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COHORT PROFILE

Cohort Profile: The Chennai prospective study of mortality among 500 000 adults in Tamil Nadu, South India

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How did the study come about?

A prospective study of half a million adults living in the city of Chennai (formerly Madras) arose out of discussions at the 1994 International Cancer Congress in Delhi about how to assess the effects of tobacco on health in different parts of India. Chennai is the capital of the South Indian state of Tamil Nadu, and it is India's fourth most populous city. Two large-scale epidemiological studies of tobacco and other factors were established: a case-control study[1] that could provide reasonably reliable results quickly, and a prospective cohort study that could provide more robust results over a longer period. (A parallel prospective study of 100 000 adults, not included in this profile, is in progress in the nearby rural area of Villupuram; Figure 1.) The case-control analyses,[1] which involved 43 000 adult deaths during 1995–97 and 35 000 controls who had been living with a case, indicated that smoking is a cause of, among other things, about half of all tuberculosis (TB) deaths among men. The prospective cohort study, which recruited half a million participants between 1998 and 2001, is described here.

What does it cover?

The Chennai Prospective Study examines the associations of tobacco smoking, quid chewing, alcohol drinking, obesity, blood pressure, respiratory function and other factors with overall mortality, and with cause-specific mortality. Table 1 shows that in the mid-1990s the age-standardized death rates for middle-aged men and women in Chennai differed very substantially from those in, for example, Japan, the United Kingdom and the United States. All-cause mortality was twice as great in Chennai as in the United Kingdom and the United States, and about three times as great as in Japan. In both sexes, about half of the excess mortality compared with these three countries was accounted for by vascular diseases other than stroke—i.e. chiefly by ischaemic heart disease (IHD). The main reasons for the high IHD mortality rates in Chennai are not fully known. Furthermore, there are still high TB death rates in Chennai, particularly among men, but not in the other three countries. Within Chennai, smoking accounts for most of the difference in TB mortality between men and women, but even among women TB is still a major cause of death. For these and other diseases, the study will help quantify the evolving importance in this population of some known causes of death such as tobacco, alcohol, high blood pressure and obesity, and help identify and quantify some other risk factors.

Who is in the sample?

The study includes one-third of all adults aged 35 and over in the city of Chennai. We sought to visit all houses in two of the 10 administrative zones into which Chennai is divided (Figure 1), as well as all houses in either 30% or 50% of the streets (selected randomly) in five of the other eight zones. Participant information was collected through in-person interviews of all aged 35 or over in each household visited. Only 5% (25 184) refused, and 500 816 took part. The mean age of participants was 49 for women and 48 for men, and 97% were aged 35–74. Eighty-five per cent were Hindu, and 7% each were Muslim and Christian. Half (53%) were men. Seventeen per cent of the men had been educated at university or college, compared with 6% of women (Table 2). Nearly one in three women, and 1 in 10 men, had received no formal education. The most commonly reported prevalent diseases at baseline were diabetes and hypertension; few reported a history of IHD, stroke or TB (Table 2).

How often are they being followed-up?

Follow-up, which can be especially challenging in lower-income countries,[3] is being conducted not only by passive but also by active methods. The passive methods involve record linkage to routine mortality data collected from the Chennai Vital Statistics Division for all adult (age 30 or more) deaths occurring in Chennai since 1998. Participant and death records are matched by manual and computerized (probabilistic[4]) record linkage based on name, age, sex, address and name of spouse or father. Even though death registration is almost complete in Chennai, reliable assessment of cause-specific mortality from the stated cause on the death certificate is not

