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## Research paper

## Health-seeking behavior and barriers to treatment of patients with upper gastrointestinal cancer detected by screening in rural China: real-world evidence from the ESECC trial

Hui Wang<sup>1,#</sup>, Zhen Liu<sup>1,#</sup>, Chuanhai Guo<sup>1</sup>, Mengfei Liu<sup>1</sup>, Yu He<sup>2</sup>, Hongrui Tian<sup>1</sup>, Yaqi Pan<sup>1</sup>, Fangfang Liu<sup>1</sup>, Ying Liu<sup>1</sup>, Zhe Hu<sup>1</sup>, Huanyu Chen<sup>1</sup>, Zhonghu He<sup>1,\*</sup>, Yang Ke<sup>1,\*</sup><sup>1</sup> Key laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Laboratory of Genetics, Peking University Cancer Hospital & Institute, Beijing, People's Republic of China<sup>2</sup> Department of Non-communicable Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK

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## ABSTRACT

**Background:** To fully realize efficacy in cancer screening, timely and appropriate treatment for participants with malignant lesions is critical. However, the health-seeking behavior of patients with upper gastrointestinal (G.I.) cancer identified in population-level screening programs in China is unknown.

**Methods:** A community-based real-world investigation was conducted with 136 upper G.I. cancer patients detected in a large screening cohort in an area of high-risk for upper G.I. cancer in China. Using local medical claims data and semi-structured face-to-face interview, we collected information regarding the clinical treatment regimen and factors which result in the lack of timely and appropriate treatment.

**Findings:** The treatment records for 133 upper G.I. cancer patients were acquired. Among these, 48 (36.09%) patients did not receive treatment within three months of initial diagnosis, and treatment of early-stage cancer was more likely to be delayed. Sixteen patients did not seek further diagnostic testing due to their low health-awareness and socio-economic status. Another 20 participants proactively sought further diagnostic evaluation in health care facilities but were prevented from receiving further treatment due to low sensitivity of given diagnostic test(s), failure to recognize the significance of screening results, and/or lack of basic knowledge of diagnosis and treatment for early cancer on the part of clinicians. The treatment regimen offered to patients depended largely on the level of health care facilities they visited, and non-medical factors were the main reasons for choice of health care facilities.

**Interpretation:** A coordinated, system-based management strategy is urgently needed to support the design of upper G.I. cancer screening programs in rural populations in China.

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\* Corresponding author. Key laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Laboratory of Genetics, Peking University Cancer Hospital & Institute, #52 Fucheng Rd, Beijing, 100142, P.R. China, Tel: +86-10-88196762

E-mail addresses: [zhonghuhe@foxmail.com](mailto:zhonghuhe@foxmail.com) (Z. He), [keyang@bjmu.edu.cn](mailto:keyang@bjmu.edu.cn) (Y. Ke).

# Authors for equal contribution

## Research in context

**Evidence before this study**

Achieving efficacy of screening relies largely on timely appropriate treatment for participants following detection of malignant lesions. Effective management of screening positive individuals is thus an important component of any screening program. We searched PubMed and Google Scholar for studies published from the inception of the database to Jan 1, 2021, with no language restrictions. Using the search terms “cancer screening program” or “cancer screening trial” or “cancer screening projects”, mass cancer screening programs were found with this specific combination. In these mass cancer screening projects in different countries we identified, roughly two management strategies were adopted including “screening & recommendation” and “screening & treatment”. A series of early diagnosis and early treatment projects for upper G.I. cancer had been launched in high-incidence rural areas of China in the past decades. In these projects, “screening & recommendation” strategy was widely adopted for management of screening positive individuals. However, whether these screening-detected cancer patients received timely and appropriate treatment is unknown, and what factors influenced their health-seeking behavior had not been well determined.

**Added value of this study**

To our knowledge, this is the first study to investigate the real-world health-seeking behavior of screening-detected upper G.I. cancer patients in a rural area with high incidence for esophageal cancer in China. We mapped out the health-seeking trajectory of screening-detected upper G.I. cancer patients, revealed the reasons for lack of timely treatment and for choice of health facilities for treatment.

**Implications of all the available evidence**

We recommend adoption of a coordinated, system-based management strategy when designing an upper G.I. cancer screening project in rural populations in China. Our findings provide important evidence for formulating and tailoring management strategy for cancer screening in rural areas in China, and also provide guidance for screening in other similar settings.

