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Time intervals experienced between first symptom recognition to pathological diagnosis and stage at time of diagnosis among oesophageal cancer patients in Ethiopia: A cross-sectional study

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3 **1 Time intervals experienced between first symptom recognition to pathological diagnosis**
4 **and stage at time of diagnosis among oesophageal cancer patients in Ethiopia: A cross-**
5 **sectional study**
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11 4 Berhe Dessalegn^{1*,2}, Sefonias Getachew², Robel Yirgu², Fikre Enqueselassie^{2†}, Mathewos
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14 5 Assefa³, Adamu Addissie²
15

16 ¹Department of Public Health, College of Medicine and Health Sciences, Adigrat University
17
18 7 Adigrat, Ethiopia
19

20 ² Department of Preventive Medicine, School of Public Health, College of Health Sciences,
21
22
23 9 Addis Ababa University, Addis Ababa, Ethiopia
24

25 ³Department of Radiotherapy Center, School of Medicine, Addis Ababa University, Addis
26
27
28 11 Ababa, Ethiopia
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30
31 12 * Corresponding Author
32

33 13 Email: berhe_dessalegn@yahoo.com(BD)
34

35 14 † Professor Fikre Enqueselassie has passed away on October 28th, 2019.
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21 Abstract

22 Objective

23 The aim of this study was to estimate the magnitude of patients and diagnostic delays, stage at
24 diagnosis, and determinant factors among oesophageal cancer patients in Ethiopia.

25 Methods

26 **Design** A cross-sectional study design was employed

27 **Settings and participants** Oesophageal cancer patients aged ≥ 18 years were included from
28 health facilities of Addis Ababa, Ethiopia (n=338) from February 2019 to August 2020. The
29 participants were selected consecutively from six health facilities provided cancer care nearly for
30 90% of patients.

31 **Main outcomes and measurements** The Aarhus statement criterias was applied to
32 classify patient interval (time from first symptom recognition to presentation), and diagnostic
33 interval (time from first presentation to diagnosis). Patient and diagnostic intervals >60 and >30
34 days were considered delays, respectively. For tumor classification, the American Joint
35 Committee on cancer was used. Data were analyzed using SPSS Version 24. Descriptive
36 statistics were applied to describe patients' characteristics. Poisson regression with robust
37 variance was used to compute prevalence ratios. In all statistical tests, significances were
38 declared at p-value of <0.05 .

39 Results

40 The mean (SD) age of the study participants was 54.30 ± 12.49 years. About 75% of the study
41 participants had never heard of oesophageal cancer before diagnosis. Dysphagia was commonly
42 mentioned symptom. About 76% of the cases were diagnosed at advanced stages. The median
43 patient interval was 108.5 days and the median diagnostic interval was 77.5 days. After adjusting
44 for confounders, marital status, awareness of oesophageal cancer, cost of transportation, level of

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3 45 first medical consultation and patient delay > two months were found statistically significant
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6 46 predictors.

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8 47 **Conclusion** Oesophageal cancer patients in Ethiopia had prolonged patient and diagnostic
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11 48 delays. Increasing awareness about the commonest symptoms of oesophageal cancer and
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13 49 shortening the time to diagnosis helps to improve the out-come of oesophageal cancer care in
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15 50 Ethiopia.

17 51 **Keywords:** Oesophageal cancer, delay, intervals, tumor stage

52 53 **Strengths and Limitations**

- 54 • In Ethiopia, in case of patient and diagnostic delays and determinant factors, it is the first
55 multifacility study
- 56 • Poisson regression with robust variance was used to compute the prevalence ratios
- 57 • It is the only research based on primary data in Ethiopia that estimates the patient and
58 diagnostic intervals on oesophageal cancer patients
- 59 • However, the onset of symptoms is a subjective measurement that patients may not recall the
60 exact time

1. Introduction

Cancers is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. Globally, cancer becomes a major public health concern[1]. Oesophageal cancer, an aggressive tumor of the esophagus that develops in the organ's tissue lining, is the fourth most prevalent cancer in developing countries[2]. Oesophageal cancer caused significant morbidity and mortality throughout the world with a unique hallmark of poor prognosis and survival rate.[3-5] It is the sixth most common cause of mortality among all cancers and the seventh most common cancer in terms of incidence[1].

Squamous cell carcinoma and adenocarcinoma are the two most common subtypes of oesophageal cancer. Squamous cell carcinoma starts in the flat cells that line the esophagus, while adenocarcinoma starts in the cells that produces and releases mucus and other fluids. Oesophageal cancer mortality and incidence rates are higher in Africa than elsewhere in the world, owing mostly to squamous cell carcinoma [6 7].

The five-year survival rate for non-metastatic oesophageal cancer is between 19 and 30%, whereas, the median overall survival time for metastatic oesophageal cancer is between four and six months. Nonetheless, it is not uncommon for oesophageal cancer patients to be diagnosed at advanced stages ,because, in most cases, the oesophageal cancer patients have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patients prognosis and survival rate[5 8 9].

Studies evidenced that the survival rate of oesophageal cancer patients has depended on the patients' commitment in early consultation and shortening the times of pathological diagnosis[10 11]. In practice, however, oesophageal cancer patients frequently have arrived late in

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3 90 presentation and commonly lately referred to the appropriate health facilities. In addition,
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5 91 literatures also showed that shortening the time to presentation is an important step in reducing
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7 92 late in diagnosis, and improving the prognosis and survival of oesophageal cancer patients[12
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13 94 Oesophageal cancer is the overwhelming disease and among the commonest cause of cancer
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15 95 deaths in the world. Though, few patients can be cured, the treatment for oesophageal cancer is
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17 96 prolonged, quality of life is significantly compromised and cases fatality rate is high [1].

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21 97 Ethiopia is a country, geographically located within the highest risk region of oesophageal cancer
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23 98 known to be the oesophageal cancer belt. And, the disease has created a huge burden interms of
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25 99 morbidity and mortality in the country[14]. In addition, few hospital reports revealed that over
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28 100 the last decades, the incidence and burden of oesophageal cancer has been increasing.

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31 101 In Eastern African countries like Ethiopia, an up-to-date oesophageal cancer data are
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33 102 unequivocally important to design appropriate and resilient strategies. Hence, able to reduce
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35 103 morbidities and mortalities from oesophageal cancer mainly due to delay in patients'
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37 104 consultation and pathological diagnosis [7 15]

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41 105 In Ethiopia, however, oesophageal cancer is not yet a public health priority, left in dark and is
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43 106 under-researched; as a result, there is no clear evidence about patient and diagnostic intervals and
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45 107 the stage at time of diagnosis. The goal of this study was to determine time to care seeking and
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47 108 pathological diagnosis, and the stage at time of diagnosis of oesophageal cancer patients.
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49 109 Meanwhile, we were also strived to identify predictors of patients and pathological diagnostic
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51 110 delays of > 60 and > 30 days, respectively.

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112 2. Materials and methods

113 2.1. Study design and sample size

114 A cross-sectional study design was employed. The study involved 338 oesophageal cancer
115 patients aged ≥ 18 years from February 2019 to August 2020 in Addis Ababa, Ethiopia. Using the
116 expected proportion ($p=32.0\%$) of patient delay to presentation (>2 months) from a similar study
117 and assuming a 95% level of confidence, a 5% precision and 5% non-response rate [16].

118 2.2. Settings and participants

119 The Ethiopian health care delivery system has three tiers: primary, secondary and tertiary level
120 health care facilities that are linked with a referral system. The setup differs slightly between
121 urban and rural settings. The main healthcare service in the metropolitan city, such as Addis
122 Ababa, Ethiopia's capital, includes public health centers, private clinics, and primary hospitals.
123 Secondary and tertiary healthcare levels are general hospitals and specialty hospitals,
124 respectively. The primary healthcare services in rural areas are made up of a health post, a health
125 center, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and
126 specialty hospitals, respectively. Nurses and health officers are the primary staff of public health
127 centers, with the goal of providing preventative and primary health care services.

128 In the case of cancers, such as oesophageal cancer, health workers at the primary level care
129 facilities are only expected to refer patients to general hospitals and other high-level facilities for
130 further diagnosis and treatments[17].

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133 **Sampling procedure**

134 A consecutive sampling method was used to recruit study participants. Six health facilities in
135 Addis Ababa (Tikur Anbesa Specialized Hospital, St. Paul Hospital Millennium Medical
136 College, Betezata Hospital, Hallelujah General Hospital, Landmark Hospital, and United Vision
137 Medical Services Centre) were selected, where nearly 90% of cancer patients being diagnosed
138 and treated. At each health facility, one focal person was assigned to identify eligible
139 oesophageal cancer patients and communicate with the principal investigator and supervisor. To
140 avoid duplication, the medical chart of the recruited patient was coded in red on the top cover
141 page. Prior to the interview, study participants were informed about the purpose of the study and
142 their right to withdraw under any circumstances without compromisation of any services.

143 **2.3. Variables and Measurements**

144 We used the Aarhus statement criteria to classify patient, diagnostic and symptoms intervals.
145 Thus, patient interval was defined as the interval between the date of first symptom recognition
146 (the time point at which the patient first noticed bodily changes and/or symptoms) and the date of
147 first clinical presentation (the date at which the patient first presented to a healthcare provider
148 after first recognizing symptoms), and symptom interval was defined as the time interval
149 between the date of first symptom recognition and the date of pathological diagnosis[18 19]. The
150 date of symptom recognition was determined based on participants recall. Furthermore, the
151 diagnostic interval was defined as the time elapsed between the date of first clinical presentation
152 and the date of the final pathological diagnosis (the date at which the first histological or
153 cytological confirmation of this malignancy was documented in the pathology report). The
154 pathology report of the patient was used to determine the date of diagnosis [18 19]. Tumors were

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3 155 classified using the Tumor-Node-Metastasis method from the 7th edition of the American Joint
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5 156 Committee on Cancer (AJCC)[20]. And cases were histologically and endoscopically confirmed.
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8 157 Stages I and II were classified as early stages of diagnosis, while stage III and IV were classified
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10 158 as late stages of diagnosis [21]. A pretest for cultural suitability and clarity was performed prior
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12 159 to administering the tool to the participants. When the eligible participants were arrived for
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14 160 treatment, trained nurses interviewed them individually in a semiprivate room in Amharic. If the
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16 161 participants couldn't recall the exact date of their first symptom recognition, they were asked to
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18 162 provide a month or year ('was it at the beginning, middle, or end of the year'). For those who
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20 163 only remembered the month, the date was estimated to be the 15th day of that month. If the
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22 164 participants only said at the beginning, middle or at the end of the year, the estimated date was
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24 165 15th of February, June or October of the year, respectively; if they only said the year, the
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26 166 estimated date was June 30th of that year. We performed sensitivity analyses excluding patients
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28 167 who had only remembered the beginning, middle or end of the year or a year for the date of first
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30 168 symptom recognition or clinical presentation[22].
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35 169 **2.4. Data Analysis**

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39 170 Epi-info version 7 was used for the data entry and SPSS Version 24 was used to analyze the data.
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41 171 Descriptive statistics were calculated for each variable. Numbers and percentages were used to
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43 172 summarize categorical variables. We presented mean and standard deviation for numerical
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45 173 variables with normal distributions, whereas median and IQR were employed for variables with
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47 174 skewed distributions. Patient and diagnostic delays were defined as >60-days patient intervals
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49 175 and >30-days diagnostic intervals, respectively, in the literature [11]. For cross-sectional
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51 176 research, OR is the default measure of association, and logistic regression is often used to
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53 177 estimate. Nevertheless, evidences suggest that when the proportion of the outcome exceeds 10%,
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3 178 an odds ratio overestimates the risk ratio, leading to incorrect interpretations. As a result, to
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5 179 avoid these limitations, the prevalence ratio is preferred measure of association[23 24]. Hence,
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8 180 Poisson regression with robust variance was used to compute the adjusted prevalence ratios of
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10 181 factors associated with the prevalence of patient and diagnostic delays, as well as factors
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12 182 associated with stage at time of diagnosis. Variables having a p value on bivariable analysis were
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15 183 chosen based on literatures that have an effect on patient and diagnostic delays and stage at time
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17 184 of diagnosis. A two-sided p value of 0.05 was declared as statistically significant.
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20 185 **Patient and public involvement** “No patient involved”
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199 3. Results:

200 Socio-demographic and socio- economic characteristics of the study participants

201 We approached 351 participants those histologically confirmed and clinically staged for
202 oesophageal cancer and among 96.3% of them were provided their oral for participation. The
203 participants in the study were 54.30 ± 12.49 years old on average (SD). Male participants
204 accounted for 52.4% of the total participants. More than half of the participants (52%) were
205 above the age of 55 years, only 7.0% of the participants were below the age of 35 years.
206 Approximately, two-thirds of the study participants were from rural areas of Ethiopia and were
207 unable to read and write. Muslims and farmers participants accounted 52% and 38% of the total
208 participants respectively. At the time of data collection, 75% of the participants in the study were
209 married. More than half of the participants in the study earned not more than one USD per day or
210 about 29 Ethiopian Birr. Among the participants, 73% had to travel long distances to receive
211 cancer-specific diagnosis and treatment services, and had to pay more than seven USD or 203
212 Ethiopian Birr for a single trip just to cover only for transportation costs. Furthermore, nearly
213 three-quarters of the study participants had paid their medical expenses out of their pockets
214 (Table 1).

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222 **Table 1:** Socio-demographic and socio-economic characteristics of esophageal cancer patients
 223 Addis Ababa, Ethiopia, February 2019 to August 2020 (n=338)

Variables	Frequency	Percent
Age categories (years)		
<35	24	7
35-44	46	14
45-54	91	27
≥55	177	52
Gender		
Male	177	52.4
Female	161	47.6
Religion		
Christianity	159	47
Islam	175	51.8
Wakefata	4	1.2
Residency		
Urban	126	37.3
Rural	212	62.7
Educational status of participants		
Unable to read and write	209	61.8
1-8 grade	72	21.3
9-12 grade	37	10.9
Diploma and above	20	5.9
Occupation of participants		
Government workers	38	1.2
House wife	118	34.9
Merchant	20	5.9
Private worker	35	10.4
Farmer	127	37.6
Marital status of participants during the data collection time		
Married	246	72.8
Single	92	27.2
Monthly income (USD)		
<35	171	50.6
35-106	130	38.5
106.6-177	21	6.2
>177	16	4.7
One way cost of transport (USD*)		
<7 dollar	93	27.5
≥7 dollar	245	72.5
Sources of medical expenses		
Employing organization	1	0.3
Free medical care	72	21.3
Government insurance	19	5.6
Out of pocket	242	71.6
Private insurance	4	1.2

224 **3.1. Pre-symptomatic and pre-diagnostic characteristics of oesophageal cancer** 225 **patients**

226 Among the total participants, 21.3 % had reported a history of at least one chronic disease, with
227 diabetes mellitus being the most common one. More than three-fourth of the study participants
228 (77.8%, 95% CI [73.4%, 82.2%]) had never heard of oesophageal cancer prior to diagnosis for
229 oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main
230 sources (48%) of the information were friends/ family members or neighbors, followed by
231 printed and electronic medias such as (TV, radio, internet) (28%). Only eight participants (2.4%)
232 had reported first degree family history of oesophageal cancer.

233 Dysphagia was the cardinal symptom mentioned by 84.6% of the study participants, followed by
234 odynophagia of 54.1%. Approximately three-fourth of the study participants had linked the first
235 symptom/s to gastritis. All patients had recognized at least one symptom. Moreover, a significant
236 number of patients reported as having more than one oesophageal cancer symptom. About half
237 of the cases stated that they did not take an immediate action for the first symptom/s because
238 they thought that the symptom/s was/ were simple and self-limited. Meanwhile, about a quarter
239 of the cases sought treatment from various traditional healers as a quick fix for the symptom/s.

240 More than half (58.9%) of the study participants felt compelled by their family members to seek
241 medical help for the symptom/s. About half of the cases first went to public health facilities for
242 their first symptom/s (health centers and health posts), followed by public hospitals (16%). At
243 their first visit to health facilities, approximately to two-third of the study participants first
244 contacted health officers and nurses as health care providers. The mean (SD) of health facilities
245 visited by the cases until the data collection time was 6.6 ± 3.2 . Meanwhile, 11% of the

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3 246 participants had visited more than 10 health facilities until data collection time. The mean (SD)
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5 247 number of visits to health facilities by participants until the data collection time was 7.45 ± 3.63 .
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8 248 The prominent reason mentioned by the participants for consultation delays was a financial issue,
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10 249 (61.5%).
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13 250 3.2. Diagnosis characteristics of oesophageal cancer patients

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16 251 Out of the total oesophageal cancer patients, about 76% (95% CI [71.0 %, 80.7%]) of the study
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18 252 participants were diagnosed at late stages (III and IV), and only 24% of the participants were
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20 253 diagnosed at early stages (I and II). In terms of histologic subtypes, 85.8%, 13.3% and 0.89%
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22 254 were oesophageal squamous cell carcinoma, oesophageal adenocarcinoma and undifferentiated
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24 255 carcinomas, respectively. For those with available grade on biopsy report, 59.8%, 15.7% and
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26 256 8.9%) were well differentiated, unspecified and poorly differentiated respectively. Endoscopic
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28 257 appearance was ulcerative in 49.4% followed by an obliterative of 34.9%. In case of tumor
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30 258 locations, middle oesophagus 41.1% and lower oesophagus 30.8%. The most noticeable single
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32 259 factor mentioned by majority (78%) the participants for the diagnostic delay was longer
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34 260 appointments primarily associated with the health care organizations (**Table 2**).
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Table 2: Diagnostic history of oesophageal cancer patients from February 2019 to August 2020 Addis Ababa, Ethiopia,

Variable	Frequency	Percent
Stage at first diagnosis		
Stage I	20	6.0
Stage II	58	17.2
Stage III	167	49.4
Stage IV	76	22.4
Unknown	17	5.0
Histological sub-type		
Oesophageal squamous carcinoma	290	85.8
Oesophageal adenocarcinoma	45	13.3
Unknown	3	0.9
Histopathological differentiations		
Well-differentiated	202	59.8
Moderate differentiated	47	13.8
Poor differentiated	30	8.9
Undifferentiated	6	1.8
Unspecified	53	15.7
Morphology of tumor during upper gastrointestinal endoscopy		
Ulcerative	167	49.4
Obliterative	118	34.9
Proliferative	45	13.3
Ulceroproliferative	8	2.4
Tumor location(Histology)		
Upper (cervical)	95	28.1
Middle oesophagus	139	41.1
Lower oesophagus	104	30.8

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273 Patient and diagnostic intervals

274 The median (IQR) patient interval was 108.5 (60.5-215) days. The magnitude of patient delay
275 was 75% (95% CI [69.8%, 79.3%]). About ten percent of the participants had visited health
276 facilities after a year of first symptom recognition. Only about 8% of the participants consulted
277 health facilities within one month. Great majority (71%) of the participants mentioned their
278 reason for late patients' consultation was financial problems (59.5%) followed by not bothering
279 about the disease. The median (IQR) of diagnostic interval was 77.5 (39-133) days. The
280 magnitude of diagnostic delay was 81.9% (95% CI [77.9%, 86.2%]). Three percent of those who
281 took part in the study received diagnostic confirmation after a year of waiting and 18% of the
282 participants got diagnosis confirmation less than a month. The median (IQR) symptom interval
283 was 215(130-353) days.

284 3.3. Determinate factors associated with patient and diagnostic delays

285 In the bivariable analysis, participants unable to read and write (PR=1.2, 95% CI [1.05, 1.43]),
286 being house wife (PR=1.14, 95%CI [1.01, 1.29]), single participants (PR=1.08, 95% CI [1.03,
287 1.14]) monthly income <35USD (PR=1.29,95%CI[1.09,1.55]) and 35-106 USD
288 (PR=1.3,95%CI[1.17]CI[1.09,1.55]family monthly income<53USD(PR=1.17,95%CI[1.02,1.33])
289 and 53-141 USD (PR=1.17,95% CI [1.02,1.34]) and never heard of oesophageal cancer prior to
290 diagnosis (PR=1.11,95%CI [1.03,1.97]) were significantly associated with higher prevalence of
291 patient delay. However, after an adjustment, we only found marital status (Adjusted PR=1.09,
292 95% CI [1.03, 1.15]) and never heard of oesophageal cancer prior to diagnosis (Adjusted
293 PR=1.08, 95% CI [1.03, 1.15]) were found statistically significant to increase the prevalence of
294 patients delay among oesophageal cancer patients (Table 3).

