Original Paper

# Effectiveness of Risk-Adapted Upper Gastrointestinal Cancer Screening in China: Prospective Cohort Study

Youqing Wang[1*], MS; Juan Zhu[1*], PhD; Huizhang Li[1*], MS; Le Wang[1], PhD; Chen Zhu[1], MS; Xue Li[1], PhD; Shi Wang[2], MD; Lingbin Du[1], MPH

[1]Department of Cancer Prevention, Zhejiang Cancer Hospital, Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences, Hangzhou, China

[2]Department of Endoscopy, Zhejiang Cancer Hospital, Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences, Hangzhou, China

*these authors contributed equally

**Corresponding Author:**

Lingbin Du, MPH
Department of Cancer Prevention, Zhejiang Cancer Hospital
Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences
Hangzhou, 310022
China
Phone: 86 13588114180
Email: dulb@zjcc.org.cn

**Related Article:**
This is a corrected version. See correction statement in: https://publichealth.jmir.org/2024/1/e67642

## Abstract

**Background:** Previous studies have proved the effectiveness of endoscopic screening in rural areas; however, long-term, high-quality evidence regarding the effectiveness of risk-adapted upper gastrointestinal cancer (UGC) sequential screening strategies in resource-rich regions is currently lacking.

**Objective:** The objectives were to validate the effectiveness of risk-adapted sequential screening strategies in UGC prevention and control and assess the potential of sequential screening to lower mortality rates.

**Methods:** Based on the Cancer Screening Program in Urban China, a prospective, large-scale cohort study based on population was conducted to recruit individuals from 4 cities in China from 2013-2019. Those identified as having a high risk of UGC according to a validated risk-score model were advised to undergo endoscopy tests. Follow-up outcomes were tracked until June 2021. Incidence of UGC, UGC-related mortality, and all-cause mortality were evaluated between the screened and nonscreened cohorts.

**Results:** The study included 153,079 participants at baseline. In total, 113,916 (74.42%) of the participants were designated as low risk of UGC. The remaining 39,163 (25.68%) participants were deemed to be at high risk of UGC and were offered gastroscopy tests. Among the high-risk participants, 9627 (compliance rate 24.6%) adhered to the gastroscopy tests. Over a median follow-up of 6.05 (IQR 3.06-7.06) years, 622 UGC cases, 180 UGC deaths, and 1958 all-cause death cases were traced. The screened cohort exhibited the highest cumulative incidence of UGC (119.2 per 100,000 person-years), followed by the nonscreened and low-risk cohorts. Obvious reductions in both all-cause mortality and UGC mortality were observed between those who undertook screening (153.7 and 4.7 per 100,000 person-years, respectively) and the nonscreened group (245.3 and 27 per 100,000 person-years, respectively). The screening population showed a significant 36% and 82% reduction in both all-cause mortality (hazard ratio [HR] 0.64, 95% CI 0.49-0.83, $P<.001$) and UGC mortality (HR 0.18, 95% CI 0.04-0.74, $P=.02$), respectively, compared to the nonscreened group. Reductions of 35% in all-cause mortality (HR 0.65, 95% CI 0.49-0.86, $P=.003$) and 81% in UGC mortality (HR 0.19, 95% CI 0.05-0.80, $P=.02$) were observed in participants aged older than 55 years in the screened group compared to the nonscreened group. The reductions in all-cause mortality and UGC mortality were statistically significant in males (all-cause mortality: HR 0.64, 95% CI 0.47-0.88, $P=.005$; UGC mortality: HR 0.10, 95% CI 0.01-0.72, $P=.02$), but significant reductions were not observed in females (all $P$ values were $>.05$).

**Conclusions:** Our study suggests the significance of one-off risk-adapted UGC screening in reducing both all-cause mortality and UGC mortality, particularly among high-risk individuals, indicating its effectiveness in UGC prevention and management.

*JMIR Public Health Surveill 2024;10:e62864;* doi: 10.2196/62864

**Keywords:** upper gastrointestinal cancer; screening; endoscopy; effectiveness, incidence, mortality, all-cause mortality

# Introduction

Upper gastrointestinal cancer (UGC), encompassing esophageal cancer (EC) and gastric cancer (GC), represents a significant global public health concern. As per GLOBOCAN 2022 data, EC stands as the seventh most common cause of cancer-related deaths worldwide, whereas GC holds the fifth position in both incidence and mortality worldwide [1]. With substantial efforts to combat UGC in recent years, both incidence and mortality rates have shown noteworthy declines in China [2]. However, UGC continues to impose a substantial burden, persistently ranking within the top 4 for cancer-attributable disability-adjusted life years [3,4]. Thus, UGC remains a formidable challenge for both health care systems and individuals.

Patients diagnosed with late-stage UGC still have a grim prognosis, characterized by a low resection rate and unfavorable survival outcomes [5]. Conversely, for early-stage UGC, a promising prognosis exists through complete surgical removal, resulting in 5-year survival rates exceeding 85% [6,7]. Prior studies have emphasized the substantial potential of gastroscopic screening in alleviating the UGC burden [8-12]. Organized and opportunistic screening programs have been extensively adopted in Asian nations characterized by a high burden of UGC, such as Japan, Korea, and China [8,13-15]. Nonetheless, gastroscopy examination remains an invasive and expertise-intensive procedure, limiting its utility in regions with lower UGC incidence and constrained health care resources. For such regions, the adoption of a risk-stratified scoring system is advised for the identification of high-risk individuals who would benefit from endoscopic evaluation [16,17].

Initiated by the Chinese government in October 2012, the Cancer Screening Program in Urban China (CanSPUC) targets the predominant cancers, including UGC [18,19]. Since 2013, Zhejiang Province has participated in the CanSPUC. This program seeks to provide free cancer screening to eligible participants and uses a cancer risk stratification system to evaluate cancer risk. This system guides individuals with a high risk of EC or GC to undergo gastroscopic evaluation at designated hospitals.

Previous studies have proved the effectiveness of endoscopic screening in rural areas [8,9,20]. Nevertheless, evidence regarding the effectiveness of sequential screening strategies in resource-rich regions is currently lacking. Considering China's large population base and the significant burden on endoscopy resources, conducting large-scale 1-time endoscopic primary screening is not feasible. Guidelines recommend conducting high-risk assessments first to discern screeners with high risk for subsequent endoscopic screening in non–high-incidence areas. However, there exists an absence of long-term, high-quality evidence supporting this approach. Therefore, our study aims to bridge this knowledge gap by analyzing UGC screening data from 2013 to 2019, involving the comparison of 3 distinct groups: low-risk cohort, high-risk but unscreened cohort, and high-risk population that underwent screening. Our primary objectives were to explore the effectiveness of sequential screening in UGC control and assess its potential to lower mortality rates.

