

Regular Article

Background Radiation and Cancer Excluding Leukemia in Kerala, India –Karunagappally Cohort Study

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The coastal belt of Karunagappally, Kerala, India is known for high natural background radiation (HNBR) from thorium-containing monazite sand. A cohort of all residents in Karunagappally was established in the 1990s to evaluate the health effects of HNBR. Following the cohort of 149,585 residents aged 30–84 for 19.1 years on average, approximately 2,851,688 person-years of observation were accumulated. The cumulative radiation dose for each individual was estimated based on outdoor and indoor dosimetry of each household, taking into account sex- and age-specific house occupancy factors. Using Karunagappally cancer registry, 6,804 cancer cases excluding leukemia were identified by the end of 2017. Poisson regression analysis of cohort data stratified by sex, attained age, follow-up periods and the original/additional subcohorts estimated an excess relative risk of cancer excluding leukemia as -0.05 Gy^{-1} (95% CI: $-0.33, 0.29$) when adjusted for education, bidi smoking, tobacco chewing, and alcohol drinking in a statistical model. In site-specific analyses, no cancer site was significantly related to cumulative radiation dose. Leukemia was not significantly related to HNBR, either.

Key words: cancer incidence, natural radiation, risk analysis, radiation protection

1. Introduction

A cancer incidence study of the Karunagappally cohort, which consists of residents in a high natural background radiation (HNBR) area along the coastal belt of Kerala, India during the period between 1990 and 2005 showed no excess cancer risk in the area¹. In that study, the analysis was limited to the cohort members in 6 panchayats in the

taluk since the database for the remaining 6 panchayats were not completed. In the present study, the cohort was expanded to the residents in the entire taluk, and the follow-up period was extended by 12 years. Herein we report the cancer incidence in relation to the cumulative dose of natural background radiation in Karunagappally taluk during 1990–2017.

2. Materials and Methods

Base-line survey

A base-line survey was conducted to measure indoor and outdoor radiation levels and collect socio-demographic

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details, lifestyle, including dietary habits, and tobacco and alcohol use covering a population of 385,103 (191,149 males and 193,954 females) in 76,773 households. This survey yielded information on 359,619 subjects in 71,674 households, which accounts for 93% of population and 94% of households¹⁻³. In total, this household survey collected personal information on study population.

Study population

Since the data input and editing for the entire cohort were considered to take a lot of time, in the previous analysis, it was decided to select four coastal panchayats of Chavara, Neendakara, Panmana and Alappad, which had high natural background radiation, and two control areas (panchayats), Oachira and Thevalakkara, which had relatively low natural radiation levels¹. This cohort will be called the original subcohort in this report. In the present study, the data for the entire cohort were used for risk analysis. The newly added cohort will be referred to as the additional subcohort in this report. Therefore, the full cohort consists of the original and additional subcohorts. In the present risk analysis, as was the case in the previous analysis, it was decided to analyze those aged 30-84.

Outdoor and indoor dosimetry

The individual radiation dose was estimated from the HNBR based on outdoor and indoor doses and sex- and age-specific occupancy factors. The radiation levels (air kerma: mGy y⁻¹) used in the cancer risk analysis were obtained by converting the scintillometer based annual dose to TLD equivalent annual dose by multiplying with the 0.97¹.

House occupancy factor

In each ward, 2% of all houses were randomly selected and information on occupancy factor on 7,711 residents (3783 males and 3928 females) in all age groups living in the selected houses was collected. The house occupancy factor varies from 0.5 to 0.89 depending on sex and age¹.

Migration

Door-to-door surveys of all the households conducted in 2001 and 2010 collected information on the extent of migration. Migration to outside the taluk was approximately 6% in the migration survey. The majority of migration took place for job opportunities in Gulf countries. Approximately 1% was lost to follow-up. This information on migration was taken into account when estimating the cumulative dose of the individuals in the cohort in the following manner: When migration occurred into Karunagappally taluk, the mean outside and inside radiation doses of Oachira panchayat (a control area) were assigned to the ages of the immigrants before

migration. When a subject moved within Karunagappally taluk, the average outdoor dose of the ward in which the house was located and the average indoor dose of all the houses in the same ward was assigned. If the ward was not known, the mean outdoor dose of the panchayat was given¹.

