24 0.9-1.6	0.83 0.4-1.5
	May	1.06 0.7-1.4	0.81 0.4-1.4
	Jun	0.95 0.6-1.3	1.06 0.6-1.8
	Jul	0.85 0.6-1.1	0.84 0.4-1.5
	Aug	1.30 0.9-1.7	0.82 0.4-1.5
	Sep	1.16 0.8-1.5	0.80 0.4-1.4
	Oct	0.85 0.6-1.1	1.18 0.6-2.0
	Nov	1.02 0.7-1.3	0.60 0.3-1.1
	Dec	0.95 0.6-1.2	0.65 0.3-1.1

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and month of diagnosis.

•NS is not significant• Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.115- Survival according to month of diagnosis for male and female NSCLC patients who received surgery: lung cancer deaths



Graph 3.116- Survival according to month of diagnosis for male and female NSCLC patients who received surgery: non-lung-cancer deaths

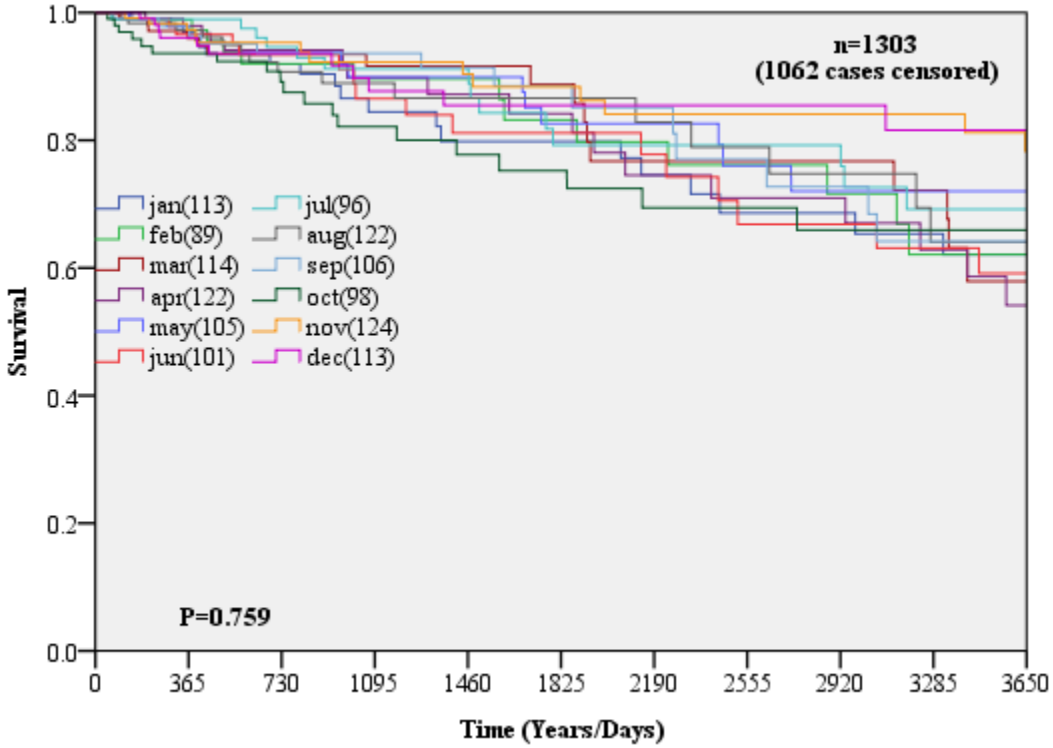


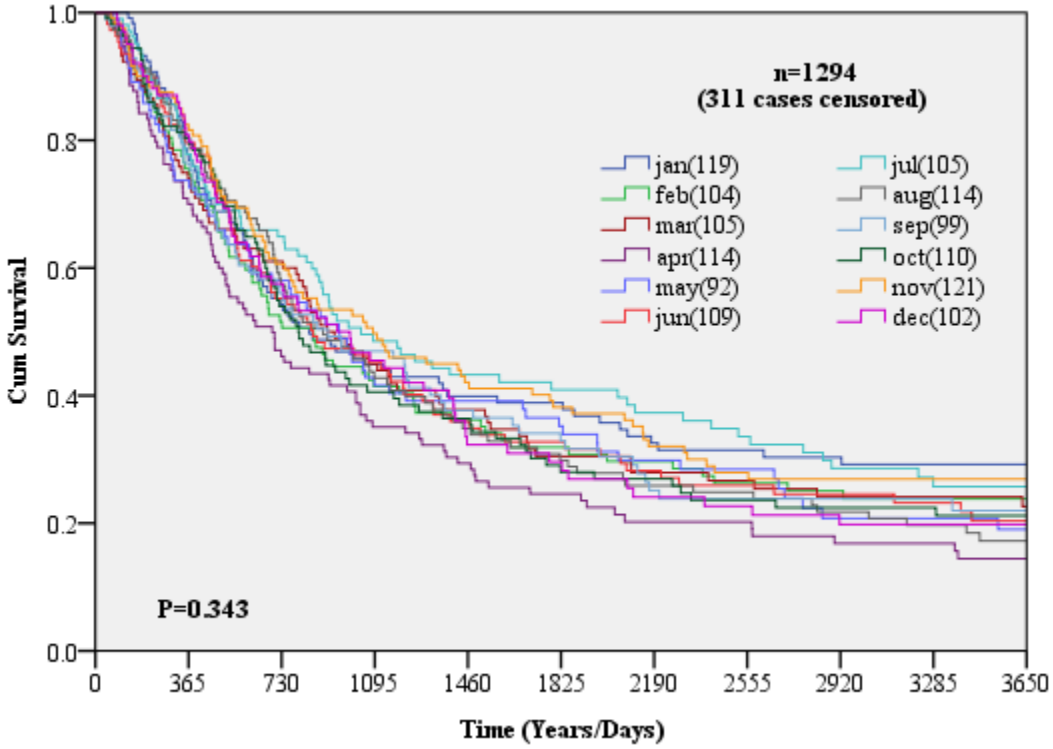
Table 3.63- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for male and female patients with NSCLC who received surgery

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		1294	1294
Number of censored cases		311	1054
HR (95% CI)	Jan	1	1
	Feb	1.09 0.8-1.4	0.91 0.5-1.6
	Mar	1.01 0.7-1.3	0.78 0.4-1.4
	Apr	1.40 1.0-1.8	0.87 0.4-1.7
	May	1.11 0.8-1.5	0.86 0.4-1.6
	Jun	1.15 0.8-1.5	1.09 0.6-1.9
	Jul	0.90 0.6-1.2	1.07 0.5-1.9
	Aug	1.15 0.8-1.5	0.82 0.4-1.5
	Sep	1.24 0.9-1.7	1.63 0.9-2.9
	Oct	1.10 0.8-1.5	1.03 0.5-1.8
	Nov	1.05 0.7-1.4	0.91 0.5-1.6
	Dec	1.10 0.8-1.5	1.14 0.6-2.0

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and month of first treatment.

•NS is not significant •Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.117- Survival according to month of first treatment for male and female NSCLC patients who received surgery: lung cancer deaths



Graph 3.118- Survival according to month of first treatment for male and female NSCLC patients who received surgery: non-lung-cancer deaths

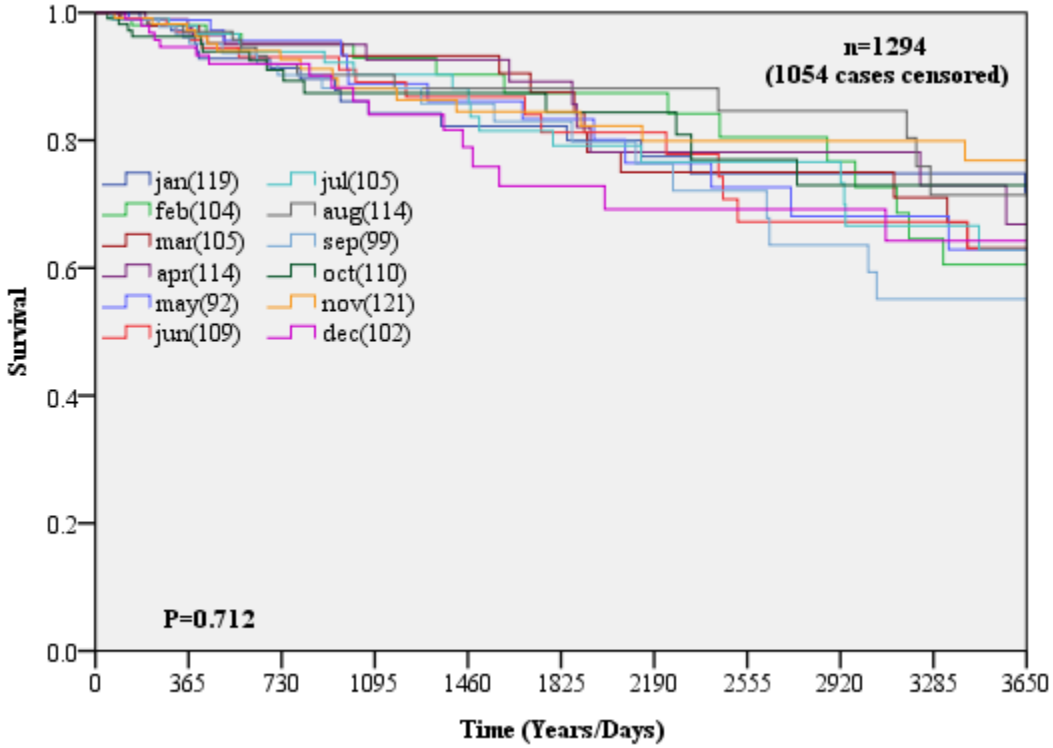


Table 3.64- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for male and female patients with NSCLC who received surgery

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	1278	307	0.085	0.052	1	1.06 0.8-1.2	1.22 1.0-1.4	1.18 0.9-1.4	0.92 0.7-1.1
Other causes	1278	1039	NS	NS	1	1.26 0.8-1.8	1.05 0.7-1.5	1.18 0.8-1.7	1.15 0.7-1.7

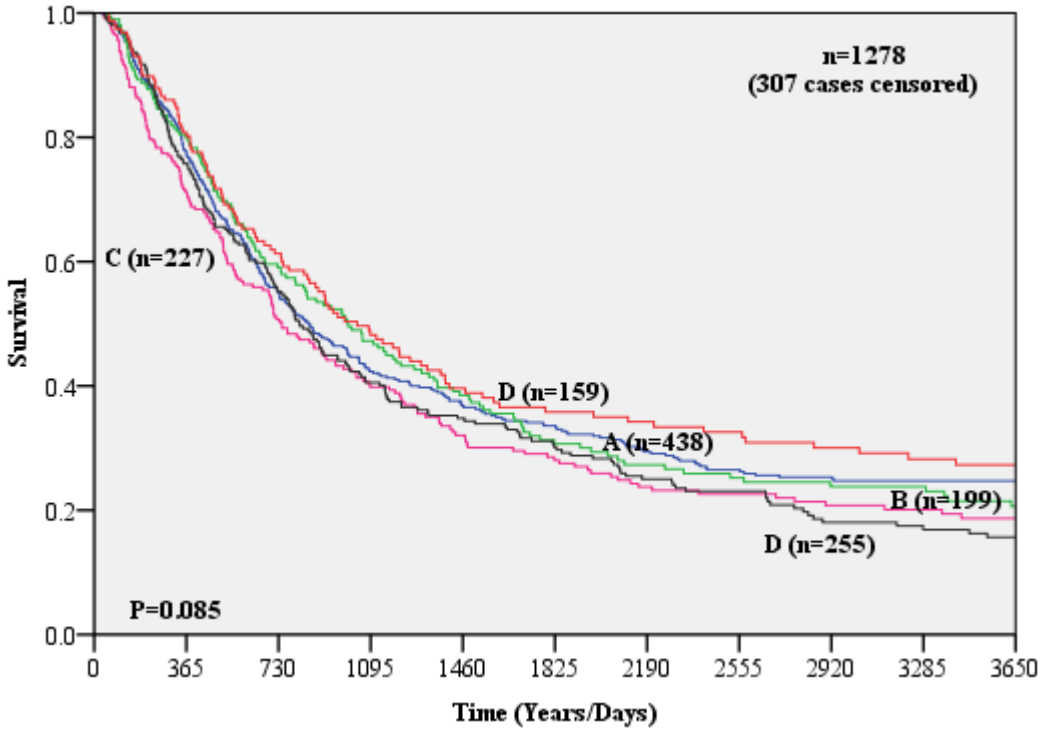
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and radiotherapy), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.119- Survival according to MMVDSI for male and female NSCLC patients who received surgery: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.120- Survival according to MMVDSI for male and female NSCLC patients who received surgery: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

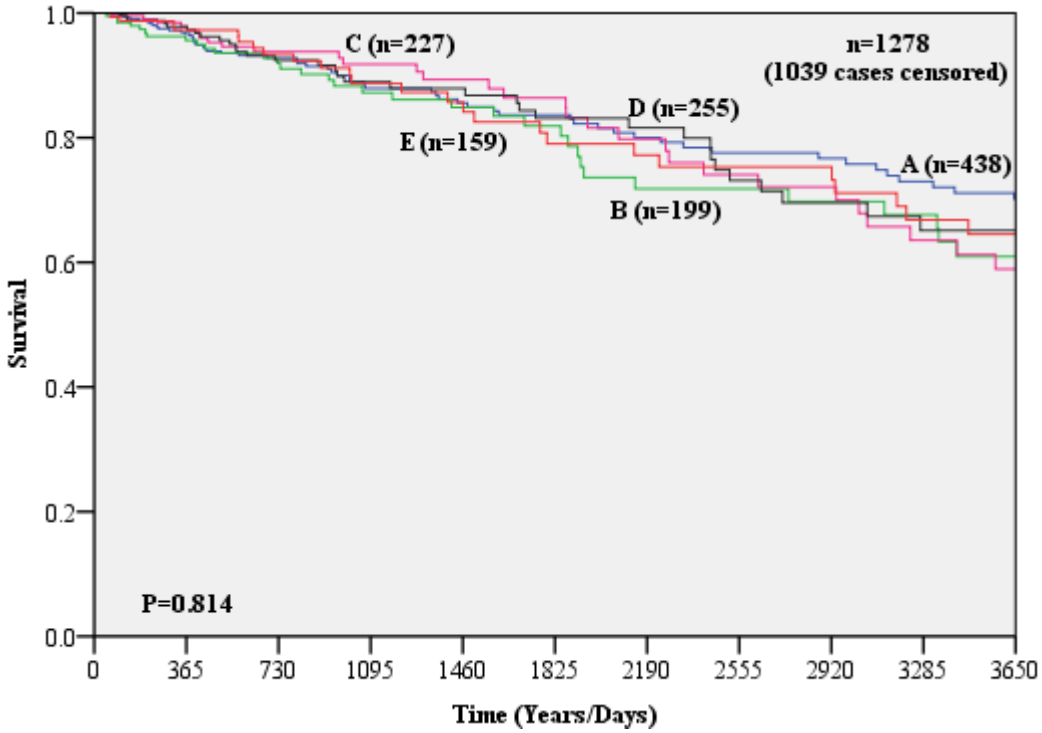


Table 3.65- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for males with NSCLC who received radiotherapy

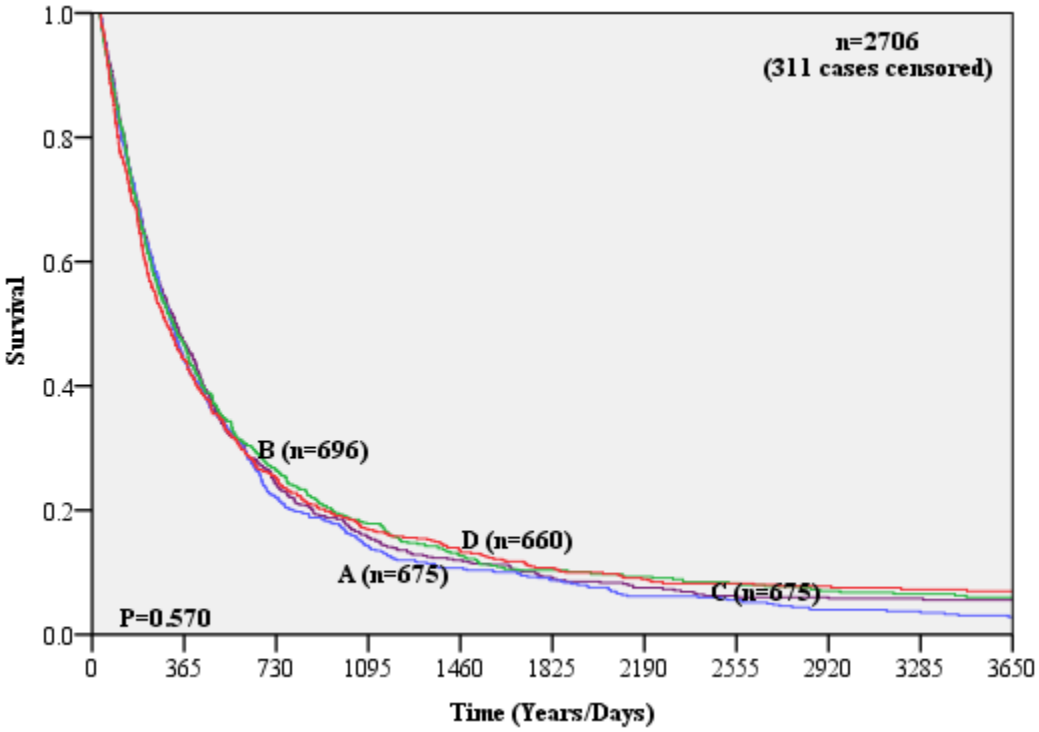
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	2706	311	NS	NS	1.03 0.9-1.16	0.92 0.8-1.0	1	0.97 0.8-1.0
Other causes	2706	2419	NS	NS	0.85 0.5-1.2	1.04 0.7-1.4	1	1.02 0.7-1.4

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.121- Survival according to season of diagnosis for males with NSCLC who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.122- Survival according to season of diagnosis for males with NSCLC who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

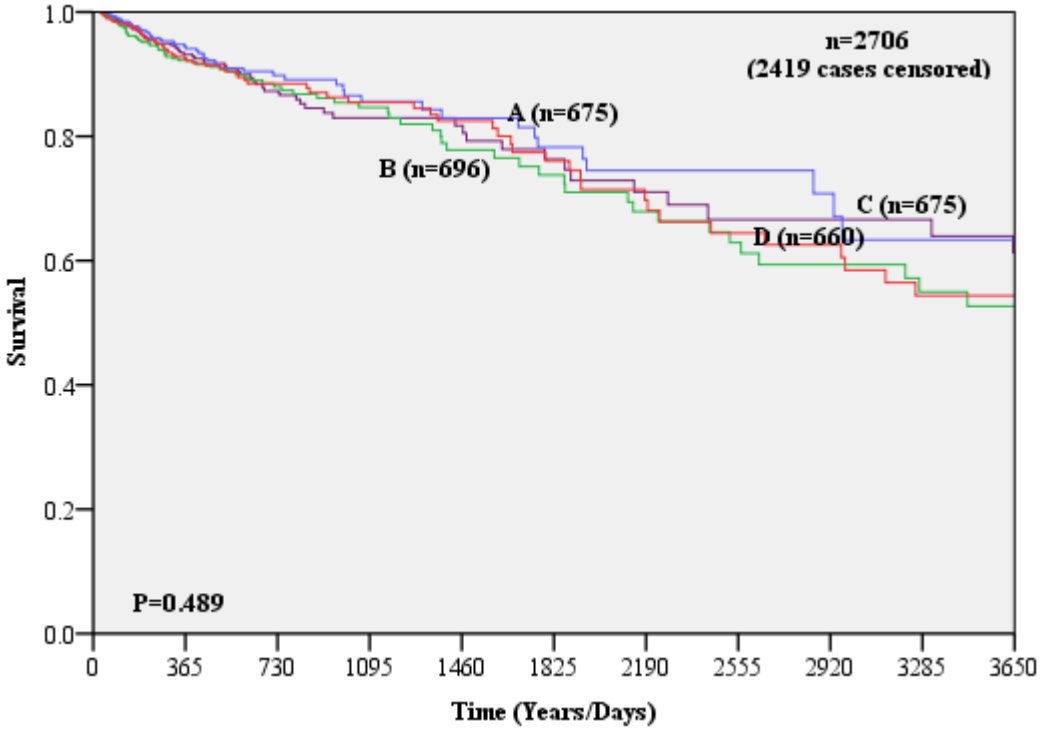


Table 3.66- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for males with NSCLC who received radiotherapy

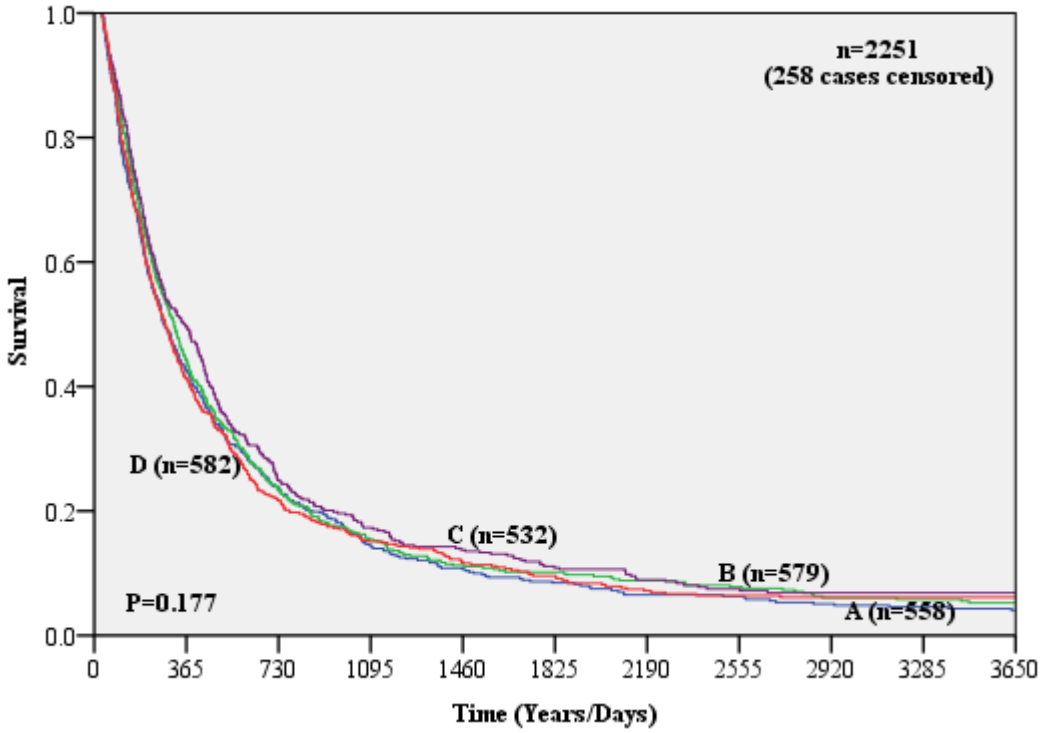
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	2251	258	NS	NS	1	0.92 0.8-1.0	0.88 0.7-1.0	0.94 0.8-1.0
Other causes	2251	2013	NS	NS	1	1.09 0.7-1.6	1.30 0.8-1.8	1.22 0.8-1.7

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.123- Survival according to season of first treatment for males with NSCLC who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.124- Survival according to season of first treatment for males with NSCLC who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

