Cancer mortality in India: a nationally representative survey

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Summary

Background **The age-specific mortality rates and total deaths from specific cancers have not been documented for the various regions and subpopulations of India. We therefore assessed the cause of death in 2001–03 in homes in small areas that were chosen to be representative of all the parts of India.**

Methods **At least 130 trained physicians independently assigned causes to 122 429 deaths, which occurred in 1·1 million homes in 6671 small areas that were randomly selected to be representative of all of India, based on a structured non-medical surveyor's field report.**

Findings **7137 of 122 429 study deaths were due to cancer, corresponding to 556 400 national cancer deaths in India in 2010. 395 400 (71%) cancer deaths occurred in people aged 30–69 years (200 100 men and 195 300 women). At 30–69 years, the three most common fatal cancers were oral (including lip and pharynx, 45 800 [22·9%]), stomach (25 200 [12·6%]), and lung (including trachea and larynx, 22 900 [11·4%]) in men, and cervical (33 400 [17·1%]), stomach (27 500 [14·1%]), and breast (19 900 [10·2%]) in women. Tobacco-related cancers represented 42·0% (84 000) of male and 18·3% (35 700) of female cancer deaths and there were twice as many deaths from oral cancers as lung cancers. Age-standardised cancer mortality rates per 100 000 were similar in rural (men 95·6 [99% CI 89·6–101·7] and women 96·6 [90·7–102·6]) and urban areas (men 102·4 [92·7–112·1] and women 91·2 [81·9–100·5]), but varied greatly between the states, and were two times higher in the least educated than in the most educated adults (men, illiterate 106·6 [97·4–115·7] *vs* most educated 45·7 [37·8–53·6]; women, illiterate 106·7 [99·9–113·6] *vs* most educated 43·4 [30·7–56·1]). Cervical cancer was far less common in Muslim than in Hindu women (study deaths 24, age-standardised mortality ratio 0·68 [0·64–0·71] *vs* 340, 1·06 [1·05–1·08]).**

Interpretation **Prevention of tobacco-related and cervical cancers and earlier detection of treatable cancers would reduce cancer deaths in India, particularly in the rural areas that are underserved by cancer services. The substantial variation in cancer rates in India suggests other risk factors or causative agents that remain to be discovered.**

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*Full list of the Million Death Study Collaborators is provided in the appendix p 9

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Introduction

Cancer is one of the leading causes of adult deaths worldwide. In India, the International Agency for Research on Cancer estimated indirectly that about 635 000 people died from cancer in 2008, representing about 8% of all estimated global cancer deaths and about 6% of all deaths in India.[1] The absolute number of cancer deaths in India is projected to increase because of population growth and increasing life expectancy. Rates of cancer deaths are expected to rise, particularly, from increases in the age-specific cancer risks of tobacco smoking, which increase the incidence of several types of cancer.[2] India is a culturally diverse country, with huge regional and rural-to-urban variation in lifestyles and in age-specific adult death rates.[3] Thus, understanding the geographical and social distribution of specific cancers is essential to target cancer control programmes and spur further research into the causes of cancer.

About three-quarters of Indians live in rural areas. Yet, mortality for specific cancers is estimated mostly with data from India's 24 urban population-based cancer registries, with only two registries representing rural areas.[4] Most deaths in India (and in most low-income or middle-income countries) occur at home and without medical attention.[3] Thus, alternative methods to obtain information about cancer and other deaths are necessary. Here, we assess cancer mortality in the Million Death Study (MDS), which is in progress in India and is one of the few, large, nationally representative studies of the causes of death in any low-income or middle-income country.[3,5–7] We focus on the geographical and social variation in specific cancers, and the degree to which these cancers might be avoidable by controlling their risk factors or causative agents.

Methods

Study design

Details of the MDS design,[3,5] assignment of the underlying causes of death, statistical methods, and preliminary results for various diseases and risk factors have been reported elsewhere.[6,7] Briefly, the Registrar General of India (RGI) divides India into 1 million small areas after each 10-year census. The RGI's Sample Registration System (SRS) randomly selected 6671 of these small areas (with about 1000 individuals per area) from the 1991 census and monitored all births and deaths in 1·1 million homes

from 1993 to 2003. From 2001, the RGI introduced an enhanced form of verbal autopsy (routine, reliable, representative, resampled household investigation of mortality with medical evaluation [RHIME])[5] to assess the cause of death recorded in the SRS. Each home in which a death had occurred between 2001 and 2003 was visited by one of 800 non-medical SRS field surveyors to obtain a structured investigation of events before death, including a written narrative in the local language. The two-page field report was converted into electronic records and assigned randomly with an automated computer system to two of 130 specially trained physicians (assignment was stratified only by their ability to read the language of the narrative), who independently and anonymously assigned codes to the causes of death using guidelines for the major causes.[8] If the two physicians did not agree on the assigned three-digit code from the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10),[9] a senior physician adjudicated. A random sample of about 5% of the areas was resurveyed independently, and the results were broadly consistent within families of ICD-10 codes.[5] Comparisons of the results of the RHIME verbal autopsy with information from hospital deaths and cancer registries have been reported previously.[10,11]

Definitions of cancer deaths

People who died from cancer between 2001 and 2003 and for whom causes of death were eventually assigned ICD-10 codes C00-C97, and for about 3% (n=213) of cancers D00-D48 was included in this study. Classification of cancers from verbal autopsy relies on grouping the broadly similar categories based on symptoms because microscopic confirmation used by cancer registries is not available. We thus grouped cancers into disorders that were diagnostically similar on verbal autopsy, such as all lip, oral cavity, and pharyngeal cancers, and all eye, brain, and other CNS cancers. Cancer categories were based on the ICD-10 codes: oral, lip, and pharynx (C00-14, D10, D11), oesophagus (C15), stomach (C16), colorectal (C17-21, D12), liver (C22), other digestive organs (C23-25, D00, D01, D13, D37), ill-defined digestive (C26), larynx, trachea, and lung (C32-34, D02, D14), bone (C40-49), urinary tract (C64-68, D30, D41), eye and brain (C69-75, D31-33,

