5. ÅRS OPPGAVE MEDISINSTUDIET VED UNIVERSITETET I TROMSØ

ADOLESCENT SMOKING AND TRENDS IN LUNG CANCER INCIDENCE AMONG YOUNG ADULTS IN NORWAY 1954–1998

Av:

Stud. med. Trond-Eirik Strand, MK-98 Stud. med. Columbo Malayeri, MK-00 Stud. med. Petri Karlo Juhani Eskonsipo, MK-00

Eksterne veiledere ved Kreftregisteret: Cand. med. Tom Kristian Grimsrud Cand. med. Jarle Norstein

Dr. med. Tom Grotmol

Intern veileder ved Universitetet i Tromsø, ISM: Dr. med. Maja-Lisa Løchen

Abstract

Background Limited information is available on trends of lung cancer incidence among young adults and the relationship to adolescent smoking.

Methods Between 1954 and 1998, a total of 1 108 lung cancers were reported to the Cancer Registry of Norway in individuals aged 20–44 years. Temporal variations were studied in age and sex specific rates, in age-adjusted rates, and by means of age-period-cohort modelling. The association between cancer incidence and smoking prevalence was evaluated.

Results The lung cancer incidence rate among women aged 40–44 in Norway continued to increase into the most recent time interval (1994–1998) whereas the rate among men aged 40–44 was essentially constant after 1970. Consequently, lung cancer incidence rates converged among male and female young adults. Lung cancer incidence rates at age 40–44 were highly correlated with smoking prevalence at age 15–19 in males (r = 0.88) and females (r = 0.82) within the same birth cohort.

Conclusions The lung cancer incidence rate in young Norwegian women now equals that of men. The risk at age 40–44 was closely associated with teenage smoking, indicating that duration and age of onset are important.

Introduction

The dramatic changes in lung cancer incidence and mortality in the 20th century have been investigated extensively in people above 50 years of age, among whom this cancer form has become one of the most common world-wide. Although the disease is comparatively rare in young adults, temporal trends in the age group 20–44 may provide a forecast of changes in the rates when these groups reach a more mature and cancer prone age (1). Tobacco smoking has been shown to be by far the most important cause of lung cancer at the age above 50 (2), and there is evidence of a strong impact even in young adults (3). Changes in trend among young adults may therefore provide an early reflection of changes in tobacco smoking.

The aim of the present study was to evaluate the incidence trends at the population level among Norwegian adults between 20 and 44 years of age during the period 1954 to 1998, according to sex, age, birth cohort, and period of diagnosis. The relationship to tobacco smoking was evaluated with aggregated data, with a focus on differences between birth cohorts. Historical information on smoking prevalence for these cohorts could be extrapolated from survey data beginning in 1954 (4).

Methods

The Cancer Registry of Norway is a population-based registry with virtually complete national data on all new cases of cancer since 1953 (5). Reporting of incident cases is compulsory from clinical hospital departments and pathology laboratories.

Every year in the observation period from 1954 to 1998, the Norwegian population counted between 590 - and 820 thousand individuals of each sex in the age group 20 to 44. On this basis of more than 60 million person-years, a total of 1 235 cases of lung cancer (ICD-7 location code 162) were reported to the Cancer Registry, 761 men and 474 women. We chose to exclude 127 cases of carcinoid tumours from the analyses, mainly because these tumours have a less aggressive growth pattern, which makes the incidence rates susceptible to bias caused by gradual improvements in the

diagnostic procedures. Furthermore, the occurrence of carcinoid tumours are much more evenly distributed according to age than the other lung cancers (data from the Cancer Registry), and consequently they would tend to mask some of the variation that was of special interest for our study. We were left with 1 108 non-carcinoid tumours, 701 in men and 407 in women. The cases were grouped according to five-year age bands and five-year observation periods. The low number of cases in the three youngest age bands made us collapse these into one (20–34 years). The distribution of cases according to sex, age, and period of observation is shown in table 1A.