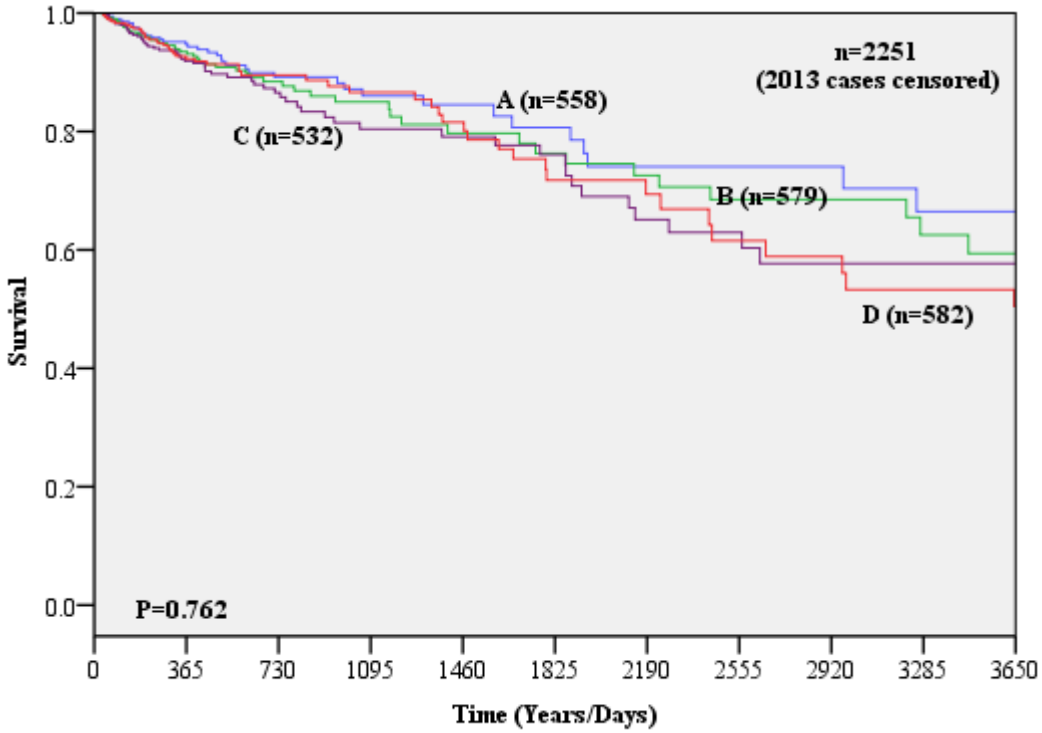


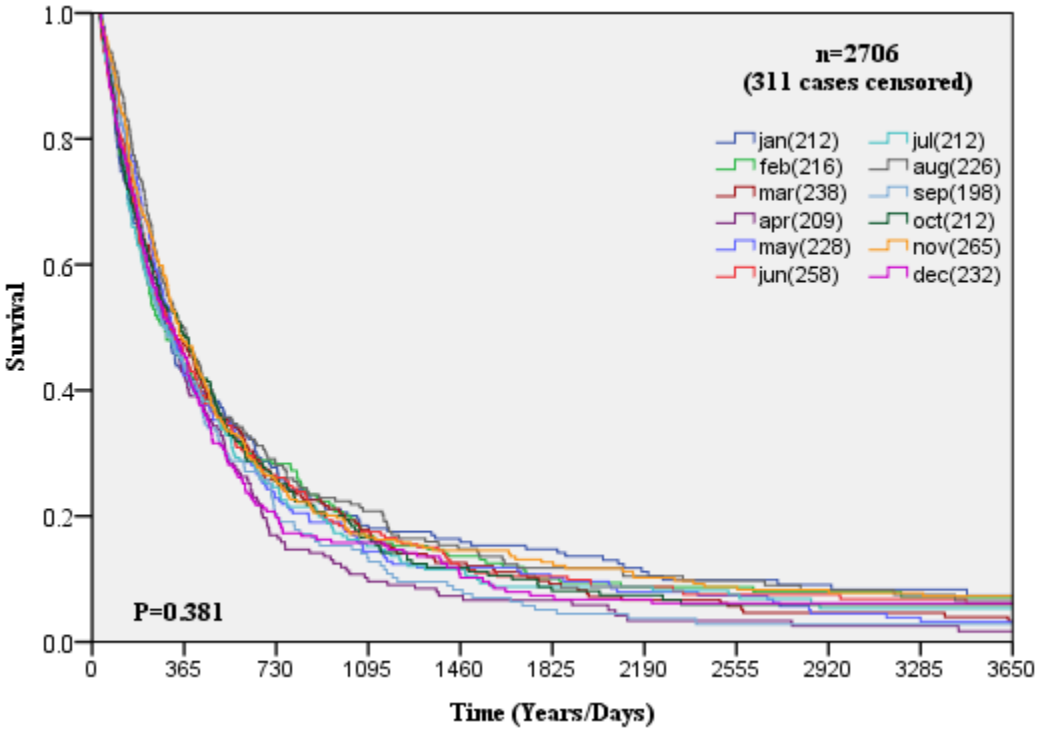
Table 3.67- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for males with NSCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.060	NS
Number of cases		2706	2706
Number of censored cases		311	2419
HR (95% CI)	Jan	1	1
	Feb	1.04 0.8-1.2	1.26 0.7-2.1
	Mar	1.12 0.9-1.3	0.91 0.5-1.6
	Apr	1.31 1.0-1.6	1.22 0.6-2.2
	May	1.05 0.8-1.2	0.83 0.4-1.5
	Jun	1.02 0.8-1.2	1.28 0.7-2.1
	Jul	1.11 0.9-1.3	0.94 0.5-1.7
	Aug	0.94 0.7-1.1	1.28 0.7-2.2
	Sep	1.22 0.9-1.5	1.37 0.7-2.5
	Oct	1.10 0.9-1.3	1.30 0.7-2.3
	Nov	1.02 0.8-1.2	0.90 0.5-1.5
	Dec	1.21 0.9-1.4	1.24 0.7-2.1

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and month of diagnosis.

●NS is not significant ●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.125- Survival according to month of diagnosis for males with NSCLC who received radiotherapy: lung cancer deaths



Graph 3.126- Survival according to month of diagnosis for males with NSCLC who received radiotherapy: non-lung-cancer deaths

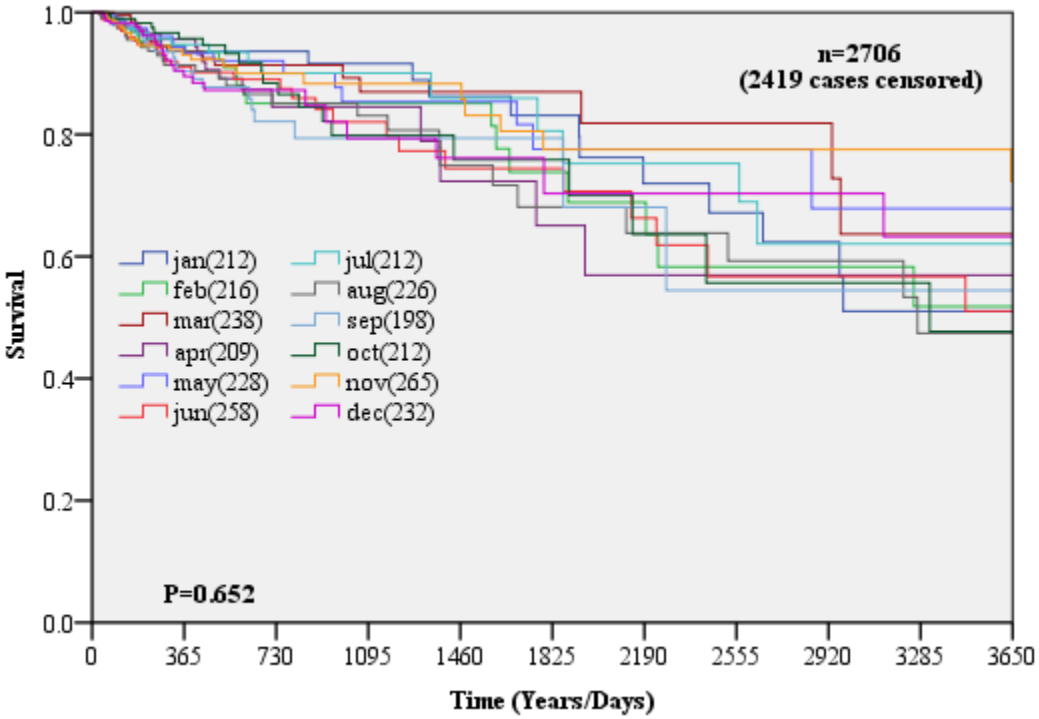


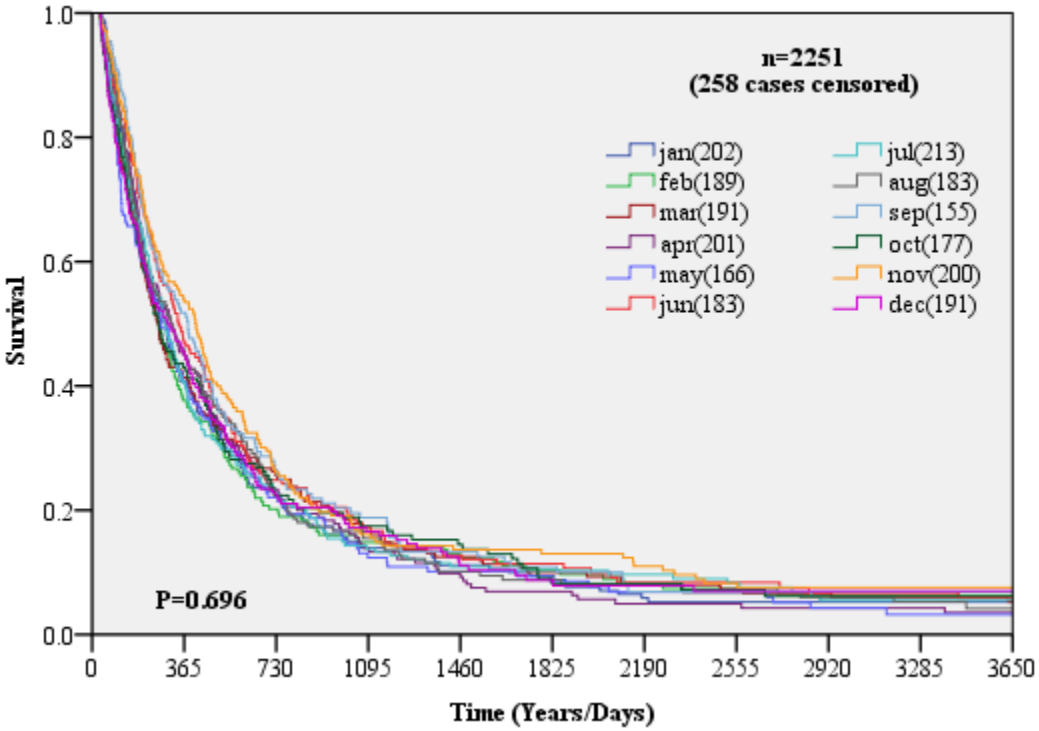
Table 3.68- Hazard ratio (HR) and 95% confidence interval (CI) according to month of first treatment for males with NSCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		2251	2251
Number of censored cases		258	2013
HR (95% CI)	Jan	1	1
	Feb	0.97 0.7-1.2	1.39 0.7-2.5
	Mar	1.04 0.8-1.2	0.88 0.4-1.7
	Apr	1.04 0.8-1.2	0.94 0.4-1.8
	May	1.07 0.8-1.3	1.16 0.5-2.3
	Jun	0.89 0.7-1.1	1.00 0.5-1.9
	Jul	0.99 0.8-1.2	1.15 0.6-2.1
	Aug	0.99 0.8-1.2	1.08 0.5-2.0
	Sep	0.81 0.6-1.0	1.18 0.6-2.2
	Oct	1.03 0.8-1.2	1.44 0.7-2.7
	Nov	0.95 0.7-1.1	1.24 0.6-2.2
	Dec	0.97 0.7-1.2	1.17 0.6-1.2

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and month of first treatment.

●NS is not significant ●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.127- Survival according to month of first treatment for males with NSCLC who received radiotherapy: lung cancer deaths



Graph 3.128- Survival according to month of first treatment for males with NSCLC who received radiotherapy: non-lung-cancer deaths

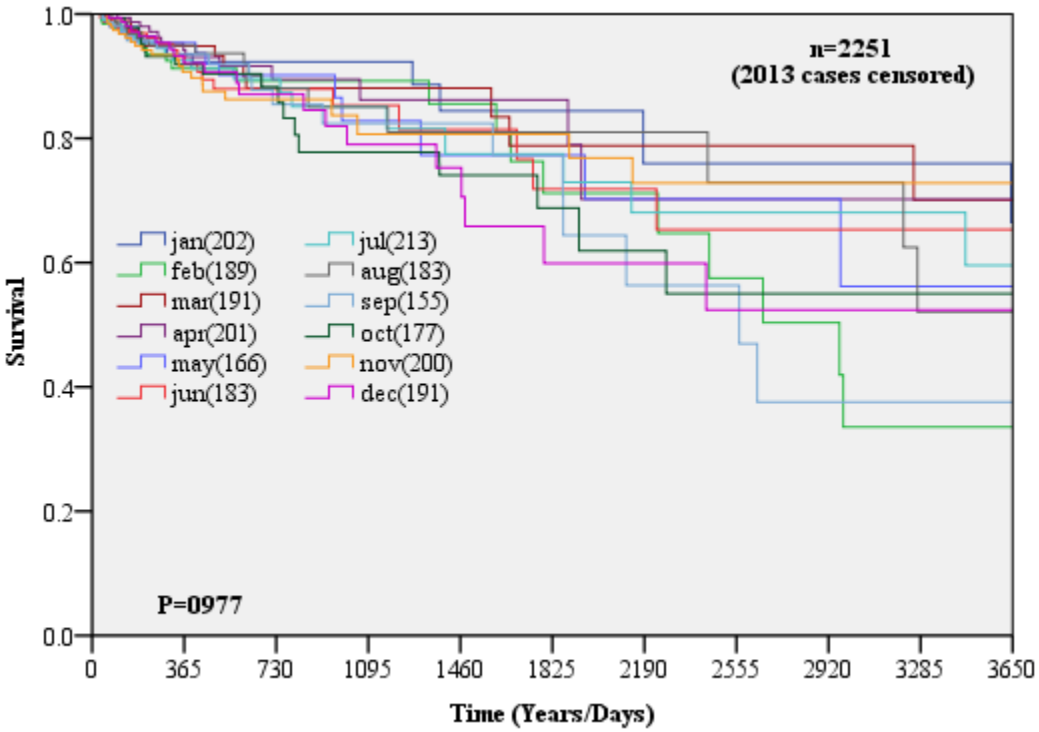


Table 3.69- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for males with NSCLC who received radiotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	2687	306	0.024	<0.01	1	1.07 0.9-1.2	1.22 1.0-1.3	0.92 0.8-1.0	1.03 0.9-1.1
Other causes	2687	2402	NS	NS	1	0.92 0.6-1.3	1.13 0.7-1.6	0.90 0.6-1.2	1.11 0.7-1.5

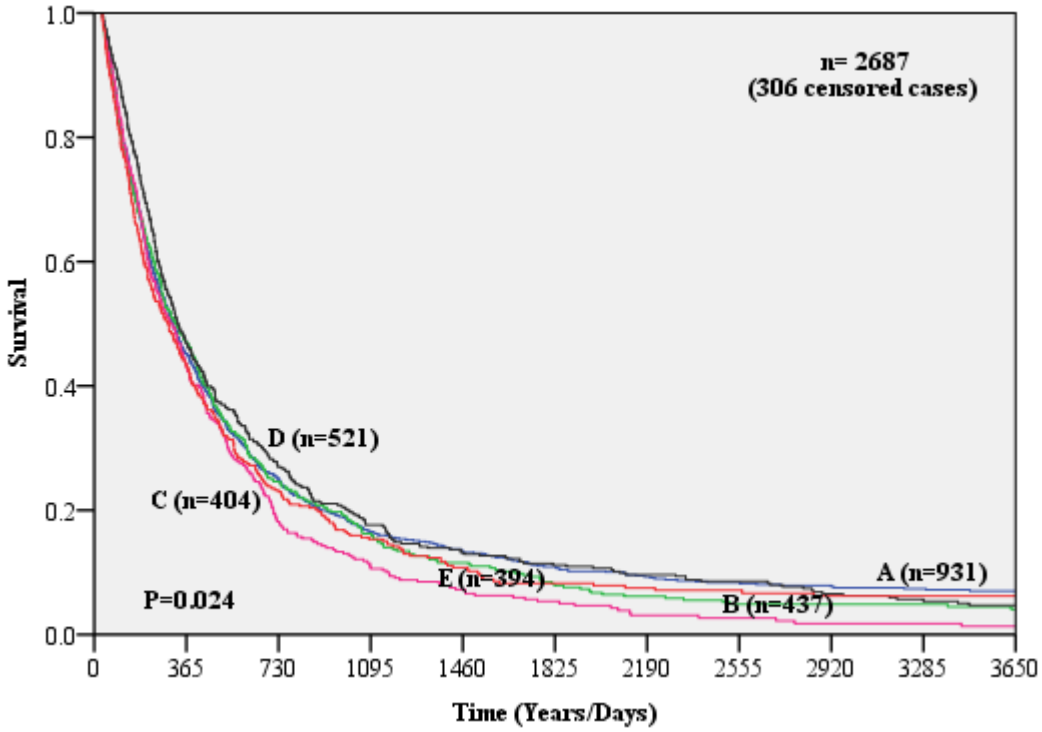
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and to monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.129- Survival according to MMVDSI for males with NSCLC who received radiotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.130- Survival according to MMVDSI for males with NSCLC who received radiotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

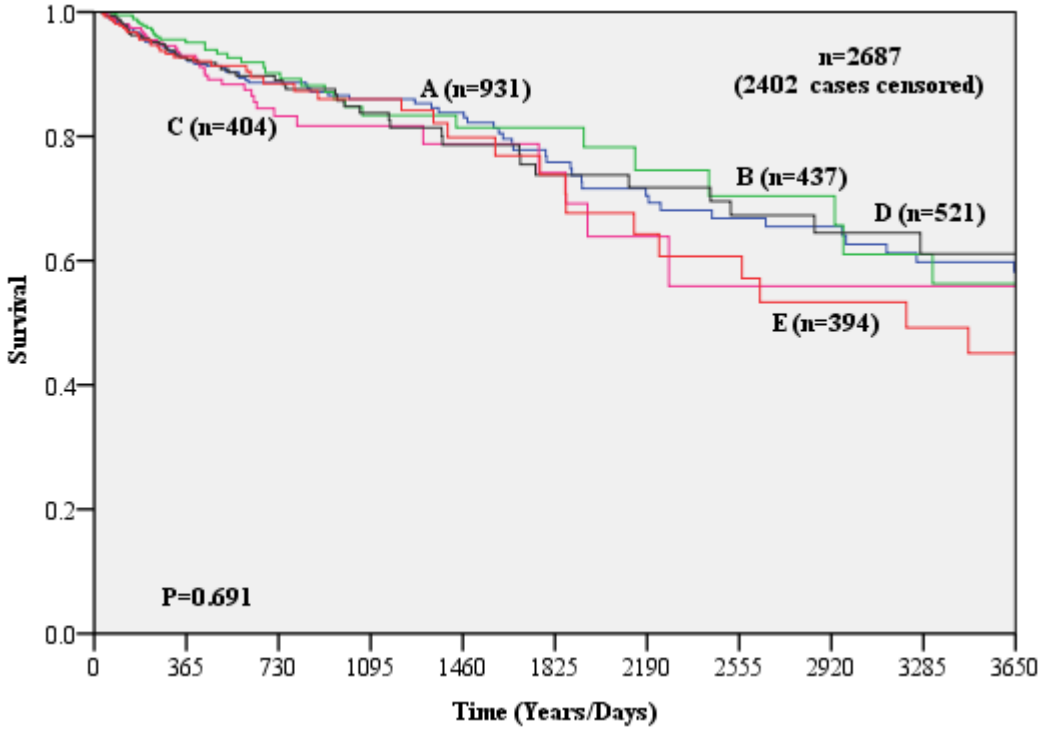


Table 3.70- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for females with NSCLC who received radiotherapy

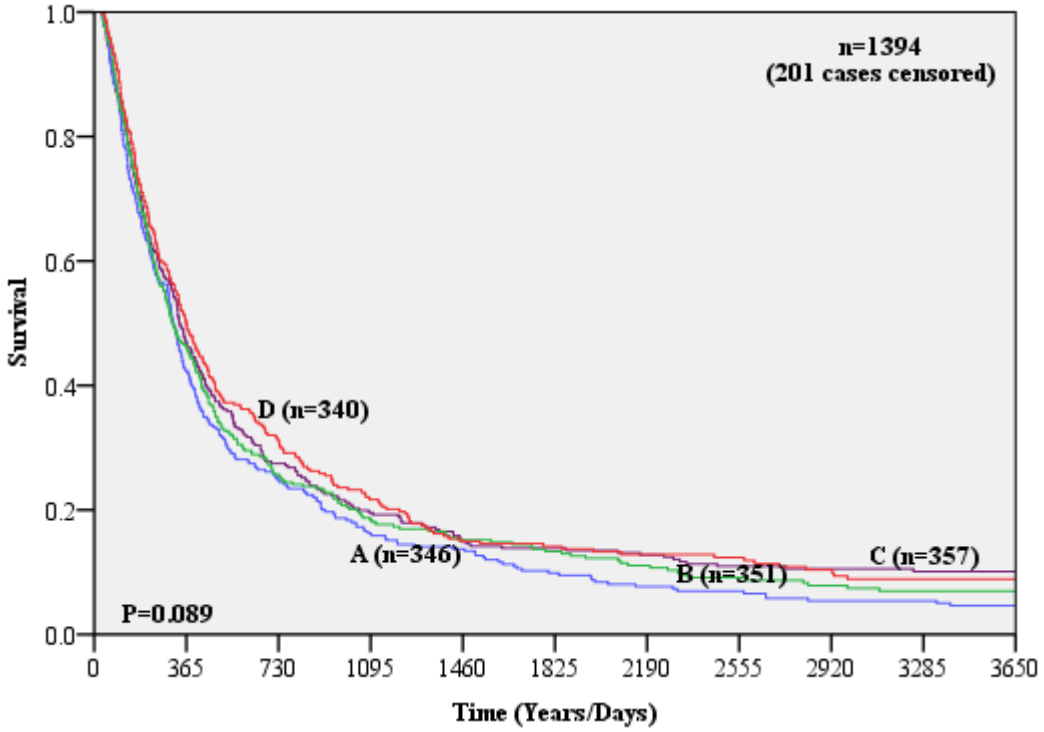
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	1394	201	0.089	NS	1.10 0.9-1.3	1.0 0.8-1.1	1	0.88 0.7-1.0
Other causes	1394	1221	NS	NS	0.95 0.5-1.5	1.06 0.6-1.6	1	1.18 0.7-1.7

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.131- Survival according to season of diagnosis for females with NSCLC who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.132- Survival according to season of diagnosis for females with NSCLC who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

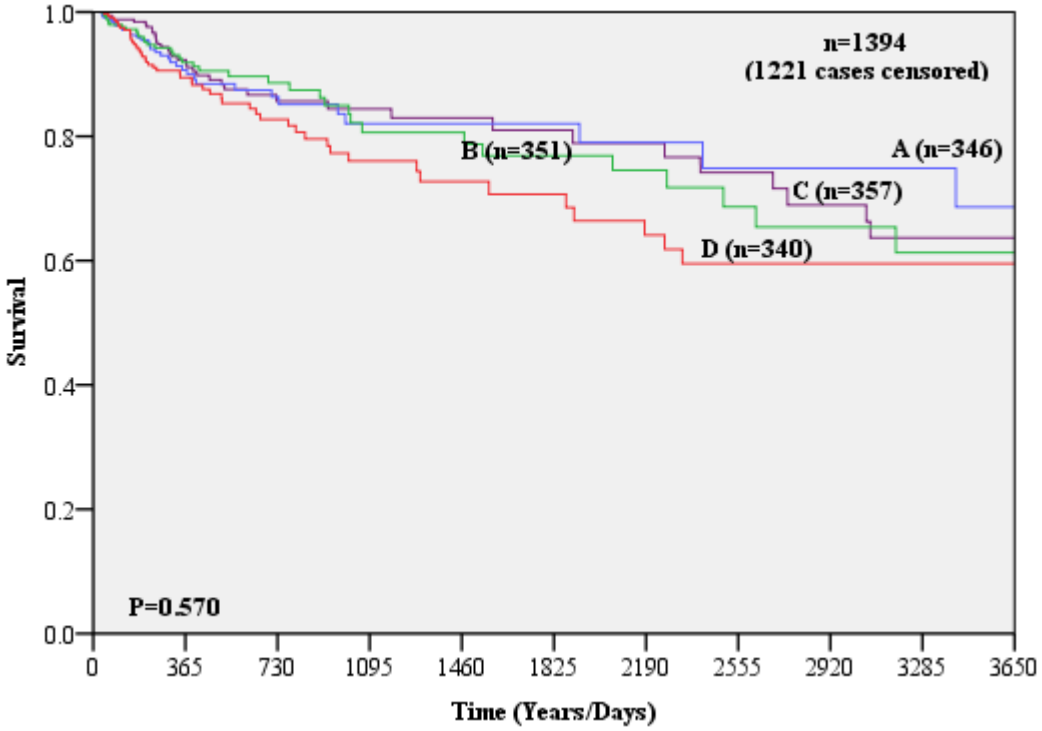


Table 3.71- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for females with NSCLC who received radiotherapy

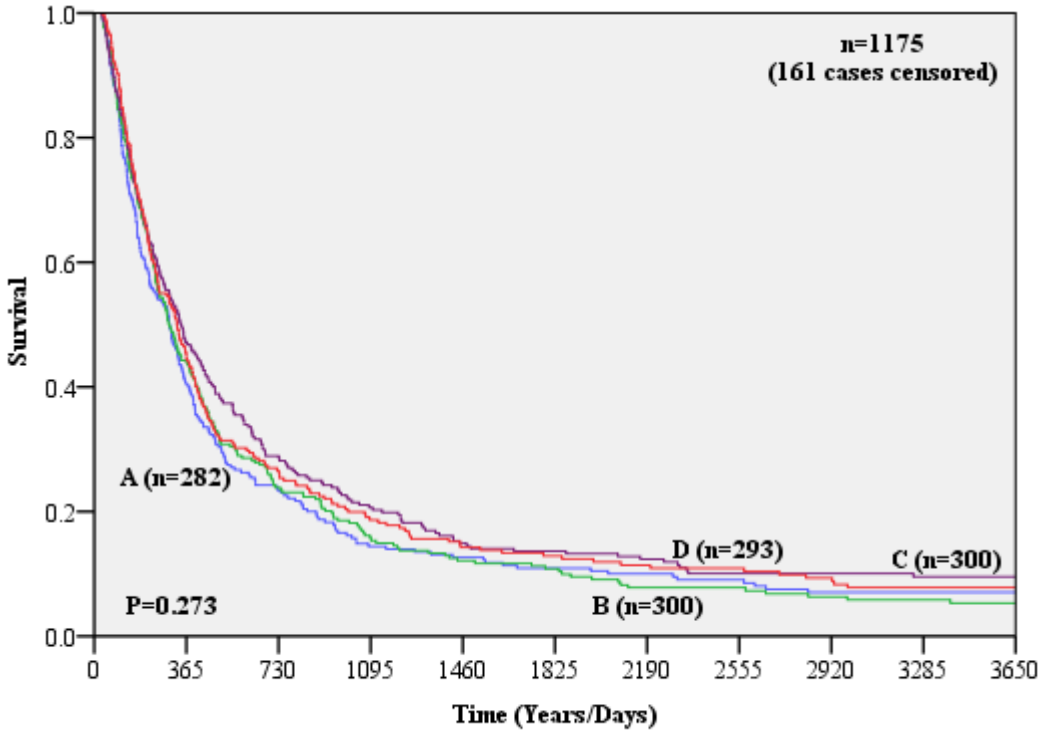
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multiivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	1175	161	NS	NS	1	0.98 0.8-1.1	0.87 0.7-1.0	0.88 0.7-1.0
Other causes	1175	1037	NS	NS	1	0.91 0.5-1.5	0.99 0.6-1.6	1.08 0.6-1.7