	Study deaths, 2001–03		All India, 2010								
			UN's estimates of deaths from all causes (×1000)		Estimated cancer deaths* (×1000)			Estimated cancer death rate (lower and upper bounds†) per 100 000		Cumulative risk‡	
	Male	Female	Male	Female	Male	Female	Total	Male	Female	Male	Female
India											
Age (years)											
0–14§	138	80	1053	1089	10·5	5·5	16·0	5·5 (3·3–6·7)	3·2 (2·1–5·0)	0·08%	0·05%
15–19	64	63	86	86	3·9	4·0	7·9	6·2 (5·1–6·5)	6·9 (5·2–8·3)	0·11%	0·08%
20–24	61	67	119	105	4·7	4·4	9·1	7·8 (6·5–9·4)	8·1 (4·3–9·7)	0·15%	0·12%
25–29	80	70	146	105	6·4	4·9	11·3	11·7 (8·6–13·3)	9·7 (7·5–11·5)	0·21%	0·17%
30–34	124	119	168	104	10·8	9·4	20·1	22·0 (16·4–25·0)	20·6 (16·4–22·3)	0·32%	0·27%
35–39	136	184	190	104	11·7	14·0	25·8	27·3 (21·8–29·7)	35·1 (31·4–36·4)	0·46%	0·45%
40–44	191	234	213	113	14·1	18·7	32·8	37·0 (29·1–42·3)	52·6 (44·2–55·6)	0·64%	0·71%
45–49	278	319	254	138	19·7	27·8	47·6	59·5 (49·2–66·1)	89·7 (74·7–93·7)	0·94%	1·16%
50–54	402	335	328	186	34·3	31·0	65·3	119·6 (96·4–130·2)	114·6 (97·8–121·8)	1·54%	1·73%
55–59	452	426	409	257	39·9	37·2	77·0	167·2 (145·0–179·3)	162·3 (139·6–171·3)	2·37%	2·54%
60–64	474	379	459	314	36·9	30·1	67·0	229·1 (197·4–254·5)	184·6 (144·8–200·0)	3·52%	3·47%
65–69	516	419	486	370	32·7	27·1	59·9	282·3 (221·1–319·7)	218·9 (166·3–238·8)	4·93%	4·56%
70–74	408	254	492	429	27·8	19·6	47·4	342·9 (285·1–378·2)	209·5 (165·7–230·8)	6·64%	5·61%
≥75	493	371	991	1051	37·3	32·1	69·4	436·5 (327·1–487·2)	312·1 (212·0–355·2)		
All ages§	3817	3320	5394	4451	290·5	265·9	556·4	58·5 (47·1–65·1)	51·6 (40·9–56·4)	6·64%	5·61%
30–69§	2573	2415	2507	1586	200·1	195·3	395·4	97·6 (80·4–108·1)	95·1 (78·1–101·5)	4·72%	4·39%
Rural§	1969	1907	1858	1230	138·3	143·8	282·1	95·6 (77·3–107·8)	96·6 (79·2–103·2)	4·63%	4·46%
Urban§	604	508	649	356	61·8	51·5	113·3	102·4 (87·8–108·8)	91·2 (75·3–97·1)	4·94%	4·21%
USA, 30–69 years	NA	NA	764	462	125·4	109·8	235·2	167·6 (162·7–172·6)	136·4 (132·1–140·7)	8·33%	6·64%
UK, 30–69 years	NA	NA	127	77	28·1	25·0	53·1	161·3 (151·4–171·2)	138·7 (129·7–147·8)	8·14%	6·77%

See appendix pp 6–7 for 99% CIs for data in this table. Data for the most recent UK (2009) and USA (2007) rates were extracted from the WHO mortality database, available at the International Agency for Research Cancer.[1] NA=not applicable. *National totals are the product of the UN-estimated number of all deaths in 2010 and the percentage in each age range, weighted for state and urban or rural status. †99% CIs are shown for USA and UK. ‡Cumulative risk for all ages row was calculated by summing the risk from 0–74 years, which gave the probability of death from cancer if there were no other causes of death. §Age-standardised cancer death rate, with rates standardised to the world population; the 5-year age groups from 15–19 years to 75 years and older are crude rates.

Table 1: **Cancer-attributed deaths in the present study and estimated national totals by age and sex in India**

D42-43), lymphoid and haemopoietic (C81-96, D45–47), cervical and uterine (C53-55), and ill-defined secondary and unspecified sites (C76-80, C97, D48). In men, other cancers were other respiratory, breast, and male cancers (C30-31, C37-39, C50, C60-63, D03-04, D07-09, D24, D29, D34-36, D38, D40, D44, N60, N62-64, R59). In women, other cancers were other respiratory and female genital organ cancers (C30-31, C37-39, C40-49, C51, C52, C56-58, C64-68, D25-28, D39, D30, D41, D03-04, D07-09, D15-23, D34-36, D38, D44, R59). All 28 uterine cancer deaths (C54) were recoded as cervical cancers after central review. We defined cancers strongly related to tobacco smoking or chewing as oral (including lip, oral, and pharynx), lung (including trachea and larynx), and other respiratory and oesophagus cancers. We defined cancers strongly related to infection as stomach cancer (*Helicobacter pylori*), liver

