



# Out-of-pocket medical expenditure and associated factors of advanced colorectal cancer in China: a multi-center cross-sectional study

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**Background:** Colorectal cancer (CRC) causes a substantial disease burden in China. Information on the medical expenditure of CRC patients is critical for decision-makers to allocate medical resources reasonably, however, relevant data is limited in China, especially advanced CRC. The aim of this survey was to quantify the out-of-pocket medical expenditure of advanced CRC and explore associated factors.

**Methods:** A nation-wide, multi-center, cross-sectional survey was conducted from March 2020 to March 2021. Nineteen hospitals in seven geographical regions were selected by multi-stage stratified sampling.

For each eligible CRC patient with stage III or IV disease in the selected hospitals, the socio-demographics, clinical information, and range of out-of-pocket medical expenditure data were collected based on patients' self-reporting or medical records. Multivariable logistic analysis was used to explore associated factors of medical expenditure. All statistical analyses were conducted using SAS 9.4.

**Results:** The mean age of the 4,428 advanced CRC patients included was  $59.5 \pm 11.6$  years, 59.6% were male, and 80.1% of patients were in stage III or IV at the time of diagnosis. Besides, 57.2% of patients had an annual household income of less than 50,000 Chinese Yuan (CNY), 40.9% of patients had an out-of-pocket medical expenditure of 50,000–99,999 CNY. As for the affordability of medical expenditure, 33.2% could afford 50,000–99,999 CNY. Multivariate analysis showed that patients who were in the southern [odds ratio (OR): 1.63, 95% confidence interval (CI): 1.31–2.03] and southwestern (OR: 1.55, 95% CI: 1.25–1.93), were in stage III at the time of diagnosis (OR: 1.33, 95% CI: 1.13–1.57), visited three or more hospitals (OR: 1.26, 95% CI: 1.04–1.52), had sought cross-regional health care (OR: 1.60, 95% CI: 1.40–1.83), used genetic testing (OR: 1.26, 95% CI: 1.10–1.45) and targeted drugs (OR: 2.12, 95% CI: 1.79–2.51) had higher out-of-pocket medical expenditure.

**Conclusions:** Patients with advanced CRC had a high out-of-pocket medical expenditure. It is necessary to strengthen the prevention and control of CRC to reduce the disease burden; also, it is critical to deepen the reform of the medical system, increase proportion of medical insurance reimbursement, and remove barriers to cross-regional health care.

**Keywords:** Colorectal cancer (CRC); medical expenditure; China

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## Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide. There were 1,931,590 new cases of CRC in the world in 2020, of which cases in China accounted for 28.8% (1). The most recently available data from the National Cancer Registry of China reported 388,000 new CRC cases diagnosed in 2015, making CRC the third most common cancer in China (2). Evidence has shown that the incidence and mortality of CRC in China has increased over the past decades and is expected to continuously increase (3–5).

It has been confirmed that there are many modifiable risk factors for CRC, such as smoking, processed meat, alcohol intake, red meat, low intake of vegetables and fruits, body fat, and obesity (6). Reducing these risk factors can effectively reduce the incidence of CRC. In addition, the role of screening in reducing the burden of CRC has reached an international consensus (7,8). In order to curb the rising incidence and mortality of CRC, China has successively launched a number of screening projects in recent years, and the coverage among the population has gradually expanded (9–14). However, despite the emergence

of screening programs, nearly half of CRCs in China are diagnosed at an advanced stage. The 5-year survival rate of CRC patients at an early stage is as high as 90%, while that of patients at an advanced stage is only about 30% (15,16), which results in a heavy burden to families and society. In recent years, several new treatments have been developed for patients with advanced CRC, such as targeted therapy, which can effectively prolong the overall survival of CRC patients, but these new treatments are expensive and may lead to a huge economic burden on patients.

Understanding the economic burden of CRC patients and the associated factors is essential to guide cancer prevention and control and inform the relevant healthcare policy in the future. First of all, discerning the true financial burden helps explain the general status of a population's health under current healthcare system, thus enabling the development of optimal policies. Second, collecting related expenditure of CRC patients is crucial for evaluating the cost-effectiveness and budget impact of population-based intervention programs such as CRC screening. Moreover, mastering the medical expenditures and associated factors can help explain the effect of the current health-care reform

policy on cost control and thus facilitate the development of optimal policies.