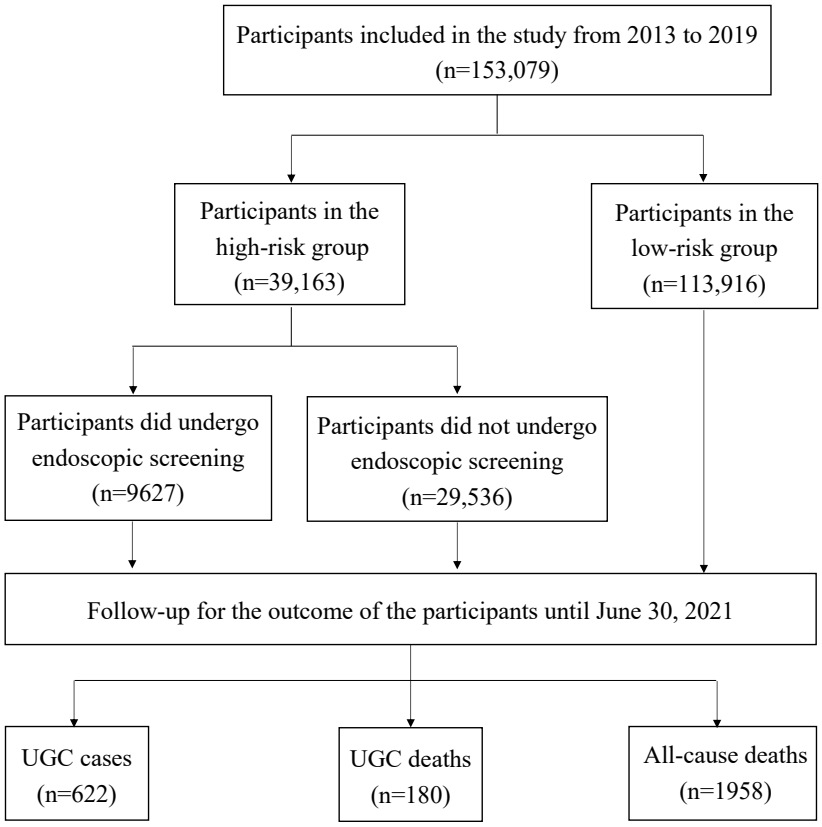
# Methods

## Study Design and Participants

We conducted a screening cohort study within the framework of the CanSPUC program. We used the household registration system in local communities to identify eligible permanent residents who were aged 40-74 years and asymptomatic for UGC with no history of cancer diagnosis. People who were unable to give informed consent, had a prior cancer diagnosis, or were receiving therapy for other serious medical conditions were ineligible for participation. Television broadcasts, brochures, and websites were used to publicize cancer screening programs. Community-based telephone calls or home visits were carried out by trained staff to reach and inform the maximum number of eligible residents.

We used data from the UGC screening performed over the initial 6 years, spanning from October 2013 to August 2019, in 4 cities within Zhejiang Province: Hangzhou, Ningbo, Quzhou, and Jinhua city. In total, 153,079 eligible participants underwent risk assessment in our UGC screening program. Figure 1 displays a flowchart of the study population.

**Figure 1.** Flow diagram of the cohort study. The study included 153,079 participants at baseline. In total, 74.42% (n=113,916) were evaluated as low risk for UGC, while 25.68% (n=39,163) were deemed to be at high risk and invited for endoscopy tests. Among the high-risk participants, 9627 (compliance rate 24.6%) adhered to the gastroscopy tests. Over a median follow-up of 6.05 (IQR 3.06-7.06) years, 622 UGC cases, 180 UGC deaths, and 1958 all-cause death cases were traced. UGC: upper gastrointestinal cancer.




## Screening Procedure

Participants deemed eligible were initially required to complete a risk evaluation before undergoing endoscopy procedure. To distinguish individuals with a high risk of developing UGC, we used a cancer-related risk assessment questionnaire developed by the CanSPUC group. This questionnaire covered a range of information, including basic information, dietary habits, living environment, lifestyle and habits, psychological and emotional aspects, medical history, and family history of cancer. To evaluate UGC risk, we used gender-specific risk scoring systems derived from the Harvard Cancer Risk Index [21]. A panel of experts assigned a score to each risk factor, considering the strength of its correlation with UGC. These individual risk scores were then totaled and divided by the average risk score in the general population, resulting in a relative risk assessment for each participant. The estimation process is illustrated in detail in Multimedia Appendix 1.

Individuals identified as high risk for UGC were advised to undertake a one-off endoscopy at a specialized tertiary-level hospital designated by the program. Further diagnostic or follow-up procedures were decided depending on the endoscopy results. Any anomalies discovered during the endoscopy were meticulously examined using biopsies. Additionally, visual documentation was made of any endoscopy findings. Individuals who did not have a complete endoscopy examination were encouraged to undergo a repeat endoscopy to fulfill the necessary clinical standards for diagnosis.

## Follow-Up Data

To address potential bias stemming from differences in the time during which participants in the screened cohort were required to stay alive and free from certain events (immortal time), we determined the entry date as the day of screening for participants in the screened group. In the nonscreened group, the cohort entry date was approximated based on the screening date of the participant in the screened group whose risk assessment date most closely matched that of the nonscreened group. The duration until the occurrence of UGC was computed as the time from the entry date to the earliest of 3 events: the development of UGC, death, or administrative censoring (up to June 30, 2021). Similarly, the duration until UGC-specific or all-cause death was calculated as the time from the cohort entry date to the earliest death or administrative censoring.

## Outcome Assessment and Quality Control

Our focus was on 3 key outcomes: new cases of UGC, UGC-related deaths, and deaths from all causes. We identified UGC using the *International Classification of Diseases, 10th Revision*, where EC was coded as C15 and GC as C16. Every 6 months, we collected outcome data from

national sources, which included the cancer registry and death surveillance system.

Our data collection involved standardized web-based forms, including an epidemiological questionnaire and endoscopy reports, which were collected by our qualified staff and physicians face-to-face. A thorough verification of consistency was carried out, and any discrepancies were rectified by referring to the original documents. Each participant was assigned a unique identification number, which helped us keep track of all relevant documentation.

### Statistical Analysis

We compared the screened versus nonscreened groups and the high-risk versus low-risk groups using standardized differences. These differences were derived by dividing the mean or proportion variations by a combined SD estimate [22]. This analytical approach is not heavily influenced by sample size and is efficacious in discerning significant discrepancies, with standardized differences exceeding 0.1 being deemed significant. For UGC outcomes, the estimation of the cumulative incidence or mortality was carried out using the cumulative incidence or mortality function, with due consideration given to the competing risk of mortality or other causes. All-cause mortality was defined as any cause of mortality, and cancer-specific mortality was regarded as mortality from UGC. The Gray test was used to evaluate discrepancies between groups concerning cumulative UGC incidence and UGC mortality. All-cause mortality was assessed using the Kaplan-Meier method with a log-rank test to discern differences between groups. We used a Cox proportional hazards model to determine the respective association of endoscopy screening with each outcome. Hazard ratios (HRs) and 95% CIs were reported. All hypothesis tests were 2-sided. Statistical analyses were conducted using R software (version 3.5.1; R Foundation for Statistical Computing), considering *P* values less than .05 as indicative of statistical significance.