	Study deaths, 2001–03				All India, 2010					
					Estimated cancer deaths (×1000)			Age-standardised cancer mortality rate per 100 000*		
	Rural	Urban	Total	Two coders agreed	Rural	Urban	Total	Rural	Urban	Total (99% CI)
Men										
Lip, oral cavity, and pharynx	411	132	543	335	31·8	14·0	45·8	21·8	22·8	22·1 (19·7–24·6)
Stomach	296	65	361	213	19·7	5·5	25·2	13·9	8·7	12·5 (10·6–14·3)
Larynx, trachea, and lung	238	76	314	173	14·9	7·9	22·9	10·7	13·8	11·6 (9·8–13·4)
Liver	127	50	177	141	9·3	4·7	14·0	6·4	7·9	6·8 (5·4–8·1)
Oesophagus	116	37	153	76	7·9	3·9	11·9	5·7	6·9	6·0 (4·7–7·3)
Ill-defined digestive	112	33	145	34	8·2	3·7	11·9	5·8	6·3	5·9 (4·6–7·2)
Lymphoid and haemopoietic	132	41	173	141	8·3	4·1	12·4	5·6	6·3	5·8 (4·6–7·0)
Eye and brain	118	37	155	127	7·4	4·3	11·7	4·6	7·5	5·3 (4·2–6·5)
Other†	73	18	91	26	5·2	1·8	7·0	3·6	2·9	3·4 (2·4–4·4)
Bone	58	19	77	49	4·5	1·9	6·4	3·2	3·2	3·2 (2·2–4·1)
Colorectal	55	22	77	43	4·4	1·7	6·1	2·9	2·8	2·9 (2·0–3·7)
Other digestive organs	33	14	47	29	2·6	1·8	4·4	1·7	2·7	2·0 (1·3–2·7)
Urinary tract	42	12	54	39	2·8	1·2	4·0	2·0	1·8	2·0 (1·3–2·7)
Ill-defined secondary and unspecified sites	158	48	206	89	11·2	5·3	16·5	7·7	8·8	8·1 (6·6–9·5)
Subtotal of tobacco-related cancer‡	800	255	1055	588	57·1	26·9	84·0	39·9	45·0	41·4 (38·0–44·8)
Subtotal of infection-related cancer§	423	115	538	354	29·0	10·2	39·2	20·3	16·6	19·2 (17·0–21·5)
Total	1964	604	2573	1515	138·3	61·8	200·1	95·6	102·4	97·6 (92·5–102·7)
Women										
Cervical	317	74	391	324	25·4	8·0	33·4	16·6	14·7	16·0 (13·9–18·1)
Stomach	282	56	338	186	21·2	6·3	27·5	14·3	11·4	13·5 (11·6–15·5)
Breast	178	62	240	203	14·0	5·9	19·9	9·2	9·8	9·4 (7·8–10·9)
Lip, oral cavity, and pharynx	196	42	238	159	14·6	4·5	19·1	9·9	7·7	9·4 (7·8–10·9)
Ill-defined digestive	156	23	179	43	12·6	2·1	14·7	8·8	3·6	7·4 (6·0–8·8)
Lymphoid and haemopoietic	133	38	171	138	9·3	3·3	12·6	6·3	5·9	6·1 (4·8–7·4)
Other¶	114	39	153	84	7·8	4·3	12·1	5·4	7·9	6·0 (4·8–7·3)
Liver	112	33	145	116	8·6	2·9	11·5	5·7	5·1	5·6 (4·4–6·8)
Eye and brain	76	32	108	80	5·7	3·6	9·3	3·7	6·2	4·4 (3·3–5·4)
Larynx, trachea, and lung	80	27	107	64	5·5	2·5	8·0	3·8	4·0	3·9 (2·9–4·9)
Oesophagus	63	25	88	52	4·4	2·5	6·9	2·9	4·8	3·4 (2·5–4·3)
Colorectal	51	11	62	36	4·1	1·4	5·4	2·8	2·5	2·7 (1·8–3·6)
Other digestive organs	33	12	45	26	2·4	0·7	3·1	1·6	1·2	1·5 (0·9–2·1)
Ill-defined secondary and unspecified sites	116	34	150	65	8·4	3·6	12·0	5·6	6·3	5·8 (4·5–7·0)
Subtotal of tobacco-related cancer‡	357	100	457	283	25·7	10·0	35·7	17·5	17·6	17·6 (15·4–19·7)
Subtotal of infection-related cancer§	711	163	874	626	55·2	17·2	72·4	36·7	31·2	35·1 (32·0–38·2)
Total	1907	508	2415	1576	143·8	51·5	195·3	96·6	91·2	95·1 (90·1–100·2)

Cancer categories are based on International Statistical Classification of Diseases and Related Health Problems, 10th revision. *Age-standardised cancer mortality rates use the method of International Agency for Research Cancer, based on the cancer mortality rate, world population weights, and the number of actual deaths.[18] See appendix pp 3–5 for comparisons of selected cancer registries with GLOBOCAN indirect estimates with the proportions reported in the Million Deaths Study (appendix pp 7–8). †Other respiratory, breast, and male cancers. ‡Oral, lung, oesophagus, and other respiratory cancers. §Stomach, liver, and cervical cancers. ¶Other respiratory and female genital organ cancers.

Table 2: **Estimated rates of cancer mortality for main cancer sites by place of residence and sex in individuals aged 30–69 years**

cancer (hepatitis B and C viruses), and cervical cancer (human papillomavirus).[12]

Analysis

We applied the age-specific and sex-specific proportion of cancer deaths within the 2001–03 survey to the UN's estimates of absolute numbers of deaths (and age-specific risks) for all causes in India in 2010.[13] The 9·8 million total deaths reported by the UN in 2010 was used because the results were similar to those of the 2011 census, to correct for the slight undercounts reported in the total death rates in the SRS,[14,15] and account for the 12% of deaths missed in our survey. The proportions of deaths from outmigration of the family or from incomplete field records that accounted for these missed deaths were similar between states. We partitioned the 2010 UN total deaths into state-specific total deaths by using the relative SRS death rates for 2007–09.[16] The proportion of cancer deaths to total deaths in our survey were weighted for sampling probability for each rural or urban stratum per state (although such weighting made little difference because the study was nationally representative). The forward projection to 2010 should not introduce important biases because the main determinant of state cancer totals (and age-specific risks) is the state-specific number of all-cause deaths that were drawn from 2007–09 SRS rates. For example, use of 2004 UN totals did not notably alter the results (data not shown). Education levels for the population were derived from the 2001 census and education levels for deaths were derived from the MDS and an earlier nationally representative survey of 50 000 deaths in 1997 in the same areas.[17] Mortality rates by education were standardised to the UN 2010 population. All other rates were standardised to the world population, as first proposed by Doll and colleagues (appendix p 3).[18] The lower bounds for the age-standardised cancer rates