There have been systematic studies on the medical expenses of cancer patients in many foreign countries, such as the United States and Australia (17,18). And studies showed that the medical expenses of cancer patients are related to the patient's age, living area, medical insurance status, availability of medical services, cancer stage and other factors (18-20). Considering that the medical system and disease burden of CRC in China are quite different from those in foreign countries, it is necessary to carry out local studies to provide reference for medical decision-making in China. However, studies on the medical expenditure of CRC patients were limited in China, especially multi-center studies with large sample sizes. One previous study indicated that the overall direct medical expenditure associated with CRC diagnosis and subsequent treatment per patient was 37,902 Chinese Yuan (CNY) (2011 value) in China between 2002 and 2011, with an average annual growth rate of 9.2% over the 10-year period (21). Another study showed that the average medical expenditure per CRC patient was 66,291 CNY (2014 value) during the period from 2005 to 2014 (22). As for the associated factors of medical expenditure, studies showed that the expenditures vary within different stages and treatment methods (21,23). However, with the continuous emergence of new diagnostic and treatment methods, previous cost surveys are no longer representative of the current situation, and it is necessary to investigate the latest medical expenses and associated factors.

To improve the understanding of the current situation of the medical expenditure of CRC in China, this study analyzed the medical expenditure and associated factors of advanced CRC patients in China based on a nation-wide multi-center survey conducted from March 2020 to March 2021. We present the following article in accordance with the SURGE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-1001/rc>).

## Methods

### *Study design and sites*

To comprehensively present the knowledge, medical experience, health-related quality of life and health-care costs among Chinese patients with advanced CRC, a cross-sectional, nation-wide, hospital-based, multi-center survey was conducted across seven geographic regions (northeastern, northern, northwestern, eastern, central,

southern, and southwestern) in China from March 2020 to March 2021, and this study is a part of the large sample study. Multi-stage stratified sampling was adopted to determine the participant hospitals. In stage one, two cities of each region were selected by convenient sampling. In stage two, one tertiary cancer hospital and/or one general hospital were selected in each city. A total of nineteen hospitals (ten tertiary cancer hospitals and nine general hospitals) were selected.

### *Study population*

All CRC patients aged  $\geq 18$  years old with stage III or IV disease in the selected hospitals were invited by the interviewer verbally to participate current study. Patients were excluded if they had severe physical, cognitive, and/or verbal impairments that interfered with the completion of the questionnaire. Patients will receive a CRC health knowledge booklet in return after being surveyed. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This research was approved by the independent review board of Henan Cancer Hospital (No. 2019273), the other 18 hospitals were informed and agreed with the study, and informed consent was taken from all the patients.

The sample size of the large-sample survey overall is estimated based on the prevalence of advanced CRC, sample representativeness and response rate. The sample size of this study is consistent with that of large sample survey. It has been estimated that there are about 400,000 advanced CRC patients in China (1,24). To ensure the representativeness of the sample, this study was expected to recruit approximately 1% of the patients. Considering the non-response rate of 10%, more than 4,445 patients would be enrolled into this survey. The sample size of each region was allocated proportionally according to the population density.

### *Data collection*

Information was collected face-to-face by interviewers via a semi-structured questionnaire, and all interviewers were systematically trained before the study was launched. The information of the questionnaire included the following aspects: (I) socio-demographics including birthdate, gender, marital status, education, occupation, annual household income, and medical insurance type; (II) clinical information including number of hospitals visited, cancer

type (colon cancer, rectal cancer, and both), duration of cancer (time from the patient's CRC diagnosis to the date of investigation), cancer stage at the time of diagnosis (CRC staging was consistent with the 8<sup>th</sup> edition of the American Joint Committee on Cancer tumor-node-metastasis staging system), phases of the disease at the time of investigation [(i) during the first treatment and did not change the regimen; (ii) during the first treatment and changed the regimen; (iii) during the treatment phase after recurrence; (iv) during the phase of regular review], whether the patient had sought cross-regional health care, use of genetic testing and targeted drugs, and therapeutic regimen; and (III) medical expenditure: range of out-of-pocket medical expenditure, including costs of diagnosis, medication, surgery, radiology, medical examinations, nursing care, hospitalization, etc. The cost was collected in the form of categorical variables in the questionnaire [(i) <50,000; (ii) 50,000–99,999; (iii) 100,000–199,999; (iv) ≥200,000]; proportion of medical insurance reimbursement; who bore the medical expenditure; affordability of treatment costs; and related measures to relieve financial pressure, etc.

