participated in the study. Excluded from analysis were 2 subjects who displayed URTI on the first day of intervention, and 1 subject who did not write in the diary at all (follow-up, 99%). Included in the analysis were a total of 384 patients, with 122 patients in the water-gargling group, 132 patients in the povidone/iodine-gargling group, and 130 patients in the control group. Baseline characteristics and outcomes of gargling and control groups are shown in Table 1.

Gargling groups were instructed to gargle with approximately 20 ml of water or povidone-iodine for about 15 s, 3 times/day. Control groups were instructed to retain previous gargling habits. The primary outcome measure was first URTI incidence within 60 days. Sample size of the trial was calculated at a power level of 0.90 and a significance level of 0.05. Analyses were performed on an intention-to-treat basis.

Frequency of gargling and presence of various URTI complaints in all subjects were also assessed using the self-administered record (gargling diary). All URTI complaints, such as nasal symptoms, pharyngeal symptoms, bronchial symptoms, pharyngeal symptoms, bronchial symptoms and general symptoms were recorded and classified by each subject into 4 grades as none, mild, moderate or severe, according to Jackson methods[6]. "Mild" was defined as being unaware of the symptom when busy, "moderate" as always feeling discomfort, and "severe" as having difficulties in completing the usual activities of daily living. Subjects who developed URTI were asked to continue completing the gargling diary for 1 week after onset of URTI symptoms to confirm the incidence and severity of URTI.

No subjects assigned to the water-gargling group skipped gargling, while 36 subjects (28%) in the control group did not gargle at all. Compared to 50 subjects (40.8% by Kaplan-Meier estimation) in the control group, 34 subjects (30.1%) in the water-gargling group ($p = 0.044$) and 46 subjects (37.2%) in the povidone/iodine-gargling group ($p = 0.59$) had developed URTI as of day 60. Incidences were lower in water-gargling subjects (0.34 episodes/60 person-days) and povidone/iodine-gargling subjects (0.48 episodes/60 person-days) than in controls (0.52 episodes/60 person-days), and rate ratios compared to controls were 0.64 (95% confidence interval (95%CI), 0.42–0.99) and 0.89 (95%CI, 0.60–1.33), respectively. In the present study, the cost and effectiveness of water gargling were determined by comparison with the control group. All study protocols were approved by the ethics committee of Kyoto University.

Costs of care

The 60-day cumulative follow-up costs for all trial participants were estimated from a societal perspective. All costs were converted into US dollars according to Purchasing Power Parities in 2005[7], with a dollar considered equivalent to about 128 Japanese yen.

Costs of gargling, physician consultations due to URTI, medications to treat URTI, and lost productivity due to severe URTI were estimated (Table 1). Costs of gargling were estimated as the opportunity costs of the time required for gargling by multiplying the time to complete a single session of gargling, the frequency of gargling in each group, and the mean wage of Japanese workers[8]. Time to complete a single session of gargling, including going to and returning from the washroom, was determined based on 12 individuals who were not participants in this trial, with gargling considered to require an average of 71 s.

The cost of a physician consultation was estimated by multiplying the proportion of subjects who visited physicians due to URTI and the costs involved in such visits. The proportion of subjects who visited physicians was obtained from the literature[9], since this information was not recorded in the gargling trial. The cost of physician consultation was estimated from the sum of the first visit fee, the cost of the time required for the consultation, and the transportation fee. The latter two costs were obtained from the Patients' Behavior Survey[10], with time converted to a cost based on national wage and labor time statistics[11]. The daily cost of medicine was estimated based on the Survey for Individual Medical Procedures[11]. The cost of lost productivity was estimated assuming that patients with severe URTI were unable to work all day. All costs are expressed in 2005 costs.

Effectiveness

Effectiveness was measured in quality-adjusted life days (QALD). Utility was assigned to each day according to the duration and severity of URTI, with the 60-day cumulative QALD gained calculated for each strategy. Utilities in severe and moderate URTI were considered to be decreased. These utilities were derived from a previous study that measured utility in influenza[12]. Health states in severe URTI were estimated as the average utility from day 1 to day 3 of influenza, and in moderate URTI as the average utility from day 4 to day 7 of influenza (Table 1).

Analysis

Differences in 60-day cumulative follow-up costs and effectiveness between gargling and control groups were compared on an intention-to-treat basis, and the incremental cost-effectiveness ratio (ICER) was derived.

In this trial, the endpoint was the onset of URTI, and affected patients were censored. The average cost and effectiveness for each day were therefore estimated based on those from the number of participants observed on

Table 2: Estimated costs and utility

Variable	Value
Cost per day	
Gargling (once)	$0.4
Visiting physicians (once)*	$47.9
Medicine (per day)	$2.0
Lost productivity due to severe URI (per day)	$97.7
Utility	
Moderate URI	0.63
Severe URI	0.24

* Only 36% of those who developed URI were assumed to visit a physician.

each day, then the 60-day average cost and effectiveness were summed to calculate differences between groups. Censoring in the cost estimation was adjusted according to the methods described by Lin et al[13]. ICER was calculated from differences between gargling and control groups in 60-day cumulative costs and QALD. The ICER unit was converted to quality-adjusted life years (QALY) for convenience. The 95%CIs were calculated using the bootstrap method, using 5000 resamplings with replacement of participants in this trial.

Sensitivity analysis

One-way sensitivity analyses were performed for all costs and utilities within ± 50% ranges to assess the effects of uncertainty related to parameter estimates. Further two-way sensitivity analyses were applied to evaluate combinations of gargling cost and utility of moderate URTI.

Results

Of the 384 participants in the gargling trial, 122 subjects assigned to water-gargling and 130 subjects assigned to the control group were included in the economic analysis. Baseline characteristics of the two groups are shown in Table 2. During the 60-day follow-up, incidence of the first URTI was 0.26 episodes/30 person-days in the control group and 0.17 episodes/30 person-days in the water-gargling group[5].

Estimated costs and effectiveness after 60 days (Table 3)

The 60-day cumulative follow-up costs were estimated at $105.3 for the gargling group and $68.2 for the control group, respectively. Difference between the groups was $37.1 (95%CI, $7.40–$65.40). The costs of gargling for each group were $80.40 in the gargling group and $17.80 in the control group, representing a $62.6 increase in the gargling group. The costs of URTI were $24.9 in the gargling group and $50.4 in the control group. Cost was thus $25.50 lower in the gargling group. The 60-day QALD was 59.52 in the gargling group and 59.10 in the control group, showing that QALD was greater by 0.43 (95%CI, 0.07–0.80) in the gargling group (Table 3).

Cost-effectiveness analysis (Table 3)

The incremental cost per QALY gained associated with gargling was $31,800 (95%CI, $1,900–$248,100). Bootstrapped estimates of the incremental costs and incremental QALD are shown in Figure 1 using the cost-effectiveness plane. Figure 2 shows that, given a willingness-to-pay threshold of $50,000/QALY, the probability of gargling being cost-effective compared with control is 69.8%. If the threshold is increased to $100,000, then the probability increases to 89.9%.

Sensitivity analyses (Table 4)

One-way sensitivity analysis showed that the ICER of gargling is highly sensitive to the cost of gargling and the utility of moderate influenza (Table 4). These 2 critical factors were studied further using two-way sensitivity analysis. Figure 3 shows the combination of gargling cost and utility of moderate URTI.

Table 3: Results of cost effectiveness analysis

	Cost($)	Incremental cost (95%CI)**	Effectiveness (QALD)	Incremental effectiveness (95%CI)	ICER($/QALY) (95%CI)**
Gargling					
Cost of gargling	80.4	62.6			
Cost of URTI	24.9	-25.5			
Total	**105.3**	**37.1 (7.4–65.4)**	**59.52**	**0.43 (0.07–0.80)**	**31,800 (1,877–248,095)**
Control					
Cost of gargling	17.8				
Cost of URTI	50.4				
Total	**68.2**		**59.10**		

QALD = quality adjusted life days.
ICER = incremental cost-effectiveness ratio.
**95% confidence intervals calculated by the bootstrap method.

ICER for gargling varied from $5,000 to $58,600 when the cost of gargling ranged from $0.2 to $0.6. In addition, ICER varied from $21,000 to $64,800 when the utility of moderate influenza ranged from 0.32 to 0.95. ICER of gargling did not exceed $50,000/QALY in sensitivity analyses involving the following variables: cost of physician consultations due to URTI; cost of medications to treat URTI; and utility of severe influenza.