See Online for appendix

	Illiterate	Less than primary	Primary	Middle or secondary	Senior secondary and above
Men					
Study deaths	899	459	402	592	221
Total population at risk (×1 000 000)	67·4	30·0	33·3	49·7	32·1
Estimated cancer deaths (99% CI; ×1000)	79·2 (72·3–86·0)	29·1 (25·6–32·6)	34·3 (29·9–38·7)	41·4 (37·0–45·8)	16·2 (13·4–19·0)
Age-standardised cancer mortality rate per 100 000					
Lip, oral cavity, and pharynx	24·7	20·1	20·8	17·1	9·0
Stomach	16·4	11·9	11·5	7·8	3·8
Larynx, trachea, and lung	11·0	10·6	9·3	9·2	6·0
Oesophagus	3·7	5·9	7·4	5·1	3·1
All other cancers	50·8	39·7	44·4	36·3	23·8
Subtotal of tobacco-related cancer*	39·3	36·5	37·5	31·4	18·2
Subtotal of infection-related cancer†	24·3	17·4	17·8	13·4	7·6
All cancers (99% CI)	106·6 (97·4–115·7)	88·1 (77·5–98·7)	93·4 (81·4–105·4)	75·5 (67·5–83·5)	45·7 (37·8–53·6)
Women					
Study deaths	1599	327	192	219	78
Total population at risk (×1 000 000)	124·0	20·0	22·6	22·1	11·8
Estimated cancer deaths (99% CI; ×1000)	140·2 (131·2–149·2)	20·3 (17·4–23·1)	15·3 (12·5–18·2)	14·2 (11·7–16·7)	5·4 (3·8–7·0)
Age-standardised cancer mortality rate per 100 000					
Cervical and uterine	19·1	13·6	11·4	10·0	5·4
Stomach	15·9	15·0	7·7	4·3	3·2
Breast	9·6	9·7	6·5	10·7	6·5
Lip, oral cavity, and pharynx	11·2	7·9	5·5	4·6	2·0
All other cancers	51·0	49·6	33·1	30·9	26·2
Subtotal of tobacco-related cancer*	19·5	15·1	10·1	8·1	7·2
Subtotal of infection-related cancer†	41·2	35·6	21·7	19·4	10·3
All cancers (99% CI)	106·7 (99·9–113·6)	95·7 (82·0–109·3)	64·2 (52·2–76·2)	60·5 (50·0–71·1)	43·4 (30·7–56·1)

Census 2001 educational groups were used, with below primary education including individuals who were literate but without having received a formal education. Mortality rates by education were based on the current mortality survey and a survey in the same areas in 1997.[17] These proportions were applied to the 2007–09 mortality rates from the Sample Registration System[16] and 2001 census population and then adjusted to the UN's estimates of deaths in India for 2010. Cause-specific mortality was calculated by applying the Million Deaths Study's cancer-specific mortality proportions. There were no substantial differences in the proportion of ill-defined cancers between the education groups, and physician agreement about any cancer was similar between the education groups. *Oral, lung, oesophagus, and other respiratory cancers. †Stomach, liver, and cervical cancers.

Table 3: **Age-standardised mortality rates for selected cancers by education level and sex of deceased individuals aged 30–69 years for all India**

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and risks in India (table 1) were based on the numbers of deaths that were immediately coded by both physicians as cancer, whereas the upper bounds was based on all deaths with cancer as the initial diagnosis by at least one coder. For site-specific cancers (tables 2–4), the numbers of deaths were fewer for each stratum, thus we estimated 99% CIs based on the actual number of cancer deaths.

In our analyses, we focused on deaths in individuals aged 30–69 years because these deaths are more likely to be avoidable than are those at older ages[19] and because the RHIME verbal autopsy method provides a greater proportion of classifiable deaths at these ages than in people older than 70 years.[5,11]

Role of the funding source

The sponsors of the study had no role in the study design, data gathering, analysis, and interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

For both sexes at all ages, 122 429 deaths occurred in 2001–03 and 7137 of these were attributable to cancer (table 1). In 2010, more than 556 000 cancer deaths were estimated in India for people of all ages, and 71·1% occurred in people aged 30–69 years (table 1). Cancer deaths accounted for 8·0% of the 2·5 million total male deaths and 12·3% of the 1·6 million total female deaths at age 30–69 years (table 1). In 2010, at all ages, the rates of cancer deaths were about 59 per 100 000 for men and about 52 per 100 000 for women (table 1). However, the rates of cancer deaths per 100 000 rose sharply with age and at age 30–69 years were about 98 for men and 95 for women. The remaining analyses focused on deaths at age 30–69 years (table 1). Based on the actual death rates and the hypothetical absence of other causes of death, a 30-year-old man in India had a 4·7% (99% CI 4·5–5·0) chance of dying from cancer before the age of 70 years. The respective risk for a 30-year-old woman was 4·4% (4·2–4·6).

In men aged 30–69 years, the most common types of fatal cancers were oral (22·9%), stomach (12·6%), and lung (11·4%; table 2; appendix pp 7–8). 42·0% of all male cancer deaths at these ages were from tobacco-related cancers, and another 19·6% were from infection-related stomach and liver cancers (table 2). In women aged 30–69 years, the most common fatal cancers were cervical (17·1%), stomach (14·1%), breast (10·2%), and oral (9·8%). 37·0% of all female cancer deaths were from infection-related cervical, stomach, and liver cancers and 18·3% were from tobacco-related cancers (table 2). Two physicians agreed on cancer as the cause of death at initial coding in about 4127 (82·7%) of 4988 deaths, but

	Hindu		Muslim		Other*	
	Study deaths	Age-standardised mortality ratio (99% CI)	Study deaths	Age-standardised mortality ratio (99% CI)	Study deaths	Age-standardised mortality ratio (99% CI)
Men						
Lip, oral cavity, and pharynx	437	0·95 (0·94–0·96)	56	1·22 (1·18–1·27)	50	1·23 (1·19–1·28)
Stomach	264	0·93 (0·91–0·94)	62	1·44 (1·38–1·51)	35	1·18 (1·12–1·25)
Larynx, trachea, and lung	246	0·99 (0·97–1·00)	45	1·38 (1·32–1·44)	23	0·68 (0·63–0·73)
Liver	142	1·02 (1·00–1·05)	20	0·92 (0·85–0·99)	15	0·87 (0·80–0·95)
Oesophagus	114	0·92 (0·89–0·94)	20	1·25 (1·16–1·33)	19	1·52 (1·42–1·62)
All other cancers	825	0·99 (0·98–1·00)	117	1·25 (1·22–1·.29)	83	0·82 (0·79–0·85)
Subtotal of tobacco-related†	834	0·96 (0·95–0·97)	123	1·23 (1·20–1·26)	98	1·15 (1·12–1·19)
Subtotal of infection-related‡	406	0·96 (0·95–0·98)	82	1·26 (1·21–1·30)	50	1·07 (1·03–1·12)
Total	2028	0·97 (0·96–0·98)	320	1·26 (1·24–1·28)	225	0·99 (0·97–1·01)
Women						
Cervical	340	1·06 (1·05–1·08)	24	0·68 (0·64–0·71)	27	0·76 (0·72–0·81)
Stomach	272	1·03 (1·02–1·05)	44	1·13 (1·08–1·18)	22	0·50 (0·46–0·54)
Lip, oral cavity, and pharynx	190	1·01 (0·99–1·03)	24	0·80 (0·74–0·85)	24	1·15 (1·08–1·22)
Breast	178	0·92 (0·90–0·94)	32	1·43 (1·37–1·50)	30	1·28 (1·21–1·36)
Lymphoid and haemopoietic	135	0·98 (0·95–1·00)	20	1·04 (0·96–1·11)	16	1·16 (1·08–1·25)
All other cancers	816	0·99 (0·98–1·00)	128	1·15 (1·12–1·18)	93	0·89 (0·86–0·92)
Subtotal of tobacco-related†	352	0·99 (0·97–1·00)	52	0·89 (0·85–0·94)	53	1·28 (1·23–1·34)
Subtotal of infection-related‡	729	1·04 (1·03–1·05)	90	0·97 (0·94–1·00)	55	0·61 (0·58–0·63)
Total	1931	1·00 (0·99–1·01)	272	1·05 (1·03–1·07)	212	0·89 (0·87–0·92)