**Introduction**

Cancer is the leading cause of death worldwide, and is an important barrier to increasing life expectancy in the 21st century.<sup>1</sup> The development of cancer is a multi-step process, and a wide variety of cancers are amenable to early detection resulting in earlier diagnosis, thus improving prognosis. Screening has therefore been widely accepted as an optimal secondary prevention strategy for cancers, especially for those cancers with etiologic factors which have not been definitively identified.<sup>2</sup>

Achieving efficacy in screening is dependent largely on timely and appropriate treatment for participants with malignant lesions which have been detected in screening.<sup>3</sup> It is therefore crucial to formulate a management strategy which ensures participants in screening programs with screening-detected abnormalities receive timely and appropriate clinical treatment consistent with local health system capacity and socio-economic level. Currently, management strategies for persons in cancer screening programs who are screening-positive can roughly be classified into two types which include “screening & recommendation” and “screening &

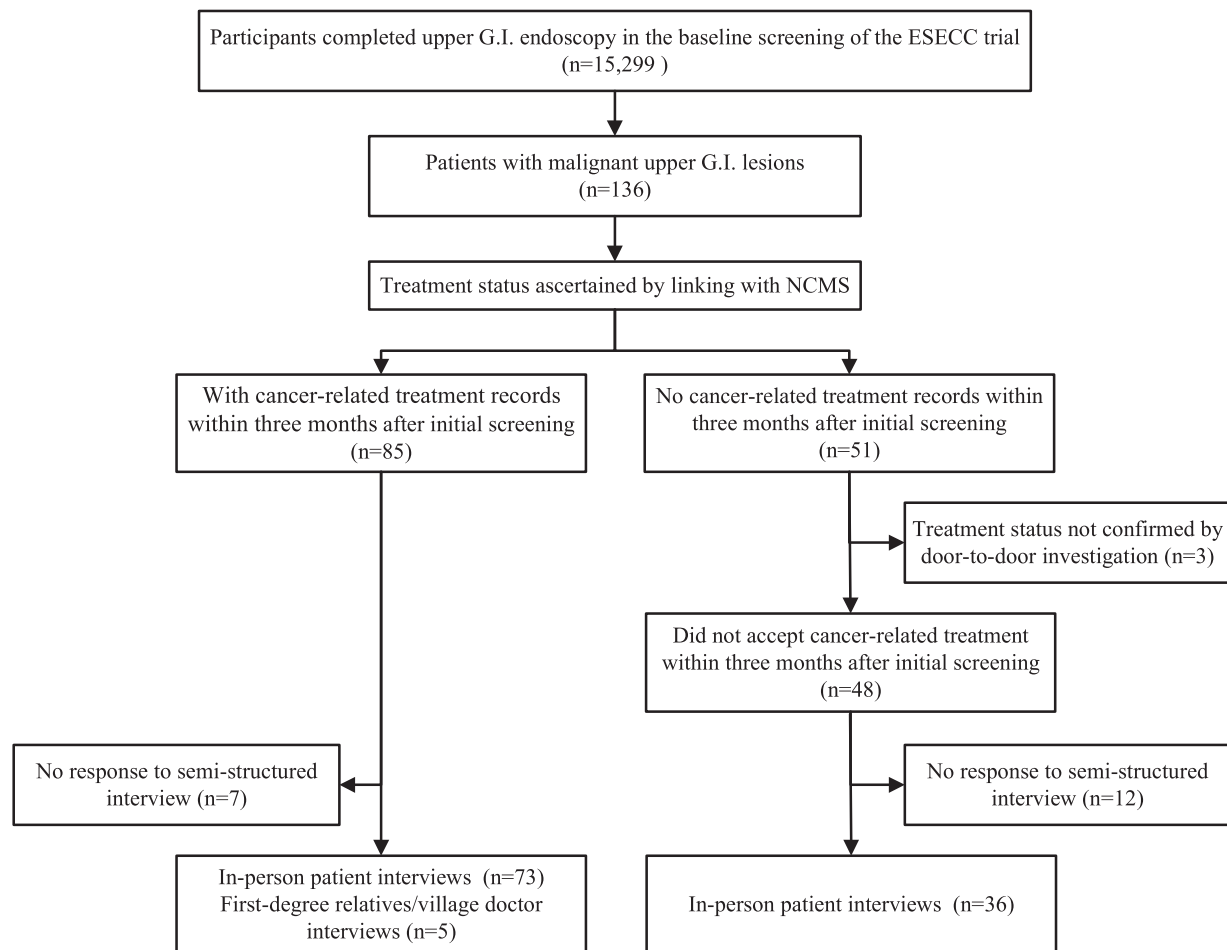
treatment”. The former has been the most widely adopted strategy. Taking the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial<sup>3</sup> and the National Lung Screening Trial<sup>4</sup> as examples, it is noteworthy that these cancer screening programs ceased after screening, together with communication of findings, and referral, and the patients were then free to choose whether to seek further diagnosis and treatment or not. The less commonly employed “screening & treatment” strategy, which was adopted in an endoscopic screening trial in China<sup>5</sup> and in a colorectal screening trial in Norway,<sup>6</sup> directly provided diagnostic testing and therapeutic procedures for individuals who were screening-positive.