295 **Table 3** : Determinant factors associated with patient delay (>60 days) among oesophageal
 296 cancer patients from February 2019 to August 2020, Addis Ababa, Ethiopia (n=324)

Patient characteristics	Patient delay		Unadjusted	P-value	Adjusted	P-value
	Yes (%)	No (%)	PR (95% CI)		PR (95% CI)	
Age of participants (years)						
<35	14 (66.7)	7 (33.3)	Ref.		Ref.	
35-44	26 (59.1)	18 (40.9)	0.96 (0.82,1.11)	0.55	0.96 (0.86,1.07)	0.43
45-54	63 (72.4)	24 (27.6)	1.03 (0.91,1.18)	0.62	1.03 (0.94, 1.12)	0.56
≥55	140 (81.4)	32 (18.6)	1.10 (0.96,1.23)	0.18	0.99 (0.91,1.08)	0.81
Gender						
Male	127 (73.8)	45 (26.2)	0.99 (0.94,1.04)	0.61		
Female	116 (76.3)	36 (23.7)	Ref.		Not included	
Residency						
Urban	88 (71.0)	36 (29.0)	Ref.		Ref.	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98,1.10)	0.19	1.04 (0.97,1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05,1.43)	0.01	1.11 (0.94, 1.29)	0.22
Grade 1-8	56 (81.2)	13 (18.8)	1.25 (1.07,1.46)	0.006	1.15 (0.97, 1.35)	0.10
Grade 9-12	23 (67.6)	11 (32.4)	1.16 (0.97,1.38)	0.11	1.08 (0.91, 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Ref.			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Ref.		Ref.	
Government workers	24 (68.6)	11 (31.4)	1.08 (0.93,1.24)	0.32	1.02 (0.94, 1.11)	0.57
House wife	82 (78.8)	22 (21.2)	1.14 (1.01,1.29)	0.03	0.94 (0.86, 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02,1.34)	0.03	1.03 (0.94,1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13(0.99,1.27)	0.06	0.93 (0.85, 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03,1.14)	0.002	1.09 (1.03, 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Ref.			
Monthly income						
<35 US dollar	124 (78.5)	34 (21.5)	1.29 (1.09,1.55)	0.004	1.22(1.005,1.48)	0.045
35-106 US dollar	101 (78.9)	27 (21.1)	1.3 (1.09,1.55)	0.004	1.22(1.22,1.48)	0.042
106.6-177 US dollar	12 (54.5)	10 (45.5)	1.12 (0.90,1.39)	0.29	0.46(1.09)	0.46
>177 US dollar	6 (37.5)	10 (62.5)	Ref.			
One way cost of transport (USD)						
<7 dollar	71 (77.2)	21 (22.8)	1.02 (0.96,1.08)	0.56	Not included	
≥7 dollar	172 (74.1)	60 (25.9)	Ref.			
Family monthly income(USD)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02, 1.33)	0.025	1.12(0.98,1.27)	0.09
53-141	84 (77.8)	24 (22.2)	1.17 (1.02,1.34)	0.024	1.13(0.99,1.28)	0.08
141.4-230	18 (72.0)	7 (28.0)	1.13 (0.96,1.33)	0.14	1.1(0.94,1.29)	0.26
>230	13 (52.0)	12 (48.0)	Ref.			

297 **Table 3 cont.....**

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Prior information about esophageal cancer						
No	198 (79.0)	53 (21.0)	1.11 (1.03,1.97)	0.007	1.08(1.02,1.17)*	0.04
Yes	44 (61.1)	29 (38.9)	Ref.			
Family size in the house hold						
<3	9(64.3)	5 (35.7)	Ref.		Not included	
3-5	108 (74.0)	38 (26.0)	1.06 (0.90, 1.24)	0.48		
>5	126 (76.8)	38 (23.2)	1.08 (0.92, 1.26)	0.36		
Visiting traditional healers						
No	180(73.2)	66(26.8)	Ref.			
Yes	63(80.8)	15(19.8)	1.04(0.99,1.11)	0.15	1.04(0.98,1.10)	0.23

298 Meanwhile, in the bivariable analysis, single participants (PR=1.8,95%CI[1.74,1.85]),family
299 monthly income 53-141 USD(PR=0.91,95%CI [0.85,0.99]),cost transport (one
300 trip)>7USD(PR=1.07,95%CI[1.06,1.13]), first medical consultation at health center
301 (PR=0.93,95%CI[0.88,0.99]) and number of health facilities visited < 3 health facilities
302 (PR=0.93, 95%CI [0.87,0.99]) were significantly associated with higher prevalence of diagnostic
303 delay. However, after an adjustment or in the multivariable analysis, we only found marital
304 status (Adjusted PR=1.2, 95% CI [1.11,2.10]), sources of medical expenses (Adjusted
305 PR=1.2,95% CI[1.13,2.40]), cost of transportation (Adjusted PR=1.2,95% CI [1.12,1.54]) and
306 first medical consultation to health facilities (Adjusted PR= 1.4, 95% CI [1.20,2.30]) were
307 statistically significant to increase the prevalence of diagnostic delay among oesophageal cancer
308 patients (Table 4).

312 **Table 4:** Factors associated with diagnostic delay (>30 days) among oesophageal cancer
 313 diagnosed from February 2019 to August 2020, Addis Ababa Ethiopia (n=326)

Patient characteristics	Diagnosis delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Ref.		Ref.	
35-44	33 (75.0)	11 (25.0)	0.94 (0.84, 1.04)	0.24	0.96(0.86,1.07)	0.45
45-54	75 (87.2)	11 (12.8)	1.01 (0.92, 1.09)	0.92	1.02(0.93,1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89, 1.05)	0.45	0.97(0.89,1.06)	0.53
Gender						
Male	144(83.2)	29(16.8)	1.02(0.97,1.06)	0.51		
Female	123(80.4)	30(19.6)	Ref.		Not included	
Residency						
Urban	102(82.9)	21(17.1)	Ref.		Not included	
Rural	165(81.3)	38(18.7)	0.99(0.95,1.04)	0.71		
Marital status of participants during the data collection time						
Single	78(88.6)	10(11.4)	1.80(1.74,1.85)	0.0001	1.2 (1.1,2.10)**	0.04
Married	189(79.4)	49(20.6)	Ref.		Ref.	
Monthly income						
<35 US dollar	129(80.1)	32(19.9)	0.96(0.88,1.05)	0.39		
35-106 US dollar	103(81.1)	24(18.9)	0.97(0.88,1.06)	0.47		
106.6-177 US dollar	17(77.3)	5(22.7)	1.04(0.95,1.15)	0.40		
>177 US dollar	12(66.7)	6(27.3)	Ref.		Not included	
Family monthly income(USD)						
<53	139(82.7)	29(17.3)	0.95(0.89,1.01)	0.11	0.98(0.88,1.09)	0.69
53-141	80(74.8)	27(25.2)	0.91(0.85,0.99)	0.008	0.91(0.82,1.002)	0.05
141.4-230	20(80.0)	5(20.0)	1.02(0.95,1.09)	0.57	1.01(0.93,1.09)	0.84
>230	19(73.1)	7(26.9)	Ref.		Ref.	
One way cost of transport (USD)						
<7 dollar	67(73.6)	24(26.4)	Ref.			
≥7 dollar	200(85.1)	35(14.9)	1.07(1.06,1.13)	0.03	1.2(1.12,1.54)**	0.04
First medical consultation						
Health post	35(87.5)	5(12.5)	0.99(0.94,1.07)	0.96	1.01(0.94,1.08)	0.83
Health center	123(77.4)	36(22.6)	0.93(0.88,0.99)	0.015	1.4 (1.2, 2.30)**	0.049
Private clinic	38(88.4)	5(11.6)	0.99(0.94,1.06)	0.78	1.01(0.94,1.08)	0.87
Private hospital	24(72.7)	9(27.3)	0.91(0.82,1.002)	0.054	0.92(0.83,1.02)	0.10
Public hospital	46(90.2)	5(9.8)	Ref.		Ref.	
Visiting traditional healers						
No	201(82.0)	44(18.0)	Ref.			
Yes	66(81.5)	15(18.5)	0.99 (0.95,1.05)	0.91	Not included	
Family size						
<3	9(64.3)	5(35.7)	Ref.		Not included	
3-5	122(83.6)	24(16.4)	0.99(0.89,1.09)	0.83		
>5	133(80.1)	33(19.9)	0.97(0.87,1.08)	0.57		

314 Table 4 cont....

Patient characteristics	Diagnosis delay		Unadjusted	P-value	Adjusted	P-value
	Yes (%)	No (%)	PR (95% CI)		PR (95% CI)	
First consulted health care provider						
HEW	38(84.4)	7(15.6)	1.018(0.95,1.09)	0.62		
Nurse	61(68.5)	14(31.5)	1.001(0.94,1.07)	0.97		
Health officer	82(82.0)	18(18.0)	1.005(0.95,1.06)	0.87		
Medical doctor	86(81.1)	20(18.9)	Ref.		Not included	
Number of health facilities visited for diagnosis						
< 3 health facilities	13(72.2)	5(27.8)	Ref.		Ref.	
3-6 health facilities	153(80.5)	37(19.5)	0.93(0.87,0.99)	0.02	0.93(0.87,1.22)	0.054
7-10 health facilities	67(81.7)	15(18.3)	0.93(0.87,1.004)	0.06	0.94(0.87,1.01)	0.108
>10 health facilities	29(82.9)	6(17.1)	0.94(0.86,1.026)	0.17	0.94(0.86,1.03)	0.19
Source of medical expenses						
Free medical care	57(79.2)	15(20.8)	Ref.			
Governmental insurance	11(61.1)	7(38.9)	0.90(0.78,1.044)	0.16	1.22 (1.13, 2.40)*	0.048
Out of pocket	199(84.3)	37(15.7)	1.03(0.97,1.09)	0.34	1.03(0.98,1.09)	0.26
Prior information about oesophageal cancer						
No	205(81.0)	48(19.0)	0.98(0.93,1.03)	0.42		
Yes	62(85.0)	11(15.0)	Ref.		Not included	

315

316 3.4. Factors associated with advanced stages at diagnosis among oesophageal 317 cancer patients

318 In the bivariable analysis, marital status, single (PR=1.16, 95% CI [1.02, 1.30]) and patients
319 delay of > two months (PR=1.38, 95% CI [1.14, 1.68]) were significantly associated with late
320 stage at first diagnosis. However, after an adjustment or multivariable analysis, marital status
321 (Adjusted PR=1.16, 95% CI [1.03, 1.31]), female participants (Adjusted PR=1.15, 95% CI
322 [1.015, 1.31]), patient delay > two months (Adjusted PR=1.41, 95% CI [1.15, 1.69]) and
323 symptom intervals (Adjusted PR=1.26, 95% CI [1.12, 1.67]) were statistically significant to
324 increase the prevalence of advanced stage at time of diagnosis (Table 5).

325 **Table 5:** Factors associated with advanced stages at diagnosis among oesophageal cancer
 326 patients from February 2019 to August 2020 Addis Ababa, Ethiopia (n=321).

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Age						
<35	5(21.7)	18(78.3)	Ref.		Not included	
35-44	12(27.3)	32(72.7)	0.88(0.68,1.14)	0.34		
45-54	22(25.6)	64(74.4)	0.90(0.72,1.13)	0.36		
≥55	40(23.8)	128(76.2)	0.92(0.75,1.13)	0.44		
Gender						
Male	45(27.1)	121(72.9)	Ref.		Ref.	
Female	33(21.3)	122(78.7)	0.93(0.82,1.05)	0.22	1.15 (1.01,1.31)*	0.049
Residency						
Urban	33(27.5)	87(72.5)	Ref.			
Rural	45(22.4)	156(77.6)	1.07(0.94,1.22)	0.32	Not included	
Educational status of participants						
Unable to read and write	44(22.2)	154(77.8)	1.14(0.83,1.56)	0.42		
Grade 1-8	17(24.6)	52(75.4)	1.10(0.79,1.54)	0.57		
Grade 9-12	11(31.4)	24(68.6)	1.01(0.69,1.46)	0.99		
Diploma and above	6(31.6)	13(68.4)	Ref.		Not included	
Occupation of participants						
Private worker	5(17.2)	24(82.8)	Ref.			
Government workers	13(35.1)	24(64.9)	0.78(0.59,1.05)	0.10	0.77 (0.57, 1.02)	0.07
House wife	28(24.8)	85(75.2)	0.91(0.75,1.11)	0.34	0.89 (0.73,1.09)	0.25
Merchant	6(30.0)	14(70.0)	1.03(0.80,1.32)	0.83	0.99 (0.78,1.28)	0.98
Farmer	29(23.8)	93(76.2)	0.92(0.76,1.12)	0.41	0.89 (0.74,1.09)	0.29
Marital status of participants during the data collection time						
Single	14(16.1)	73(83.9)	1.16(1.02,1.30)	0.02	1.16 (1.03,1.31)*	0.015
Married	64(27.4)	170(72.6)	Ref.		Ref.	
Monthly income (USD)						
<35	37(22.8)	125(77.2)	0.95(0.74,1.20)	0.69		
35-106	31(25.6)	90(74.4)	0.92(0.71,1.18)	0.50		
106.6-177	7(31.8)	15(68.2)	0.84(0.58,1.22)	0.35		
>177	5 (31.3)	11(68.7)	Ref.		Not included	
Family monthly income(USD)						
<53	38(22.9)	128(77.1)	1.01(0.80,1.26)	0.98		
53-141	30(28.3)	76(71.7)	0.93(0.73,1.19)	0.57		
141.4-230	5(21.7)	18(78.3)	1.07(0.81,1.42)	0.62		
>230	6(23.1)	20(76.9)	Ref.		Not included	
Prior information about esophageal cancer						
No	59(23.5)	192(76.5)	1.05(0.89,1.23)	0.55	Not included	
Yes	19(27.1)	51(72.8)	Ref.			

327

328 Table 5 cont...

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Family size in the house hold						
<3	6(37.5)	10 (62.5)	Ref.			
3-5	38(26.6)	105(73.4)	0.84(0.68,1.04)	0.10	0.82 (0.66, 1.03)	0.08
>5	38(23.5)	124(76.5)	0.88(0.71,1.07)	0.20	0.87 (0.69 ,1.07)	0.19
Visiting traditional healers						
No	61(25.2)	181(74.8)	Ref.			
Yes	17(21.5)	62(78.5)	1.05(0.92,1.20)	0.49	Not included	
One way cost of transport (USD)						
<7 dollar	28(31.1)	62(68.9)	Ref.			
>7 dollar	50(21.6)	181(78.4)	1.14(0.98,1.33)	0.10	1.12 (0.96 , 1.30)	0.15
First medical consultation						
Health post	6(15.4)	33(84.6)	1.11(0.94,1.32)	0.22	1.11 (0.92, 1.33)	0.27
Health center	48(30.6)	109(69.4)	0.86(0.73,1.02)	0.08	0.87 (0.73 ,1.04)	0.12
Private clinic	6(14.3)	36(85.7)	1.06(0.88,1.27)	0.52	1.05 (0.88 , 1.30)	0.57
Private hospital	10(32.2)	21(67.8)	0.84(0.64,1.11)	0.21	0.83 (0.63 , 1.09)	0.18
Public hospital	10(19.2)	42(80.8)	Ref.			
Source of medical expenses						
Free medical care	19(26.8)	52(73.2)	Ref.		Not included	
Governmental insurance	7(38.9)	11(61.9)	1.06(0.91,1.24)	0.47		
Out of pocket	52(22.4)	180(77.6)	0.83(0.56,1.24)	0.37		
Patient delay (> 2 months)						
No	31(40.8)	45(59.2)	Ref.		Ref.	
Yes	42(18.2)	189(81.8)	1.38(1.14,1.68)	0.001	1.41 (1.15, 1.69)*	0.001
Diagnosis delay(> 1 month)						
No	16(29.1)	39(70.9)	Ref.			
Yes	58(22.7)	197(77.3)	1.09(0.91,1.31)	0.36	Not included	
Number of health facilities visited						
<3	6(30.0)	14(70.0)	Ref.			
3-6	50(27.0)	135(73.0)	1.04(0.77,1.41)	0.79		
7-10	19(23.5)	62(76.5)	1.09(0.80,1.49)	0.57		
>10	5(14.3)	30(85.7)	1.31(0.96,1.77)	0.08		
Number of times visited health facilities prior to final diagnosis						
< 3 times	7(31.8)	15(68.2)	Ref.		Ref.	
3-6 times	40(26.8)	109(73.2)	1.07(0.79,1.45)	0.65	0.89 (0.69 , 1.16)	0.39
7-10 times	19(21.8)	68(78.2)	1.15(0.84,1.56)	0.38	0.93 (0.70 , 1.23)	0.61
>10 times	12(19.0)	51(81.0)	1.19(0.87,1.62)	0.24	1.12 (0.85 , 1.46)	0.43
Symptom interval						
< 3 months	12(36.4)	21(63.6)	Ref.		Ref.	
3-6 months	26(29.5)	62(70.3)	1.11(0.83,1.48)	0.49	1.09 (0.81 , 1.46)	0.51
> 6months	37(19.7)	151(80.3)	1.26(0.97,1.65)	0.08	1.26 (1.12 , 1.67)*	0.048

329

330 Discussion

331 Longer consultation and diagnostic delays, as well as late stages at the time of diagnosis, were
332 hypothesized before we started this study. We estimated prolonged presentation and diagnostic
333 delays. In addition, most of the cases were diagnosed at advanced stages. The most common
334 reason for patient delays was financial constraints. About 11% of the cases were forced to visit
335 an average of 10 different health facilities looking for affordable care. The dominant histological
336 subtype was oesophageal squamous carcinoma. In addition, risk factors for late consultation,
337 diagnostic and late stage at the time of diagnosis were identified.

338 The median patient intervals were much lower in studies [11 21 25-27]. compared to the patient
339 interval estimated from our study. This significant variation could be related to the socio-
340 cultural, socio-economic differences in health-seeking behavior and a lack of awareness about
341 oesophageal cancer symptoms across the groups/communities. Furthermore, the late presentation
342 is heavily attributed to limited access to care as most of our participants were from rural areas
343 and cancer care is provided by secondary and tertiary level care facilities located far from the
344 most rural dwellers and mostly illiterates. Our study, however, is analogous to a study conducted
345 in South Africa[28]. The comparable socio-economic, socio-cultural and literacy rates of the
346 societies may explain for the parallel presentation delays.

347 The median diagnostic interval estimated from our study is higher than that of prior studies.[11
348 21 25 26]. The discrepancy may be the differences in diagnostic workups and the availability of
349 experienced and trained health professionals in cancer related diagnostic and treatment services.
350 On the other hand, our study is in line with the study[28]. The similarities could be attributed to
351 the fact that diagnostic workups and health facilities status are comparable throughout African
352 countries.

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3 353 The proportion of advanced stages at first diagnosis is higher compared to study [21] this could
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5 354 be related to longer patient and diagnostic intervals and socio-economic difference among the
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8 355 communities. The cardinal symptom reported by majority of our participants was dysphagia this
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10 356 result is comparable with studies [21 26 27]. We discovered that oesophageal squamous
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12 357 carcinoma was the most prevalent, which is consistent with other studies. [21 29 30].

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14 358 Sizable amount of oesophageal cancer patients were diagnosed at advanced stages and this is
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16 359 comparable with studies. [29 31]. However, the proportion of those diagnosed with oesophageal
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19 360 cancer early is relatively higher in this study [30]. Increased patient delay (> two months) was
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21 361 found to be exacerbated by socio-economic level in our study. Our finding is equivalent to this
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23 362 study [32] , which evidenced those patients with lower socio-economic status sought medical
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25 363 help later. Furthermore, socioeconomic status has had an important influence in patients being
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27 364 diagnosed at advanced stages, which is similar to the findings of the study [32].