### Statistical analysis

In the current study, if more than 95% of items were filled, the questionnaire was regarded as complete and was included in the analysis. Unfilled items were included in the analysis as missing values. For continuous variables conforming to a normal distribution, such as age, data were presented as the mean ± standard deviation (SD). Otherwise, the median, upper, and lower quartiles were used for description. Categorical variables were presented as frequencies and percentages. To determine the factors associated with medical expenditure, an ordinal logistic regression model was constructed, in which stepwise regression was performed to choose variables included in the final model ( $P_{\text{entry}}=0.05$ ,  $P_{\text{stay}}=0.05$ ). In the model, medical expenditure was taken as the dependent variable, and independent variables included socio-demographics (age, gender, marital status, occupation, education, region, annual household income of the patients, annual household income of the patients' children), and clinical information (number of hospitals visited, cancer type, duration of cancer, cancer stage when diagnosis, phase of the disease at the time of investigation, whether the patients sought cross-region health care, use of gene testing, and use of targeted drugs). All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA), and the significance level was set

to two-sided  $\alpha=0.05$ .

## Results

### Patient characteristics

A total of 4,589 CRC patients with stage III or IV disease were investigated, of whom 161 patients were just diagnosed at the time of investigation and had not started any treatment. Therefore, a total 4,428 CRC patients with stage III or IV disease were included in the current analysis. The mean age of the included patients at the time of investigation was  $59.5 \pm 11.6$  years, and 46.4% of the patients were aged 50–64 years. Among the patients, 59.6% were male, 17.7% were unemployed, 55.2% had an education of junior or senior high school, 99.0% of patients had medical insurance, and most of the patients (57.2%) or their children (43.1%) had an annual household income of less than 50,000 CNY (Table 1).

At the time of investigation, 47.2% of the patients were undergoing the first treatment and did not change the regimen, and the median [P25, P75] duration of cancer was 9 [3, 23] months; 80.1% of the patients were at a stage of III or IV at the time of diagnosis, and 53.7% of the patients had rectal cancer; 51.8% of the patients had visited two hospitals, and 19.1% had visited three or more hospitals. Among the patients, 37.0% had sought cross-regional health care, 47.2% had used genetic testing, and 32.0% had used targeted drugs. The most commonly used treatment methods included chemotherapy (87.9%), surgery (84.4%), targeted therapy (29.3%) and radiotherapy (22.4%) (Table 1).

### Medical expenditure and related information

A total of 40.9% of the patients had an out-of-pocket medical expenditure of 50,000–99,999 CNY, and the median [P25, P75] medical insurance reimbursement ratio was 60% [50%, 70%]. Most patients bore the medical expenditure themselves coupled with their spouses (81.4%) or their children (49.3%). When asked about the treatment cost that patients could afford, 33.2% answered that 50,000–99,999 CNY was an affordable treatment cost, and 28.4% of the patients could afford less than 50,000 CNY. With the financial pressure derived from CRC treatment, only 20.9% of patients could afford the current treatment costs without changing their living conditions. In contrast, nearly 80% of patients had taken actions to relieve financial pressure, including reducing household expenses (66.2%), reducing

**Table 1** Characteristics of advanced colorectal cancer patients

Variables	No.	%
Age (years), mean ± SD	59.5±11.6	
<50	825	18.6
50–64	2,053	46.4
≥65	1,550	35.0
Gender		
Male	2,638	59.6
Female	1,790	40.4
Marital status*		
Married	4,178	94.4
Other	249	5.6
Occupation		
Employees of enterprise, or government	1,750	39.5
Service staff, farmer, collar-blue worker	1,895	42.8
Unemployed	783	17.7
Education*		
Primary school or below	1,272	28.8
Junior or senior high school	2,442	55.2
Undergraduate or above	711	16.1
Region		
Northeastern	351	7.9
Northern	545	12.3
Eastern	1,271	28.7
Southern	646	14.6
Central	657	14.8
Northwestern	313	7.1
Southern	645	14.6
Health-care insurance type (multiple response)		
Urban employees basic medical insurance	1,868	42.4
Urban residents basic medical insurance	958	21.7
New rural cooperative medical scheme	1,503	34.1
Critical illness insurance program	215	4.9
Commercial medical insurance	220	5.0
Uninsured	46	1.0