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.133- Survival according to season of first treatment for females with NSCLC who received radiotherapy: lung cancer death (A is spring, B is summer, C is fall and D is winter)



Graph 3.134- Survival according to season of first treatment for females with NSCLC who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

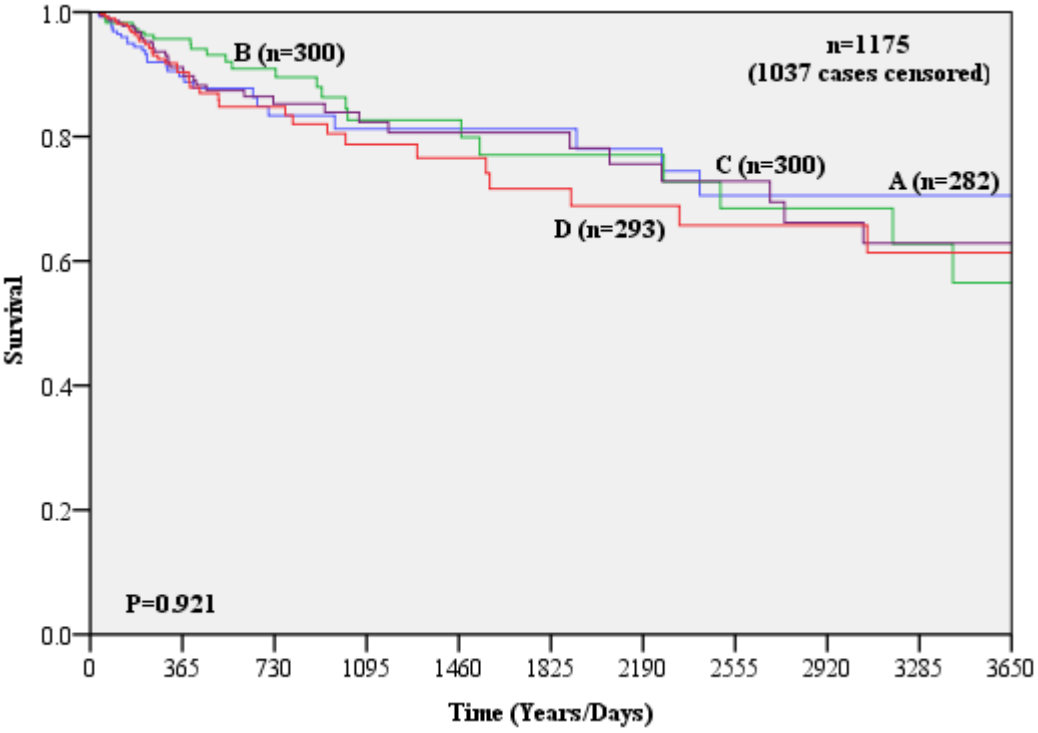


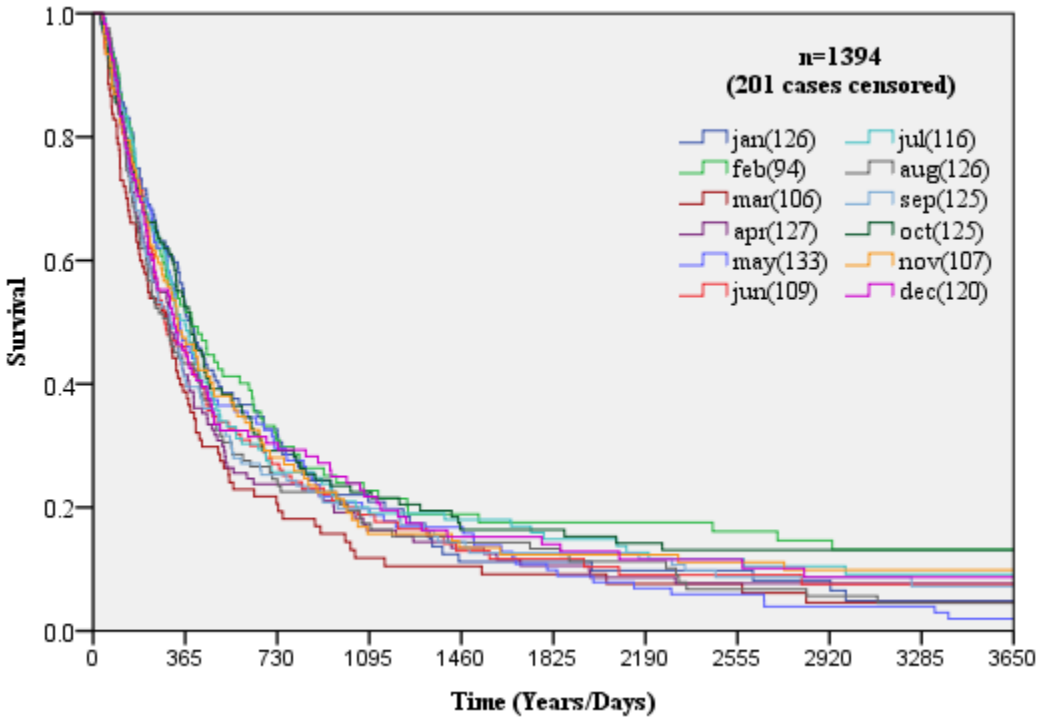
Table 3.72- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for females with NSCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		1394	1394
Number of censored cases		201	1221
HR (95% CI)	Jan	1	1
	Feb	0.90 0.6-1.2	0.53 0.2-1.0
	Mar	1.34 1.0-1.7	1.02 0.5-2.0
	Apr	1.29 0.9-1.6	0.73 0.3-1.4
	May	1.09 0.8-1.4	0.35 0.1-0.8
	Jun	1.10 0.8-1.4	0.54 0.2-1.1
	Jul	1.00 0.7-1.3	0.69 0.3-1.3
	Aug	1.26 0.9-1.6	1.01 0.5-1.9
	Sep	1.16 0.8-1.5	0.63 0.3-1.2
	Oct	0.99 0.7-1.3	0.69 0.3-1.3
	Nov	1.20 0.9-1.6	0.76 0.3-1.5
	Dec	1.04 0.7-1.3	0.93 0.4-1.7

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and month of diagnosis.

●NS is not significant ●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.135- Survival according to month of diagnosis for females with NSCLC who received radiotherapy: lung cancer deaths



Graph 3.136- Survival according to month of diagnosis for females with NSCLC who received radiotherapy: non-lung-cancer deaths

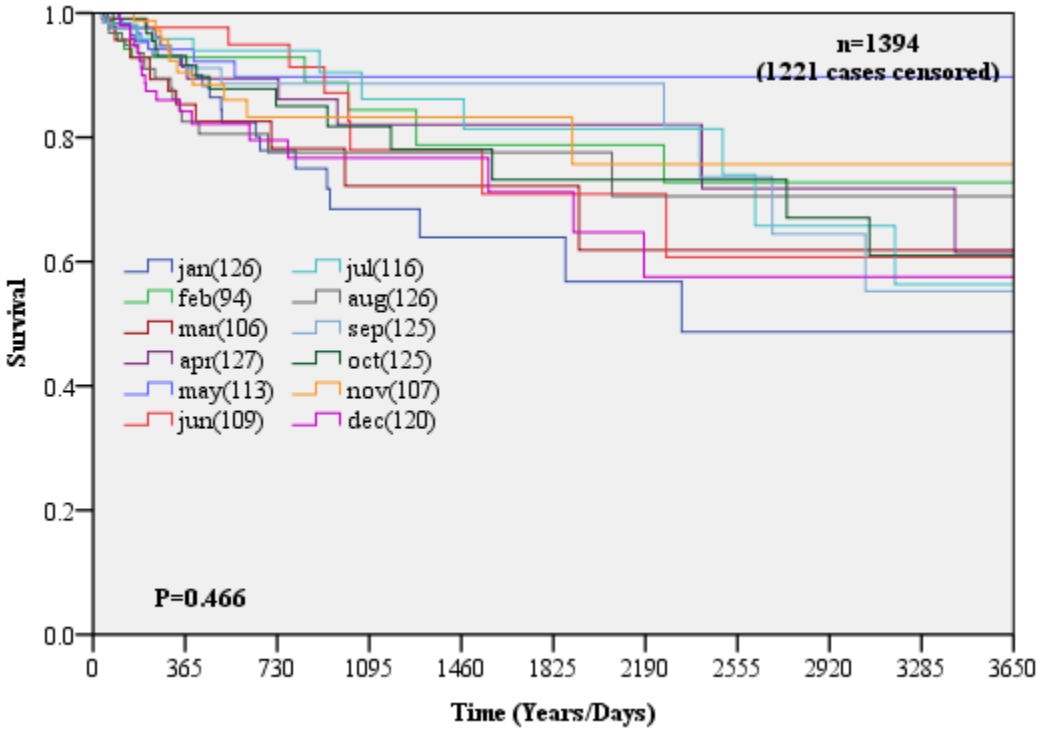


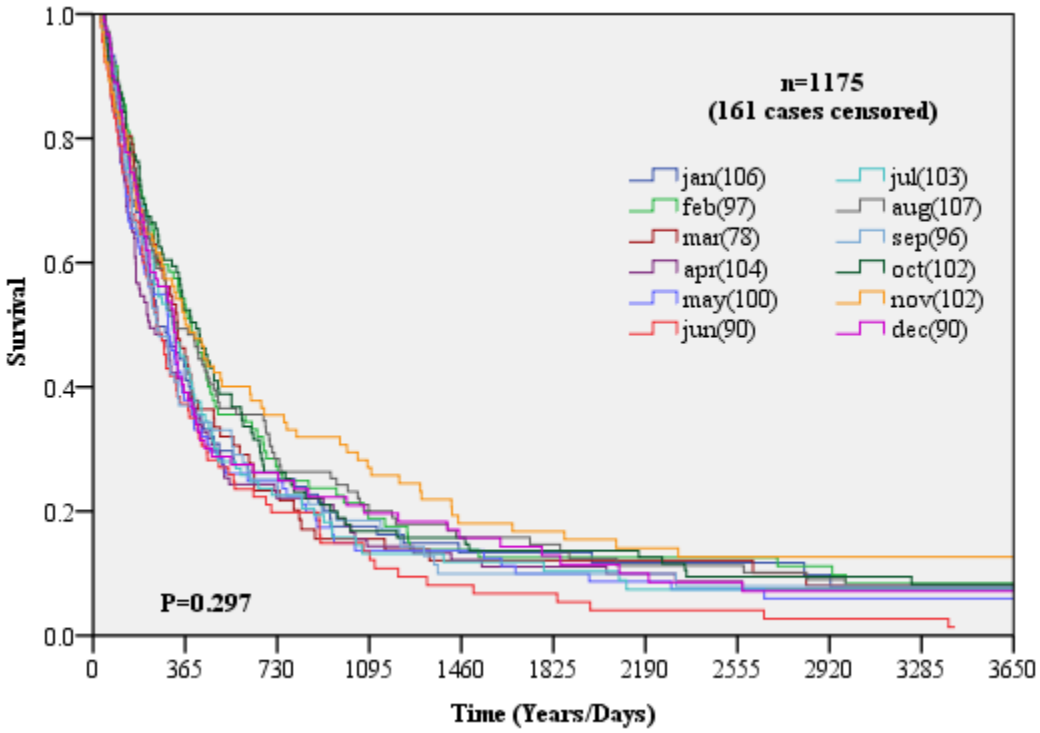
Table 3.73- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for females with NSCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	<0.01
Multivariate P value		NS	NS
Number of cases		1175	1175
Number of censored cases		161	1037
HR (95% CI)	Jan	1	1
	Feb	0.92 0.6-1.2	0.49 0.2-1.1
	Mar	1.00 0.7-1.3	0.72 0.3-1.6
	Apr	1.23 0.9-1.6	0.50 0.2-1.1
	May	1.11 0.8-1.5	0.73 0.3-1.5
	Jun	1.30 0.9-1.7	0.43 0.1-1.1
	Jul	1.01 0.7-1.3	0.87 0.4-1.7
	Aug	1.05 0.7-1.4	0.46 0.2-1.0
	Sep	1.12 0.8-1.5	1.19 0.6-2.3
	Oct	0.89 0.6-1.2	0.23 0.0-0.6
	Nov	0.94 0.6-1.2	0.70 0.3-1.4
	Dec	1.06 0.7-1.4	0.64 0.2-1.4

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and month of first treatment.

●NS is not significant ●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.137- Survival according to month of first treatment for females with NSCLC who received radiotherapy: lung cancer deaths



Graph 3.138- Survival according to month of first treatment for females with NSCLC who received radiotherapy: non-lung-cancer deaths

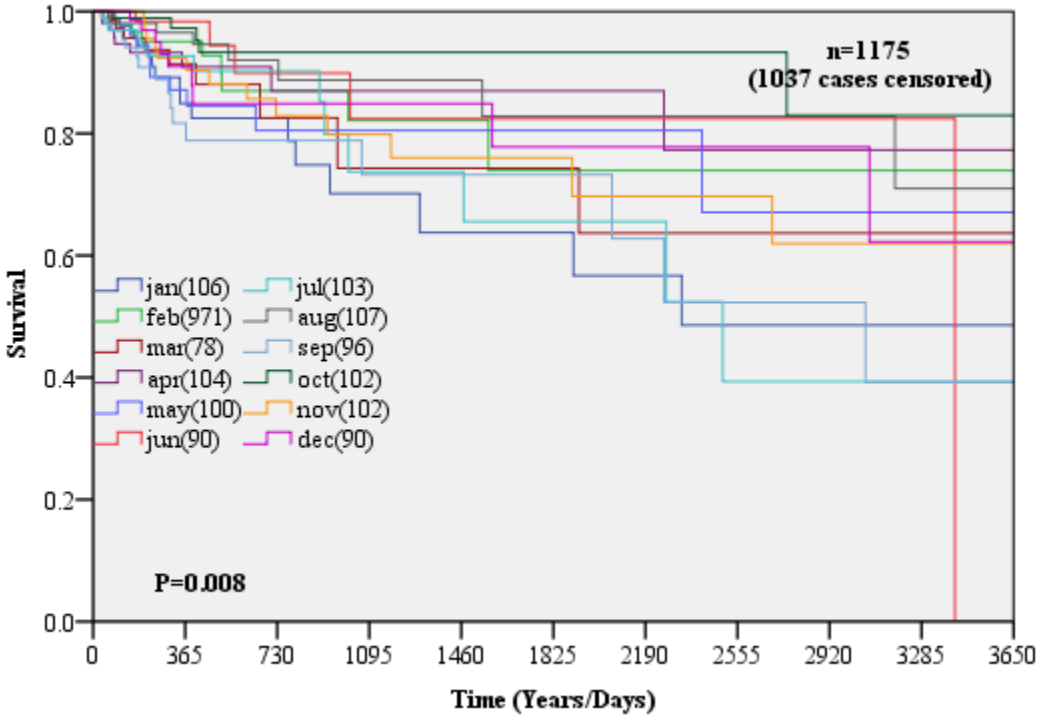


Table 3.74- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for females with NSCLC who received radiotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	1377	198	NS	NS	1	1.09 0.9-1.3	1.21 1.0-1.4	1.12 0.9-1.3	1.01 0.8-1.2
Other causes	1377	1206	NS	NS	1	1.05 0.6-1.6	0.84 0.5-1.3	0.85 0.5-1.3	0.72 0.4-1.2

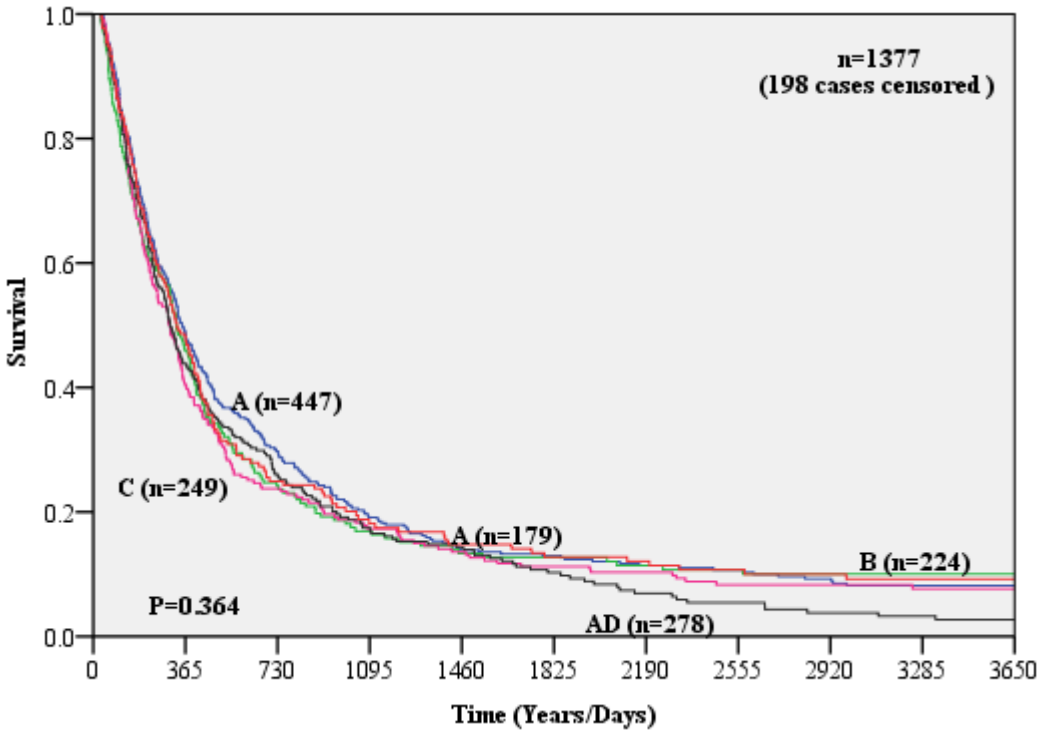
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.139- Survival according to MMVDSI for females with NSCLC who received radiotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.140- Survival according to MMVDSI for females with NSCLC who received radiotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

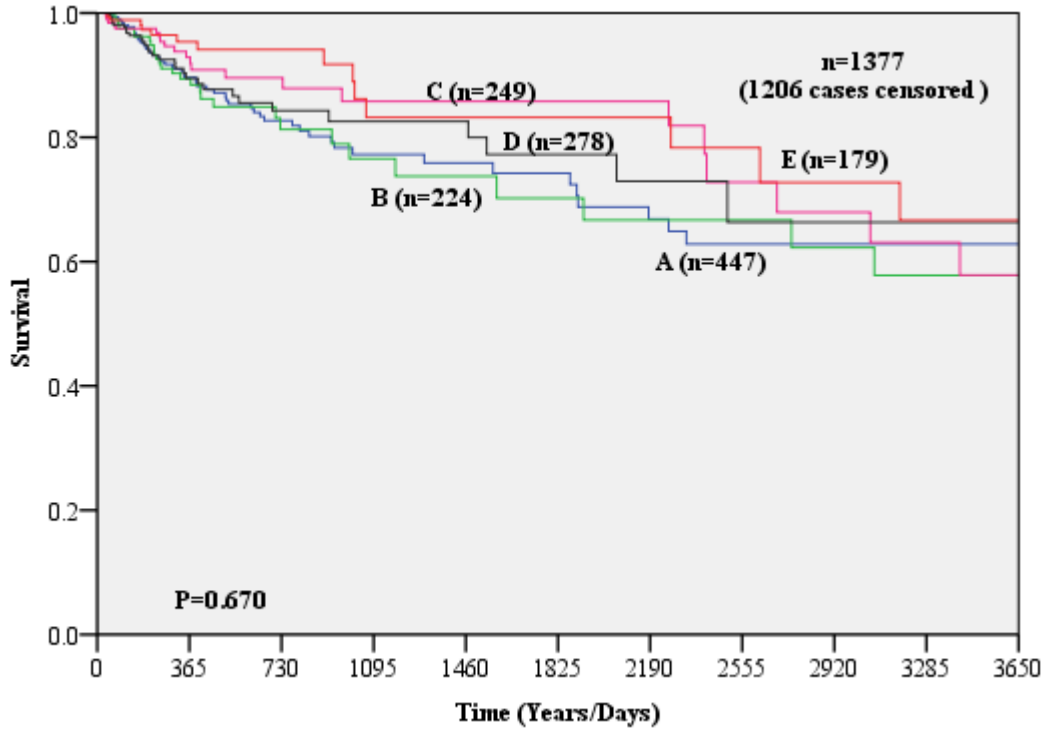


Table 3.75- Hazard ratio (HR) and 95% confidence interval (CI) according to season of diagnosis for male and female patients with NSCLC who received radiotherapy

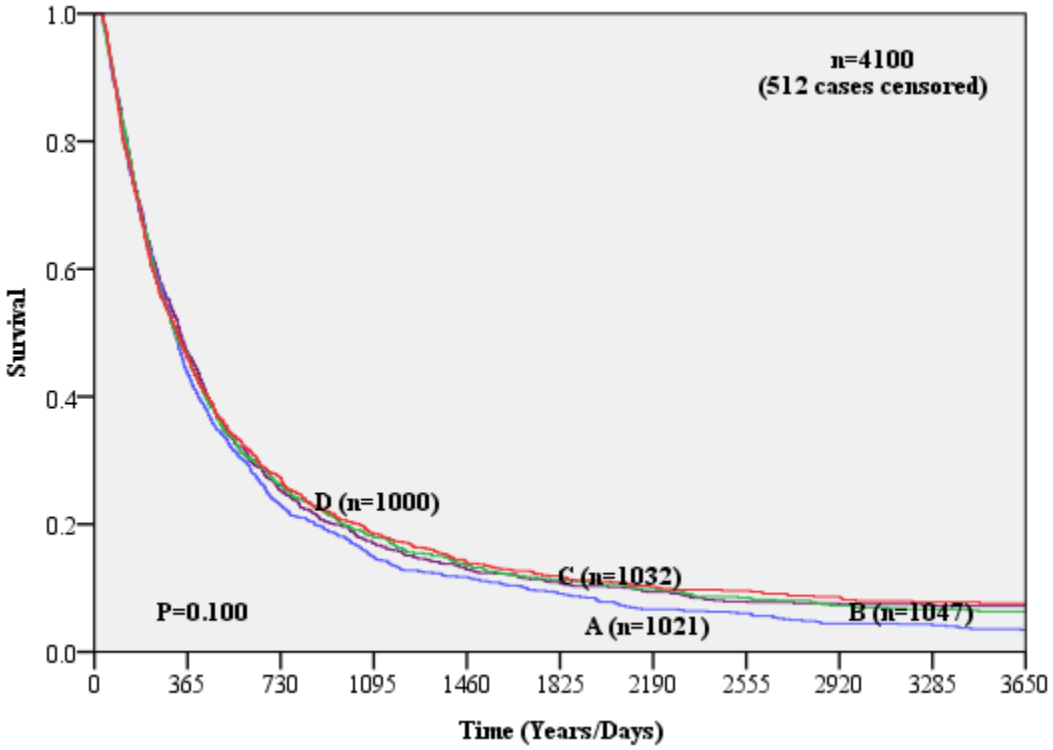
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	4100	512	NS	0.064	1.05 0.9-1.1	0.95 0.8-1.0	1	0.93 0.8-1.4
Other causes	4100	3640	NS	NS	0.89 0.6-1.1	1.06 0.8-1.3	1	1.12 0.8-1.4

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.141- Survival according to season of diagnosis for male and female NSCLC patients who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.142- Survival according to season of diagnosis for male and female NSCLC patients who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

