# Effects of bidi smoking on all-cause mortality and cardiorespiratory outcomes in men from south Asia: an observational community-based substudy of the Prospective Urban Rural Epidemiology Study (PURE)

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## Summary

**Background** Bidis are minimally regulated, inexpensive, hand-rolled tobacco products smoked in south Asia. We examined the effects of bidi smoking on baseline respiratory impairment, and prospectively collected data for all-cause mortality and cardiorespiratory events in men from this region.

**Methods** This substudy of the international, community-based Prospective Urban Rural Epidemiology (PURE) study was done in seven centres in India, Pakistan, and Bangladesh. Men aged 35–70 years completed spirometry testing and standardised questionnaires at baseline and were followed up yearly. We used multilevel regression to compare cross-sectional baseline cardiorespiratory symptoms, spirometry measurements, and follow-up events (all-cause mortality, cardiovascular events, respiratory events) adjusted for socioeconomic status and baseline risk factors between non-smokers, light smokers of bidis or cigarettes (≤10 pack-years), heavy smokers of cigarettes only (>10 pack-years), and heavy smokers of bidis (>10 pack-years).

**Findings** 14 919 men from 158 communities were included in this substudy (8438 non-smokers, 3321 light smokers, 959 heavy cigarette smokers, and 2201 heavy bidi smokers). Mean duration of follow-up was 5·6 years (range 1–13). The adjusted prevalence of self-reported chronic wheeze, cough or sputum, dyspnoea, and chest pain at baseline increased across the categories of non-smokers, light smokers, heavy cigarette smokers, and heavy bidi smokers (p<0·0001 for association). Adjusted cross-sectional age-related changes in forced expiratory volume in 1 s ($FEV_1$) and $FEV_1$/forced vital capacity (FVC) ratio were larger for heavy bidi smokers than for the other smoking categories. Hazard ratios (relative to non-smokers) showed increasing hazards for all-cause mortality (light smokers 1·28 [95% CI 1·02–1·62], heavy cigarette smokers 1·59 [1·13–2·24], heavy bidi smokers 1·56 [1·22–1·98]), cardiovascular events (1·45 [1·13–1·84], 1·47 [1·05–2·06], 1·55 [1·17–2·06], respectively) and respiratory events (1·30 [0·91–1·85], 1·21 [0·70–2·07], 1·73 [1·23–2·45], respectively) across the smoking categories.

**Interpretation** Bidi smoking is associated with severe baseline respiratory impairment, all-cause mortality, and cardiorespiratory outcomes. Stricter controls and regulation of bidis are needed to reduce the tobacco-related disease burden in south Asia.

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## Introduction

Tobacco use is the world's leading preventable cause of premature death.[1] The harmful effects of cigarette smoking have been extensively studied and are universally accepted. Less is known about the health effects of non-cigarette tobacco products, such as bidis (also known as beedis), which are commonly used in populations of low socioeconomic status.

Bidis are inexpensive, small, hand-rolled tobacco products commonly smoked in south Asia. Estimates suggest that there were 53 million users of bidis in India and Bangladesh in 2003–09.[2] Outside this region, bidi use has mainly been reported in young adults in developed countries,[3] where unregulated marketing over the internet and in ethnic stores has allowed easy access to this vulnerable population. Bidis are manufactured in south Asia by a cottage industry that has avoided many of the local and international tobacco regulations and taxes enforced on factory-made cigarettes. Consequently, bidis are sold cheaply, at various prices and in packaging with poorly visible health warnings.[4–6] Furthermore, herbal and flavoured varieties are made to appeal to young adults as

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## Research in context

**Evidence before this study**

We searched PubMed, Embase, the Cochrane database, and bibliographies of retrieved articles for relevant reports published in English between Jan 1, 1960, and Jan 1, 2016. We used key search terms "beedi", "beedis", "bidi", "bidis", "tobacco-smoking", and "India", "south Asia" to identify reports of bidi smoking on health outcomes including mortality, cardiorespiratory health, and lung function in south Asia. We found few reports published after 2000. Previous publications were not methodologically robust, and reported data derived from retrospective, cross-sectional, or case-control studies with limited and variable adjustments for potential confounders such as differences in socioeconomic and baseline risk factors. Furthermore, very few studies directly compared the effects of bidi smoking with cigarette smoking on cardiorespiratory outcomes and lung function.

**Added value of this study**

To our knowledge, this is the largest prospective multisite study with standardised approaches for data collection (covariates, cardiorespiratory symptoms, and lung function measurements) and ascertainment of follow-up outcomes (deaths and cardiorespiratory events) in India, Bangladesh, and Pakistan. We examined the effects of cigarette and bidi smoking on several outcomes, adjusting for important differences in socioeconomic and baseline risk factors. A coherent pattern of worst outcomes was seen for bidi smokers, including highest self-reported baseline respiratory symptoms, obstructive ventilatory impairment, and follow-up mortality and cardiorespiratory events compared with cigarette smokers and non-smokers.

**Implications of all the available evidence**

Our findings fill an important gap in knowledge about the many harmful health effects of bidi smoking. These findings can be used for evidence-based practice and policy making that will help bring about greater controls on bidi use in south Asia.