China has a high incidence of esophageal cancer (EC), and most high-risk regions in China are rural areas where people have relatively low socio-economic status and limited access to health services.<sup>7</sup> The central government of China has implemented a series of early diagnosis and early treatment projects for upper gastrointestinal (G.I.) cancer in high-incidence rural areas beginning in 2005, and most of these programs have adopted the “screening & recommendation” strategy. A total of 2.16 million people underwent upper G.I. cancer screening up to 2018, and among these individuals over 34 thousand were found to have upper G.I. cancer; 70% of these individuals were diagnosed at early stage.<sup>8</sup> Given the lack of a strict referral mechanism in China’s health system,<sup>9</sup> these screening-detected patients were often left to decide for themselves whether, and at which health care facility to seek further diagnosis and treatment. Such decisions are strongly affected by individual health literacy, socio-economic status and health system-related factors such as health care availability and accessibility.<sup>10</sup> However, to date no study has reported on the performance of the “screening & recommendation” strategy in China. Therefore, mapping out the health-seeking trajectory of individuals who are screening-positive together with the factors associated with their health-seeking behavior is a matter of importance. Such information has potential to inform planning of cancer screening in China in the future.

In this study, for the first time we conducted a community-based mixed methods study based on the Endoscopic Screening for Esophageal Cancer in China (ESECC) trial, which was a population-based randomized controlled trial in a region that is high-risk for EC in China.<sup>11,12</sup> This study aimed to evaluate the performance of the “screening & recommendation” strategy in a real-world screening project in rural China. We investigated the health-seeking behavior of participants in whom malignant lesions were detected in the upper digestive tract at baseline screening in the ESECC trial, and interviewed these participants face-to-face to identify the reasons for lack of timely and appropriate treatment. Factors affecting their decision-making in choosing health care facilities for treatment were also evaluated.

**Methods***The parent study*

This study was based on the ESECC randomized controlled trial (ClinicalTrials.gov: NCT01688908) and a detailed description of the original design of this trial has been reported elsewhere.<sup>11</sup> Briefly, this trial was initiated in 2012, and 668 villages were randomly selected from Hua county, Henan Province, China, which is a high-incidence area for esophageal squamous cell carcinoma (ESCC). A blocked randomization procedure was used to allocate these villages into the screening arm or the control arm at a ratio of 1:1 (334 villages, ~16,000 participants aged 45-69 in each arm). In the screening arm, standard upper G.I. endoscopy with iodine staining was performed at baseline screening. A computer-aided one-on-one questionnaire was completed by all participants at the baseline



**Figure 1.** Procedure for collecting data on the treatment history of 136 screening-detected upper G.I. cancer patients from the ESECC trial, rural Hua County, China. G.I.: gastrointestinal; ESECC: Endoscopic Screening for Esophageal Cancer in China; NCMS: New Rural Cooperative Medical Scheme.

investigation to collect information on characteristics (demographics and potential risk factors for EC) of the participants.

The ESECC trial adopted a “screening & recommendation” strategy to manage participants with malignant lesions detected at baseline screening. When participants were diagnosed with malignant upper G.I. lesion(s), a designated endoscopist with standardized training informed the participant, or informed their first-degree relatives of the results in a face-to-face communication, and provided these individuals with appropriate medical advice about further diagnostic testing and clinical treatment according to current guidelines.

#### Study participants

Baseline endoscopic screening for the ESECC trial was completed by September 2016, and 15,299 participants in the screening arm underwent upper G.I. endoscopic examination. Among these individuals, 136 were found to have malignant lesions, including 113 malignant esophageal lesions, 12 malignant lesions of the gastric cardia, and 11 malignant gastric non-cardial lesions. All of these 136 participants were analyzed in this study.

#### Data collection

“Timely treatment” was defined in this study as initial cancer-related clinical treatment undertaken within three months of the diagnosis in the baseline screening. We adopted a two-stage procedure to collect data on the treatment history of these 136 patients (Figure 1).