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31 365 As an immediate measure for their symptom/s, a large percentage of oesophageal cancer patients
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33 366 contacted various traditional healers. This finding is consistent with the findings of a qualitative
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35 367 study conducted in Ethiopia's in Oromia Regional State [33]. The study's comparability is owing
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37 368 to the societies' similar socio-economic and socio-cultural characteristics. The prevalence of
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39 369 diagnostic delay was higher in single patients than the married participants. Thus, being married
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41 370 might have a better chance to seek medical care than unmarried participants. The reason could
42
43 371 be, partners may influence each other on decision making to seek care as early as possible. In our
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45 372 findings, oesophageal cancer that paid their medical expense from their own pocket had longer
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47 373 patient interval than patients whose medical expenses covered by other organizations. The reason
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49 374 could be, they ignore the symptoms because patients with low socio-economic status had other
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51 375 unmet survival felt needs than investing money for medical cares [34].
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376 4. Conclusion

377 Oesophageal cancer patients in Ethiopia had longer patients' presentation, diagnostic and
378 symptom intervals. Moreover, majority of the oesophageal cancer patients had diagnosed at
379 advanced stages (III and IV). Marital status and having never heard of oesophageal cancer prior
380 to diagnosis were found to be predictors of increased patient intervals. The levels of first health
381 facilities visited for medical consultation and the cost of transportation were identified as key
382 factors in increasing diagnostic intervals. Furthermore, marital status, gender, patient delay of
383 more than two months and symptom interval were revealed to be statistically significant factors
384 in the occurrence of advanced stages at time of diagnosis. Patients' intervals could be shortened
385 by increasing their awareness of oesophageal cancer symptoms.

386 Abbreviations

387 AJCC: American Joint Committee on Cancer

388 APR: Adjusted Prevalence Ratio

389 SD: Standard Deviation

390 IQR: Inter Quartile Range

391 P: Proportion

392 PR: Prevalence Ratio

393 USD: United States Dollar

394 Ethics approval and informed consent

395 The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa
396 University College of Health Sciences with a protocol number of 080/18/SPH. The study
397 followed basic ethical principles of Helsinki declaration for medical research involving human

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2
3 398 participants[35]. All of the study participants were informed about the purpose and procedure of
4
5 399 the research and their right to withdrawal from the study at any time. Written informed consent
6
7
8 400 was obtained from each of the study participants. Meanwhile, the study participants were agreed
9
10 401 to the extent that the finding of this study will be subjected to publication. Participants were well
11
12 402 informed not to disclose their information to a third person. The information was kept secured
13
14
15 403 and put confidentially with the first author.

18 404 **Data availability**

21 405 Data will be available up on request

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28 407 There is no fund for this research project

31 408 **Competing interests**

35 409 There is no competing interest of this research

38 410 **Authors' contributions**

41 411 All authors contributed from the conception of idea up to data analysis and write up. They also
42
43 412 participated in drafting or revising of the article and have agreed on to which journal the article
44
45 413 shall be submitted and have given final approval of the version to be published, and agreed to be
46
47
48 414 accountable for all aspects of the work. Specifically, BD was conceptualized the topic of interest,
49
50 415 involved in data collection, coding, cleaning, analysis, interpretation of the result unto
51
52
53 416 preparation of the manuscript. FE was involved in proposal development, planning the fieldwork
54
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3 417 and result section. And RY, MA, SG and AA were involved in proposal development, data
4
5 418 analysis and write up and in critical reviewing of manuscript.
6
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27 430 **References**

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Time intervals from first symptom recognition to pathological diagnosis among oesophageal cancer patients in Ethiopia: A cross-sectional study

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4 1 **Time intervals from first symptom recognition to pathological diagnosis**
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6 2 **among oesophageal cancer patients in Ethiopia: A cross-sectional study**
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9 3 Berhe Dessalegn^{1*,2}, Sefonias Getachew², Robel Yirgu², Fikre Enqueselassie^{2†}, Mathewos
10 4 Assefa³, Adamu Addissie²
11

12
13
14 5 ¹Department of Public Health, College of Medicine and Health Sciences, Adigrat University
15
16 6 Adigrat, Ethiopia
17
18

19 7 ² Department of Preventive Medicine, School of Public Health, College of Health Sciences,
20
21 8 Addis Ababa University, Addis Ababa, Ethiopia
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23
24 9 ³Department of Radiotherapy Center, School of Medicine, Addis Ababa University, Addis
25
26 10 Ababa, Ethiopia
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29 11 * Corresponding Author
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31 12 Email: berhe_dessalegn@yahoo.com(BD)
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33 13 † Professor Fikre Enqueselassie has passed away on October 28th, 2019.
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21 Abstract

22 Objective

23 The aim of this study was to estimate the time intervals from first symptom recognition to
24 pathological diagnosis among oesophageal cancer patients in Ethiopia.

25 Methods

26 **Design** A cross-sectional study design was employed

27 **Settings and participants** Oesophageal cancer patients aged ≥ 18 years were included from
28 health facilities of Addis Ababa, Ethiopia (n=338) from February 2019 to August 2020. The
29 participants were selected consecutively from six health facilities provided cancer care nearly for
30 90% of patients.

31 **Main outcomes and measurements** The Aarhus statement criterias was applied to
32 classify patient interval (time from first symptom recognition to presentation), and diagnostic
33 interval (time from first presentation to diagnosis). Patient and diagnostic intervals >60 and >30
34 days were considered as delays, respectively. For tumor classification, the American Joint
35 Committee on cancer was used. Data were analyzed using SPSS Version 24. Descriptive
36 statistics were applied to describe patients' characteristics. Poisson regression with robust
37 variance was used to compute prevalence ratios. In all statistical tests, significances were
38 declared at p-value of <0.05 .

39 Results

40 The mean (SD) age of the participants was 54.30 ± 12.49 years.

41 Prior to diagnosis, 78% of the study participants had never heard of oesophageal cancer and
42 believed suffering from gastritis. Dysphagia was commonly mentioned symptom. About 76% of
43 the cases were diagnosed at advanced stages (III and IV). The median patient interval was 108.5
44 days and the median diagnostic interval was 77.5 days. After adjusting for confounders, marital

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3 45 status, lack of awareness of oesophageal cancer, cost of transportation, first medical consultation
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5 46 and patient delay > two months were found statistically significant predictors.
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9 47 **Conclusion** Oesophageal cancer patients in Ethiopia had prolonged patient and diagnostic
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11 48 intervals. Increasing awareness about the commonest symptoms of oesophageal cancer and
12
13 49 shortening the time to diagnosis will help to improve the out-come of oesophageal cancer care in
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16 50 Ethiopia.

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18 51 **Keywords:** Oesophageal cancer, delay, intervals, tumor stage
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21 52 22 23 24 53 **Strengths and Limitations**

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27 54 • In Ethiopia, in case of patient and diagnostic interval and associated factors, it is the first
28
29 55 multifacility study
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31 56 • Poisson regression with robust variance was used to compute the prevalence ratios
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33 57 • It is the only research based on primary data in Ethiopia that estimates the patient and
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35 58 diagnostic intervals on oesophageal cancer patients
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37 59 • However, the onset of symptoms is a subjective measurement that patients may not recall the
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39 60 exact time
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1. Introduction

Cancer is a group of diseases in which abnormal cells grow and spread uncontrollably. Cancer has become a major public health concern on a global scale [1]. Oesophageal cancer is the fourth most common cancer in developing countries, and it is an aggressive tumor of the esophagus that develops in the organ's tissue lining [2]. Oesophageal cancer, which has a dismal prognosis and survival rate, has caused considerable morbidity and mortality around the world from the last three decades [3-5]. Globally, oesophageal cancer was the sixth most common cause of mortality among all cancers and the seventh most common cancer in terms of incidence[1].

The two most prevalent subtypes of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. Adenocarcinoma begins in the cells that produce and release mucus and other fluids, whereas squamous cell carcinoma begins in the flat cells that line the esophagus. Oesophageal cancer mortality and incidence are higher in Africa than the rest of the world, with squamous cell carcinoma being the most common type [6 7].

The five-year survival rate of non-metastatic oesophageal cancer is between 19 and 30%, whereas, the median overall survival time for metastatic oesophageal cancer is between four and six months. Nonetheless, it is not uncommon for oesophageal cancer patients to be diagnosed at advanced stages ,because, in most cases, the oesophageal cancer patients have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patients prognosis and survival rate[5 8 9]. The prognosis and time intervals of oesophageal cancer patients has been solely depended on the patients' awareness on symptoms and literates rate that contribute to early consultation and shorter pathological diagnosis periods, according to studies[10 11]. In practice, however, oesophageal cancer patients frequently have arrived late in presentation and commonly lately referred to the appropriate health facilities. In addition,

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3 91 literatures also showed that shortening the time to presentation is an important step in reducing
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5 92 late in diagnosis, and improving the prognosis and survival of oesophageal cancer patients[12
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11 94 Oesophageal cancer is the overwhelming disease and among the commonest cause of cancer
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13 95 deaths in the world. Though, few patients can be cured, the treatment for oesophageal cancer is
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15 96 prolonged, quality of life is significantly compromised and cases fatality rate is high [1].
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19 97 Ethiopia is a country, geographically located within the highest risk region of oesophageal cancer
20
21 98 known to be the oesophageal cancer belt. And, the disease has created a huge burden interms of
22
23 99 morbidity and mortality in the country[14]. In addition, few hospital reports revealed that over
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25 100 the last decades, the incidence and burden of oesophageal cancer has been increasing.
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29 101 Diagnostic and consultation delays on cancers are common in underdeveloped countries, such as
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31 102 the Eastern part of Africa, and are closely linked to poor survival rates. As a result, obtaining
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33 103 updated information is crucial for establishing a resilient plan to reduce oesophageal cancer
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35 104 related morbidity and mortality [7 15].
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39 105 In Ethiopia, however, oesophageal cancer is not yet a public health priority, left in dark and is
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41 106 under-researched; as a result, there is no clear evidence about patient and diagnostic intervals and
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43 107 the stage at time of diagnosis. The goal of this study was to determine time to care seeking and
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45 108 pathological diagnosis, and the stage at time of diagnosis of oesophageal cancer patients.
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47 109 Meanwhile, we were also strived to identify predictors of patients and pathological diagnostic
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49 110 delays of > 60 and > 30 days, respectively.
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112 2. Materials and methods

113 2.1. Study design and sample size

114 A cross-sectional study design was employed. The study involved 338 oesophageal cancer
115 patients aged ≥ 18 years from February 2019 to August 2020 in Addis Ababa, Ethiopia. Using the
116 expected proportion ($p=32.0\%$) of patients delay to presentation (>2 months) from another
117 similar study [16] by assuming a 95% level of confidence, a 5% precision and 5% non-response
118 rate

119 2.2. Settings and participants

120 The Ethiopian health care delivery system has three tiers: primary, secondary and tertiary level
121 health care facilities that are linked with a referral system. The setup differs slightly between
122 urban and rural settings. The main healthcare service in the metropolitan city, such as Addis
123 Ababa, Ethiopia's capital, includes public health centers, private clinics, and primary hospitals.
124 Secondary and tertiary healthcare levels are general hospitals and specialty hospitals,
125 respectively. The primary healthcare services in rural areas are made up of a health post, a health
126 center, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and
127 specialty hospitals, respectively. Nurses and health officers are the primary staff of public health
128 centers, with the goal of providing preventative and primary health care services. In the case of
129 cancers, such as oesophageal cancer, health workers at the primary level care facilities are only
130 expected to refer patients to general hospitals and other high-level facilities for further diagnosis
131 and treatments[17].

132

133 **Sampling procedure**

134 A consecutive sampling method was used to recruit study participants. Oesophageal cancer
135 patients histologically confirmed and clinically staged came to the selected health facilities were
136 included in the study, whereas critically ill, diagnosed to other cancer types and non-Ethiopian
137 patients were excluded from participation. Six health facilities in Addis Ababa (Tikur Anbesa
138 Specialized Hospital, St. Paul Hospital Millennium Medical College, Betezata Hospital,
139 Hallelujah General Hospital, Landmark Hospital, and United Vision Medical Services Centre)
140 were selected, where nearly 90% of cancer patients being diagnosed and treated. At each health
141 facility, one focal person was assigned to identify eligible oesophageal cancer patients and
142 communicate with the principal investigator and supervisor. To avoid duplication, the medical
143 chart of the recruited patient was coded in red on the top cover page. Prior to the interview,
144 study participants were informed about the purpose of the study and their right to withdraw
145 under any circumstances without compromisation of any services.

146 **2.3. Variables and Measurements**

147 We used the Aarhus statement criteria to classify patient, diagnostic and symptoms intervals.
148 Thus, patient interval was defined as the interval between the date of first symptom recognition
149 (the time point at which the patient first noticed bodily changes and/or symptoms) and the date of
150 first clinical presentation (the date at which the patient first presented to a healthcare provider
151 after first recognizing symptoms), and symptom interval was defined as the time interval
152 between the date of first symptom recognition and the date of pathological diagnosis[18 19]. The
153 date of symptom recognition was determined based on participants recall. Furthermore, the
154 diagnostic interval was defined as the time elapsed between the date of first clinical presentation
155 and the date of the final pathological diagnosis (the date at which the first histological or

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3 156 cytological confirmation of the malignancy was documented in the pathology report). The
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5 157 pathology report of the patient was used to determine the date of diagnosis [18 19]. Tumors were
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8 158 classified using the Tumor-Node-Metastasis method from the 7th edition of the American Joint
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10 159 Committee on Cancer (AJCC)[20]. And cases were histologically and endoscopically confirmed.
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12 160 Stages I and II were classified as early stages of diagnosis, while stage III and IV were classified
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14 161 as late stages of diagnosis [21]. The interviews were conducted in Amharic, the country's
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16 162 working language. The study tool was initially prepared in English, then translated into Amharic
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18 163 by language translators, and finally back to English to ensure that the two versions were
19
20 164 consistent. Experts in cancer research assessed the tool to ensure that the questions were clear
21
22 165 and two days training was given data collectors and the supervisor about the objective of the
23
24 166 study. A pretest for cultural suitability and clarity was performed prior to administering the tool
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26 167 to the participants. When the eligible participants were arrived for treatment, trained nurses
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28 168 interviewed them individually in a semiprivate room in Amharic. If the participants couldn't
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30 169 recall the exact date of their first symptom recognition, they were asked to provide a month or
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32 170 year ('was it at the beginning, middle, or end of the year'). For those who only remembered the
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34 171 month, the date was estimated to be the 15th day of that month. If the participants only said at the
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36 172 beginning, middle or at the end of the year, the estimated date was 15th of February, June or
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38 173 October of the year, respectively; if they only said the year, the estimated date was June 30th of
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40 174 that year. We performed sensitivity analyses excluding patients who had only remembered the
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42 175 beginning, middle or end of the year or a year for the date of first symptom recognition or
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44 176 clinical presentation[22].
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179 2.4. Data Analysis

180 Epi-info version 7 was used for the data entry and SPSS Version 24 was used to analyze the data.
181 Descriptive statistics were calculated for each variable. Numbers and percentages were used to
182 summarize categorical variables. We presented mean and standard deviation for numerical
183 variables with normal distributions, whereas median and IQR were employed for variables with
184 skewed distributions. Patient and diagnostic delays were defined as >60-days patient intervals
185 and >30-days diagnostic intervals, respectively, from previous similar study [11]. For cross-
186 sectional research, OR is the common measure of association, and logistic regression is often
187 used to estimate. Nevertheless, evidences suggest that when the proportion of the outcome
188 exceeds 10%, an odds ratio overestimates the risk ratio, leading to incorrect interpretations. As a
189 result, to avoid these limitations, the prevalence ratio is preferred measure of association [23 24].
190 Hence, Poisson regression with robust variance was used to compute the adjusted prevalence
191 ratios of factors associated with the prevalence of patient and diagnostic delays, as well as factors
192 associated with stage at time of diagnosis. Variables having a p value of <0.25 on bivariable
193 analysis were chosen for the multivariable analysis based on literatures that have an effect on
194 patient and diagnostic delays and stage at time of diagnosis. A two-sided p value of 0.05 was
195 declared as statistically significant.

196 **Patient and public involvement** “No patient involved”

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201 3. Results:

202 Socio-demographic and socio- economic characteristics of the study participants

203 We approached 351 participants those histologically confirmed and clinically staged for
204 oesophageal cancer and among 96.3% (338) of them were provided their oral consent for
205 participation. The participants in the study were 54.30 ± 12.49 years old on average (SD). Male
206 participants accounted for 52.4% of the total participants. More than half of the participants
207 (52%) were above the age of 55 years, only 7.0% of the participants were below the age of 35
208 years. Two-thirds of the study participants were from rural areas of Ethiopia and were unable to
209 read and write. Muslims and farmers participants accounted 52% and 38% of the total
210 participants respectively. At the time of data collection, 75% of the participants in the study were
211 married. More than half of the participants in the study earned not more than one USD per day or
212 about 29 Ethiopian Birr. Among the participants, 73% had to travel long distances to receive
213 cancer-specific diagnosis and treatment services, and had to pay more than seven USD or 203
214 Ethiopian Birr for a single trip just to cover only for transportation costs. Furthermore, nearly
215 three-quarters of the study participants had paid their medical expenses out of their pockets
216 **(Table 1).**

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224 **Table 1:** Socio-demographic and socio-economic characteristics of esophageal cancer patients
 225 Addis Ababa, Ethiopia, February 2019 to August 2020 (n=338)

Variables	Frequency	Percent
Age categories (years)		
<35	24	7
35-44	46	14
45-54	91	27
≥55	177	52
Gender		
Male	177	52.4
Female	161	47.6
Religion		
Christianity	159	47
Islam	175	51.8
Wakefata	4	1.2
Residency		
Urban	126	37.3
Rural	212	62.7
Educational status of participants		
Unable to read and write	209	61.8
1-8 grade	72	21.3
9-12 grade	37	10.9
Diploma and above	20	5.9
Occupation of participants		
Government workers	38	1.2
House wife	118	34.9
Merchant	20	5.9
Private worker	35	10.4
Farmer	127	37.6
Marital status of participants during the data collection time		
Married	246	72.8
Single	92	27.2
Monthly income (USD)		
<35	171	50.6
35-106	130	38.5
106.6-177	21	6.2
>177	16	4.7
One way cost of transport (USD*)		
<7 dollar	93	27.5
≥7 dollar	245	72.5
Sources of medical expenses		
Employing organization	1	0.3
Free medical care	72	21.3
Government insurance	19	5.6
Out of pocket	242	71.6
Private insurance	4	1.2

3.1. Symptoms and awareness of oesophageal cancer

Among the total participants, 21.3 % had reported a history of at least one chronic disease, with diabetes mellitus being the commonest one. More than three-fourth of the study participants (77.8%, 95% CI [73.4%, 82.2%]) had never heard of oesophageal cancer prior to diagnosis for oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main sources (48%) of the information were friends/ family members or neighbors, followed by printed and electronic medias such as (TV, radio, internet) (28%). Only eight participants (2.4%) had reported first degree family history of oesophageal cancer.

Dysphagia was the cardinal symptom mentioned by 84.6% of the study participants, followed by odynophagia of 54.1%. Approximately three-fourth of the study participants had linked the first symptom/s to gastritis. All patients had recognized at least one symptom. Moreover, a significant number of patients reported as having more than one oesophageal cancer symptom. About half of the cases stated that they did not take an immediate action for the first symptom/s because they thought that the symptom/s was/ were simple and self-limited. Meanwhile, about a quarter of the cases sought treatment from various traditional healers as a quick fix for the symptom/s.