"natural and safe" tobacco alternatives to cigarettes.[3] This claim contrasts with the toxicology data, which have shown higher nicotine, tar, and carbon monoxide levels delivered for a lower content of tobacco in bidis than in cigarettes.[7] However, there is a paucity of clinical data on the health effects of bidis. Most of these data are derived from retrospective, cross-sectional, or case-control studies, most with small sample sizes and limited adjustments for a wide range of potential confounders.[8–11]

We prospectively assessed the effects of bidi and cigarette smoking on mortality, respiratory, and cardiovascular outcomes in an unselected community-based cohort of men in south Asia. All comparisons were adjusted for differences in socioeconomic status, user-specific characteristics, and baseline risk factors. Furthermore, cross-sectional comparisons of self-reported baseline respiratory symptoms and spirometry measurements were done to provide information about baseline respiratory morbidity. The high prevalence of low-intensity smoking (ie, ≤10 pack-years) in this cohort provided an opportunity to assess the effects of low-intensity tobacco smoking on health outcomes.

## Methods

### Study design and participants

This substudy of the Prospective Urban Rural Epidemiology (PURE) study included community-based participants from India (five centres), Pakistan (one centre), and Bangladesh (one centre). Details of the overall PURE study design have been described elsewhere[12] and are summarised in the appendix (pp 5–9). The centres were purposely chosen to provide a diverse range of economic, physical, and sociocultural environments, balanced by the feasibility of centres to achieve long-term follow-up. Standardised approaches were used for the enumeration of households, identification of individuals, recruitment, and data collection. The methods of approaching households differed between countries, but aimed to avoid biases in participant selection. Households with at least one member aged 35–70 years who were intending to stay locally for more than 4 years were approached. The final sample size for analysis varied by the outcome of interest and included only men with no missing data relevant for the outcome of interest. Only men were selected because the rate of smoking in women in south Asia were low. Similarly, former and current smokers were combined as ever-smokers for all analyses.

See Online for appendix

All eligible individuals who provided written informed consent were enrolled. Baseline data were collected from Jan 1, 2003, to Dec 30, 2009, and follow-up data from Jan 1, 2008, to Dec 30, 2013. The study was coordinated by the Population Health Research Institute (Hamilton, ON, Canada) and approved by the Hamilton Health Sciences Research Ethics Board and by the local ethics committee at each site.

### Procedures

Standardised interview-based questionnaires adapted from previous cohort studies (appendix p 10) were administered by trained personnel to household members aged 35–70 years. The questionnaire elicited demographic, household, behavioural, and medical information (risk factors, symptoms, comorbid disorders). Bidi and cigarette use was defined as self-reported duration of use more than 0 days or quantity more than none per day. Former smokers were defined as individuals who had not smoked for at least 12 months. Participants were classified into four categories based on the number of pack-years of smoking (duration [years]×quantity [sticks per day] divided by 20) and tobacco type: non-smokers of bidis or cigarettes (never-smokers), light smokers of either or both products (≤10 pack-years), heavy smokers of cigarettes only (>10 pack-years), and heavy smokers of bidis (including concurrent use of cigarettes; >10 pack-years). Other relevant data included cooking fuel (solid or kerosene *vs* gas or electricity), education, asset index, proportion of income spent on food, physical activity, dietary intake, and cardiorespiratory symptoms (dyspnoea with usual activity; wheeze; cough or sputum; chest pain) occurring at least weekly in the previous 6 months.

Household owned items were used to generate an asset index, an indicator of wealth. Physical activity was assessed with the International Physical Activity Questionnaire (IPAQ).[13] Dietary intake was assessed with a validated food frequency questionnaire.[14] Physical measurements were collected by standardised methods for anthropometrics, blood pressure, handgrip strength, and spirometry. An individualised INTERHEART risk score was calculated with the version excluding cholesterol concentration. This score provided a validated and quantitative measure of the risk-factor burden for cardiovascular disease, which incorporates information about self-reported age, sex, cigarette use, diabetes, family history of cardiovascular disease, psychosocial factors, diet, physical activity, and measured waist-to-hip ratio and hypertension (≥140/90 mm Hg).[15]

Lung function was measured with a portable spirometer (MicroGP, MicroMedical Ltd, Chatham, IL, USA), which did not generate spirograms. Each participant attempted up to six forced prebronchodilator manoeuvres while standing and wearing a nose clip. Each manoeuvre was closely observed for maximal effort, with exhalation time 6 s or more and without coughing. Spirometers were calibrated monthly (3 L syringe) or before each use in extreme temperature or handling. For analyses, we selected participants with at least two forced expiratory volume in 1 s ($FEV_1$) and forced vital capacity (FVC) measurements within 200 mL variability. The quality of the spirometry data in PURE have previously been