### Ethical Considerations

The study was approved by the ethics committee of the Cancer Hospital Chinese Academy of Medical Sciences (approval 15-070/997) and Zhejiang Cancer Hospital (approval IRB-2022-271). All participants provided written informed consent.

## Results

In total, 153,079 participants were included in this study from 2013 to 2019. Of these, 113,916 (74.42%) of the participants were designated as low risk of UGC. The remaining 39,163 (25.68%) participants were deemed to be at high risk of UGC and were offered gastroscopy tests. Among the high-risk participants, 9627 (compliance rate 24.6%) adhered to the gastroscopy tests.

The baseline characteristics of participants in the high-risk and low-risk groups are summarized in Table 1. The mean age was 55.86 (SD 8.43) years among the entire population. The distributions of age, sex, BMI, education, marriage, and tea drinking among the high-risk group were similar to those in the low-risk group (standardized difference <0.1). In contrast to individuals in the low-risk group, participants in the high-risk group exhibited a higher likelihood of being smokers, being alcohol drinkers, being passive smokers, not performing frequent exercises, having a history of trauma and upper gastrointestinal system disease, and having family history of UGC (standardized difference >0.1).

After a median follow-up of 6.05 (IQR 3.06-7.06) years, a total of 51 UGC cases, 2 UGC deaths, and 66 all-cause deaths were identified in the screened cohort, whereas 146 UGC cases, 40 UGC deaths, and 364 all-cause deaths occurred in the nonscreened group. There were 425 UGC cases, 138 UGC deaths, and 1528 all-cause deaths in the low-risk group. The crude UGC incidence densities were 119.2 and 98.6 per 100,000 person-years in the screened and the nonscreened cohort, respectively. Obvious reductions in both the all-cause mortality and UGC mortality were observed between the screened group (153.7 and 4.7 per 100,000 person-years) and the nonscreened group (245.3 and 27 per 100,000 person-years; Table 2).

In Figure 2A, the screened group exhibited the highest cumulative incidence of UGC, followed by the nonscreened and low-risk groups; regarding all-cause cumulative mortality (Figure 2B), the screened group recorded the lowest rate, succeeded by the nonscreened and low-risk group; Figure 2C illustrates that cumulative UGC mortality was most pronounced in the nonscreened group, followed by the low-risk and screened group.

Figure 3 shows the adjusted HRs indicating the correlation between an endoscopy test and each outcome from Cox regression models. The screened group showed a significant 36% and 82% reduction in both all-cause mortality (HR 0.64, 95% CI 0.49-0.83, *P*<.001) and UGC mortality (HR 0.18, 95% CI 0.04-0.74, *P*=.02) compared to the nonscreened group. Reductions of 35% in all-cause mortality (HR 0.65, 95% CI 0.49-0.86, *P*=.003) and 81% in UGC mortality (HR 0.19, 95% CI 0.05-0.80, *P*=.02) were observed in participants aged older than 55 years in the screened group compared to the nonscreened group, and a reduction of 82% in UGC mortality (HR 0.18, 95% CI 0.04-0.74, *P*=.02) was also observed in participants aged 40-54 years. The reductions in all-cause mortality and UGC mortality were statistically significant in males (all-cause mortality: HR 0.64, 95% CI 0.47-0.88, *P*=.005; UGC mortality: HR 0.10, 95% CI 0.01-0.72, *P*=.02), but significant reductions were not observed in females (all *P* values were >.05). Compared to the nonscreened group, all-cause mortality decreased by 39% (HR 0.61, 95% CI 0.44-0.86, *P*=.004) for smokers and 38% (HR 0.62, 95%CI 0.41-0.95, *P*=.03) for nonsmokers in the screened group. Significant UGC mortality reductions were observed in smokers (HR 0.10, 95% CI 0.01-0.76; *P*=.03), but not for nonsmokers (*P*=.40).

**Table 1.** Baseline characteristics of the study population from 2013 to 2019 (N=153,079).

| Characteristics | Overall (n=153,079) | High-risk group | | | | Low-risk group (n=113,916) | Standardized difference (high-risk vs low risk) |
|---|---|---|---|---|---|---|---|
| | | High-risk group (n=39,163) | Screened (n=29,536) | Nonscreened (n=9627) | Standardized difference (screened vs nonscreened) | | |
| **Age (years)** | | | | | | | |
| Mean (SD) | 55.86 (8.43) | 56.42 (8.08) | 56.45 (8.16) | 56.33 (7.81) | 0.014 | 55.67 (8.54) | 0.090 |
| 40-54, n (%) | 66,838 (43.66) | 15,763 (40.25) | 11,865 (40.17) | 3898 (40.49) | 0.007 | 51,075 (44.84) | 0.093 |
| 55-74, n (%) | 86,241 (56.34) | 23,400 (59.75) | 17,671 (59.83) | 5729 (59.51) | 0.007 | 62,841 (55.16) | 0.093 |
| **Sex, n (%)** | | | | | 0.027 | | 0.008 |
| Male | 67,584 (44.15) | 17,177 (43.86) | 12,857 (43.53) | 4320 (44.87) | | 50,407 (44.25) | |
| Female | 5495 (55.85) | 21,986 (56.14) | 16,679 (56.47) | 5307 (55.13) | | 63,509 (55.75) | |
| **BMI (kg/m$^2$), n (%)** | | | | | 0.033 | | 0.033 |
| <24 | 56,535 (57.60) | 14,897 (58.80) | 11,212 (59.21) | 3685 (57.59) | | 41,638 (57.18) | |
| ≥24 | 41,620 (42.40) | 10,437 (41.20) | 7723 (40.79) | 2714 (42.41) | | 31,183 (42.82) | |
| **Education, n (%)** | | | | | 0.010 | | 0.028 |
| No primary education | 9139 (5.97) | 2532 (6.47) | 1928 (6.53) | 604 (6.27) | | 6607 (5.80) | |
| Primary education or more | 143,940 (94.03) | 36,631 (93.53) | 27,608 (93.47) | 9023 (93.73) | | 107,309 (94.20) | |
| **Marriage, n (%)** | | | | | 0.037 | | 0.033 |
| Unmarried | 7232 (4.72) | 2057 (5.25) | 1610 (5.45) | 447 (4.64) | | 5175 (4.54) | |
| Married | 145,847 (95.28) | 37,106 (94.75) | 27,926 (94.55) | 9180 (95.36) | | 108,741 (95.46) | |
| **Smoking, n (%)** | | | | | 0.114 | | 0.245 |
| No | 112,580 (73.54) | 25,583 (65.32) | 19,690 (66.66) | 5893 (61.21) | | 86,997 (76.37) | |
| Yes | 40,499 (26.46) | 13,580 (34.68) | 9846 (33.34) | 3734 (38.79) | | 26,919 (23.63) | |
| **Alcohol drinking, n (%)** | | | | | 0.107 | | 0.365 |
| No | 109,242 (71.36) | 23,037 (58.82) | 17,757 (60.12) | 5280 (54.85) | | 86,205 (75.67) | |
| Yes | 43,835 (28.64) | 16,126 (41.18) | 11,779 (39.88) | 4347 (45.15) | | 27,709 (24.32) | |
| **Passive smoking, n (%)** | | | | | 0.181 | | 0.473 |
| No | 94409 (61.67) | 17496 (44.67) | 13,841 (46.86) | 3655 (37.97) | | 76,913 (67.52) | |
| Yes | 58,668 (38.33) | 21667 (55.33) | 15,695 (53.14) | 5972 (62.03) | | 37,001 (32.48) | |
| **Tea drinking, n (%)** | | | | | 0.021 | | 0.030 |
| No | 85,398 (55.79) | 21,409 (54.67) | 16,224 (54.93) | 5185 (53.86) | | 63,989 (56.17) | |
| Yes | 67,679 (44.21) | 17,754 (45.33) | 13,312 (45.07) | 4442 (46.14) | | 49,925 (43.83) | |
| **Physical activity, n (%)** | | | | | 0.090 | | 0.189 |
| No | 82,587 (53.95) | 23,844 (60.88) | 17,665 (59.81) | 6179 (64.18) | | 58,743 (51.57) | |