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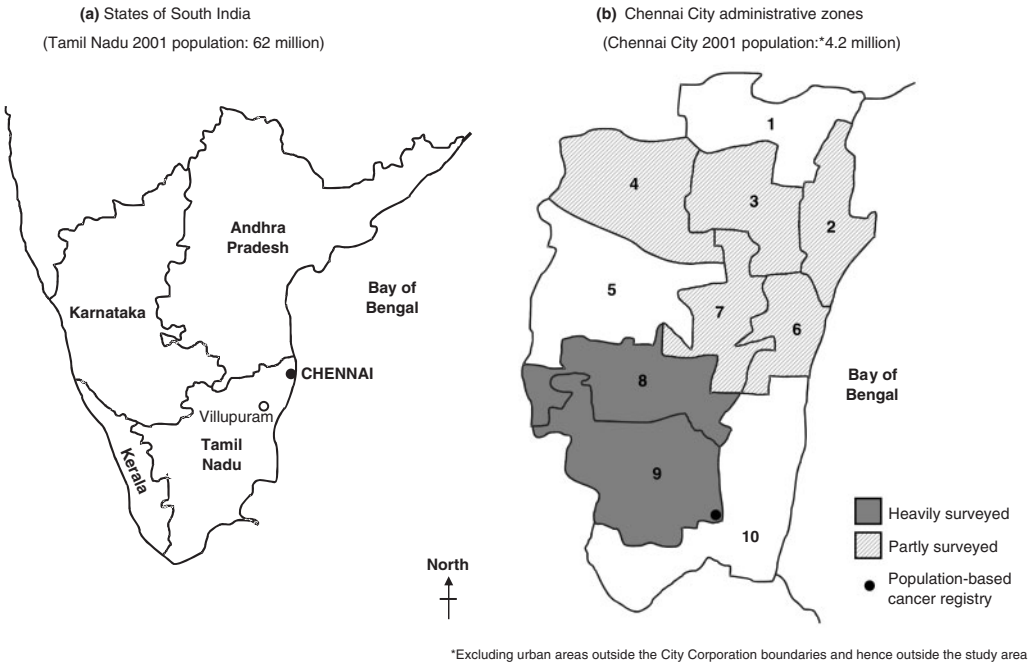

Figure 1 Map showing locations of (a) the city of Chennai (formerly Madras) within Tamil Nadu, South India, and (b) the study area in Chennai

Table 1 Age-standardized mortality rates[a] at ages 35 to 69 in Chennai (1995–97) and, for comparison, three high-income countries

	Annual death per 100 000							
	Men				Women			
Cause of death[c]	Chennai 1995–97	Japan 1994[b]	UK 1996	USA 1996	Chennai 1995–97	Japan 1994[b]	UK 1996	USA 1996
Tuberculosis	152	4	1	1	43	1	1	0
Other respiratory diseases	109	51	74	64	60	17	49	46
Other infectious diseases	70	13	7	15	49	7	5	11
Neoplastic diseases	177	310	314	311	156	152	249	237
Stroke	89	71	50	38	62	37	37	29
IHD/other vascular diseases	685	113	326	324	428	45	123	143
Diabetes	58	10	10	29	58	5	7	25
Peptic ulcer	6	3	6	2	5	1	3	1
Hepatic diseases	92	32	19	26	22	9	11	11
Renal diseases	52	10	4	10	40	6	3	8
Pregnancy complications	0	0	0	0	0[d]	0	0	0
Other 'medical' causes	181	37	49	95	186	21	37	52
External causes	135	78	42	81	48	27	17	28
All causes	1805	732	901	996	1158	327	540	591

[a]For Chennai, calculated from a verbal autopsy study of 48 000 adult deaths;[2] for the three countries, calculated from WHO mortality[10] and UN Population Division[11] data. Rates are means of the age-specific rates for the seven five-year age bands from 35 to 69.

[b]Japan changed from ICD-9 to ICD-10 in 1995, so the 1994 data have been used for comparability.

[c]ICD-9 codes for Chennai as defined previously,[2] except 'other infectious diseases' excludes tuberculosis (011, 012, 018). ICD-9 codes for the three countries as for Chennai except (because of the way routinely available WHO mortality data are categorized) for: slightly more liberal definitions of tuberculosis (010–018) and 'IHD/other vascular diseases' (390–429 and 440–529); and slightly less liberal definitions of 'other infectious diseases' (001–009, 020–139, 320–322, 590, 680–686), 'other respiratory diseases' (460–519) and hepatic diseases (571).

[d]0.49

yet possible because more than half the medical causes of death are non-specific or inaccurate; hence, all these deaths have to be supplemented by verbal autopsy reports.