Individual dose estimation

Assuming the air kerma values for the cosmic ray component of the measured radiation level to be 0.227 mGy y⁻¹ for indoor and 0.252 mGy y⁻¹ for outdoor^{1, 4-6}, the annual absorbed dose for each individual was calculated using the formula:

$$\begin{aligned} \text{Annual dose (mGy)} \\ &= \{[\text{Indoor dose y}^{-1} - 0.227] \times \text{OF}_{\text{indoor}} \\ &+ [\text{outdoor dose y}^{-1} (\text{mean}) \text{ of ward or panchayat} - 0.252] \times \\ &\text{OF}_{\text{outdoor}}\} \times \text{CF}, \end{aligned}$$

where OF is Occupancy factor based on sex and age ranging from 0.5 to 0.89¹ and CF is the conversion factor for air kerma to organ-specific absorbed dose presented in ICRP 116 report⁷. The CFs of ²³²Th used for men and women in the present study were 0.785 and 0.813, respectively, for the colon. The CFs of children aged 1-14 years and infants aged less than 1 year were increased by 10% and 30%, respectively. Colon dose was used for risk analysis since Life-Span study reports of cancer risk analysis of atomic bomb survivors used it⁸. The cosmic ray component was subtracted from the measured dose in order to estimate the radiation dose from terrestrial radiation exposure. The individual cumulative dose was calculated by adding up the annual effective dose in a time-dependent manner, using EPICURE software⁹. The internal dose consisting of ingested and inhaled radionuclides was not considered for the cumulative dose estimation.

Cancer case ascertainment

Cancer cases among the cohort were ascertained by the cancer registry in Karunagappally as described in an earlier paper¹.

Statistical analysis

Statistical analysis was based on the data in cross-classifications by sex, attained age (5-year category), follow-up interval (1990-1996, 1997-2003, 2004-2010, 2011-2017), and other covariates, which are shown in the footnotes of each table. The categories of covariates are those shown in Table 1. Migration surveys were conducted in 2001 and in 2010. Person-years and number of cancer cases were calculated by DATAB procedure of EPICURE program. Poisson regression analysis of grouped survival data (Breslow and Day 1987) was conducted, using the AMFIT module of EPICURE software⁹.

Table 1. Socio-demographic features of study population and cases of cancer excluding leukemia

	men				women			
	N (%)	cases	RR	95%CI	N (%)	cases	RR	95%CI
Religion								
Hindu	49,768	2,745	1	reference	58,227	2,192	1	reference
Muslim	12,276	697	1.0	0.95 - 1.1	15,799	548	0.95	0.87 - 1.0
Christian	6,290	331	0.93	0.83 - 1.0	7,225	291	1.1	0.95 - 1.2
	P for heterogeneity=0.257				P for heterogeneity=0.242			
Education								
Illiterate	4,483	297	1	reference	14,452	537	1	reference
Primary	18,015	1,202	1.0	0.92 - 1.2	23,253	888	1.0	0.91 - 1.1
Middle	18,093	1,085	1.0	0.89 - 1.2	19,290	747	1.1	0.95 - 1.2
High	21,183	912	0.79	0.67 - 0.90	19,564	702	1.1	0.95 - 1.2
College	5,808	238	0.76	0.64 - 0.91	4,186	139	1.1	0.91 - 1.3
Unknown	752	39	0.83	0.59 - 1.2	506	18	1.0	0.65-1.7
	P for heterogeneity < 0.001				P for heterogeneity > 0.5			

*RRs for each variable were obtained from the following model: H_0 (attained age, follow-up interval, subcohort membership) $[\exp(\sum \beta_i X_i)]$, where R_s are dummy variables representing categories of each variable. RRs and 95% CIs are expressed in two effective digits. All the P values presented are two sided.

Assuming a linear dose-response, the excess relative risk (ERR) of all cancer excluding leukemia in relation to cumulative dose 10 years prior to the time at risk was also estimated using the following model;

H_0 (sex, attained age, follow-up interval, original/additional sub-cohorts) $[1 + \beta D]$, where D is cumulative organ specific absorbed radiation dose calculated in a time-dependent manner, and β , the regression coefficient of D, describes the relative change in rates associated with the dose. H_0 is the baseline cancer rate.

For adjusting for life-style related factors and socioeconomic factors, the following model was used; H_0 (sex, attained age, follow-up interval, original/additional sub-cohorts) $[\exp(\sum \gamma_i X_i)] [1 + \beta D]$, where X_i are covariables such as education, bidi smoking, tobacco chewing and/or; alcohol drinking; and γ_i are their regression coefficients.