Incidence rates were computed with data from the Central Population Register. Time trends for age-specific rates were displayed in graphs with 95 percent confidence intervals (6,7). The yearly rates for the whole age group 20–44 were age-adjusted according to the world standard population, displayed in a scatter plot, and smoothed by a locally weighted least-squares curve-fitting method (loess). A span of 0.3 was chosen for the smoothing procedure, which means that for each data point to be fitted the nearest 30% of all observations were used. The loess regressions were prepared by the S-PLUS statistical package (8).

Statistical analysis

Before introducing the birth cohort approach, we wanted to explore the age, period, and cohort effects in an age-period-cohort (APC) modelling, based on the Poisson distribution. Due to low number of cases, the data were organised in the same 3 age bands as described above (20–34, 35–39, 40–44), 11 five-year non-overlapping birth cohorts (1910–1914, ..., 1960–1964), and 9 synthetic (partly overlapping) diagnostic periods. A total of 1054 cases were used for the APC modelling. Estimation and testing were carried out with the statistical program Stata (9).

The model fit was evaluated in terms of deviance and compared with nested models using the chi-square distribution (likelihood-ratio test). When the deviance was close to the degrees of freedom of the model, the fit was considered adequate. A statistical significance level of 0.05 was chosen.

Smoking habits

Data on smoking habits according to birth cohort were obtained from a study by Rønneberg and co-workers based on annual or biannual surveys of smoking habits from 1954 to 1992, performed in large and representative samples of the population, and individual lifetime smoking histories collected in 1965 in a representative sample of people born between 1893 and 1927 (4). These data were supplemented with results from yearly surveys performed by Statistics Norway for the Norwegian Council on Tobacco and Health, covering the last 16 years. Access to unpublished data on the prevalence of pipe smoking and combined pipe and cigarette smoking, which mainly involved men in the oldest birth cohorts, was provided by Tor Haldorsen at the Cancer Registry of Norway.

Since lung cancer is more weakly associated with pipe smoking than with cigarette smoking, possibly due to a lower consumption of tobacco (10-13), we decided to take only cigarette smoking into consideration. We estimated the number of daily cigarette smokers as the sum of smokers of cigarettes only and half the number of combined smokers of pipe and cigarettes, considering smokers of pipe only as non-smokers for the purpose of this study. The cancer rates at age 40 to 44 and the smoking prevalence at different ages within the respective birth cohorts were inspected in graphs and evaluated by correlation analysis.

Results

In men, an increase in the age-specific incidence rate of lung cancer was found in the oldest age group (40–44 years) until 1970, with a levelling off during the last 3 decades (table 1B, figure 1). In women, the oldest age group (40–44 years) showed a pronounced increase throughout the whole observation period. A less marked rise was seen among women aged 35 to 39 until 1980. For the most recent five-year period, the rates for the two oldest age groups were equally high in men and women.

BI

The yearly age-adjusted rates were unstable, but the smoothed curves suggested a downward trend in men during the last 8 years, barely intercepting the rising trend in women in the last year of observation (figure 2).

In men, the full age-period-cohort model did not provide any significantly better fit (deviance = 11.0, degrees of freedom (df) = 7) than the age-period or age-cohort models. Although the latter two models cannot be compared formally, a highly adequate fit was suggested for the age-cohort submodel (deviance = 14.6, df = 14), as opposed to that of the age-period submodel (deviance = 23.5, df = 16), suggesting a more important contribution from the cohort than from the period parameter. In women, the full age-period-cohort model provided a significantly better fit (deviance = 5.6, df = 7) than the age-period or the age-cohort models (deviance = 23.6, df = 16; and deviance = 20.9, df = 14, respectively).