Discussion

Although several limitations are inherent to performing an economic analysis alongside a randomized trial[14], this approach allowed quantification of the cost-effectiveness of gargling. Gargling generated a 0.43 increase in QALD and $37.1 higher costs compared with the control group. Although gargling generated a higher QALD by preventing URTI, the daily cost of gargling exceeded the cost of the URTI saved by gargling. ICER of the gargling group was $31,800/QALY (95%CI, $1,900–$248,100). This is similar to many acceptable forms of medical intervention, including URTI preventive methods such as influenza vaccination[12,15,16]. Although ICER of gargling was within the range of acceptable forms of URTI preventive methods such as influenza vaccination[12,15,16], the broad confidence interval indicates uncertainty surrounding our results. In addition, one-way sensitivity analysis showed that the cost of gargling and the utility of moderate URTI exerted a large impact on the cost-effectiveness of gargling. Careful evaluation is thus required for those variables.

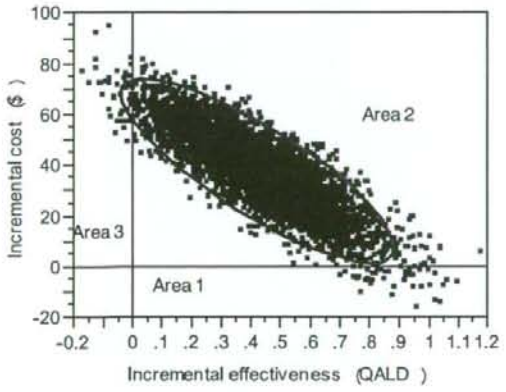

Figure 1
Scatter plot of simulated mean cost and effect differences in 60 days. Five thousand bootstrap samplings were used for the incremental cost and effectiveness of the gargling group compared to the control group. The plot indicates that 0.9% of all cases are located in area 1 indicating that gargling is dominant, 98.2% of total cases are located in area 2 indicating that gargling is more costly and effective than control, and 0.9% of all cases are located in area 3 indicating that gargling is dominated by control.

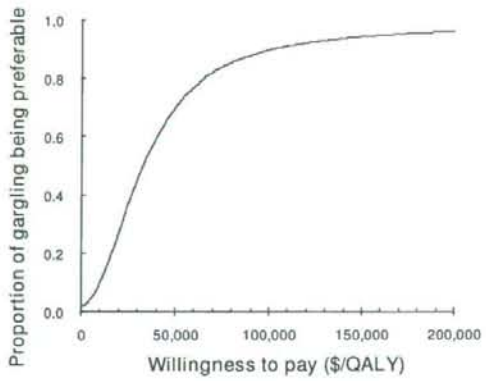

Figure 2
Acceptability curve. The curve indicates the probability of gargling being preferable to the control for potential maximum amounts that a decision-maker is willing to pay for an additional increase in QALY. WTP, willingness to pay.

We estimated the cost of gargling based on the average wage of Japanese workers based on the assumption that patients lost productivity due to gargling. If the impact on productivity is minimized and the cost of gargling can be maintained at lower than $0.16 (lower than the lower limit of the cost used in sensitivity analysis) gargling will be dominant.

The cost effectiveness of gargling also depends on how effectively it can reduce the incidence of influenza-like illnesses (ILI). The gargling trial was designed to evaluate the effectiveness of gargling for preventing URTI among healthy individuals, and therefore excluded ILI. Further analysis focusing on ILI was subsequently performed using the same data set[17]. Although no statistical significance was achieved due to the small number of ILI, analysis indicated a tendency toward decreased incidence of ILI with water gargling (hazard ratio, 0.75; 95%CI, 0.32–1.72). If the effectiveness of gargling in preventing ILI were to be demonstrated in a further study involving a large sample, the cost-effectiveness of gargling would be improved due to decreases in the number of patients suffering from complications of ILI and decreased use of oseltamivir.

Table 4: Results of sensitivity analysis

	Estimated costs and utilities			ICER ($/QALY)*		
	-50%	Baseline	+50%	-50%	Baseline	+50%
Costs ($)						
Gargling (one time)	0.2	0.4	0.6	5,000	31,800	58,600
Physician consultation because of URTI	8.6	17.2	25.9	33,900	31,800	29,600
Medication to treat URTI	0.6	1.2	1.8	31,900	31,800	31,700
Lost productivity due to severe URTI	48.9	97.7	146.6	41,400	31,800	22,100
Utility						
Utility in moderate influenza	0.32	0.63	0.95	21,000	31,800	64,800
Utility in severe influenza	0.12	0.24	0.36	29,900	31,800	33,900

ICER = incremental cost-effectiveness ratio.
*ICERs for each group are rounded to the nearest $100.

The major limitation of our study was that this trial was conducted in winter, the season of maximum URTI prevalence. Care must therefore be taken when applying our results to seasons in which URTI is less prevalent, since the ICER will increase with a lower URTI incidence. Second, estimated costs for URTI, particularly for physician consultations resulting from URTI, were based on the assumption that the proportion of patients who visit clinics is 36%[9]. We examined the impact of variability of costs for URTI with one-way sensitivity analysis and showed the variability did not significantly affect the result. Finally, we were unable to estimate all opportunity costs, such as time required for dedicated trips to the washroom to gargle, as no precise data were available.

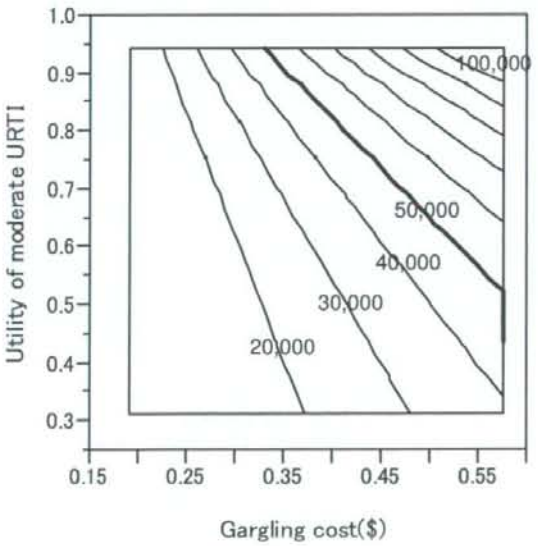

Figure 3
Two-way sensitivity analysis of two factors: gargling cost and utility of moderate URTI. Lines indicate the incremental cost effectiveness ratio ($/QALY) for gargling. The thick line indicates 50,000 $/QALY.

Conclusion

In conclusion, the present study suggests that gargling has potential as a cost-effective preventive strategy for URTI that is acceptable from both third-party payer and societal perspectives. However, careful consideration of the uncertainties surrounding the estimation of ICER for gargling is required.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MS drafted the manuscript and helped with data analysis. TS analyzed the cost effectiveness. KO and YT helped with data analysis. KS and TK conceived of this randomized controlled trial, designed the protocol, enrolled participants, and participated in data collection. TK managed the whole project as chief investigator. HB, MY, and HI contributed to the enrollment of patients. The Great Cold Investigators worked very well as a team during the study period.

All authors have read and approved the final manuscript.

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The relationship between trust in mass media and the healthcare system and individual health: evidence from the AsiaBarometer Survey

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Abstract

Background: Vertical and horizontal trust, as dimensions of social capital, may be important determinants of health. As mass media campaigns have been used extensively to promote healthy lifestyles and convey health-related information, high levels of individual trust in the media may facilitate the success of such campaigns and, hence, have a positive influence on health. However, few studies have investigated the relationship between trust levels in mass media, an aspect of vertical trust, and health.

Methods: Based on cross-sectional data of the general population from the AsiaBarometer Survey (2003–2006), we analyzed the relationship between self-rated health and trust in mass media, using a multilevel logistic model, adjusted for age, gender, marital status, income, education, occupation, horizontal trust, and trust in the healthcare system.

Results: In a total of 39082 participants (mean age 38; 49% male), 26808 (69%) were classified as in good health. By the levels of trust in mass media, there were 6399 (16%) who reported that they trust a lot, 16327 (42%) reporting trust to a degree, 9838 (25%) who do not really trust, 3307 (9%) who do not trust at all, and 191 (0.5%) who have not thought about it. In the multilevel model, trust in mass media was associated with good health (do not trust at all as the base group): the odds ratios (OR) of 1.16 (95% confidence interval (CI) = 1.05–1.27) for do not really trust; OR of 1.35 (95% CI = 1.23–1.49) for trust to a degree, and 1.57 (95% CI = 1.36–1.81) for trust a lot. Horizontal trust and trust in the healthcare system were also associated with health.

Conclusion: Vertical trust in mass media is associated with better health in Asian people. Since mass media is likely an important arena for public health, media trust should be enhanced to make people healthier.

Background

Social capital has developed as a concept indicating the quantity and quality of social interactions in the community and has emerged recently as an important determinant of health [1]. A society with high levels of social capital has high social participation among its citizens, high interpersonal trust, and high levels of institutional or organizational trust [2,3]. Studies suggest that societies and individuals with higher social capital have positive effects on various aspects of physical and psychological health among individuals in those societies [4,5]. Social capital is considered to promote health through mechanisms including effective reciprocal support, mutual respect, better access to local services, social control of deviant behavior and violence, and enhanced transmission of health information and healthy behavior [6].