The modifying effect of sex, age or other factors on ERR was examined by replacing $[1 + \beta D]$ with $[1 + \beta D \exp(\delta X)]$, where X is the modifying factor and δ is its coefficient corresponding to the magnitude of modification.

In the analysis to estimate relative risks (RRs) for different cumulative radiation dose categories, the following model was used;

H_0 (sex, attained age, follow-up interval, original/additional sub-cohorts) $[\exp(\beta_1 D_1 + \beta_2 D_2 + \beta_3 D_3 + \beta_4 D_4 + \beta_5 D_5)]$. The estimates of β_1 , β_2 , β_3 , β_4 and β_5 correspond to log RRs for dose categories (mGy) of 50-, 100-, 200-, 300- and 500+, respectively. The dose category 0-49 mGy was the reference category. In Tables 3 and 4, risk analysis used lagged cumulative dose, which was calculated in a time-dependent manner. To allow for a

possible latent period between radiation exposure and its consequences, cumulative doses were lagged by 10 years for all cancer except leukemia¹⁰. With a lag of 10 years, a dose was included in the calculation of the cumulative dose at time t if it had been received at or before time $t-10$ year. A similar approach was used to estimate relative RRs for different environmental dose categories.

The entry into the cohort was the date of interview, which ranged from 1 January 1990 to 31 December 1997. The end of follow-up was the date of diagnosis of cancer cases, the date of death for those deceased, the date of migration out of the study area, the end of follow-up (31 December 2017) or the date attaining the age of 85, whichever occurred first. In person-year calculation, migrations that had taken place and identified by the migration surveys in 2001 and 2010 were taken into account. The migration, being very low, was ignored for the period after the survey.

3. Results

The present study examined 149,585 residents (68,334 men and 81,251 women) who were 30-84 years old at the time of interview. The original and additional subcohort members numbered 69,958 and 79,627, respectively. By the end of 2017, 2,458,250 person-years of observation were accumulated. During the follow-up, 6,804 cases of cancer excluding leukemia (3,773 males and 3,031 females), and 135 leukemia cases were ascertained. Diagnosis of cancer was based on histopathology or cytology in 78% of the cases, and 6% of the cancer cases were ascertained from the Vital Statistics Division based on death certificate information. The rest was based

Table 2. Tobacco use and alcohol drinking of study population and cases of cancer excluding leukemia

	men				women			
	N (%)	cases	RR	95%CI	N (%)	cases	RR	95%CI
Bidi smoking (the number of bidis smoked per day)								
Never	32,062	1,260	1	reference	79,751	2,973	1	reference
Ex-smoker	6,531	379	1.3	1.2 - 1.5	376	11	0.92	0.51 - 1.7
Current smokers								
1-4/day	3,081	141	1.2	0.97 - 1.4	593	23	1.1	0.74 - 1.7
5-14/day	10,155	641	1.6	1.4 - 1.7	351	18	1.4	0.90 - 2.3
15-24/day	8,060	652	1.9	1.7 - 2.1	66	2	0.81	0.20 - 3.3
25+/day	5,108	493	2.1	1.9 - 2.4	19	1	1.2	0.17 - 8.4
Unknown	3,337	207	1.6	1.4 - 1.9	95	3	1.1	0.36 - 3.5
	P for heterogeneity < 0.001				P for heterogeneity > 0.5			
Tobacco chewing								
Never	43,926	2,257	1	reference	60,677	2,170	1	reference
Ex-chewer	4,825	351	1.2	1.1 - 1.4	2,873	118	1.2	0.99 - 1.4
Current								
1-years	12,134	713	1.1	1.0 - 1.2	8,999	388	1.1	0.99 - 1.2
15-years	5,512	350	1.1	0.97 - 1.2	7,473	298	1.0	0.90 - 1.2
30-years	677	40	0.98	0.72 - 1.3	726	41	1.5	1.1 - 2.0
45+years	126	10	1.3	0.70 - 2.4	95	5	1.3	0.54 - 3.1
Unknown	1,134	52	0.97	0.73 - 1.3	408	11	0.74	0.41 - 1.3
	P for heterogeneity = 0.002				P for heterogeneity = 0.051			
Alcohol drinking								
Never	34,760	1,682	1	reference	81,185	3,024	1	reference
Ex-drinker	8,607	558	1.2	1.1 - 1.4	32	1	1.1	0.16 - 8.1
Current								
-70mg/day*	9,412	500	1.2	1.0 - 1.3	17	4	7.5	2.8 = 20
70 + mg/day	13,294	883	1.3	1.2 - 1.4	17	2	3.4	0.84 = 13
Unknown	2,261	150	1.4	1.1 - 1.7	0	0		
	P for heterogeneity < 0.001				P for heterogeneity = 0.011			