The proportion of cigarette smokers at age 40 to 44 was in the range 36% to 50% for men, and 30% to 39% for women, with a slightly declining trend in men and a more stable one in women. Among teenagers (aged 15 to 19), there was a rise in smoking prevalence. The trend towards taking up smoking at an earlier age was marked among women.

The proportions of smokers within birth cohorts at age 40 to 44 and 15 to 19 were plotted together with the rates of lung cancer at age 40 to 44 (figure 3). Judged by inspection, an association was suggested between the two latter variables, while cancer and smoking at the same age appeared much less correlated.

In the analyses, the lung cancer rates at age 40 to 44 were highly correlated to the teenage smoking prevalence within the corresponding cohorts, with a Pearson correlation coefficient r of 0.88 and 0.82 for men and women, respectively. Similar correlations were found when the cancer rates were compared to smoking prevalence in the early twenties (20 to 24 years) with coefficients of 0.81 and 0.87 in men and women, respectively; p < 0.01 for all r-values.

Discussion

The incidence rate of lung cancer in Norwegian adults under the age of 45 increased from the 1950s, with a levelling off in men around 1970, and a sustained rise in women throughout the study period. The rate in females caught up with that of males in the second half of the 1990s. Cohort specific factors appeared to be important, and a high correlation was found between the cancer incidence at age 40 to 44 and the smoking prevalence when the same individuals were in their teens or early twenties.

The rise of the lung cancer trends started much later in Norway than in UK and the USA, and the problem with underdiagnosis, which was imminent during the first decades of the century, was probably less of a problem after 1950. The smoking data were based on representative and large samples of the population with information collected through standardised telephone interviews or questionnaires (4).

Compared with studies in older age groups, our age-period-cohort modelling was hampered by a low number of cases and only three age-bands of observation for each cohort. Still it was possible to recognise a pattern with an important contribution from the cohort parameter, and to obtain a quite satisfactory fit from the age-cohort models. The data suggested that the proportion of long-term smokers who began early in life was predictive of the lung cancer risk in young adulthood.

Correlation analysis represent a simple way of describing the association between cancer and the proportion of teenage smokers, but the inferences that can be made from such an ecological study are limited. The relationship between smoking and lung cancer has been described in a large number of cohort and case-control studies, and in 1982, Day and Charnay suggested that lung cancer incidence may reflect the number of cigarettes that a cohort becomes addicted to early in life (14). Such a pattern was recently recognised in a German study when lung cancer at all ages was included (15).

Case-control studies from Europe have identified smoking as an important risk factor

MBI

This interpretation does, however, depend upon the assumption that the teenage smokers were the same people as those who were smoking in their forties. Indeed, the tendency among smokers to continue their habit is well documented, as are the addictive properties of nicotine. These characteristics have made it possible to conduct meaningful prospective epidemiological lung cancer studies even on the basis of single cross-sectional smoking surveys (11).

The average amount of tobacco smoked by each smoker has been increasing from about 8.5 g per day in men and 6 g per day in women in the period 1930–1950, until the year 1985 when 15 g and 12 g per day were smoked by men and women, respectively (4). The rise in consumption may therefore explain part of the lung cancer trends. Whether or not there is an additional separate effect from age at onset of smoking early in life, independent of duration, has been a topic for discussion (20,21). A separate effect may exist (22), but it is probably not of the same order of magnitude as that of duration.

We disregarded pipe smoking, which may have had a minor effect on the risk in the oldest male cohorts. The consumption of other types of tobacco has been negligible, especially in women. We find it reasonable to conclude that duration of smoking, remained the strongest candidate to explain the changes in rates during the study period, with as much as a sevenfold rise among 40- to 44-year-old women.

Occupational exposures have been shown to be important for lung cancer risk in men younger than 46 years (3). In our study, we had no access to information on occupational histories, but the effect from workplace exposures was considered negligible in women (23). The observed low rates in females during the 1950s and early –60s may therefore be regarded as a baseline occurrence of lung cancer, minimally affected by smoking and occupation, and illustrating the potential for prevention in young adulthood, even among men.

