Prevalence and sociodemographic determinants of dyspepsia in the general population of Rwanda

Jean Bosco Bangamwabo,[1] John David Chetwood [iD],[2] Vincent Dusabejambo,[3,4] Cyprien Ntirenganya,[5] George Nuki,[6] Arcade Nkurunziza,[7,8] Kelly A Kieffer,[9] Michael Jones,[10] Timothy D Walker[2,11]

ABSTRACT

Introduction Dyspepsia accounts for a significant burden of worldwide disease, but there is a relative paucity of data from the sub-Saharan African setting. We undertook to describe the burden, risk factors and severity of dyspepsia across Rwanda.

Methods We performed a population-based clustered cross-sectional survey between November 2015 and January 2016, nationwide in Rwanda, using the Short Form Leeds Dyspepsia Questionnaire to describe the presence and severity of dyspepsia, and the Short Form Nepean Dyspepsia Index to describe the concomitant quality of life effects. Univariate and multivariate logistic regression models were constructed to correlate measured sociodemographic factors with dyspepsia.

Results The prevalence of clinically significant dyspepsia in the general Rwandan population was 14.2% (283/2000). The univariate factors that significantly predicted severity were gender, profession, socioeconomic status, and non-steroidal anti-inflammatory drug, aspirin and alcohol use, with gender, current smoking, aspirin use both in the past and currently, and alcohol use in the past remaining significant on multivariate modelling. Dyspeptics had a significantly lower gastrointestinal-related quality of life, though the sociodemographic factors measured did not modify the observed quality of life.

Conclusion Dyspepsia is prevalent in the Rwandan setting and is associated with a significant burden on quality of life. More work is required to determine the pathological entities involved, and the optimal approach to mitigating this burden.

Summary

What is already known about this subject?
► Dyspepsia is common globally, yet there is a lack of evidence from the African, sub-Saharan African and specifically Rwandan setting including the prevalence, and factors associated with its presence and severity.

What are the new findings?
► The national dyspepsia prevalence was 14.2% (283/2000). Thus, study validates multiple risk factors such as gender, aspirin, alcohol non-steroidal anti-inflammatory medication use, and profession/socioeconomic status as associated with dyspepsia prevalence. Dyspeptics had a significantly lower gastrointestinal-related quality of life, though the sociodemographic factors measured did not modify the observed quality of life.

How might it impact on clinical practice in the foreseeable future?
► This study validates the increasing importance that is being placed on global dyspepsia—but specifically the high burden of disease attributable to the Rwandan and sub-Saharan Africa. This corroborates gender, aspirin and alcohol as associated with the prevalence of dyspepsia. Further studies might further explore these associations as well as explore dose–response relations.

INTRODUCTION

Dyspepsia is a constellation of symptoms referable to the gastroduodenal territory of the upper gastrointestinal tract, specifically unpleasant sensations of epigastric pain, burning, postprandial fullness or early satiety, sometimes in association with heartburn.[1] [2] Dyspepsia is an extremely common symptom, accounting for 3%–4% of worldwide primary healthcare visits,[3] and the resultant social, psychological, and healthcare-related[4] burden of worldwide disease[1] is both economically significant and associated with reduced quality of life among those afflicted.[5]

The burden of dyspepsia in the primary care setting in sub-Saharan Africa is significant, but poorly characterised,[6] as most patients do not seek medical investigation,[7] with most prior evidence arising from work done in Nigeria.[8–10] Two prior studies have sought to the burden of dyspepsia in Rwanda among hospital-based healthcare workers[6] and patients referred for endoscopy,[11] but such data cannot be easily extrapolated to predict overall disease burden among the general population.

Strengths and limitations of this study

► A large population data set with a stratified sampling technique.
► Validated and internationally comparable questionnaires used in data collection, with a strict dyspepsia definition.
► Native Rwandan and Kinyarwanda speakers used to approach the participants.
► However, as a cross-sectional survey, we are unable to comment on causality, nor specifically whether the symptoms had attributable organic pathology or were from functional dyspepsia—and whether uninvestigated dyspepsia has a different natural history in this population to others.
► We were also unable to assess changes in the participants' dyspepsia and quality of life scores over time.

There is thus a lamentable deficit in population-level data about the prevalence of dyspepsia in sub-Saharan Africa, and its sociodemographic determinants, which limits public health and health system interventions aimed at reducing the burden of disease in these settings. Therefore, we undertook to investigate the prevalence of dyspepsia and its effects on gastrointestinal-related quality of life (GI-QoL) in a representative sample of the Rwandan general population, using locally validated, internationally accepted tools.

METHODS

We undertook a population-based clustered cross-sectional survey between November 2015 and January 2016, nationwide in Rwanda, with study subjects recruited from Kigali city and each of the four provinces.

Rwanda has a higher ordered local governance structure and this was leveraged to assist recruitment for the study. All residents in Rwanda are part of a 'village' which is in turn part of an administrative district, and these administrative districts in turn coalesce to give rise to four provinces, and a separate administrative area for the capital, Kigali, each with separate local governments. The vast majority of people identifying as Rwandan speak a single common language, Kinyarwanda, and all study consent and questionnaire processes were conducted in Kinyarwanda.