National sex-specific rates were used as the standard rates. *117 Christian, 76 Sikh, Buddhist, and Jain, and 32 male cancer deaths, and 88 Christian, 98 Sikh, Buddhist, and Jain, and 26 female cancer deaths. †Oral, lung, oesophagus, and other respiratory cancers. ‡Stomach, liver, and cervical cancers.

Table 4: **Age-standardised mortality ratios for main cancer sites by religion for men and women aged 30–69 years**

agreed less often (3091 [62·0%]) about the specific type of cancer. Physician agreement or the proportion of ill-defined cancers did not vary greatly by region, education, or religion (data not shown). Only 843 (16·9%) of 4988 cancer deaths occurred in a health facility.

At ages 30–69 years, the age-standardised cancer mortality rates per 100 000 were similar in rural and urban men and similar in rural and urban women (table 1). However, the age-standardised rates for specific types of cancer differed somewhat between rural and urban areas (table 2). In men, oral cancers were the leading fatal cancers in both rural and urban areas and age-standardised rates were similar in both areas. Lung cancer rates were higher in urban areas and stomach cancer rates were higher in rural areas (table 2). Rates of tobacco-related cancer deaths were higher in urban than in rural men. In women, cervical cancers were the leading fatal cancers in both rural and urban areas, with somewhat higher rates in rural areas. Rates of female breast cancer mortality were similar in rural and urban areas. Stomach cancer rates were higher in rural than in urban areas of India. For both sexes, death rates from infection-related cancers were higher in rural than in urban areas.

The risks of dying from cancer differed by a factor of at least four between the major states of India (figure 1). In the hypothetical absence of other diseases and based on the actual death rates, we noted that a 30-year old man in northeast India had the highest chance (11·2%) of dying from cancer before 70 years of age (figure 2). By contrast, the risk was less than 3% for men in the adjacent states of Bihar, Jharkhand, and Odissa in eastern India (figure 2). For women, the highest risk (6·0%) of dying from cancer before 70 years of age was in the northeast states (figure 3). Women and men in the poorest nine states (Assam, Bihar, Chhattisgarh, Jharkhand, Madhya Pradesh, Odissa, Rajasthan, Uttarakhand, and Uttar Pradesh) had lower risks of cancer deaths than did their counterparts in the remaining richer 26 states and union territories.

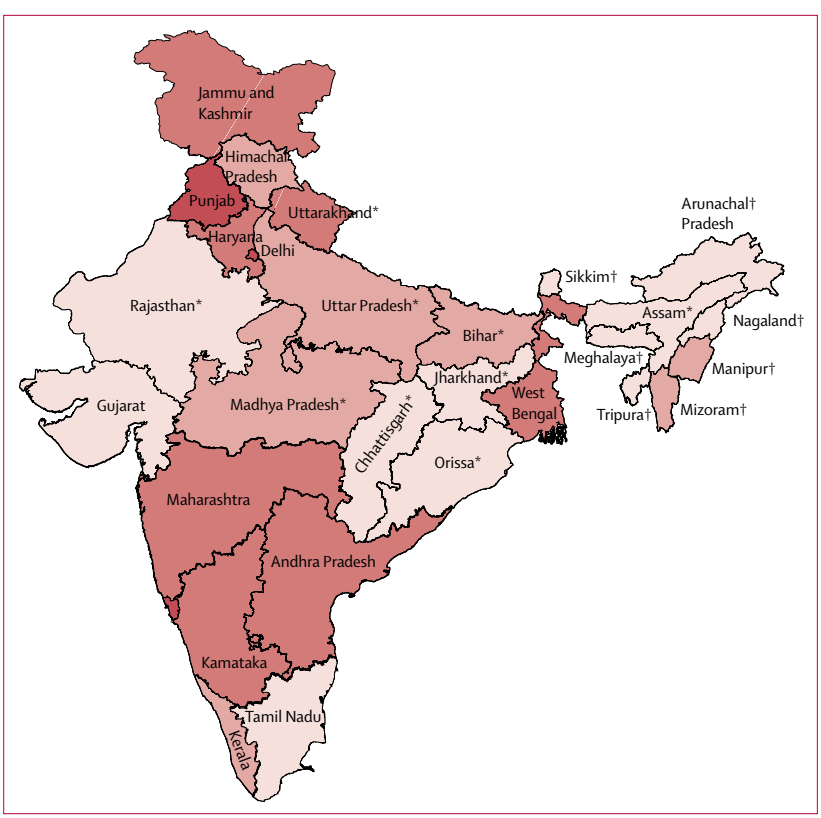

Figure 1: **Map of India showing the states and regions**
*Poorest states. †Northeast states.

In men, the age-standardised death rate of 41·4 per 100 000 from tobacco-related cancers corresponds to a cumulative risk of 1·9% (1·7–2·1) of dying at age 30–69 years in the absence of other diseases. In women, the age-standardised death rate from tobacco-related cancers of 17·6 per 100 000 corresponds to a cumulative risk of dying at age 30–69 years in the absence of other diseases of 0·8% (0·7–0·9). Rates of tobacco-related cancer deaths varied substantially by state for both men and women (figures 2 and 3). Indeed, rates of tobacco-related cancer deaths in men in Assam and other northeastern states were greater than the national rates of deaths from all cancers. The age-standardised rates for cervical cancer in women in Jammu and Kashmir and Assam (where 75% and 40% of the total populations, respectively, are Muslim), were less than a quarter of the national rates for cervical cancer. Taking data for both sexes together, cancers common to both sexes (excluding tobacco-related oral, respiratory, and oesophagus cancers, or sex-specific sites, such as breast, cervical, or prostate cancers), showed a variation of nearly four-times between states (appendix p 2). Particularly high rates of these specific cancers were noted in the northeast states, Kashmir, Kerala, and West Bengal (appendix p 2).