More than half (58.9%) of the study participants felt compelled by their family members to seek medical help for the symptom/s. About half of the cases first went to public health facilities for their first symptom/s (health centers and health posts), followed by public hospitals (16%). At their first visit to health facilities, approximately to two-third of the study participants first contacted health officers and nurses as health care providers. The mean (SD) of health facilities visited by the cases until the data collection time was 6.6 ± 3.2 . Meanwhile, 11% of the participants had visited more than 10 health facilities until data collection time. The mean (SD)

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3 248 number of visits to health facilities by participants until the data collection time was 7.45 ± 3.63 .
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5 249 The prominent reason mentioned by the participants for consultation delays was a financial issue,
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8 250 (61.5%).
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10 11 251 3.2. Diagnosis characteristics of oesophageal cancer patients 12

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14 252 Out of the total oesophageal cancer patients, about 76% (95% CI [71.0 %, 80.7%]) of the study
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16 253 participants were diagnosed at late stages (III and IV), and only 24% of the participants were
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18 254 diagnosed at early stages (I and II). In terms of histologic subtypes, 85.8%, 13.3% and 0.89%
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20 255 were oesophageal squamous cell carcinoma, oesophageal adenocarcinoma and unknown
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22 256 carcinomas, respectively. For those with available grade on biopsy report, 59.8%, 15.7% and
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24 257 8.9%) were well differentiated, unspecified and poorly differentiated respectively. Endoscopic
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26 258 appearance was ulcerative in 49.4% followed by an obliterative of 34.9%. In case of tumor
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28 259 locations, middle oesophagus, lower oesophagus and upper (cervical) were 41.1%, 30.8% and
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30 260 28.1% respectively (**Table 2**).
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267 **Table 2:** Diagnostic history of oesophageal cancer patients from February 2019 to August
 268 2020 Addis Ababa, Ethiopia,

Variable	Frequency	Percent
Stage at first diagnosis		
Stage I	20	6.0
Stage II	58	17.2
Stage III	167	49.4
Stage IV	76	22.4
Unknown	17	5.0
Histological sub-type		
Oesophageal squamous carcinoma	290	85.8
Oesophageal adenocarcinoma	45	13.3
Unknown	3	0.9
Histopathological differentiations		
Well-differentiated	202	59.8
Moderate differentiated	47	13.8
Poor differentiated	30	8.9
Undifferentiated	6	1.8
Unspecified	53	15.7
Morphology of tumor during upper gastrointestinal endoscopy		
Ulcerative	167	49.4
Obliterative	118	34.9
Proliferative	45	13.3
Ulceroproliferative	8	2.4
Tumor location(Histology)		
Upper (cervical)	95	28.1
Middle oesophagus	139	41.1
Lower oesophagus	104	30.8

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275 **Patient and diagnostic intervals**

276 The median (IQR) patient interval was 108.5 (60.5-215) days. The proportion of patient delay
277 was 75% (95% CI [69.8%, 79.3%]). About ten percent of the participants had visited health
278 facilities after 365 days of first symptom recognition. Only about 8% of the participants visited
279 health facilities within thirty days. Great majority (71%) of the participants mentioned their
280 reason for late patients' consultation was financial problems (59.5%) followed by not bothering
281 about the disease. The median (IQR) of diagnostic interval was 77.5 (39-133) days. The
282 proportion of diagnostic delay was 81.9% (95% CI [77.9%, 86.2%]). Three percent of those who
283 took part in the study received diagnostic confirmation after 365 days of waiting and 18% of the
284 participants got diagnosis confirmation less than thirty days. The median (IQR) symptom
285 interval was 215(130-353) days. The most noticeable single factor mentioned by majority (78%)
286 the participants for the diagnostic delay was longer appointments primarily associated with the
287 health care organizations.

288 **3.3. Factors associated with patient delay**

289 In the bivariable analysis, participants unable to read and write (PR=1.2, 95% CI [1.05, 1.43]),
290 being house wife (PR=1.14, 95%CI [1.01, 1.29]), single participants (PR=1.08, 95% CI [1.03,
291 1.14]) monthly income <35USD (PR=1.29,95%CI[1.09,1.55]) and 35-106 USD
292 (PR=1.3,95%CI[1.17]CI[1.09,1.55]family monthly income<53USD(PR=1.17,95%CI[1.02,1.33])
293 and 53-141 USD (PR=1.17,95% CI [1.02,1.34]) and never heard of oesophageal cancer prior to
294 diagnosis (PR=1.11,95%CI [1.03,1.97]) were significantly associated with higher prevalence of
295 patient delay and adjusted for multivariable analysis. Therefore, after an adjustment, we only
296 found marital status (Adjusted PR=1.09, 95% CI [1.03, 1.15]) and never heard of oesophageal

297 cancer prior to diagnosis (Adjusted PR=1.08, 95% CI [1.03, 1.15]) were found statistically
 298 significant to increase the prevalence of patients delay among oesophageal cancer patients
 299 (Table 3).

300 **Table 3** : Determinant factors associated with patient delay (>60 days) among oesophageal
 301 cancer patients from February 2019 to August 2020, Addis Ababa, Ethiopia (n=324)

Patient characteristics	Patient delay		Unadjusted	P-value	Adjusted	P-value
	Yes (%)	No (%)	PR (95% CI)		PR (95% CI)	
Age of participants (years)						
<35	14 (66.7)	7 (33.3)	Ref.		Ref.	
35-44	26 (59.1)	18 (40.9)	0.96 (0.82,1.11)	0.55	0.96 (0.86,1.07)	0.43
45-54	63 (72.4)	24 (27.6)	1.03 (0.91,1.18)	0.62	1.03 (0.94, 1.12)	0.56
≥55	140 (81.4)	32 (18.6)	1.10 (0.96,1.23)	0.18	0.99 (0.91,1.08)	0.81
Residency						
Urban	88 (71.0)	36 (29.0)	Ref.		Ref.	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98,1.10)	0.19	1.04 (0.97,1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05,1.43)	0.01	1.11 (0.94, 1.29)	0.22
Grade 1-8	56 (81.2)	13 (18.8)	1.25 (1.07,1.46)	0.006	1.15 (0.97, 1.35)	0.10
Grade 9-12	23 (67.6)	11 (32.4)	1.16 (0.97,1.38)	0.11	1.08 (0.91, 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Ref.			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Ref.		Ref.	
Government workers	24 (68.6)	11 (31.4)	1.08 (0.93,1.24)	0.32	1.02 (0.94, 1.11)	0.57
House wife	82 (78.8)	22 (21.2)	1.14 (1.01,1.29)	0.03	0.94 (0.86, 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02,1.34)	0.03	1.03 (0.94,1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13(0.99,1.27)	0.06	0.93 (0.85, 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03,1.14)	0.002	1.09 (1.03, 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Ref.			
Monthly income						
<35 US dollar	124 (78.5)	34 (21.5)	1.29 (1.09,1.55)	0.004	1.22(1.005,1.48)	0.045
35-106 US dollar	101 (78.9)	27 (21.1)	1.3 (1.09,1.55)	0.004	1.22(1.22,1.48)	0.042
106.6-177 US dollar	12 (54.5)	10 (45.5)	1.12 (0.90,1.39)	0.29	0.46(1.09)	0.46
>177 US dollar	6 (37.5)	10 (62.5)	Ref.			
Family monthly income(USD)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02, 1.33)	0.025	1.12(0.98,1.27)	0.09
53-141	84 (77.8)	24 (22.2)	1.17 (1.02,1.34)	0.024	1.13(0.99,1.28)	0.08
141.4-230	18 (72.0)	7 (28.0)	1.13 (0.96,1.33)	0.14	1.1(0.94,1.29)	0.26
>230	13 (52.0)	12 (48.0)	Ref.			

302 **Table 3 cont.....**

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Prior information about esophageal cancer						
No	198 (79.0)	53 (21.0)	1.11 (1.03,1.97)	0.007	1.08(1.02,1.17)*	0.04
Yes	44 (61.1)	29 (38.9)	Ref.			
Visiting traditional healers						
No	180(73.2)	66(26.8)	Ref.			
Yes	63(80.8)	15(19.8)	1.04(0.99,1.11)	0.15	1.04(0.98,1.10)	0.23

303 **3.4. Factors associated with diagnostic delay**

304 Meanwhile, in the bivariable analysis, single participants (PR=1.8,95%CI[1.74,1.85]),family
305 monthly income 53-141 USD(PR=0.91,95%CI [0.85,0.99]),cost transport (one
306 trip)>7USD(PR=1.07,95%CI[1.06,1.13]), first medical consultation at health center
307 (PR=0.93,95%CI[0.88,0.99]) and number of health facilities visited < 3 health facilities
308 (PR=0.93, 95%CI [0.87,0.99]) were significantly associated with higher prevalence of diagnostic
309 delay. However, after an adjustment or in the multivariable analysis, we only found single
310 participants (Adjusted PR=1.2, 95% CI [1.11,2.10]), sources of medical expenses (Adjusted
311 PR=1.2,95% CI[1.13,2.40]), cost of transportation (Adjusted PR=1.2,95% CI [1.12,1.54]) and
312 first medical consultation to health facilities (Adjusted PR= 1.4, 95% CI [1.20,2.30]) were
313 statistically significant to increase the prevalence of diagnostic delay among oesophageal cancer
314 patients (Table 4).

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318 **Table 4:** Factors associated with diagnostic delay (>30 days) among oesophageal cancer patients
 319 from February 2019 to August 2020, Addis Ababa Ethiopia (n=326)

Patient characteristics	Diagnosis delay		Unadjusted	P-value	Adjusted	P-value
	Yes (%)	No (%)	PR (95% CI)		PR (95% CI)	
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Ref.		Ref.	
35-44	33 (75.0)	11 (25.0)	0.94 (0.84, 1.04)	0.24	0.96(0.86,1.07)	0.45
45-54	75 (87.2)	11 (12.8)	1.01 (0.92, 1.09)	0.92	1.02(0.93,1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89, 1.05)	0.45	0.97(0.89,1.06)	0.53
Marital status of participants during the data collection time						
Single	78(88.6)	10(11.4)	1.80(1.74,1.85)	0.0001	1.2 (1.1,2.10)**	0.04
Married	189(79.4)	49(20.6)	Ref.		Ref.	
Family monthly income(USD)						
<53	139(82.7)	29(17.3)	0.95(0.89,1.01)	0.11	0.98(0.88,1.09)	0.69
53-141	80(74.8)	27(25.2)	0.91(0.85,0.99)	0.008	0.91(0.82,1.002)	0.05
141.4-230	20(80.0)	5(20.0)	1.02(0.95,1.09)	0.57	1.01(0.93,1.09)	0.84
>230	19(73.1)	7(26.9)	Ref.		Ref.	
One way cost of transport (USD)						
<7 dollar	67(73.6)	24(26.4)	Ref.		Ref.	
≥7 dollar	200(85.1)	35(14.9)	1.07(1.06,1.13)	0.03	1.2(1.12,1.54)**	0.04
First medical consultation						
Health post	35(87.5)	5(12.5)	0.99(0.94,1.07)	0.96	1.01(0.94,1.08)	0.83
Health center	123(77.4)	36(22.6)	0.93(0.88,0.99)	0.015	1.4 (1.2, 2.30)**	0.049
Private clinic	38(88.4)	5(11.6)	0.99(0.94,1.06)	0.78	1.01(0.94,1.08)	0.87
Private hospital	24(72.7)	9(27.3)	0.91(0.82,1.002)	0.054	0.92(0.83,1.02)	0.10
Public hospital	46(90.2)	5(9.8)	Ref.		Ref.	
Number of health facilities visited for diagnosis						
< 3 health facilities	13(72.2)	5(27.8)	Ref.		Ref.	
3-6 health facilities	153(80.5)	37(19.5)	0.93(0.87,0.99)	0.02	0.93(0.87,1.22)	0.054
7-10 health facilities	67(81.7)	15(18.3)	0.93(0.87,1.004)	0.06	0.94(0.87,1.01)	0.108
>10 health facilities	29(82.9)	6(17.1)	0.94(0.86,1.026)	0.17	0.94(0.86,1.03)	0.19
Source of medical expenses						
Free medical care	57(79.2)	15(20.8)	Ref.		Ref.	
Governmental insurance	11(61.1)	7(38.9)	0.90(0.78,1.044)	0.16	1.22 (1.13, 2.40)*	0.048
Out of pocket	199(84.3)	37(15.7)	1.03(0.97,1.09)	0.34	1.03(0.98,1.09)	0.26

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3 324 **3.5 Factors associated with advanced stages at diagnosis among oesophageal cancer**
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6 325 **patients**
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9 326 In the bivariable analysis, marital status, single (PR=1.16, 95% CI [1.02, 1.30]) and patients
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11 327 delay of > two months (PR=1.38, 95% CI [1.14, 1.68]) were significantly associated with late
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14 328 stage at first diagnosis. However, after an adjustment or multivariable analysis, marital status
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16 329 (Adjusted PR=1.16, 95% CI [1.03, 1.31]), female participants (Adjusted PR=1.15, 95% CI
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18 330 [1.015, 1.31]), patient delay > two months (Adjusted PR=1.41, 95% CI [1.15, 1.69]) and
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21 331 symptom intervals (Adjusted PR=1.26, 95% CI [1.12, 1.67]) were statistically significant to
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23 332 increase the prevalence of advanced stage at time of diagnosis (**Table 5**).
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341 **Table 5:** Factors associated with advanced stages at diagnosis among oesophageal cancer
 342 patients from February 2019 to August 2020 Addis Ababa, Ethiopia (n=321).

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Gender						
Male	45(27.1)	121(72.9)	Ref.		Ref.	
Female	33(21.3)	122(78.7)	0.93(0.82,1.05)	0.22	1.15 (1.01,1.31)*	0.049
Occupation of participants						
Private worker	5(17.2)	24(82.8)	Ref.			
Government workers	13(35.1)	24(64.9)	0.78(0.59,1.05)	0.10	0.77 (0.57, 1.02)	0.07
House wife	28(24.8)	85(75.2)	0.91(0.75,1.11)	0.34	0.89 (0.73,1.09)	0.25
Merchant	6(30.0)	14(70.0)	1.03(0.80,1.32)	0.83	0.99 (0.78,1.28)	0.98
Farmer	29(23.8)	93(76.2)	0.92(0.76,1.12)	0.41	0.89 (0.74,1.09)	0.29
Marital status of participants during the data collection time						
Single	14(16.1)	73(83.9)	1.16(1.02,1.30)	0.02	1.16 (1.03,1.31)*	0.015
Married	64(27.4)	170(72.6)	Ref.		Ref.	
Family size in the house hold						
<3	6(37.5)	10 (62.5)	Ref.			
3-5	38(26.6)	105(73.4)	0.84(0.68,1.04)	0.10	0.82 (0.66, 1.03)	0.08
>5	38(23.5)	124(76.5)	0.88(0.71,1.07)	0.20	0.87 (0.69 ,1.07)	0.19
One way cost of transport (USD)						
<7 dollar	28(31.1)	62(68.9)	Ref.			
≥7 dollar	50(21.6)	181(78.4)	1.14(0.98,1.33)	0.10	1.12 (0.96 , 1.30)	0.15
First medical consultation						
Health post	6(15.4)	33(84.6)	1.11(0.94,1.32)	0.22	1.11 (0.92, 1.33)	0.27
Health center	48(30.6)	109(69.4)	0.86(0.73,1.02)	0.08	0.87 (0.73 ,1.04)	0.12
Private clinic	6(14.3)	36(85.7)	1.06(0.88,1.27)	0.52	1.05 (0.88 , 1.30)	0.57
Private hospital	10(32.2)	21(67.8)	0.84(0.64,1.11)	0.21	0.83 (0.63 , 1.09)	0.18
Public hospital	10(19.2)	42(80.8)	Ref.			
Patient delay (> 2 months)						
No	31(40.8)	45(59.2)	Ref.		Ref.	
Yes	42(18.2)	189(81.8)	1.38(1.14,1.68)	0.001	1.41 (1.15, 1.69)*	0.001
Number of times visited health facilities prior to final diagnosis						
< 3 times	7(31.8)	15(68.2)	Ref.		Ref.	
3-6 times	40(26.8)	109(73.2)	1.07(0.79,1.45)	0.65	0.89 (0.69 , 1.16)	0.39
7-10 times	19(21.8)	68(78.2)	1.15(0.84,1.56)	0.38	0.93 (0.70 , 1.23)	0.61
>10 times	12(19.0)	51(81.0)	1.19(0.87,1.62)	0.24	1.12 (0.85 , 1.46)	0.43
Symptom interval						
< 3 months	12(36.4)	21(63.6)	Ref.		Ref.	
3-6 months	26(29.5)	62(70.3)	1.11(0.83,1.48)	0.49	1.09 (0.81 , 1.46)	0.51
> 6months	37(19.7)	151(80.3)	1.26(0.97,1.65)	0.08	1.26 (1.12 , 1.67)*	0.048

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344 Discussion

345 Longer consultation and diagnostic intervals, as well as late stages at the time of diagnosis, were
346 hypothesized before we started this study. We estimated prolonged consultation and diagnostic
347 intervals. In addition, most of the cases were diagnosed at advanced stages. The most common
348 reason for patient delays was financial constraints. About 11% of the cases were forced to visit
349 an average of 10 different health facilities in search of better and more effective care and
350 treatment in areas where they believe they can afford it.

351 The dominant histological subtype was oesophageal squamous carcinoma. In addition, risk
352 factors for late consultation, diagnostic and late stage at the time of diagnosis were identified.

353 The median patient intervals were much lower in studies conducted elsewhere [11 21 25-27]
354 compared to the patient interval estimated from our study. This substantial gap could be
355 attributed to socio-cultural and socio-economic disparities in health-seeking behavior, as well as
356 a lack of understanding of oesophageal cancer symptoms among different groups/communities.
357 Furthermore, because the majority of our participants were from rural areas, and cancer care is
358 provided by secondary and tertiary care institutions that are located far from the majority of rural
359 residents, the majority of them were illiterate, late presentation is strongly associated with poor
360 access to care. Our research, on the other hand, is similar to the study conducted in South Africa
361 [28]. The similarities in socioeconomic, sociocultural, and literacy rates could explain the same
362 presentation delays The median diagnostic interval estimated from our study is higher than
363 previous studies conducted in different part of the world [11 21 25 26]. The discrepancy may be
364 the differences in diagnostic workups and the availability of experienced and trained health
365 professionals in cancer related diagnostic and treatment services. On the other hand, our study is
366 in line with the study conducted in South Africa [28]. The similarities could be explained by the

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3 367 fact that the diagnostic procedures and health-care facilities are more or less similar among many
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5 368 of the African countries The proportion of advanced stages at time of first diagnosis is higher
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8 369 compared the study conducted Shandong University in Jinan (China) [21] this could be related
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10 370 to longer patient and diagnostic intervals and socio-economic difference among the communities.
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12 371 The cardinal symptom reported by majority of our participants was dysphagia this result is
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14 372 comparable with studies [21 26 27]. We discovered that oesophageal squamous carcinoma was
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16 373 the most prevalent, which is consistent with other studies conducted elsewhere in the world [21
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18 374 29 30]. A significant number of patients with oesophageal cancer were diagnosed at advanced
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20 375 stages, which are consistent with previous studies [29 31]. However, the proportion of those
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22 376 diagnosed delay in oesophageal cancer was relatively higher in a nationwide cohort study
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24 377 conducted in Korean patients [30]. Increased patient delay (> two months) was found to be
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26 378 exacerbated by socio-economic characteristics in our study. Our finding is equivalent to this
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28 379 study [32] , which evidenced those patients with lower socio-economic status sought medical
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30 380 help later. Furthermore, socioeconomic status has had an important influence in patients being
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32 381 diagnosed at advanced stages, which is similar to the findings of the study conducted in China
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34 382 [32]. As an immediate measure for their symptom/s, a large percentage of oesophageal cancer
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36 383 patients contacted various traditional healers. This finding is consistent with the findings of a
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38 384 qualitative study conducted in Ethiopia's in Oromia Regional State [33]. The study's
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40 385 comparability is owing to the societies' similar socio-economic and socio-cultural characteristics.
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42 386 The prevalence of diagnostic delay was higher in single patients than the married participants.
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44 387 Thus, being married might have a better chance to seek medical care than unmarried participants.
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46 388 The reason could be partners may influence each other on decision making to seek care as early
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48 389 as possible. In our findings, oesophageal cancer patients that paid their medical expense from
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390 their own pocket had longer patient interval than patients whose medical expenses covered by
391 other organizations. The reason could be, they ignore the symptoms because patients with low
392 socio-economic status had other unmet survival felt needs than investing money for medical care
393 [34].

394 **4. Conclusion**

395 Oesophageal cancer patients in Ethiopia had longer patients' presentation, diagnostic and
396 symptom intervals. Moreover, majority of the oesophageal cancer patients had diagnosed at
397 advanced stages (III and IV). Being single and never heard of oesophageal cancer prior to
398 diagnosis was found to be predictors of increased patient intervals. The levels of first health
399 facilities visited for medical consultation and the cost of transportation were identified as key
400 factors in increasing diagnostic intervals.

401 Furthermore, being single, being female, waiting more than two months for a diagnosis, and
402 symptom interval were found to be statistically significant predictors in the incidence of
403 advanced stages at diagnosis. Patients' intervals could be shortened by increasing their awareness
404 of oesophageal cancer symptoms.