First, information regarding the clinical treatment regimen of the participants was collected with linkage to claims data from the New Rural Cooperative Medical Scheme (NCMS), which is a government-run health insurance program in rural China with coverage of nearly 100% in the study area that had previously proved to be a reliable data source regarding cancer diagnosis and treatment.<sup>13-15</sup> Detailed claims records from the NCMS for all participants from January 2012 to September 2017 were carefully reviewed to confirm whether they had received cancer-related therapy, which included endoscopic therapy, radical surgery, radiotherapy, and chemotherapy.

Second, door-to-door investigation was conducted from December 2016 to May 2018, during which all study participants were interviewed face-to-face with a semi-structured questionnaire. The treatment status of the participants without cancer-related therapy records in the NCMS was confirmed. Individuals who did not receive timely treatment were asked to describe the reasons underlying the delay, and those who received treatment were asked about the details of the clinical diagnosis and therapeutic process, such as tumor stage, date of initial treatment, the level of the health care facility where they were treated, the treatment regimen which was adopted and the factors most important to them when choosing health care facilities. The level of a given health care facility (primary, secondary, or tertiary) is decided based on the official database of the National Health Commission of China.<sup>16</sup>

A telephone interview was used if the patient was not home during the door-to-door interviews. If the patient had died before the interview, their first-degree relatives or the village doctors who were responsible for the primary health care of local rural residents were interviewed. All interviews were audio-recorded and transcribed.

#### Data analysis

We used a conventional analysis approach, and inductively analyzed transcripts to identify reasons for lack of timely treatment, and reasons for choice of health care facilities. We developed a codebook, which was refined iteratively. Two authors analyzed the transcripts independently and resolved disagreements through discussion. Once all interviews were coded using NVivo 12 software (QSR International Pty Ltd.), we summarized the reasons for a lack of timely treatment and for choice of health care facilities. "Early-stage lesions" in the stratified analysis refers to severe dysplasia and carcinoma in situ; and "non-early-stage lesions" includes ESCC, gastric cardia and gastric non-cardial adenocarcinoma.

All variables were first evaluated with unconditional univariate logistic regression analysis to identify potential factors associated with lack of timely treatment. Age, gender and variables with  $p < 0.05$  were subject to multivariable logistic regression analysis. Risk difference was calculated for each variable, and 95% confidence intervals (CI) were estimated using the Wilson method. All statistical analysis was performed using STATA version 15.1 (STATA, College Station, Texas, USA). All tests were two-sided and had a significance level of 0.05.

#### Ethics statement

Research protocols for the present study were approved by the Institutional Review Board of the Peking University School of Oncology, Beijing, China (No. 2011101110). All participants provided informed consent.

#### Role of the funding source

The funding sources had no role in the study design, data collection, analysis, interpretation, or writing of the report.

#### Results

Among the 136 patients with screening-detected malignant lesions in the ESECC trial, treatment records for 133 (97.79%) were acquired and 114 (83.82%) responded to semi-structured interviews (109 face-to-face, five over the telephone). As shown in Table 1, 48 (36.09%) of the participants had not received clinical treatment targeting malignant upper G.I. lesion(s) within three months after the initial screening, and of these individuals 47 remained untreated at the time the interview was conducted (at least 586 days after the baseline screening). Only one patient sought treatment six months after the initial screening, due to obvious symptoms. Hence, this patient was not deemed to have received screening-related treatment.

As shown in Table 2, tumor stage was found to be an independent risk factor for lack of timely treatment. The proportion of participants who did not receive timely treatment was significantly higher in patients with early-stage lesions than in those with non-early-stage lesions [51.14% vs. 6.67%, OR:16.46, 95% CI (4.62, 58.62)]. This discrepancy was larger for participants with esophageal malignant lesions, where 53.95% of early-stage and 5.88% of non-early-stage lesions were not treated in a timely manner [OR:23.36, 95%CI (4.97, 109.85)]. Other factors, including age, gender, education, job type, annual per capita household income,

marital status, living arrangements, family history of EC and G.I. cancer-related symptoms, had no statistical correlation with lack of timely treatment (Data was not shown).

Among the 48 participants who did not receive timely treatment, 36 participated in our face-to-face interviews. Findings of this qualitative analysis are presented below.

A total of 20 participants proactively sought further diagnostic evaluation in health care facilities after screening, but were prevented from receiving further treatment for three reasons: (1) 55% (11/20) had an endoscopy re-examination in which no malignant lesion was detected. (2) 25% (5/20) consulted clinicians, who told patients that they could be cured with oral medication or traditional Chinese medicine and did not refer the patients for endoscopic re-examination. (3) 20% (4/20) consulted clinicians who suggested only regular surveillance.