39·6% of cancers in men occurred in those who were illiterate, although these men constituted less than a third of India's male total population (table 3). The corresponding proportion for women was 71·8%, with illiterate women constituting about three-fifths of India's female total population. For both sexes, the age-standardised rates of cancer deaths were more than twice as high in the least educated (illiterate) compared with the most educated (secondary or higher education; table 3). The ratio of the age-standardised death rates for the least and most educated men were largest for stomach cancer, followed by oral and lung cancers. The ratio of the age-standardised death rates between the least and most educated women were largest for oral cancers, followed by stomach and cervical cancers. By contrast, rates of breast cancer deaths in women varied little with education level. Most cancer deaths occurred in Hindus in roughly similar proportion to the national Hindu population. Muslim men had higher age-standardised mortality ratios for most cancers than did Hindus and other religious groups, but a

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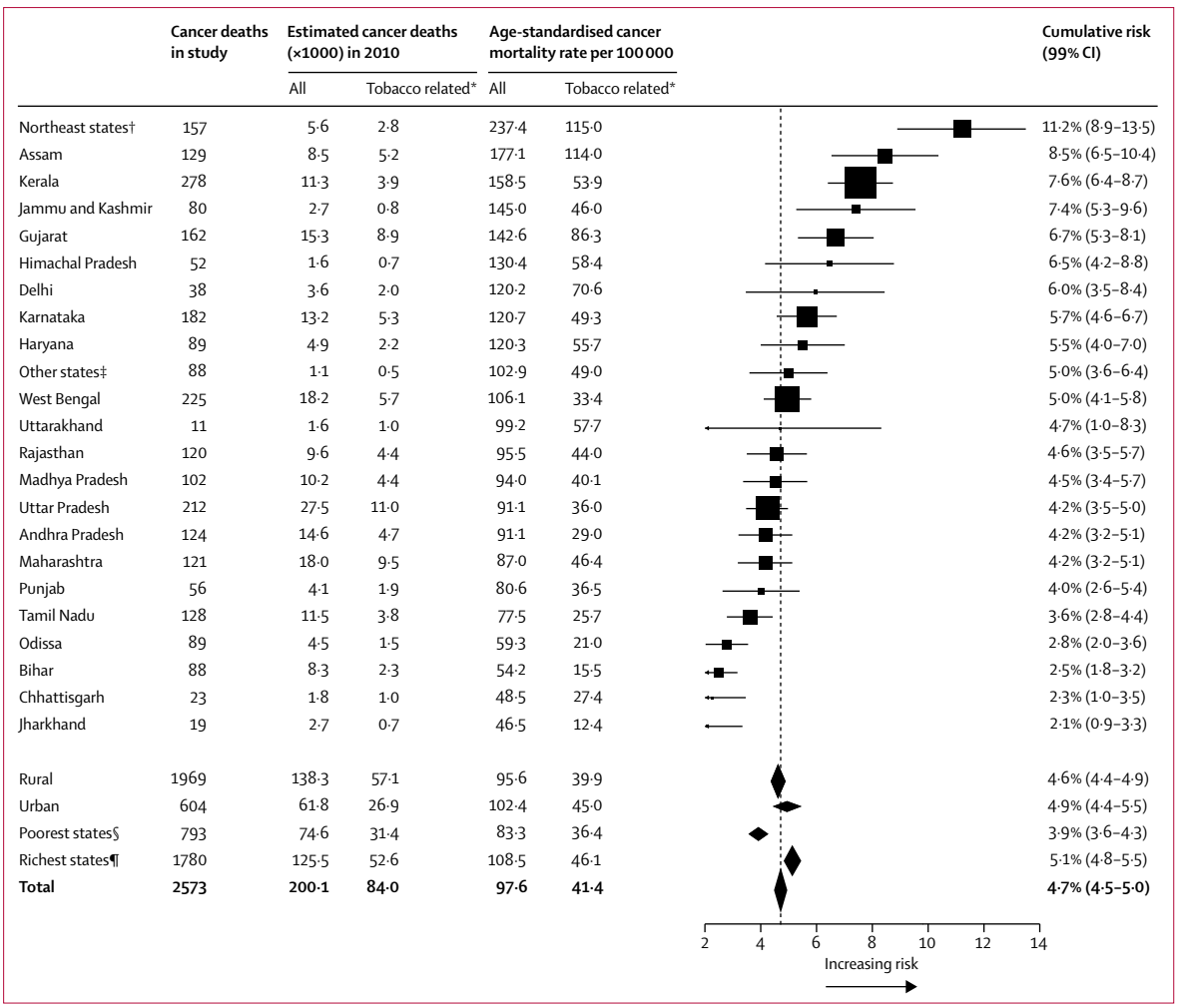

Figure 2: **Estimated deaths, age-standardised mortality rates, and cumulative risks from all and tobacco-related cancers for men aged 30–69 years in the states and regions of India**

Rates are standardised to the world population. The size of the squares and the height of the diamonds are proportional to the weighted cancer deaths in the study. Diamonds indicate the aggregated values and the widths were determined by the widths of the 99% CIs. *Oral, lung, oesophagus, and other respiratory cancers. †Arunachal Pradesh, Manipur, Meghalaya, Mizoram, Nagaland, Tripura, and Sikkim. ‡Andaman and Nicobar Islands, Chandigarh, Dadra and Nagar Haveli, Daman and Diu, Goa, Lakshadweep, and Puducherry. §The poorest states are the Empowered Action Group of States (Bihar, Chhattisgarh, Jharkhand, Madhya Pradesh, Odissa, Rajasthan, Uttarakhand, and Uttar Pradesh) plus Assam. ¶Remaining 26 states or union territories.

slightly lower ratio for liver cancer than did Hindus (table 4). Muslim women had notably low age-standardised mortality ratios for cervical and oral cancers, but higher ratios for breast and stomach cancers (table 4).