405 **Abbreviations**

406 AJCC: American Joint Committee on Cancer

407 APR: Adjusted Prevalence Ratio

408 SD: Standard Deviation

409 IQR: Inter Quartile Range

410 P: Proportion

411 PR: Prevalence Ratio

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3 412 USD: United States Dollar
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6 413 **Ethics approval and informed consent** 7 8

9 414 The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa
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11 415 University College of Health Sciences with a protocol number of 080/18/SPH. The study
12
13 416 followed basic ethical principles of Helsinki declaration for medical research involving human
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15 417 participants[35]. All of the study participants were informed about the purpose and procedure of
16
17 418 the research and their right to withdrawal from the study at any time. Written informed consent
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19 419 was obtained from each of the study participants. Meanwhile, the study participants were agreed
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21 420 to the extent that the finding of this study will be subjected to publication. Participants were well
22
23 421 informed not to disclose their information to a third person. The information was kept secured
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25 422 and put confidentially with the first author.
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30 423 **Data availability** 31 32

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34 424 Data will be available up on request
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47 428 There is no competing interest of this research
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50 429 **Authors' contributions** 51 52 53 54 55 56 57 58 59 60

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3 430 All authors contributed from the conception of idea up to data analysis and write up. They also
4
5 431 participated in drafting or revising of the article and have agreed on to which journal the article
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7 432 shall be submitted and have given final approval of the version to be published, and agreed to be
8
9 433 accountable for all aspects of the work. Specifically, BD was conceptualized the topic of interest,
10
11 434 involved in data collection, coding, cleaning, analysis, interpretation of the result unto
12
13 435 preparation of the manuscript. FE was involved in proposal development, planning the fieldwork
14
15 436 and result section. And RY, MA, SG and AA were involved in proposal development, data
16
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Time intervals from first symptom recognition to pathological diagnosis among oesophageal cancer patients in Ethiopia: A cross-sectional study

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4 1 **Time intervals from first symptom recognition to pathological diagnosis**
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6 2 **among oesophageal cancer patients in Ethiopia: A cross-sectional study**
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9 3 Berhe Dessalegn^{1*,2}, Sefonias Getachew², Robel Yirgu², Fikre Enqueselassie^{2†}, Mathewos
10
11
12 4 Assefa³, Adamu Addissie²
13

14 5 ¹Department of Public Health, College of Medicine and Health Sciences, Adigrat University
15
16
17 6 Adigrat, Ethiopia
18

19 7 ² Department of Preventive Medicine, School of Public Health, College of Health Sciences,
20
21
22 8 Addis Ababa University, Addis Ababa, Ethiopia

23
24 9 ³Department of Radiotherapy Center, School of Medicine, Addis Ababa University, Addis
25
26 10 Ababa, Ethiopia
27

28
29 11 * Corresponding Author
30

31 12 Email: berhe_dessalegn@yahoo.com(BD)
32

33 13 † Professor Fikre Enqueselassie has passed away on October 28th, 2019.
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21 Abstract

22 Objective

23 The aim of this study was to estimate the time intervals from first symptom recognition to
24 pathological diagnosis among oesophageal cancer patients in Ethiopia.

25 Methods

26 **Design** Cross-sectional study design was employed

27 **Settings and participants** Oesophageal cancer patients aged ≥ 18 years were included from
28 Addis Ababa, Ethiopia (n=338) from February 2019 to August 2020. The participants were
29 selected consecutively from six health facilities provided cancer care nearly for 90% of patients.

30 **Main outcomes and measurements** The Aarhus statement criterias was applied to
31 classify patient intervals (time from first symptom recognition to presentation), and diagnostic
32 intervals (time from first presentation to diagnosis). Patient and diagnostic intervals >60 and >30
33 days were considered as delays, respectively. For tumor classification, the American Joint
34 Committee on cancer was used. Data were analyzed using SPSS Version 24. Descriptive
35 statistics were applied to describe patients' characteristics. Poisson regression with robust
36 variance was used to compute prevalence ratios. In all statistical tests, significances were
37 declared at p-value of <0.05 .

38 Results

39 The mean (SD) age of the participants was 54.30 ± 12.49 years.

40 Approximately 78 percent of study participants had never heard of oesophageal cancer and
41 thought they had gastritis. Dysphagia was commonly mentioned symptom. About 76% of the
42 cases were diagnosed at advanced stages (III and IV). Median patient interval was 108.5 (60.5-
43 215) days and median diagnostic interval was 77.5 (39-133) days. After adjusting confounders,
44 being single and unawareness of oesophageal cancer had association with consultation delay,

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3 45 cost of transportation and medical consultation had association with diagnostic delay and patient
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5 46 delay > two months had association with late stage at diagnosis.
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9 47 **Conclusion** Oesophageal cancer patients in Ethiopia had prolonged patient and diagnostic
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11 48 intervals. Increasing awareness on symptoms of oesophageal cancer and shortening time to
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13 49 diagnosis will help to improve the out-come of oesophageal cancer care in Ethiopia.
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16 50 **Keywords:** Oesophageal cancer, delay, intervals, tumor stage
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21 52 **Strengths and Limitations**
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- 25 53 • In Ethiopia, in case of patient and diagnostic interval and associated factors, it is the first
26 54 multifacility study
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28 55 • Poisson regression with robust variance was used to compute the prevalence ratios
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30 56 • It is the only research based on primary data in Ethiopia that estimates the patient and
31 57 diagnostic intervals on oesophageal cancer patients
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33 58 • However, the onset of symptoms is a subjective measurement that patients may not recall the
34 59 exact time
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1. Introduction

Cancer is a group of diseases in which abnormal cells grow and spread uncontrollably. Cancer has become a major public health concern on a global scale [1]. Oesophageal cancer is the fourth most common cancer in developing countries, and it is an aggressive tumor of the esophagus that develops in the organ's tissue lining [2]. Oesophageal cancer, which has a dismal prognosis and survival rate, has caused considerable morbidity and mortality around the world from the last three decades [3-5]. Globally, oesophageal cancer was the sixth most common cause of mortality among all cancers and the seventh most common cancer in terms of incidence[1].

The two most prevalent subtypes of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. Adenocarcinoma begins in the cells that produce and release mucus and other fluids, whereas squamous cell carcinoma begins in the flat cells that line the esophagus. Oesophageal cancer mortality and incidence are higher in Africa than the rest of the world, with squamous cell carcinoma being the most common type [6 7].

The five-year survival rate of non-metastatic oesophageal cancer is between 19 and 30%, whereas, the median overall survival time for metastatic oesophageal cancer is between four and six months. Nonetheless, it is not uncommon for oesophageal cancer patients to be diagnosed at advanced stages ,because, in most cases, the oesophageal cancer patients have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patients prognosis and survival rate[5 8 9]. The prognosis and time intervals of oesophageal cancer patients has been solely depended on the patients' awareness on symptoms and literates rate that contribute to early consultation and shorter pathological diagnosis periods, according to studies[10 11]. In practice, however, oesophageal cancer patients frequently have arrived late in presentation and commonly lately referred to the appropriate health facilities. In addition,

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3 90 literatures also showed that shortening the time to presentation is an important step in reducing
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5 91 late in diagnosis, and improving the prognosis and survival of oesophageal cancer patients[12
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11 93 Oesophageal cancer is the overwhelming disease and among the commonest cause of cancer
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13 94 deaths in the world. Though, few patients can be cured, the treatment for oesophageal cancer is
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15 95 prolonged, quality of life is significantly compromised and cases fatality rate is high [1].
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19 96 Ethiopia is a country, geographically located within the highest risk region of oesophageal cancer
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21 97 known to be the oesophageal cancer belt. And, the disease has created a huge burden interms of
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23 98 morbidity and mortality in the country[14]. In addition, few hospital reports revealed that over
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25 99 the last decades, the incidence and burden of oesophageal cancer has been increasing.
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29 100 Diagnostic and consultation delays on cancers are common in underdeveloped countries, such as
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31 101 the Eastern part of Africa, and are closely linked to poor survival rates. As a result, obtaining
32
33 102 updated information is crucial for establishing a resilient plan to reduce oesophageal cancer
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35 103 related morbidity and mortality [7 15].
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39 104 In Ethiopia, however, oesophageal cancer is not yet a public health priority, left in dark and is
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41 105 under-researched; as a result, there is no clear evidence about patient and diagnostic intervals and
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43 106 the stage at time of diagnosis. The goal of this study was to determine time to care seeking and
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45 107 pathological diagnosis, and the stage at time of diagnosis of oesophageal cancer patients.
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47 108 Meanwhile, we were also strived to identify predictors of patients and pathological diagnostic
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49 109 delays of > 60 and > 30 days, respectively.
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111 2. Materials and methods

112 2.1. Study design and sample size

113 A cross-sectional study design was employed. The study involved 338 oesophageal cancer
114 patients aged ≥ 18 years from February 2019 to August 2020 in Addis Ababa, Ethiopia. Using the
115 expected proportion ($p=32.0\%$) of patients delay to presentation (>2 months) from another
116 similar study [16] by assuming a 95% level of confidence, a 5% precision and 5% non-response
117 rate

118 2.2. Settings and participants

119 The Ethiopian health care delivery system has three tiers: primary, secondary and tertiary level
120 health care facilities that are linked with a referral system. The setup differs slightly between
121 urban and rural settings. The main healthcare service in the metropolitan city, such as Addis
122 Ababa, Ethiopia's capital, includes public health centers, private clinics, and primary hospitals.
123 Secondary and tertiary healthcare levels are general hospitals and specialty hospitals,
124 respectively. The primary healthcare services in rural areas are made up of a health post, a health
125 center, and primary hospitals. Secondary and tertiary healthcare levels are general hospitals and
126 specialty hospitals, respectively. Nurses and health officers are the primary staff of public health
127 centers, with the goal of providing preventative and primary health care services. In the case of
128 cancers, such as oesophageal cancer, health workers at the primary level care facilities are only
129 expected to refer patients to general hospitals and other high-level facilities for further diagnosis
130 and treatments[17].

131

132 **Sampling procedure**

133 A consecutive sampling method was used to recruit study participants. Oesophageal cancer
134 patients histologically confirmed and clinically staged came to the selected health facilities were
135 included in the study, whereas critically ill, diagnosed to other cancer types and non-Ethiopian
136 patients were excluded from participation. Six health facilities in Addis Ababa (Tikur Anbesa
137 Specialized Hospital, St. Paul Hospital Millennium Medical College, Betezata Hospital,
138 Hallelujah General Hospital, Landmark Hospital, and United Vision Medical Services Centre)
139 were selected, where nearly 90% of cancer patients being diagnosed and treated. At each health
140 facility, one focal person was assigned to identify eligible oesophageal cancer patients and
141 communicate with the principal investigator and supervisor. To avoid duplication, the medical
142 chart of the recruited patient was coded in red on the top cover page. Prior to the interview,
143 study participants were informed about the purpose of the study and their right to withdraw
144 under any circumstances without compromisation of any services.

145 **2.3. Variables and Measurements**

146 We used the Aarhus statement criteria to classify patient, diagnostic and symptoms intervals.
147 Thus, patient interval was defined as the interval between the date of first symptom recognition
148 (the time point at which the patient first noticed bodily changes and/or symptoms) and the date of
149 first clinical presentation (the date at which the patient first presented to a healthcare provider
150 after first recognizing symptoms), and symptom interval was defined as the time interval
151 between the date of first symptom recognition and the date of pathological diagnosis[18 19]. The
152 date of symptom recognition was determined based on participants recall. Furthermore, the
153 diagnostic interval was defined as the time elapsed between the date of first clinical presentation
154 and the date of the final pathological diagnosis (the date at which the first histological or

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3 155 cytological confirmation of the malignancy was documented in the pathology report). The
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5 156 pathology report of the patient was used to determine the date of diagnosis [18 19]. Tumors were
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8 157 classified using the Tumor-Node-Metastasis method from the 7th edition of the American Joint
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10 158 Committee on Cancer (AJCC)[20]. And cases were histologically and endoscopically confirmed.
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12 159 Stages I and II were classified as early stages of diagnosis, while stage III and IV were classified
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15 160 as late stages of diagnosis [21]. The interviews were conducted in Amharic, the country's
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17 161 working language. The study tool was initially prepared in English, then translated into Amharic
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19 162 by language translators, and finally back to English to ensure that the two versions were
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22 163 consistent. Experts in cancer research assessed the tool to ensure that the questions were clear
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24 164 and two days training was given data collectors and the supervisor about the objective of the
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26 165 study. A pretest for cultural suitability and clarity was performed prior to administering the tool
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28 166 to the participants. When the eligible participants were arrived for treatment, trained nurses
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31 167 interviewed them individually in a semiprivate room in Amharic. If the participants couldn't
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33 168 recall the exact date of their first symptom recognition, they were asked to provide a month or
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35 169 year ('was it at the beginning, middle, or end of the year'). For those who only remembered the
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38 170 month, the date was estimated to be the 15th day of that month. If the participants only said at the
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40 171 beginning, middle or at the end of the year, the estimated date was 15th of February, June or
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42 172 October of the year, respectively; if they only said the year, the estimated date was June 30th of
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45 173 that year. We performed sensitivity analyses excluding patients who had only remembered the
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47 174 beginning, middle or end of the year or a year for the date of first symptom recognition or
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178 2.4. Data Analysis

179 Epi-info version 7 was used for the data entry and SPSS Version 24 was used to analyze the data.
180 Descriptive statistics were calculated for each variable. Numbers and percentages were used to
181 summarize categorical variables. We presented mean and standard deviation for numerical
182 variables with normal distributions, whereas median and IQR were employed for variables with
183 skewed distributions. Patient and diagnostic delays were defined as >60-days patient intervals
184 and >30-days diagnostic intervals, respectively, from previous similar study [11]. For cross-
185 sectional research, OR is the common measure of association, and logistic regression is often
186 used to estimate. Nevertheless, evidences suggest that when the proportion of the outcome
187 exceeds 10%, an odds ratio overestimates the risk ratio, leading to incorrect interpretations. As a
188 result, to avoid these limitations, the prevalence ratio is preferred measure of association [23 24].
189 Hence, Poisson regression with robust variance was used to compute the adjusted prevalence
190 ratios of factors associated with the prevalence of patient and diagnostic delays, as well as factors
191 associated with stage at time of diagnosis. Variables having a p value of <0.25 on bivariable
192 analysis were candidates for the multivariable analysis and other variables were also considered
193 based on literatures had impacts on patient and diagnostic delays and stage at time of diagnosis.
194 A two-sided p value of 0.05 was declared as statistically significant.

195 **Patient and public involvement** “No patient involved”

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3. Results:

Socio-demographic and socio- economic characteristics of the study participants

We approached 351 participants those histologically confirmed and clinically staged for oesophageal cancer and among 96.3% (338) of them were provided their oral consent for participation. The participants in the study were 54.30 ± 12.49 years old on average (SD). Male participants accounted for 52.4% of the total participants. More than half of the participants (52%) were above the age of 55 years, only 7.0% of the participants were below the age of 35 years. Two-thirds of the study participants were from rural areas of Ethiopia and were unable to read and write. Muslims and farmers participants accounted 52% and 38% of the total participants respectively. At the time of data collection, 75% of the participants in the study were married. More than half of the participants in the study earned not more than one USD per day or about 29 Ethiopian Birr. Among the participants, 73% had to travel long distances to receive cancer-specific diagnosis and treatment services, and had to pay more than seven USD or 203 Ethiopian Birr for a single trip just to cover only for transportation costs. Furthermore, nearly three-quarters of the study participants had paid their medical expenses out of their pockets (Table 1).

223 **Table 1:** Socio-demographic and socio-economic characteristics of esophageal cancer patients
 224 Addis Ababa, Ethiopia, February 2019 to August 2020 (n=338)

Variables	Frequency	Percent
Age categories (years)		
<35	24	7
35-44	46	14
45-54	91	27
≥55	177	52
Gender		
Male	177	52.4
Female	161	47.6
Religion		
Christianity	159	47
Islam	175	51.8
Wakefata	4	1.2
Residency		
Urban	126	37.3
Rural	212	62.7
Educational status of participants		
Unable to read and write	209	61.8
1-8 grade	72	21.3
9-12 grade	37	10.9
Diploma and above	20	5.9
Occupation of participants		
Government workers	38	1.2
House wife	118	34.9
Merchant	20	5.9
Private worker	35	10.4
Farmer	127	37.6
Marital status of participants during the data collection time		
Married	246	72.8
Single	92	27.2
Monthly income (USD)		
<35	171	50.6
35-106	130	38.5
106.6-177	21	6.2
>177	16	4.7
One way cost of transport (USD*)		
<7 dollar	93	27.5
≥7 dollar	245	72.5
Sources of medical expenses		
Employing organization	1	0.3
Free medical care	72	21.3
Government insurance	19	5.6
Out of pocket	242	71.6
Private insurance	4	1.2

3.1. Symptoms and awareness of oesophageal cancer

Among the total participants, 21.3 % had reported a history of at least one chronic disease, with diabetes mellitus being the commonest one. More than three-fourth of the study participants (77.8%, 95% CI [73.4%, 82.2%]) had never heard of oesophageal cancer prior to diagnosis for oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main sources (48%) of the information were friends/ family members or neighbors, followed by printed and electronic medias such as (TV, radio, internet) (28%). Only eight participants (2.4%) had reported first degree family history of oesophageal cancer.

Dysphagia was the cardinal symptom mentioned by 84.6% of the study participants, followed by odynophagia of 54.1%. Approximately three-fourth of the study participants had linked the first symptom/s to gastritis. All patients had recognized at least one symptom. Moreover, a significant number of patients reported as having more than one oesophageal cancer symptom. About half of the cases stated that they did not take an immediate action for the first symptom/s because they thought that the symptom/s was/ were simple and self-limited. Meanwhile, about a quarter of the cases sought treatment from various traditional healers as a quick fix for the symptom/s.

More than half (58.9%) of the study participants felt compelled by their family members to seek medical help for the symptom/s. About half of the cases first went to public health facilities for their first symptom/s (health centers and health posts), followed by public hospitals (16%). At their first visit to health facilities, approximately to two-third of the study participants first contacted health officers and nurses as health care providers. The mean (SD) of health facilities visited by the cases until the data collection time was 6.6 ± 3.2 . Meanwhile, 11% of the participants had visited more than 10 health facilities until data collection time. The mean (SD)

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3 247 number of visits to health facilities by participants until the data collection time was 7.45 ± 3.63 .
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5 248 The prominent reason mentioned by the participants for consultation delays was a financial issue,
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8 249 (61.5%).
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10 11 250 3.2. Diagnosis characteristics of oesophageal cancer patients 12

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14 251 Out of the total oesophageal cancer patients, about 76% (95% CI [71.0 %, 80.7%]) of the study
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16 252 participants were diagnosed at late stages (III and IV)., In terms of histologic subtypes, 85.8%,
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18 253 13.3% and 0.89% were oesophageal squamous cell carcinoma, oesophageal adenocarcinoma and
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20 254 unknown carcinomas, respectively. For those with available grade on biopsy report, 59.8%,
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22 255 15.7% and 8.9%) were well differentiated, unspecified and poorly differentiated respectively.
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24 256 Endoscopic appearance was ulcerative in 49.4% followed by an obliterative of 34.9%. In case of
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26 257 tumor locations, middle oesophagus, lower oesophagus and upper (cervical) were 41.1%, 30.8%
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28 258 and 28.1% respectively (**Table 2**).
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265 **Table 2:** Diagnostic history of oesophageal cancer patients from February 2019 to August
 266 2020 Addis Ababa, Ethiopia,

Variable	Frequency	Percent
Stage at first diagnosis		
Stage I	20	6.0
Stage II	58	17.2
Stage III	167	49.4
Stage IV	76	22.4
Unknown	17	5.0
Histological sub-type		
Oesophageal squamous carcinoma	290	85.8
Oesophageal adenocarcinoma	45	13.3
Unknown	3	0.9
Histopathological differentiations		
Well-differentiated	202	59.8
Moderate differentiated	47	13.8
Poor differentiated	30	8.9
Undifferentiated	6	1.8
Unspecified	53	15.7
Morphology of tumor during upper gastrointestinal endoscopy		
Ulcerative	167	49.4
Obliterative	118	34.9
Proliferative	45	13.3
Ulceroproliferative	8	2.4
Tumor location(Histology)		
Upper (cervical)	95	28.1
Middle oesophagus	139	41.1
Lower oesophagus	104	30.8

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273 Patient and diagnostic intervals

274 The median (IQR) patient interval was 108.5 (60.5-215) days. The proportion of patient delay
275 was 75% (95% CI [69.8%, 79.3%]). About ten percent of the participants had visited health
276 facilities after 365 days of first symptom recognition. Only about 8% of the participants visited
277 health facilities within thirty days. Great majority (71%) of the participants mentioned their
278 reason for late patients' consultation was financial problems (59.5%) followed by not bothering
279 about the disease. The median (IQR) of diagnostic interval was 77.5 (39-133) days. The
280 proportion of diagnostic delay was 81.9% (95% CI [77.9%, 86.2%]). Three percent of those who
281 took part in the study received diagnostic confirmation after 365 days of waiting and 18% of the
282 participants got diagnosis confirmation less than thirty days. The median (IQR) symptom
283 interval was 215(130-353) days. The most noticeable single factor mentioned by majority (78%)
284 the participants for the diagnostic delay was longer appointments primarily associated with the
285 health care organizations.