The other 16 participants did not seek further clinical diagnostic testing after screening for the following five principal reasons: (1) 56.25% (9/16) chose to ignore the screening results and the advice of the screening team professionals. These individuals believed that they were healthy, as no symptoms were identified. (2) 18.75% (3/16) were concerned about incurring financial burden, as they were of low economic status and could not get sufficient support from their families. (3) 12.50% (2/16) felt their social value was low and gave up seeking further diagnosis and treatment. Old age was the main reason underlying this perspective. (4) 12.50% (2/16) experienced fear, anxiety, or uneasiness about the endoscopic examination per se. (5) Non-disclosure was observed in 12.50% (2/16) participants. The patients' first-degree relatives (spouse, offspring etc.) were informed of the screening results, but did not discuss the results with the patients themselves.

For the 85 participants who received timely treatment after screening, the types of therapies they accepted are tabulated in Table 3. In patients with early-stage lesions, only about 1/4 received endoscopic treatment, and the rest received radical surgery or combined radical surgery and radio-chemotherapy. Among the patients treated in secondary health care facilities, none received endoscopic therapy, while the proportion of endoscopic therapy in tertiary health care facilities was 35.48%. For patients with lesions which were not early-stage, no significant differences in types of therapy were found in secondary versus tertiary health care facilities.

Regarding the reasons for choosing given health care facilities for treatment, 32 participants treated in secondary health care facilities and 46 treated in tertiary health care facilities participated in our semi-structured interview and described their choices (Figure 2).

The main reasons for choice of secondary health care facilities were: (1) "Convenience". 46.88% (15/32) chose secondary health care facilities based on close location, and convenience for relatives taking care of them during treatment/hospitalization. (2) "Medical expenses". 21.88% (7/32) believed secondary health care facilities have lower treatment fees and a higher medical insurance reimbursement rate as compared with tertiary health care facilities. (3) "Expert effect". 18.75% (6/32) reported that a secondary health care facility could invite experts from the prefecture- and province-level hospitals to provide medical service for local residents.

The main reasons for choosing tertiary health care facilities were: (1) "Social network". 45.65% (21/46) reported that they knew someone who could help arrange clinical treatment in prefecture- or province-level hospitals. (2) "Quality of care". 34.78% (16/46) believed tertiary health care facilities provide better medical service. (3) "Family support". 26.09% (12/46) chose a tertiary hospital because of advice or financial support from their offspring.

Among the patients who received timely treatment, only 10.26% (8/78) indicated that the decision was made based on the advice of the screening team endoscopists, and 2.56% (2/78) con-

**Table 1**

The characteristics of 133 individuals with malignant upper G.I. lesions detected at baseline screening of the ESECC trial in rural Hua County, China.

Variable	Timely treatment, N (%)	No timely treatment, N (%)	Total, N (%)
<b>N<sup>a</sup></b>	85 (63·91)	48 (36·09)	133 (100·00)
<b>Age</b>			
45-54	1 (1·18)	5 (10·42)	6 (4·51)
55-64	52 (61·18)	29 (60·42)	81 (60·90)
65-69	32 (37·65)	14 (29·17)	46 (34·59)
<b>Gender</b>			
Male	50 (58·82)	29 (60·42)	79 (59·40)
Female	35 (41·18)	19 (39·58)	54 (40·60)
<b>Education</b>			
Primary school or below	63 (74·12)	29 (60·42)	92 (69·17)
Middle school or above	22 (25·88)	19 (39·58)	41 (30·83)
<b>Job type</b>			
Official	0 (0·00)	1 (2·08)	1 (0·75)
Farmer	85 (100·00)	47 (97·92)	132 (99·25)
<b>Annual per capita household income</b>			
≤2000RMB	27 (31·76)	16 (33·33)	43 (32·33)
>2000RMB	26 (30·59)	20 (41·67)	46 (34·59)
Unknown	32 (37·65)	12 (25·00)	44 (33·08)
<b>Marital status</b>			
Married	75 (88·24)	43 (89·58)	118 (88·72)
Unmarried	10 (11·76)	5 (10·42)	15 (11·28)
<b>Living arrangements</b>			
Living alone or with spouse only	37 (43·53)	18 (37·50)	55 (41·35)
Living with offspring	48 (56·47)	30 (62·50)	78 (58·65)
<b>Family history of esophageal cancer</b>			
No	68 (80·00)	40 (83·33)	108 (81·20)
Yes	17 (20·00)	8 (16·67)	25 (18·80)
<b>G.I. cancer-related symptoms<sup>b</sup></b>			
No	44 (51·76)	28 (58·33)	72 (54·14)
Yes	41 (48·24)	20 (41·67)	61 (45·86)

G.I.: gastrointestinal; ESECC: Endoscopic Screening for Esophageal Cancer in China.