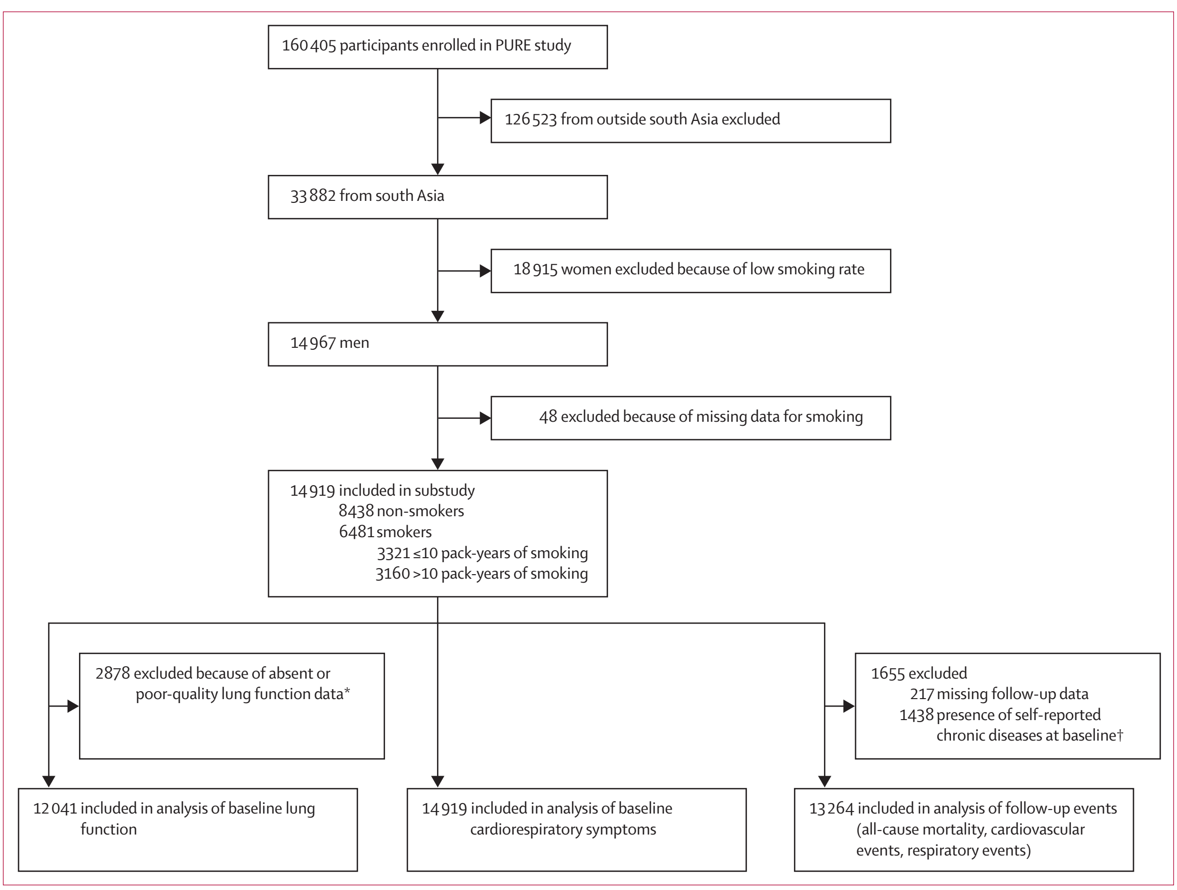


***Figure 1:* Participant selection for the substudy**
PURE=Prospective Urban Rural Epidemiology Study. *Participants with poor-quality lung function data were those with less than two measurements of forced expiratory volume in 1 s ($FEV_1$) or forced vital capacity (FVC), or with variability between two the highest $FEV_1$ or FVC measurements of >200 mL. †Participants with self-reported diagnoses of cardiorespiratory disease, stroke, cancer, tuberculosis, or HIV infection at baseline were excluded from the analysis of follow-up events.

validated for external, internal, and face validity (appendix pp 11–16).[16] The highest $FEV_1$, FVC, and $FEV_1$/FVC ratio recorded for each individual was included in the analysis.

Participants were followed up with yearly telephone calls and face-to-face interviews every 3 years. At each contact, participants, or close relatives in cases of deaths (via verbal autopsy[17]), were questioned as to whether any clinical events had occurred and if so, documentation was obtained for event adjudication by the site investigators using standard definitions (appendix pp 17–20). Furthermore, a random subset of events from each site was assessed centrally (Population Health Research Institute) to ensure consistency in the adjudicated events.

To ensure standardisation and data quality, comprehensive operations manuals, reinforced by periodic training workshops, training DVDs, and regular communication were used in all sites. Data were entered locally by each site into a customised database programmed with range and consistency checks and transmitted electronically to the coordinating centre, where further quality control measures were implemented.

| | Non-smokers (n=8438) | Light smokers (n=3321) | Heavy cigarette smokers (n=959) | Heavy bidi smokers (n=2201) |
|---|---|---|---|---|
| Tobacco type | | | | |
| Cigarettes only | .. | 1811 (55%) | 959 (100%) | 0 |
| Bidis only | .. | 1330 (40%) | 0 | 1627 (74%) |
| Both | .. | 180 (5%) | 0 | 574 (26%) |
| Smokeless tobacco use* | 696 (8%) | 227 (7%) | 57 (6%) | 121 (5%) |
| Age (years) | 49·3 (10·6) | 47·9 (10·0) | 53·0 (9·1) | 51·9 (10·1) |
| Height (cm) | 164·9 (7·4) | 165·1 (7·2) | 165·4 (6·9) | 164·2 (6·7) |
| Weight (kg) | 63·6 (13·7) | 59·8 (13·4) | 63·2 (13·6) | 54·0 (10·8) |
| Body-mass index (kg/m²) | 23·4 (4·4) | 22·0 (4·3) | 23·0 (3·9) | 20·2 (3·5) |
| Urban residency | 4649 (55%) | 1414 (43%) | 578 (60%) | 504 (23%) |
| Education | | | | |
| Secondary or higher | 5595 (67%) | 1836 (56%) | 633 (66%) | 615 (28%) |
| Primary or none | 2695 (33%) | 1456 (44%) | 321 (34%) | 1573 (72%) |
| Missing data | 148 (2%) | 29 (1%) | 5 (1%) | 13 (1%) |
| Asset index† | −0·8 (1·0) | −1·3 (0·8) | −0·7 (0·7) | −1·5 (0·5) |
| Proportion of income spent on food (%)‡ | 54·3% (26·2) | 62·3% (25·0) | 58·5% (23·1) | 68·3% (22·4) |
| Cooking fuel | | | | |
| Gas or electricity | 4735 (61%) | 1338 (43%) | 583 (62%) | 394 (21%) |
| Kerosene or solid fuel | 3021 (39%) | 1751 (57%) | 353 (38%) | 1502 (79%) |
| Missing data | 682 (8%) | 232 (7%) | 23 (2%) | 305 (14%) |
| Manual labour occupations§ | 2267/8438 (45%) | 987/3321 (63%) | 421/959 (60%) | 1114/ (87%) |
| Location¶ | | | | |
| Bangladesh | 572 (7%) | 312 (9%) | 211 (22%) | 238 (11%) |
| Chandigarh, India | 1392 (16%) | 89 (3%) | 18 (2%) | 127 (6%) |
| Chennai, India | 1265 (15%) | 473 (14%) | 116 (12%) | 306 (14%) |
| Thiruvananthapuram, India | 985 (12%) | 549 (17%) | 309 (32%) | 228 (10%) |
| Bengaluru, India | 2487 (29%) | 1426 (43%) | 146 (15%) | 792 (36%) |
| Jaipur, India | 1190 (14%) | 344 (10%) | 13 (1%) | 507 (23%) |
| Pakistan | 547 (6%) | 128 (4%) | 146 (15%) | 3 (<1%) |