286 3.3. Factors associated with patient delay

287 Based on the cut of point, age, residency ,educational status, occupation, marital status, income,
288 awareness about oesophageal cancer prior to diagnosis for oesophageal cancer, being house wife
289 and visiting traditional healers were potential candidates and included in the multivariable
290 analysis and among participants unable to read and write (PR=1.2, 95% CI [1.05, 1.43]), being
291 house wife (PR=1.14, 95%CI [1.01, 1.29]), single participants (PR=1.08, 95% CI [1.03, 1.14])
292 monthly income <35USD (PR=1.29,95%CI[1.09,1.55]) and 35-106 USD
293 (PR=1.3,95%CI[1.17]CI[1.09,1.55]family monthly income<53USD(PR=1.17,95%CI[1.02,1.33])
294 and 53-141 USD (PR=1.17,95% CI [1.02,1.34]) and never heard of oesophageal cancer prior to

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3 295 diagnosis (PR=1.11,95%CI [1.03,1.97]) were significantly associated with higher prevalence of
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5 296 patient delay and adjusted for multivariable analysis. Therefore, after an adjustment, single
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8 297 participants (Adjusted PR=1.09, 95% CI [1.03, 1.15]) and never heard of oesophageal cancer
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10 298 prior to diagnosis (Adjusted PR=1.08, 95% CI [1.03, 1.15]) were found statistically significant to
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12 299 increase the prevalence of patients delay among oesophageal cancer patients (**Table 3**).

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312 **Table 3** : Factors associated with patient delay (>60 days) among oesophageal cancer patients
 313 from February 2019 to August 2020, Addis Ababa, Ethiopia (n=324)

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	14 (66.7)	7 (33.3)	Ref.		Ref.	
35-44	26 (59.1)	18 (40.9)	0.96 (0.82,1.11)	0.55	0.96 (0.86,1.07)	0.43
45-54	63 (72.4)	24 (27.6)	1.03 (0.91,1.18)	0.62	1.03 (0.94, 1.12)	0.56
>55	140 (81.4)	32 (18.6)	1.10 (0.96,1.23)	0.18	0.99 (0.91,1.08)	0.81
Residency						
Urban	88 (71.0)	36 (29.0)	Ref.		Ref.	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98,1.10)	0.19	1.04 (0.97,1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05,1.43)	0.01	1.11 (0.94, 1.29)	0.22
Grade 1-8	56 (81.2)	13 (18.8)	1.25 (1.07,1.46)	0.006	1.15 (0.97, 1.35)	0.10
Grade 9-12	23 (67.6)	11 (32.4)	1.16 (0.97,1.38)	0.11	1.08 (0.91, 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Ref.			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Ref.		Ref.	
Government workers	24 (68.6)	11 (31.4)	1.08 (0.93,1.24)	0.32	1.02 (0.94, 1.11)	0.57
House wife	82 (78.8)	22 (21.2)	1.14 (1.01,1.29)	0.03	0.94 (0.86, 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02,1.34)	0.03	1.03 (0.94,1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13(0.99,1.27)	0.06	0.93 (0.85, 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03,1.14)	0.002	1.09 (1.03, 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Ref.			
Monthly income						
<35 US dollar	124 (78.5)	34 (21.5)	1.29 (1.09,1.55)	0.004	1.22(1.005,1.48)	0.045
35-106 US dollar	101 (78.9)	27 (21.1)	1.3 (1.09,1.55)	0.004	1.22(1.22,1.48)	0.042
106.6-177 US dollar	12 (54.5)	10 (45.5)	1.12 (0.90,1.39)	0.29	0.46(1.09)	0.46
>177 US dollar	6 (37.5)	10 (62.5)	Ref.			
Family monthly income(USD)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02, 1.33)	0.025	1.12(0.98,1.27)	0.09
53-141	84 (77.8)	24 (22.2)	1.17 (1.02,1.34)	0.024	1.13(0.99,1.28)	0.08
141.4-230	18 (72.0)	7 (28.0)	1.13 (0.96,1.33)	0.14	1.1(0.94,1.29)	0.26
>230	13 (52.0)	12 (48.0)	Ref.			

314 **Table 3 cont.....**

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Prior information about esophageal cancer						
No	198 (79.0)	53 (21.0)	1.11 (1.03,1.97)	0.007	1.08(1.02,1.17)*	0.04

Yes	44 (61.1)	29 (38.9)	Ref.			
Visiting traditional healers						
No	180(73.2)	66(26.8)	Ref.			
Yes	63(80.8)	15(19.8)	1.04(0.99,1.11)	0.15	1.04(0.98,1.10)	0.23

3.4. Factors associated with diagnostic delay

Based on the cut off age, marital status, family size, transportation, first medical consultation, number of health facilities visited and sources of medical expenses were included in the multivariable analysis and among single participants (PR=1.8,95%CI[1.74,1.85]),family monthly income 53-141 USD(PR=0.91,95%CI [0.85,0.99]),cost transport (one trip)>7USD(PR=1.07,95%CI[1.06,1.13]), first medical consultation at health center (PR=0.93,95%CI[0.88,0.99]) and number of health facilities visited < 3 health facilities (PR=0.93, 95%CI [0.87,0.99]) were significantly associated with higher prevalence of diagnostic delay. However, after an adjustment or in the multivariable analysis, we found single participants (Adjusted PR=1.2, 95% CI [1.11,2.10]), sources of medical expenses (Adjusted PR=1.2,95% CI[1.13,2.40]), cost of transportation (Adjusted PR=1.2,95% CI [1.12,1.54]) and first medical consultation to health facilities (Adjusted PR= 1.4, 95% CI [1.20,2.30]) were statistically significant to increase the prevalence of diagnostic delay among oesophageal cancer patients (Table 4).

333 **Table 4:** Factors associated with diagnostic delay (>30 days) among oesophageal cancer patients
 334 from February 2019 to August 2020, Addis Ababa Ethiopia (n=326)

Patient characteristics	Diagnosis delay		Unadjusted	P-value	Adjusted	P-value
	Yes (%)	No (%)	PR (95% CI)		PR (95% CI)	
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Ref.		Ref.	
35-44	33 (75.0)	11 (25.0)	0.94 (0.84, 1.04)	0.24	0.96(0.86,1.07)	0.45
45-54	75 (87.2)	11 (12.8)	1.01 (0.92, 1.09)	0.92	1.02(0.93,1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89, 1.05)	0.45	0.97(0.89,1.06)	0.53
Marital status of participants during the data collection time						
Single	78(88.6)	10(11.4)	1.80(1.74,1.85)	0.0001	1.2 (1.1,2.10)**	0.04
Married	189(79.4)	49(20.6)	Ref.		Ref.	
Family monthly income(USD)						
<53	139(82.7)	29(17.3)	0.95(0.89,1.01)	0.11	0.98(0.88,1.09)	0.69
53-141	80(74.8)	27(25.2)	0.91(0.85,0.99)	0.008	0.91(0.82,1.002)	0.05
141.4-230	20(80.0)	5(20.0)	1.02(0.95,1.09)	0.57	1.01(0.93,1.09)	0.84
>230	19(73.1)	7(26.9)	Ref.		Ref.	
One way cost of transport (USD)						
<7 dollar	67(73.6)	24(26.4)	Ref.		Ref.	
≥7 dollar	200(85.1)	35(14.9)	1.07(1.06,1.13)	0.03	1.2(1.12,1.54)**	0.04
First medical consultation						
Health post	35(87.5)	5(12.5)	0.99(0.94,1.07)	0.96	1.01(0.94,1.08)	0.83
Health center	123(77.4)	36(22.6)	0.93(0.88,0.99)	0.015	1.4 (1.2, 2.30)**	0.049
Private clinic	38(88.4)	5(11.6)	0.99(0.94,1.06)	0.78	1.01(0.94,1.08)	0.87
Private hospital	24(72.7)	9(27.3)	0.91(0.82,1.002)	0.054	0.92(0.83,1.02)	0.10
Public hospital	46(90.2)	5(9.8)	Ref.		Ref.	
Number of health facilities visited for diagnosis						
< 3 health facilities	13(72.2)	5(27.8)	Ref.		Ref.	
3-6 health facilities	153(80.5)	37(19.5)	0.93(0.87,0.99)	0.02	0.93(0.87,1.22)	0.054
7-10 health facilities	67(81.7)	15(18.3)	0.93(0.87,1.004)	0.06	0.94(0.87,1.01)	0.108
>10 health facilities	29(82.9)	6(17.1)	0.94(0.86,1.026)	0.17	0.94(0.86,1.03)	0.19
Source of medical expenses						
Free medical care	57(79.2)	15(20.8)	Ref.		Ref.	
Governmental insurance	11(61.1)	7(38.9)	0.90(0.78,1.044)	0.16	1.22 (1.13, 2.40)*	0.048
Out of pocket	199(84.3)	37(15.7)	1.03(0.97,1.09)	0.34	1.03(0.98,1.09)	0.26

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3 339 **3.5 Factors associated with advanced stages at diagnosis among oesophageal cancer**
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6 340 **patients**
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9 341 Based on the cutoff point, gender, occupation, family size, transport, first medical consultation,
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11 342 patients delay > two months and number of times visiting for diagnosis were included in the
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13 343 multivariable analysis and among, marital status, single (PR=1.16, 95% CI [1.02, 1.30]) and
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15 344 patients delay of > two months (PR=1.38, 95% CI [1.14, 1.68]) were significantly associated
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17 345 with late stage at first diagnosis. However, after an adjustment or multivariable analysis, marital
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19 346 status (Adjusted PR=1.16, 95% CI [1.03, 1.31]), female participants (Adjusted PR=1.15, 95% CI
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21 347 [1.015, 1.31]), patient delay > two months (Adjusted PR=1.41, 95% CI [1.15, 1.69]) and
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23 348 symptom intervals (Adjusted PR=1.26, 95% CI [1.12, 1.67]) were statistically significant to
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25 349 increase the prevalence of advanced stage at time of diagnosis (**Table 5**).
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358 **Table 5:** Factors associated with advanced stages at diagnosis among oesophageal cancer
 359 patients from February 2019 to August 2020 Addis Ababa, Ethiopia (n=321).

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Gender						
Male	45(27.1)	121(72.9)	Ref.		Ref.	
Female	33(21.3)	122(78.7)	0.93(0.82,1.05)	0.22	1.15 (1.01,1.31)*	0.049
Occupation of participants						
Private worker	5(17.2)	24(82.8)	Ref.			
Government workers	13(35.1)	24(64.9)	0.78(0.59,1.05)	0.10	0.77 (0.57, 1.02)	0.07
House wife	28(24.8)	85(75.2)	0.91(0.75,1.11)	0.34	0.89 (0.73,1.09)	0.25
Merchant	6(30.0)	14(70.0)	1.03(0.80,1.32)	0.83	0.99 (0.78,1.28)	0.98
Farmer	29(23.8)	93(76.2)	0.92(0.76,1.12)	0.41	0.89 (0.74,1.09)	0.29
Marital status of participants during the data collection time						
Single	14(16.1)	73(83.9)	1.16(1.02,1.30)	0.02	1.16 (1.03,1.31)*	0.015
Married	64(27.4)	170(72.6)	Ref.		Ref.	
Family size in the house hold						
<3	6(37.5)	10 (62.5)	Ref.			
3-5	38(26.6)	105(73.4)	0.84(0.68,1.04)	0.10	0.82 (0.66, 1.03)	0.08
>5	38(23.5)	124(76.5)	0.88(0.71,1.07)	0.20	0.87 (0.69 ,1.07)	0.19
One way cost of transport (USD)						
<7 dollar	28(31.1)	62(68.9)	Ref.			
≥7 dollar	50(21.6)	181(78.4)	1.14(0.98,1.33)	0.10	1.12 (0.96 , 1.30)	0.15
First medical consultation						
Health post	6(15.4)	33(84.6)	1.11(0.94,1.32)	0.22	1.11 (0.92, 1.33)	0.27
Health center	48(30.6)	109(69.4)	0.86(0.73,1.02)	0.08	0.87 (0.73 ,1.04)	0.12
Private clinic	6(14.3)	36(85.7)	1.06(0.88,1.27)	0.52	1.05 (0.88 , 1.30)	0.57
Private hospital	10(32.2)	21(67.8)	0.84(0.64,1.11)	0.21	0.83 (0.63 , 1.09)	0.18
Public hospital	10(19.2)	42(80.8)	Ref.			
Patient delay (> 2 months)						
No	31(40.8)	45(59.2)	Ref.		Ref.	
Yes	42(18.2)	189(81.8)	1.38(1.14,1.68)	0.001	1.41 (1.15, 1.69)*	0.001
Number of times visited health facilities prior to final diagnosis						
< 3 times	7(31.8)	15(68.2)	Ref.		Ref.	
3-6 times	40(26.8)	109(73.2)	1.07(0.79,1.45)	0.65	0.89 (0.69 , 1.16)	0.39
7-10 times	19(21.8)	68(78.2)	1.15(0.84,1.56)	0.38	0.93 (0.70 , 1.23)	0.61
>10 times	12(19.0)	51(81.0)	1.19(0.87,1.62)	0.24	1.12 (0.85 , 1.46)	0.43
Symptom interval						
< 3 months	12(36.4)	21(63.6)	Ref.		Ref.	
3-6 months	26(29.5)	62(70.3)	1.11(0.83,1.48)	0.49	1.09 (0.81 , 1.46)	0.51
> 6months	37(19.7)	151(80.3)	1.26(0.97,1.65)	0.08	1.26 (1.12 , 1.67)*	0.048

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361 Discussion

362 Longer consultation and diagnostic intervals, as well as late stages at the time of diagnosis, were
363 hypothesized before we started this study. This research has estimated prolonged patients
364 consultation and diagnostic intervals. In addition, most of the cases were diagnosed at advanced
365 stages. The most common reason mentioned by the patients for their delays was financial
366 constraints. About 11% of the cases were forced to visit an average of 10 different health
367 facilities in search of better and more effective cancer care and treatments in areas where they
368 believe they can afford it.

369 The dominant histological subtype was oesophageal squamous carcinoma. In addition, risk
370 factors for late consultation, diagnostic and late stage at the time of diagnosis were identified.

371 The median patient intervals were much lower in studies conducted elsewhere [11 21 25-27]
372 compared to the patient interval estimated from our study. This substantial difference could be
373 attributed to socio-cultural and socio-economic disparities in health-seeking behavior, as well as
374 a lack of understanding of oesophageal cancer symptoms among different groups/communities.

375 Furthermore, the bulk of our participants were from rural areas, and cancer care is given by
376 secondary and tertiary care institutions located far from the majority of rural populations.
377 Furthermore, the majority of the individuals were illiterate, implying that late presentation is
378 closely linked to a lack of access to care.

379 .Our research, on the other hand, is similar to the study conducted in South Africa [28]. The
380 similarities in socioeconomic, sociocultural, and literacy rates could explain the same
381 presentation delays. The median diagnostic interval estimated from our study was higher than the
382 previous studies conducted in different part of the world [11 21 25 26]. The discrepancy may be

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3 383 the differences in diagnostic workups and the availability of experienced and trained health
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5 384 professionals in cancer related diagnostic and treatment services. On the other hand, our study is
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8 385 in line with the study conducted in South Africa [28]. The similarities could be explained by the
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10 386 fact that the diagnostic procedures and health-care facilities are more or less similar among many
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12 387 of the African countries. The prevalence of diagnostic delay was higher in single patients than
13
14 388 the married participants. Thus, being married might have a better chance to seek medical care
15
16 389 than unmarried participants. The reason could be partners may influence each other on decision
17
18 390 making to seek care as early as possible.

21
22 391 In our findings, oesophageal cancer patients that paid their medical expense from their own
23
24 392 pocket had longer patient interval than patients whose medical expenses covered by other
25
26 393 organizations. The reason could be, they ignore the symptoms because patients with low socio-
27
28 394 economic status had other unmet survival felt needs than investing money for medical care [29]

29
30
31
32 395 The proportion of advanced stages at time of first diagnosis is higher compared the study
33
34 396 conducted Shandong University in Jinan (China) by Wang J, et al [21] this could be related to
35
36 397 longer patient and diagnostic intervals and socio-economic difference among the communities.
37
38 398 The cardinal symptom reported by majority of our participants was dysphagia this result is
39
40 399 comparable with studies [21 26 27]. We discovered that oesophageal squamous carcinoma was
41
42 400 the most prevalent, which is consistent with other studies conducted elsewhere in the world [21
43
44 401 30 31]. A significant number of patients with oesophageal cancer were diagnosed at advanced
45
46 402 stages, which are consistent with previous studies [30 32]. However, the proportion of those
47
48 403 diagnosed delay in oesophageal cancer was relatively higher in a nationwide cohort study
49
50 404 conducted in Korean patients [31]. Increased patient delay (> two months) was found to be
51
52 405 exacerbated by socio-economic characteristics in our study. Our finding is equivalent to this
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3 406 study [33] , which evidenced those patients with lower socio-economic status sought medical
4
5 407 help later. Furthermore, socioeconomic status has had an important influence in patients being
6
7 408 diagnosed at advanced stages, which is similar to the findings of the study conducted in China
8
9
10 409 [33]. In our study, the majority of oesophageal cancer patients sought rapid relief for their
11
12 410 symptoms by contacting several traditional healers. This conclusion is in line with that of a
13
14 411 qualitative study conducted in Ethiopia's Oromia Regional State.
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18 412 **4. Conclusion**

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21 413 Oesophageal cancer patients in the study area had longer patients' presentation, diagnostic and
22
23 414 symptom intervals. Moreover, majority of the oesophageal cancer patients had diagnosed at
24
25 415 advanced stages (III and IV). Being single and never heard of oesophageal cancer prior to
26
27 416 diagnosis was found to be predictors of increased patient intervals. The levels of first health
28
29 417 facilities visited for medical consultation and the cost of transportation were identified as key
30
31 418 factors in increasing diagnostic intervals.
32
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36 419 Furthermore, being single, being female, waiting more than two months for a diagnosis, and
37
38 420 symptom interval were found to be statistically significant predictors in the incidence of
39
40 421 advanced stages at diagnosis. Patients' intervals could be shortened by increasing their awareness
41
42 422 of oesophageal cancer symptoms.
43
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45

46 423 **Abbreviations**

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48
49 424 AJCC: American Joint Committee on Cancer

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51 425 APR: Adjusted Prevalence Ratio

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53 426 SD: Standard Deviation
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3 427 IQR: Inter Quartile Range
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5 428 P: Proportion
6

7 429 PR: Prevalence Ratio
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9
10 430 USD: United States Dollar
11

12 431 **Ethics approval and informed consent** 13 14

15
16 432 The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa
17
18 433 University College of Health Sciences with a protocol number of 080/18/SPH. The study
19
20 434 followed basic ethical principles of Helsinki declaration for medical research involving human
21
22 435 participants[34]. All of the study participants were informed about the purpose and procedure of
23
24 436 the research and their right to withdrawal from the study at any time. Written informed consent
25
26 437 was obtained from each of the study participants. Meanwhile, the study participants were agreed
27
28 438 to the extent that the finding of this study will be subjected to publication. Participants were well
29
30 439 informed not to disclose their information to a third person. The information was kept secured
31
32 440 and put confidentially with the first author.
33
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36

37 441 **Data availability** 38 39

40
41 442 Data will be available up on request
42
43

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48
49

50 445 **Competing interests** 51 52

53
54 446 There is no competing interest of this research
55
56
57

447 **Authors' contributions**

448 All authors contributed from the conception of idea up to data analysis and write up. They also
449 participated in drafting or revising of the article and have agreed on to which journal the article
450 shall be submitted and have given final approval of the version to be published, and agreed to be
451 accountable for all aspects of the work. Specifically, BD was conceptualized the topic of interest,
452 involved in data collection, coding, cleaning, analysis, interpretation of the result unto
453 preparation of the manuscript. FE was involved in proposal development, planning the fieldwork
454 and result section. And RY, MA, SG and AA were involved in proposal development, data
455 analysis and write up and in critical reviewing of manuscript.