Although social capital has been assessed as social participation or social trust [3], recent studies have suggested that a society with high social participation but with low social trust is associated with high-risk adverse behaviors to health [7-10]. Trust has emerged recently as the central means of achieving cooperation in inter-organizational and inter-individual relationships and promoting the accumulation of social capital [3,11].

Social trust reflects the expectation that an individual or institution will act competently, fairly, openly, and with concern [12], and can be divided into horizontal (interpersonal) trust and vertical (institutional) trust [3]. Horizontal trust flows across and among ordinary people. Vertical trust flows upward from people to public institutions in a society [13]. Development of the capacity to trust others is an essential element for successful social adjustment [14], and is considered an important predictor of health and psychological well-being [15,16].

Persons with high vertical trust consider public institutions or organizations as trustful social resources and the levels of this vertical trust may vary between societies with the level of social connectedness [17]. For instance, the healthcare system is one of the important institutions in which people may feel different levels of trust. A higher vertical trust in the healthcare system has been shown to be associated with better self-rated health [17]. Patients with high trust in the healthcare system are likely to gain access to healthcare services, provide important medical information to healthcare providers, and may be better at following advice and completing prescriptions.

However, little is known about the nature or role of vertical trust in terms of health determinants between other institutions and individuals in society. In addition to the healthcare system, mass media is also considered one of the most important public institutions, and may have a considerable effect on public health through the levels of trust the people have in this institution [13], and vertical trust in mass media may be an important determinant of health.

Mass media may function well with respect to improving health, along with relevant aspects of trust. A potential pathway from high trust in mass media to better health is increased acceptance of health-related messages and the resultant dissemination of good behavior related to health throughout communities. For instance, a recent study has shown that improvements in exercise and diet mediated by community-level projects are associated with better mental health [18]. The authors of the study on the New Deal for Communities in the UK suggest that better mental health and health-related behavior occur through increasing community cohesion and social capital more widely in the neighborhood, beyond people involved directly in lifestyle interventions [18].

In addition, a recent study has shown that public health agencies, using their communication and marketing resources effectively to support people in making healthful decisions and to foster health-promoting environments, have considerable opportunity to advance public health [19]. Thus, those with high trust in both the healthcare system and mass media may be more likely to receive these positive, and possibly synergistic, effects on health.

Furthermore, the links between vertical and horizontal trust are well founded and are positively correlated in an amplifying cycle [20]. Indeed, a recent study has supported the trust propagation cycle, in which there are two types of vertical trust: vertical trust in representative institutions (input vertical trust) and trust arising from experience of the services provided (directly or indirectly) by such institutions (output vertical trust) [20]. Satisfaction with community services promotes vertical trust, as well as horizontal trust, and a trust cycle propagates trust within a community [20]. Thus, those with output vertical trust in mass media may be more likely to have higher trust in other institutions and horizontal trust, which can in turn lead to better health.

Despite the importance of examining the relationships between vertical trust in mass media, few studies have addressed these issues. Therefore, in this study, we aim at evaluating the association between distrust in mass media and poor health among Asians, using data from the Asia-Barometer Survey, comprising trans-national and multidimensional surveys conducted throughout Asia.

Methods

Study participants

We used data from the AsiaBarometer Survey (2003–2006), which included information on individuals from 29 Asian countries on a vast range of subjects [21]. The countries included in our analysis were Afghanistan, Bangladesh, Bhutan, Brunei, Cambodia, China, Hong Kong, India, Indonesia, Japan, Kazakhstan, Kyrgyzstan, Laos, Malaysia, the Maldives, Mongolia, Myanmar, Nepal, Pakistan, Singapore, South Korea, Sri Lanka, Taiwan, Tajikistan, Thailand, the Philippines, Turkmenistan, Uzbekistan, and Vietnam. For the purpose of the study, Hong Kong and Taiwan were considered independent countries, in view of their socioeconomic characteristics. Prior ethics committee approval was obtained from the Chuo University. We received written informed consent from the survey participants.

Data collection

We used face-to-face interviews to administer structured questionnaires. The detailed content of the questionnaires has been published previously [21]. Data collection included demographics, marital status, socioeconomic factors (income, education, and occupation), self-rated health, interpersonal trust, and trust in the healthcare system and mass media, as well as information on political, environmental, and daily-life issues that were related to the AsiaBarometer Survey.

The individual-level independent variables included gender, age (range between 20 and 69 years), marital status, religious belief, income, education, employment, and individual-level social trust. Age was categorized into five groups of 20–29, 30–39, 40–49, 50–59, and 60–69 years old. Categories of marital status included single, married, divorced/separated, or widowed.

Annual household income was used as an income variable in this study. Categories of the income groups included low, middle, and high, based on the income distribution of each country (see Appendix A, in Additional file 1). For educational achievement, we also used three categories (low, middle, and high) based on the distribution of educational achievement in each country (see Appendix B, in additional file 1). For occupational status, six categorical classes were used: self-employed, employed, unemployed, retired, homemaker, and student. The self-employed group included: self-employed in agriculture, forestry or fisheries; business owner in mining or manufacturing industry of an organization with up to 30 employees; vendor or street trader; business owner or manager of an organization; and self-employed professional. The employed group included senior manager, employed professional or specialist, clerical worker, sales, manual worker, driver, and "other" worker.

In this study, self-rated health was defined as the individual's personal satisfaction with their overall health. In the survey, we asked "Please tell me how satisfied or dissatisfied you are with your health? Would you say you are very satisfied, somewhat satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied, or very dissatisfied with your health?". These categories were collapsed to form a dichotomous outcome of self-rated health: poor health (1) for very dissatisfied, somewhat dissatisfied, or neither satisfied nor dissatisfied; and good health (0) for very satisfied, or somewhat satisfied.

Horizontal trust, a dimension of cognitive social capital, was measured by a composite index constructed from a factor (principal component) score of three questionnaire items related to general trust, interpersonal trust, and mutual help. The general trust question was, "Would you say that most people can be trusted or that you can't be too careful in dealing with people?". The question for interpersonal trust in merit-based utility was, "Would you say that most of the time people try to be helpful or that they are mostly looking out for themselves?". The question for mutual help was, "If you saw somebody on the street looking lost, would you stop to help?". For the last question, the responses were: "I would always stop to help", "I would help if nobody else did", and "It is highly likely I wouldn't stop to help". These questions have been widely used in previous studies to measure cognitive social trust [2,5,22,23]. Factor analysis of these items provided a one-factor solution with an eigenvalue of 1.4. All items were loaded above 0.4 and no other factors exceeded unity. The individual scores were calculated using the regression equation with the factor loadings, and a higher score indicated lower trust. The scores were then standardized (mean 0; standard deviation 1). Before being included into the multivariable multilevel model, the scores were further collapsed to form a dichotomized variable: low social trust (0) for the values less than 0 and high social trust (1) for the values of 0 or more.

Trust in institutions (vertical trust) is an item that reflects the participant's trust in the healthcare system and in mass media (specified as newspapers and television). The item "Please indicate to what extent you trust the following institutions to operate in the best interests of society" offered the alternatives (a) the healthcare system and (b) mass media, with the six alternative responses: (1) "Trust a lot"; (2) "Trust to a degree"; (3) "Don't really trust"; (4) "Don't trust at all"; (5) "Haven't thought about it"; and (6) "I don't know".

Statistical analysis

Descriptive statistics were calculated and presented as the mean with standard deviation or the count number in proportion to the overall sample population where

appropriate. Bivariate correlation analyses were conducted among the trust variables using Pearson's correlation coefficients.

We used the multilevel (mixed-effects) logistic regression model to analyze the relationship of individual characteristics to self-rated health by considering individuals nested in each country, as data structures in the Asia Barometer Survey were hierarchical multilevels (level 1, individual; level 2, country). The data provide information on individuals, while the individuals are also grouped in their countries. Analyzing hierarchical data at the individual level by conventional regression models does not meet the assumption of independence of observations. When ignoring the nesting of individuals in countries, the estimated standard errors would be smaller, thus inflating the risk of Type I errors [24]. The mixed-effects model can be used to analyze hierarchical data [24], and is used widely in social and epidemiological research. The random-effects covariance matrix was set to an unstructured form and we utilized three trust measures (horizontal trust, trust in the healthcare, and trust in mass media) as the random-effects parameters in the model. Variances and their standard errors were estimated for these random-effects parameters.