The sex ratio of lung cancer mortality in adults below age 45 has been reported to be close to 1 in Norway, Denmark, Sweden, and the Netherlands (24). In Sweden, lung cancer mortality in young women passed that of men during the 1990s (25). In Tasmania, the incidence rate has been reported to be at the same level among young females and males (26,27). Norwegian 5-year mortality data from Statistics Norway were recently evaluated and the lung cancer rate among women passed that of men (28). This finding was, however, based on the most recent two-year observation period, and may turn out to be a random fluctuation.

The Norwegian population is rather small with its 4.5 million by January 2002, but the completeness of the data and the ethnic homogeneity strengthen our study. Since the early 1960s the unique 11 digit personal identity numbers have secured a high quality of the population register and facilitated cancer registration.

The exclusion of carcinoid tumours, which constituted 10% of all lung tumours in 20-to 44-year-olds, probably enhanced the demonstration of an association between smoking and lung cancer. The age distribution of this tumour form, found in the registry data, suggested that the carcinoid tumours do not have the same close relation to smoking habits as do other lung tumours.

Conclusion

The time trends in lung cancer incidence at young age belong to a full description of this man-made epidemic and have particular relevance for prevention purposes. During the last 45 years, there has been an alarming rise in the lung cancer rate among Norwegian females under 45, continuing through the 1990s. The rate now equals that of men, and in the absence of marked changes in smoking habits one would expect an

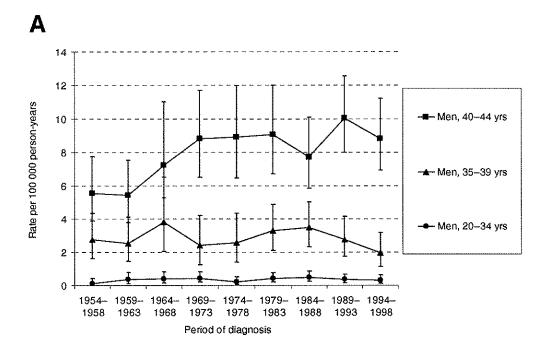
equally high rate in both sexes even at an older and more cancer-prone age. The finding of a high correlation between lung cancer incidence at age 40 to 44 and the proportion of smokers when these people were in their teens is in agreement with earlier findings that duration of smoking, and hence the age at onset, is important.

Reference List

- 1. Doll R. Progress against cancer: an epidemiologic assessment. The 1991 John C. Cassel Memorial Lecture. *Am J Epidemiol* 1991; **134** (7): 675-88.
- 2. International Agency for Research on Cancer. Tobacco Smoking. Lyon: IARC, 1986: 1-421. *IARC Monogr Eval Carcinogenic Risks Hum*, Vol 38.
- 3. Kreuzer M, Kreienbrock L, Gerken M, Heinrich J, Bruske-Hohlfeld I, Muller KM et al. Risk factors for lung cancer in young adults. *Am J Epidemiol* 1998; **147** (11): 1028-37.
- 4. Rønneberg A, Lund KE, Hafstad A. Lifetime smoking habits among Norwegian men and women born between 1890 and 1974. *Int J Epidemiol* 1994; **23** (2): 267-76.
- Association of Nordic Cancer Registries. Survey of Nordic Cancer Registries. World Wide Web URL: http://www.cancer.dk/ANCR/report.pdf, 7-18. 2001. Copenhagen, Denmark: Danish Cancer Society.
- Haenszel W, Loveland DB, Sirken MG. Lung-Cancer Mortality as Related to Residence and Smoking Histories. I. White Males. *J Natl Cancer Inst* 1962; 947-1001.
- 7. dos Santos Silva I. Cancer Epidemiology: Principles and Methods. Second ed. Lyon, France: International Agency for Reserarch on Cancer, 1999.
- 8. Insightful Corporation. S-Plus 2000 Professional Release 2. Seattle, WA: Insightful Corporation, 1999.
- 9. StataCorp. Stata Statistical Software: Release 7.0. College Station, TX: Stata Corporaion, 2001.
- 10. Lubin JH, Richter BS, Blot WJ. Lung cancer risk with cigar and pipe use. *J Natl Cancer Inst* 1984; **73** (2): 377-81.