The verbal autopsy[1,2] is a systematic retrospective inquiry, generally of family members, about the circumstances, events, symptoms and signs of illness and treatment details prior to a participant's death. It is an interactive process, with the respondent taking the lead in providing the narrative information, and the interviewer prompting where necessary for more details. The interviewers use an open narrative format for their report

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Table 2 Study population: baseline (1998–2001) characteristics of 500 816 adults aged 35 or more, by age and sex

	Percent					
	264 848 men, by age (years)			253 968 women, by age (years)		
	35–54	55–74	⩾75	35–54	55–74	⩾75
Number of participants	194 703	62 205	7940	164 420	63 778	7770
Vegetarian	3.7	6.2	10.2	8.4	10.1	12.1
Religion						
Hindu	85.1	85.5	87.0	84.9	85.7	86.4
Muslim	7.5	7.4	6.2	7.5	6.9	5.5
Christian	6.8	6.6	6.3	7.0	7.0	7.4
Other	0.6	0.5	0.5	0.6	0.4	0.6
Highest educational level						
University/college	18.8	12.1	7.6	7.6	2.4	1.2
9–11 years at school	41.8	34.3	29.0	30.1	14.8	7.1
6–8 years	20.6	21.6	20.7	22.2	17.0	10.6
1–5 years	10.4	16.8	21.7	16.1	18.7	17.3
<1 year/no schooling	8.4	15.2	21.1	23.9	47.0	63.8
Ever diagnosed with:						
Tuberculosis	0.4	0.7	0.9	0.2	0.3	0.2
Diabetes	3.5	9.5	8.5	3.9	9.4	6.0
Ischaemic heart disease	0.2	0.7	0.6	0.2	0.3	0.4
Stroke	0.1	0.7	1.1	0.1	0.4	0.6
Hypertension	2.5	7.5	8.1	3.9	9.6	8.8

Table 3 Summary of baseline questionnaire and physical measurement data

Personal information
Name, age, sex
Mother tongue
Religion
Marital status
Socioeconomic status
Educational level
Occupation
House type/ownership/room number/cooking fuel
Household luxury items
Health behaviour
Tobacco smoking (cigarette, bidi, chutta, cigar, pipes, hookah)
Chewing (betel leaf/areca nut/tobacco)
Tobacco powder (nasal/oral)
Alcohol drinking
Vegetarian diet
Personal disease history: ever diagnosed with
Tuberculosis
Diabetes
Ischaemic heart disease
Stroke
Hypertension
Cancer (specify site)
Family history of cancer
Measurements
Resting blood pressure (SBP/DBP measured twice)
Waist circumference (men only)
Height
Weight
Peak expiratory flow rate (measured three times)

rather than taking the respondent through detailed questionnaires, as these would have to be impracticably long to cover a sufficiently wide range of possible causes for adult deaths. However, each interviewer has a short checklist of symptoms and signs that are used to help ensure the reports are appropriately informative. The verbal autopsy report, written in the local language by the interviewer, describes the chronological order of the appearance of various signs and symptoms and their progress, with details of treatment received, if any, the name(s) of the hospital(s) attended and any history of similar episodes. The interviewers are carefully trained non-medical graduates, and each report is independently reviewed centrally by two specifically trained medical doctors to arrive at a probable underlying cause of death. Strict supervision of the fieldwork and of the quality of the narratives is maintained by random checking of 5% of the interviews, partly to discover any inadvertent errors and partly to ensure that the original interviewer knows there is a 5% chance that the quality of the work will be checked just a few days later.

This verbal autopsy tool for adult deaths was originally developed and validated in 80 000 deaths in urban and rural areas of Tamil Nadu.[1,5] It appeared generally satisfactory, so in recent years its use in nationwide surveys by the Registrar-General of India has been piloted.[6] It is now being adapted for use in India's Sample Registration System, a large nationally representative survey of a million households in several thousand randomly chosen study areas, with prospective follow-up of all births and deaths.

The active component of follow-up in the Chennai study involves the field interviewers revisiting all households once during 2002–05, and then once in every two years (2006–07, etc.) indefinitely, supplemented where deaths have occurred by a verbal autopsy. In addition to repeat assessment of a few risk factors (tobacco smoking, quid chewing

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and alcohol drinking), surviving participants are asked about the occurrence (after the baseline interview) of any clinical events such as the onset of TB, diabetes, IHD, stroke, hypertension or cancer. If the study participant is not living at the address noted at the time of collecting the baseline data, then neighbours are asked when the person moved out and where he or she went.

