There is evidence that 15% of gastric cancer patients in Zambia survive more than one-year after diagnosis. The major contributing factor to these poor outcomes is late case detection. We set out to investigate the time course of gastric cancer diagnosis in Zambia. The study was conducted at the University Teaching Hospital, in Lusaka. Consenting patients presenting to the endoscopy unit were enrolled and their endoscopic findings recorded. An interviewer-administered questionnaire was used to collect information on basic characteristics, presenting symptoms and duration. We enrolled 388 patients, 92 (24%) of whom had gastric cancer. About two-thirds of the gastric cancers were located in the distal part of the stomach. The median time to endoscopic gastric cancer diagnosis was 12 weeks, IQR 4-32 weeks after the first health care consultation. This was despite gastric cancer patients seeking healthcare attention within a median of 2 weeks, IQR 0-4 weeks of noticing the symptoms. Patients presenting with persistent vomiting or evidence of blood loss had significantly shorter delays than those with abdominal pain (p<0.05 and p<0.001 respectively). Delayed referral for diagnostic endoscopy is a contributing factor to late gastric cancer diagnosis in Zambia. The delay is highest in patients presenting with abdominal pain.

INTRODUCTION
Gastric cancer is a malignant tumour that can arise from any part of the stomach, including the cardia, fundus, body and antrum. It is the fifth most common cancer globally and the third leading cause of cancer related deaths. [1] Gastric cancer is commoner among men than women and the highest recorded incidence rates are from Korea, Mongolia and Japan. In Africa, data on gastric cancer are scarce mainly due to fragmented diagnostic facilities in these low resource countries. [2] There are very few African countries with reliable population-based registries region. [3] The Global Cancer Incidence, Mortality and Prevalence estimates the incidence of gastric cancer in Africa to be between 5.2 per 100,000 in some countries such as Angola to more than 20.2 per 100,000 in Mali. [1] In Zambia, gastric cancer is estimated to be the tenth among common cancers but this is similarly limited by challenges of case detection. Gastric cancer is the third most commonly diagnosed gastrointestinal cancer after oesophageal and liver cancers in the gastrointestinal unit at the University Teaching Hospital (UTH), unpublished observation. The outcome of gastric cancer patients in Zambia is poor. We previously reported evidence that less than 15% of these patients live beyond one year after the initial diagnosis. [4] The advanced stage at which gastric cancer is diagnosed is one of the major contributors to the poor outcomes. Zambia has a referral system, in which patient’s first contact with healthcare is at primary care centres located in all districts of the country. Depending on the condition, the health care provider can then elect to refer them for secondary care offered at larger district and provincial hospitals. If specialist opinion is required, patients are then sent to tertiary institutions such as the UTH. Gastric cancer diagnosis can only be confirmed by examining a tissue sample obtained either endoscopically or during surgery, services that are not available in primary and most of the secondary care facilities. For a gastric cancer patient to be seen in a tertiary centre for confirmatory diagnosis, healthcare providers at the primary and secondary care levels have to promptly identify that such a patient needs urgent referral. This also depends on how quickly the patients present themselves at the health centres. With the poor outcomes and delayed gastric cancer diagnoses observed at UTH, we endeavoured to analyse the time frames from the onset of symptoms to clinical diagnosis in order to establish the contributors to late diagnosis. The University of Zambia Biomedical Research Ethics committee, reference number 000-03-16, approved this study.

METHODS
Patient enrolment
The study was carried out between July 2016 and April 2018 at the University Teaching Hospital (UTH) gastroenterology unit. All consenting patients above the age 18 years coming in for upper gastrointestinal endoscopy were considered for enrolment. Excluded were those with history of ingesting a caustic substance or an obvious oesophageal or other extra gastric malignancy. Informed and written consent was obtained from all participating patients.

Study procedures
Upper gastrointestinal endoscopy was carried out on all patients following standard guidelines. Any lesions seen were recorded. After the procedure, an interviewer-administered questionnaire was used to collect information on the onset of symptoms and first healthcare consultation. In addition the data on basic characteristic were also collected.