| Characteristics | Overall (n=153,079) | High-risk group | | | | Low-risk group (n=113,916) | Standardized difference (high-risk vs low risk) |
|---|---|---|---|---|---|---|---|
| | | High-risk group (n=39,163) | Screened (n=29,536) | Nonscreened (n=9627) | Standardized difference (screened vs nonscreened) | | |
| Yes | 70,492 (46.05) | 15,319 (39.12) | 11,871 (40.19) | 3448 (35.82) | | 55,173 (48.43) | |
| **History of trauma, n (%)** | | | | | 0.136 | | 0.443 |
| No | 139,294 (90.99) | 31,469 (80.35) | 24,136 (81.72) | 7333 (76.17) | | 107,825 (94.65) | |
| Yes | 13,785 (9.01) | 7694 (19.65) | 5400 (18.28) | 2294 (23.83) | | 6091 (5.35) | |
| **History of mental depression, n (%)** | | | | | 0.203 | | 0.397 |
| No | 142,098 (92.83) | 3,2945 (84.12) | 25,408 (86.02) | 7537 (78.29) | | 109,153 (95.82) | |
| Yes | 10,981 (7.17) | 6218 (15.88) | 4128 (13.98) | 2090 (21.71) | | 4763 (4.18) | |
| **History of upper gastrointestinal system disease, n (%)** | | | | | 0.252 | | 2.165 |
| No | 115,287 (75.31) | 8335 (21.28) | 6995 (23.68) | 1340 (13.92) | | 106,952 (93.89) | |
| Yes | 37,788 (24.69) | 30,827 (78.71) | 22,541 (76.32) | 8286 (86.07) | | 6961 (6.11) | |
| **Family history of UGC[a], n (%)** | | | | | 0.094 | | 0.986 |
| No | 137,908 (90.09) | 25,322 (64.66) | 19,427 (65.77) | 5895 (61.23) | | 112,586 (98.83) | |
| Yes | 15,171 (9.91) | 13,841 (35.34) | 10,109 (34.23) | 3732 (38.77) | | 1330 (1.17) | |

[a]UGC: upper gastrointestinal cancer.

**Table 2.** Crude incidence of upper gastrointestinal cancer (UGC), all-cause mortality, and UGC mortality among all participants, high-risk group (screened and nonscreened), and low-risk group.

| | Overall | | High-risk group | | | | Low-risk group | |
|---|---|---|---|---|---|---|---|---|
| | Number | Rate (95% CI)[a] | Screened | | Nonscreened | | Number | Rate (95% CI)[a] |
| | | | Number | Rate (95% CI)[a] | Number | Rate (95% CI)[a] | | |
| **UGC incidence** | | | | | | | | |
| Overall | 622 | 79.9 (73.9-86.5) | 51 | 119.2 (90.6-156.9) | 146 | 98.6 (83.9-116.0) | 425 | 72.4 (65.8-79.6) |
| **Age (years)** | | | | | | | | |
| 40-54 | 121 | 35.0 (29.3-41.8) | 5 | 29.4 (12.3-70.7) | 26 | 42.9 (29.2-63.0) | 90 | 33.5 (27.3-41.2) |
| 55-74 | 501 | 115.9 (106.2-126.5) | 46 | 178.3 (133.6-238.1) | 120 | 137.2 (114.8-164.1) | 335 | 105.0 (94.4-116.9) |
| **Sex** | | | | | | | | |
| Male | 456 | 134.3 (122.6-147.3) | 34 | 179.7 (128.4-251.5) | 114 | 176.7 (147.0-212.3) | 308 | 120.3 (107.6-134.5) |
| Female | 166 | 37.8 (32.5-44.1) | 17 | 71.3 (44.3-114.6) | 32 | 38.3 (27.1-54.2) | 117 | 35.3 (29.5-42.3) |
| **Smoking** | | | | | | | | |
| No | 298 | 52.2 (46.6-58.4) | 22 | 82.0 (54.0-124.5) | 56 | 56.9 (43.8-74.0) | 220 | 49.3 (43.2-56.3) |
| Yes | 324 | 156.7 (140.6-174.8) | 29 | 182.0 (126.5-262.0) | 90 | 181.2 (147.4-222.8) | 205 | 145.3 (126.7-166.6) |
| **All-cause mortality** | | | | | | | | |
| Overall | 1958 | 251.6 (240.7-263.0) | 66 | 153.7 (120.7-195.6) | 364 | 245.3 (221.3-271.8) | 1528 | 259.7 (247.0-273.1) |
| **Age (years)** | | | | | | | | |
| 40-54 | 397 | 114.8 (104.0-126.6) | 9 | 53.0 (27.6-101.9) | 64 | 105.6 (82.7-135.0) | 324 | 120.7 (108.3-134.6) |
| 55-74 | 1561 | 361.2 (343.7-379.6) | 57 | 221.0 (170.5-286.5) | 300 | 343.1 (306.4-384.2) | 1204 | 377.5 (356.8-399.4) |
| **Sex** | | | | | | | | |