**Table 1** (continued)**Table 1** (continued)

Variables	No.	%
Annual household income of patients (CNY)		
<50,000	2,533	57.2
50,000–99,999	1,254	28.3
≥100,000	641	14.5
Annual household income of patient's children (CNY)		
<50,000	1,907	43.1
50,000–99,999	1,547	34.9
≥100,000	974	22.0
Duration of cancer (months), median [P25, P75]	9 [3, 23]	
Number of hospitals visited*		
1	1,267	29.2
2	2,248	51.8
≥3	829	19.1
Cancer stages at diagnosis*		
I/II	849	19.9
III	1,909	44.8
IV	1,506	35.3
Cancer type*		
Colon	1,995	45.1
Rectum	2,379	53.7
Other	53	1.2
Phases of the disease at the time of investigation		
During the first treatment and did not change the regimen	2,088	47.2
During the first treatment and changed the regimen	532	12.0
During the treatment phase after recurrence	1,138	25.7
During the phase of regular review	670	15.1
Has the patient ever sought cross-region health care*		
No	2,789	63.0
Yes	1,637	37.0
Use of genetic testing*		
No	2,336	52.8
Yes	2,086	47.2

**Table 1** (continued)



**Table 1** (continued)

Variables	No.	%
Use of targeted drugs*		
No	3,005	68.0
Yes	1,415	32.0
Treatment method (multiple response)		
Surgery	3,734	84.4
Endoscopic interventional therapy	130	2.9
Radiotherapy	991	22.4
Chemotherapy	3,888	87.9
Targeted therapy	1,298	29.3
Immunotherapy	104	2.4
Traditional Chinese medicine treatment	507	11.5
Palliative treatment	218	4.9

\*, some data are missing. SD, standard deviation; CNY, Chinese Yuan.

the purchase of large items (57.3%), and borrowing from relatives and friends (25.5%) (Table 2).

### Factors associated with out-of-pocket medical expenditure

A multivariate logistic regression analysis was conducted to identify potential associated factors that may be associated with the medical expenditure of advanced CRC patients, and the results are shown in Table 3. Compared with patients under the age of 50, patients aged 50–64 [odds ratio (OR): 0.83, 95% confidence interval (CI): 0.70–0.99] and patients over the age of 65 (OR: 0.66, 95% CI: 0.55–0.80) had lower medical expenditure. Compared to patients in the central area, patients in the eastern area (OR: 0.73, 95% CI: 0.60–0.88) had lower medical expenditure, while those in the southern (OR: 1.63, 95% CI: 1.31–2.03) and southwestern (OR: 1.55, 95% CI: 1.25–1.93) areas had higher medical expenditure. Patients with higher annual household incomes (themselves or their children) had higher medical expenditure. Moreover, patients had higher medical expenditure if they had longer duration of cancer (OR: 1.02, 95% CI: 1.01–1.02), visited three or more hospitals (OR: 1.26, 95% CI: 1.04–1.52), were in stage III at the time of diagnosis (OR: 1.33, 95% CI: 1.13–1.57), were undergoing treatment phases and changed the regimen (OR: 1.66, 95% CI: 1.36–2.03), had recurrence (OR: 3.28, 95%

CI: 2.75–3.90), were in the course of regular review (OR: 1.77, 95% CI: 1.48–2.13), had ever sought cross-regional health care (OR: 1.60, 95% CI: 1.40–1.83), used genetic testing (OR: 1.26, 95% CI: 1.10–1.45), and used targeted drugs (OR: 2.12, 95% CI: 1.79–2.51).

### Discussion

To the best of our knowledge, this study was the latest largest multi-center survey in China to analyze the medical expenditure and associated factors of advanced CRC patients. The findings showed that the out-of-pocket medical expenditure of advanced CRC patients was high, especially in patients who were in southern and southwestern China, visited more hospitals, were in the advanced stage at the time of diagnosis, sought cross-regional health care, and used genetic testing and targeted drugs. Although the medical expenditure of most patients was within the affordable range, they were still higher than the annual household income level.

In the current study, most advanced CRC patients had an average total out-of-pocket medical expenditure of 50,000–99,999 CNY. In a multicenter study that enrolled 14,536 CRC patients diagnosed from 2002 to 2011, the average medical expenditure for patients with stage III and IV disease were 38,918 and 42,614 CNY (2011 value), respectively (21). Another cross-sectional study conducted from 2012 to 2014 reported that the average medical expenditure of 2,356 CRC patients was 61,829 CNY (2014 value), ranging from 51,366 CNY for stage I to 75,673 CNY for stage IV (23). Meanwhile, a more recently conducted multi-center retrospective survey found that the average medical expenditure of 8,465 CRC patients diagnosed between 2012 and 2014 in mainland China was 66,291 CNY (2014 value), however, this study included all clinical stages of CRC patients (22). Notably, the above two retrospective studies suggested that the medical expenditure of CRC patients in China showed a significant growth trend (21,22), of which, one suggested that the annual growth rate was as high as 9.2% (21). Considering the medical insurance reimbursement, the increasing trend of medical expenditure, and currency inflation in recent years, the medical expenditure of advanced CRC patients in the current study seems to be comparable with those in the above studies.