The model was constructed to evaluate the relations of trust in the healthcare system and mass media to self-rated health, adjusted for age, gender, marital status, income, education, occupation, and horizontal trust. We constructed a total of six models, including only baseline sociodemographic variables (base), such as age, gender, marital status, income, education, and occupation (Model 1), base plus horizontal trust (Model 2), base plus trust in the healthcare system (Model 3), base plus trust in mass media (Model 4), base minus income and education plus horizontal trust, trust in the healthcare system and trust in mass media (Model 5), and base plus horizontal trust, trust in the healthcare system and trust in mass media (Model 6; full model). Model 5 was constructed by eliminating income and education from the full model for examining the possible endogeneity to health of income and education.

No interaction terms were included in the model. To check the robustness of the model, we also conducted the logistic regression analysis including country fixed effects as well as the ordered probit model analysis using original dependent variable (self-rated health). The odds ratios (ORs) along with 95% confidence interval (CIs) were estimated in each variable for poor health. An OR value greater than one indicates greater effects that were positively related to poor health. All statistical analyses were performed using STATA 10.0 (College Station, TX, USA). Two-tailed *P*-values less than 0.05 were considered statistically significant.

Results

Table 1 presents the descriptive statistics of the study participants. The sample population was split almost evenly between women and men. The mean age was 37.8 years (standard deviation (SD) = 11.9). The majority of participants were married (72.4%). The three levels of both income and education were distributed almost evenly. In terms of job status, the majority were employed: employed (48.2%) and self-employed (16.5%).

In terms of self-rated health, 68.6% considered themselves to be in good health, while 30.9% were in poor health. More than half (55.4%) of the participants were classified as having low horizontal trust (Table 2). For the questionnaire involving trust in the healthcare system and mass media, the majority (64.1%) of participants were classified as having trust ("trust a lot" and "trust to a degree") in the healthcare system, and similarly, 58.1% of

Table 1: Sociodemographics of all participants (N = 39082)

Characteristic	No.	%
Demographics		
Gender		
* Women	19800	50.7
Men	19282	49.3
Age, yr		
* 20–29	11413	29.2
30–39	11128	28.5
40–49	9147	23.4
50–59	5784	14.8
60–69	1610	4.1
Marital status		
* Married/partnered	28278	72.4
Others	10772	27.6
NA	32	0.1
Socioeconomic Status		
Income		
* High	12420	31.8
Mid	12219	31.3
Low	12426	31.8
NA	2017	5.2
Education		
* High	11861	30.3
Mid	14549	37.2
Low	12518	32.0
NA	154	0.4
Employment		
* Self-employed	6467	16.5
Employed	18843	48.2
Unemployed	13681	35.0
NA	91	0.2

NA = data not available.
* Reference categories used for subsequent regression analyses.

Table 2: Levels of Horizontal Trust and Trust in the Healthcare System and in Mass Media by Health Status

Characteristic	All participants (N = 39082)		Good health (n = 26808)		Poor health (n = 12080)	
	No.	%	No.	%	No.	%
Horizontal trust						
High	14450	37.0	10170	37.9	4206	34.8
* Low	21642	55.4	14637	54.6	6918	57.3
NA	2990	7.7	2001	7.5	956	7.9
Trust in the healthcare system						
Trust a lot	7568	19.4	5971	22.3	1551	12.8
Trust to a degree	17475	44.7	12364	46.1	5062	41.9
Don't really trust	7934	20.3	4732	17.7	3161	26.2
* Don't trust at all	2344	6.0	1234	4.6	1086	9.0
Haven't thought about it	71	0.2	48	0.2	23	0.2
NA	3690	9.4	2459	9.2	1197	9.9
Trust in mass media						
Trust a lot	6399	16.4	4801	17.9	1554	12.9
Trust to a degree	16327	41.8	11716	43.7	4571	37.8
Don't really trust	9838	25.2	6401	23.9	3406	28.2
* Don't trust at all	3307	8.5	1948	7.3	1346	11.1
Haven't thought about it	191	0.5	119	0.4	72	0.6
NA	3020	2.6	1823	6.8	1131	9.4

NA = data not available. * Reference categories used for subsequent regression analyses.

the participants were classified as having trust in mass media.

For horizontal trust, 37.9% of the participants with good health and 34.8% with poor health had high trust ($P < 0.001$). For trust in the healthcare system, 22.3% of the participants with good health and 12.8% with poor health reported as "having trust a lot" ($P < 0.001$). In addition, for trust in mass media, 17.9% of the participants with good health and 12.9% with poor health reported as "having trust a lot" ($P < 0.001$).

The correlation coefficient between trust in the healthcare system and trust in mass media was 0.3434 ($P < 0.001$). The correlation coefficients between horizontal trust and trust in the healthcare system and between horizontal trust and trust in mass media were 0.0159 and 0.0160, respectively ($P < 0.001$ for both).

Table 3 presents the mean scores and standard deviations of health and trust for each of the 29 countries. By construction, the horizontal trust score of all participants was centered at 0 with a standard deviation of 1. In terms of self-rated health, people in Brunei also reported the highest level, followed by those in Bhutan and Indonesia. People in Turkmenistan reported the lowest level of health, followed by those in Cambodia and Mongolia.

People in the Maldives reported the highest level of trust in mass media, followed by those in Brunei and the Philippines, while people in Hong Kong reported the lowest level of trust in mass media, followed by those in Taiwan and Uzbekistan. In addition, for the horizontal trust score, people in the Maldives reported the greatest level of trust, followed by those in China and Pakistan. People in Cambodia reported the lowest level of trust, followed by those in the Philippines and Kazakhstan. Lastly, people in Brunei reported the highest level of trust in the healthcare system, followed by those in the Maldives and Malaysia, while people in Tajikistan reported the lowest level of trust in the healthcare system, followed by those in Uzbekistan and South Korea. Data for trust in the healthcare system in Myanmar was not available at the time of the survey.

Table 4 presents the results from six multilevel logistic regression models for good health, adjusted for age, gender, marital status, income, education, occupation, horizontal trust, and trust in the healthcare system and mass media. In Models 1, 2, 3, 4, and 6, the sociodemographic variables that were associated significantly with better health included women, younger age, marital status, high income, and high education (not mid education). Employment status was not associated with health in any of the models. Horizontal trust, trust in the healthcare system, and media trust were all significantly associated with good health in Models 2–6.

Based on the full model (Model 6), horizontal trust was associated significantly with good health, with an OR of

Table 3: Health, Horizontal Trust, and Trust in the Healthcare System and in Mass Media in 29 Asian countries

Country	No.	Health *		Horizontal **		Trust			
						Healthcare system ***		Mass media ***	
		mean	SD	mean	SD	mean	SD	mean	SD
Afghanistan	874	4.11	0.98	0.25	1.00	1.96	0.81	1.83	0.92
Bangladesh	1008	3.87	1.04	-0.18	0.82	2.05	0.79	2.14	0.86
Bhutan	801	4.38	0.81	0.01	0.97	2.38	0.67	2.09	0.71
Brunei	804	4.62	0.57	0.21	0.94	2.71	0.49	2.20	0.68
Cambodia	812	3.29	1.05	-0.64	0.65	1.86	0.80	1.91	0.75
China	3800	3.71	0.95	0.54	1.02	1.54	0.75	1.48	0.79
Hong Kong	1000	3.57	0.71	0.06	1.06	1.65	0.73	0.95	0.72
India	2060	4.25	0.94	-0.08	0.97	1.84	0.82	2.12	0.84
Indonesia	825	4.35	0.84	0.07	0.90	2.27	0.67	2.06	0.68
Japan	2685	3.66	0.98	-0.01	1.01	1.56	0.67	1.16	0.68
Kazakhstan	800	3.47	1.16	-0.41	0.80	1.72	0.81	1.66	0.80
Kyrgyzstan	800	3.57	1.27	-0.32	0.73	1.66	0.90	1.72	0.83
South Korea	2642	3.55	0.91	0.46	1.02	1.41	0.69	1.33	0.74
Laos	800	3.92	0.98	-0.33	0.86	2.16	0.65	1.82	0.72
Malaysia	1600	4.22	0.75	-0.28	0.92	2.42	0.60	1.78	0.72
Maldives	821	4.34	0.87	0.55	0.97	2.69	0.56	2.67	0.75
Mongolia	800	3.42	1.09	-0.18	0.88	1.84	0.78	1.73	0.76
Myanmar	1600	3.78	1.12	-0.17	0.84	NA		1.94	0.70
Nepal	800	3.81	0.78	-0.24	0.79	1.74	0.70	2.11	0.64
Pakistan	1086	3.51	1.02	0.49	1.01	1.51	0.86	1.63	0.87
the Philippines	800	4.21	0.84	-0.50	0.80	2.17	0.68	2.16	0.70
Singapore	1838	4.06	0.75	0.10	1.02	2.21	0.57	1.74	0.69
Sri Lanka	1613	4.13	0.86	-0.32	0.93	1.92	0.72	1.59	0.84
Taiwan	1006	3.62	0.84	0.09	1.13	1.67	0.72	1.05	0.82
Tajikistan	800	3.85	1.04	-0.07	0.97	1.23	0.91	1.71	0.89
Thailand	1600	3.82	1.07	-0.33	0.89	2.17	0.70	1.80	0.70
Turkmenistan	800	3.07	1.56	0.02	1.31	1.55	1.18	2.02	1.01
Uzbekistan	1600	3.43	1.15	-0.25	0.94	1.32	0.89	1.11	0.92
Vietnam	2607	3.56	0.95	0.11	0.94	2.05	0.75	2.16	0.74
Total	39082	3.81	1.02	0.00	1.00	1.86	0.83	1.72	0.86

* Based on 5-point Likert scale from very dissatisfied with health (1) to very satisfied with health (5).
** Based on 1-factor analysis from the three questionnaires. The greater value indicates the higher trust.
*** Based on 4-point Likert scale from "Don't trust at all" (0) to "Trust a lot" (3). NA = data not available. SD = standard deviation.