A repeat survey of 20 000 individuals will be carried out in 2007–08 in randomly chosen streets in the study area to help correct for the 'regression dilution' bias[7] that can result from random errors in baseline measurements. Participants will be re-assessed with repeat interviews and re-measurements as in the baseline survey. Further such surveys are planned at approximately five-year intervals thereafter.

What has been measured?

Among the items recorded at the baseline assessment were age, sex, educational level, occupation, religion, mother tongue, diet (vegetarian/not), tobacco smoking (including not only cigarettes but also tobacco in the form of bidis, chuttas, cigars, pipes and hookahs), quid chewing (with or without tobacco in the quid), use of tobacco powder, alcohol drinking, family history of cancer, and whether the participant had ever been diagnosed as having TB, stroke, IHD, diabetes, hypertension or cancer (Table 3). In addition, height, weight, blood pressure, peak expiratory flow rate and (in men only, for cultural reasons) waist circumference were measured.

The questionnaires were checked centrally for consistency and missing values by coding clerks, and then double-entered into computers by 16 data-entry operators. As with the verbal autopsies, a random 5% of the baseline assessments were checked one week later by a fieldwork supervisor who re-interviewed and re-measured participants in randomly selected households while blinded to the original data. This random checking was done partly to ensure that the fieldwork was reliably motivated (the original interviewer knew that there was a 5% chance that the quality of their work would be checked just a few days later).

What is attrition like?

Participants will be lost to follow-up if they move permanently out of Chennai City, but only a very small proportion of participants is likely to do so each year. It is hoped that those who move address within the city can continue to be followed, but this is not yet known. Hence, estimates of actual losses to follow-up are not yet available.

What has it found?

Analyses of associations between possible risk factors and cause-specific mortality will not start until 2008 when the second round of follow-up is complete. By then, over 25 000 deaths will have been recorded. On the basis of the verbal autopsy study of 48 000 deaths in 1998–99,[2] about 5% of the deaths that occur at ages 35–69 in either sex will be due to stroke, about 40% will be due to IHD or other vascular diseases, and about 4% (women) or 8% (men) will be due to TB (Table 1).

Table 4 shows the baseline distributions of various risk factors by age and sex. About one-third of the men aged 35–74 were current smokers of tobacco, and about one-third of these smokers used bidis. Bidis, which are widely smoked throughout South Asia, are smaller than Western-style cigarettes, and instead of the tobacco being wrapped in paper it is wrapped in the leaf of another plant (temburni). Smoking was rare among women: 99.9% reported never having smoked. In contrast, more women than men in every age group (and 10% vs 6% overall) reported quid chewing (either with or without tobacco in the quid). In both sexes, quid chewing was more prevalent at older ages. A quarter of men overall (and even more at younger ages) reported being current drinkers of alcohol, but almost all women (99.9%) reported never having been a regular drinker. One-third of the younger men who chewed tobacco also smoked it (whereas almost none of the women who chewed tobacco smoked it too). Figure 2 shows the distributions of the main smoking, chewing and drinking habits by educational level. Independently of age, bidi-smoking men tended to be less educated, as did beer- or brandy-drinking men, and also quid-chewing men and quid-chewing women (particularly, for both sexes, when the quid contained tobacco).

In both sexes, the mean body mass index (BMI, kg/m^2) was higher at younger ages, and at all ages the mean BMI was higher among women than men. The mean BMI levels for men and older women were much lower than in most Western countries, but the mean for women aged 35–54 ($24.0\,kg/m^2$) was similar to that in some European countries (e.g. France, Sweden and Belgium[8]). Of the women aged 35–54, 24% had a BMI of 25–30 kg/m^2 and 10% had a BMI of $30\,kg/m^2$ or more. Unusually, in comparison with Western countries, the mean systolic blood pressure above age 55 was 1–2 mmHg higher among women than among men. However, at ages 35–54 it was 1.5 mmHg lower among women than among men, despite the mean BMI being higher among women.

What are the main strengths and weaknesses?