(Table 1 continues on next page)

## Statistical analysis

We used multilevel marginal regression to estimate the effect size by smoking category on outcomes relative to non-smokers adjusted for age, body-mass index, asset index, education, cooking fuel, INTERHEART risk score, diabetes, hypertension, and centre (except for spirometry measurements and respiratory events). Community was treated as a random effect to account for data clustering. Logistic regression provided estimates on the adjusted prevalence and odds ratios (ORs) for cross-sectional baseline symptoms. We used linear regression to compare the cross-sectional age-related changes on baseline $FEV_1$ and $FEV_1$/FVC ratio by smoking category adjusted for height, weight, centre, and education ($FEV_1$) or age, height, and centre ($FEV_1$/FVC ratio). We used Cox proportional hazards models to estimate the incidences and hazard ratios (HRs) for all-cause mortality and cardiovascular events (myocardial infarction, stroke, heart failure, sudden death, cardiovascular-related death, and cardiovascular-related hospital admission). For respiratory events (chronic obstructive pulmonary disease, asthma, pneumonia, tuberculosis), the same Cox model was used but without INTERHEART risk score, diabetes, and hypertension as covariates. To compare the effect size estimates by smoking category, smoking category was fitted as a categorical variable and its coefficient reflects the nature of association between effect size and smoking category.

There was no formal sample size calculation for this substudy. We assessed the adequacy of the sample size using guidelines proposed by Concato and colleagues,[18] which recommend that for Cox regression at least ten events for each degree of freedom (df) are needed to provide stable models. There were 685 deaths, 552 cardiovascular events, and 269 respiratory events recorded during follow-up. The model for deaths and cardiovascular events contained nine covariates including the smoking categories, giving a total of 22 df. For the respiratory event model, there were five covariates giving a total of 16 df. Thus the events per df for mortality, cardiovascular, and respiratory events were 31 (685/22), 25 (552/22), and 16 (269/16), respectively. These estimates are all greater than ten events per df, indicating the sample size was adequate to provide stable models for all three event outcomes.

Some sensitivity analyses were carried out to examine for any changes to our main findings on outcome events using different criteria for selection of study population (including participants with significant baseline comorbidities); classification of smoking categories (excluding former smokers or smokers of both bidis and cigarettes) and using different socioeconomic status covariates (education, rural or urban location, percent income spent of food, and the combination of these). All analyses were done with SAS version 9.2. No adjustments for multiplicity of analysis were made.

## Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data 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

14 919 men from 158 communities across seven centres in south Asia were included in this substudy (figure 1). Bidi smoking was more common in India, whereas cigarette smoking was more common in Bangladesh and Pakistan (table 1). A small proportion of smokers reported using both tobacco types; bidis were the predominant type. The demographics of participants who smoked both bidis and cigarettes were similar to the demographics of those who smoked bidis only; we therefore reclassified this group as bidi smokers (appendix p 21). A small and similar proportion of participants across the smoking categories reported the use of smokeless tobacco. There was a small proportion of former smokers and the numbers were evenly distributed across the smoking categories. Overall, heavy bidi smokers were more likely to come from rural communities and have a low socioeconomic status than were men in all other smoking categories (lower education and asset index; higher percentages of income spent on food, manual labour occupations, and use of solid or kerosene cooking fuels).

The adjusted prevalence of self-reported chronic cardiorespiratory symptoms at baseline was significantly higher in heavy cigarette smokers and heavy bidi smokers than in non-smokers (table 2, figure 2). The largest effect was seen for chronic cough and sputum. Light smokers showed a modest increase in adjusted prevalence of chronic symptoms relative to non-smokers; however, because of low reported rates of wheeze and dyspnoea, the increase in these symptoms was not significant. The prevalence of chronic symptoms at baseline increased across the categories of non-smokers, light smokers, heavy cigarette smokers, and heavy bidi smokers ($p<0 \cdot 001$ for association).

For the cross-sectional analysis of spirometry measurements, centres from Pakistan, Jaipur (India), and Bangladesh were excluded because of high proportions of participants with missing spirometry data (figure 1). We therefore examined spirometry data from the five centres in India. The adjusted cross-sectional age-related changes in $FEV_1$ and $FEV_1$/FVC ratio were significantly larger for heavy bidi smokers than for men in the other smoking categories (table 3, figure 3). This finding suggests increasingly lower lung function in the older age groups of bidi smokers. By contrast, age-related changes in $FEV_1$ did not differ between non-smokers, light smokers, and heavy cigarette smokers. However, similar pairwise comparison showed a significantly reduced $FEV_1$/FVC ratio, suggesting mild obstructive ventilatory impairment, in light smokers and heavy cigarette smokers compared with non-smokers.