Approximately 80% of advanced CRC patients in the current research were diagnosed with stage III or IV at the time of diagnosis, which may be related to the fact that the target population of this study were patients with stage

**Table 2** Medical expenditure and related information of advanced colorectal cancer patients

Variables	No.	%
Total out-of-pocket medical expenditure (CNY)*		
<50,000	1,065	24.1
50,000–99,999	1,807	40.9
100,000–199,999	1,034	23.4
≥200,000	510	11.6
Medical insurance reimbursement ratio (%), median [P25, P75]	60 [50, 70]	
Who bore the medical expenditure (multiple response)		
Patient and his/her spouse	3,593	81.4
Siblings of patients	306	6.9
Children of patients	2,175	49.3
Parents of patients	163	3.7
Other relatives of patients	183	4.1
Other social financing	44	1.0
Affordability of treatment cost (CNY)*		
<50,000	1,250	28.4
50,000–99,999	1,461	33.2
100,000–199,999	1,077	24.5
200,000–499,999	521	11.8
≥500,000	95	2.2
Things done to relieve financial pressure derived from the treatment of CRC (multiple response)		
The treatment cost is sufficient and there is no need to change the living standard	926	20.9
Reduce household expenses	2,927	66.2
Reduce the purchase of large items	2,532	57.3
Borrowing from relatives and friends	1,127	25.5
Borrowing from financial institutions	74	1.7
Selling house property	102	2.3
Selling cars	44	1.0
Selling other valuables	61	1.4
Other	43	1.0

\*, some data are missing. CNY, Chinese Yuan; CRC, colorectal cancer.

III or IV disease. However, other studies, which included CRC patients with all stages, also found that about half of patients were in an advanced stage at the time of diagnosis (21-23). In addition, both the current study and other studies indicated that patients with stage I disease accounted for less than 20% of all CRC patients in China, which is far

lower than that in countries with national CRC screening programs available, such as Australia (22.1% for stage I) and the United States (38.1% for localized CRC) (25,26). However, with the increasing coverage for cancer screening in China, which is recognized by the Chinese government as a priority (27), downstage shift can be expected.

**Table 3** Multivariable analysis of medical expenditure in advanced colorectal cancer patients

Variables	$\beta$ -coefficient	OR (95% CI)	P
Age (years)			
<50	Reference	1	–
50–64	–0.185	0.83 (0.70, 0.99)	0.034
$\geq 65$	–0.414	0.66 (0.55, 0.80)	<0.001
Region			
Central	Reference	1	–
Northeastern	–0.023	0.98 (0.75, 1.27)	0.861
Northern	0.018	1.02 (0.81, 1.28)	0.878
Eastern	–0.317	0.73 (0.60, 0.88)	0.001
Southern	0.488	1.63 (1.31, 2.03)	<0.001
Northwestern	–0.102	0.90 (0.70, 1.17)	0.447
Southwestern	0.440	1.55 (1.25, 1.93)	<0.001
Annual household income of patients and spouses (CNY)			
<50,000	Reference	1	–
50,000–99,999	0.179	1.20 (1.04, 1.37)	0.012
$\geq 100,000$	0.306	1.36 (1.13, 1.64)	0.002
Annual household income of patient's children (CNY)			
<50,000	Reference	1	–
50,000–99,999	–0.048	0.95 (0.83, 1.10)	0.511
$\geq 100,000$	0.251	1.29 (1.08, 1.53)	0.005
Duration time of cancer (months)	0.015	1.02 (1.01, 1.02)	<0.001
Number of hospitals visited			
1	Reference	1	–
2	–0.104	0.90 (0.78, 1.04)	0.162
$\geq 3$	0.231	1.26 (1.04, 1.52)	0.018
Cancer stage at the time of diagnosis			
I/II	Reference	1	–
III	0.286	1.33 (1.13, 1.57)	0.001
IV	0.056	1.06 (0.88, 1.27)	0.550
Phases of the disease at the time of investigation			
During the first treatment and did not change the regimen	Reference	1	–
During the first treatment and changed the regimen	0.509	1.66 (1.36, 2.03)	<0.001
During the treatment phase after recurrence	1.187	3.28 (2.75, 3.90)	<0.001
During the phase of regular review	0.573	1.77 (1.48, 2.13)	<0.001