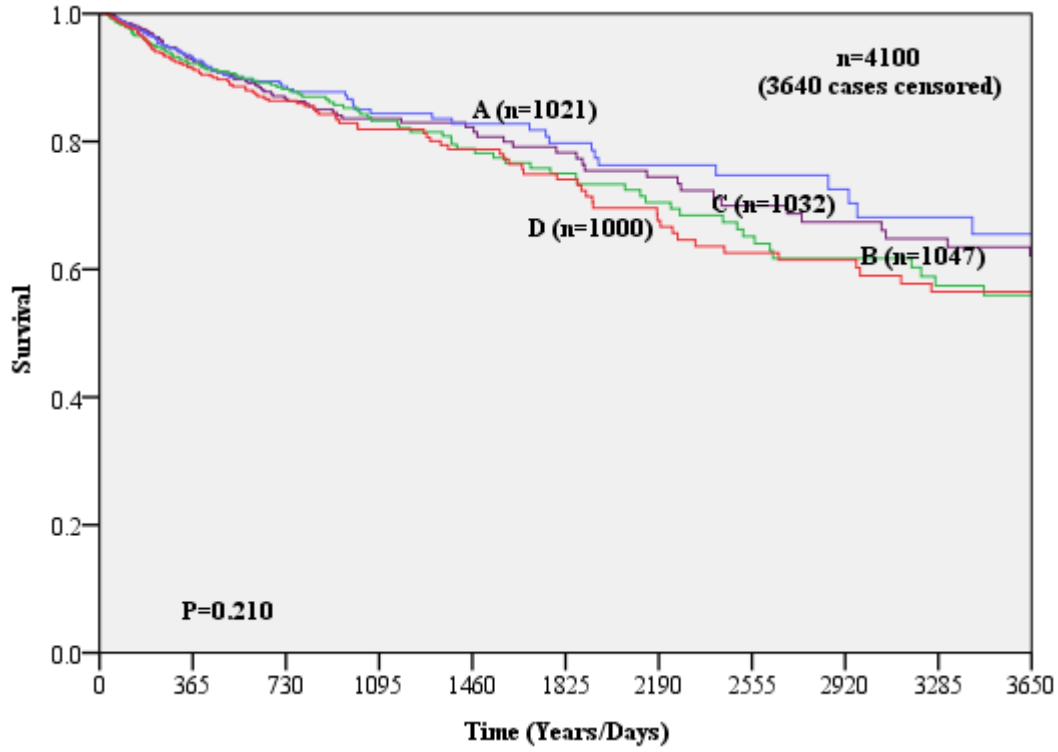


Table 3.76- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for male and female patients with NSCLC who received radiotherapy

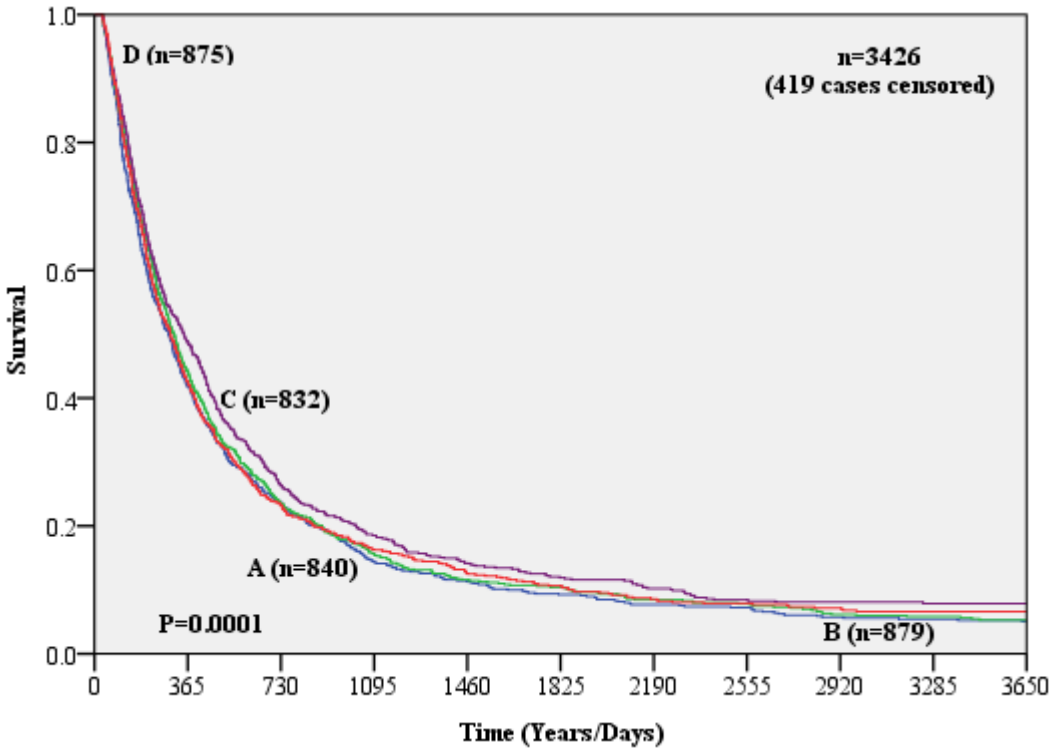
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	3426	419	<0.01	<0.01	1	0.94 0.8-1.0	0.88 0.8-0.9	0.92 0.8-1.0
Other causes	3426	3050	NS	NS	1	1.03 0.7-1.4	1.17 0.8-1.5	1.13 0.8-1.5

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and season of first treatment.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.143- Survival according to season of first treatment for male and female NSCLC patients who received radiotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.144- Survival according to season of first treatment for male and female NSCLC patients who received radiotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

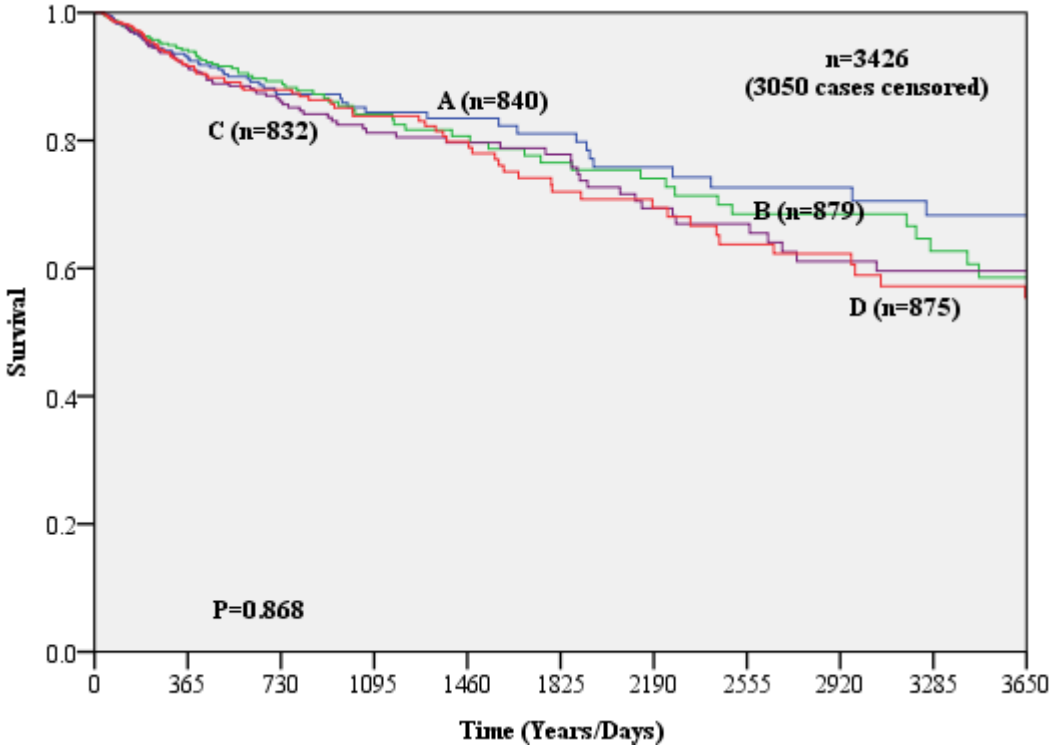


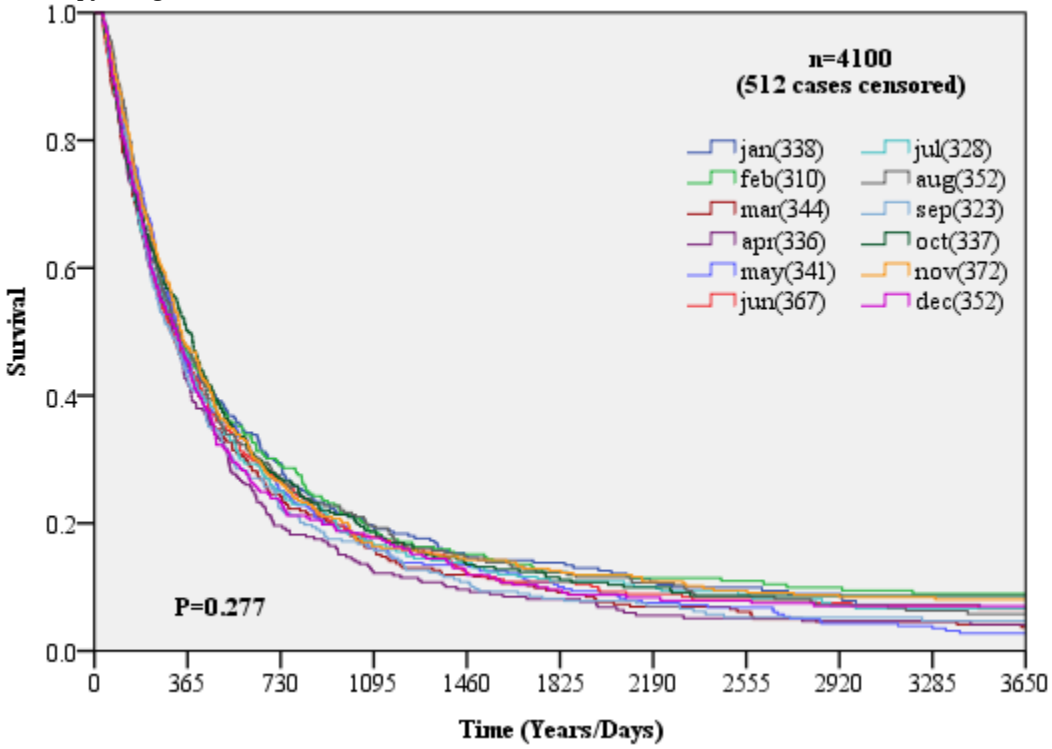
Table 3.77- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for male and female patients with NSCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.046	NS
Number of cases		4100	4100
Number of censored cases		512	3640
HR (95% CI)	Jan	1	1
	Feb	0.99 0.8-1.1	0.91 0.5-1.3
	Mar	1.18 1.0-1.3	0.87 0.5-1.3
	Apr	1.29 1.1-1.5	0.94 0.5-1.4
	May	1.05 0.8-1.2	0.59 0.3-0.9
	Jun	1.05 0.8-1.2	0.92 0.6-1.4
	Jul	1.07 0.9-1.2	0.80 0.5-1.2
	Aug	1.04 0.8-1.2	1.06 0.7-1.6
	Sep	1.20 1.0-1.4	0.96 0.6-1.5
	Oct	1.05 0.8-1.2	0.91 0.5-1.4
	Nov	1.08 0.9-1.2	0.79 0.5-1.2
	Dec	1.13 0.9-1.3	1.06 0.7-1.6

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and month of diagnosis.

●NS is not significant ●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.145- Survival according to month of diagnosis for male and female NSCLC patients who received radiotherapy: lung cancer deaths



Graph 3.146- Survival according to month of diagnosis for male and female NSCLC patients who received radiotherapy: non-lung-cancer deaths

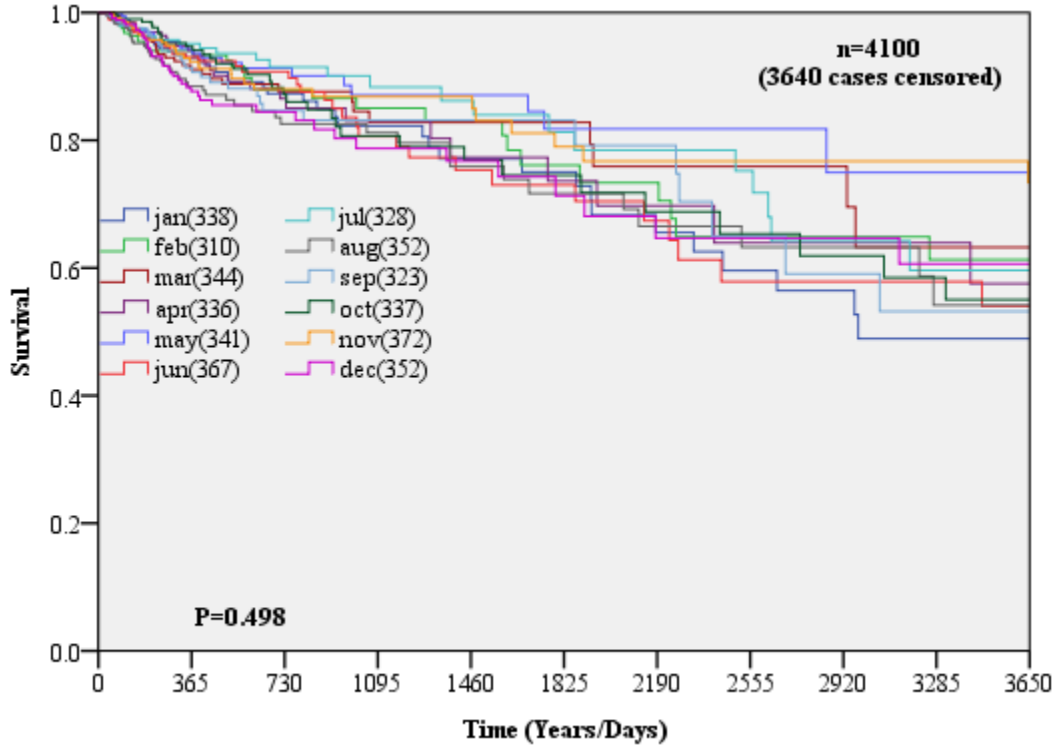


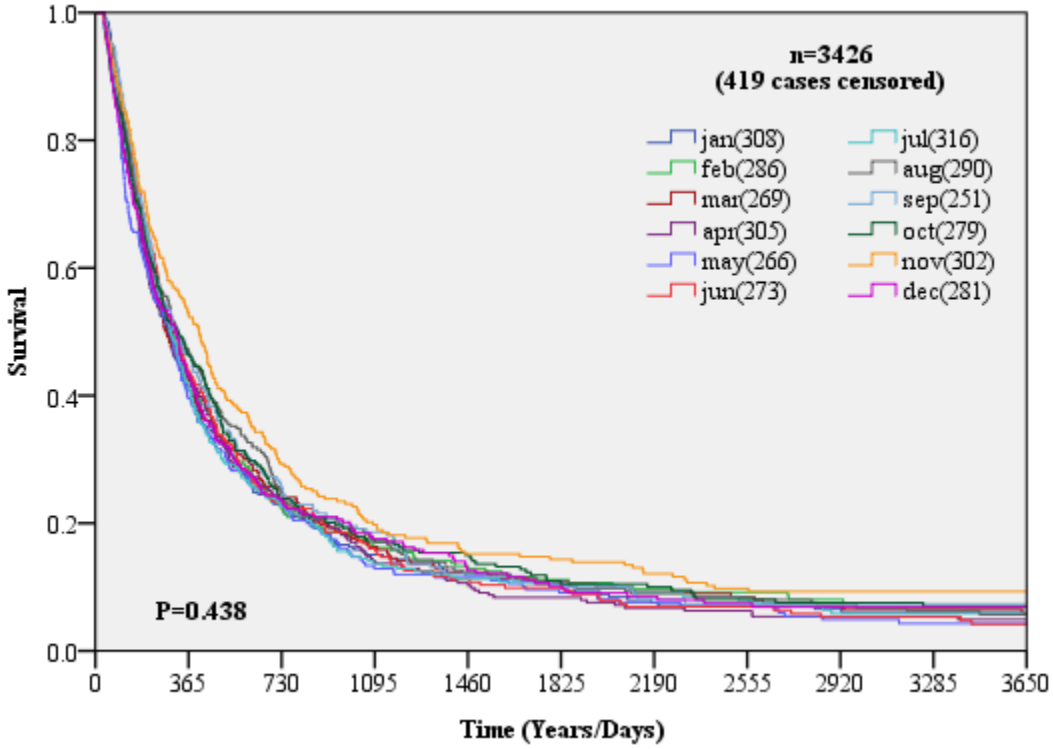
Table 3.78- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for male and female patients with NSCLC who received radiotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		3426	3426
Number of censored cases		419	3050
HR (95% CI)	Jan	1	1
	Feb	0.95 0.8-1.1	0.85 0.5-1.3
	Mar	1.03 0.8-1.2	0.81 0.4-1.3
	Apr	1.09 0.9-1.2	0.70 0.4-1.1
	May	1.08 0.9-1.2	0.85 0.5-1.4
	Jun	1.01 0.8-1.2	0.70 0.4-1.1
	Jul	1.00 0.8-1.1	0.98 0.6-1.5
	Aug	1.00 0.8-1.1	0.76 0.4-1.2
	Sep	0.95 0.7-1.0	1.12 0.7-1.7
	Oct	0.97 0.8-1.1	0.73 0.4-1.2
	Nov	0.94 0.7-1.1	0.97 0.6-1.5
	Dec	1.00 0.8-1.2	0.88 0.5-1.4

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and month of first treatment.

•NS is not significant• Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.147- Survival according to month of first treatment for male and female NSCLC patients who received radiotherapy: lung cancer deaths



Graph 3.148- Survival according to month of first treatment for male and female NSCLC patients who received radiotherapy: non-lung-cancer deaths

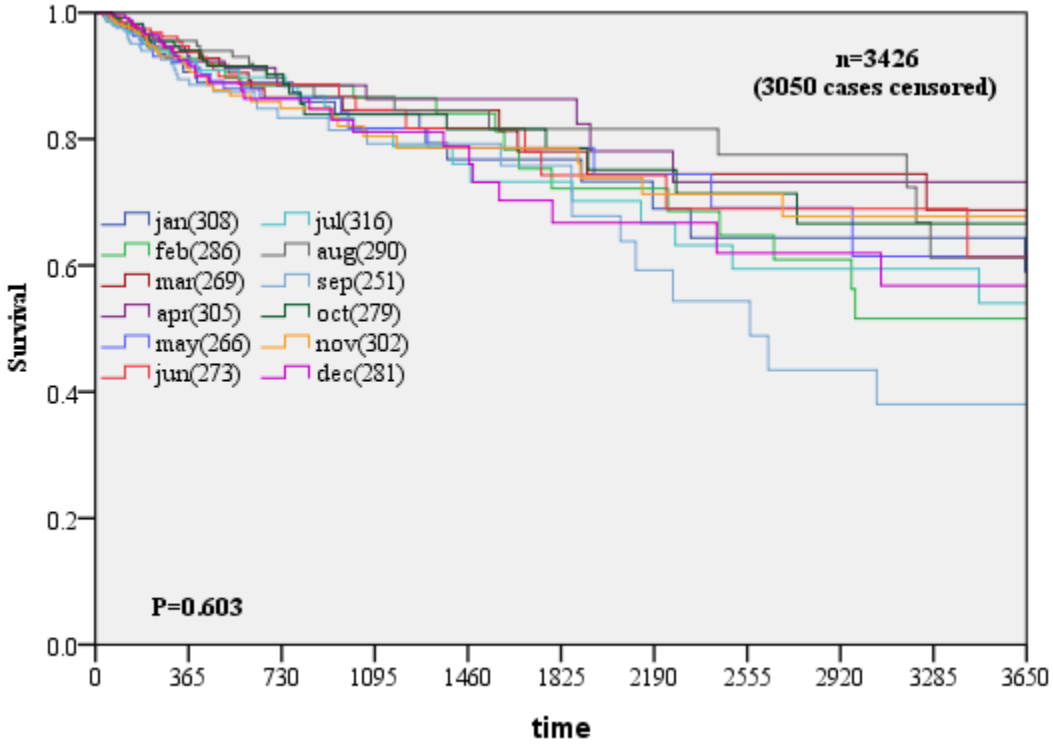


Table 3.79- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index male and female patients with NSCLC who received radiotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	4064	504	0.06	<0.01	1	1.07 0.9-1.1	1.21 1.0-1.3	0.98 0.8-1.0	1.03 0.9-1.13
Other causes	4064	3608	NS	NS	1	0.92 0.6-1.2	0.97 0.7-1.3	0.87 0.6-1.1	0.95 0.7-1.2

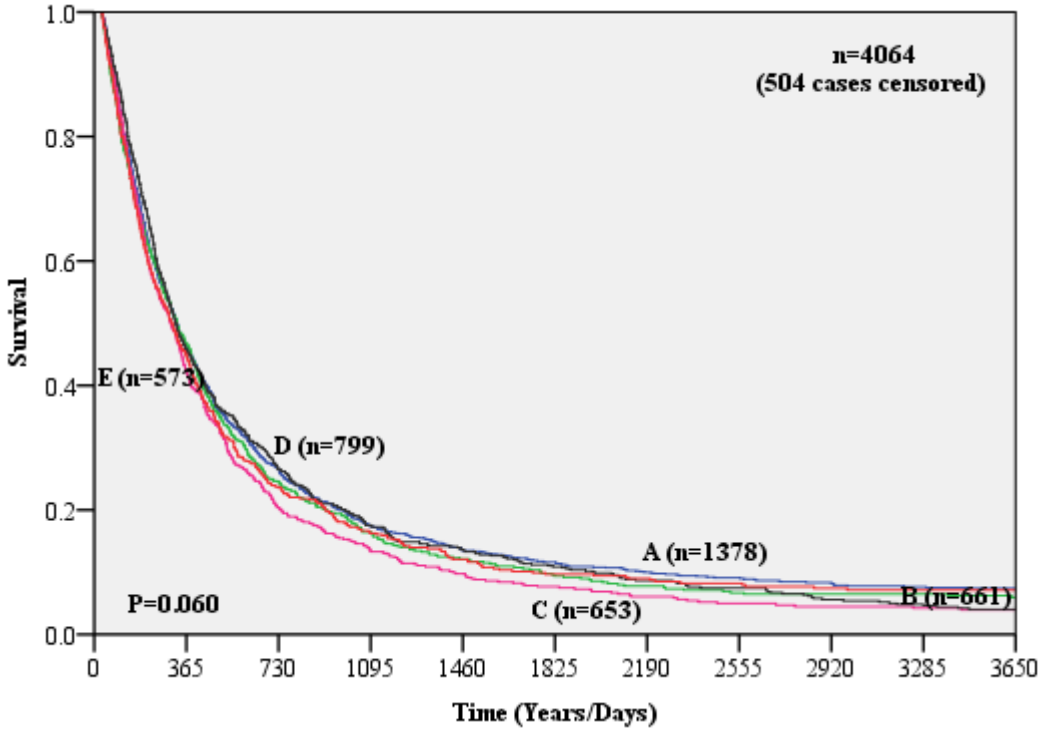
(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (chemotherapy and surgery), disease site and monthly mean vitamin D sunshine index.