Mean duration of follow-up was 5·6 years (range 1–13). 13 264 (98%) participants completed follow-up, with a similar proportion in each smoking category (7554 [98%] non-smokers; 2966 [98%] light smokers; 819 [99%] heavy cigarette smokers; 1925 [98%] heavy bidi smokers). Participants with self-reported baseline cardiovascular disease, respiratory disease, cancer, or HIV infection were excluded from the analysis of follow-up events (figure 1). The demographics of the excluded and included participants were similar (appendix pp 21). In the analysis population, there were 685 deaths, 552 cardiovascular events, and 269 respiratory events (table 4). Heavy bidi smokers had the highest incidence of follow-up events compared with men in the other smoking categories (table 4, figure 4). The largest effect of heavy bidi smoking was on respiratory events. The incidence of follow-up events in light smokers and heavy cigarette smokers was intermediate between that for non-smokers and heavy bidi smokers; however, the increase in incidence of respiratory events in light smokers and heavy cigarette smokers compared with non-smokers was not significant. The HRs for follow-up events increased across the categories of light smokers, heavy cigarette smokers, and heavy bidi smokers.

We did sensitivity analyses that included all participants with complete vital statistics; adjusted for other indicators

| | Non-smokers (n=8438) | Light smokers (n=3321) | Heavy cigarette smokers (n=959) | Heavy bidi smokers (n=2201) |
|---|---|---|---|---|
| (Continued from previous page) | | | | |
| Smoking history | | | | |
| Age of smoking initiation (years) | ·· | 31·0 (11·6) | 22·7 (8·4) | 22·7 (9·1) |
| Duration of smoking (years) | ·· | 15·7 (10·6) | 29·2 (10·1) | 28·7 (11·0) |
| Tobacco sticks smoked per day | ·· | 6·1 (5·0) | 18·2 (13·6) | 21·0 (11·7) |
| Tobacco stick-years¶ | ·· | 83·0 (61·4) | 494·3 (378·6) | 575·4 (393·3) |
| Pack-years‖ | ·· | 4·2 (3·1) | 24·7 (18·9) | 28·8 (19·7) |
| Current smokers** | ·· | 2934 (88%) | 807 (84%) | 1995 (91%) |
| Former smokers | ·· | 364 (11%) | 145 (15%) | 192 (9%) |
| Missing data | ·· | 23 (1%) | 7 (1%) | 14 (1%) |

Data are n (%) or mean (SD). Non-smokers self-reported no bidi or cigarette use at baseline survey; light smokers reported smoking ten or fewer pack-years of either bidis, cigarettes, or both; and heavy smokers (>10 pack-years) are divided into those who smoked cigarettes only and those who smoked bidis with or without cigarettes. ··=not applicable. *Smokeless tobacco use was defined as self-reported duration of use more than 0 days or quantity more than none per day of smokeless tobacco (chewed tobacco, snuff, or rolled tobacco leaves). †Asset index is the non-monetary aspect of wealth based on the number and type of household items owned (a high positive value indicates greater wealth). ‡Lower-income families spend a greater percentage of total income on food. §Manual labour includes workers in agricultural, fishery, and craft industries, plant/machine operators, assemblers, and elementary workers; missing data mainly due to retirement. ¶Tobacco stick-years=number of tobacco sticks smoked per day × duration of smoking (years). ‖Pack-years=tobacco stick-years/20. **Current smokers were defined as individuals who reported use of at least one tobacco stick per day within 12 months.

*Table 1:* **Baseline characteristics**

| | Non-smokers (n=8438) | Light smokers (n=3321) | Heavy cigarette smokers (n=959) | Heavy bidi smokers (n=2201) |
|---|---|---|---|---|
| **Wheeze** | | | | |
| Number | 425 | 234 | 69 | 242 |
| Adjusted prevalence (95% CI) | 4·3% (3·4–5·4) | 5·1% (3·9–6·6) | 6·1% (4·2–8·7) | 8·0% (6·2–10·2) |
| Adjusted OR (95% CI) | 1·0 | 1·20 (0·97–1·50) | 1·45 (1·10–1·92) | 1·95 (1·59–2·39) |
| p value | ·· | 0·092 | 0·009 | <0·0001 |
| **Cough or sputum** | | | | |
| Number | 1094 | 686 | 214 | 696 |
| Adjusted prevalence (95% CI) | 12·9% (11·0–15·2) | 17·9% (15·2–20·8) | 21·4% (18·1–25·1) | 26·7% (23·2–30·5) |
| Adjusted OR (95% CI) | 1·0 | 1·46 (1·27–1·69) | 1·83 (1·49–2·24) | 2·45 (2·07–2·89) |
| p value | ·· | 0·0001 | 0·0001 | 0·0001 |
| **Dyspnoea with usual activity** | | | | |
| Number | 966 | 469 | 170 | 508 |
| Adjusted prevalence (95% CI) | 12·8% (11·4–14·3) | 15·0% (13·3–16·8) | 19·7% (16·4–23·4) | 19·6% (16·6–23·0) |
| Adjusted OR (95% CI) | 1·0 | 1·20 (1·05–1·39) | 1·67 (1·36–2·06) | 1·67 (1·36–2·04) |
| p value | ·· | 0·010 | <0·0001 | <0·0001 |
| **Chest pain** | | | | |
| Number | 1241 | 677 | 181 | 612 |
| Adjusted prevalence (95% CI) | 15·9% (14·5–17·5) | 19·9% (17·9–22·1) | 20·2% (17·5–23·1) | 23·6% (20·9–26·5) |
| Adjusted OR (95% CI) | 1·0 | 1·31 (1·16–1·48) | 1·33 (1·09–1·63) | 1·63 (1·40–1·89) |
| p value | ·· | 0·0001 | 0·006 | 0·0001 |

Self-reported baseline symptoms defined as those occurring at least weekly in the 6 months before the baseline survey. ORs (relative to non-smokers) were estimated with multilevel marginal logistic regression with age, asset index, body-mass index, and centre as covariates. Community was treated as a random effect to account for data clustering. OR=odds ratio.