- 11. Engeland A, Haldorsen T, Andersen A, Tretli S. The impact of smoking habits on lung cancer risk: 28 years' observation of 26,000 Norwegian men and women. Cancer Causes Control 1996; 7 (3): 366-76.
- 12. Boffetta P, Pershagen G, Jockel KH, Forastiere F, Gaborieau V, Heinrich J et al. Cigar and pipe smoking and lung cancer risk: a multicenter study from Europe. *J Natl Cancer Inst* 1999; **91** (8): 697-701.
- 13. Engeland A. Trends in the incidence of smoking-associated cancers in Norway, 1954-93. *Int J Cancer* 1996; **68** (1): 39-46.
- 14. Day NE, Charnay B. Time trends, cohort effects, and aging as influence on cancer incidence. In: Magnus K, editor. *Trends in cancer incidence*. London: Hemisphere Publishing Corporation, 1982: 51-65.
- 15. Knorr-Held L, Rainer E. Projections of lung cancer mortality in West Germany: a case study in Bayesian prediction. *Biostatistics* 2001; **2** (1): 109-29.
- 16. Boffetta P, Kreuzer M, Benhamou S, Agudo A, Wichmann HE, Gaborieau V et al. Risk of lung cancer from tobacco smoking among young women from Europe. *Int J Cancer* 2001; **91** (5): 745-6.
- 17. Jemal A, Chu KC, Tarone RE. Recent trends in lung cancer mortality in the United States. *J Natl Cancer Inst* 2001; **93** (4): 277-83.
- 18. Doll R, Peto R. Cigarette smoking and bronchial carcinoma: dose and time relationships among regular smokers and lifelong non-smokers. *J Epidemiol Community Health* 1978; **32** (4): 303-13.
- 19. Haldorsen T, Grimsrud TK. Cohort analysis of cigarette smoking and lung cancer incidence among Norwegian women. *Int J Epidemiol* 1999; **28** (6): 1032-6.
- 20. Hegmann KT, Fraser AM, Keaney RP, Moser SE, Nilasena DS, Sedlars M et al. The effect of age at smoking initiation on lung cancer risk. *Epidemiology* 1993; 4 (5): 444-8.
- 21. Benhamou S, Benhamou E. The effect of age at smoking initiation on lung cancer risk. *Epidemiology* 1994; **5** (5): 560.

- 22. Wiencke JK, Thurston SW, Kelsey KT, Varkonyi A, Wain JC, Mark EJ et al. Early age at smoking initiation and tobacco carcinogen DNA damage in the lung. *J Natl Cancer Inst* 1999; **91** (7): 614-9.
- 23. Dreyer L, Andersen A, Pukkala E. Avoidable cancers in the Nordic countries. Occupation. *APMIS Suppl* 1997; **76**: 68-79.
- 24. Levi F, La Vecchia C, Lucchini F, Negri E. Trends in cancer mortality sex ratios in Europe, 1950-1989. *World Health Stat Q* 1992; **45** (1): 117-64.
- 25. Wramner B, Zatonski W, Pellmer K. Premature mortality in lung cancer as an indicator of effectiveness of tobacco use prevention in a gender perspective—a comparison between Poland and Sweden. *Cent Eur J Public Health* 2001; **9** (2): 69-73.
- 26. Dwyer T, Blizzard L, Shugg D, Hill D, Ansari MZ. Higher lung cancer rates in young women than young men: Tasmania, 1983 to 1992. *Cancer Causes Control* 1994; **5** (4): 351-8.
- 27. Blizzard L, Dwyer T. Case-control study of lung cancer during 1994-1997 in the birth cohort in Tasmania, Australia, with an excess of female cases during 1983-1992. *Cancer Causes Control* 2003; **14** (2): 123-9.
- 28. Tverdal A. Dødelighet av lungekreft--nå høyere hos kvinner enn hos menn under 50 år [Lung cancer mortality--now higher in women than in men under 50 years]. *Tidsskr Nor Lægeforen* 2001; **121** (21): 2487-8.