1.27 (95% CI = 1.17–1.38). For institutional trust ("don't trust at all" as the base group), trust in the healthcare system was associated significantly with good health, with ORs of 1.29 (95% CI = 1.14–1.45) for "don't really trust", 1.75 (95% CI = 1.54–1.99) for "trust to a degree", and, similarly, 2.29 (95% CI = 1.95–2.68) for "trust a lot". Overall, these results indicate a linear relationship between the levels of trust in the healthcare system and the ORs for good health (Model 3, 5, and 6 of Table 4). Similarly, trust in mass media was associated significantly with good health, with ORs of 1.16 (95% CI = 1.05–1.27) for "don't really trust", 1.35 (95% CI = 1.23–1.49) for "trust to a degree", and 1.57 (95% CI = 1.36–1.81) for "trust a lot". Again, these results indicate a linear relationship between the levels of trust in mass media and the ORs for good health (Models 4, 5, and 6 of Table 4). In addition to covariates in the full model, the regression model including country fixed effects showed similar findings and did not affect the results. Further, the ordered probit model analysis using the original dependent variable (self-rated health) produced the similar findings and did not affect the results.

Discussion

The results of the current study suggest that trust in mass media is associated significantly with self-rated health. Slightly over 50% of the Asian participants reported that they "trust a lot" or "trust to a degree" in mass media. Trust in mass media remains associated significantly with health in multilevel modeling. Consistent with previous studies, this study also indicated significant associations between horizontal trust and self-rated health and between vertical (institutional) trust in the healthcare system and health. Further, significant sociodemographic determinants for health include younger age, male gender, marital status, high income, and high education.

Table 4: Estimated Odds Ratios from Multilevel Logistic Models (outcome of good health)

Variable	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6 **
Fixed parameters						
Male gender	1.21 (1.15–1.27) *	1.22 (1.16–1.29) *	1.22 (1.15–1.28) *	1.21 (1.15–1.28) *	1.25 (1.18–1.32) *	1.23 (1.16–1.30) *
Age						
30–39 yr	0.73 (0.68–0.78) *	0.73 (0.68–0.79) *	0.73 (0.68–0.79) *	0.76 (0.70–0.81) *	0.71 (0.66–0.77) *	0.75 (0.69–0.81) *
40–49	0.59 (0.55–0.63) *	0.59 (0.55–0.64) *	0.60 (0.55–0.65) *	0.62 (0.57–0.67) *	0.57 (0.53–0.62) *	0.62 (0.57–0.67) *
50–59	0.45 (0.41–0.49) *	0.44 (0.41–0.48) *	0.46 (0.42–0.50) *	0.47 (0.43–0.51) *	0.42 (0.39–0.46) *	0.46 (0.42–0.50) *
60–69	0.41 (0.36–0.47) *	0.40 (0.35–0.45) *	0.42 (0.37–0.48) *	0.43 (0.37–0.49) *	0.36 (0.32–0.41) *	0.40 (0.35–0.46) *
Marital status						
Others	0.78 (0.74–0.83) *	0.80 (0.75–0.85) *	0.79 (0.74–0.84) *	0.82 (0.77–0.87) *	0.81 (0.76–0.86) *	0.81 (0.76–0.87) *
Income						
Mid	0.87 (0.82–0.93) *	0.87 (0.82–0.93) *	0.87 (0.82–0.93) *	0.88 (0.82–0.93) *		0.87 (0.81–0.93) *
Low	0.73 (0.69–0.77) *	0.73 (0.68–0.78) *	0.73 (0.69–0.78) *	0.73 (0.68–0.78) *		0.73 (0.68–0.78) *
Education						
Mid	1.00 (0.94–1.06)	1.01 (0.95–1.08)	0.99 (0.93–1.05)	1.00 (0.93–1.06)		1.00 (0.93–1.07)
Low	0.82 (0.76–0.88) *	0.82 (0.76–0.88) *	0.79 (0.74–0.86) *	0.82 (0.76–0.88) *		0.80 (0.74–0.87) *
Employment						
Employed	1.00 (0.94–1.07)	1.01 (0.94–1.08)	1.01 (0.94–1.09)	1.03 (0.96–1.11)	1.07 (0.99–1.15)	1.03 (0.95–1.11)
Unemployed	0.97 (0.90–1.05)	0.98 (0.91–1.06)	0.99 (0.92–1.08)	0.99 (0.92–1.08)	1.00 (0.92–1.09)	1.01 (0.93–1.10)
Horizontal trust						
High		1.29 (1.19–1.40) *			1.28 (1.17–1.39) *	1.27 (1.17–1.38) *
Trust in the healthcare system						
Don't really trust			1.32 (1.19–1.46) *		1.27 (1.13–1.43) *	1.29 (1.14–1.45) *
Trust to a degree			1.85 (1.64–2.08) *		1.72 (1.52–1.94) *	1.75 (1.54–1.99) *
Trust a lot			2.55 (2.18–2.97) *		2.27 (1.93–2.66) *	2.29 (1.95–2.68) *
Trust in mass media						
Don't really trust				1.25 (1.15–1.37) *	1.17 (1.07–1.28) *	1.16 (1.05–1.27) *
Trust to a degree				1.55 (1.42–1.69) *	1.34 (1.22–1.47) *	1.35 (1.23–1.49) *
Trust a lot				1.98 (1.73–2.27) *	1.56 (1.35–1.79) *	1.57 (1.36–1.81) *
Random parameters						
Between-country variation	0.22 (0.83)	0.22 (0.82)	0.18 (0.64)	0.20 (0.74)	0.17 (0.61)	0.18 (0.63)

Figures in parentheses are the 95% confidence intervals (except for between-country variation, for which each of the numbers corresponds to the standard error and the variance.

* Statistically significant at the 0.05 level.

** The regression model including country fixed effects showed the similar findings. In addition, the ordered probit model analysis using original dependent variable (self-rated health) produced the similar findings.

Although the current study has inferential limitations for causal direction due to the cross-sectional study design, the interpretation could be made that the levels of trust in mass media may be able to influence the individual's health status. Enhancement of trust in mass media among the general population could be utilized to promote people's health.

Regarding causal pathways for how trust in mass media operates to influence health, the following mechanism can be considered: greater media trust may lead to higher use of mass media for health information; this in turn may lead to higher awareness of important health information and may result in better health-related decision-making and behavior. Alternatively, media trust could reflect higher credibility of public information on health issues, and may lead to greater dissemination of accurate health information, which may, in turn, lead to better health-related behavior. However, since there may be intermediate variables that underlie the relationship between media trust and health, further studies are needed to explore these causal mechanisms.

Mass media can have beneficial effects on people's health through conveying useful information related to health by various approaches, such as educational campaigns, series programs, and advertisements. In particular, mass media campaigns can have beneficial effects on public health, because mass media, particularly newspaper and television, can reach population-wide consumers throughout Asian countries. Given the widespread influence of mass media, well-designed mass media campaigns can have

beneficial effects not only on health knowledge and attitudes, but also on health behaviors, with a potentially huge public health impact [25].

TV advertisements can increase public knowledge and awareness of the important symptoms of various diseases. For instance, TV delivery of information regarding the early warning symptoms of stroke increases the number of presentations to the emergency department during the early stages of stroke, providing increased opportunity to receive potentially life-saving thrombolytic therapies that are only indicated during the early stage [26,27]. A US study also showed that TV advertisements are the most frequently mentioned source of help among recent quitters of smoking [28]. Furthermore, a number of studies have shown that mass media campaigns enhance improvements in attitude toward healthy behavior, such as better diet, exercise, illegal drug prevention, safe sex, and smoking cessation [29-36]. The World Health Organization (WHO) reports on developing countries also support mass media interventions to increase the knowledge of HIV transmission and boost awareness of health providers [37].