Table 3 (continued)



Table 3 (continued)

Variables	$\beta$ -coefficient	OR (95% CI)	P
Has the patient ever sought cross-regional health care			
No	Reference	1	–
Yes	0.470	1.60 (1.40, 1.83)	<0.001
Use of genetic testing			
No	Reference	1	–
Yes	0.232	1.26 (1.10, 1.45)	0.001
Use of targeted drugs			
No	Reference	1	–
Yes	0.750	2.12 (1.79, 2.51)	<0.001

OR, odds ratio; CI, confidence interval; CNY, Chinese Yuan.

This study found that the out-of-pocket medical expenditure of CRC patients was associated with many factors. Consistent with other studies (21,23), we found that medical expenditure was higher for patients with advanced stage at the time of diagnosis compared to those with early stage at the time of diagnosis, suggesting that advanced CRC patients in China bear a higher economic burden. Moreover, the use of genetic testing and targeted therapy could significantly increase the medical costs for CRC patients. Targeted therapy is a new treatment method for advanced CRC patients that has been applied in recent years (28). Considering its high price, relevant government departments have taken measures, and some of the targeted drugs have been included in the catalogue of drugs for national basic medical insurance (29), which will greatly reduce the economic burden of CRC patients in the future. In addition, medical expenditure was also related to the region in which the patient was located. Compared with patients in central China, patients in the eastern area had a lower medical expenditure, whereas patients in the southern and southwestern had a higher medical expenditure, which was not consistent with our expectations. It is generally believed that the economic development level of a region is positively correlated with the medical expenditure of patients. We suspect that the out-of-pocket medical expenditure may be related to the proportion of medical insurance reimbursement between regions. The surveyed data showed that the average proportion of medical insurance reimbursement of patients from the central area was 57.9%, and the proportion in the eastern, southern and southwestern areas were 61.5%,

55.1%, and 51.7%, respectively. The out-of-pocket medical expenditure of patients may be relatively low in areas with a high reimbursement ratio.

In terms of the financial burden of advanced CRC patients, this study found that most patients' out-of-pocket medical expenditure were affordable; however, they also exceeded the annual household income of patients, and patients needed to reduce some daily household expenses to relieve financial pressures. At the same time, some patients needed to seek help from relatives, friends, or other social organizations. In fact, the financial burden of medical expenditure on patients can be expressed by the catastrophic health expenditure, which was measured by the household's capacity to pay and the threshold was set as equal to or greater than 40% of capacity to pay (30). Previously, a multi-center cross-sectional study involving 2,356 CRC patients conducted from 2012 to 2014 showed that patients spent 59.9% of their household income for the diagnosis and treatment of CRC in a year (23), reaching the level of catastrophic health expenditure. Therefore, the economic burden of CRC patients, especially advanced CRC patients, deserves more attention. It is also necessary to expand the coverage of CRC screening and increase the rate of early diagnosis to reduce the disease burden of CRC, and formulate corresponding policies to control out-of-pocket expenditure.

Nevertheless, the study had several limitations that should be noted. Firstly, the self-reported data may be affected by recall bias and social expectations. Secondly, the cost information collected in this study was only the approximate range of medical expenditure, and the specific

expenditure, breakdown of expenditure, and indirect expenditure were not collected. Finally, generalization of the findings could be limited because only advanced CRC patients were enrolled in current study. However, we are planning to conduct further follow-up of the investigated patients with CRC and establish a longitudinal cohort. If possible, we will collect the medical expenditure, non-medical expenditure, and indirect expenditure of the whole disease course of the patients, so as to provide more detailed data support for the prevention and control of CRC in the future.

In summary, this nation-wide multi-center survey illustrated the current medical expenditure and associated factors of advanced CRC patients in China. The findings indicated that the out-of-pocket medical expenditure of advanced CRC patients was high. Although most of them were affordable, they were still higher than the average annual household income. In addition, the treatment cost varied among subgroups. More attention needs to be paid to patients who were in southern and southwestern China, were in the advanced stage at the time of diagnosis, had sought cross-regional health care, and those who used genetic testing and targeted drugs.

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### Footnote

*Reporting Checklist:* The authors have completed the SURGE reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-22-1001/rc>

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This research was approved by the independent review board of Henan Cancer Hospital (No. 2019273), the other 18 hospitals were informed and agreed with the study, and informed consent was taken from all the patients.

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