*Table 2:* **Self-reported cardiorespiratory symptoms at baseline**

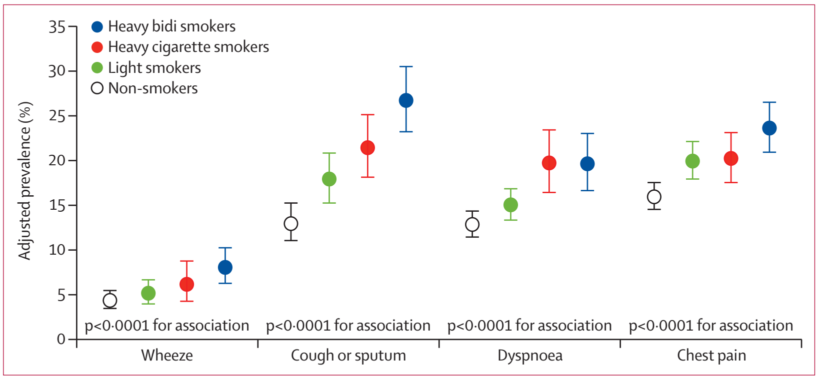


***Figure 2:*** **Self-reported cardiorespiratory symptoms at baseline**
Self-reported baseline symptoms defined as those occurring at least weekly in the 6 months before the baseline survey. p value for association examined the order effect in effect size by different smoking groups (as categorical variable). Error bars represent 95% CI.

of socioeconomic status alone or in combination; and excluded former smokers and smokers of both bidis and cigarettes (appendix p 23–24). Results of sensitivity analyses showed the conclusions remained unchanged.

## Discussion

In this prospective community-based cohort study of unselected men in south Asia, we recorded a high prevalence of bidi and cigarette use. Bidi smokers were more likely to be from rural areas and have low socioeconomic status. Accounting for these differences and additional baseline risk factors, bidi use was consistently associated with significantly increased prevalences and relative risks of baseline cardiorespiratory symptoms, low ventilatory capacity, and follow-up mortality and cardiorespiratory outcomes. Light smokers and heavy cigarette smokers also showed increased risks of death and cardiovascular events relative to non-smokers, but not for respiratory events. The observed pattern of greater baseline respiratory morbidity and higher risks of mortality and cardiorespiratory outcomes in heavy bidi smokers suggest that bidis are at least as harmful as cigarettes and contribute to the burden of tobacco-related disease and deaths in south Asia.

Our reported rates and pattern of bidi use are consistent with previous data, indicating a high prevalence of bidi smoking in south Asia, with geographical[19] and socioeconomic variation.[20,21] These baseline differences could potentially confound the relation between bidi smoking and health outcomes. Our large sample size and data on socioeconomic status and other characteristics made it possible to adjust for a large number of potentially important confounders, in order to derive an unbiased estimate of the independent effect of bidi smoking on cardiorespiratory health and mortality. In addition to the covariates included in the final model, we also explored other potential confounders in several sensitivity analyses and found their effects were small and did not substantially change the overall model or conclusions.

| | Non-smokers (n=6701) | Light smokers (n=2849) | Heavy cigarette smokers (n=800) | Heavy bidi smokers (n=1691) |
|---|---|---|---|---|
| **$FEV_1$** | | | | |
| Change per year, mL/s (95% CI) | –22·1 (–23·8 to –20·4) | –22·5 (–24·2 to –20·8) | –22·7 (–24·7 to –20·8) | –23·8 (–25·6 to –22·0) |
| Difference from non-smokers | 0 | –0·3 (–0·9 to 0·2) | –0·6 (–1·5 to 0·3) | –1·7 (–2·3 to –1·0) |
| p value | .. | 0·198 | 0·191 | <0·0001 |
| **$FEV_1$/FVC ratio** | | | | |
| Change per year (95% CI) | –0·145% (–0·171 to –0·119) | –0·160% (–0·184 to –0·136) | –0·158% (–0·184 to –0·132) | –0·180% (–0·207 to –0·153) |
| Difference from non-smokers | 0 | –0·015% (–0·027 to –0·003) | –0·013% (–0·028 to 0·002) | –0·035% (–0·049 to –0·022) |
| p value | .. | 0·012 | 0·097 | <0·0001 |

Multilevel marginal linear regression was used to estimate the cross-sectional age-related change in forced expiratory volume in 1 s ($FEV_1$) or $FEV_1$/forced vital capacity (FVC) ratio by smoking category adjusted for height, weight, centre, and education ($FEV_1$) or age, height, and centre ($FEV_1$/FVC ratio). Community was treated as a random effect. Differences in the cross-sectional age-related change relative to non-smokers were also adjusted for the same covariates.