Sample size

A sample size of 1876 was calculated as necessary to detect the population prevalence of dyspepsia to within a 3.2% margin of error at a two-sided 95% CI, with a design effect factor of 2 and using an estimated dyspepsia prevalence of 5%, an intentionally more statistically conservative figure than the 30% used in previous studies for sample size calculation.[6 11] This number was increased by 6.5% to cater for possible non-responders, giving a total target sample size of 2000 participants.

Sampling strategy

Villages were chosen from across Rwanda for inclusion as recruitment sites in the study according to two levels of stratification. First, a list was made of all administrative districts within each of the four provinces as well as Kigali city (to make five 'provinces' in total), and four separate administrative districts in each province were randomly selected. A list of villages (a smaller administrative unit covering the whole of the population in both rural and urban areas) containing more than 100 households within each chosen administrative district was then compiled, and four villages were chosen at random from this list. In Kigali city there are only three districts, therefore two villages were selected from one district and one from each of the other two districts to make a total of four villages. Subsequently in each of these villages, consecutive households were visited in person by study research personnel and all willing eligible participants within each household recruited until 100 people had been recruited in total in that village. One hundred people were recruited in each village to make a total of 2000 participants from 20 villages, representing 19 different districts (four from each province and three from Kigali) across Rwanda.

Participant inclusion criteria:
► Participants over 21 years of age.
► Those able to give written informed consent (participants unable to read and write were enrolled if accompanied by a relative or friend who could assist them with the consent process).

Participant exclusion criteria:
► People with known mental health or intellectual disorders where assessing informed consent would be problematic.
► People who were not fluent in Kinyarwanda language and valid informed consent could therefore not be gained.

Questionnaire

The study questionnaire compiled after piloting, included sociodemographic data, the Short Form Leeds Dyspepsia Questionnaire (SF-LDQ) and the Short Form Nepean Dyspepsia Index (SF-NDI), both of which have been translated and validated for use in this context in Kinyarwanda.[6 11]

Sociodemographic data

The collected information included gender, age, province of residence, occupation, and socioeconomic status. Socioeconomic status was grouped into four strata according to established Rwandan governmental categories: the lowest income who did not own their house and did not have food security (category 1), those with low incomes but who owned their house and had food security (category 2), those with their own house and a modest income (category 3), and the more affluent (category 4).

Short Form Leeds Dyspepsia Questionnaire

The SF-LDQ is an eight-item symptom-based questionnaire based on the frequency and severity of dyspepsia symptoms, measured in the symptom domains of indigestion, heartburn, regurgitation and nausea. Scores

are ascribed according to the frequency and severity of each symptom, with larger scores indicating more severe dyspepsia, a possible score range of 0–32, and a discriminatory cut-off score of 16 for severe dyspepsia.[12] The questionnaire has been internationally validated[12] as well as specifically in the Rwandan context.[6 11] Specifically, the cut-off score of ≥16 has been validated in this context to accurately detect dyspepsia that correlates with the clinical diagnosis of experienced clinicians.[11]

Short Form Nepean Dyspepsia Index
The SF-NDI was created based on the Nepean Dyspepsia Index, which was developed to study quality of life in functional dyspepsia.[13 14] It comprises a 10-item questionnaire with two questions on each of five quality of life indicators known to be affected by dyspepsia (tension/anxiety; interference with daily activities; disruption to regular eating/drinking; knowledge and control over disease symptoms; and interference with work/study). Each aspect is rated according to severity by a 5-point Likert scale, from 0 ('not at all' or 'not applicable') to 5 ('extremely'), and the total score from the subscale is aggregated and collated to generate a total score from 0 (the lowest health score) up to 100 (the highest score), with higher scores indicating a worse health-related quality of life. The questionnaire has again been validated internationally[15 16] as well as specifically in the Rwandan context.[6 11]

Data and statistical analysis
Data were manually captured on paper forms, and double entered into a database software package STATA (V.13) with manual cross-checking by a second researcher. Determination of the risk of dyspepsia via SF-LDQ score, and severity of dyspepsia using SF-NDI score (once the diagnosis of dyspepsia was made) was via univariate and multiple unconditional logistic regression, in order to analyse the relative contribution of each factor to the overall model.

RESULTS
Demographics
Two thousand participants were recruited from November 2015 to January 2016, with equal numbers (n=400/2000 (20%)) taken from each of Kigali city and the four provinces.

There was a slight preponderance of females (1168/2000, 58%) among recruited participants. There was a roughly equal number of participants in each of the age demographics, 33.1% (661/2000) were 30 years of age or younger, 36.5% (730/2000) were 31–45 years of age while the remaining 30.4% (609/2000) were over the age of 45 years. A demographic breakdown is available in table 1.

The prevalence of clinically significant dyspepsia in the general Rwandan population was 14.1% (283/2000), when defined by an SF-LDQ score greater than or equal to 16.

Univariate analysis of dyspepsia risk factors (SF-LDQ)
Risk factors for dyspepsia that reached significance in a univariate model (see table 1) included: gender, profession, socioeconomic status, non-steroidal anti-inflammatory drug (NSAID), aspirin and alcohol use. Factors that did not reach significance included age, marital status, having children, and smoking. Where the stated profession was unsure/other or where the respondent was unsure of an exposure, as a subgroup this response was thought to be heterogeneous and not statistically analysed—hence subgroup totals may not always equal 2000.