<sup>a</sup> Three participants whose treatment status was not confirmed were not included.

<sup>b</sup> G.I. cancer-related symptoms included dysphagia, chest pain, heartburn/reflux, appetite change/indigestion, black stool, upper abdominal pain or weight loss.

**Table 2**

Correlation of tumor stage with treatment status in 133 patients with malignant upper G.I. lesions detected at baseline screening in the ESECC trial in rural Hua County, China.

Lesions	Timely treatment, N (%)	No timely treatment, N (%)	Adjusted OR (95%CI) <sup>c</sup>	Risk differences(95%CI) <sup>d</sup>
<b>Total upper G.I. malignant lesions<sup>a</sup></b>				
Non-early-stage lesions	42 (93·33)	3 (6·67)	Ref	Ref
Early-stage lesions	43 (48·86)	45 (51·14)	16·46 (4·62, 58·62)	0·45 (0·29, 0·56)
Total <sup>b</sup>	85 (63·91)	48 (36·09)		
<b>Esophagus</b>				
Squamous cell carcinoma	32 (94·12)	2 (5·88)	Ref	Ref
Severe dysplasia/carcinoma in situ	35 (46·05)	41 (53·95)	23·36 (4·97, 109·85)	0·48 (0·31, 0·60)
Total	67 (60·91)	43 (39·09)		
<b>Gastric cardia/Gastric non-cardia</b>				
Adenocarcinoma	10 (90·91)	1 (9·09)	Ref	Ref
Severe dysplasia/carcinoma in situ	8 (66·67)	4 (33·33)	5·46 (0·33, 89·25)	0·24 (-0·10, 0·53)
Total	18 (78·26)	5 (21·74)		

G.I.: gastrointestinal; ESECC: Endoscopic Screening for Esophageal Cancer in China; OR: odd ratio; CI: confidence intervals; Ref: reference.

<sup>a</sup> The early-stage lesions included severe dysplasia and carcinoma in situ, the non-early-stage lesions included esophageal squamous cell carcinoma, gastric cardia and gastric non-cardial adenocarcinoma.

<sup>b</sup> Three participants whose treatment status was not confirmed were not included.

<sup>c</sup> The OR was adjusted for age and gender.

<sup>d</sup> Risk refers to the proportion of no timely treatment in each group (row percentage).

sulted their village doctors before choosing a health care facility for treatment.

## Discussion

Cancer screening has long been an important strategy for reducing the burden of cancer mortality. The efficacy of a screening modality depends on identification and removal of cancer at an early stage. Timely and appropriate treatment for lesions detected with screening is therefore crucial to ensure the protective effect of screening. However, in real-world screening practice de-

lay of treatment after screening is common, and this may lead to lower actual “effectiveness” of screening than the putative “efficacy” of screening. Thus, effective management of individuals who are screening-positive is an important component in the screening program. Considering the two common management strategies, the “screening & treatment” strategy may ensure that more people will receive treatment, but a professional team with sufficient resources is needed to satisfactorily complete treatment. In contrast, the “screening & recommendation” strategy, which requires fewer resources and incurs fewer ethical problems has been widely used in China. Most EC screening programs in China have been con-



**Table 3**

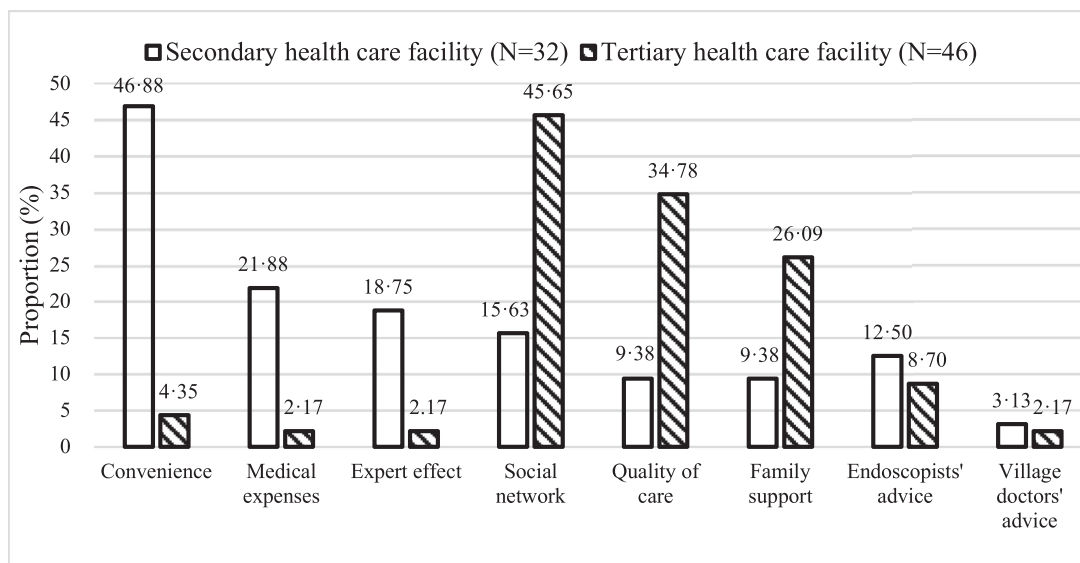
Treatment modalities used in 85 patients with malignant upper G.I. lesions detected at baseline screening in the ESECC trial in rural Hua County, China.