Despite increased interest in obtaining health information by the public, a significant proportion of those diagnosed with a serious disease, such as cancer, report that they do not seek health information beyond that given by healthcare providers. One study, based on a national survey of American adults, demonstrated that compared with information-seeking groups, non-seeker patients showed low trust in mass media and paid less attention to health information in mass media [38]. Thus, trust in mass media is related to seeking behavior for health information and low trust may be associated with low levels of knowledge regarding important information relevant to their own health.

There are several strengths of our study. This may be one of the first studies to suggest a significant association between trust in mass media and health. Second, our results are based on the multilevel and multivariable model adjusted for potential confounders, such as demographic and socioeconomic factors. In evaluating the relationship between trust and well-being, these factors should be adjusted for to avoid confounding effects. Individuals with higher socioeconomic status may perceive their societies as being friendly and may have high trust in most public institutions, compared with those with a lower socioeconomic status [39]. Furthermore, socioeconomic status is related to health status [40]. Marital status is also associated with an individual's health and may be related to trust in public institutions [4]. The results based on the adjusted model are more reliable for estimating the association between trust and health.

Third, we assessed the potential association between sociodemographic factors and health after accounting for horizontal and vertical trust. The results of our study confirmed previous reports that found several factors for good health: including younger age, marital status, high income, high education, horizontal trust, and trust in the healthcare system [4,6,41]. In contrast, employment was not associated with health in our study.Thus, the typical 'healthy' Asians may be young, married, high-income, and highly educated men with a high trust in interpersonal relations as well as in the healthcare system and mass media.

Our study is based on the analysis of cross-sectional data and thus it has inferential limitations. It is possible that poor health leads to social isolation and distrust in any institutions due to psychosocial mechanisms. In addition, health and trust may reflect different facets of a common underlying psychological construct of general well-being. Alternatively, media trust might act as a surrogate marker for other types of output vertical trust, economic development or income equity in a country, or it might approximate the political systems, such as democracy, freedom of the press, and multi-ethnic cohesion. These parameters are known to be related to health status. Another limitation of our study was the use of the self-reported health satisfaction measure. It would have been more accurate to obtain more explicit self-reported health dimensions, such as those from the SF-36, although these data were not available in the AsiaBarometer Survey. Finally, our study has both cross-sectional causality problems and the absence of objective measures of physical health [42]. Future studies with a panel structure with individual fixed effects and more objective health measures, such as healthcare access or disability, are needed to mitigate the bias from omitting unobservable, personal, psychosocial characteristics, and to address measurement problems relating to self-reported health status [42].

In summary, this study is the first to analyze the relationship between high institutional trust in mass media and good health. These results indicate that individuals with high trust in mass media have better health. Mass media programs may contribute towards better health, especially among those people who have trust in mass media. Mass media may need to recognize the importance of their social role in terms of public health. Further research is necessary to determine the characteristics of high-quality mass media with high trust among the public.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

YT was involved in the analysis and interpretation of data, critical revision of the manuscript for important intellectual content, statistical analysis, and also had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. SF was involved in the acquisition, analysis, and interpretation of data and critical revision of the manuscript for important intellectual content. MJ was involved in interpretation of data and critical revision of the manuscript for important intellectual content. TI was responsible for the study concept and design, obtaining funds, administrative, technical, and material support, and study supervision, and was also involved in the acquisition, analysis, and interpretation of data and critical revision of the manuscript for important intellectual content.

Additional material

Additional file 1

Appendix A and Appendix B
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□ ORIGINAL ARTICLE □

Modifiable Risk Factors for Colorectal Neoplasms and Hyperplastic Polyps

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Abstract

Purpose Obesity, smoking and alcohol are modifiable putative risk factors for colorectal neoplasms (CRN) and hyperplastic polyps (HP). The aim of this study was to evaluate the strength of association between these modifiable risk factors and colorectal polyps.

Methods These risk factors were assessed by using a questionnaire completed by the patient prior to colonoscopy. Eight hundred-seventy consecutive patients satisfying inclusion criteria who had undergone a complete colonoscopy were divided into 4 groups: CRN (n=194), HP (n=132), CRN and HP (n=42) and control (neither CRN nor HP; n=586). Multiple logistic regression was performed.

Results The ORs [95%CI] of both CRN and HP for incremental body mass index expressed in 2 categories (≧22, ≧25) were 2.12 [1.00, 4.50] and 1.41 [0.53, 3.77], respectively. The ORs [95%CI] of CRN and HP for heavy smoking of over 20 pack-years were 1.66 [1.05, 2.64] and 1.67 [1.01, 2.77], respectively. The ORs of CRN and HP for habitual alcohol drinking (median ethanol intake 32 g/day and interquartile range 18-40 g/day) were 1.31 [0.86, 1.98] and 1.91 [1.06, 3.47], respectively. CRN and HP were correlated with each other (p=0.0043, chi-square test). Aging was a significant risk factor for all three groups of colorectal polyps.

Conclusion These findings are especially important since smoking and alcohol consumption are modifiable risk factors. Heavy smokers should be encouraged to quit to reduce their risk of CRN and HP. Habitual drinkers should be warned of the risk of HP. HP can be a marker of coincidence of CRN.

Key words: colorectal neoplasms, hyperplastic polyps, body mass index, smoking, alcohol, aging

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Introduction

Colorectal polyps are classified histologically as adenomatous, hyperplastic, mixed hyperplastic-adenomatous polyps (serrated adenomas) or non-neoplastic hamartoma (juvenile polyp). The reported prevalence of adenomatous and hyperplastic polyps, even in asymptomatic individuals is substantial and increases with age. For example, Lieberman et al (1) reported that the prevalence of colorectal neoplasms (CRN) and hyperplastic polyps (HP) in men from 50 to 75 years of age is 37.7% and 12.5%, respectively. The number and prevalence of CRN and HP are reported to be correlated (2). Both genetic and non-genetic modifiable factors, such as obesity, smoking and alcohol drinking are thought to be potentially important in causation of these lesions.

Obesity, smoking and alcohol drinking are common risk factors of several kinds of diseases. For example, smoking is thought to be a risk factor for cardiovascular disease, cancer, respiratory disease and several maternal complications of pregnancy (3). However, the association between these factors and colon polyps is not established. These factors may be more important than genetic factors because they are modifiable, either in primary prevention of polyp development or in the prevention of metachronous polyps after polypectomy or resection of colonic cancers.

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Obesity and alcohol abuse are recognized health issues. The prevalence of adult smoking is high in Japan (43% in men and 12% in women in 2004) (4). Several epidemiologic studies have suggested an association between colorectal polyps, especially adenoma and smoking (1, 5-14). However, only a few studies using full colonoscopy to detect polyps have investigated the association between HP and smoking and between colorectal polyps and obesity or alcohol consumption (1, 9, 13, 15, 16). It is important to investigate the association between modifiable risk factors, such as obesity, smoking and alcohol and adenoma because most colorectal cancers arise from adenomas (17). It may be meaningful to examine modifiable risk factors in relation to HP also because some of these polyps may have a malignant potential (18, 19). Therefore, we conducted a case-control study, using full colonoscopy as an outcome measure, to examine the relationships between certain modifiable risk factors and CRN and HP.

Methods

We performed a retrospective case-control study of 870 consecutive patients who underwent full colonoscopy at Tokai University Oiso Hospital in Kanagawa, Japan. These patients presented to the outpatient clinic with various signs and symptoms, such as abdominal pain, hematochezia and positive fecal occult blood test. Body mass index (BMI), history of smoking and alcohol consumption were investigated by use of a questionnaire administered just before colonoscopy. We excluded patients who had a history of inflammatory bowel disease, colonic polyps, hereditary polyposis syndrome or non-steroidal anti-inflammatory drug use. We also excluded patients with colorectal polyps who could not undergo biopsy due to a medical contraindication, such as taking anti-coagulation or anti-platelet medicine. Tissue samples were evaluated anonymously from colonoscopies. The term CRN was used to include adenoma and colorectal cancer. The findings of colonoscopy, combined with histopathological findings, served to measure the main outcome, i. e., the presence of CRN or HP. We included 19 patients who had colorectal cancer in the CRN group because the causal pathway to cancer, other than de novo cancer, by these modifiable factors is assumed to be the same as for adenoma.

The proportions of CRN and HP among non-smokers were 0.19 and 0.15, respectively. By using an odds ratio for CRN and HP of 1.9 and 3.2, respectively, as reported by Potter et al (9), the expected proportions of CRN and of HP among heavy smokers were 0.32 and 0.36, respectively. If the number of cases is the same for controls in both CRN and HP groups, 191 cases of CRN and 75 cases of HP would be necessary for 80% power. In our study, 194 cases of CRN and 132 cases of HP, and 586 controls, were analyzed. Therefore, our study should have at least 80% power for detecting significant association between smoking and CRN or HP.