Multivariate analysis of dyspepsia risk factors (SF-LDQ)
A multivariate model using an adjusted Wald test found that gender, current smoking, aspirin in the past and currently and alcohol use in the past remained significant for predicting dyspepsia while profession, socioeconomic status, and NSAID use did not (see table 2). The logistic regression was able to predict dyspepsia under the receiver operating characteristic curve being 0.6501 (95% CI 0.615 to 0.685).

Analysis of dyspepsia symptoms (by SF-LDQ)
In our study, among those who suffered from dyspepsia, the most frequent severe symptom was upper abdominal pain and heartburn (both 42.4%), followed by nausea (33.6%) then regurgitation (27.2%). See table 3 for more information.

Effect of dyspepsia on quality of life (SF-NDI)
For all the assessed quality of life indicators, dyspepsia was associated with significantly lower GI-QoL when compared with non-dyspeptic controls. The presence of dyspepsia was therefore associated with a negative impact on all of: feelings of tension and anxiety, with interference with daily activities score, disruption to regular eating and drinking habits, knowledge towards control disease, and interference with work (all p<0.0001, table 4).

Univariate analysis of dyspepsia severity (SF-NDI)
Risk factors for a worse dyspepsia severity (via the SF-NDI, once dyspepsia was established) that reached significance in a univariate model (see table 5) were socioeconomic status only.

Multivariate analysis of dyspepsia severity (SF-NDI)
Using a multivariate logistic regression model, none of the univariate factors reached significance with regard to dyspepsia severity.

DISCUSSION
This study describes a high prevalence of 14.2% of clinically significant dyspepsia among the community-based Rwandan population. It demonstrates a major reduction of GI-QoL among those with dyspepsia, and shows that, as in other populations, gender, socioeconomic status and lifestyle factors are significant modifiers of dyspepsia

Table 1 Socioeconomic data with univariate dyspepsia risk factors (SF-LDQ)

Variable	Proportion with dyspepsia (n/total (%))	OR	SE	P value	95% CI
Age					
≤30	87/661 (13.2)	1.003	0.005	0.58	0.989 to 1.018
31–45	105/730 (14.4)				
≥45	91/609 (14.9)				
Gender					
Male	79/832 (9.5)	–	–	–	
Female	204/1168 (17.5)	2.017	0.16	0.001*	1.618 to 2.514
Profession					
Unemployed	20/135 (14.8)	–	–	–	
Farmer	209/1350 (15.5)	0.979	0.309	0.95	0.408 to 2.351
Student	17/123 (13.8)	0.857	0.297	0.68	0.327 to 2.246
Private sector	26/253 (10.3)	0.612	0.17	0.152	0.283 to 1.323
Public sector	5/109 (4.6)	0.257	0.081	0.012*	0.107 to 0.615
Socioeconomic status					
Category 1	44/221 (19.9)	–	–	–	
Category 2	165/1230 (13.4)	0.623	0.103	0.045*	0.395 to 0.985
Category 3	72/541 (13.3)	0.618	0.204	0.219	0.246 to 1.548
Category 4	2/8 (25.0)	1.341	0.524	0.495	0.453 to 3.968
Marital status					
Single	54/391 (13.8)	–	–	–	
Married	191/1387 (13.8)	0.997	0.124	0.98	0.705 to 1.409
Divorced	3/20 (15.0)	1.101	0.404	0.805	0.398 to 3.047
Widow	35/202 (17.3)	1.308	0.471	0.498	0.481 to 3.556
Having children					
Has children	224/1554 (14.4)	–	–	–	
No children	59/446 (13.2)	0.905	0.074	0.292	0.721 to 1.137
Smoking					
Never	211/1600 (13.8)	–	–	–	
In the past	39/222 (17.6)	1.403	0.282	0.167	0.803 to 2.451
Currently	31/173 (17.9)	1.437	0.236	0.091	0.912 to 2.265
NSAID use					
Never	104/738 (14.1)	–	–	–	
In the past	149/1164 (12.8)	0.895	0.166	0.581	0.535 to 1.497
Currently	27/81 (33.3)	3.048	1.217	0.049*	1.006 to 9.233
Aspirin use					
Never	114/963 (10.6)	–	–	–	
In the past	136/681 (16.7)	1.687	0.173	0.007*	1.27 to 2.241
Currently	25/59 (29.8)	3.579	0.648	0.002*	2.166 to 5.916
Alcohol use					
Never	70/590 (11.9)	–	–	–	
In the past	84/415 (20.2)	1.885	0.125	0.001*	1.569 to 2.265
Currently	128/990 (12.9)	1.103	0.157	0.528	0.743 to 1.637

*Denotes a significant value with p<0.05.
NSAID, non-steroidal anti-inflammatory drug; SF-LDQ, Short Form Leeds Dyspepsia Questionnaire.