| | Overall | | High-risk group | | | | Low-risk group | |
|---|---|---|---|---|---|---|---|---|
| | Number | Rate (95% CI)[a] | Screened | | Nonscreened | | Number | Rate (95% CI)[a] |
| | | | Number | Rate (95% CI)[a] | Number | Rate (95% CI)[a] | | |
| Male | 1325 | 390.4 (369.9-412.0) | 47 | 248.4 (186.6-330.6) | 255 | 395.2 (349.5-446.8) | 1023 | 399.6 (375.9-424.9) |
| Female | 633 | 144.3 (133.5-156.0) | 19 | 79.7 (50.8-124.9) | 109 | 130.6 (108.2-157.5) | 505 | 152.4 (139.7-166.3) |
| **Smoking** | | | | | | | | |
| No | 1085 | 189.9 (178.9-201.5) | 25 | 93.1 (62.9-137.8) | 149 | 151.5 (129.0-177.9) | 911 | 204.2 (191.3-217.9) |
| Yes | 873 | 422.3 (395.2-451.3) | 41 | 257.4 (189.5-349.5) | 215 | 432.9 (378.7-494.8) | 617 | 437.2 (404.0-473.1) |
| **UGC mortality** | | | | | | | | |
| Overall | 180 | 23.1 (20.0-26.8) | 2 | 4.7 (1.2-18.6) | 40 | 27.0 (19.8-36.7) | 138 | 23.5 (19.9-27.7) |
| **Age (years)** | | | | | | | | |
| 40-54 | 24 | 6.9 (4.6-10.3) | 0 | —[b] | 4 | 6.6 (2.5-17.6) | 20 | 7.5 (4.8-11.6) |
| 55-74 | 156 | 36.1 (30.9-42.2) | 2 | 7.8 (1.9-31.0) | 36 | 41.2 (29.7-57.1) | 118 | 37.0 (30.9-44.3) |
| **Sex** | | | | | | | | |
| Male | 149 | 43.9 (37.4-51.5) | 1 | 5.3 (0.7-37.5) | 36 | 55.8 (40.2-77.3) | 112 | 43.8 (36.4-52.7) |
| Female | 31 | 7.1 (5.0-10.0) | 1 | 4.2 (0.6-29.8) | 4 | 4.8 (1.8-12.8) | 26 | 7.8 (5.3-11.5) |
| **Smoking** | | | | | | | | |
| No | 70 | 12.3 (9.7-15.5) | 1 | 3.7 (0.5-26.4) | 9 | 9.2 (4.8-17.6) | 60 | 13.4 (10.4-17.3) |
| Yes | 110 | 53.2 (44.1-64.1) | 1 | 6.3 (0.9-44.6) | 31 | 62.4 (43.9-88.8) | 78 | 55.3 (44.3-69.0) |

[a]Rate is the number of cases per 100,000 person-years.
[b]Not available.

**Figure 2.** (A) Cumulative incidence of UGC, (B) all-cause mortality, and (C) UGC mortality. UGC: upper gastrointestinal cancer.

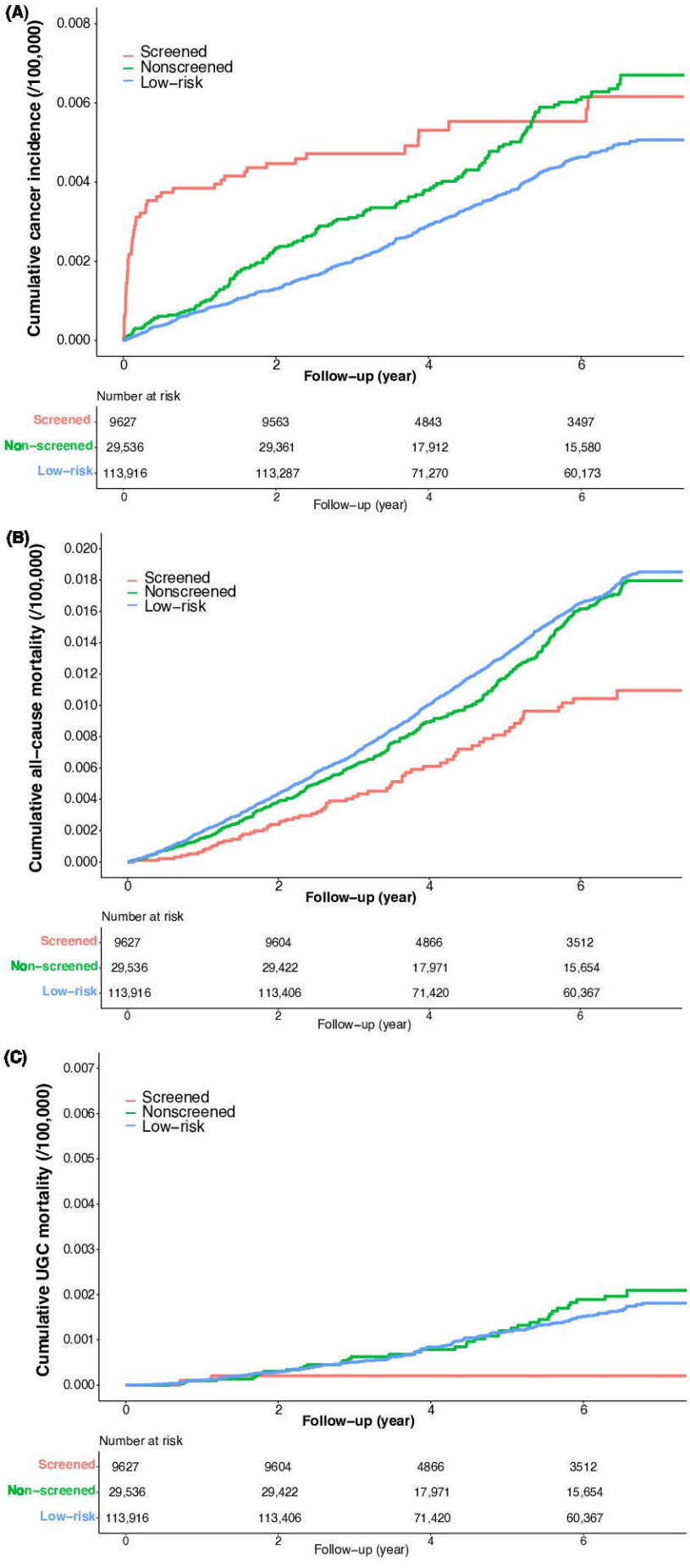
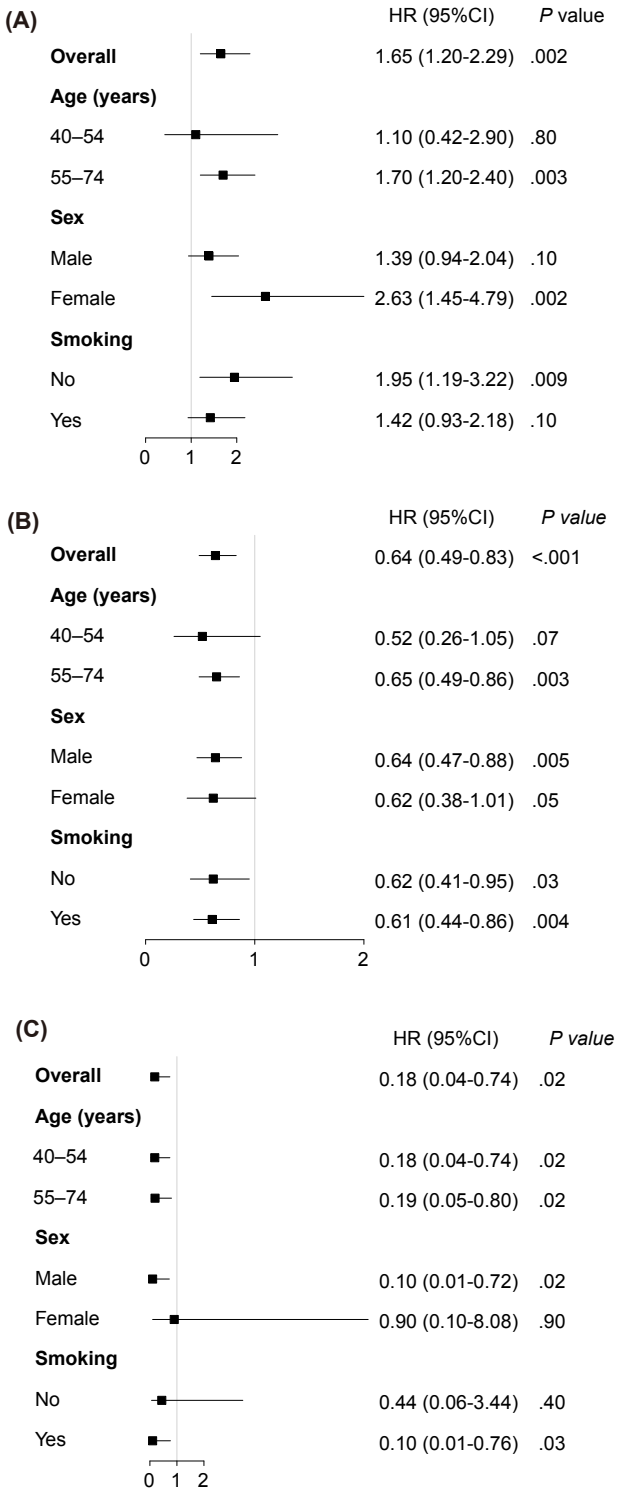