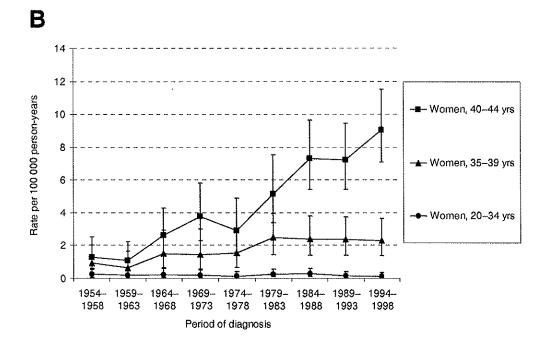


Figure 1 Age-specific incidence rates of lung cancer, exclusive of carcinoid tumours, in young Norwegian men (Panel A) and women (Panel B) by period of diagnosis. The vertical bars represent 95% confidence intervals.

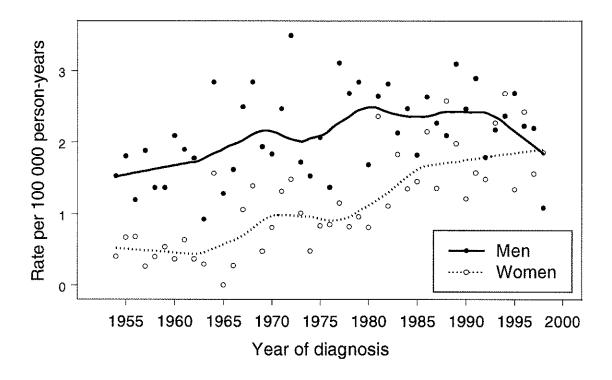
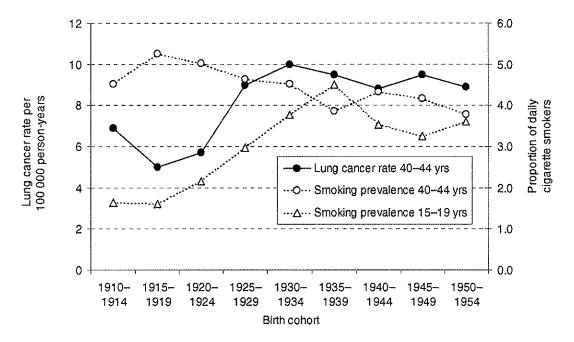


Figure 2 Age-adjusted incidence rates of lung cancer, exclusive of carcinoid tumours, in young Norwegian adults aged 20 to 44 by year of diagnosis. The yearly rates were age-adjusted according to the world standard population and displayed in a scatter plot (circles), and subsequently smoothed (lines) by a locally weighted least-squares curvefitting method (loess). The weighting of the regression was based on a span of 0.3, *i.e.* a proportion of 30% of all the observations (those lying closest to the data point to be fitted).