Table 2 Multivariate dyspepsia risk factors

Variable	OR	SE	P value	95% CI
Gender				
Male	–	–	–	
Female	2.209	0.165	<0.0001*	1.794 to 2.72
Smoking				
Never	–	–	–	
In the past	1.349	0.322	0.279	0.695 to 2.619
Currently	1.941	0.321	0.016*	1.227 to 3.07
Aspirin use				
Never	–	–	–	
In the past	1.608	0.191	0.016*	1.157 to 2.234
Currently	3.606	0.67	0.002*	2.153 to 6.039
Alcohol use				
Never	–	–	–	
In the past	1.751	0.172	0.005*	1.333 to 2.3
Currently	1.136	0.212	0.531	0.677 to 1.907

*Denotes a significant value with p<0.05.

prevalence in Rwanda.[6 11] This is the first study of which we are aware to describe in depth the epidemiology and burden of dyspepsia in Rwanda. It validates the growing concern for dyspepsia as a major driver of reduced quality of life and increased healthcare utilisation in sub-Saharan Africa, which is still poorly characterised and understood.

This is the first African study to use a rigorous sampling method and definition of dyspepsia applied to the general population instead of those already presenting to healthcare for other potentially related reasons. Other studies from Africa reporting high headline dyspepsia prevalence have either enrolled an endoscopy referral population, used a liberal definition of dyspepsia, or both, leaving the extrapolation of their findings to clinical and public health practice in the wider population open to question. For example, the general population dyspepsia prevalence of 14.1% found in this study is lower than the prevalences of 45%, 26% and 29% found in prior African work conducted in Nigeria.[8–10] Similarly, in a study from Kenya, in adult diabetics attending an outpatient setting, 53.3% suffered from dyspepsia.[17] In lower income settings further afield, dyspepsia has been reported at prevalences of 29.9% and 54.6% in Iran,[18 19] 30.4% in India,[20] and 60.1% in Jordan.[21] Globally, the prevalence of dyspepsia has been estimated at 21%, though with geographical and methodological variation.[22]

Many of these studies used different tools to assess dyspepsia, many using a much looser definition of any upper abdominal discomfort and others using older Rome criteria. Although a direct comparison is not possible, if our study was to assume a definition of dyspepsia that included any upper abdominal pain in the last month, the reported headline prevalence would dramatically increase (from 14.1% to 92.9%). A strength to our study is this rigorous, internationally validated,

definition. It is unclear whether the international prevalence differences noted above are due to corresponding differences in disease definition, true disease burden or both. Further work at an epidemiological level in other African countries is certainly required.

Bitwayiki *et al*'s previous Rwandan study,[6] conducted in a single tertiary hospital survey of healthcare workers and using a liberal definition of dyspepsia, had estimated the prevalence to be 38.9%[6] in that population. The definition of dyspepsia used in the current study was much stricter, corresponding to the category of 'severe dyspepsia' in that study, with 10.2% being the corresponding comparator prevalence from that study. The current work thus suggests that clinically significant (or 'severe') dyspepsia is more prevalent among the general population than healthcare workers in Rwanda, possibly due to differences in health literacy, illness behaviour and access to care between healthcare workers and the wider population.

Dyspepsia risk factors
Gender
We found female gender to be a significant risk factor in both the univariate and multivariate models for the prevalence of dyspepsia, but not dyspepsia's impact on quality of life. The two previous studies in Rwanda suggest a female preponderance among those with dyspepsia,[6 11] which was also found in this study (36.3% for females vs 21.4% for males). This gender-based risk accords with other international studies,[6 18 23] and a recent global meta-analysis by Ford *et al*[22] also found that for uninvestigated dyspepsia, the prevalence was slightly higher in females compared with males (25.3% vs 21.9%, OR 1.24; 95% CI 1.13 to 1.36), but with significant heterogeneity among studies. In Ford's meta-analysis this did not

Table 3 SF-LDQ in dyspeptics and non-dyspeptics

	Symptom frequency (n, %)				Interference with lifestyle (n, %)			
	No dyspepsia		Dyspepsia		No dyspepsia		Dyspepsia	
Total	1717	(100%)	283	(100%)	1717	(100%)	283	(100%)
Upper abdominal pain								
Never	1232	71.8%	8	2.8%	1347	78.5%	13	4.6%
<Monthly	211	12.3%	12	4.2%	229	13.3%	26	9.2%
>Monthly, <weekly	172	10.0%	60	21.2%	101	5.9%	73	25.8%
>Weekly, <daily	55	3.2%	83	29.3%	24	1.4%	74	26.1%
>Daily	47	2.7%	120	42.4%	16	0.9%	97	34.3%
Heartburn								
Never	1159	67.5%	9	3.2%	1321	76.9%	13	4.6%
<Monthly	243	14.2%	9	3.2%	231	13.5%	20	7.1%
>Monthly, <weekly	191	11.1%	57	20.1%	110	6.4%	65	23.0%
>Weekly, <daily	86	5.0%	88	31.1%	41	2.4%	89	31.4%
>Daily	38	2.2%	120	42.4%	14	0.8%	96	33.9%
Regurgitation								
Never	1349	78.6%	23	8.1%	1444	84.1%	27	9.5%
<Monthly	186	10.8%	20	7.1%	170	9.9%	31	11.0%
>Monthly, <weekly	111	6.5%	62	21.9%	75	4.4%	72	25.4%
>Weekly, <daily	57	3.3%	101	35.7%	24	1.4%	90	31.8%
>Daily	14	0.8%	77	27.2%	4	0.2%	63	22.3%
Nausea								
Never	1291	75.2%	21	7.4%	1410	82.1%	23	8.1%
<Monthly	246	14.3%	22	7.8%	205	11.9%	38	13.4%
>Monthly, <weekly	108	6.3%	74	26.1%	68	4.0%	84	29.7%
>Weekly, <daily	52	3.0%	71	25.1%	27	1.6%	67	23.7%
>Daily	20	1.2%	95	33.6%	7	0.4%	71	25.1%