This study's main strength is the large number of participants in a previously unstudied population, and the high background mortality rate in that population, meaning that the study will not need to wait a long time for a large number of deaths to occur. It should, therefore, be able fairly quickly to assess in detail many predictors of common causes of death in Chennai. Cause-and-effect relationships will be generalizable not only to Indian populations, but also more widely—for example, the case-control finding that smoking is a major cause of death from TB[1] has recently been confirmed by David Zaridze and his colleagues in Siberia. Robust data collection methods—including strict supervision, random checking and active follow-up—ensure that all of the collected information is reasonably accurate. The verbal autopsy tool is expected to overcome many of the well-known shortcomings of cause-of-death information on adult death certificates in most lower-income (and some higher-income[9]) countries. Correctly linking

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Table 4 Baseline distributions of selected disease risk factors in 500 816 adults aged 35 or more, by age and sex

	Percent, or mean (and standard deviation)					
	264 848 men, by age (years)			235 968 women, by age (years)		
	35–54	55–74	⩾75	35–54	55–74	⩾75
Number of participants	194 703	62 205	7940	164 420	63 778	7770
Current tobacco smokers	36.0	31.5	18.7	0.03	0.09	0.2
Bidi only	8.4	11.2	8.6	0.01	0.03	0.05
Cigarette only	25.2	18.4	8.4	0.01	0.02	0.04
Only bidi & cigarette	2.2	1.4	0.6	0	0.002	0
Other (chutta, cigar, pipe, hookah)	0.2	0.5	1.1	0.01	0.04	0.1
Ex-smokers	1.5	4.4	5.6	0.003	0.01	0.04
Never smokers	62.5	64.1	75.6	99.9	99.9	99.7
Current quid chewers	5.4	8.0	8.6	7.5	16.7	17.1
With tobacco	4.0	6.2	7.1	5.0	12.6	13.5
Not with tobacco	1.4	1.8	1.5	2.5	4.1	3.6
Ex-chewers	0.1	0.6	1.1	0.2	1.1	1.7
Never chewers	94.5	91.4	90.3	92.3	82.3	81.2
[% of tobacco chewers who smoke]	[34.9]	[22.9]	[15.7]	[0.1]	[0.2]	[0.3]
Current alcohol drinkers	27.5	21.3	11.3	0.04	0.08	0.04
Only Indian toddy/arrack	0.5	0.6	0.6	0.01	0.01	0
Only beer/brandy[a]	23.7	18.4	9.6	0.03	0.06	0.04
Only wine/whisky/rum/gin[a]	2.2	1.5	0.6	0.003	0.002	0
Any combination	1.1	0.8	0.5	0.001	0.002	0
Ex-drinkers	1.2	2.6	3.6	0.004	0.01	0
Never drank	71.3	76.1	85.0	99.96	99.91	99.96
BMI, kg/m^2	22.6 (3.3)	22.1 (3.6)	20.8 (3.7)	24.0 (4.4)	23.2 (4.6)	21.5 (4.5)
BMI <20	15.1	22.3	37.7	14.1	20.3	35.2
BMI 20–25	61.2	55.7	47.9	44.7	44.8	41.9
BMI 25–30	20.7	19.0	12.5	30.9	26.4	18.0
BMI ⩾30	3.0	3.0	2.0	10.3	8.5	4.9
Waist circumference, cm	82.8 (8.8)	82.8 (9.7)	80.0 (10.1)	–	–	–
PEFR, never smokers, L/min	412 (82)	347 (92)	277 (96)	297 (69)	251 (76)	202 (80)
PEFR, current smokers, L/min	393 (82)	328 (92)	260 (98)	–	–	–
SBP, mmHg	126.0 (12.5)	133.7 (17.9)	136.8 (21.2)	124.5 (15.7)	135.1 (20.6)	138.7 (24.3)
DBP, mmHg	83.0 (8.5)	84.9 (10.6)	83.7 (12.4)	81.8 (9.9)	84.7 (11.6)	84.0 (13.3)

Missing values: BMI (body mass index) M: 5%, F: 12%; waist circumference M: 7%, F: 100%; PEFR (peak expiratory flow rate) M: 6%, F: 13%; SBP/DBP (systolic/diastolic blood pressure) M: 5%, F: 12%.

[a]Beer and brandy are widely produced in India; wine, whisky, rum and gin are generally imported.

mortality data (from the Vital Statistics Division) and baseline data for the same individual is more challenging than in many settings because of the absence of a unique identifier and the varying usage (including spelling) of last names. However, modern computerized probabilistic matching methods[4] can help with this problem, although some human judgement (plus in some cases, extra fieldwork) is still necessary. Owing to resource limitations, the study was not able to collect and store biological specimens.

Where can I find out more?