Clinical therapy	Level of health care facility, N (%)		Total, N (%)	Absolute differences (95%CI) <sup>b</sup>
	Secondary	Tertiary		
<b>Early-stage lesions<sup>a</sup></b>				
Endoscopic therapy	0 (0.00)	11 (35.48)	11 (25.58)	0.36 (0.07, 0.53)
Radical surgery/radical surgery combined with radio-chemotherapy	12 (100.00)	20 (64.52)	32 (74.42)	-0.36 (-0.53, -0.07)
Total	12 (100.00)	31 (100.00)	43 (100.00)	
<b>Non-early-stage lesions<sup>a</sup></b>				
Radical surgery	17 (73.91)	15 (78.95)	32 (76.19)	0.05 (-0.21, 0.29)
Radical surgery combined with radio-chemotherapy/radio-chemotherapy	6 (26.09)	4 (21.05)	10 (23.81)	-0.05 (-0.29, 0.21)
Total	23 (100.00)	19 (100.00)	42 (100.00)	

G.I.: gastrointestinal; ESECC: Endoscopic Screening for Esophageal Cancer in China; CI: confidence intervals.

<sup>a</sup> Early-stage lesions included severe dysplasia and carcinoma in situ, non-early-stage lesions included esophageal squamous cell carcinoma, gastric cardia and gastric non-cardial adenocarcinoma.

<sup>b</sup> The proportion of different treatment modalities in health care facilities of each level (column percentage), where secondary health care facilities served as a reference group.



**Figure 2.** Factors influencing the choice of health care facilities in 78 upper G.I. cancer patients who were treated in a timely manner detected at baseline screening in ESECC trial, rural Hua County, China.

G.I.: gastrointestinal; ESECC: Endoscopic Screening for Esophageal Cancer in China.

ducted in rural high-risk areas that are economically underdeveloped.<sup>8</sup> No study has investigated whether screening-positive participants received timely and appropriate treatment, and what factors influenced their health-seeking behavior. This study, for the first time has mapped out the real-world health-seeking behavior of screening-detected upper G.I. cancer patients from an area at high-risk for EC in China based on a large population-level screening trial. Our findings may provide evidence for formulating and tailoring management strategy for cancer screening in rural areas in China, and also provide guidance for screening in other similar settings.

In this study, we found that more than a third of patients with malignant lesions which were detected in the initial screening were not treated in a timely manner, and persons with early-stage cancer were more likely to delay treatment. By use of interviews, we identified the reasons for lack of timely treatment. First, low health awareness and socio-economic status were the main reasons which deterred 44.44% (16/36) patients from seeking further diagnosis and treatment. Second, 30.56% (11/36) of the untreated patients had undergone an endoscopic re-examination as a diagnostic test, but no abnormality was detected, so the screening result was considered to be a false positive. This inconsistency was largely due to the fact that no iodine staining was used in the

diagnostic test. Endoscopic examination with Lugol's iodine staining has high sensitivity for detection of early-stage lesions in the esophagus, and was adopted in the ESECC trial.<sup>17</sup> But this staining procedure has not been routinely adopted for endoscopy in general clinical settings, and the sensitivity of routine white light endoscopy for detecting early-stage lesions is as low as 11.1%.<sup>18</sup> Esophageal lesions, and in particular early-stage esophageal lesions are therefore likely to be missed. In addition, without a full evaluation and understanding of screening results, physicians performing endoscopic re-examination would not have specific expectations regarding the risk in a given patient prior to the endoscopy, which would further limit the application of more sensitive methods (e.g. Lugol's iodine staining,<sup>17</sup> narrow-band imaging,<sup>19</sup> etc.) and targeted biopsy. Third, 25% (9/36) patients were not referred for further endoscopic re-examination or clinical treatment by gastroenterologists; and oral medication or regular surveillance alone was suggested by clinicians who were consulted. This reflected the doctors' lack of awareness of the significance of screening results and basic knowledge of diagnosis and treatment of early upper G.I. cancer.