SF-LDQ, Short Form Leeds Dyspepsia Questionnaire.

reach significance in the sub-Saharan African context (OR 0.93, 95% CI 0.73 to 1.19), which may be attributable to the paucity of data, as the subgroup meta-analysis only included two studies both from Nigeria. As yet there has not been a convincing mechanism asserted for the gender discrepancy observed.

Smoking

Smoking has become increasingly socially taboo in the Rwandan context, and although current smoking has been recognised as a risk factor by Ford et al in their meta-analysis (OR 1.25; 95% CI 1.12 to 1.40)[22] based on 19 pooled studies, we did not find tobacco use to be a

Table 4 SF-NDI comparison (dyspeptics vs non-dyspeptics)

SF-NDI variables	Dyspeptics (mean)	Non-dyspeptics (mean)	Difference (means)	95% CI (difference)	P value
Tension/anxiety score	10.61	2.75	7.86	7.34 to 8.37	<0.0001
Interference with daily activities score	10.46	2.56	7.90	7.40 to 8.40	<0.0001
Disruption with regular eating/drinking score	11.01	2.87	8.14	7.62 to 8.66	<0.0001
Knowledge/control disease score	8.4	2.16	6.24	5.83 to 6.65	<0.0001
Interference with work score	10.69	2.57	8.12	7.62 to 8.62	<0.0001
Overall score	47.44	10.18	37.27	34.97 to 39.56	<0.0001

SF-NDI, Short Form Nepean Dyspepsia Index.

Table 5 Univariate dyspepsia severity risk factors (SF-NDI)

Variable	Coefficient	SE	P value	95% CI
Age	−0.06	0.056	0.347	−0.215 to 0.096
Gender				
Male	–	–	–	
Female	−8.597	4.928	0.156	−22.28 to 5.087
Profession				
Unemployed	–	–	–	
Farmer	−3.666	5.151	0.516	−17.966 to 10.635
Student	−9.095	16.587	0.613	−55.147 to 36.957
Private sector	−10.538	6.123	0.16	−27.539 to 6.462
Public sector	−27.354	9.927	0.051	−54.916 to 0.208
Socioeconomic status				
Category 1	–	–	–	
Category 2	−6.773	3.119	0.118	−16.699 to 3.153
Category 3	−9.058	2.428	0.034*	−16.787 to −1.33
Category 4	−22.864	2.856	0.004*	−31.953 to −13.774
Marital status				
Single	–	–	–	
Married	−5.668	4.174	0.246	−17.258 to 5.922
Divorced	−29.815	20.635	0.222	−87.106 to 27.476
Widow	−1.815	8.613	0.843	−25.729 to 22.099
Having children				
Has children	–	–	–	
No children	8.105	5.661	0.225	−7.612 to 23.823
Smoking				
Never	–	–	–	
In the past	2.178	3.841	0.601	−8.488 to 12.843
Currently	6.75	7.993	0.446	−15.441 to 28.941
NSAID use				
Never	–	–	–	
In the past	−2.364	4.744	0.644	−15.536 to 10.808
Currently	−5.991	8.297	0.51	−29.026 to 17.045
Aspirin use				
Never	–	–	–	
In the past	0.859	1.691	0.638	−3.835 to 5.554
Currently	−3.996	6.825	0.59	−22.945 to 14.952
Alcohol use				
Never	–	–	–	
In the past	0.219	5.767	0.972	−15.793 to 16.231
Currently	1.593	5.767	0.796	−14.418 to 17.605

*Denotes a significant value with p<0.05.
NSAID, non-steroidal anti-inflammatory drug; SF-NDI, Short Form Nepean Dyspepsia Index.

predictor of dyspepsia prevalence or severity in Rwanda in this or our prior study.

Tobacco smoking may impair barrier function via reduced prostaglandin synthesis, mucous secretion, and epidermal growth factor secretion, as well as reducing gastric blood flow[24] and potentiating the relaxation of the lower oesophageal sphincter.[25] Furthermore, nicotine, a key component of tobacco, potentiates mucosal injury by augmenting pepsin and acid secretion, duodenogastric reflux, and production of free radicals.[26] Smoking

has also been linked with duodenal eosinophilia, which in turn has been linked with functional dyspepsia.[27] However, with the prevalence of current smoking in our study being only 7%, the most likely reason for the lack of any significant effect for smoking on dyspepsia is inadequate power, with the observed effect statistically similar to Ford's work, but with wide CIs.

Aspirin and NSAIDs
We observed current and past aspirin use to be a significant risk factor in univariate analysis and multivariate analysis for the presence of dyspepsia, but not severity. Current NSAID use was a risk factor in univariate but not multivariate analysis for the presence of dyspepsia, but also did not predict severity.