***Table 3:*** **Cross-sectional age-related changes in $FEV_1$ and $FEV_1$/FVC ratio**

Few contemporary data exist about the respiratory effects of bidis. Early studies showed an association between bidi smoking with chronic cough and sputum.[22–25] In keeping with these findings, we noted that the prevalence and risk of cardiorespiratory symptoms were consistently higher in heavy bidi smokers than in men in the other smoking categories; bidi smokers also had the lowest adjusted ventilatory capacity. The finding for ventilatory capacity had not been consistently documented across earlier studies, which were limited by small sample sizes and variability in their adjustments of potential confounders.[24,26,27] Our study is the largest study so far to compare spirometry data between bidi and cigarette smokers. Our findings suggest lower ventilatory capacity and greater airflow obstruction in heavy bidi smokers, and together with a higher prevalence of cardiorespiratory symptoms indicate substantially higher rates of obstructive respiratory impairment in bidi smokers compared with other smokers. Heavy cigarette smokers and light smokers also showed lower adjusted lung function than did non-smokers, but the magnitude of this difference did not reach significance. This finding might relate to the smaller sample size in these subgroups or the greater variability in the effect of cigarette smoking on lung function.

Large population-based studies have examined the incidence of cancer, cardiovascular disease, and all-cause mortality in tobacco users in south Asia.[9,10,28–31] To our knowledge, only one other publication has reported on the effect of bidis separately from cigarettes on all-cause mortality (HR relative to never-smokers 1·64 [95% CI 1·47–1·81] for bidi smokers *vs* 1·37 [1·23–1·53] for cigarette smokers).[9] Our work supports and extends this finding by showing that the risks of cardiorespiratory events are also significantly increased with bidi smoking independent of socioeconomic status.

Several aspects of this study are worthy of discussion. First, our study population included a large number of light smokers, particularly of cigarettes. Separating out the light smokers provided a more balanced and matched distribution of smoking intensity and smoking pattern between heavy bidi smokers and heavy cigarette smokers for comparison. We found that low-intensity smoking can also be associated with respiratory impairment at an

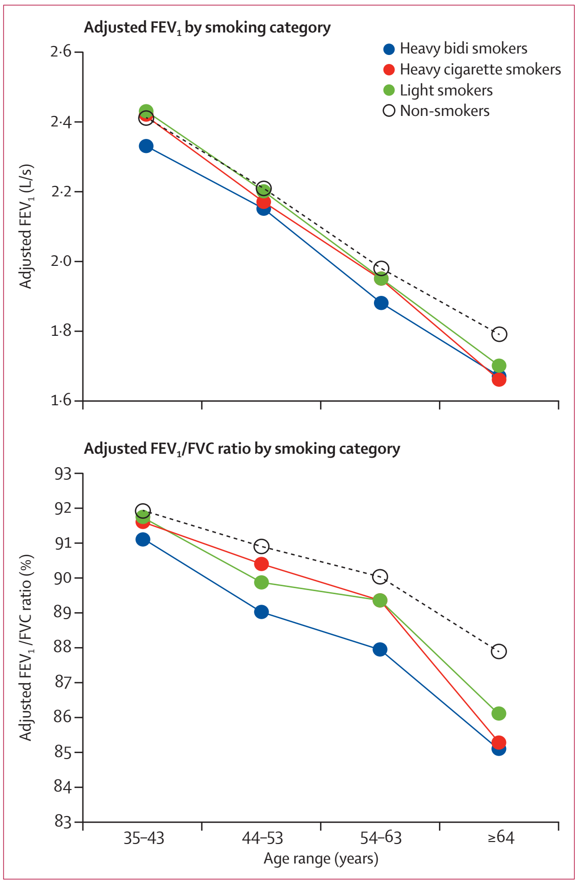


***Figure 3:*** **Mean adjusted $FEV_1$ and $FEV_1$/FVC ratio by age group**
Multilevel marginal linear regression was used to model forced expiratory volume in 1 s ($FEV_1$) by age group and smoking category with height, weight, centre, and education as covariates (reference: non-smokers) and community as a random effect. A similar model was used for the comparison of $FEV_1$/forced vital capacity (FVC) ratio by age group and smoking category with age, height, and centre as covariates (reference: non-smokers) and community as a random effect.

| | Non-smokers (n=7554) | Light smokers (n=2966) | Heavy cigarette smokers (n=819) | Heavy bidi smokers (n=1925) |
|---|---|---|---|---|
| **Cardiovascular events** | | | | |
| Number | 234 | 144 | 65 | 109 |
| Adjusted incidence (95% CI) | 3·1% (2·4–3·9) | 4·6% (3·4–6·3) | 4·4% (3·0–6·3) | 5·1% (3·5–7·3) |
| Adjusted HR (95% CI) | 1·0 | 1·45 (1·13–1·84) | 1·47 (1·05–2·06) | 1·55 (1·17–2·06) |
| p value | .. | 0·003 | 0·023 | 0·002 |
| **Respiratory events** | | | | |
| Number | 99 | 61 | 27 | 82 |
| Adjusted incidence (95% CI) | 0·7% (0·4–1·1) | 0·9% (0·6–1·5) | 0·8% (0·4–1·5) | 1·3% (0·8–2·2) |
| Adjusted HR (95% CI) | 1·0 | 1·30 (0·91–1·85) | 1·21 (0·70–2·07) | 1·73 (1·23–2·45) |
| p value | .. | 0·154 | 0·496 | 0·002 |
| **Deaths** | | | | |
| Number | 279 | 165 | 58 | 183 |
| Adjusted incidence (95% CI) | 2·3% (1·7–3·0) | 3·1% (2·1–4·5) | 3·3% (2·2–5·0) | 3·8% (2·7–5·5) |
| Adjusted HR (95% CI) | 1·0 | 1·28 (1·02–1·62) | 1·59 (1·13–2·24) | 1·56 (1·22–1·98) |
| p value | .. | 0·034 | 0·008 | <0·0003 |