- NS is not significant

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.149- Survival according to MMVDSI for male and female NSCLC patients who received radiotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.150- Survival according to MMVDSI for male and female NSCLC patients who received radiotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

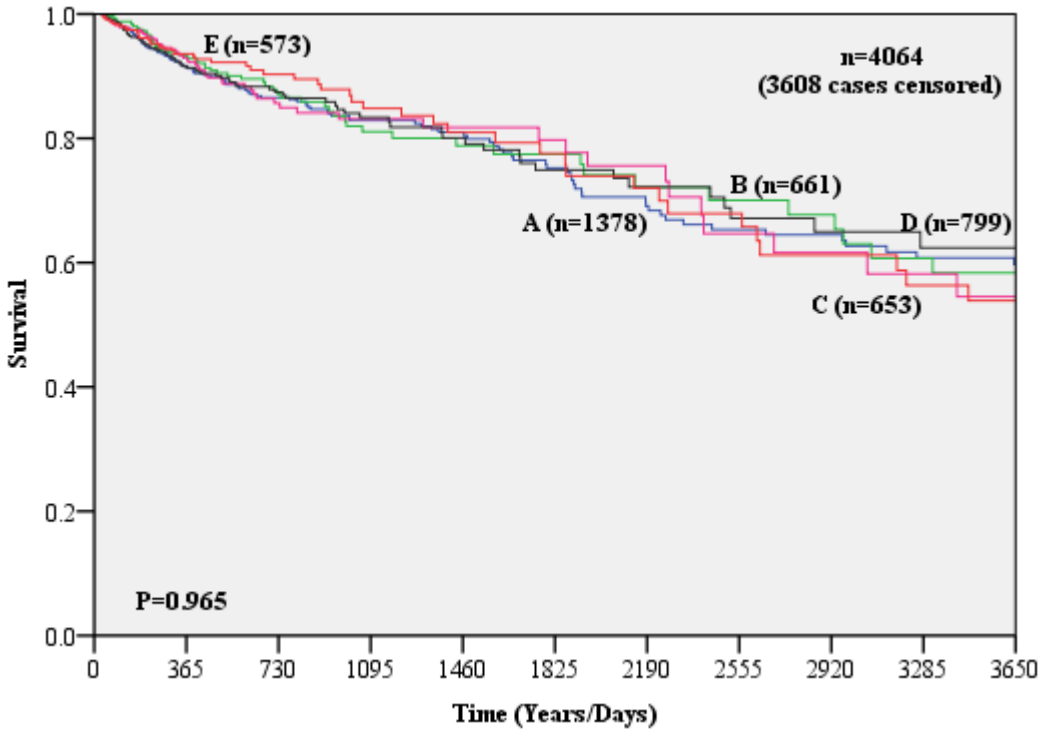
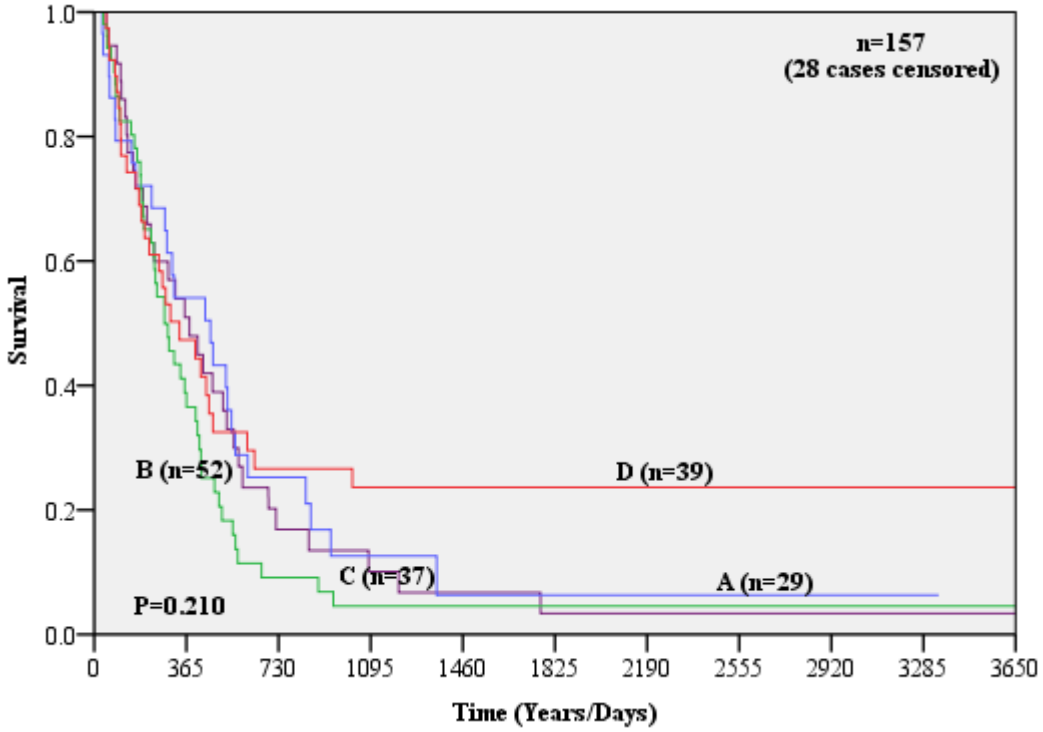


Table 3.80- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for males with NSCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	157	28	NS	NS	1.81 0.9-3.5	1.26 0.7-2.1	1	0.90 0.5-1.5
Other causes	157	132	NS	NS	N<5	0.60 0.1-2.4	1	0.55 0.1-2.2

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and season of diagnosis.
- NS is not significant; A is spring, B is summer, C is fall and D is winter.
- N is number of uncensored cases
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.151- Survival according to season of diagnosis for males with NSCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.152- Survival according to season of diagnosis for males with NSCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

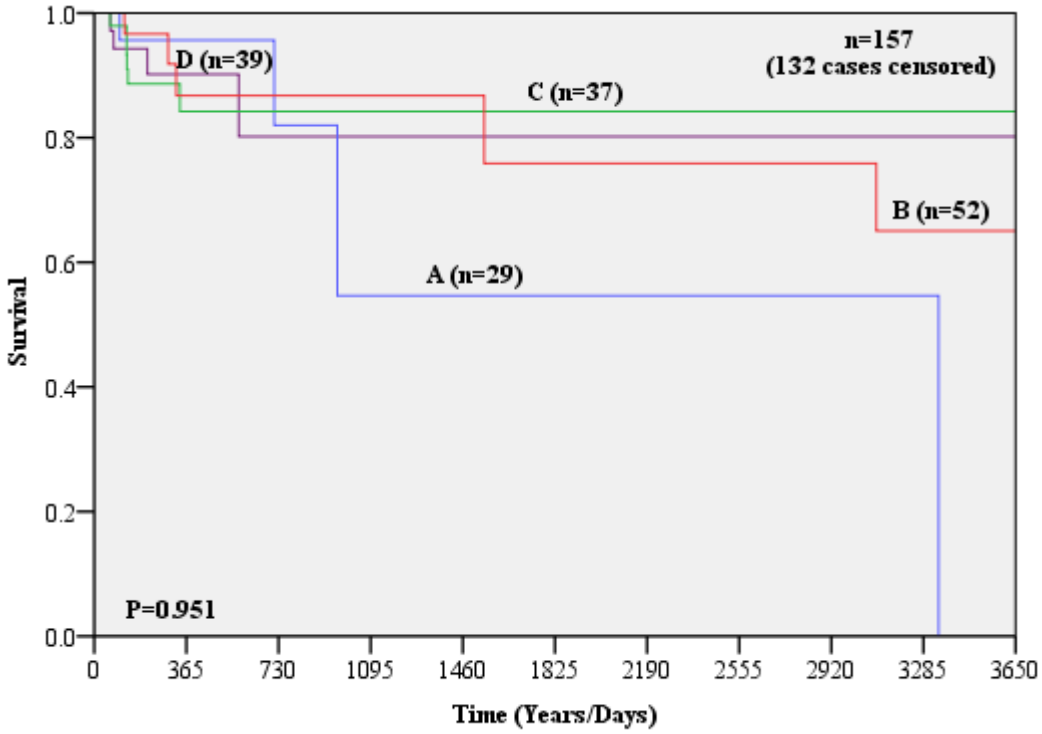


Table 3.81- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for males with NSCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	154	28	NS	NS	1	1.20 0.6-2.1	1.19 0.6-2.0	1.16 0.6-2.0
Other causes	154	129	NS	NS	1	N<5	N<5	6.13 1.2-29.6

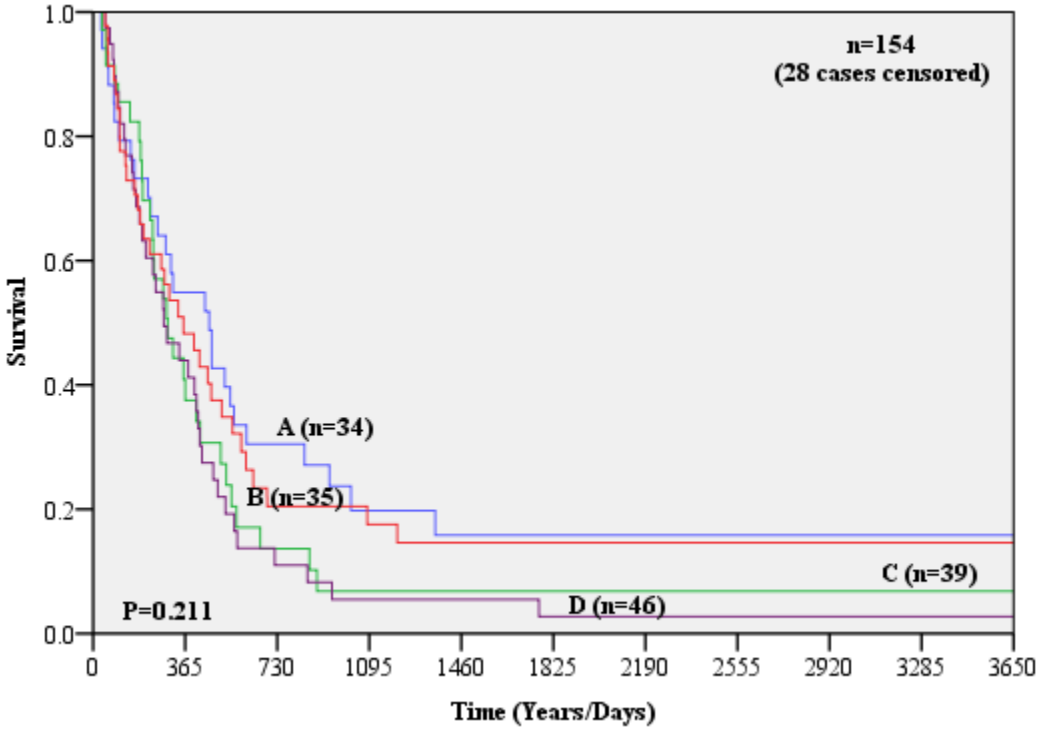
- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- N is number of uncensored cases

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.153 Survival according to season of first treatment for males with NSCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.154- Survival according to season of first treatment for males with NSCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

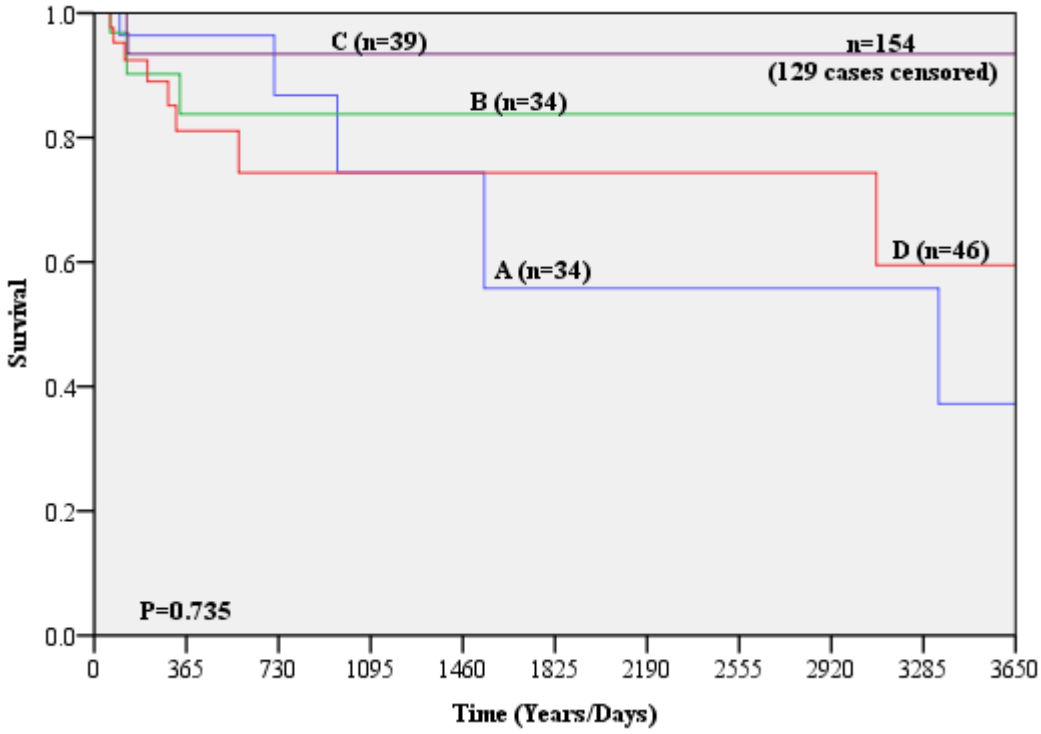


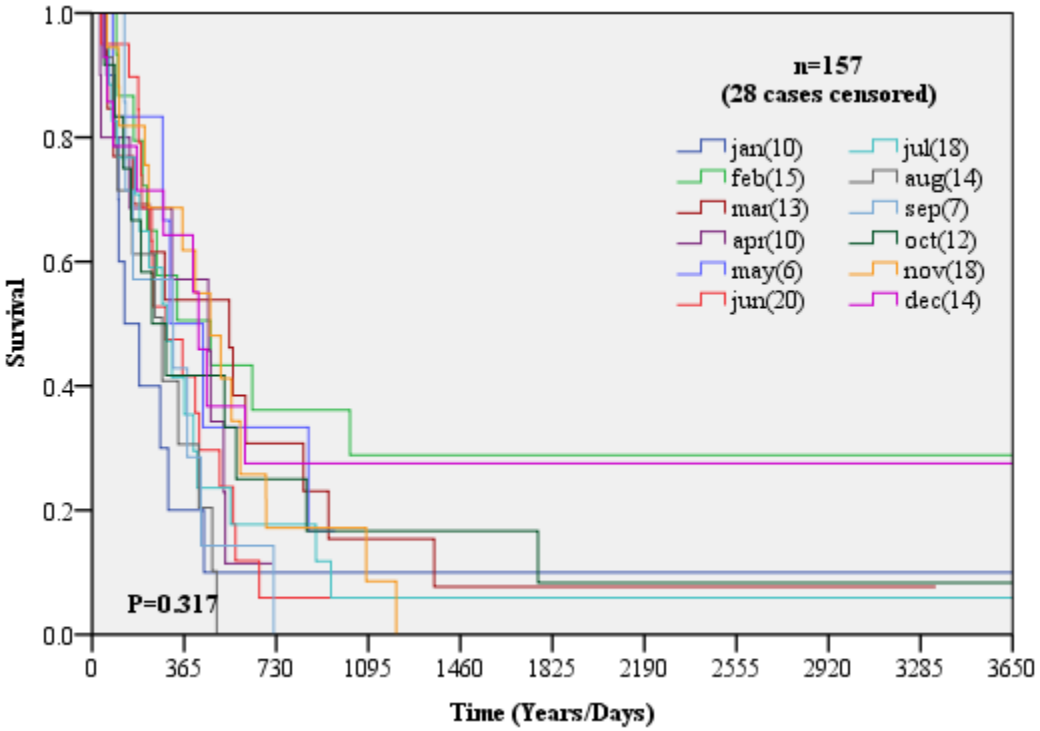
Table 3.82- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for males with NSCLC who received chemotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.057	NS
Number of cases		157	157
Number of censored cases		28	132
HR (95% CI)	Jan	1	1
	Feb	0.19 0.0-0.5	N<5
	Mar	0.62 0.2-1.7	N<5
	Apr	0.90 0.3-2.6	N<5
	May	0.68 0.1-2.5	N<5
	Jun	0.41 0.1-1.0	N<5
	Jul	0.43 0.1-1.1	N<5
	Aug	0.88 0.3-2.4	N<5
	Sep	0.61 0.1-1.9	N<5
	Oct	0.28 0.0-0.7	N<5
	Nov	0.37 0.1-1.0	N<5
	Dec	0.45 0.1-1.4	N<5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and month of diagnosis.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.155- Survival according to month of diagnosis for males with NSCLC who received chemotherapy: lung cancer deaths



Graph 3.156- Survival according to month of diagnosis for males with NSCLC who received chemotherapy: non-lung-cancer deaths

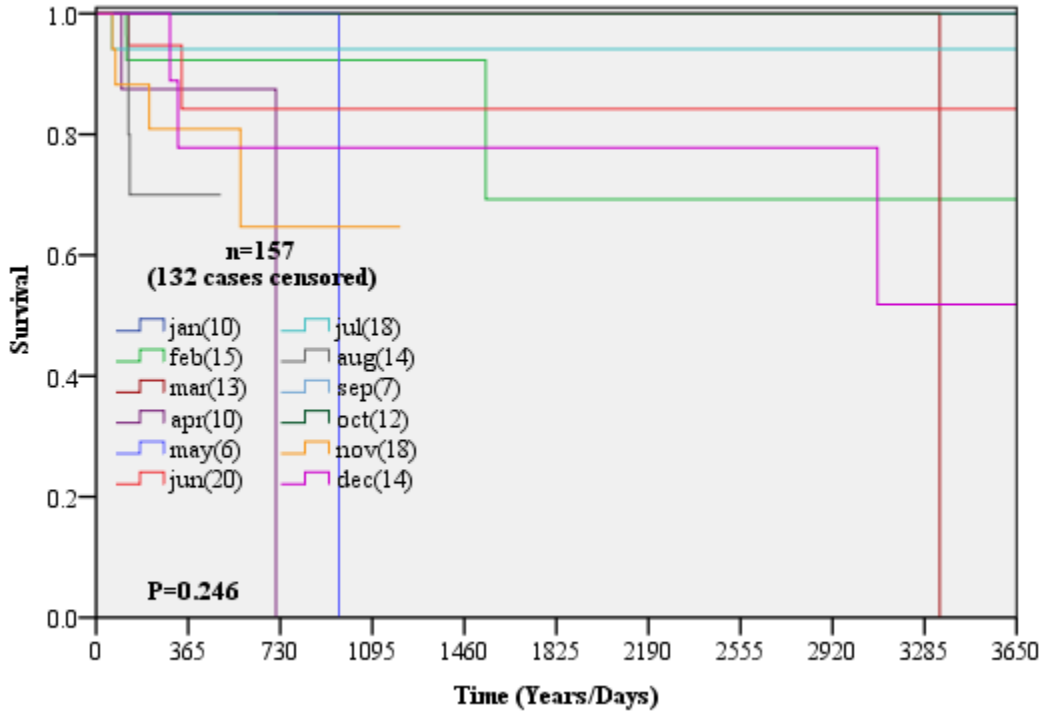


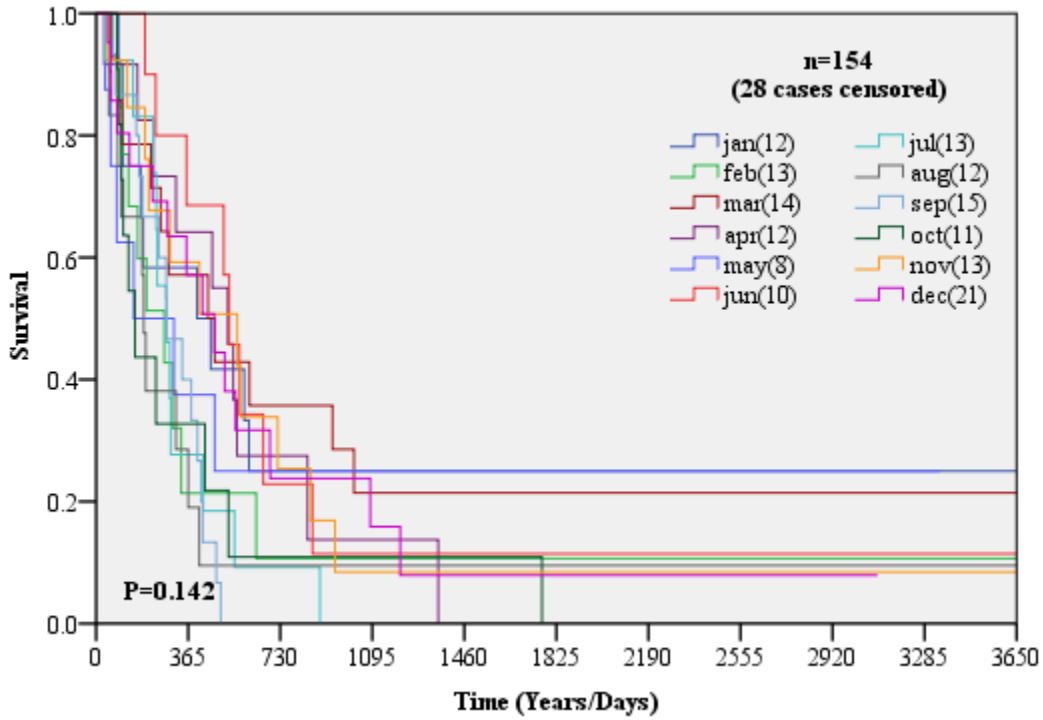
Table 3.83- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for males with NSCLC who received chemotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		154	154
Number of censored cases		28	129
HR (95% CI)	Jan	1	1
	Feb	1.18 0.4-3.2	N<5
	Mar	0.64 0.2-1.7	N<5
	Apr	1.22 0.4-3.4	N<5
	May	1.83 0.5-6.07	N<5
	Jun	0.63 0.2-1.8	N<5
	Jul	1.18 0.4-3.3	N<5
	Aug	2.18 0.8-5.9	N<5
	Sep	1.75 0.6-0.4	N<5
	Oct	0.78 0.2-2.2	N<5
	Nov	0.85 0.3-2.3	N<5
	Dec	1.01 0.4-2.4	18.91 1.2->100

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and month of first treatment.

●NS is not significant●N is number of uncensored cases●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.157- Survival according to month of first treatment for males with NSCLC who received chemotherapy: lung cancer deaths



Graph 3.158- Survival according to month of first treatment for males with NSCLC who received chemotherapy: non-lung-cancer deaths

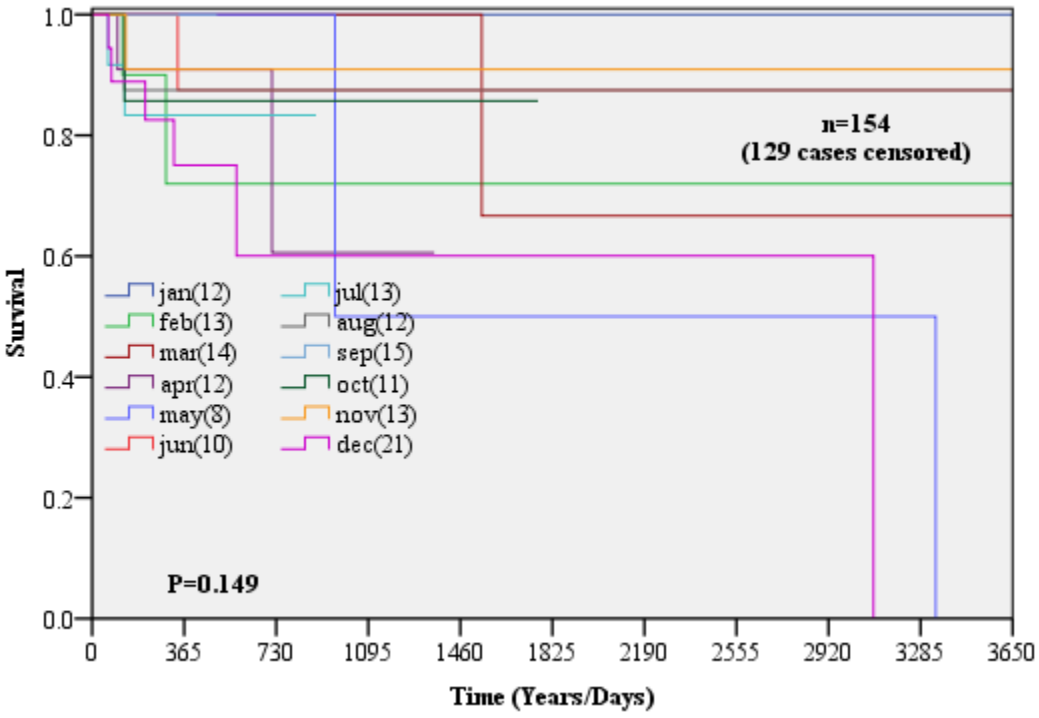


Table 3.84- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for males with NSCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	157	28	NS	NS	1	1.14 0.6-2.0	2.02 1.0-3.9	1.44 0.8-2.5	1.33 0.7-2.3
Other causes	157	132	NS	NS	1	N<5	N<5	N<5	N<5

(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

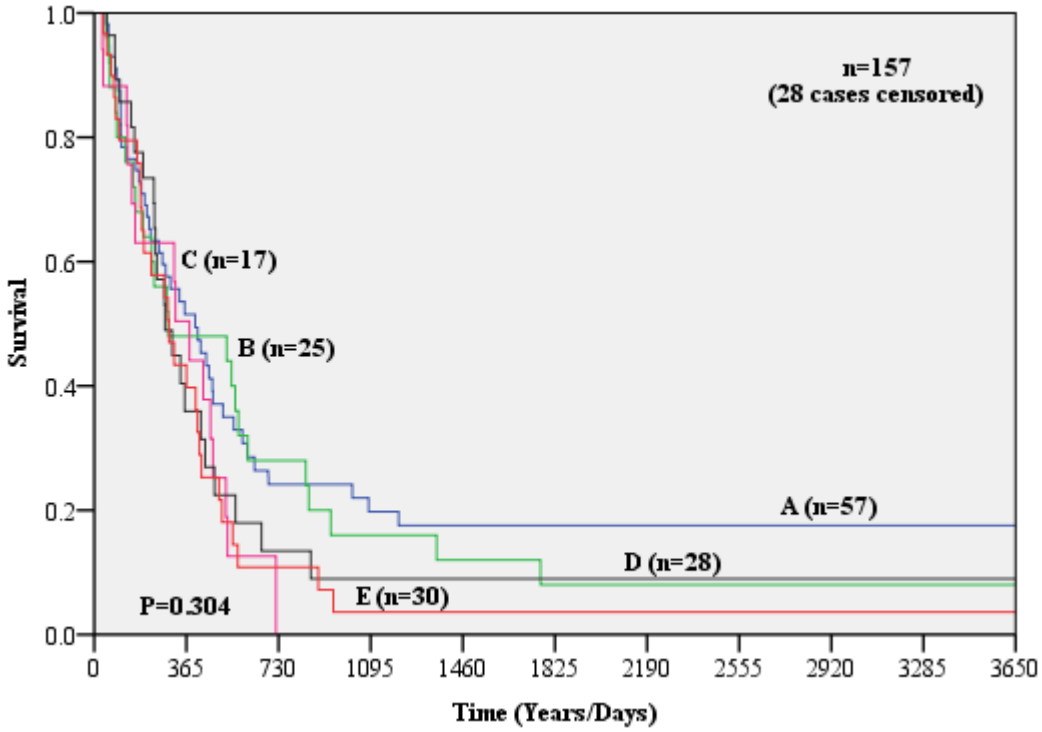
●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and monthly mean vitamin D sunshine index.