**Figure 3.** (A) Forest plot of the adjusted HRs for the association between an endoscopy test and incidence of upper gastrointestinal cancer, (B) all-cause mortality, and (C) upper gastrointestinal cancer mortality. Note: comparisons are between the screened group and the nonscreened group. HR: hazard ratio.




# Discussion

## *Principal Findings*

We conducted a multicenter, large-scale, prospective cohort study to investigate the effectiveness of sequential UGC screening in a real-world situation. Our results highlight a substantial decrease in both all-cause mortality and UGC mortality among high-risk individuals subjected to one-off endoscopic screening compared to the nonscreened group. These findings carry significant implications for clinical practice and public health, emphasizing the real benefits associated with the implementation of effective UGC screening programs.

UGC continues to represent a substantial population health challenge on a global scale. While evaluations of the program's effectiveness have been conducted over several decades, the routine impact of the screening program remains unclear. Countries such as Japan and Korea in East Asia have also implemented nationwide population-based screening strategies to address the high burden of UGC and reduce its incidence and mortality, showing that implementing gastroscopic screening in high-risk rural areas can lower the mortality related to EC and GC [5]. The Korean National Cancer Screening Program found an overall odds ratio of GC mortality among individuals ever screened as 0.79 (95% CI 0.77-0.81) relative to those who had never undergone screening [13,23]. On the other hand, Hamashima et al [24] revealed a standardized mortality risk ratio of 0.43 (95% CI 0.30-0.57) for the gastroscopic screening participants in Japan. Another study illustrated decreases in cumulative mortality from UGC, with a standardized mortality rate of 0.47 (95% CI 0.25-0.88) [25]. Despite these studies, the effectiveness of UGC screening programs remains a topic of ongoing research and discussion. The effectiveness of UGC screening in lowering mortality may be ascribed to the identification of precancerous abnormalities. The majority of cancers detected through screening were in their early stages, including precancerous lesions. These early-stage malignancies have a lower likelihood of progressing compared to advanced-stage cancers if treated promptly. Hence, the sustained decrease in UGC mortality over time aligns with the natural course of UGC, affirming the continued impact of timely intervention.

Apart from the above studies, evidence derived from large-scale, high-quality cohort studies regarding the association with all-cause mortality is sparse. One of the most compelling aspects of our results is the impact on all-cause mortality. The fact that screening significantly lowered 36% of all-cause mortality indicates that the benefits of UGC screening extend beyond merely reducing UGC-related deaths. A positive impact on overall mortality may be more conspicuous in nations with constrained medical resources and fewer diagnostic capabilities compared to countries with ample medical provisions. Individuals who participate in such screening programs experience better overall health outcomes and a lower risk of death from various causes. This suggests that the positive effects of screening are not limited to cancer-specific outcomes but can have a broader impact on an individual's overall well-being. However, research conducted among Western populations did not consistently demonstrate a meaningful correlation [26]. The disparity could be attributed to lower UGC incidences and mortality rates in Western populations compared to East Asian populations [1]. In Europe, Areia et al [26] pointed out that the cost-effectiveness of gastroscopic screening was only evident when accompanied by colonoscopy screening in countries where the risk of GC is ≥10 per 100,000.

As expected, a greater UGC incidence density was observed in both the high-risk and screened groups, which can be attributed to increased opportunities for early diagnosis and treatment. Early detection is a key determinant of improved cancer treatment outcomes [27,28]. When UGC is diagnosed at an advanced stage, the treatment options become limited, and the prognosis tends to be less favorable. However, screening programs, as demonstrated in our study, offer a powerful tool to address this issue. One of the notable outcomes we observed was a marked increase in incidence rates within the screened group. This is a positive outcome, and it underscores the fact that screening programs effectively identify cases of UGC at earlier, more treatable stages. By increasing the opportunities for early diagnosis, screening facilitates timely medical intervention, which is known to lead to better treatment success rates. The rationale behind this increase in incidence rates within the screened group is that the screening process identifies UGC cases that might have otherwise gone undetected until they reached a more advanced and less treatable stage. When UGC is diagnosed early, patients can receive appropriate medical care, including surgical intervention, targeted therapy, or radiation treatment, all of which are associated with higher success rates in terms of disease management and patient survival. Additionally, early detection allows for a more focused and less aggressive treatment approach. This means that patients with UGC detected through screening may undergo less invasive surgical procedures, experience fewer treatment-related side effects, and have a higher likelihood of achieving complete remission. As a result, the quality of life for these individuals can be significantly improved.

We also highlight variations in the effectiveness of screening among different age groups and genders. Notably, the benefits of screening appear more pronounced in older participants, particularly concerning UGC mortality. This may be linked to age-related differences in cancer progression and treatment response. It has been reported that advanced age is associated with an increased risk of developing UGC [29]. The UGC incidence, all-cause mortality, and UGC mortality in the age group of 55-74 years are all remarkably higher than those in the age group of 40-54 years, consistent with findings from other studies [30,31]. In addition, our study showed that older adult individuals showed markedly reduced risks of all-cause mortality (HR 0.65, 95% CI 0.49-0.86) and UGC mortality (HR 0.19, 95% CI 0.05-0.80) after the endoscopic screening in contrast to the younger group. Furthermore, we observed a more pronounced effect of screening in males, with significant reductions in both all-cause mortality and UGC mortality, whereas the effect was less significant in females. This could reflect gender-specific disparities in UGC incidence and survival. These differences may be associated with unfavorable lifestyle habits in males, such as smoking, alcohol consumption, and irregular dietary patterns [32]. Moreover, we observed similar reductions in all-cause mortality for smokers (0.61, 95% CI 0.44-0.86) and nonsmokers (0.62, 95% CI 0.41-0.95) after endoscopic screening, which means the screening initiative contributes to overall health outcomes, irrespective of smoking status. While the study reveals significant reductions in UGC mortality among smokers (HR 0.10, 95% CI 0.01-0.76), the absence of a similar effect in nonsmokers raises intriguing questions. The explanation for this may lie in several factors, including distinct etiological pathways of

UGC in smokers and nonsmokers, or differences in health awareness among these 2 populations. Further exploration of these nuances could enhance our understanding of the intricate interplay among risk exposures, screening effectiveness, and mortality outcomes.