Discussion

The results of our nationally representative mortality survey confirm that cancer is an important cause of adult deaths in India, with more than 70% of fatal cancers occurring during the productive ages of 30–69 years. Contrary to the common perception that cancer kills urban and educated people, we noted that rates of cancer deaths were generally similar between rural and urban areas and about twice as high in the least versus the most educated. One in 22 men or women aged 30 years alive today in rural India is likely to die of cancer before 70 years of age based on the rates of actual deaths and in the absence of other disorders; in urban areas, the risks are one in 20 for men and one in 24 for women. Rural cancer registries, of which there are only two in India, might have low ascertainment of the incidence of cancer[4,20] because they report about half the incidence of cancer compared with registries in urban areas (panel). Even with possibly lower incidence of cancer, rural Indians have a higher prevalence of bidi (small hand-rolled cigarette) smoking and tobacco chewing (but not cigarette smoking),[26] their cancers are diagnosed at a later stage and they have fewer cancer treatment facilities available to them.

The very high levels of cancer deaths among illiterate women might represent deaths in a cohort of women older than 50 years who also had the highest prevalence of bidi

	Cancer deaths in study	Estimated cancer deaths (×1000) in 2010			Age-standardised cancer mortality rate per 100 000			Cumulative risk (99% CI)
		All	Tobacco related*	Cervical	All	Tobacco related*	Cervical	
Northeast states†	118	3·2	0·4	0·4	138·0	21·0	15·2	6·0% (4·6–7·4)
Himachal Pradesh	63	1·7	0·4	0·3	127·5	27·9	19·7	5·9% (4·0–7·8)
Assam	73	5·3	1·7	0·2	116·0	37·5	3·5	5·5% (3·8–7·1)
Punjab	80	5·5	1·3	0·8	113·2	25·8	16·7	5·3% (3·8–6·9)
Jammu and Kashmir	60	2·0	0·3	0·04	113·7	17·2	2·3	5·3% (3·6–7·1)
Karnataka	173	13·2	4·0	1·8	114·8	34·1	16·5	5·3% (4·2–6·3)
West Bengal	212	18·0	2·7	2·7	110·5	17·5	15·5	5·0% (4·1–5·9)
Uttar Pradesh	260	31·2	4·1	4·0	108·2	14·6	13·6	4·8% (4·1–5·6)
Andhra Pradesh	137	17·6	3·3	3·0	104·2	20·3	17·6	4·7% (3·7–5·8)
Uttarakhand	10	1·5	0·4	..	91·9	27·2	..	4·6% (0·9–8·4)
Tamil Nadu	175	15·7	1·9	5·4	102·5	12·3	35·7	4·5% (3·6–5·4)
Kerala	184	7·5	1·4	0·9	90·3	16·8	11·1	4·3% (3·5–5·1)
Gujarat	118	9·6	2·3	2·0	92·1	22·5	16·8	4·3% (3·3–5·3)
Delhi	34	2·6	0·3	0·3	90·9	9·1	9·4	4·0% (2·3–5·8)
Madhya Pradesh	98	9·8	2·3	1·2	87·4	21·2	10·1	4·0% (2·9–5·0)
Maharashtra	134	18·1	4·2	3·8	88·6	20·3	19·0	3·9% (3·1–4·8)
Other states‡	66	0·9	0·2	0·2	83·7	15·7	17·5	3·9% (2·7–5·1)
Chhattisgarh	31	3·0	0·4	0·9	80·4	9·7	24·6	3·8% (2·0–5·5)
Rajasthan	103	8·1	1·5	1·0	77·3	13·7	10·3	3·4% (2·6–4·3)
Haryana	63	3·0	0·8	0·4	73·8	18·3	11·4	3·3% (2·3–4·4)
Bihar	119	10·4	1·0	2·0	68·2	7·1	12·9	2·9% (2·2–3·6)
Odissa	85	5·0	0·7	0·9	63·5	9·6	10·9	2·8% (2·0–3·6)
Jharkhand	19	2·9	0·2	1·1	53·0	2·8	19·5	2·1% (0·9–3·4)
Rural	1907	143·8	25·7	25·4	96·6	17·5	16·6	4·5% (4·2–4·7)
Urban	508	51·6	10·0	8·0	91·2	17·6	14·7	4·2% (3·7–4·7)
Poorest states§	798	77·0	12·2	11·4	87·1	14·2	12·5	3·9% (3·5–4·3)
Richest states¶	1617	118·4	23·4	22·0	101·2	20·1	18·7	4·6% (4·3–4·9)
Total	**2415**	**195·4**	**35·7**	**33·4**	**95·1**	**17·6**	**16·0**	**4·4% (4·2–4·6)**

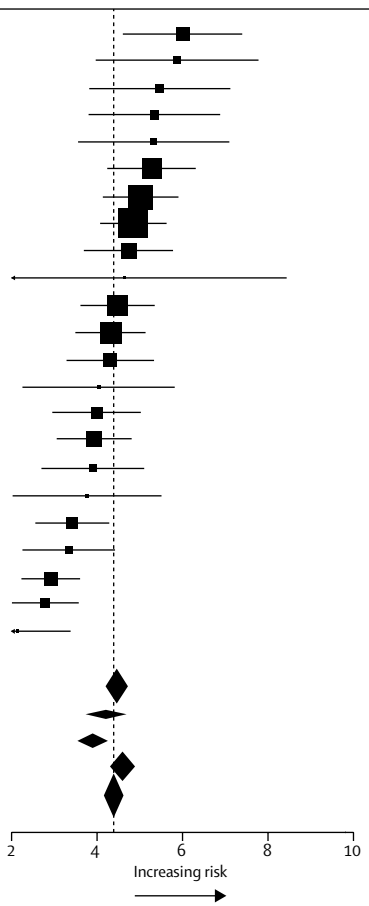

Figure 3: **Estimated deaths, age-standardised mortality rates, and cumulative risks from all, tobacco-related, and cervical cancers for women aged 30–69 in the states and regions of India**
Rates are standardised to the world population. The size of the squares and the height of the diamonds are proportional to the weighted cancer deaths in the study. Diamonds indicate the aggregated values and the widths were determined by the widths of the 99% CIs. The correlation of death rates for tobacco-related cancers between men and women was high (R^2=0·68). *Oral, lung, oesophagus, and other respiratory cancers. †Arunachal Pradesh, Manipur, Meghalaya, Mizoram, Nagaland, Tripura, and Sikkim. ‡Andaman and Nicobar Islands, Chandigarh, Dadra and Nagar Haveli, Daman and Diu, Goa, Lakshadweep, and Puducherry. §The poorest states are the Empowered Action Group of States (Bihar, Chhattisgarh, Jharkhand, Madhya Pradesh, Odissa, Rajasthan, Uttarakhand, and Uttar Pradesh) plus Assam. ¶Remaining 26 states or union territories.