*RRs for each variable were obtained from the following model: H_0 (attained age, follow-up interval, subcohort membership) $[\exp(\sum \beta_i X_i)]$, where R_s are dummy variables representing categories of each variable.

RRs and 95% CIs are expressed in two effective digits.

All the P values presented are two sided.

* <70mg of alcohol consumed a day

on clinical observation and investigations like special biochemical and immunological tests. The five most common cancers among men were cancers of the lung (833 cases), oropharynx (623 cases), stomach (233 cases), esophagus (218 cases), and larynx (160 cases). Among women, these were cancers of the breast (705 cases), uterus (432 cases), oropharynx (307 cases), thyroid (137 cases), lung (140 cases) and esophagus (111 cases). There were 276 and 196 cases of unknown primary cancer sites for men and women, respectively.

Tables 1 and 2 present relative risks (RR) of religion, education, and lifestyles of study subjects, which were considered to be potential confounders in our preliminary analysis of radiation related cancer risk. Occupation or annual income was not a strong enough confounder once education was adjusted for.

Table 3 summarizes the risk analysis of cancer excluding leukemia, using Poisson regression models. In all the analysis, data were stratified by sex, attained age,

and follow-up periods. For full cohort, the ERR estimate is obtained from analysis with stratification for original/additional sub-cohorts. Adjustment for education, bidi smoking, tobacco chewing and alcohol and drinking gave an ERR estimate of -0.05 Gy^{-1} (95% CI: $-0.33, 0.29$; $P > 0.5$). For men and women, ERR estimates per gray were -0.20 (95% CI = $-0.52, 0.20$; $P = 0.307$) and 0.24 (95% CI = $-0.27, 0.89$; $P = 0.386$), respectively. The sex difference was not statistically significant ($P = 0.154$).

Table 4 shows the results of risk analysis using the annual environmental dose of each house, which is the sum of (0.7 x annual indoor dose) and (0.3 x annual outdoor dose) of each house at the time of household dosimetry survey conducted during the period 1990-1997. The risk of cancer excluding leukemia was not related to annual environmental dose in any groups of attained age.

Table 5 presents dose category-specific RRs. No evident heterogeneity of RRs among dose groups was observed. This table also presents sex-specific RRs. No evident sex

Table 3. ERR estimates per 1 gray for cancer other than leukemia

Cohort	cases	person years
Full cohort, stratified*	6,804	2,851,688
original subcohort	3,213	1,325,425
additional subcohort	3,591	1,526,263
	ERR/Gy	95%CI
Full cohort, stratified*	0.12	-0.19, 0.48
Original subcohort	0.17	-0.17, 0.57
Additional subcohort	-0.29	nd(-1.16), 0.75
analysis adjusted for education		
Full cohort, stratified	0.06	-0.24, 0.41
Original cohort	0.10	-0.22, 0.49
Additional cohort	-0.33	nd(-1.19), 0.70
analysis adjusted for bidi smoking (numbers of bidi smoked a day)		
Full cohort, stratified*	-0.01	-0.30, 0.33
Original subcohort	0.02	-0.29, 0.38
Additional subcohort	-0.28	nd(-1.14), 0.76
analysis adjusted for tobacco chewing (numbers of chewed tobacco used a day)		
Full cohort, stratified*	0.15	-0.17, 0.52
Original subcohort	0.20	-0.15, 0.60
Additional subcohort	-0.22	nd(-1.11), 0.84
analysis adjusted for alcohol drinking (amount of alcohol consumed a day)		
Full cohort, stratified*	0.007	-0.29, 0.35
Original subcohort	-0.03	-0.28, 0.41
Additional subcohort	-0.33	nd(-1.19), 0.69
analysis adjusted for education, bidi smoking, tobacco chewing, and alcohol drinking		
Full cohort, stratified*	-0.05	-0.33, 0.29
Original subcohort	-0.05	-0.35, 0.31
Additional subcohort	-0.28	nd(-1.14), 0.6

ERRs were obtained from the following statistical model: H_0 (sex, attained age, follow-up interval) $[\exp(\sum \gamma_i X_i)] [1 + \beta D]$

*The analysis was stratified by sub-cohorts (original/additional cohorts), using the following model: H_0 (sex, attained age, follow-up interval, subcohort membership) $[\exp(\sum \gamma_i X_i)] [1 + \beta D]$

ERRs are expressed to the second decimal place.

difference was observed.