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4 1 **Time intervals from first symptom recognition to pathological diagnosis among**
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6 2 **oesophageal cancer patients in Ethiopia: A cross-sectional study**
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9 3 Berhe Dessalegn^{1*,2}, Sefonias Getachew², Robel Yirgu², Fikre Enqueselassie^{2†}, Mathewos
10 4 Assefa³, Adamu Addissie²
11

12
13
14 5 ¹Department of Public Health, College of Medicine and Health Sciences, Adigrat University
15
16 6 Adigrat, Ethiopia

17
18
19 7 ²Department of Preventive Medicine, School of Public Health, College of Health Sciences, Addis
20
21 8 Ababa University, Addis Ababa, Ethiopia

22
23
24 9 ³Department of Radiotherapy Center, School of Medicine, Addis Ababa University, Addis Ababa,
25
26 10 Ethiopia

27
28
29 11 * Corresponding Author

30
31 12 Email: berhe_dessalegn@yahoo.com(BD)

32
33 13 † Professor Fikre Enqueselassie has passed away on October 28th, 2019.
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21 Abstract

22 Objective

23 The aim of this study was to estimate the time intervals from first symptom recognition to
24 pathological diagnosis among oesophageal cancer patients in Ethiopia.

25 Methods

26 **Design** Cross-sectional study design was employed

27 **Settings and participants** Oesophageal cancer patients aged ≥ 18 years were included from
28 Addis Ababa, Ethiopia (n=338) from February 2019 to August 2020. The participants were
29 selected consecutively from six health facilities provided cancer care nearly for 90% of patients.

30 **Main outcomes and measurements** The Aarhus statement criterias was applied to classify
31 patient intervals (time from first symptom recognition to presentation), and diagnostic intervals
32 (time from first presentation to diagnosis). Patient and diagnostic intervals >60 and >30 days were
33 considered as delays, respectively. For tumor classification, the American Joint Committee on
34 cancer was used. Data were analyzed using SPSS Version 24. Descriptive statistics were applied
35 to describe patients' characteristics. Poisson regression with robust variance was used to compute
36 prevalence ratios. In all statistical tests, significances were declared at p-value of <0.05 .

37 Results

38 The mean (SD) age of the participants was 54.30 ± 12.49 years.

39 Approximately 78 percent of study participants had never heard of oesophageal cancer and thought
40 they had gastritis. Dysphagia was commonly mentioned symptom. About 76% of the cases were
41 diagnosed at advanced stages (III and IV). Median patient interval was 108.5 (60.5-215) days and
42 median diagnostic interval was 77.5 (39-133) days. After adjusting confounders, being single and
43 unawareness of oesophageal cancer had association with consultation delay, cost of transportation

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3 44 and medical consultation had association with diagnostic delay and patient delay > two months
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5 45 had association with late stage at diagnosis.
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9 46 **Conclusion** Oesophageal cancer patients in Ethiopia had prolonged patient and diagnostic
10
11 47 intervals. Increasing awareness on symptoms of oesophageal cancer and shortening time to
12
13 48 diagnosis will help to improve the out-come of oesophageal cancer care in Ethiopia.
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16 49 **Keywords:** Oesophageal cancer, delay, intervals, tumor stage
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22 51 **Strengths and Limitations**
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25

- 26 52 • In Ethiopia, in case of patient and diagnostic interval and associated factors, it is the first
27
28 53 multifacility study
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30 54 • Poisson regression with robust variance was used to compute the prevalence ratios
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32 55 • It is the only research based on primary data in Ethiopia that estimates the patient and
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34 56 diagnostic intervals on oesophageal cancer patients
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36 57 • However, the onset of symptoms is a subjective measurement that patients may not recall the
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38 58 exact time
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1. Introduction

Cancer is a group of diseases in which abnormal cells grow and spread uncontrollably. Cancer has become a major public health concern on a global scale [1]. Oesophageal cancer is the fourth most common cancer in developing countries, and it is an aggressive tumor of the esophagus that develops in the organ's tissue lining [2]. Oesophageal cancer, which has a dismal prognosis and survival rate, has caused considerable morbidity and mortality around the world from the last three decades [3-5]. Globally, oesophageal cancer was the sixth most common cause of mortality among all cancers and the seventh most common cancer in terms of incidence[1].

The two most prevalent subtypes of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. Adenocarcinoma begins in the cells that produce and release mucus and other fluids, whereas squamous cell carcinoma begins in the flat cells that line the esophagus. Oesophageal cancer mortality and incidence are higher in Africa than the rest of the world, with squamous cell carcinoma being the most common type [6 7].

The five-year survival rate of non-metastatic oesophageal cancer is between 19 and 30%, whereas, the median overall survival time for metastatic oesophageal cancer is between four and six months.

Nonetheless, it is not uncommon for oesophageal cancer patients to be diagnosed at advanced stages ,because, in most cases, the oesophageal cancer patients have identified symptoms by the time the disease has reached its advanced stages, then lead to poor patients prognosis and survival rate[5 8 9]. The prognosis and time intervals of oesophageal cancer patients has been solely depended on the patients' awareness on symptoms and literates rate that contribute to early consultation and shorter pathological diagnosis periods, according to studies[10 11]. In practice, however, oesophageal cancer patients frequently have arrived late in presentation and commonly lately referred to the appropriate health facilities. In addition, literatures also showed that

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3 89 shortening the time to presentation is an important step in reducing late in diagnosis, and improving
4
5 90 the prognosis and survival of oesophageal cancer patients[12 13].
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9 91 Oesophageal cancer is the overwhelming disease and among the commonest cause of cancer deaths
10
11 92 in the world. Though, few patients can be cured, the treatment for oesophageal cancer is prolonged,
12
13 93 quality of life is significantly compromised and cases fatality rate is high [1].
14
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16 94 Ethiopia is a country, geographically located within the highest risk region of oesophageal cancer
17
18 95 known to be the oesophageal cancer belt. And, the disease has created a huge burden interms of
19
20 96 morbidity and mortality in the country[14]. In addition, few hospital reports revealed that over the
21
22 97 last decades, the incidence and burden of oesophageal cancer has been increasing.
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26 98 Diagnostic and consultation delays on cancers are common in underdeveloped countries, such as
27
28 99 the Eastern part of Africa, and are closely linked to poor survival rates. As a result, obtaining
29
30 100 updated information is crucial for establishing a resilient plan to reduce oesophageal cancer related
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32 101 morbidity and mortality [7 15].
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36 102 In Ethiopia, however, oesophageal cancer is not yet a public health priority, left in dark and is
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38 103 under-researched; as a result, there is no clear evidence about patient and diagnostic intervals and
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40 104 the stage at time of diagnosis. The goal of this study was to determine time to care seeking and
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42 105 pathological diagnosis, and the stage at time of diagnosis of oesophageal cancer patients.
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44 106 Meanwhile, we were also strived to identify predictors of patients and pathological diagnostic
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46 107 delays of > 60 and > 30 days, respectively.
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110 **2. Materials and methods**

111 **2.1. Study design and sample size**

112 A cross-sectional study design was employed. The study involved 338 oesophageal cancer patients
113 aged ≥ 18 years from February 2019 to August 2020 in Addis Ababa, Ethiopia. Using the expected
114 proportion (p=32.0%) of patients delay to presentation (>2 months) from another similar study
115 [16] by assuming a 95% level of confidence, a 5% precision and 5% non-response rate

116 **2.2. Settings and participants**

117 The Ethiopian health care delivery system has three tiers: primary, secondary and tertiary level
118 health care facilities that are linked with a referral system. The setup differs slightly between urban
119 and rural settings. The main healthcare service in the metropolitan city, such as Addis Ababa,
120 Ethiopia's capital, includes public health centers, private clinics, and primary hospitals. Secondary
121 and tertiary healthcare levels are general hospitals and specialty hospitals, respectively. The
122 primary healthcare services in rural areas are made up of a health post, a health center, and primary
123 hospitals. Secondary and tertiary healthcare levels are general hospitals and specialty hospitals,
124 respectively. Nurses and health officers are the primary staff of public health centers, with the goal
125 of providing preventative and primary health care services. In the case of cancers, such as
126 oesophageal cancer, health workers at the primary level care facilities are only expected to refer
127 patients to general hospitals and other high-level facilities for further diagnosis and treatments[17].

128

129 **Sampling procedure**

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3 130 A consecutive sampling method was used to recruit study participants. Oesophageal cancer
4
5 131 patients histologically confirmed and clinically staged came to the selected health facilities were
6
7 132 included in the study, whereas critically ill, diagnosed to other cancer types and non-Ethiopian
8
9 133 patients were excluded from participation. Six health facilities in Addis Ababa (Tikur Anbesa
10
11 134 Specialized Hospital, St. Paul Hospital Millennium Medical College, Betezata Hospital, Hallelujah
12
13 135 General Hospital, Landmark Hospital, and United Vision Medical Services Centre) were selected,
14
15 136 where nearly 90% of cancer patients being diagnosed and treated. At each health facility, one focal
16
17 137 person was assigned to identify eligible oesophageal cancer patients and communicate with the
18
19 138 principal investigator and supervisor. To avoid duplication, the medical chart of the recruited
20
21 139 patient was coded in red on the top cover page. Prior to the interview, study participants were
22
23 140 informed about the purpose of the study and their right to withdraw under any circumstances
24
25 141 without compromisation of any services.

142 **2.3. Variables and Measurements**

143 We used the Aarhus statement criteria to classify patient, diagnostic and symptoms intervals. Thus,
144 patient interval was defined as the interval between the date of first symptom recognition (the time
145 point at which the patient first noticed bodily changes and/or symptoms) and the date of first
146 clinical presentation (the date at which the patient first presented to a healthcare provider after first
147 recognizing symptoms), and symptom interval was defined as the time interval between the date
148 of first symptom recognition and the date of pathological diagnosis[18 19]. The date of symptom
149 recognition was determined based on participants recall. Furthermore, the diagnostic interval was
150 defined as the time elapsed between the date of first clinical presentation and the date of the final
151 pathological diagnosis (the date at which the first histological or cytological confirmation of the
152 malignancy was documented in the pathology report). The pathology report of the patient was used

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3 153 to determine the date of diagnosis [18 19]. Tumors were classified using the Tumor-Node-
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5 154 Metastasis method from the 7th edition of the American Joint Committee on Cancer (AJCC)[20].
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8 155 And cases were histologically and endoscopically confirmed. Stages I and II were classified as
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10 156 early stages of diagnosis, while stage III and IV were classified as late stages of diagnosis [21].
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12 157 The interviews were conducted in Amharic, the country's working language. The study tool was
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14 158 initially prepared in English, then translated into Amharic by language translators, and finally back
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17 159 to English to ensure that the two versions were consistent. Experts in cancer research assessed the
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19 160 tool to ensure that the questions were clear and two days training was given data collectors and the
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21 161 supervisor about the objective of the study. A pretest for cultural suitability and clarity was
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23 162 performed prior to administering the tool to the participants. When the eligible participants were
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25 163 arrived for treatment, trained nurses interviewed them individually in a semiprivate room in
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27 164 Amharic. If the participants couldn't recall the exact date of their first symptom recognition, they
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29 165 were asked to provide a month or year ('was it at the beginning, middle, or end of the year'). For
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31 166 those who only remembered the month, the date was estimated to be the 15th day of that month. If
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33 167 the participants only said at the beginning, middle or at the end of the year, the estimated date was
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35 168 15th of February, June or October of the year, respectively; if they only said the year, the estimated
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37 169 date was June 30th of that year. We performed sensitivity analyses excluding patients who had only
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39 170 remembered the beginning, middle or end of the year or a year for the date of first symptom
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41 171 recognition or clinical presentation[22].
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176 2.4. Data Analysis

177 Epi-info version 7 was used for the data entry and SPSS Version 24 was used to analyze the data.
178 Descriptive statistics were calculated for each variable. Numbers and percentages were used to
179 summarize categorical variables. We presented mean and standard deviation for numerical
180 variables with normal distributions, whereas median and IQR were employed for variables with
181 skewed distributions. Patient and diagnostic delays were defined as >60-days patient intervals and
182 >30-days diagnostic intervals, respectively, from previous similar study [11]. For cross-sectional
183 research, OR is the common measure of association, and logistic regression is often used to
184 estimate. Nevertheless, evidences suggest that when the proportion of the outcome exceeds 10%,
185 an odds ratio overestimates the risk ratio, leading to incorrect interpretations. As a result, to avoid
186 these limitations, the prevalence ratio is preferred measure of association [23 24]. Hence, Poisson
187 regression with robust variance was used to compute the adjusted prevalence ratios of factors
188 associated with the prevalence of patient and diagnostic delays, as well as factors associated with
189 stage at time of diagnosis. Variables having a p value of <0.25 on bivariable analysis were
190 candidates for the multivariable analysis and other variables were also considered based on
191 literatures had impacts on patient and diagnostic delays and stage at time of diagnosis. A two-sided
192 p value of 0.05 was declared as statistically significant.

193 **Patient and public involvement** “No patient involved”

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198 3. Results:

199 Socio-demographic and socio- economic characteristics of the study participants

200 We approached 351 participants those histologically confirmed and clinically staged for
201 oesophageal cancer and among 96.3% (338) of them were provided their oral consent for
202 participation. The participants in the study were 54.30 ± 12.49 years old on average (SD). Male
203 participants accounted for 52.4% of the total participants. More than half of the participants (52%)
204 were above the age of 55 years, only 7.0% of the participants were below the age of 35 years. Two-
205 thirds of the study participants were from rural areas of Ethiopia and were unable to read and write.
206 Muslims and farmers participants accounted 52% and 38% of the total participants respectively.
207 At the time of data collection, 75% of the participants in the study were married. More than half
208 of the participants in the study earned not more than one USD per day or about 29 Ethiopian Birr.
209 Among the participants, 73% had to travel long distances to receive cancer-specific diagnosis and
210 treatment services, and had to pay more than seven USD or 203 Ethiopian Birr for a single trip just
211 to cover only for transportation costs. Furthermore, nearly three-quarters of the study participants
212 had paid their medical expenses out of their pockets (**Table 1**).

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220 **Table 1:** Socio-demographic and socio-economic characteristics of esophageal cancer patients
 221 Addis Ababa, Ethiopia, February 2019 to August 2020 (n=338)

Variables	Frequency	Percent
Age categories (years)		
<35	24	7
35-44	46	14
45-54	91	27
≥55	177	52
Gender		
Male	177	52.4
Female	161	47.6
Religion		
Christianity	159	47
Islam	175	51.8
Wakefata	4	1.2
Residency		
Urban	126	37.3
Rural	212	62.7
Educational status of participants		
Unable to read and write	209	61.8
1-8 grade	72	21.3
9-12 grade	37	10.9
Diploma and above	20	5.9
Occupation of participants		
Government workers	38	1.2
House wife	118	34.9
Merchant	20	5.9
Private worker	35	10.4
Farmer	127	37.6
Marital status of participants during the data collection time		
Married	246	72.8
Single	92	27.2
Monthly income (USD)		
<35	171	50.6
35-106	130	38.5
106.6-177	21	6.2
>177	16	4.7
One way cost of transport (USD*)		
<7 dollar	93	27.5
≥7 dollar	245	72.5
Sources of medical expenses		
Employing organization	1	0.3
Free medical care	72	21.3
Government insurance	19	5.6
Out of pocket	242	71.6
Private insurance	4	1.2

222 3.1. Symptoms and awareness of oesophageal cancer

223 Among the total participants, 21.3 % had reported a history of at least one chronic disease, with
224 diabetes mellitus being the commonest one. More than three-fourth of the study participants
225 (77.8%, 95% CI [73.4%, 82.2%]) had never heard of oesophageal cancer prior to diagnosis for
226 oesophageal cancer. For those who heard of oesophageal cancer prior to diagnosis, the main
227 sources (48%) of the information were friends/ family members or neighbors, followed by printed
228 and electronic medias such as (TV, radio, internet) (28%). Only eight participants (2.4%) had
229 reported first degree family history of oesophageal cancer.

230 Dysphagia was the cardinal symptom mentioned by 84.6% of the study participants, followed by
231 odynophagia of 54.1%. Approximately three-fourth of the study participants had linked the first
232 symptom/s to gastritis. All patients had recognized at least one symptom. Moreover, a significant
233 number of patients reported as having more than one oesophageal cancer symptom. About half of
234 the cases stated that they did not take an immediate action for the first symptom/s because they
235 thought that the symptom/s was/ were simple and self-limited. Meanwhile, about a quarter of the
236 cases sought treatment from various traditional healers as a quick fix for the symptom/s.

237 More than half (58.9%) of the study participants felt compelled by their family members to seek
238 medical help for the symptom/s. About half of the cases first went to public health facilities for
239 their first symptom/s (health centers and health posts), followed by public hospitals (16%). At their
240 first visit to health facilities, approximately to two-third of the study participants first contacted
241 health officers and nurses as health care providers. The mean (SD) of health facilities visited by
242 the cases until the data collection time was 6.6 ± 3.2 . Meanwhile, 11% of the participants had
243 visited more than 10 health facilities until data collection time. The mean (SD) number of visits to

244 health facilities by participants until the data collection time was 7.45 ± 3.63 . The prominent reason
245 mentioned by the participants for consultation delays was a financial issue, (61.5%).

246 3.2. Diagnosis characteristics of oesophageal cancer patients

247 Out of the total oesophageal cancer patients, about 76% (95% CI [71.0 %, 80.7%]) of the study
248 participants were diagnosed at late stages (III and IV)., In terms of histologic subtypes, 85.8%,
249 13.3% and 0.89% were oesophageal squamous cell carcinoma, oesophageal adenocarcinoma and
250 unknown carcinomas, respectively. For those with available grade on biopsy report, 59.8%, 15.7%
251 and 8.9%) were well differentiated, unspecified and poorly differentiated respectively. Endoscopic
252 appearance was ulcerative in 49.4% followed by an obliterative of 34.9%. In case of tumor
253 locations, middle oesophagus, lower oesophagus and upper (cervical) were 41.1%, 30.8% and
254 28.1% respectively (**Table 2**).

262 **Table 2:** Diagnostic history of oesophageal cancer patients from February 2019 to August
 263 2020 Addis Ababa, Ethiopia,

Variable	Frequency	Percent
Stage at first diagnosis		
Stage I	20	6.0
Stage II	58	17.2
Stage III	167	49.4
Stage IV	76	22.4
Unknown	17	5.0
Histological sub-type		
Oesophageal squamous carcinoma	290	85.8
Oesophageal adenocarcinoma	45	13.3
Unknown	3	0.9
Histopathological differentiations		
Well-differentiated	202	59.8
Moderate differentiated	47	13.8
Poor differentiated	30	8.9
Undifferentiated	6	1.8
Unspecified	53	15.7
Morphology of tumor during upper gastrointestinal endoscopy		
Ulcerative	167	49.4
Obliterative	118	34.9
Proliferative	45	13.3
Ulceroproliferative	8	2.4
Tumor location(Histology)		
Upper (cervical)	95	28.1
Middle oesophagus	139	41.1
Lower oesophagus	104	30.8

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270 Patient and diagnostic intervals

271 The median (IQR) patient interval was 108.5 (60.5-215) days. The proportion of patient delay was
272 75% (95% CI [69.8%, 79.3%]). About ten percent of the participants had visited health facilities
273 after 365 days of first symptom recognition. Only about 8% of the participants visited health
274 facilities within thirty days. Great majority (71%) of the participants mentioned their reason for
275 late patients' consultation was financial problems (59.5%) followed by not bothering about the
276 disease. The median (IQR) of diagnostic interval was 77.5 (39-133) days. The proportion of
277 diagnostic delay was 81.9% (95% CI [77.9%, 86.2%]). Three percent of those who took part in
278 the study received diagnostic confirmation after 365 days of waiting and 18% of the participants
279 got diagnosis confirmation less than thirty days. The median (IQR) symptom interval was
280 215(130-353) days. The most noticeable single factor mentioned by majority (78%) the
281 participants for the diagnostic delay was longer appointments primarily associated with the health
282 care organizations.

283 3.3. Factors associated with patient delay

284 Based on the cut of point, age, residency ,educational status, occupation, marital status, income,
285 awareness about oesophageal cancer prior to diagnosis for oesophageal cancer, being house wife
286 and visiting traditional healers were potential candidates and included in the multivariable analysis
287 and among participants unable to read and write (PR=1.2, 95% CI [1.05, 1.43]), being house wife
288 (PR=1.14, 95%CI [1.01, 1.29]), single participants (PR=1.08, 95% CI [1.03, 1.14]) monthly
289 income <35USD (PR=1.29,95%CI[1.09,1.55]) and 35-106 USD
290 (PR=1.3,95%CI[1.17]CI[1.09,1.55]family monthly income<53USD(PR=1.17,95%CI[1.02,1.33])
291 and 53-141 USD (PR=1.17,95% CI [1.02,1.34]) and never heard of oesophageal cancer prior to

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3 292 diagnosis (PR=1.11,95%CI [1.03,1.97]) were significantly associated with higher prevalence of
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5 293 patient delay and adjusted for multivariable analysis. Therefore, after an adjustment, single
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7 294 participants (Adjusted PR=1.09, 95% CI [1.03, 1.15]) and never heard of oesophageal cancer prior
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9 295 to diagnosis (Adjusted PR=1.08, 95% CI [1.03, 1.15]) were found statistically significant to
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11 296 increase the prevalence of patients delay among oesophageal cancer patients (**Table 3**).