Initial enquiries should be made to the principal investigator (VG) in Chennai (see www.ercchennai.com). An English-language version of the questionnaire, and associated coding conventions, is available at: www.ctsu.ox.ac.uk/chennai on the Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU) website.

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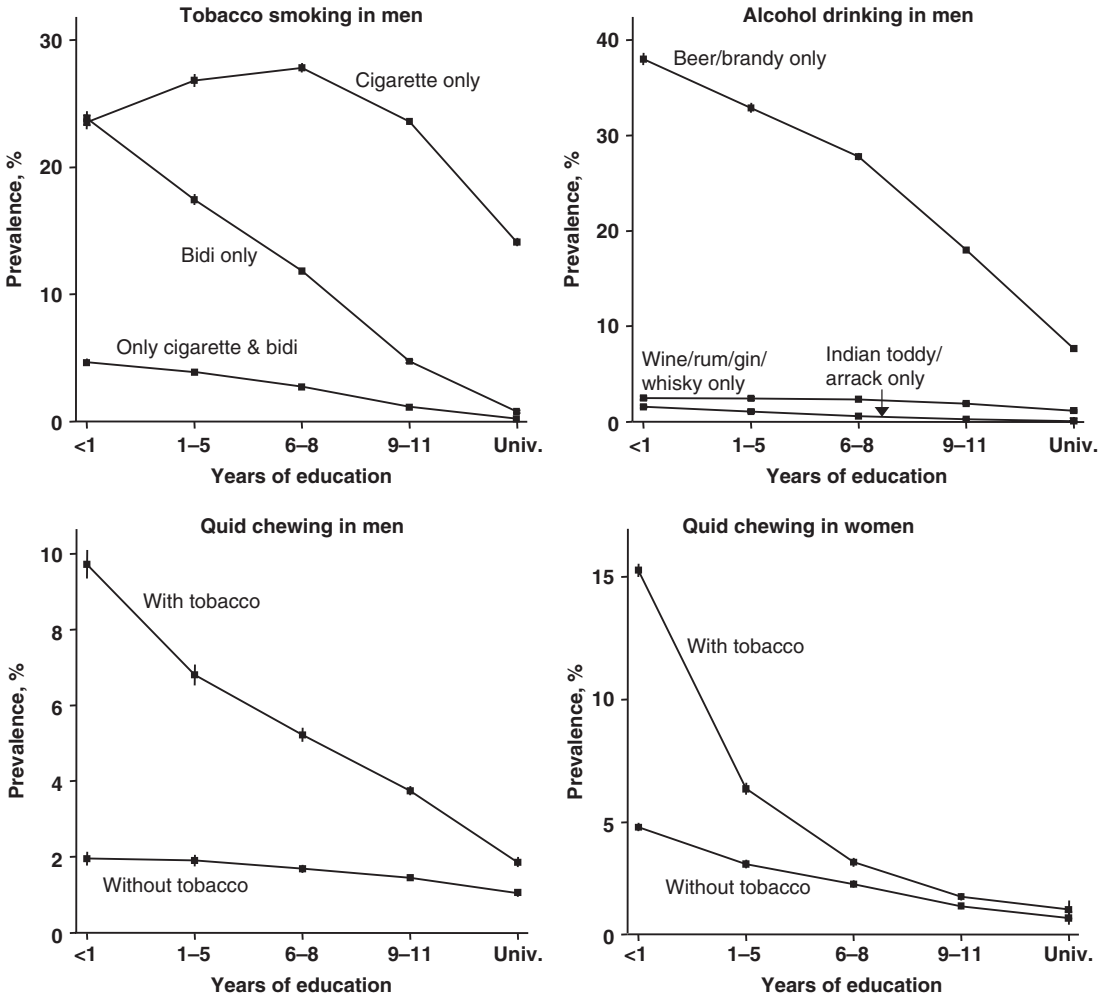

Figure 2 Smoking, alcohol drinking and chewing habits in 264 848 men, and chewing habits in 235 968 women, by highest education level. Prevalences standardized for age using the age distribution of the study population. Boxes are point estimates, and vertical lines are 95% confidence intervals (not visible if smaller than box). 'Univ.' means university or college. The smoking graph omits about 0.3% of men who smoked things other than cigarettes or bidis, and the alcohol graph omits about 1% of men who drank any combination of the three categories of alcohol displayed

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