Aspirin and NSAIDs may cause gastroduodenal toxicity via various mechanisms, including prostaglandin and nitric oxide inhibition which may cause increased gastric acid secretion, decreased mucus and bicarbonate secretion, decreased cell proliferation, decreased mucosal blood flow and increased intestinal permeability.[28] However, similar to tobacco, the relationship between medication use and dyspepsia is complex, as the presence of dyspepsia may in turn discourage clinicians and patients from using aspirin and NSAIDs.

NSAIDs have been implicated internationally as a risk factor for dyspepsia (OR 1.59; 95% CI 1.27 to 1.99)[22] and 'Indulgence in self-medication' was found to be a significant risk factor for unexplained dyspepsia in Nigeria.[8] However, generally, there are a paucity of data in this area to further delineate the association, and a longitudinal study of African population-based cohorts may be required to tease out the temporal relationships involved.

Alcohol
Alcohol use in the past was found to be a significant risk factor in both the univariate and multivariate models, but did not predict severity. Current use of alcohol was not predictive of dyspepsia presence or severity.

Alcohol decreases gastric motility in mice[29] and human subjects[30] as well as increasing intestinal permeability and microbiotal alterations.[31] The association of alcohol with dyspepsia has been inconsistent, and it has previously not been demonstrated to be significant in the Rwandan[6] and wider sub-Saharan African[32] context. While other explanations are possible, including the lack of any true effect of alcohol on dyspepsia, this may be due to cultural or clinical beliefs encouraging those with dyspepsia to reduce or cease their alcohol intake. Once again, a cohort study would be required to better delineate the nature of this potentially complex relationship over time.

Socioeconomic status and profession
Socioeconomic status did not predict the presence, but did predict the severity of dyspepsia in a univariate but not multivariate model (with greater affluence being protective).

The link with dyspepsia and socioeconomic status has not been consistently identified, with many negative studies.[33 34] However, there may be a socioeconomic link with *Helicobacter pylori* infection,[12 35–37] and which was also found in Denmark by Wildner-Christensen *et al*[37] and the UK,[38] and unemployment was implicated in a study across seven international sites.[39] In the Rwandan context, higher educational attainment has previously been found to be protective,[6] suggesting that there may be true variation depending on the prevalence of *H. pylori* in the population.

One issue with evaluating an association in general is the different socioeconomic status strata, cultures, average incomes, professions and sanitary conditions in these groups internationally. This means that international comparisons of lower socioeconomic groups involve significant heterogeneity and are generally problematic.

Impact on quality of life
In our study, the most frequent and most troublesome symptoms for dyspeptic participants were abdominal pain and heartburn, followed by nausea. This result is similar to those previously found in Rwanda,[6] the UK,[12] and Malaysia.[7]

Participants with dyspepsia had significant reduced GI-QoL, with SF-NDI mean subscores ranging from 8.4 to 11.0, compared with 2.2 to 2.9 in non-dyspeptics (p<0.0001 for each). This severe impact on participants' quality of life further validates the clinical relevance of the strict definition of dyspepsia used. It also shows the importance that should be placed on dyspepsia at a population level, as untreated dyspepsia debilitates people, and some pathologies underlying dyspepsia can cause major morbidity or death.

Strengths and limitations
This is the first study we are aware of characterising the prevalence and burden of dyspepsia in the Rwandan general population.

Some specific strengths of this study are the large population data set and the stratified sampling technique used. Whereas previous studies have characterised certain subpopulations or locations, we endeavoured to accurately recruit a representative population across the whole country in a systematic matter. A further strength is the validated and internationally comparable questionnaire used in data collection, and the native Rwandan and Kinyarwanda speakers used to approach the participants.

We used a much stricter definition of dyspepsia than most other studies, a definition which is robust and well validated in this context. Though compared with more liberal definitions of dyspepsia, our approach underestimates the headline dyspepsia prevalence figure, the major impact on observed quality of life demonstrates the merit of our approach identifying those with significant afflictions, who could be the target for further research on endoscopy findings and targeted interventions. On

the other hand, we could not assess early satiety or post-prandial fullness as these are not included on the SF-LDQ and it is possible we underestimated the prevalence of dyspepsia.

We recruited a female preponderance, and predominantly participants from a low socioeconomic background. However, given the general population of Rwanda and the 1994 genocide that predominantly affected males,[40] this likely describes the Rwandan population and therefore validates our sampling technique. Due to the sampling technique, we were unable to recruit participants from small villages (under 100 people), and though we are not aware of any evidence this would affect the data collection, we cannot know and therefore rule out that this would introduce a small bias. Because participants were recruited from their own homes and clustered sampling in villages was done, there is a possibility of systematic bias in that those available at home may differ from those not available.

As a cross-sectional survey, the study could not inform us about causality, nor specifically whether the symptoms had attributable organic pathology or were from functional dyspepsia—and whether uninvestigated dyspepsia has a different natural history in this population to others. We were also unable to assess changes in the participants' dyspepsia and quality of life scores over time, as is usual with single time point cross-sectional surveys. Further follow-up and investigation in the studied cohort may be informative in this regard.