●NS is not significant

●N is number of uncensored cases

●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.159- Survival according to MMVDSI for males with NSCLC who received chemotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.160- Survival according to MMVDSI for males with NSCLC who received chemotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

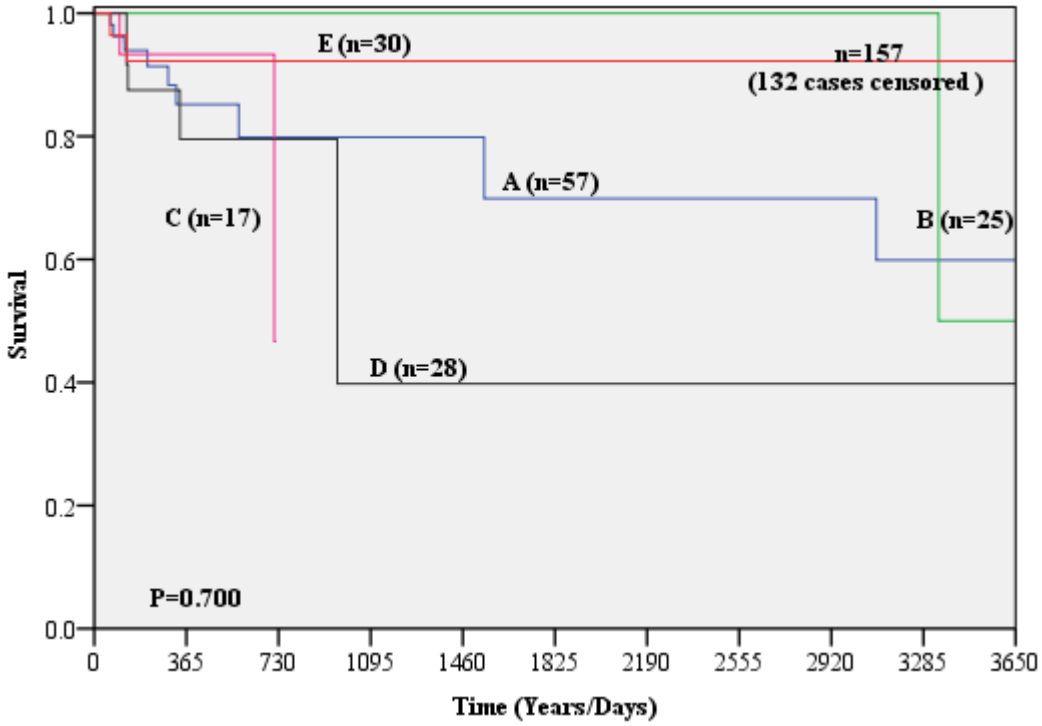
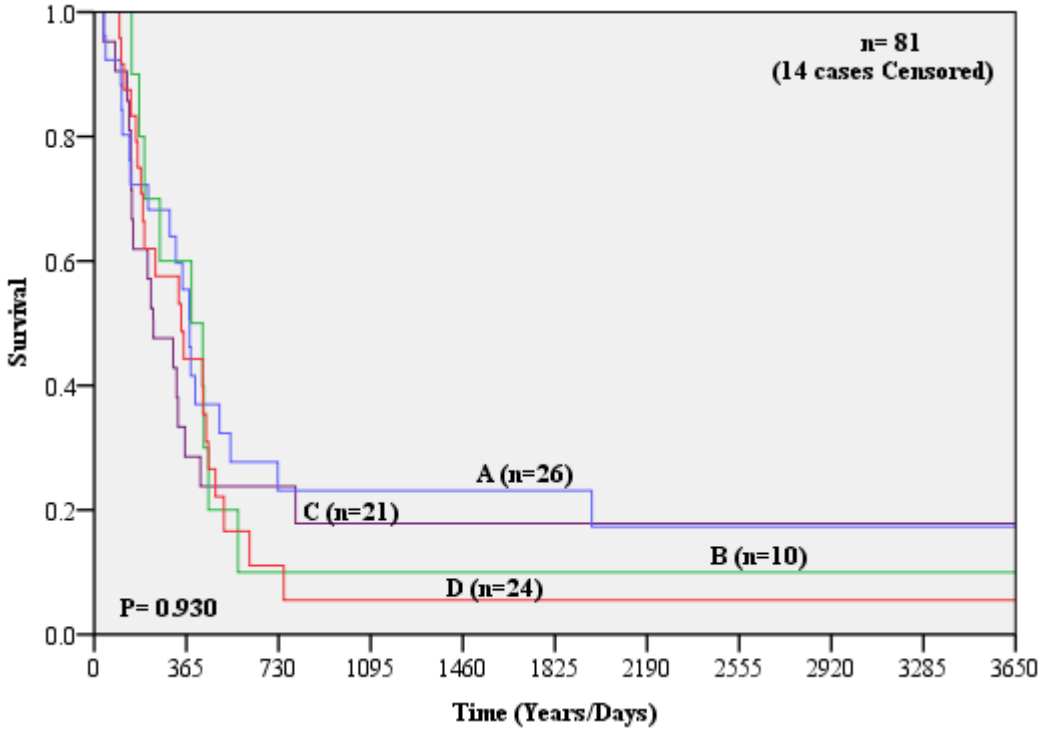


Table 3.85- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for females with NSCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	81	14	NS	NS	1.06 0.4-2.2	0.98 0.3-2.6	1	1.05 0.5-2.1
Other causes	81	72	NS	NS	N<5	N<5	1	N<5

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and season of diagnosis.
- NS is not significant; A is spring, B is summer, C is fall and D is winter.
- N is number of uncensored cases
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.161- Survival according to season of diagnosis for females with NSCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.162- Survival according to season of diagnosis for females with NSCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

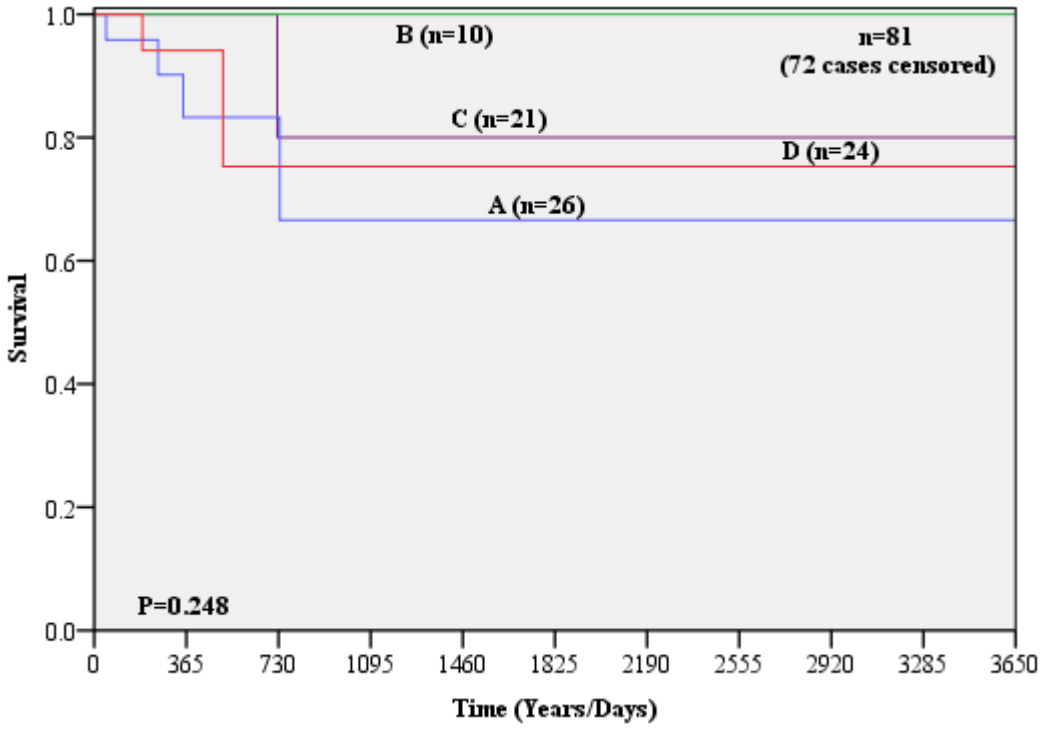
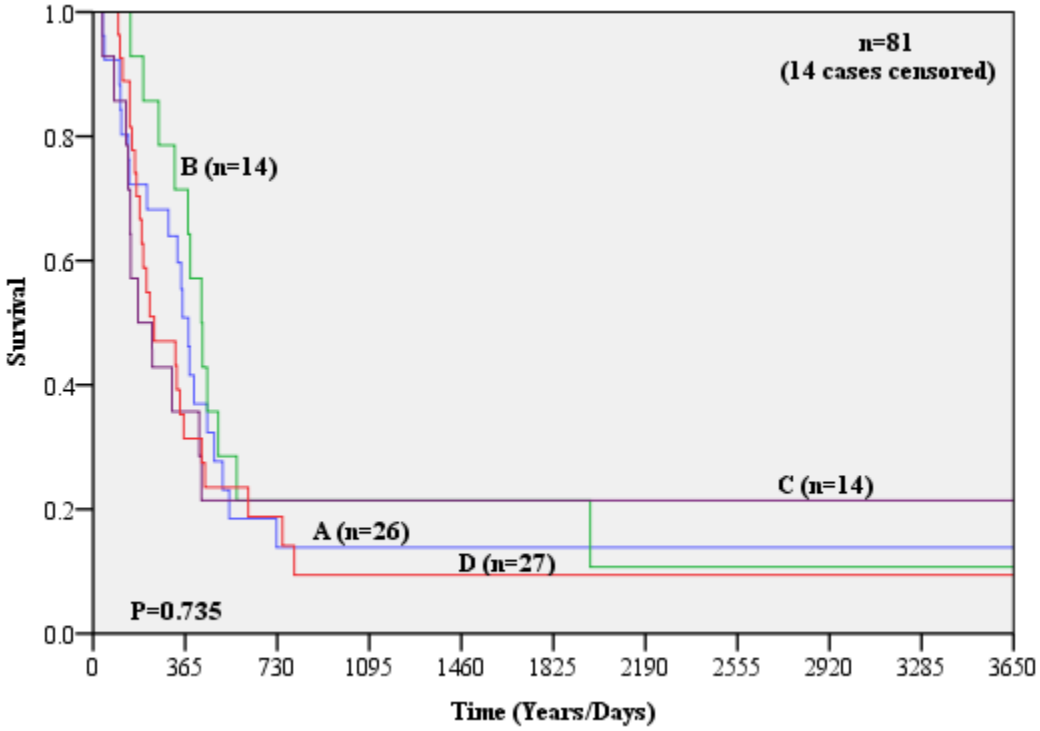


Table 3.86- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for females with NSCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	81	14	NS	NS	1	0.75 0.3-1.6	1.02 0.4-2.4	0.95 0.5-1.8
Other causes	81	72	NS	NS	1	N<5	N<5	N<5

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and season of first treatment.
- NS is not significant; A is spring, B is summer, C is fall and D is winter.
- N is number of uncensored cases
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.163- Survival according to season of first treatment for females with NSCLC who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.164- Survival according to season of first treatment for females with NSCLC who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

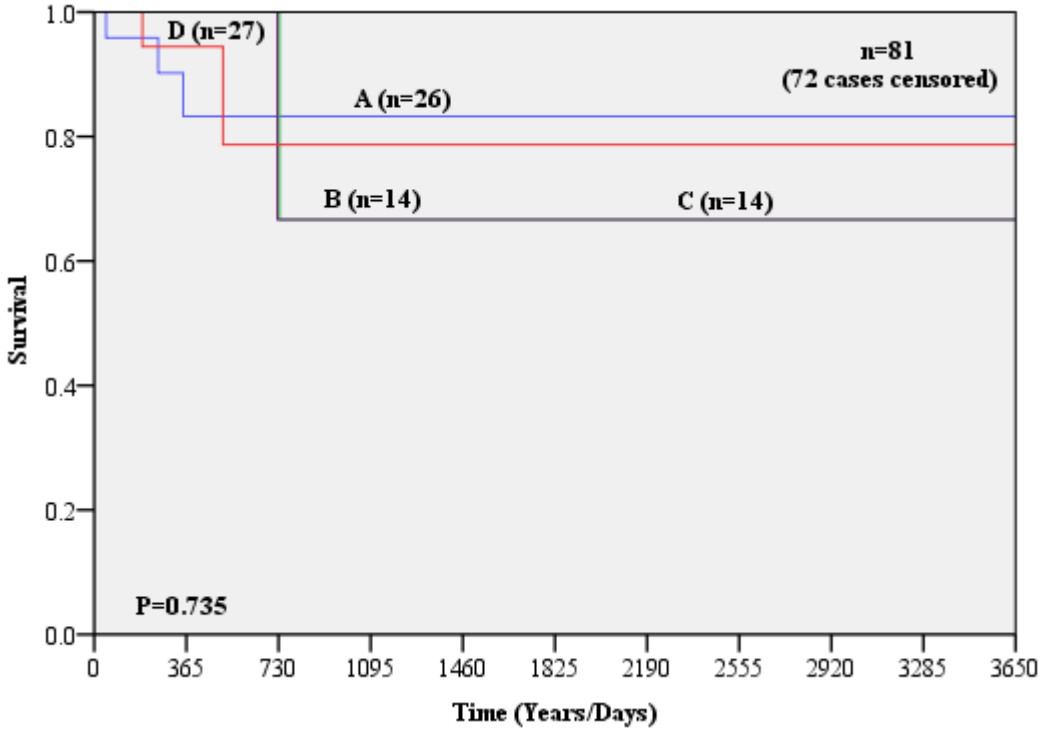


Table 3.87- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for females with NSCLC who received chemotherapy

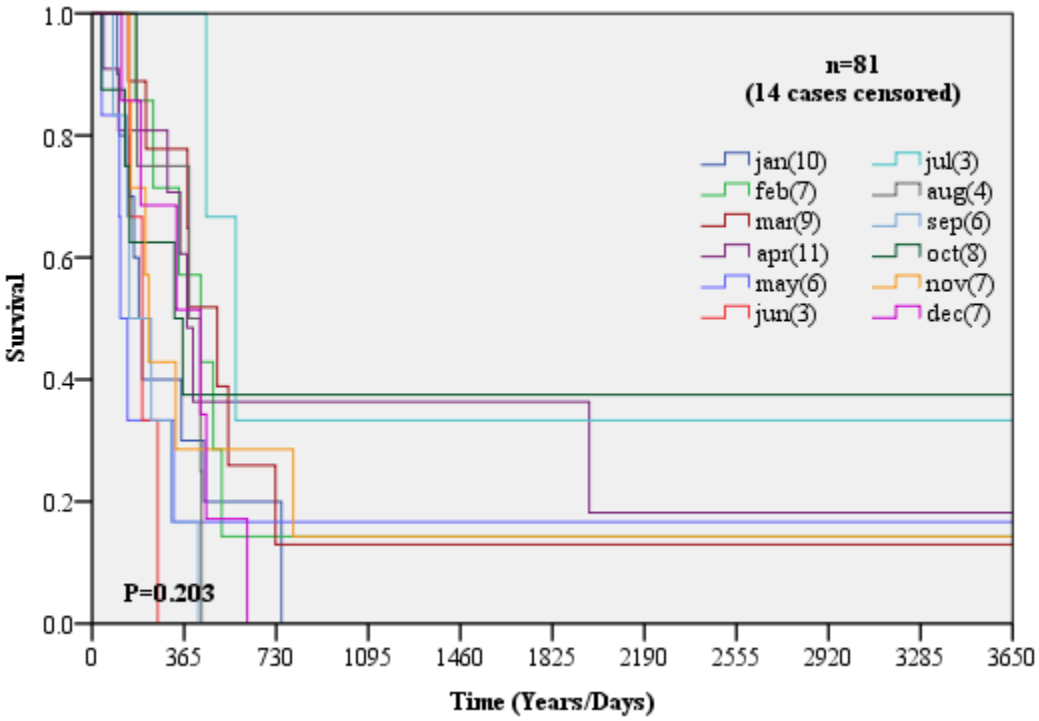
Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.025	NS
Number of cases		81	81
Number of censored cases		14	72
HR (95% CI)	Jan	1	1
	Feb	0.87 0.2-3.2	N<5
	Mar	0.55 0.1-1.6	N<5
	Apr	1.43 0.4-4.9	N<5
	May	2.93 0.7-12.2	N<5
	Jun	N<5	N<5
	Jul	N<5	N<5
	Aug	N<5	N<5
	Sep	2.35 0.6-9.1	N<5
	Oct	0.68 0.2-2.2	N<5
	Nov	0.81 0.2-2.5	N<5
	Dec	1.15 0.3-3.7	N<5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and month of diagnosis.

●NS is not significant

●N is number of uncensored cases ●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.165- Survival according to month of diagnosis for females with NSCLC who received chemotherapy: lung cancer deaths



Graph 3.166- Survival according to month of diagnosis for females with NSCLC who received chemotherapy: non-lung-cancer deaths

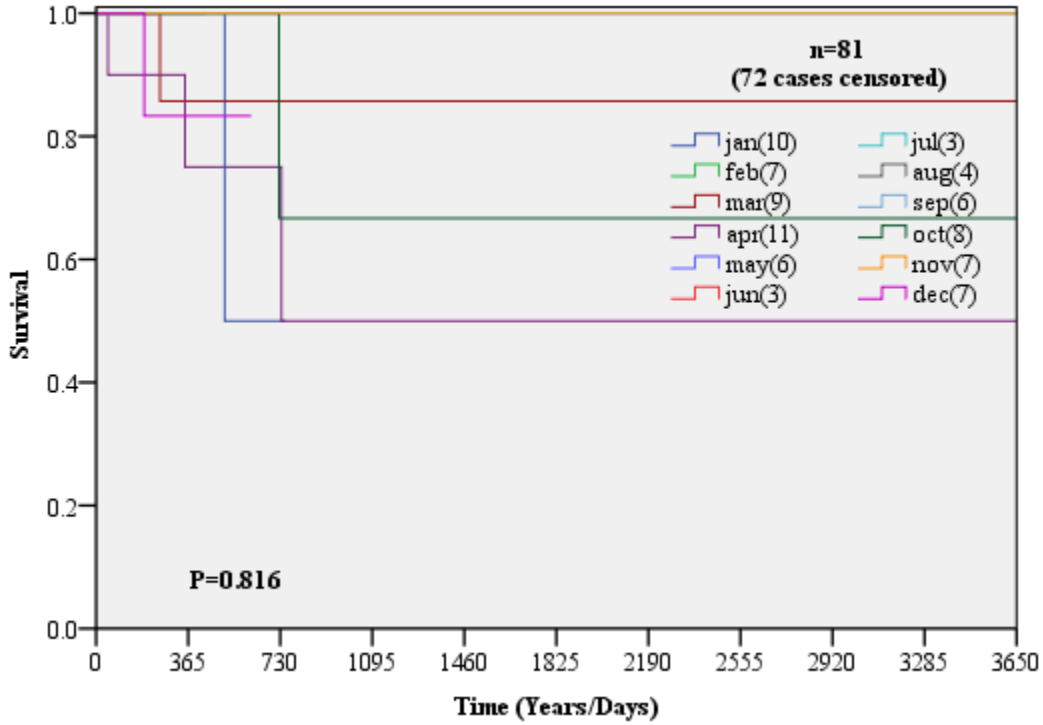


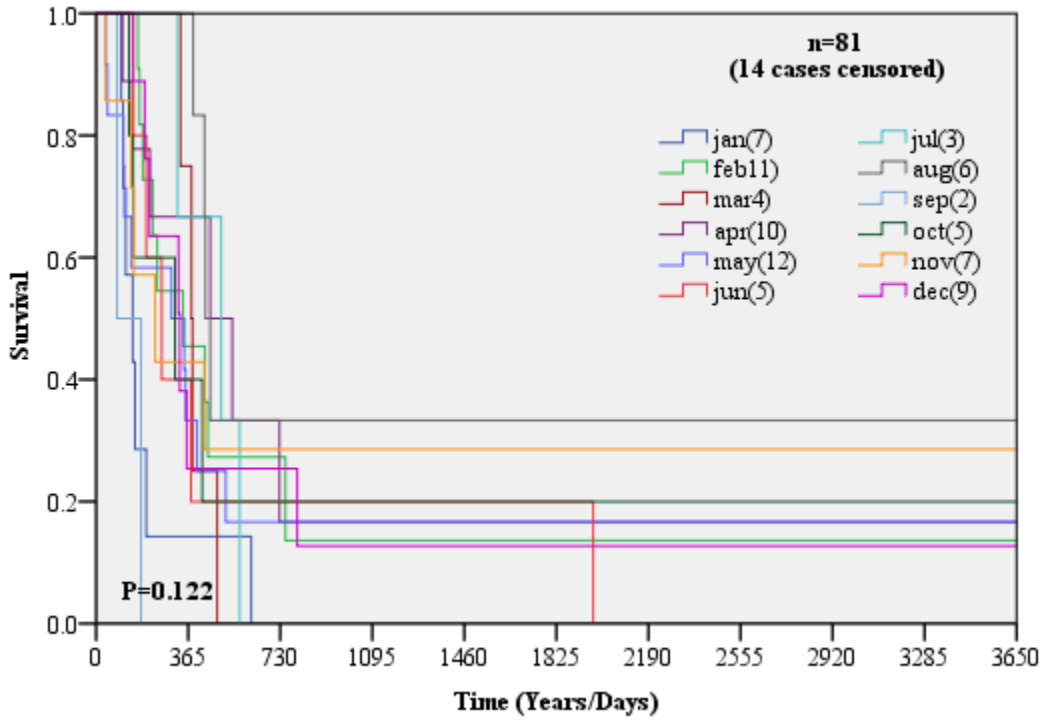
Table 3.88- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for females with NSCLC who received chemotherapy

Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.025	NS
Number of cases		81	81
Number of censored cases		14	72
HR (95% CI)	Jan	1	1
	Feb	0.16 0.0-0.5	N<5
	Mar	N<5	N<5
	Apr	0.26 0.0-0.9	N<5
	May	0.44 0.1-1.4	N<5
	Jun	0.55 0.1-2.3	N<5
	Jul	N<5	N<5
	Aug	N<5	N<5
	Sep	N<5	N<5
	Oct	N<5	N<5
	Nov	0.21 0.0-0.8	N<5
	Dec	0.19 0.0-0.8	N<5

●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and season of first treatment.

●NS is not significant ●N is number of uncensored cases ●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.167- Survival according to month of first treatment for females with NSCLC who received chemotherapy: lung cancer deaths



Graph 3.168- Survival according to month of first treatment for females with NSCLC who received chemotherapy: non-lung-cancer deaths

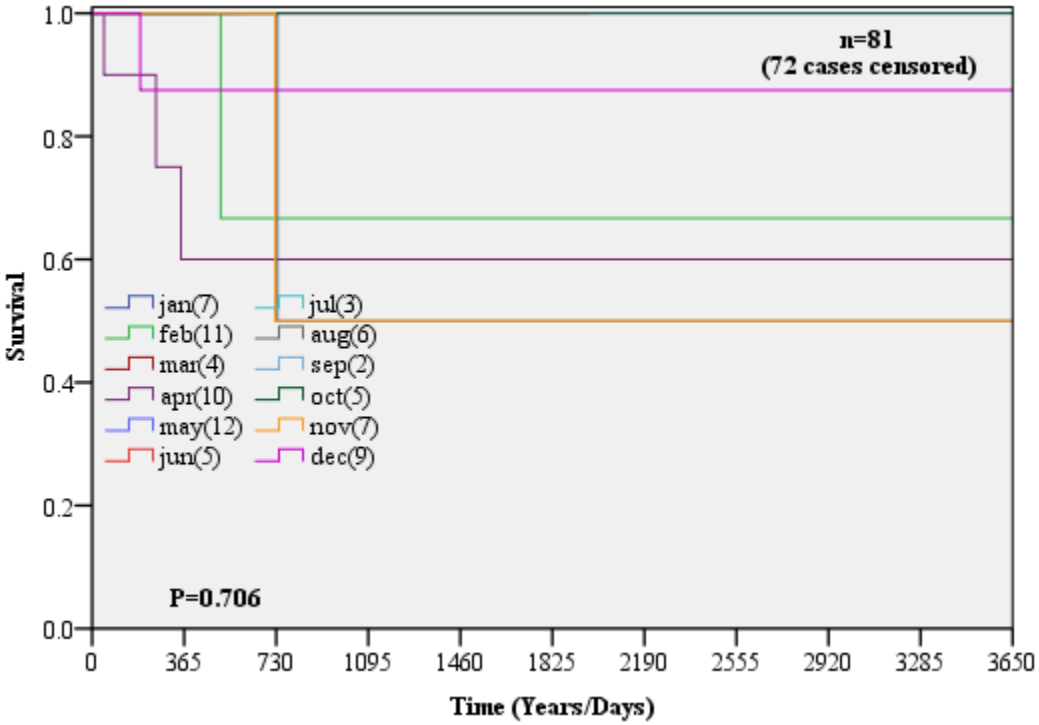


Table 3.89- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for females with NSCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	81	14	0.071	NS	1	0.70 0.3-1.4	1.82 0.8-4.0	2.77 1.0-7.6	0.66 0.2-2.0
Other causes	81	72	NS	NS	1	N<5	N<5	N<5	N<5

(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

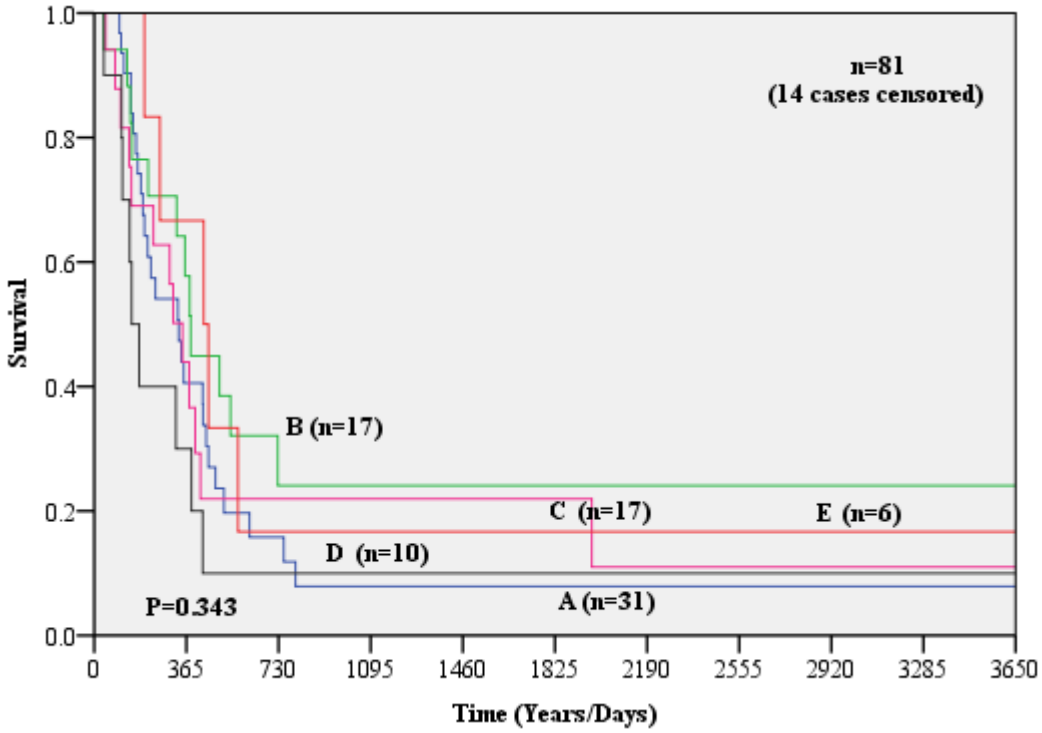
•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and Monthly mean vitamin D sunshine index.