We performed unconditional logistic regression for both bivariate and multivariate analyses by using gender, four categories of age (less than 44, 45-54, 55 -64, more than 65 years), three categories of BMI (less than 21, 22-25, more than 25), three categories of cigarette smoking status (never smoked, ex-smoker, current smoker), three categories of cigarette consumption (non-smoker; moderate smoker, less than 20 pack-years; heavy smoker, more than 20 pack-years), alcohol drinker, three categories of alcoholic-beverage preference (sake, whisky, beer), three categories of drinking status (never, ex-drinker, current drinker). The odds ratios of outcomes were adjusted for potential confounders. All analyses were conducted using STATA® version 10 (StataCorp, College Station, TX).

Results

Patient characteristics

Table 1 shows the baseline patient characteristics of the 870 patients divided into four groups (CRN, HP, both CRN and HP and control). Among the 870 patients, 194 patients (22.2%) had CRN (180 adenoma, 19 carcinoma and 5 both adenoma and carcinoma) and 132 patients (15.1%) had HP. Forty-two patients had both CRN and HP. Five hundred eighty-six patients had neither CRN nor HP.

Comparing the three groups to the control group, the proportions of male, smoker, heavy smoker, and drinker were higher among patients with CRN. Alcohol drinker regularly took alcohol daily (median ethanol intake 32 g/day and interquartile range 18-40 g/day) for at least one year. The proportion of beer drinkers was higher in the HP group (Table 1).

Bivariate analysis

The existence of CRN was associated with HP (p=0.0043, Chi-square test). Aging, male gender, BMI over or equal to 22, ever smoking, current smoker, heavy smoking, alcohol drinker and current drinker were significantly associated with the three groups of polyp (Table 2).

Multivariate analysis

The odds ratios (ORs) [95% confidence interval (CI)] of incremental age by 3 categories (≧45, ≧55, ≧65 years-old) for CRN and HP were 3.73 [1.92, 7.23], 7.81 [4.08, 15.0], 10.39 [5.42, 19.89] and 2.06 [1.17, 3.63], 2.06 [1.13, 3.78], 2.90 [1.60, 5.30], respectively. The trend tests of increasing risk of three polyp groups by incremental age were significant. The ORs [95%CI] of incremental BMI by 2 categories (≧22, ≧25) for both CRN and HP for were 2.12 [1.00, 4.50] and 1.41 [0.53, 3.77], respectively. The ORs [95%CI] of heavy smoking over 20 pack-years for CRN and HP were 1.66 [1.05, 2.64] and 1.67 [1.01, 2.77], respectively. The ORs of alcohol drinker for CRN and HP were 1.31 [0.86, 1.98] and 1.91 [1.06, 3.47], respectively. The ORs of alcohol drinking with smoking for CRN and HP

Table 1. Basic Characteristics of All Patients

Characteristics N (%)	CRN N=194 (22.2)	HP N=132 (15.1)	Both CRN and HP N=42 (4.8)	Control N=586 (67.3)	All patients N=870
Mean age (SD)	60.8 (10.4)	55.3 (13.2)	61.2 (10.0)	49.2 (14.6)	52.2 (14.5)
Male gender (%)	127 (65.4)	90 (68.1)	29 (69)	301 (51.3)	489 (56.2)
Coincidence of CRN or HP (%)	42 (21.6) (HP)	42 (31.8) (CRN)	N/A	N/A	N/A
Obesity (%)	37 (19.1)	25 (18.9)	7 (16.7)	90 (15.7)	145 (16.7)
Ever smoker (Ex and Current) (%)	94 (48.4)	68 (51.5)	23 (54.8)	210 (35.8)	349 (40.1)
Moderate smoker (%)	17 (8.76)	19 (14.3)	3 (7.1)	95 (16.2)	128 (14.7)
Heavy smoker (%)	77 (39.7)	49 (37.1)	20 (47.6)	115 (19.6)	221 (25.4)
Ex smoker (%)	29 (14.9)	11 (8.3)	4 (9.5)	47 (8.0)	83 (9.5)
Current smoker (%)	65 (33.5)	57 (43.2)	19 (45.2)	163 (27.8)	266 (30.6)
Alcohol drinker (%)	95 (49.0)	71 (53.8)	25 (59.5)	204 (34.8)	345 (39.7)
Sake (%)	50 (25.8)	27 (20.5)	12 (28.6)	87 (14.9)	152 (17.5)
Whisky (%)	20 (10.3)	19 (14.4)	5 (11.9)	44 (7.5)	78 (9.0)
Beer (%)	39 (20.1)	60 (45.5)	9 (21.4)	120 (20.5)	184 (21.2)
Ex drinker (%)	18 (9.3)	11 (8.3)	3 (7.1)	28 (4.8)	54 (6.2)
Current drinker (%)	77 (39.7)	60 (45.5)	22 (52.4)	176 (30.0)	291 (33.5)

SD, standard deviation; CRN, colorectal neoplasms; HP, hyperplastic polyps; N/A, not applicable
Obesity was defined as body mass index over 25

Table 2. Unadjusted Odds Ratios for Colorectal Neoplasia and Hyperplastic Polyp

Characteristics	OR for CRN [95%CI]	OR for HP [95%CI]	OR for both CRN and HP [95%CI]
Age>=45 (vs. <45)	3.88 [2.01, 7.45]	2.14 [1.23, 3.70]	6.6 [1.44, 30.19]
Age>=55 (vs. <45)	9.14 [4.84, 17.28]	2.47 [1.38, 4.42]	10.64 [2.34, 48.39]
Age>=65 (vs. <45)	11.65 [6.15, 22.05]	3.29 [1.85, 5.86]	17.88 [4.05, 78.92]
Male gender	1.79 [1.28, 2.51]	2.02 [1.36, 3.03]	2.11 [1.08, 4.14]
BMI over 22 (vs under 22)	1.62 [1.13, 2.32]	1.77 [1.17, 2.70]	2.63 [1.30, 5.35]
BMI over 25 (vs under 22)	1.61 [1.02, 2.55]	1.68 [0.98, 2.86]	1.81 [0.70, 4.67]
Ever smoking (vs. never)	1.68 [1.21, 2.34]	1.90 [1.30, 2.78]	2.16 [1.15, 4.07]
Smoking status			
Ex-smoker (vs. never)	1.82 [1.12, 2.94]	1.10 [0.56, 2.16]	1.24 [0.41, 3.75]
Current smoker (vs. never)	1.62 [1.12, 2.35]	2.25 [1.50, 3.38]	2.58 [1.33, 5.00]
Pack-years			
Moderate smoking (vs. non)	0.67 [0.38, 1.17]	1.17 [0.67, 2.05]	0.62 [0.18, 2.16]
Heavy smoking (vs. non)	2.51 [1.75, 3.62]	2.5 [1.63, 3.83]	3.44 [1.78, 6.67]
Alcohol drinker	1.81 [1.30, 2.52]	2.17 [1.48, 3,19]	2.75 [1.45, 5.22]
Sake	1.99 [1.34, 2.95]	1.48 [0.91, 2.38]	2.29 [1.13, 4.65]
Whisky	1.42 [0.81, 2.47]	2.07 [1.17, 3.68]	1.66 [0.62, 4.45]
Beer	0.98 [0.65, 1.46]	1.35 [0.87, 2.09]	1.06 [0.49, 2.27]
Drinking status			
Ex-drinker (vs. never)	2.48 [1.32, 4.67]	2.46 [1.16, 5.20]	2.41 [0.67, 8.71]
Current drinker (vs. never)	1.68 [1.19, 2.39]	2.13 [1.43, 3.18]	2.80 [1.46, 5.42]

OR, odds ratio; 95%CI, 95% confidence interval; CRN, colorectal neoplasms; HP, hyperplastic polyps
"alcohol drinker" means a person who regularly takes alcohol every day for at least one year

were 0.71 [0.32, 1.59] and 0.66 [0.28, 1.57], respectively (Table 3).

Discussion

Our study showed that aging was a significant risk factor for all three groups of colonic polyps as expected (CRN, HP and combined CRN and HP). When age was categorized into four groups (less than 44, 45-54, 55-64 and >=65 years), the ORs tended to increase in all three polyp groups. The increase of OR with age in the CRN group was greater than in the HP group. Increasing BMI was not associated with either the CRN or HP group alone, but a BMI of 22-25 was significantly associated with the combined polyp group (a BMI over 25 was not, however). Current smoking was associated with the HP group and the combined polyp group. Heavy smoking was associated with the CRN and the HP groups but not with the combined polyp group. Regular alcohol drinking was associated with HP but not with CRN.