CONCLUSION

This study describes a high dyspepsia prevalence, and major associated quality of life burden, in the general Rwandan population. These data add weight to the increasing importance that is being placed on dyspepsia in the sub-Saharan and global context, and emphasise the need for further efforts directed towards investigating the causes of this symptom burden, as well as effective public health and clinical strategies to reducing dyspepsia prevalence and burden in Africa. We believe further research efforts should be directed towards eliciting the aetiology and associated factors directing both dyspepsia prevalence and severity, and particularly whether such factors are global in nature or unique to the Rwandan or sub-Saharan African setting.

Author affiliations
[1]Department of Internal Medicine, Kibuye Referral Hospital, Kibuye, Rwanda
[2]Calvary Mater Newcastle, Waratah, New South Wales, Australia
[3]Department of Internal Medicine, Kigali University Teaching Hospital, Kigali, Rwanda
[4]Department of Internal Medicine, School of Medicine and Pharmacy, College of Medicine and Health Sciences, University of Rwanda, Kigali, Rwanda
[5]Department of Internal Medicine, University Teaching Hospital of Butare, Butare, Rwanda
[6]University of Edinburgh, Edinburgh, UK
[7]Kibungo Hospital, Kibungo, Eastern Province, Rwanda
[8]Department of Internal Medicine, Kibungo Referral Hospital, Ngoma District, Rwanda
[9]Geisel School of Medicine at Dartmouth, Hanover, New Hampshire, USA
[10]Psychology Faculty, Macquarie University, Sydney, New South Wales, Australia
[11]School of Medicine and Public Health, University of Newcastle, Newcastle, New South Wales, Australia

ORCID iD
John David Chetwood http://orcid.org/0000-0002-8947-9817

REFERENCES

1 Talley NJ, Ford AC, Dyspepsia F. Functional dyspepsia. *N Engl J Med* 2015;373:1853–63.
2 Beers MH, Porter RS, *et al*. *The Merck manual of diagnosis and therapy*. 8th edition. White house station, NJ: Merck Research Laboratories, 2006.
3 Bodger K, Eastwood PG, Manning SI, *et al*. Dyspepsia workload in urban general practice and implications of the British Society of gastroenterology dyspepsia guidelines (1996). *Aliment Pharmacol Ther* 2000;14:413–20.
4 Nellesen D, Yee K, Chawla A, *et al*. A systematic review of the economic and humanistic burden of illness in irritable bowel syndrome and chronic constipation. *J Manag Care Pharm* 2013;19:755–64.
5 Aro P, Talley NJ, Agréus L, *et al*. Functional dyspepsia impairs quality of life in the adult population. *Aliment Pharmacol Ther* 2011;33:1215–24.
6 Bitwayiki R, Orikiiriza JT, Kateera F, *et al*. Dyspepsia prevalence and impact on quality of life among Rwandan healthcare workers: a cross-sectional survey. *S Afr Med J* 2015;105:1064–9.
7 Mahadeva S, Yadav H, Rampal S, *et al*. Ethnic variation, epidemiological factors and quality of life impairment associated with dyspepsia in urban Malaysia. *Aliment Pharmacol Ther* 2010;31:1141–51.
8 Ihezue CH, Oluwole FS, Onuminya JE, *et al*. Dyspepsias among the highlanders of Nigeria: an epidemiological survey. *Afr J Med Med Sci* 1996;25:23–9.
9 Holcombe C, Omotara BA, Padonu MK, *et al*. The prevalence of symptoms of dyspepsia in North eastern Nigeria. A random community based survey. *Trop Geogr Med* 1991;43:209–14.
10 Hameed L, Onyekwere CA, Otegbayo JA, *et al*. A clinicopathological study of dyspeptic subjects in Lagos, Nigeria. *Gastroenterol Insights* 2012;4:11.
11 Nkurunziza A, Dusabejambo V, Everhart K, *et al*. Validation of the Kinyarwanda-version short-form Leeds dyspepsia questionnaire and short-form Nepean dyspepsia index to assess dyspepsia prevalence and quality-of-life impact in Rwanda. *BMJ Open* 2016;6:e011018.

12 Fraser A, Delaney BC, Ford AC, *et al*. The short-form Leeds dyspepsia questionnaire validation study. *Aliment Pharmacol Ther* 2007;25:477–86.

13 Talley NJ, Verlinden M, Jones M. Validity of a new quality of life scale for functional dyspepsia: a United States multicenter trial of the Nepean dyspepsia index. *Am J Gastroenterol* 1999;94:2390–7.

14 Talley NJ, Verlinden M, Jones M. Quality of life in functional dyspepsia: responsiveness of the Nepean dyspepsia index and development of a new 10-item short form. *Aliment Pharmacol Ther* 2001;15:207–16.

15 Tian X-P, Li Y, Liang F-R, *et al*. Translation and validation of the Nepean dyspepsia index for functional dyspepsia in China. *World J Gastroenterol* 2009;15:3173–7.

16 Mahadeva S, Wee H-L, Goh K-L, *et al*. Quality of life in South East Asian patients who consult for dyspepsia: validation of the short form Nepean dyspepsia index. *Health Qual Life Outcomes* 2009;7:45.

17 Wafula JM, Lule GN, Otieno CF, *et al*. Upper gastrointestinal findings in diabetic outpatients at Kenyatta national Hospital, Nairobi. *East Afr Med J* 2002;79:232–6.