smoking and tobacco chewing[26] and perhaps other undetermined exposures associated with extreme illiteracy and poverty. Tobacco use is likely to be a strong explanation for the large differences in rates of cancer deaths by education (smoking is a key determinant of social differences in mortality in developed countries).[27] Indeed, in men, the differences in oral cancers are consistent with higher prevalence of tobacco chewing in those who are illiterate, and the differences in lung cancers are consistent with higher cigarette smoking in educated men.[26,28] The number of oral cancers was more than twice the number of lung cancers in individuals aged 30–69 years, indicating that the range of fatal cancers caused by tobacco in India differs substantially from that in high-income countries.[2,6,29] A large proportion of cancer deaths in middle age (30–69 years) arise from tobacco-related cancers, particularly in the northeastern states of India. A priority for cancer prevention is tobacco control, particularly through higher taxation of tobacco products[30] to increase the very low levels of cessation.[26]

Cervical cancer is the leading cause of cancer death in women in both rural and urban areas. The cervical cancer death rate of 16 per 100 000 reported in table 2 suggests that a 30-year old Indian woman has about 0·7% risk of dying from cervical cancer before 70 years of age in the absence of other diseases. By contrast, the risk of dying during pregnancy for Indian women aged 15–49 years is about 0·6%.[31] Cervical cancer risks were much lower in Muslim women and in states where the proportion of Muslims was larger, as noted internationally.[1] Circumcision

among Muslim men, which reduces the sexual transmission of human papillomavirus,[32] is a likely explanation although other factors might also account for this difference. Strategies to reduce cervical cancer deaths include vaccination against human papillomavirus before marriage and for married women a once-only testing or screening followed by visual inspection with acetic acid and further referral for treatment.[33,34]

In women, breast cancer mortality was similar in rural and urban India. Breast cancer is likely to be diagnosed at earlier stages in urban women than in rural women and is therefore more treatable. Trends recorded in urban cancer registries show increases in the incidence of breast cancer of about 0·5% per year from 1991 to 2005, and an increase in the proportion presenting with localised breast cancer,[20] suggesting, partly, enhanced awareness and screening. Low-cost treatments, such as tamoxifen with surgery for early stage breast cancer, have helped to substantially reduce the breast cancer mortality rates in the UK[35] and could be implemented in urban facilities in India, but less so in rural areas.

Stomach cancer was about twice as common in our study compared with the records of cancer registries (appendix pp 3–5), partly because there are few registries in rural areas where stomach cancer and, presumably, chronic *H pylori* infection are more common. The regional patterns of stomach cancer in this analysis are very similar to the pattern seen in railway workers in the 1960s.[36] Higher stomach cancer rates might arise if other cancers (eg, pancreatic cancer) were misdiagnosed as stomach cancer. This explanation does not account for the higher rates of stomach cancer in women than reported elsewhere for worldwide data.

Primary liver cancer is difficult to diagnose with verbal autopsy and the liver cancer deaths that we report might include deaths caused by cancers metastasising from other sites, particularly from other digestive cancers, and deaths resulting from cirrhosis. Prevalence of hepatitis B virus in India was less than 1·9% in 72 000 pregnant women aged 15–49 years who were tested in 2002.[37] Vaccination against hepatitis B virus in neonates would reduce future liver cancer deaths and cirrhosis.[38]

In our study, more than 80% of cancer deaths in individuals older than 15 years had a crude previous diagnosis of cancer by the physician, suggesting some medical confirmation of cancers. In view of the high mortality rates noted in our study, many of these cancers are likely to represent late presentation of disease. Earlier comparisons of verbal autopsy methods with cancer registries showed a sensitivity of 95% and specificity of 100% for identifying cancer deaths.[11] Nonetheless, diagnosis of specific cancers based on verbal autopsy is inherently difficult. Misclassification of cancers is expected most for metastatic cancers from lesions that are adjacent to each other, such as those within the abdomen, thorax, or brain. It might account for why our mortality rates for stomach cancer are higher than those recorded in urban registries, and higher in women than expected. However, misclassification is less of a concern for cancers occurring in distinct anatomical sites, such as oral, cervical, and breast cancers. Moreover, the distribution of the top five cancer sites in our study corresponded reasonably well with that recorded by Indian cancer registries or with indirect estimates based on cancer incidence and survival, although there are some exceptions especially for cancers in women (appendix pp 3–5).[4] We have probably underestimated the total number of cancer deaths at older ages, mainly because cancers might be common in the roughly one-fifth of deaths in people older than 70 years, for which no medical cause of death could be assigned.

Rates of cancer deaths in India are about 40% lower in adult men and 30% lower in women than in men and women in the USA or UK (table 1). However, cancer death rates are expected to rise, particularly with increases in age-specific exposure to tobacco smoking.[2] Many cancer deaths before 70 years of age are avoidable, most notably through prevention of cervical, liver, and tobacco-related cancers, and with early diagnosis of oral, cervical, and breast cancers that enables effective treatment. The large differences in cancer rates between the states of India and in subpopulations suggest substantial and measurable differences in other causative factors and, in some, intermediate determinants of disease risk that await discovery. Specific investigation of this huge variation in cancer risks might involve case-control studies of the common cancers, and blood-based cohort studies to investigate unidentified environmental and genetic determinants of cancer.[39,40]

Panel: Research in context

Systematic review

We used the search terms "India" (Title) AND "cancer" (Title) AND "rates" OR "estimates" (all fields) OR "epidemiology" (all fields) and identified 177 studies published after 1970. The national site-specific mortality values were estimated in only five studies, using cancer registry data.[21–25] 123 were small studies or site-specific cancer studies and the remainder were comments, correspondence, editorials, or studies in which trends or rates reported to the cancer registries were compared with other countries.

Interpretation

The results of our study are the first to provide direct nationally representative estimates and rates of cancer deaths in men and women in India. Although the National Cancer Registry Programme provides cancer data for the country,[4] the data were mostly obtained from urban cancer registries and thus less applicable to rural India where most Indians live.

Contributors

The MDS Collaborators (appendix p 9) planned the MDS in close collaboration with the Office of the RGI. RD, CR, WS, and PJ undertook the analyses. All authors were involved in data interpretation and critical revisions of the report, and approved the final version; PJ is the guarantor for the report.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

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