## Limitations

Our study has several limitations. First, the follow-up duration of 6.05 years might be insufficient for capturing all death cases, potentially leading to an underestimation of the long-term impact of the screening program. Ideally, a more extended follow-up period would afford a comprehensive understanding of sustained benefits and potential late-emerging effects. Future research endeavors should consider prolonging follow-up periods to fully evaluate the program's long-term effectiveness. Second, one must consider that the findings might not be universally representative across the entire general population of China. However, the study does offer a valuable scientific foundation for areas exhibiting equivalent socioeconomic profiles. Third, the screening compliance rate of 24.6% among high-risk individuals raises concerns about the generalizability of the findings to the entire high-risk individuals. The relatively low uptake rate may give rise to selection bias, influencing observed outcomes. However, it marginally surpassed the figure reported for UGC screening in Henan Province (18.4%) and Liaoning Province (22.3%), China [10,31,32]. Future research could explore strategies to enhance participation, such as community engagement programs, targeted awareness campaigns, or initiatives aimed at overcoming potential barriers to screening. These measures would ensure a more representative study population and enhance the generalizability of the findings. Future randomized controlled trials may be warranted to further validate the efficacy of risk-adapted sequential screening strategies.

## Conclusions

In conclusion, our study suggests the significance of UGC screening in reducing both all-cause mortality and UGC mortality, particularly among high-risk individuals. Screening offers the opportunity for early UGC detection, enhancing treatment success rates and alleviating the disease burden for patients. However, screening effectiveness may vary by age and gender, necessitating consideration when implementing screening programs. Our research provides robust support for further exploration and implementation of UGC screening, with the potential to alleviate the disease burden of UGC.

### Acknowledgments

The study was supported by the Cancer Screening Program in Urban China, Healthy Zhejiang One Million People Cohort (K-20230085), Medical and Health Research Project of Zhejiang Province (2024KY050), Zhejiang Cancer Hospital's National Natural Science Foundation Cultivation Fund (PY2022042), and Zhejiang Cancer Hospital Youth Research Fund (QN202201). We express gratitude to all the participants and investigators who contributed to this study for their assistance with data collection, organization, validation, and database establishment. The authors assume full responsibility for the analysis of data and interpretation of results presented in this paper.

### Data Availability

The data can be provided after contact with LD upon reasonable request.

### Authors' Contributions

YW designed the study and drafted the paper. JZ performed and validated the data analysis and data interpretation. HL and LW performed data collection. CZ and XL assisted data interpretation. SW and LD conceived and supervised the project. All authors reviewed and approved the final version.

### Conflicts of Interest

None declared.

### Multimedia Appendix 1

The flow of risk estimation process [21].
[DOCX File (Microsoft Word File), 78 KB-Multimedia Appendix 1]

### References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263. [doi: 10.3322/caac.21834] [Medline: 38572751]
2. Han B, Zheng R, Zeng H, et al. Cancer incidence and mortality in China, 2022. J Natl Cancer Cent. Mar 2024;4(1):47-53. [doi: 10.1016/j.jncc.2024.01.006] [Medline: 39036382]
3. Arnold M, Abnet CC, Neale RE, et al. Global burden of 5 major types of gastrointestinal cancer. Gastroenterology. Jul 2020;159(1):335-349. [doi: 10.1053/j.gastro.2020.02.068] [Medline: 32247694]
4. Sun D, Li H, Cao M, et al. Cancer burden in China: trends, risk factors and prevention. Cancer Biol Med. Nov 15, 2020;17(4):879-895. [doi: 10.20892/j.issn.2095-3941.2020.0387] [Medline: 33299641]