18 Khademolhosseini F, Mehrabani D, Zare N, *et al*. Prevalence of dyspepsia and its correlation with demographic factors and lifestyle in Shiraz, southern Iran. *Middle East J Dig Dis* 2010;2:24-30.

19 Yazdanpanah K, Moghimi N, Yousefinejad V, *et al*. Dyspepsia prevalence in general population aged over 20 in the West part of Iran. *J Pak Med Assoc* 2012;62:672–6.

20 Shah SS, Bhatia SJ, Mistry FP. Epidemiology of dyspepsia in the general population in Mumbai. *Indian J Gastroenterol* 2001;20:103–6.

21 Farsakh NA, Saadeh A, Rawshdeh M, *et al*. Dyspepsia in the general population in Jordan. *Indian J Gastroenterol* 2000;19:68–70.

22 Ford AC, Marwaha A, Sood R, *et al*. Global prevalence of, and risk factors for, uninvestigated dyspepsia: a meta-analysis. *Gut* 2015;64:1049–57.

23 Shaib Y, El-Serag HB. The prevalence and risk factors of functional dyspepsia in a multiethnic population in the United States. *Am J Gastroenterol* 2004;99:2210–6.

24 Guslandi M, Sorghi M, Pontikaki I, *et al*. Gastric microcirculation and bicarbonate production in heavy smokers. *Eur J Gastroenterol Hepatol* 1995;7:985–7.

25 Dodds WJ, Hogan WJ, Helm JF, *et al*. Pathogenesis of reflux esophagitis. *Gastroenterology* 1981;81:376–94.

26 Nandurkar S, Talley NJ, Xia H, *et al*. Dyspepsia in the community is linked to smoking and aspirin use but not to Helicobacter pylori infection. *Arch Intern Med* 1998;158:1427–33.

27 Walker MM, Aggarwal KR, Shim LS, *et al*. Duodenal eosinophilia and early satiety in functional dyspepsia: confirmation of a positive association in an Australian cohort. *J Gastroenterol Hepatol* 2014;29:474–9.

28 Bjarnason I, Scarpignato C, Holmgren E, *et al*. Mechanisms of Damage to the Gastrointestinal Tract From Nonsteroidal Anti-Inflammatory Drugs. *Gastroenterology* 2018;154:500–14.

29 Bagyánszki M, Krecsmarik M, De Winter BY, *et al*. Chronic alcohol consumption affects gastrointestinal motility and reduces the proportion of neuronal NOS-immunoreactive myenteric neurons in the murine jejunum. *Anat Rec* 2010;293:1536–42.

30 Bode C, Bode JC. Alcohol's role in gastrointestinal tract disorders. *Alcohol Health Res World* 1997;21:76–83.

31 Reding KW, Cain KC, Jarrett ME, *et al*. Relationship between patterns of alcohol consumption and gastrointestinal symptoms among patients with irritable bowel syndrome. *Am J Gastroenterol* 2013;108:270–6.

32 Seid A, Tamir Z, Demsiss W. Uninvestigated dyspepsia and associated factors of patients with gastrointestinal disorders in Dessie referral Hospital, northeast Ethiopia. *BMC Gastroenterol* 2018;18:13.

33 Furman SN, Cheetham RF, Becker PJ, *et al*. Demographic, socioeconomic, and stress factors in patients with upper-gastrointestinal symptoms (dyspepsia): impact on the therapeutic response to cisapride. *Current Therapeutic Research* 1995;56:545–55.

34 Hollnagel H, Nørrelund N, Larsen S. [Gastrointestinal symptoms among 40-year olds in Glostrup. An epidemiological study]. *Ugeskr Laeger* 1982;144:267–73.

35 Mahadeva S, Chan W-K, Mohazmi M, *et al*. Validation study of the Leeds dyspepsia questionnaire in a multi-ethnic Asian population. *J Gastroenterol Hepatol* 2011;26:1669–76.

36 Karaca C, Güler N, Yazar A, *et al*. Is lower socio-economic status a risk factor for Helicobacter pylori infection in pregnant women with hyperemesis gravidarum? *Turk J Gastroenterol* 2004;15:86–9.

37 Wildner-Christensen M, Hansen JM, De Muckadell OBS. Risk factors for dyspepsia in a general population: non-steroidal anti-inflammatory drugs, cigarette smoking and unemployment are more important than Helicobacter pylori infection. *Scand J Gastroenterol* 2006;41:149–54.

38 Moayyedi P, Forman D, Braunholtz D, *et al*. The proportion of upper gastrointestinal symptoms in the community associated with Helicobacter pylori, lifestyle factors, and nonsteroidal anti-inflammatory drugs. Leeds help Study Group. *Am J Gastroenterol* 2000;95:1448–55.

39 Stanghellini V. Relationship between upper gastrointestinal symptoms and lifestyle, psychosocial factors and comorbidity in the general population: results from the Domestic/International gastroenterology surveillance study (digest). *Scand J Gastroenterol* 1999;231:29–37.

40 de Walque D, Verwimp P. The demographic and socio-economic distribution of excess mortality during the 1994 genocide in Rwanda. *J Afr Econ* 2010;19:141–62.