Full colonoscopy with biopsy, as conducted in our study, is the most reliable way to conclusively identify CRN and HP, thus minimizing misclassification bias and increasing internal validity. Therefore, we included in the literature reviewed reports of studies in which colorectal polyps were diagnosed by full colonoscopy, not by flexible sigmoidoscopy or questionnaire.

The most common colorectal polyp is sporadic colorectal adenoma. Mutation of the adenomatous polyp gene in both alleles is needed for the development of adenoma. The mutations are thought to result from a two-hit phenomenon (20), which supports the increasing odds ratio of adenoma by aging. Our results about an effect of aging for CRN are compatible with this theory.

Regarding the association between colorectal adenoma and obesity, we have found four studies (21-24). The results of three of the studies suggested a significant association between obesity and adenoma when the BMI was more than or equal to 30. The mean (SD) of BMI of our sample was 22.4 (3.1) and patients with BMI over 30 were 17 (2%), too few to permit analysis of an association between BMI over 30 and colonic polyps. Otake et al (25) reported that high BMI is not associated with colorectal adenoma but visceral

Table 3. Adjusted Odds Ratios for Colorectal Neoplasia and Hyperplastic Polyp

Characteristics	OR for CRN [95%CI]	OR for HP [95%CI]	OR for Both CRN and HP [95%CI]
Age			
Age>=45 (vs. <45)	3.73 [1.92, 7.23]	2.06 [1.17, 3.63]	6.00 [1.29, 27.89]
Age>=55 (vs. <45)	7.81 [4.08, 15.0]	2.06 [1.13, 3.78]	8.10 [1.75, 37.56]
Age>=65 (vs. <45)	10.39 [5.42, 19.89]	2.90 [1.60, 5.30]	14.35 [3.16, 65.25]
Trend test by age categories	p=0.000	p=0.001	p=0.000
Male gender	1.40 [0.92, 2.12]	1.54 [0.97, 2.44]	1.37 [0.61, 3.11]
BMI over 22 (vs under 22)	1.43 [0.96, 2.12]	1.51 [0.97, 2.33]	2.12 [1.00, 4.50]
BMI over 25 (vs under 22)	1.29 [0.79, 2.12]	1.41 [0.81, 2.44]	1.41 [0.53, 3.77]
Ever smoker (vs never)	1.43 [0.93, 2.18]	1.53 [0.97, 2.40]	1.80 [0.82, 3.93]
Smoking status			
Ex-smoker (vs never)	1.17 [0.66, 2.08]	0.71 [0.34, 1.48]	0.76 [0.22, 2.64]
Current smoker (vs never)	1.56 [0.99, 2.47]	1.95 [1.21, 3.12]	2.33 [1.04, 5.19]
Pack-years			
Moderate smoker (vs non)	0.95 [0.50, 1.81]	1.30 [0.70, 2.40]	0.89 [0.23, 3.38]
Heavy smoker (vs non)	1.66 [1.05, 2.64]	1.67 [1.01, 2.77]	2.20 [0.96, 4.99]
Alcohol drinker	1.31 [0.86, 1.98]	1.91 [1.06, 3.47]	1.99 [0.90, 4.38]
Sake	1.15 [0.72, 1.84]	0.85 [0.50, 1.44]	1.20 [0.54, 2.68]
Whisky	1.12 [0.60, 2.08]	1.53 [0.82, 2.83]	1.04 [0.35, 3.10]
Beer	0.94 [0.60, 1.49]	1.19 [0.74, 1.92]	1.07 [0.46, 2.48]
Drinking status			
Ex-drinker (vs never)	1.78 [0.86, 3.67]	1.54 [0.68, 3.48]	1.48 [0.35, 6.24]
Current drinker (vs never)	1.23 [0.80, 1.90]	1.53 [0.95, 2.44]	2.08 [0.93, 4.64]
Drinking with smoking	0.71 [0.32, 1.59]	0.66 [0.28, 1.57]	0.54 [0.12, 2.30]

OR, odds ratio; 95%CI, 95% confidence interval; CRN, colorectal neoplasms; HP, hyperplastic polyps
*alcohol drinker" means a person who regularly takes alcohol every day for at least one year

fat accumulation and decreased plasma adiponectin are. Kim et al (26) suggested that the metabolic syndrome is associated with CRN and that of the individual components of metabolic syndrome, abdominal obesity is an important risk factor for CRN. Giovannucci et al (27) reviewed past publications and reported that the association between waist circumference or waist-to-hip ratio and colon cancer risk has generally been more consistent than that for BMI. Therefore, it is suggested that we should focus more on visceral fat accumulation and adiponectin rather than BMI when investigating risk factors of CRN.

Regarding the association between CRN and smoking, Botteri et al (28) performed a stratified meta-analysis of patients examined by full colonoscopy including 42 independent observational studies. They reported that pooled relative risks [95%CI] for former smokers, ever smokers and current smokers were 1.47 [1.29, 1.67] based on 17 studies, 1.82 [1.65, 2.00] based on 23 studies and 2.14 [1.86, 2.46] based on 19 studies, respectively. Our study showed a significant association between heavy smoking of over 20 pack-years and CRN, but did not suggest an association with current, ever or former smoking. The difference between our results and those of the meta-analysis may be due to exclusion of some studies (1, 7, 9, 11, 29) from the meta-analysis.

Morimoto et al (15) and Shrubsole et al (16) raised the possibility that the association between CRN and smoking might be erroneously strengthened by including CRN cases with concomitant HP in CRN group. They performed full colonoscopy-based study, which categorized participants into CRN-only and HP-only groups. The former suggested a significant association only between smoking and HP-only group. The latter showed a significant association between smoking and both groups and suggested a stronger association between the HP-only group and smoking than the CRN-only group and smoking. Our study also showed higher ORs of smoking for HP than for CRN, though patients with both types of polyps were included in both the CRN group and the HP group in order to satisfy appropriate sample size requirements.

It is reported that nicotine induces methylation of candidate tumor suppressor gene (TSG), fragile histidine triad, in human esophageal squamous epithelial cells (30) and that tobacco smoking is associated with hypermethylation of TSG in nonsmall cell lung cancer (31). Chan et al (32) reported concordant cytosines that precede a guanosine (CpG) island methylation in multiple HP in patients with serrated adenoma and right-sided hyperplastic polyposis (>20 HP). We assume that hypermethylation of the CpG island in the promoter of TSG is one of the mechanisms linking smoking to colorectal polyps.

We found ten studies (1, 5, 7, 10, 12, 13, 16, 29, 33, 34) regarding the association between ethanol consumption and colon polyps where all polyps were diagnosed by full colonoscopy. Three (1, 13, 16) of the ten studies also investigated the association between ethanol and HP. None of the three suggested a significant association. Seven (1, 5, 7, 10, 12, 29, 34) found some association between drinking and adenoma (26). Cope et al (7), interestingly, suggested that smoking is a significant effect modifier for the association between adenoma and ethanol consumption. Our study showed an association between drinking and HP but not between drinking and CRN. Also, our study did not show that smoking is an effect modifier for the association between the three kinds of polyps and ethanol consumption.

Alcohol or its metabolite, acetaldehyde may induce DNA hypomethylation, an early step of colonic carcinogenesis, via its antifolate effects (35). Alcohol and its metabolites are suggested to interfere with absorption of potentially anticarcinogenic nutrients such as folate and calcium (36, 37). Rectal mucosal hyperproliferation, a condition associated with an increased cancer risk, is reported to be induced by alcohol abuse (38). These reports support the assumption of an association between CRN and alcohol intake but not between HP and alcohol consumption.

We recognize certain limitations in our study. We did not analyze risk factors for colorectal cancer because the number of cancer patients was small. Also, in an observational study such as ours, unknown confounders of obesity, smoking or alcohol to CRN and HP may have been present. We did not exclude patients with diabetes mellitus or hypertriglycemia or metabolic syndrome although recent studies (26, 39, 40) suggested that these diseases are risk factor of CRN. Moreover, most of our samples were taken from patients for whom colonoscopy was indicated for abnormalities such as abdominal symptoms or positive fecal occult blood test. Thus, although we may be able to generalize our data to patients who visit gastroenterology clinics, we cannot extrapolate them to the general population. The number of patients with both CRN and HP is relatively small and the statistical power of this group may not be sufficient, so it is possible that a significant association between smoking and patients with both types of polyps was not identified because of type II error.

In conclusion, the existence of CRN was correlated with HP. Heavy smoking was associated with CRN but former, ever or current smoking status was not. Heavy smoking and current smoking status were associated with HP. Regular daily alcohol consumption for at least one year was associated with HP but not with CRN. These findings are especially important since smoking and alcohol consumption are modifiable risk factors in the pathogenesis of colon polyps, and therefore may be amenable to improvement through patient education and awareness.

Further cohort study or systematic review, including meta-analysis, will be needed in order to conclusively determine the association between colon polyps and other plausible risk factors, such as obesity.

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