•NS is not significant

•N is number of uncensored cases

•Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.169- Survival according to MMVDSI for females with NSCLC who received chemotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.170- Survival according to MMVDSI for females with NSCLC who received chemotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)

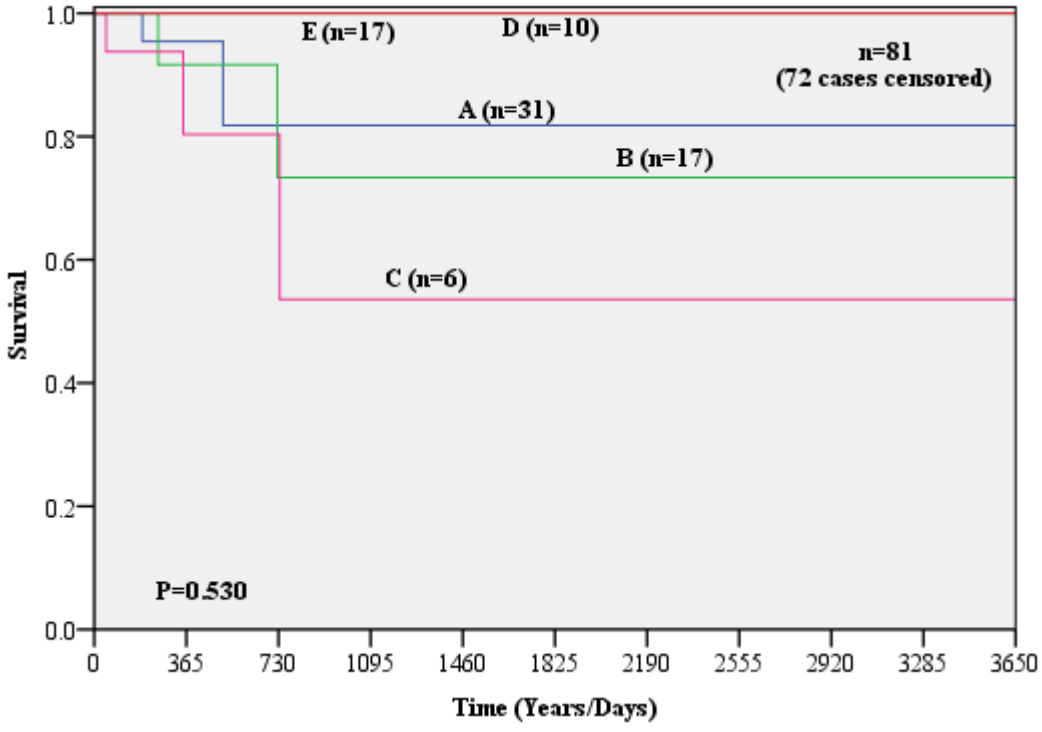


Table 3.90- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of diagnosis for male and female patients with NSCLC who received chemotherapy

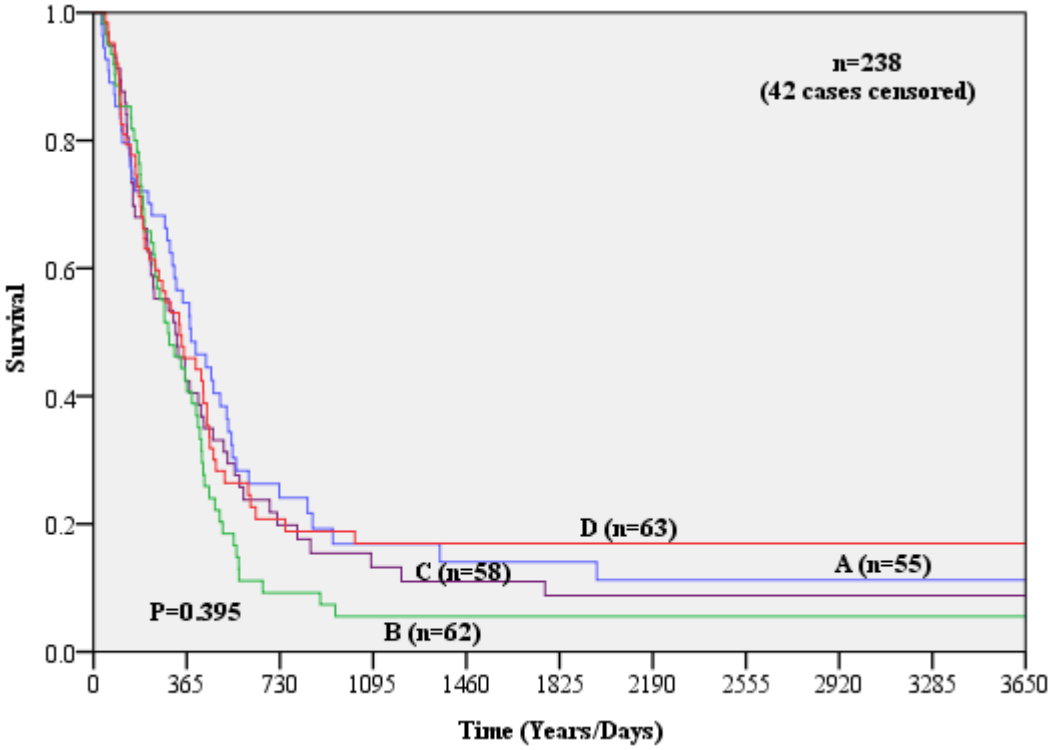
Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	238	42	NS	NS	1.07 0.6-1.6	1.22 0.7-1.8	1	0.86 0.5-1.3
Other causes	238	204	NS	NS	1.81 0.5-6.2	1.12 0.3-3.9	1	1.41 0.4-4.3

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and season of diagnosis.

- NS is not significant; A is spring, B is summer, C is fall and D is winter.

- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.171- Survival according to season of diagnosis for male and female NSCLC patients who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.172- Survival according to season of diagnosis for male and female NSCLC patients who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

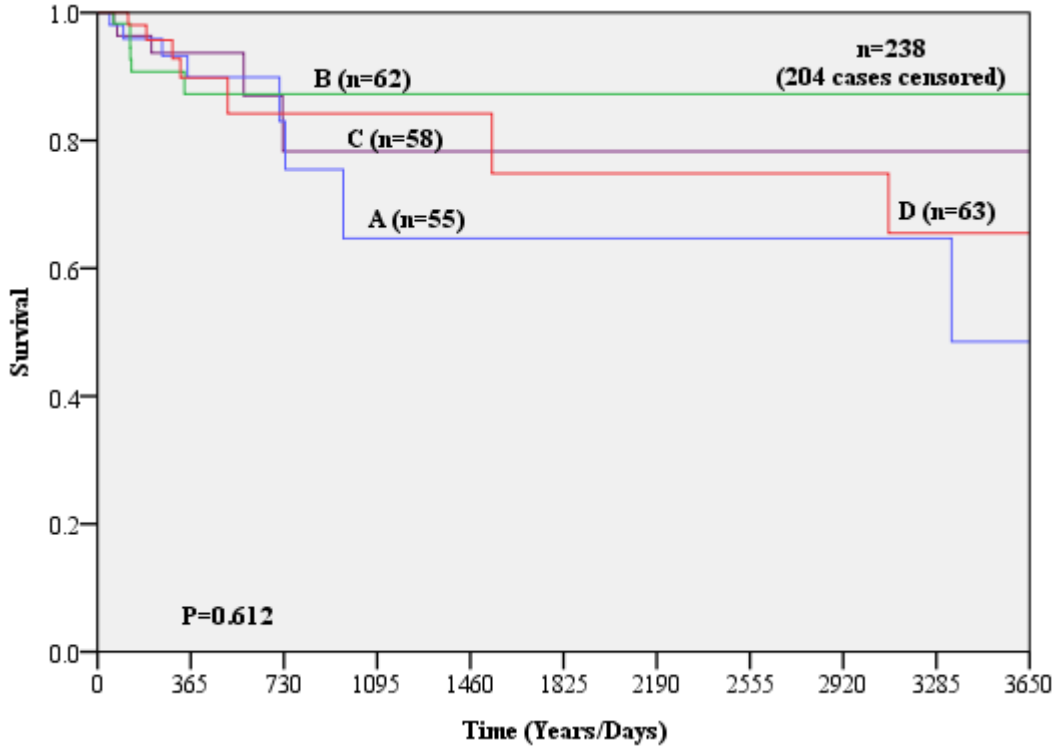
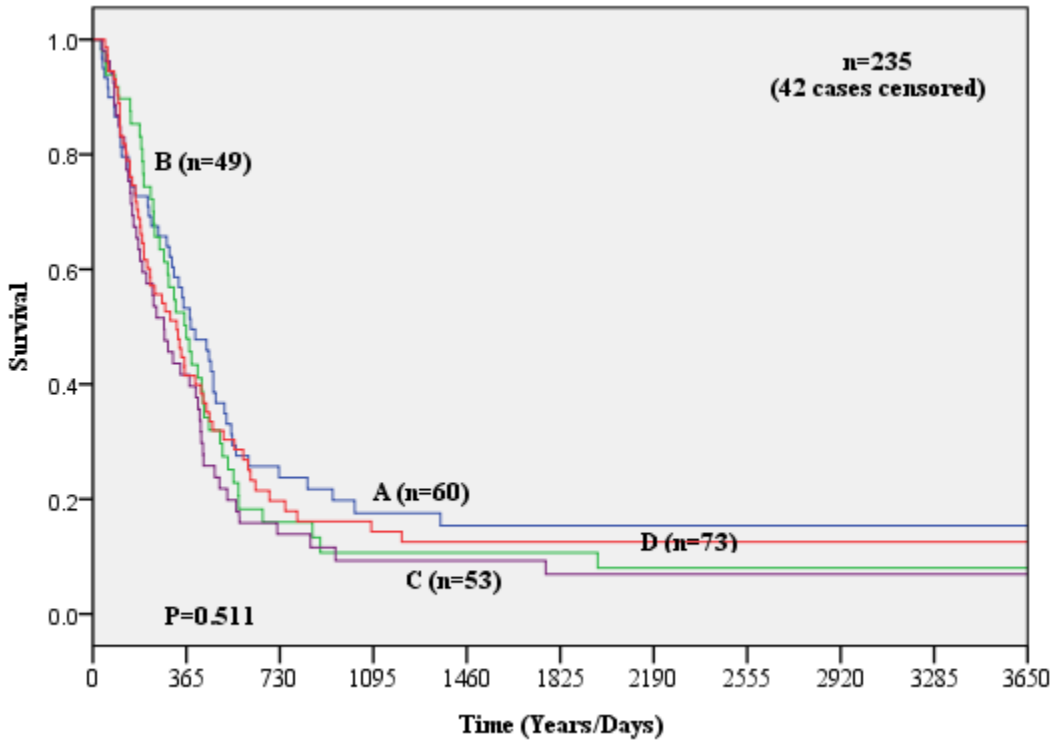


Table 3.91- Hazard ratio (HR) and 95% confidence interval (CI) associated with season of first treatment for male and female patients with NSCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)			
					Spring (A)	Summer (B)	Fall (C)	Winter (D)
Lung cancer	235	42	NS	NS	1	1.15 0.7-1.7	1.31 0.8-2.0	1.07 0.7-1.6
Other causes	235	201	NS	NS	1	0.57 0.1-1.9	N<5	1.90 0.7-4.9

- Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and season of first treatment.
- NS is not significant; A is spring, B is summer, C is fall and D is winter.
- N is number of uncensored cases
- Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.173- Survival according to season of first treatment for male and female NSCLC patients who received chemotherapy: lung cancer deaths (A is spring, B is summer, C is fall and D is winter)



Graph 3.174- Survival according to season of first treatment for male and female NSCLC patients who received chemotherapy: non-lung-cancer deaths (A is spring, B is summer, C is fall and D is winter)

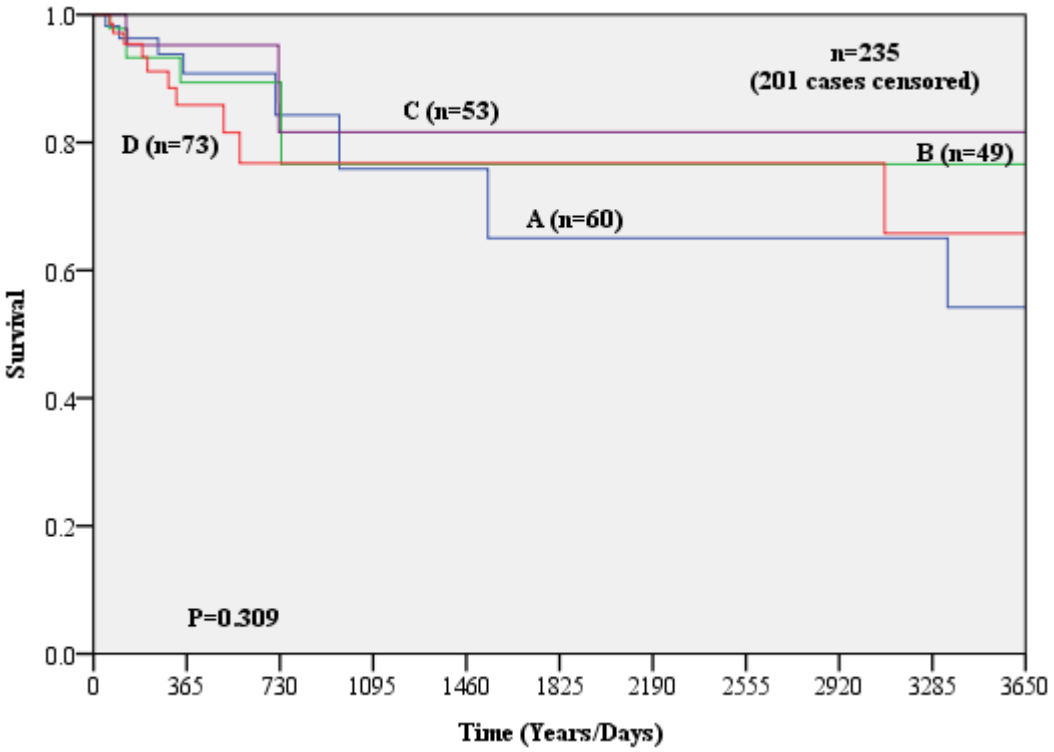


Table 3.92- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of diagnosis for male and female patients with NSCLC who received chemotherapy

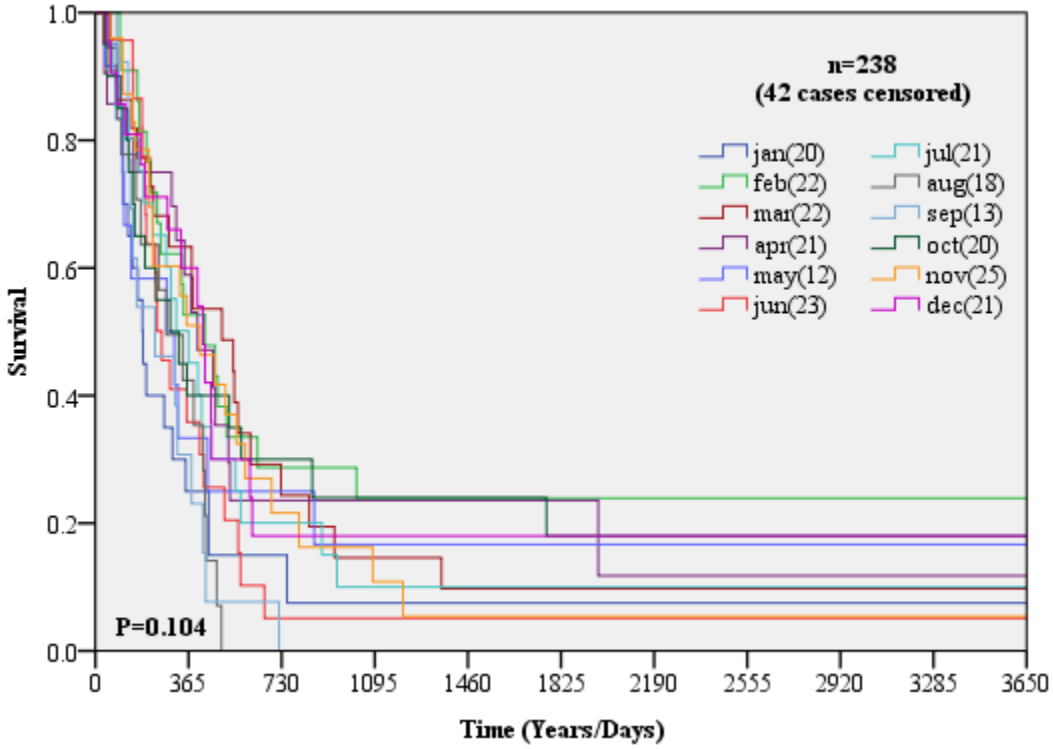
Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		0.065	NS
Number of cases		238	238
Number of censored cases		42	204
HR (95% CI)	Jan	1	1
	Feb	0.40 0.1-0.8	0.59 0.0-4.5
	Mar	0.60 0.3-1.1	n<5
	Apr	0.91 0.4-1.9	6.79 0.8-57.4
	May	1.02 0.4-2.4	N<5
	Jun	0.85 0.4-1.6	N<5
	Jul	0.70 0.3-1.4	N<5
	Aug	1.22 0.5-2.5	N<5
	Sep	1.37 0.6-2.9	N<5
	Oct	0.57 0.2-1.1	N<5
	Nov	0.59 0.3-1.1	2.07 0.2-16.3

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and month of diagnosis.

•NS is not significant

•N is number of uncensored cases •Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.175- Survival according to season of month of diagnosis for male and female NSCLC patients who received chemotherapy: lung cancer deaths



Graph 3.176- Survival according to season of month of diagnosis for male and female NSCLC patients who received chemotherapy: non-lung-cancer deaths

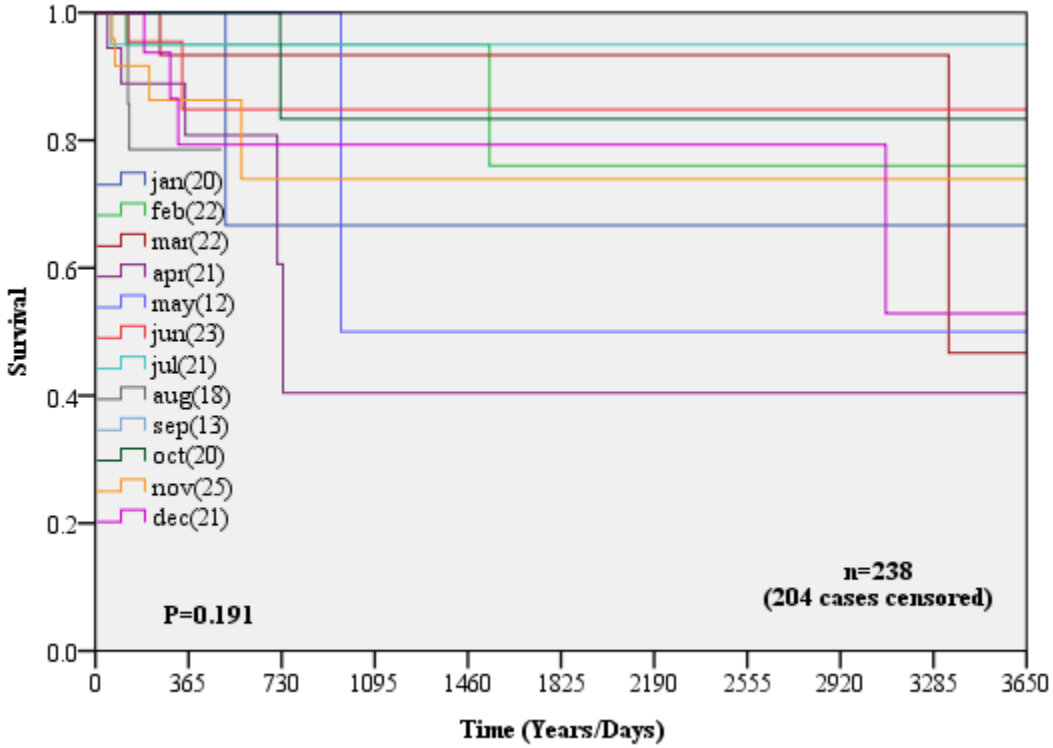


Table 3.93- Hazard ratio (HR) and 95% confidence interval (CI) associated with month of first treatment for male and female patients with NSCLC who received chemotherapy

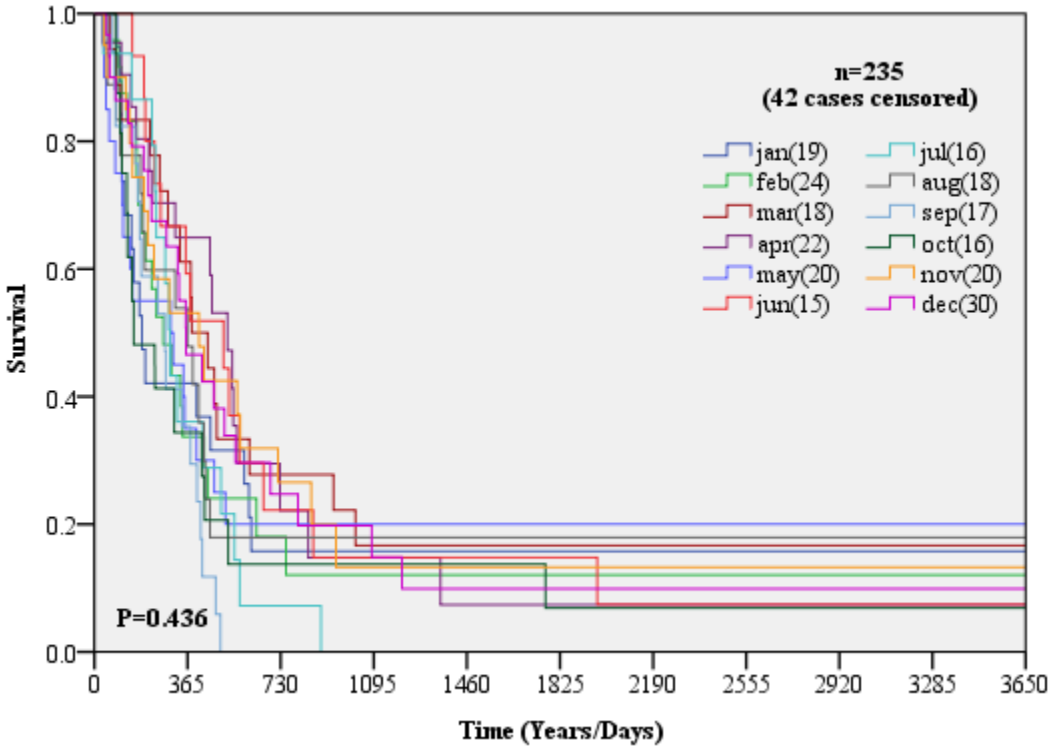
Cause of death		Lung cancer	Other Causes
Univariate P value		NS	NS
Multivariate P value		NS	NS
Number of cases		235	235
Number of censored cases		42	201
HR (95% CI)	Jan	1	1
	Feb	0.77 0.3-1.5	2.78 0.4-18.7
	Mar	0.52 0.2-1.0	N<5
	Apr	0.90 0.4-1.9	7.39 0.9-56.7
	May	0.90 0.4-1.9	N<5
	Jun	0.70 0.3-1.5	N<5
	Jul	0.94 0.4-2.0	N<5
	Aug	0.98 0.4-2.1	N<5
	Sep	1.34 0.6-2.8	N<5
	Oct	0.90 0.4-1.9	N<5
	Nov	0.71 0.3-1.5	1.35 0.1-10.6

•Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and month of first treatment.