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309 **Table 3** : Factors associated with patient delay (>60 days) among oesophageal cancer patients
 310 from February 2019 to August 2020, Addis Ababa, Ethiopia (n=324)

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Age of participants (years)						
<35	14 (66.7)	7 (33.3)	Ref.		Ref.	
35-44	26 (59.1)	18 (40.9)	0.96 (0.82,1.11)	0.55	0.96 (0.86,1.07)	0.43
45-54	63 (72.4)	24 (27.6)	1.03 (0.91,1.18)	0.62	1.03 (0.94, 1.12)	0.56
>55	140 (81.4)	32 (18.6)	1.10 (0.96,1.23)	0.18	0.99 (0.91,1.08)	0.81
Residency						
Urban	88 (71.0)	36 (29.0)	Ref.		Ref.	
Rural	155 (77.5)	45 (22.5)	1.04 (0.98,1.10)	0.19	1.04 (0.97,1.11)	0.29
Educational status of participants						
Unable to read and write	155 (77.1)	46 (22.9)	1.2 (1.05,1.43)	0.01	1.11 (0.94, 1.29)	0.22
Grade 1-8	56 (81.2)	13 (18.8)	1.25 (1.07,1.46)	0.006	1.15 (0.97, 1.35)	0.10
Grade 9-12	23 (67.6)	11 (32.4)	1.16 (0.97,1.38)	0.11	1.08 (0.91, 1.29)	0.38
Diploma and above	9 (45.0)	11 (55.0)	Ref.			
Occupation of participants						
Private worker	17 (56.7)	13 (43.3)	Ref.		Ref.	
Government workers	24 (68.6)	11 (31.4)	1.08 (0.93,1.24)	0.32	1.02 (0.94, 1.11)	0.57
House wife	82 (78.8)	22 (21.2)	1.14 (1.01,1.29)	0.03	0.94 (0.86, 1.02)	0.14
Merchant	24 (82.8)	5 (17.2)	1.17 (1.02,1.34)	0.03	1.03 (0.94,1.12)	0.54
Farmer	96 (76.2)	30 (23.8)	1.13(0.99,1.27)	0.06	0.93 (0.85, 1.02)	0.12
Marital status of participants during the data collection time						
Single	76 (85.4)	13 (14.6)	1.08 (1.03,1.14)	0.002	1.09 (1.03, 1.15)*	0.001
Married	167 (71.1)	68 (28.9)	Ref.			
Monthly income						
<35 US dollar	124 (78.5)	34 (21.5)	1.29 (1.09,1.55)	0.004	1.22(1.005,1.48)	0.045
35-106 US dollar	101 (78.9)	27 (21.1)	1.3 (1.09,1.55)	0.004	1.22(1.22,1.48)	0.042
106.6-177 US dollar	12 (54.5)	10 (45.5)	1.12 (0.90,1.39)	0.29	0.46(1.09)	0.46
>177 US dollar	6 (37.5)	10 (62.5)	Ref.			
Family monthly income(USD)						
<53	128 (77.1)	38 (22.9)	1.17 (1.02, 1.33)	0.025	1.12(0.98,1.27)	0.09
53-141	84 (77.8)	24 (22.2)	1.17 (1.02,1.34)	0.024	1.13(0.99,1.28)	0.08
141.4-230	18 (72.0)	7 (28.0)	1.13 (0.96,1.33)	0.14	1.1(0.94,1.29)	0.26
>230	13 (52.0)	12 (48.0)	Ref.			

311 **Table 3 cont.....**

Patient characteristics	Patient delay		Unadjusted		Adjusted	
	Yes (%)	No (%)	PR (95% CI)	P-value	PR (95% CI)	P-value
Prior information about esophageal cancer						

No	198 (79.0)	53 (21.0)	1.11 (1.03,1.97)	0.007	1.08(1.02,1.17)*	0.04
Yes	44 (61.1)	29 (38.9)	Ref.			
Visiting traditional healers						
No	180(73.2)	66(26.8)	Ref.			
Yes	63(80.8)	15(19.8)	1.04(0.99,1.11)	0.15	1.04(0.98,1.10)	0.23

3.4. Factors associated with diagnostic delay

Based on the cut off age, marital status, family size, transportation, first medical consultation, number of health facilities visited and sources of medical expenses were included in the multivariable analysis and among single participants (PR=1.8,95%CI[1.74,1.85]), family monthly income 53-141 USD(PR=0.91,95%CI [0.85,0.99]), cost transport (one trip)>7USD(PR=1.07,95%CI[1.06,1.13]), first medical consultation at health center (PR=0.93,95%CI[0.88,0.99]) and number of health facilities visited < 3 health facilities (PR=0.93, 95%CI [0.87,0.99]) were significantly associated with higher prevalence of diagnostic delay. However, after an adjustment or in the multivariable analysis, we found single participants (Adjusted PR=1.2, 95% CI [1.11,2.10]), sources of medical expenses (Adjusted PR=1.2,95% CI[1.13,2.40]), cost of transportation (Adjusted PR=1.2,95% CI [1.12,1.54]) and first medical consultation to health facilities (Adjusted PR= 1.4, 95% CI [1.20,2.30]) were statistically significant to increase the prevalence of diagnostic delay among oesophageal cancer patients (Table 4).

330 **Table 4:** Factors associated with diagnostic delay (>30 days) among oesophageal cancer patients
 331 from February 2019 to August 2020, Addis Ababa Ethiopia (n=326)

Patient characteristics	Diagnosis delay		Unadjusted	P-value	Adjusted	P-value
	Yes (%)	No (%)	PR (95% CI)		PR (95% CI)	
Age of participants (years)						
<35	17 (77.2)	5 (22.8)	Ref.		Ref.	
35-44	33 (75.0)	11 (25.0)	0.94 (0.84, 1.04)	0.24	0.96(0.86,1.07)	0.45
45-54	75 (87.2)	11 (12.8)	1.01 (0.92, 1.09)	0.92	1.02(0.93,1.11)	0.69
≥55	140 (80.5)	34 (19.5)	0.97 (0.89, 1.05)	0.45	0.97(0.89,1.06)	0.53
Marital status of participants during the data collection time						
Single	78(88.6)	10(11.4)	1.80(1.74,1.85)	0.0001	1.2 (1.1,2.10)**	0.04
Married	189(79.4)	49(20.6)	Ref.		Ref.	
Family monthly income(USD)						
<53	139(82.7)	29(17.3)	0.95(0.89,1.01)	0.11	0.98(0.88,1.09)	0.69
53-141	80(74.8)	27(25.2)	0.91(0.85,0.99)	0.008	0.91(0.82,1.002)	0.05
141.4-230	20(80.0)	5(20.0)	1.02(0.95,1.09)	0.57	1.01(0.93,1.09)	0.84
>230	19(73.1)	7(26.9)	Ref.		Ref.	
One way cost of transport (USD)						
<7 dollar	67(73.6)	24(26.4)	Ref.		Ref.	
≥7 dollar	200(85.1)	35(14.9)	1.07(1.06,1.13)	0.03	1.2(1.12,1.54)**	0.04
First medical consultation						
Health post	35(87.5)	5(12.5)	0.99(0.94,1.07)	0.96	1.01(0.94,1.08)	0.83
Health center	123(77.4)	36(22.6)	0.93(0.88,0.99)	0.015	1.4 (1.2, 2.30)**	0.049
Private clinic	38(88.4)	5(11.6)	0.99(0.94,1.06)	0.78	1.01(0.94,1.08)	0.87
Private hospital	24(72.7)	9(27.3)	0.91(0.82,1.002)	0.054	0.92(0.83,1.02)	0.10
Public hospital	46(90.2)	5(9.8)	Ref.		Ref.	
Number of health facilities visited for diagnosis						
< 3 health facilities	13(72.2)	5(27.8)	Ref.		Ref.	
3-6 health facilities	153(80.5)	37(19.5)	0.93(0.87,0.99)	0.02	0.93(0.87,1.22)	0.054
7-10 health facilities	67(81.7)	15(18.3)	0.93(0.87,1.004)	0.06	0.94(0.87,1.01)	0.108
>10 health facilities	29(82.9)	6(17.1)	0.94(0.86,1.026)	0.17	0.94(0.86,1.03)	0.19
Source of medical expenses						
Free medical care	57(79.2)	15(20.8)	Ref.		Ref.	
Governmental insurance	11(61.1)	7(38.9)	0.90(0.78,1.044)	0.16	1.22 (1.13, 2.40)*	0.048
Out of pocket	199(84.3)	37(15.7)	1.03(0.97,1.09)	0.34	1.03(0.98,1.09)	0.26

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336 3.5 Factors associated with advanced stages at diagnosis among oesophageal cancer 337 patients

338 Based on the cutoff point, gender, occupation, family size, transport, first medical consultation,
339 patients delay > two months and number of times visiting for diagnosis were included in the
340 multivariable analysis and among, marital status, single (PR=1.16, 95% CI [1.02, 1.30]) and
341 patients delay of > two months (PR=1.38, 95% CI [1.14, 1.68]) were significantly associated with
342 late stage at first diagnosis. However, after an adjustment or multivariable analysis, marital status
343 (Adjusted PR=1.16, 95% CI [1.03, 1.31]), female participants (Adjusted PR=1.15, 95% CI [1.015,
344 1.31]), patient delay > two months (Adjusted PR=1.41, 95% CI [1.15, 1.69]) and symptom
345 intervals (Adjusted PR=1.26, 95% CI [1.12, 1.67]) were statistically significant to increase the
346 prevalence of advanced stage at time of diagnosis (**Table 5**).

347 **Table 5:** Factors associated with advanced stages at diagnosis among oesophageal cancer patients
348 from February 2019 to August 2020 Addis Ababa, Ethiopia (n=321).

Patient characteristics	Advanced-stage		Unadjusted		Adjusted	
	No (%)	Yes (%)	PR (95% CI)	P-value	aPR (95% CI)	P-value
Gender						
Male	45(27.1)	121(72.9)	Ref.		Ref.	
Female	33(21.3)	122(78.7)	0.93(0.82,1.05)	0.22	1.15 (1.01,1.31)*	0.049
Occupation of participants						
Private worker	5(17.2)	24(82.8)	Ref.			
Government workers	13(35.1)	24(64.9)	0.78(0.59,1.05)	0.10	0.77 (0.57, 1.02)	0.07
House wife	28(24.8)	85(75.2)	0.91(0.75,1.11)	0.34	0.89 (0.73,1.09)	0.25
Merchant	6(30.0)	14(70.0)	1.03(0.80,1.32)	0.83	0.99 (0.78,1.28)	0.98
Farmer	29(23.8)	93(76.2)	0.92(0.76,1.12)	0.41	0.89 (0.74,1.09)	0.29
Marital status of participants during the data collection time						
Single	14(16.1)	73(83.9)	1.16(1.02,1.30)	0.02	1.16 (1.03,1.31)*	0.015
Married	64(27.4)	170(72.6)	Ref.		Ref.	
Family size in the house hold						
<3	6(37.5)	10 (62.5)	Ref.			
3-5	38(26.6)	105(73.4)	0.84(0.68,1.04)	0.10	0.82 (0.66, 1.03)	0.08
>5	38(23.5)	124(76.5)	0.88(0.71,1.07)	0.20	0.87 (0.69 ,1.07)	0.19

One way cost of transport (USD)						
<7 dollar	28(31.1)	62(68.9)	Ref.			
>7 dollar	50(21.6)	181(78.4)	1.14(0.98,1.33)	0.10	1.12 (0.96 , 1.30)	0.15
First medical consultation						
Health post	6(15.4)	33(84.6)	1.11(0.94,1.32)	0.22	1.11 (0.92, 1.33)	0.27
Health center	48(30.6)	109(69.4)	0.86(0.73,1.02)	0.08	0.87 (0.73 , 1.04)	0.12
Private clinic	6(14.3)	36(85.7)	1.06(0.88,1.27)	0.52	1.05 (0.88 , 1.30)	0.57
Private hospital	10(32.2)	21(67.8)	0.84(0.64,1.11)	0.21	0.83 (0.63 , 1.09)	0.18
Public hospital	10(19.2)	42(80.8)	Ref.			
Patient delay (> 2 months)						
No	31(40.8)	45(59.2)	Ref		Ref.	
Yes	42(18.2)	189(81.8)	1.38(1.14,1.68)	0.001	1.41 (1.15, 1.69)*	0.001
Number of times visited health facilities prior to final diagnosis						
< 3 times	7(31.8)	15(68.2)	Ref.		Ref.	
3-6 times	40(26.8)	109(73.2)	1.07(0.79,1.45)	0.65	0.89 (0.69 , 1.16)	0.39
7-10 times	19(21.8)	68(78.2)	1.15(0.84,1.56)	0.38	0.93 (0.70 , 1.23)	0.61
>10 times	12(19.0)	51(81.0)	1.19(0.87,1.62)	0.24	1.12 (0.85 , 1.46)	0.43
Symptom interval						
< 3 months	12(36.4)	21(63.6)	Ref.		Ref.	
3-6 months	26(29.5)	62(70.3)	1.11(0.83,1.48)	0.49	1.09 (0.81 , 1.46)	0.51
> 6months	37(19.7)	151(80.3)	1.26(0.97,1.65)	0.08	1.26 (1.12 , 1.67)*	0.048

Discussion

Longer consultation and diagnostic intervals, as well as late stages at the time of diagnosis, were hypothesized before we started this study. This research has estimated prolonged patients consultation and diagnostic intervals. In addition, most of the cases were diagnosed at advanced stages. The most common reason mentioned by the patients for their delays was financial constraints. About 11% of the cases were forced to visit an average of 10 different health facilities in search of better and more effective cancer care and treatments in areas where they believe they can afford it.

The dominant histological subtype was oesophageal squamous carcinoma. In addition, risk factors for late consultation, diagnostic and late stage at the time of diagnosis were identified.

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3 360 The median patient intervals were much lower in studies conducted elsewhere [11 21 25-27]
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5 361 compared to the patient interval estimated from our study. This substantial difference could be
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7 362 attributed to socio-cultural and socio-economic disparities in health-seeking behavior, as well as a
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9 363 lack of understanding of oesophageal cancer symptoms among different groups/communities.

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13 364 Furthermore, the bulk of our participants were from rural areas, and cancer care is given by
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15 365 secondary and tertiary care institutions located far from the majority of rural populations.
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17 366 Furthermore, the majority of the individuals were illiterate, implying that late presentation is
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19 367 closely linked to a lack of access to care.

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23 368 Our research, on the other hand, is similar to the study conducted in South Africa [28]. The
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25 369 similarities in socioeconomic, sociocultural, and literacy rates could explain the same presentation
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27 370 delays. The median diagnostic interval estimated from our study was higher than the previous
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29 371 studies conducted in different part of the world [11 21 25 26]. The discrepancy may be the
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31 372 differences in diagnostic workups and the availability of experienced and trained health
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33 373 professionals in cancer related diagnostic and treatment services. On the other hand, our study is
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35 374 in line with the study conducted in South Africa [28]. The similarities could be explained by the
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37 375 fact that the diagnostic procedures and health-care facilities are more or less similar among many
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39 376 of the African countries. The prevalence of diagnostic delay was higher in single patients than the
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41 377 married participants. Thus, being married might have a better chance to seek medical care than
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43 378 unmarried participants. The reason could be partners may influence each other on decision making
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45 379 to seek care as early as possible.

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51 380 In our findings, oesophageal cancer patients that paid their medical expense from their own pocket
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53 381 had longer patient interval than patients whose medical expenses covered by other organizations.

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3 382 The reason could be, they ignore the symptoms because patients with low socio-economic status
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5 383 had other unmet survival felt needs than investing money for medical care [29]
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9 384 The proportion of advanced stages at time of first diagnosis is higher compared the study
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11 385 conducted in Shandong University in Jinan (China) by Wang J, et al [21] this could be related to
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13 386 longer patient and diagnostic intervals and socio-economic difference among the communities.
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16 387 The cardinal symptom reported by majority of our participants was dysphagia this result is
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18 388 comparable with studies [21 26 27]. We discovered that oesophageal squamous carcinoma was the
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20 389 most prevalent, which is consistent with other studies conducted elsewhere in the world [21 30
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22 390 31]. A significant number of patients with oesophageal cancer were diagnosed at advanced stages,
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24 391 which are consistent with previous studies [30 32]. However, the proportion of those diagnosed
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26 392 delay in oesophageal cancer was relatively higher in a nationwide cohort study conducted in
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28 393 Korean patients [31]. Increased patient delay (> two months) was found to be exacerbated by
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30 394 socio-economic characteristics in our study. Our finding is equivalent to this study [33] , which
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32 395 evidenced those patients with lower socio-economic status sought medical help later. Furthermore,
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34 396 socioeconomic status has had an important influence in patients being diagnosed at advanced
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36 397 stages, which is similar to the findings of the study conducted in China [33]. In our study, the
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38 398 majority of oesophageal cancer patients sought rapid relief for their symptoms by contacting
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40 399 several traditional healers. This conclusion is in line with that of a qualitative study conducted in
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42 400 Ethiopia's Oromia Regional State.
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404 **4. Conclusion**

405 Oesophageal cancer patients in the study area had longer patients' presentation, diagnostic and
406 symptom intervals. Moreover, majority of the oesophageal cancer patients had diagnosed at
407 advanced stages (III and IV). Being single and never heard of oesophageal cancer prior to diagnosis
408 was found to be predictors of increased patient intervals. The levels of first health facilities visited
409 for medical consultation and the cost of transportation were identified as key factors in increasing
410 diagnostic intervals.

411 Furthermore, being single, being female, waiting more than two months for a diagnosis, and
412 symptom interval were found to be statistically significant predictors in the incidence of advanced
413 stages at diagnosis. Patients' intervals could be shortened by increasing their awareness of
414 oesophageal cancer symptoms.

415 **Ethics approval and informed consent**

416 The ethical clearance was obtained from the Institutional Review Board (IRB) of Addis Ababa
417 University College of Health Sciences with a protocol number of 080/18/SPH. The study followed
418 basic ethical principles of Helsinki declaration for medical research involving human
419 participants[34]. All of the study participants were informed about the purpose and procedure of
420 the research and their right to withdrawal from the study at any time. Written informed consent
421 was obtained from each of the study participants. Meanwhile, the study participants were agreed
422 to the extent that the finding of this study will be subjected to publication. Participants were well
423 informed not to disclose their information to a third person. The information was kept secured and
424 put confidentially with the first author.

425 **Abbreviations**

426 AJCC: American Joint Committee on Cancer

427 APR: Adjusted Prevalence Ratio

428 SD: Standard Deviation

429 IQR: Inter Quartile Range

430 P: Proportion

431 PR: Prevalence Ratio

432 USD: United States Dollar

433 **Data availability**

434 Data will be available up on request

435 **Funding**

436 There is no fund for this research project

437 **Competing interests**

438 There is no competing interest of this research

439 **Authors' contributions**

440 All authors contributed from the conception of idea up to data analysis and write up. They also
441 participated in drafting or revising of the article and have agreed on to which journal the article
442 shall be submitted and have given final approval of the version to be published, and agreed to be
443 accountable for all aspects of the work. Specifically, BD was conceptualized the topic of interest,
444 involved in data collection, coding, cleaning, analysis, interpretation of the result unto preparation

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3 445 of the manuscript. FE was involved in proposal development, planning the fieldwork and result
4
5 446 section. And RY, MA, SG and AA were involved in proposal development, data analysis and write
6
7
8 447 up and in critical reviewing of manuscript.
9

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12
13
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17
18 451 facilities for their cooperation.
19

20 21 22 452 **Ethics approval statement**

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25 453 We have obtained verbal consent from the study participants and the ethical clearance was
26
27 454 obtained from the Institutional Review Board (IRB) of Addis Ababa University College of
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29 455 Health Sciences with a protocol number of 080/18/SPH.
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31 32 33 456 **References**

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