Data analysis
Categorical and continuous variables were summarised using proportions, medians and interquartile ranges. Binary variables were compared using Fisher’s exact test and Kruskal-Wallis test was used to compare continuous variables. In all instances, a two-sided P value of <0.05 was considered statistically significant. Statistical analysis was done in STATA 15 (College Station, TX, USA).

RESULTS
Basic characteristics of patients stratified by endoscopic diagnosis
### Table 1: Time from onset of symptoms to first consultation and endoscopic evaluation in patients stratified by endoscopic findings

<table>
<thead>
<tr>
<th>Endoscopic findings</th>
<th>Normal (n=186)</th>
<th>Cancer (n=92)</th>
<th>Other diagnoses* (n=110)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to first consultation</td>
<td>0 (0-13) weeks</td>
<td>2 (0-4) weeks</td>
<td>1 (0-8) weeks</td>
<td>1.000</td>
</tr>
<tr>
<td>Time to endoscopic diagnosis</td>
<td>16 (4-104)</td>
<td>12 (4-32)</td>
<td>8 (3-52)</td>
<td>0.120</td>
</tr>
</tbody>
</table>

#### Figure 1: Anatomical location of gastric cancer as seen during upper gastrointestinal endoscopy

- 35% Antrum
- 21% Body
- 30% Fundus
- 14% GE Junction
Figure 2: Presenting symptoms of patients with or without gastric tumours. Significance testing done with the Fisher’s exact test.

Figure 3: Time in weeks from onset of symptoms to diagnosis. Each horizontal line represents a gastric cancer patient. The x-axis shows time in weeks.
Figure 4: Time to endoscopic diagnosis stratified by presenting symptoms. Significance tested using the Kruskal-Wallis test, * p-value<0.05, ***p-value<0.001
We enrolled 388 patients, 207 (53%) of whom were female with median age of 51 years (IQR 41-65 years). Gastric cancer was seen endoscopically in 92 (24%) patients. Of those without gastric cancer 110/296 (37%) had benign mucosal lesions including gastric or duodenal ulcers, gastric erosions, varices, polyps and other oesophageal lesions. 

**Anatomical location and clinical presentation of gastric cancer.**

During the endoscopic procedures, the location of gastric cancer was recorded, and we found that 30% and 35% of the cancers were located in the antrum and body respectively. These are known as distal gastric cancers. The remaining 35 % were proximal cancers (Figure 1). The major presenting symptoms of each of the patients was then compared between gastric cancer patients and those without cancer. Gastric cancer patients were more likely to present with vomiting [OR 3.3, 95% CI 1.6-6.6; p=0.0005] or dysphagia [OR 9.9, 95% CI 2.8-43; p<0.0001] while those without cancer were more likely to present with abdominal pain [OR 0.5; 95% CI 0.3-0.9; p=0.01] (Figure 2).

**Time in weeks from onset of symptoms to first consultation, then endoscopy for gastric cancer patients**

Enrolled patients were asked about the time when their symptoms were first noticed and their first health care consultation. The median time from onset of symptoms to the first health care consultation was 2 weeks, IQR 0-4 weeks. It then took another median of 12 weeks, IQR 4-34 weeks for these patients to be sent for endoscopic diagnosis. The difference between these two time frames was statistically significant (p<0.0001). In Figure 3, the time to first consultation for each of the gastric cancer patients is shown in green, while the time to endoscopic diagnosis is shown in orange (Figure 3).

**Time in weeks from onset of symptoms to first consultation, then endoscopy for all enrolled patients**

The median time in weeks from onset of symptoms to first health care consultation was less than three weeks for all the patient groups. The time to endoscopic diagnosis was much longer with the highest median being 16 weeks for patients without mucosal lesions. The time to endoscopic diagnosis was highest in patients presenting with abdominal pain or anaemia and lowest among those with persistent vomiting or evidence of blood loss (Figure 4).