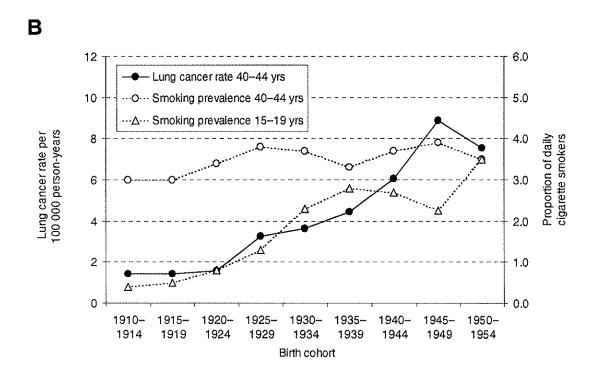


Figure 3 Observed lung cancer rates and prevalence of cigarette smoking among Norwegian men (Panel A) and women (Panel B), according to age and birth cohort. The lung cancer rates are given on the left Y-axis, and the smoking prevalences on the right Y-axis.

Table 1 A Distribution of 1108 cases of lung cancer, exclusive of carcinoid tumours, among Norwegian adults aged 20 to 44 by sex, age, and period of diagnosis.

	and a separate supplementaries					Period	Period of diagnosis				
Sex	Age	19541958	19541958 19591963 19641968	1964–1968	1969–1973	1969-1973 1974-1978 1979-1983	19791983	1984–1988 1989–1993	1989–1993	1994–1998	1954–1998
Men	2034 yrs	2	မ	7	Ø	ഗ	10	12	6	బ	89
	35-39 yrs	\$	16	21	12	14	24	28	52	16	171
	40-44 yrs	35	35	45	48	44	49	26	80	70	462
Sur	Sum 20-44 yrs	55	57	73	69	63	83	8	=	24	701
Women	2034 yrs	4	ო	4	4	ღ	9	7	4	ဇ	38
	35~39 yrs	9	4	æ	7	۵	17	18	18	18	104
	40-44 yrs	œ	7	16	20	4	27	50	54	69	265
Sum	Sum 20-44 yrs	18	14	28	31	25	20	75	92	06	407

Table 1 B Incidence rates of lung cancer among Norwegian adults aged 20 to 44 by sex, age, and period of diagnosis, carcinoid tumours excluded, rates given per 100 000 person—years with 95 percent confidence intervals in parentheses

					Apriliate middless made	Period of diagnosis	nosis			
Sex	Age	1954–1958	19591963	1964–1968	1969–1973	1974–1978	1979–1983	19841988	1989–1993	1994–1998
Men	20-34 yrs	0.12 (0.01–0.42)	0.12 0.37 (0.01–0.42) (0.14–0.80)	0.40	0.20-0.83)	0.22 (0.07–0.51)	0.20-0.77)	0.49 (0.25–0.86)	0.36	0.32
	35–39 yrs	2.75 (1.63–4.35)	2.55 (1.46–4.13)	3.82 (2.03-6.53)	2.42 (1.25–4.23)	2.58 (1.41–4.33)	3.30 (2.12–4.89)	3.49 (2.32–5.06)	2.76 (1.73–4.17)	1.96 (1.12–3.17)
	40-44 yrs	5.58 (3.89–7.75)	5.43 (3.78–7.55)	7.25 (5.29–11.0)	8.83 (6.50–11.7)	8.91 (6.47–12.0)	9.08 (6.72–12.0)	7.73 (5.87–10.1)	10.1 (8.02–12.6)	8.83 (6.93–11.2)
Women	2034 yrs	0.24 (0.07–0.61)	0.19	0.24 (0.06–0.61)	0.21	0.14	0.27	0.30	0.17	0.13 (0.03-0.37)
	35–39 yrs	0.93	0.65 (0.18–1.67)	1.50 (0.65~2.96)	1.45 (0.58–2.99)	1.53 (0.66–3.01)	2.49 (1.45–3.98)	2.40 (1.42–3.79)	2.37	2.30 (1.37~3.64)
	40-44 yrs	1.29 (0.55–2.53)	1.09 (0.44–2.25)	2.64 (1.51–4.27)	3.77 (2.31–5.81)	2.91 (1.59–4.88)	5.16 (3.40–7.53)	7.32 (5.43–9.66)	7.21 (5.43–9.46)	9.05 (7.0 9 –11.5)