For patients with early lesions such as severe dysplasia and carcinoma in situ or intramucosal carcinomas, endoscopic therapy has been recommended as a less-invasive alternative to traditional surgery.<sup>20</sup> In China, most upper G.I. cancer screening projects in

high-risk areas were undertaken in a secondary health care facility, that is, the county-level hospital.<sup>16</sup> Currently, the health service capacity of secondary facilities in most areas of China do not meet the requirements for independent endoscopic treatment. Patients who choose these facilities therefore lose the opportunity to receive endoscopic therapy. In this study, we found that patients were strongly influenced by subjective factors in choosing facilities for clinical treatment, and often gave priority to factors not directly related to disease such as “Convenience”, “Social network”, or “Medical expense” for choice of a treatment facility, rather than basing decisions on quality and capacity of the medical services. We speculate the main reasons for this are likely related to the fact that most of these patients had a low level of education together with poor health awareness.<sup>21</sup> Many of these individuals were hardly able to understand the disease with which they presented, the differences between various clinical treatments, and the suggestions made by the screening team professionals. This led to poor accessibility of high-quality medical resources and health services suitable for these persons.

Based on the findings of this study, we suggest adopting a “co-ordinated, system-based” patient management strategy when designing an upper G.I. cancer screening project for use in a rural population to ensure timely and appropriate clinical treatment of malignant lesions detected by screening. First, before a screening program is initiated, a medical alliance comprising general and cancer hospitals at different levels in a given local area should be established, so that screening results can be mutually recognized among members of the alliance. Standardized training for endoscopists and gastroenterologists should be routinely conducted to improve their understanding of the screening procedure and criteria, and the guidelines for the diagnosis and treatment of early upper G.I. cancer. For example, techniques with higher sensitivity for detection of early lesions should be used during the endoscopic re-examination. Through close cooperation among alliance members, a “fast track” referral system for individuals who are screening-positive should be established where patients can get professional advice and standardized referral to an appropriate health care facility.

Second, cancer screening programs may incorporate a primary care network for more integrated management of cancer patients. Village doctors have played an irreplaceable role in rural health care in China. They are often residents of the villages they serve and well respected by local residents. By introducing village doctors into screening programs, the barriers in communication with rural residents would be diminished, facilitating supervision and guidance for the health-seeking process, hence improving management of cancers detected by screening.

In order to verify the performance of a proposed method of management after screening, a small alliance was established in the re-examination phase of the ESECC trial which consisted of a secondary local health care facility, Hua County People’s Hospital, and Anyang Cancer Hospital which is a tertiary health care facility, where 2/3 of cases identified at baseline screening received timely treatment. A referral arrangement was made to help patients with subsequent endoscopic re-examination and clinical treatment. As a result, the proportion of patients with malignant lesions who received timely treatment increased from 63•91% at baseline to 81•48%, and the proportion of endoscopic therapy used in cases which were diagnosed early increased from 25•58% at baseline to 41•67%.

There are also limitations in this study that should be noted. This was a single center study, and our findings should therefore be interpreted with caution when applied in other areas in China and in other countries. In addition, since information about health-seeking behavior was collected via retrospective interviews, recall bias and reporting bias may exist where the respondents could not

accurately recall the health-seeking experiences, or intentionally exaggerated or concealed the true information.

This study has described for the first time the health-seeking trajectory of screening-detected upper G.I. cancer patients and the main barriers to access of timely and appropriate clinical treatment in rural China in areas of high ESCC incidence. Results of this study will provide a fundamental basis for the efficacy and cost-effectiveness evaluation in the ESECC trial in the future. In addition, establishing a regional medical alliance and involving primary care networks will help overcome identified barriers and facilitate the management of patients with cancer detected by screening in these programs. It is expected that this will improve the efficiency of diagnostic testing and clinical treatment after the initial screening. This study will inform planning of screening for upper G.I. cancer in rural China and other settings with similar social-economic conditions.

### Contributors

YK and ZH contributed to the study concept, design and supervision. CG, ML, YH, HT, YP, FL, YL, ZH and HC contributed to acquisition of data. HW and ZL contributed to drafting of the manuscript and statistical analysis. All authors have read and approved the final version of manuscript.

### Declaration of Competing Interest

We declare no competing interests.

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### Data sharing statement

De-identified data generated and analyzed in the current study are available from the corresponding author upon reasonable request.

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