**DISCUSSION**

In this study, we present evidence that delayed gastric cancer diagnosis in Zambia is not just due to late patient presentation. Gastric cancer patients enrolled in this study did seek medical attention soon after noticing their symptoms but were not sent for diagnostic gastrointestinal endoscopy promptly. The referral system in Zambia is designed to reduce patient burden in tertiary institutions by making primary and secondary health facilities available in centres close to the communities. It is therefore, incumbent upon the healthcare providers in these centres to identify patients in need of referral for specialised care. Similar to other African countries such as South Africa, Rwanda and Malawi, [5, 6, 7] gastric cancer patients in Zambia present with very advanced disease and can therefore only be offered palliative care. Another example is Nigeria where it was reported that only 30% of gastric cancer patients presented within a year of the symptom development. [8]

Late diagnosis is one of the major contributors to poor outcomes. Until now, reasons for late gastric cancer diagnosis in Zambia have just been speculative, mainly focussing on late patient presentation. Our data show that the median time from onset of symptoms to first contact with health care providers was not as long as the time it took for patients to be given the final diagnosis. This difference was statistically significant. Our data do not allow us to determine if healthcare providers fail to identify the need for endoscopy. Another contributing factor could have been the non-specific nature of gastric cancer symptoms. Gastric cancer is one of those cancers without very distinct symptoms. In very early stages of disease, it is virtually asymptomatic making detection difficult. When symptoms are present, they are non-specific: poor appetite, unintentional weight loss, abdominal pain with fullness or swelling, reflux symptoms, nausea, vomiting (with or without blood), melaena or anaemia. [9] A patient might have just one or two of these symptoms which could also be a manifestation of other diseases that do not necessarily require endoscopic evaluation. In addition, many of these symptoms become obvious in advanced disease. In a breast cancer study done in Zambia, authors concluded that one of the reasons for late diagnosis was ignorance about the existence of the disease. [10] This might also be true for gastric cancer as well.

We then endeavoured to identify which symptoms most likely to be associated with delayed presentation. The least delay was in patients with blood loss or persistent vomiting, suggesting that health care providers did identify these symptoms as suspicious for conditions requiring endoscopy. It should be noted that overt bleeding and persistent vomiting which could be a sign of luminal occlusion are late symptoms of gastric cancer. [11] The longest delay to diagnosis was in patients with abdominal pain. This is not surprising as abdominal pain is a very common symptom and is usually not indicative of gastric cancer. It can be due to many other diseases some of which are outside the gastrointestinal tract.

Such delays in diagnoses could contribute towards patients by-passing the set out referral system in preference for direct consultation at tertiary centres. A study by Atkinson et al., showed that some patients in Zambia deliberately by-pass primary care centres and go directly to tertiary institutions. [12] There is some evidence that setting up screening camps for cancer diagnosis close to the communities could reduce diagnostic delays, [13] but the cost effectiveness for gastric cancer in Zambia has not be established. We recently published data in support of a non-invasive strategy that might be useful for early identification of patients with gastric cancer, but this is yet to be validated. [14]

This study has brought out information on gastric cancer diagnosis in Zambia that might be relevant to other cancers and medical conditions as well. Awareness of gastric cancer among health care workers needs to be increased. There is also need to conduct conduct more studies that will investigate particular reasons for each source of delay from onset of symptoms to final diagnosis and treatment.

**CONCLUSION**

Gastric cancer is diagnosed late in Zambia and this is not only due to late patient presentation. Patients presenting with abdominal pain have the longest delay.

**ACKNOWLEDGEMENTS**

We would like to acknowledge the three endoscopy nurses; Themb Baanda, Rose Soko and Joyce Sibwani for their assistance rendered during all the endoscopic procedures.

**FUNDING**

Research reported in this publication was supported by the Fogarty International Center of the United States National Institutes of Health under Award number D43 TW009744. The content is solely the responsibility of the authors and does not necessarily represent the views of the National Institutes of Health.
LIST OF REFERENCES