5. Zhang X, Li M, Chen S, et al. Endoscopic screening in Asian countries is associated with reduced gastric cancer mortality: a meta-analysis and systematic review. Gastroenterology. Aug 2018;155(2):347-354. [doi: 10.1053/j.gastro.2018.04.026] [Medline: 29723507]
6. Zeng H, Chen W, Zheng R, et al. Changing cancer survival in China during 2003-15: a pooled analysis of 17 population-based cancer registries. Lancet Glob Health. May 2018;6(5):e555-e567. [doi: 10.1016/S2214-109X(18)30127-X] [Medline: 29653628]
7. Katai H, Ishikawa T, Akazawa K, et al. Five-year survival analysis of surgically resected gastric cancer cases in Japan: a retrospective analysis of more than 100,000 patients from the nationwide registry of the Japanese Gastric Cancer Association (2001-2007). Gastric Cancer. Jan 2018;21(1):144-154. [doi: 10.1007/s10120-017-0716-7] [Medline: 28417260]
8. Chen R, Liu Y, Song G, et al. Effectiveness of one-time endoscopic screening programme in prevention of upper gastrointestinal cancer in China: a multicentre population-based cohort study. Gut. Feb 2021;70(2):251-260. [doi: 10.1136/gutjnl-2019-320200] [Medline: 32241902]
9. Liu M, Yang W, Guo C, et al. Effectiveness of endoscopic screening on esophageal cancer incidence and mortality: a 9-year report of the endoscopic screening for esophageal cancer in China (ESECC) randomized trial. J Clin Oncol. May 10, 2024;42(14):1655-1664. [doi: 10.1200/JCO.23.01284] [Medline: 38457759]
10. He Z, Liu Z, Liu M, et al. Efficacy of endoscopic screening for esophageal cancer in China (ESECC): design and preliminary results of a population-based randomised controlled trial. Gut. Feb 2019;68(2):198-206. [doi: 10.1136/gutjnl-2017-315520] [Medline: 29306867]
11. Xia R, Zeng H, Liu W, et al. Estimated cost-effectiveness of endoscopic screening for upper gastrointestinal tract cancer in high-risk areas in China. JAMA Netw Open. Aug 2, 2021;4(8):e2121403. [doi: 10.1001/jamanetworkopen.2021.21403] [Medline: 34402889]
12. Xia R, Li H, Shi J, et al. Cost-effectiveness of risk-stratified endoscopic screening for esophageal cancer in high-risk areas of China: a modeling study. Gastrointest Endosc. Feb 2022;95(2):225-235. [doi: 10.1016/j.gie.2021.08.008] [Medline: 34418461]
13. Kim JH, Han KD, Lee JK, et al. Association between the National Cancer Screening Programme (NSCP) for gastric cancer and oesophageal cancer mortality. Br J Cancer. Aug 2020;123(3):480-486. [doi: 10.1038/s41416-020-0883-x] [Medline: 32398860]
14. Shiratori Y, Ishii N, Kalloo A. Disparities in gastric cancer screening: a comparative analysis of Japan and South Korea. Gastroenterology. Sep 2024;167(4):815-816. [doi: 10.1053/j.gastro.2024.03.013] [Medline: 38494036]
15. Hamashima C, Systematic Review Group and Guideline Development Group for Gastric Cancer Screening Guidelines. Update version of the Japanese guidelines for gastric cancer screening. Jpn J Clin Oncol. Jul 1, 2018;48(7):673-683. [doi: 10.1093/jjco/hyy077] [Medline: 29889263]
16. He J, Chen WQ, Li ZS, et al. China guideline for the screening, early detection and early treatment of gastric cancer (2022, Beijing). Zhonghua Zhong Liu Za Zhi. Jul 23, 2022;44(7):634-666. [doi: 10.3760/cma.j.cn112152-20220617-00430] [Medline: 35880331]
17. He J, Chen WQ, Li ZS, et al. China guideline for the screening, early detection and early treatment of esophageal cancer (2022, Beijing). Zhonghua Zhong Liu Za Zhi. Jun 23, 2022;44(6):491-522. [doi: 10.3760/cma.j.cn112152-20220517-00348] [Medline: 35754225]
18. Li N, Tan F, Chen W, et al. One-off low-dose CT for lung cancer screening in China: a multicentre, population-based, prospective cohort study. Lancet Respir Med. Apr 2022;10(4):378-391. [doi: 10.1016/S2213-2600(21)00560-9] [Medline: 35276087]
19. Wang Y, Shi J, Du L, et al. Health-related quality of life in patients with esophageal cancer or precancerous lesions assessed by EQ-5D: a multicenter cross-sectional study. Thorac Cancer. Apr 2020;11(4):1076-1089. [doi: 10.1111/1759-7714.13368] [Medline: 32130756]
20. Zhang N, Li Y, Chang X, et al. Long-term effectiveness of one-time endoscopic screening for esophageal cancer: a community-based study in rural China. Cancer. Oct 15, 2020;126(20):4511-4520. [doi: 10.1002/cncr.33119] [Medline: 33460056]
21. Colditz GA, Atwood KA, Emmons K, et al. Harvard report on cancer prevention volume 4: Harvard Cancer Risk Index. Risk Index Working Group, Harvard Center for Cancer Prevention. Cancer Causes Control. Jul 2000;11(6):477-488. [doi: 10.1023/a:1008984432272] [Medline: 10880030]
22. Mamdani M, Sykora K, Li P, et al. Reader's guide to critical appraisal of cohort studies: 2. assessing potential for confounding. BMJ. Apr 23, 2005;330(7497):960-962. [doi: 10.1136/bmj.330.7497.960] [Medline: 15845982]
23. Jun JK, Choi KS, Lee HY, et al. Effectiveness of the Korean National Cancer Screening Program in reducing gastric cancer mortality. Gastroenterology. May 2017;152(6):1319-1328. [doi: 10.1053/j.gastro.2017.01.029] [Medline: 28147224]

24. Hamashima C, Ogoshi K, Narisawa R, et al. Impact of endoscopic screening on mortality reduction from gastric cancer. World J Gastroenterol. Feb 28, 2015;21(8):2460-2466. [doi: 10.3748/wjg.v21.i8.2460] [Medline: 25741155]
25. Liu M, He Z, Guo C, et al. Effectiveness of intensive endoscopic screening for esophageal cancer in China: a community-based study. Am J Epidemiol. Apr 1, 2019;188(4):776-784. [doi: 10.1093/aje/kwy291] [Medline: 30608546]
26. Areia M, Spaander MC, Kuipers EJ, Dinis-Ribeiro M. Endoscopic screening for gastric cancer: a cost-utility analysis for countries with an intermediate gastric cancer risk. United European Gastroenterol J. Mar 2018;6(2):192-202. [doi: 10.1177/2050640617722902] [Medline: 29511549]
27. Zong L, Abe M, Seto Y, Ji J. The challenge of screening for early gastric cancer in China. Lancet. Nov 26, 2016;388(10060):2606. [doi: 10.1016/S0140-6736(16)32226-7] [Medline: 27894662]
28. Xia C, Basu P, Kramer BS, et al. Cancer screening in China: a steep road from evidence to implementation. Lancet Public Health. Dec 2023;8(12):e996-e1005. [doi: 10.1016/S2468-2667(23)00186-X] [Medline: 38000379]
29. Li Y, Ren N, Zhang B, et al. Gastric cancer incidence trends in China and Japan from 1990 to 2019: disentangling age-period-cohort patterns. Cancer. Jan 1, 2023;129(1):98-106. [doi: 10.1002/cncr.34511] [Medline: 36284481]
30. Yu Z, Zuo T, Yu H, et al. Outcomes of upper gastrointestinal cancer screening in high-risk individuals: a population-based prospective study in Northeast China. BMJ Open. Feb 15, 2022;12(2):e046134. [doi: 10.1136/bmjopen-2020-046134] [Medline: 35168959]
31. Guo L, Zhang S, Liu S, et al. Determinants of participation and detection rate of upper gastrointestinal cancer from population-based screening program in China. Cancer Med. Nov 2019;8(16):7098-7107. [doi: 10.1002/cam4.2578] [Medline: 31560836]
32. White AM. Gender differences in the epidemiology of alcohol use and related harms in the United states. Alcohol Res. 2020;40(2):01. [doi: 10.35946/arcr.v40.2.01] [Medline: 33133878]


## Abbreviations

**CanSPUC:** Cancer Screening Program in Urban China
**EC:** esophageal cancer
**GC:** gastric cancer
**HR:** hazard ratio
**UGC:** upper gastrointestinal cancer


*Edited by Amaryllis Mavragani; peer-reviewed by Deepa Valvi, Ru Chen; submitted 03.06.2024; final revised version received 08.08.2024; accepted 09.08.2024; published 10.10.2024*

*Please cite as:*
*Wang Y, Zhu J, Li H, Wang L, Zhu C, Li X, Wang S, Du L*
*Effectiveness of Risk-Adapted Upper Gastrointestinal Cancer Screening in China: Prospective Cohort Study*
*JMIR Public Health Surveill 2024;10:e62864*
*URL: https://publichealth.jmir.org/2024/1/e62864*
*doi: 10.2196/62864*


© Youqing Wang, Juan Zhu, Huizhang Li, Le Wang, Chen Zhu, Xue Li, Shi Wang, Lingbin Du. Originally published in JMIR Public Health and Surveillance (https://publichealth.jmir.org), 10.10.2024. This is an open-access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Public Health and Surveillance, is properly cited. The complete bibliographic information, a link to the original publication on https://publichealth.jmir.org, as well as this copyright and license information must be included.