New cardiovascular events (cardiovascular-related death, myocardial infarction, heart failure, stroke, and cardiovascular-related hospital admission), respiratory events (chronic obstructive pulmonary disease [COPD], pneumonia, tuberculosis, asthma), and all-cause mortality at a mean follow-up of 5·6 years. Incidence and HRs (relative to non-smokers) for all-cause mortality and cardiovascular events were adjusted for age, body-mass index, asset index, education, handgrip, INTERHEART risk score, diabetes, and hypertension, and centre as fixed-effect covariates, and community as a random effect in a multilevel marginal Cox proportional hazards model. For respiratory events, the same model was used but without INTERHEART risk score, diabetes, and hypertension as covariates in the model. HR=hazard ratio. *Participants with missing data or with self-reported diagnoses of stroke, heart disease, cancer, COPD, asthma, tuberculosis, or HIV infection were excluded from the analysis.

***Table 4:*** **Respiratory events, cardiovascular events, and deaths during follow-up***

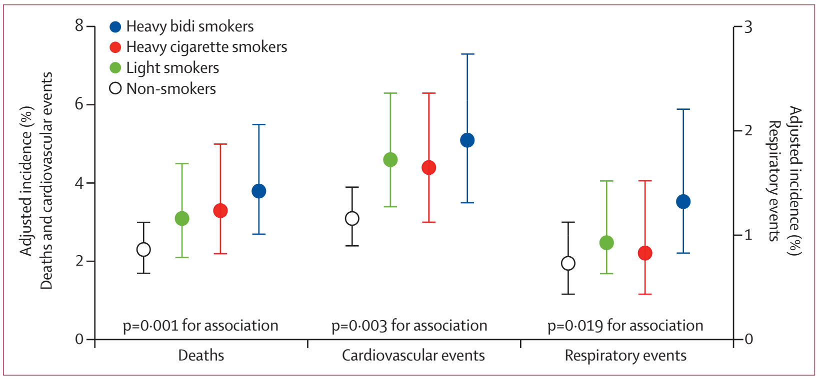


***Figure 4:*** **Respiratory events, cardiovascular events, and deaths during follow-up**
New cardiovascular events (cardiovascular-related death, myocardial infarction, heart failure, stroke, and cardiovascular-related hospital admission), respiratory events (chronic obstructive pulmonary disease, pneumonia, tuberculosis, asthma), and all-cause mortality at a mean follow-up of 5·6 years. Hazard ratios (relative to non-smokers) for all-cause mortality and cardiovascular events were estimated with a marginal Cox proportional hazards model with age, education, asset index, body-mass index, handgrip, self-reported diabetes, hypertension, INTERHEART risk score, and centre as fixed effects and community as a random effect. For respiratory events, the same model was used but without INTERHEART risk score, diabetes, and hypertension as covariates in the model. p value for association examined the order effect in effect size by different smoking groups (as categorical variable). Error bars represent 95% CI.

exposure level that is often considered to be clinically trivial. Furthermore, this level of exposure was associated with increased risks of cardiovascular events and mortality compared with not smoking. This finding suggests that there is no threshold that can be considered safe from the harmful effects of tobacco smoking. Second, bidis are smaller with less tobacco content and are generally sold in different quantities from cigarettes. These differences make comparison of the two tobacco types using a common unit of exposure such as pack-years difficult. To maintain consistency and allow ease of comparison with the literature on tobacco, we continued to use pack-years to define the groups. However, any interpretation of the effect size of bidi use on outcomes must take into account of the lower tobacco content in bidis compared with cigarettes.[7] Finally, only participants with no previous cardiorespiratory morbidity, cancer, or HIV infection were analysed for follow-up events to avoid the effect of reverse causality on our findings.

There are limitations and strengths to our study. It was not feasible to aim for strict proportionate sampling in this large prospective cohort study. The design did not use standard random sampling but adopted a design that avoided biases in levels of risk factors and prevalence of disease conditions. Second, lung function was measured with a portable spirometer that did not provide flow-volume curves and therefore verification of individual effort was not possible. However, we had previously validated this method by comparing data obtained in certified pulmonary function laboratories with data obtained by PURE methods for 531 participants from participating sites including south Asia; we noted high correlations without biases.[16] Further, there is no a-priori reason to expect differential effects in methods on spirometry measurements between different smoking groups. The major strengths of our study include the large sample size, the prospective and standardised approach to data collection and outcome ascertainment, all of which provide for a robust and systematic analysis, and adjustment for a large number of potential confounders.

Our findings have important public health implications. South Asia is the second largest consumer of tobacco in the world, with more than 130 million tobacco smokers.[2] More than half these smokers use bidis, particularly among the poorest and most vulnerable sectors of the population. Therefore the health impact of bidis is highly relevant in this region. Furthermore, as the current trend of bidi exportation continues, the global impact of bidis will rise, particularly among young adults. Our findings suggest that bidis are at least as harmful as cigarettes on cardiorespiratory health and mortality, despite having substantially less tobacco content than cigarettes. Control of bidis should be an integral part of any anti-tobacco framework, both regionally and globally, with the greatest potential effects to be seen in poor and young people.

**Contributors**
All authors contributed to the intellectual conceptualisation of PURE, study design, planning, and collection of PURE data. MD, SR, XZ, KK,

and SY contributed to the statistical analysis and wrote the report. All authors contributed to the final approval of the report. MD, KK, POB, and SY take full responsibility for the overall content of this work.

**Declaration of interests**

We declare no competing interests.

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