Table 6 summarizes the results of analysis which used childhood dose (radiation doses exposed during ages 0-14). No excess risk was observed. ERRs per gray for all the subjects, men and women were -0.35 (95%CI = -1.28, 0.72; P = 0.491), -0.58 (95% = -1.68, 0.77; P = 0.372), 0.03 (95%CI = -1.49, 1.87; P > 0.5), respectively.

4. Discussion

Poisson regression analysis of Karunagappally cohort data stratified by sex, attained age and follow-up periods

and subcohort membership gave an excess relative risk of cancer excluding leukemia as -0.09 Gy^{-1} (95%CI: -0.37, 0.23) when adjusted for education, bidi smoking, tobacco chewing, and alcohol drinking. Leukemia was not significantly related to HNBR, either. Cigarette smoking was not taken into account since its users in the study area were small in number as already reported¹⁾.

As discussed in our previous paper¹⁾ there are several limitations in this study. One is the uncertainties regarding individual dose estimation due to the lack of occupancy factors over a lifetime, and possible changes of indoor and outdoor doses. In the present study, as was the case in the previous study, if the study subjects were from outside the taluk, an average indoor and outdoor doses in Kerala state were used for the period when they lived outside the taluk. Information on individual medical exposure was not available, either. Note, however, that its annual per caput dose from medical and dental X ray examinations is only 0.15mSv in India¹¹⁾. The data for the Kerala state is not available.

DDREF (Dose and Dose Rate Effectiveness Factor) is one of the biggest concerns in radiation protection¹²⁾. In recent years, the Low Dose Effectiveness Factor and Dose-Rate Effectiveness Factor have been considered to be treated separately¹³⁾, and the effects of low dose rates are of particular concern. In UNSCEAR 2017¹⁴⁾, the Karunagappally cohort study in Kerala, India and the Techa River cohort study in Russia were reviewed as particularly important studies in assessing the risk of cancer from low dose rate exposure. However, it was concluded that more studies are needed to draw clear conclusions about the low dose rate effect.

The analysis of the entire cohort with the follow-up extended by 12 years gave essentially the same ERR estimate per radiation dose (ERR = -0.05 Gy^{-1} ; 95%CI = -0.33, 0.29) as the one in the previous study (ERR = -0.13 Gy^{-1} ; 95%CI = -0.58, 0.46). However, the confidence interval obtained from the present study is much narrower than that in the previous study, suggesting a possibility that the solid cancer risk associated with the continuous exposure to low-dose rate radiation is significantly lower than that associated with acute exposure. However, such a comparison requires matching of age at exposure since the magnitude of radiation associated RRs are known to be dependent on age at exposure.

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Table 4. Risk of all cancers excluding leukemia according to household dose rate

		Environmental radiation dose (mGy year ⁻¹)				
		0-	1-	2-	5-	10-
	mean dose (mGy)	0.8	1.4	3.0	6.6	14.6
	SD	0.1	0.2	0.6	1.1	4.7
Attained age						
Total	Case	835	3,028	2,349	451	141
	Person-years	367,012	1,272,810	967,898	187,313	56,655
	RR	1	1.05	1.05	1.00	1.01
	95%CI	reference	0.97 - 1.13	0.97 - 1.13	0.89 - 1.12	0.84 - 1.21
	P for trend > 0.5					
30-	Case	116	363	261	49	13
	Person-years	123,864	422,096	315,208	62,526	19,101
	RR	1	0.91	0.90	0.87	0.75
	95%CI	reference	0.74 - 1.12	0.72 - 1.12	0.62 - 1.23	0.42 - 1.34
	P for trend = 0.300					
50-	Case	495	1,844	1,422	270	83
	Person-years	186,542	653,785	495,001	95,494	28,655
	RR	1	1.07	1.08	1.01	1.02
	95%CI	reference	0.97 - 1.18	0.97 - 1.20	0.87 - 1.18	0.81 - 1.29
	P for trend > 0.5					
70-	Case	224	821	666	132	45
	Person-years	56,605	196,929	157,690	29,294	8,899
	RR	1	1.08	1.06	1.03	1.11
	95%CI	reference	0.93 - 1.25	0.91 - 1.24	0.82 - 1.28	0.81 - 1.54
	P for trend > 0.5					