•NS is not significant

•N is number of uncensored cases •Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.177- Survival according to month of first treatment for male and female NSCLC patients who received chemotherapy: lung cancer deaths



Graph 3.178- Survival according to month of first treatment for male and female NSCLC patients who received chemotherapy: non-lung-cancer deaths

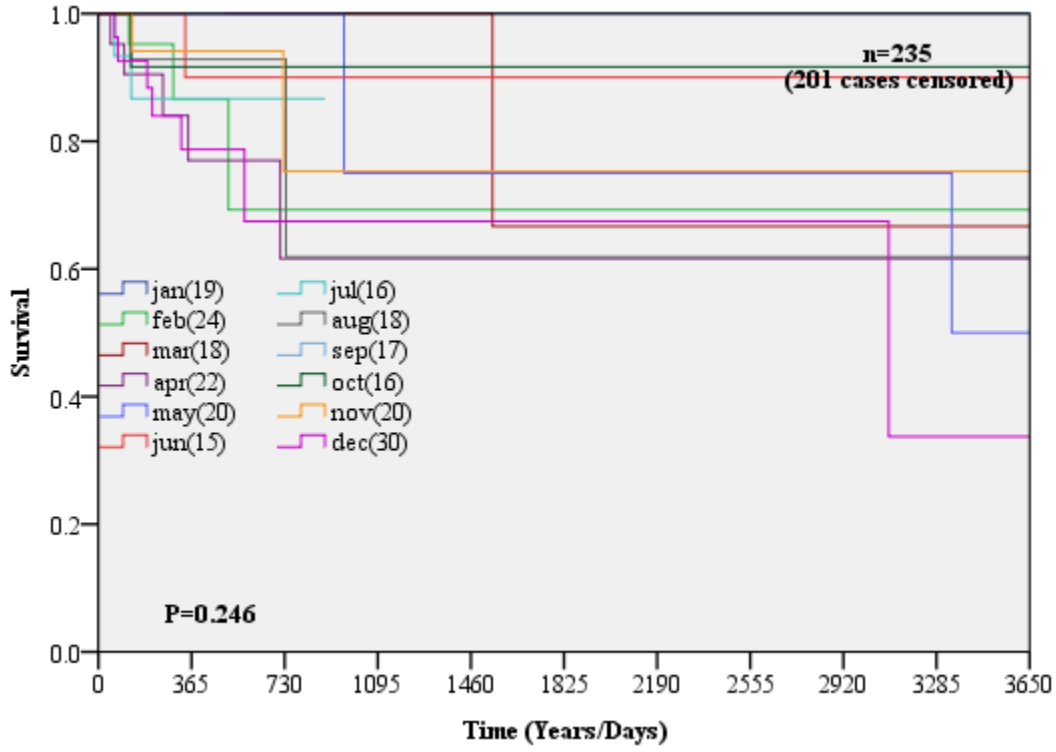


Table 3.94- Hazard ratio (HR) and 95% confidence interval (CI) associated with monthly mean vitamin D sunshine index for male and female patients with NSCLC who received chemotherapy

Cause of Death	Number of cases	Number of Censored Cases	Univariate P-value	Multivariate P-value	HR (95% CI)				
					A	B	C	D	E
Lung cancer	238	42	NS	0.058	1	0.95 0.6-1.4	1.61 1.0-2.5	1.70 1.0-2.7	1.41 0.9-2.2
Other causes	238	204	NS	NS	1	N<5	1.58 0.4-5.0	0.84 0.2-2.9	N<5

(A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU)

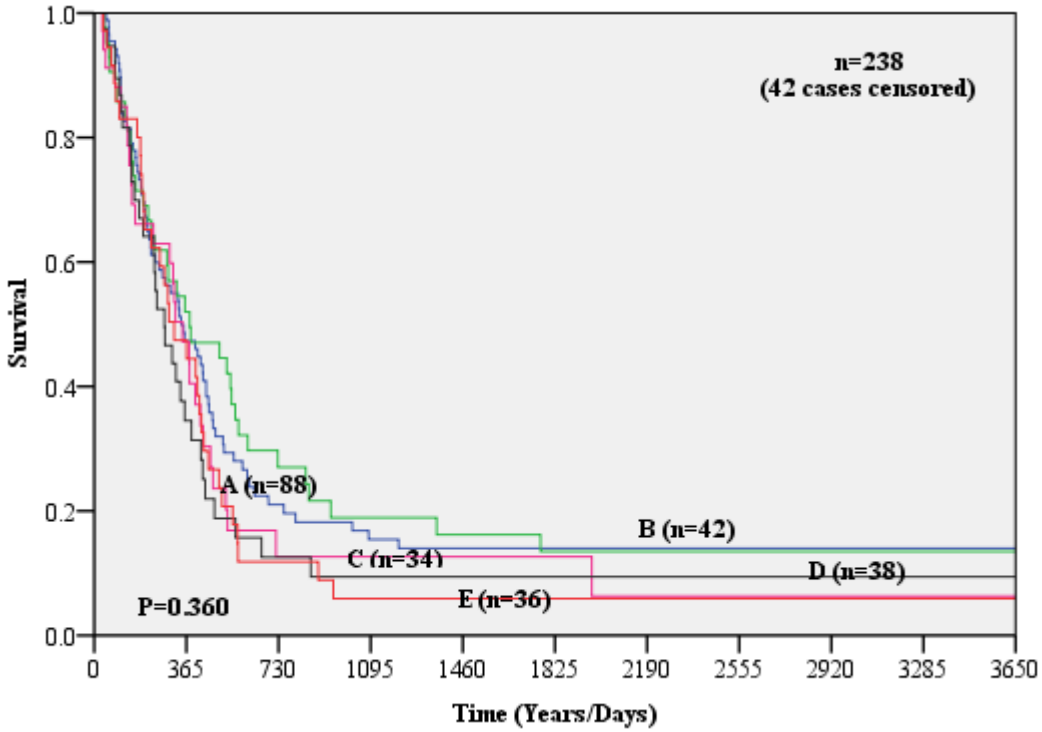
●Multivariate P-value is adjusted for age at diagnosis, cancer laterality, stage at time of diagnosis, other treatments (radiotherapy and surgery), disease site and monthly mean vitamin D sunshine index.

●NS is not significant

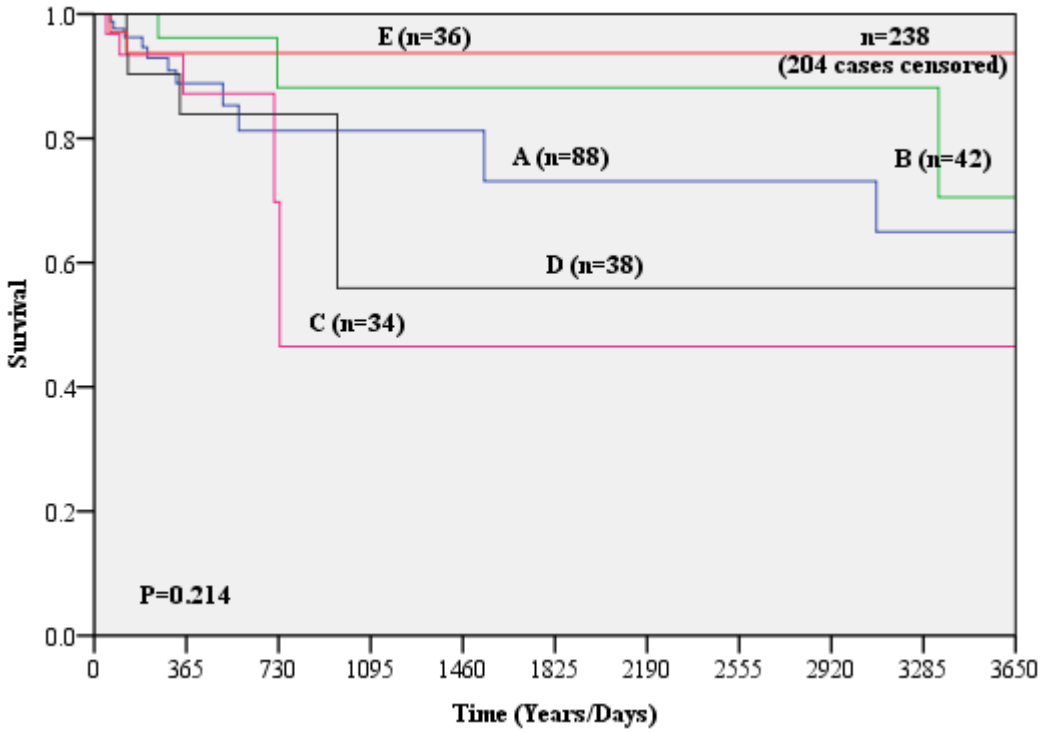
●N is number of uncensored cases

●Number of cases is the cumulative number of SCLC and NSCLC before censoring for cause of death

Graph 3.179- Survival according to MMVDSI for male and female NSCLC patients who received chemotherapy: lung cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



Graph 3.180- Survival according to MMVDSI for male and female NSCLC patients who received chemotherapy: non-lung-cancer deaths (**A**: ≤0.406 IU **B**: 0.406-0.812 IU **C**: 0.812-1.218 IU **D**: 1.218-1.624 IU **E**: ≥1.624 IU)



4. Discussion

4.1 Sunlight and cancer survival association

These results suggest that sun exposure could improve prognosis in some lung cancer patients. This might imply sun-induced vitamin D affects some lung cancer patients. In particular, I found:

A- According to table 3.2, survival was significantly associated with season of diagnosis, season of first treatment, month of diagnosis and month of first treatment in females with SCLC who received radiotherapy and died because of lung cancer. However, survival was not significantly associated with monthly mean MMVDSI in these same patients.

B- According to table 3.3, survival was significantly associated with (MMVDSI) in females with NSCLC who received surgery and died because of lung cancer. However, survival was not significantly associated with other sunshine variables (i.e., month and season) in these same patients.

C- According to table 3.4, survival was significantly associated with (MMVDSI) in males with NSCLC who received radiotherapy and died because of lung cancer. However, survival was not significantly associated with other sunshine variables (i.e., month and season) in these same patients.

In additional analyses, I separately examined patients who received monotherapy, (i.e., only chemotherapy, surgery or radiotherapy), patients age <50 and ≥50 years (at time of diagnosis). The results were:

- Survival was significantly associated with all of the sunshine variables in SCLC patients who received only radiotherapy and died because of lung cancer.
- Survival was significantly associated with (MMVDSI) in NSCLC patients age ≥50y who received only surgery and died because of lung cancer.
- Survival was significantly associated with (MMVDSI) in NSCLC patients who received only radiotherapy and died because of lung cancer.

4.2 Study strengths

Compared to previous work that was done by other groups, my study has some strong points:

- The study population was large. I considered more than 9000 patients with lung cancer and a remarkable amount of information.
- I used five different sunshine variables, which allowed us to compare with previous studies' results. This allowed me to compare this study with the previous ones and also analyze some novel sunshine variables.
- In comparing our study to other studies we used a novel method to find the association of sun-induced vitamin D and cancer survival which was monthly mean vitamin D sunshine index.
- Unlike previous studies, our study's analyses were stratified by different types of treatment. Moreover, not only we considered the types of treatment, but also we analyzed each type of treatment individually.
- The amount of missing information was small in my study. BC cancer registry, between 1980 and 1989, gathered treatment information of about 70% of patients who had lung cancer, which was an outstanding percentage at that period.

4.3 Study limitations

Having discussed our study's strength, it is important to mention that this study is not flawless. Most of the following limitations were difficult to avoid.

- Our data didn't include smoking information, which could be a potential effect modifier for the sunshine measure. There are many reasons why this might be true, but smoking is one of the important prognostic factors in lung cancer patients and smoking could interfere with sun-induced vitamin D production. Smoking information is not usually recorded in the BCCR, and it would have been very time consuming, or even impossible, to call each of the patients' families for the information.
- Our data didn't include a patient's race. Skin pigmentation is different in races, and vitamin D production depends on race. Like smoking information, The BCCR doesn't usually record information about race. A partial solution might involve taking a sample of our data set and trying to find the patients' races. Another solution might involve using each patient's name to determine his or her race.
- The sample size for SCLC patients who received surgery was not big. SCLC has the worst survival among different types of lung cancer and many patients already have metastases disease. Accordingly, few patients are candidates for surgery.
- Since we have done a considerable number of analyses, the significant results may be because of chance.
- We did not find out the amount of actual sunlight exposure in our study.
- One of the sources of vitamin D for our body is diet and vitamin D supplements. It was not possible for us to consider this variable since we had no access to this information.

4.4 Comparing the results with previous studies

Few studies have assessed the association between sun exposure and cancer survival. Most of the existing studies have been done in Norway by Porojnicu and colleagues. They have done several studies in which they found the prognostic advantage of sun-induced 25-hydroxy vitamin D in Hodgkins disease, colon, breast, prostate and lung cancers.
In addition, there are some other, non-epidemiologic, studies in which the association of vitamin D and cancer survival was evaluated. In all of these studies, researchers have tried to show the protective effect of vitamin D, either directly or indirectly (sun exposure) in different types of cancer which I have already mentioned them in section 1.4.

I also performed analyses using season of diagnosis, thereby allowing me to compare results with those of earlier studies. In Porojnicu's results, male NSCLC patient's age < 50 years had better survival during sunny seasons. In my study, of patients with the same age, sex and histology group, only those who received surgery had a better prognosis (univariate analysis only).

4.5 Future work

There are several studies to further the things I discovered in this project. My study shows that there is a good chance that sunlight exposure, specifically the range which induces vitamin D production, could increase the survival in lung cancer patients. But, I would like to repeat my study for another time period to determine whether the result would be similar. Another project would involve a prospective patient cohort so that I could address some of our project's weaknesses. If vitamin D improves a lung cancer patient's prognosis, then I might propose vitamin D supplements as adjuvant or neoadjuvant treatment for lung cancer patients.

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Appendices

Appendix A: MMVDSI data set generation process

Table A-1 on next page, is a small version of MnDph data set. For example the number 0.3423 represents the10- average (1980-1980) of vitamin D UV-B spectrum in lat 54 and lon -119 in 1 am in January 1st. In the first step, I calculated the average of the first day of each month for each corresponding lat and lon. For example, in table A-2, the number 0.3451 represents the10- average (1980-1980) of vitamin D UV-B spectrum in lat 54 and lon -119 in first day of January. In the next step, I calculated the average of each month for each corresponding lat and lon. For example, in table A-3, the number 0.3482 represents the10- average (1980-1980) of vitamin D UV-B spectrum in lat 54 and lon -119 in January. I called the last number for each month, Monthly mean vitamin D sunshine index.

The next step in generating the new data set was converting each patient postal code at the time of diagnosis to lat and lon. After this step, I had a lat and lon for each patient at the month of diagnoses. Then, I merged the data set of MMVDSI to this new data set. Finally, I had a new data set in which I had a number for each patient at the time of diagnosis representing of MMVDSI for that patient. (You can see the process in the diagram)

In the analyses since I used the Cox-proportional model, I decided to divide the MMVDSI actual range to five subgroups; A: ≤0.406 IU B: 0.406-0.812 IU C: 0.812-1.218 IU D: 1.218-1.624 IU E: ≥1.624 IU. I thought it would be fine to do it this way specially when the number of cases in each group were approximately the same

Table A-1: Hourly average of MnDph

Lat			54
Lon			-119
January First	(24 hrs MnDph)	1	0.3423
		2	0.3425
		3	.....
		4	.....
		5	.....
		6	.....
		7	.....
		8	.....
		9	.....
		10	.....
		11	.....
		12	.....
		13	.....
		14	.....
		15	.....
		16	.....
		17	.....
		18	.....
		19	.....
		20	.....
		21	.....
		22	.....
		23	.....
		24	.....

Table A-2: Daily average of MnDph

Lat			54
Lon			-119
January	(Mean of hourly MnDph for each day)	1	0.3451
		2	0.3672
		3	----------
		4	----------
		5	----------
		6	----------
		7	----------
		8	----------
		9	----------
		10	----------
		11	----------
		12	----------
		13	----------
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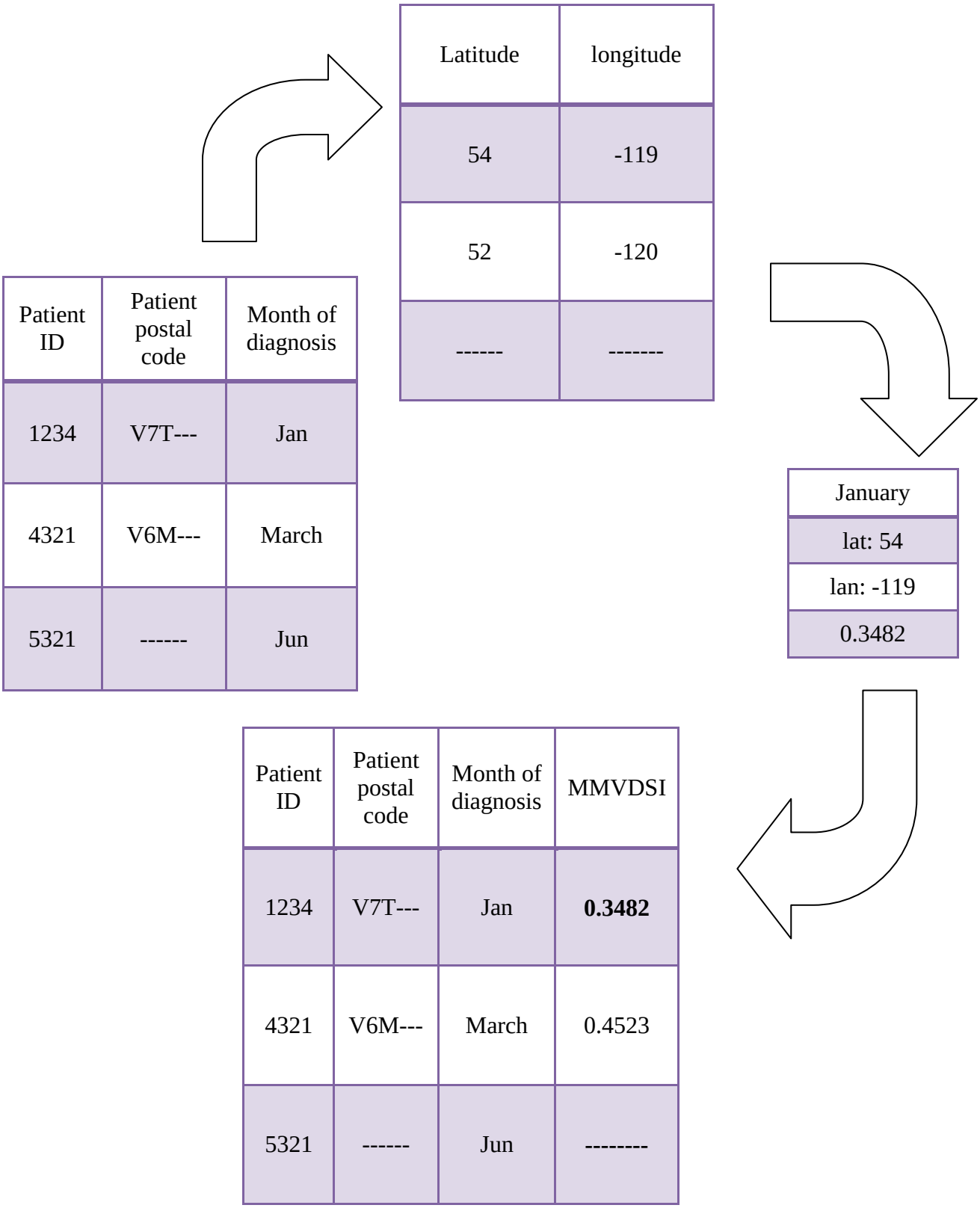
		30	----------
		31	----------

Table A-3: Monthly average of MnDph

Lat		54
Lon		-119
(Mean of hourly MnDph for each month)	Jan	**0.3482**
	Feb	0.3582
	Mar	0.3921
	Apr	----------
	May	----------
	Jun	----------
	Jul	----------
	Aug	----------
	Sep	----------
	Oct	----------
	Nov	----------
	Dec	----------

Figure A-1: Diagram of MMVDSI calculation



Appendix B: Lung cancer population details

Total number of cases in data set=9953, Number of exclusion due to 30-day period=651, Number of exclusion due to another type of cancer=6, Number of exclusion due to missing postal code=781)

Table A-4: Total number of cases in all sunshine measures except MMVDSI

Total number of cases	Exclusion due to 30-day period	exclusion due to another type of cancer	Final study population for the rest of sunshine measures but *MnDph* (after considering exclusion criteria
9953	651	6	9302

Table A-5: Total number of cases in MMVDSI

Total number of cases after considering exclusion criteria	exclusion due to missing postal code	Final study population for the *MnDph*
9302	781	8521

Appendix C: Summary of additional analyses' significant results

Histology		Sex			Cause of death		Type of Tx			MMVDSI	Season of Diagnosis	Season of 1st Tx	Month of diagnosis	Month of 1st Tx	P-value		n
SCLC	NSCLC	M	F	B	LC	NLC	C	S	R						U	M	
+			+		+				+		+				0.020	0.012	37
+			+		+				+	+						0.042	37
+				+	+				+					+	0.032	<0.01	74
+				+	+				+				+			0.041	74
+				+	+				+		+					0.033	74
+				+	+				+				+			0.019	74
+		+			+		+			+						0.028	28
+		+			+		+				+					0.017	28
+		+			+		+					+			0.047	<0.01	
+				+	+		+							+	<0.01		56
+				+	+		+				+					0.036	56
+				+	+		+					+			0.019	<0.01	56
	+		+		+			+			+				0.018		52
	+		+		+				+			+			0.045	<0.01	161
	+			+	+			+				+			0.41		118
	+			+	+			+			+				0.035		118
	+			+	+			+						+		0.043	117
	+			+	+			+					+		<0.01	<0.01	118
	+			+	+				+			+			<0.01	<0.01	321

Table A-6: Significant results for Patients age <50 years who received monotherapy

M=male, F=female, B= both sexes together, LC= lung cancer, NL=non-lung cancer, Tx=treatment, U=univariate, M=multivariate, n=number of uncensored cases in each analysis.
How to read this table: + Sign means that the topic of that column is considered in that row for analysis. For example red row means: Univariate and multivariate analyses for month of first treatment were significant (0.032, <0.01) for SCLC patients who died because of lung cancer when the analyses considered both sexes.

Histology		Sex			Cause of death		Type of Tx			MMVDSI	Season of Diagnosis	Season of 1st Tx	Month of diagnosis	Month of 1st Tx	P-value		n
SCLC	NSCLC	M	F	B	LC	NLC	C	S	R						U	M	
+				+	+			+					+			0.017	66
+		+			+				+			+				0.011	495
+			+		+				+			+				<0.01	379
+				+	+				+			+				<0.01	874
	+			+	+				+	+						<0.01	3745
	+		+		+				+			+				<0.01	1233
	+			+	+				+				+			0.022	3779
	+	+			+				+					+	0.041		122
	+		+		+				+					+		<0.01	49
	+	+			+				+			+				<0.01	2546
	+	+			+				+	+						<0.01	2528
	+			+	+				+			+			0.012	<0.01	3779
	+		+		+		+			+						0.030	49
	+			+	+			+		+						0.043	1162
	+		+		+		+							+		<0.01	49

Table A-7: Significant results for patients age ≥50 years who received monotherapy

M=male, F=female, B= both sexes together, LC= lung cancer, NL=non-lung cancer, Tx=treatment, U=univariate, M=multivariate, n=number of uncensored cases in each analysis.
How to read this table: + Sign means that the topic of that column is considered in that row for analysis. For example red row means: Multivariate analyses for season of first treatment was significant (<0.01) for females who had SCLC and died because of lung cancer.

Histology		Sex			Cause of death		Type of Tx			MMVDSI	Season of Diagnosis	Season of 1st Tx	Month of diagnosis	Month of 1st Tx	P-value		n
SCLC	NSCLC	M	F	B	LC	NLC	C	S	R						U	M	
+			+		+				+				+			<0.01	153
+			+		+				+		+				0.023	<0.01	153
+		+			+				+			+			<0.01	<0.01	190
+			+		+				+			+			<0.01	<0.01	153
+			+		+				+					+	0.021		87
+		+			+				+					+	<0.01	0.01	92
+		+			+		+							+	0.028		118
+				+	+				+	+					0.22	0.25	341
+				+	+				+		+				<0.01	<0.01	343
+				+	+				+			+			<0.01	<0.01	343
+				+	+				+				+		0.013	0.017	343
+				+	+				+					+	<0.01	0.028	179
	+		+		+				+			+			<0.01	<0.01	1019
	+	+			+				+			+			<0.01	<0.01	2001
	+	+			+				+	+					0.045	0.040	1991
	+			+	+				+			+			<0.01	<0.01	3020
	+			+	+				+	+						0.022	3000
	+	+			+		+				+					0.043	28
	+			+	+		+							+	0.027	0.012	40
	+			+	+		+						+			0.039	41

Table A-8: Significant results for Monotherapy without age categorization

M=male, F=female, B= both sexes together, LC= lung cancer, NL=non-lung cancer, Tx=treatment, U=univariate, M=multivariate, n=number of uncensored cases in each analysis.
How to read this table: + Sign means that the topic of that column is considered in that row for analysis. For example red row means: Univariate and multivariate analyses for season of first treatment was significant (<0.01, <0.01) for males who had NSCLC and died because of lung cancer.