RRs were obtained from the following model:

H_0 (sex, attained age, follow-up interval, bidi smoking, education, occupation) $[\exp(\beta_1 D_1 + \beta_2 D_2 + \beta_3 D_3 + \beta_4 D_4)]$. The estimates of β_1 , β_2 , β_3 , and β_4 correspond to log RRs for dose categories, 1-, 2-, 5-, and 10+ mGy year⁻¹, respectively. The dose category 0-1 mGy year⁻¹ was the reference category.

Table 5. Cumulative-dose-category specific relative risk of cancer excluding leukemia

		Cumulative radiation dose (mGy)					
		0-	50-	100-	200-	300-	500-
Mean dose		40	72	135	237	370	617
SD		7	13	24	26	53	120
Total							
cancer cases*		1,018	2,954	2,160	420	198	54
Person-years		681,463	1,250,960	710,542	138,197	56,854	13,675
RR**		1	0.97	1.03	0.91	0.98	0.93
95%CI		reference	0.90 - 1.04	0.95 - 1.12	0.81 - 1.03	0.84 - 1.16	0.70 - 1.22
	P for heterogeneity=0.139						
Male							
cancer cases		546	1,579	1,246	244	124	34
Person-years		302,948	536,406	321,811	63,970	28,239	6,832
RR		1	0.93	0.98	0.85	0.93	0.83
95%CI		reference	0.84 - 1.03	0.88 - 1.09	0.72 - 0.996	0.76 - 1.15	0.58 - 1.18
	P for heterogeneity=0.210						
Female							
cancer cases		472	1,375	914	176	74	20
Person-years		378,515	714,551	388,731	74,227	28,614	6,843
RR		1	1.02	1.10	1.00	1.05	1.11
95%CI		reference	0.91 - 1.14	0.97 - 1.24	0.83 - 1.20	0.81 - 1.35	0.70 - 1.74
	P for heterogeneity>0.5						

**RRs and 95%CI were obtained from the following model:

H_0 (sex, attained age, follow-up interval, subcohort membership) $\times [\exp(\text{education} + \text{bidi smoking} + \text{tobacco chewing} + \text{alcohol drinking} + \text{colon dose groups})]$.

Radiation dose is a cumulative colon dose lagged by 10 years. The dose category 0-49 mGy is the reference category.

RRs are expressed to the second decimal place.

All the P values presented are two sided.

Table 6. Childhood-dose-category specific relative risk of cancer excluding leukemia

	Cumulative radiation dose (mGy)				
	0-	20-	50-	100-	150-
Mean dose	16	32	68	122	193
SD	2	8	13	11	45
Total					
cancer cases*	2,772	3,092	775	121	44
Person-years	1,202,682	1,258,129	324,351	49,855	16,670
RR**	1	1.02	0.98	0.90	1.05
95%CI	reference	0.97 - 1.08	0.90 - 1.07	0.75 - 1.09	0.77 - 1.41
	P for heterogeneity>0.5				
Male					
cancer cases	1,427	1,800	444	74	28
Person-years	470,740	603,026	151,135	26,364	8,940
RR	1	1.00	0.97	0.84	1.03
95%CI	reference	0.93 - 1.07	0.87 - 1.09	0.66 - 1.07	0.70 - 2.48
	P for heterogeneity>0.5				
Female					
cancer cases	1,345	1,292	331	47	16
Person-years	731,942	655,103	173,216	23,491	7,730
RR	1	1.05	0.99	1.01	1.07
95%CI	reference	0.98 - 1.14	0.88 - 1.12	0.75 - 1.35	0.65 - 1.75
	P for heterogeneity> 0.5				

**RRs and 95%CI were obtained from the following model:

H_0 (sex, attained age, follow-up interval, subcohort membership) \times [exp (education + bidi smoking + tobacco chewing + alcohol drinking + colon dose groups)].

Radiation dose is a cumulative colon dose lagged by 10 years. The dose category 0-49 mGy is the reference category.

RRs are expressed to the second decimal place.

All the P values presented are two sided.

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