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AN OVERVIEW OF ADULT CORROSIVE INGESTION INJURIES IN A SUB-SAHARAN AFRICAN SETTING

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DECLARATION

I, Matthias Frank Scriba, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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LIST OF FIGURES AND TABLES

Supplementary Table:

ABBREVIATIONS

BP	Blood pressure
CT	Computerised tomography
CXR	Chest X-ray
ECMO	Extracorporeal membrane oxygenation
FT necrosis	Full thickness necrosis
HIV	Human immunodeficiency virus
ICU	Intensive care unit
NPV	Negative predictive value
PPV	Positive predictive value
ROC AUC	Receiver operator characteristic area under the curve
SSA	sub-Saharan Africa
WCC	White cell count

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ADULT ACUTE CORROSIVE INGESTION INJURIES IN A SUB-SAHARAN AFRICAN SETTING

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ABSTRACT

BACKGROUND

Corrosive ingestion remains an important global pathology with high associated morbidity and mortality. Data on the acute management of adult corrosive injuries from sub-Saharan Africa (SSA) is scarce, with international investigative algorithms, relying heavily on computerised tomography (CT), having limited availability in this setting.

AIM

To investigate the corrosive injury spectrum in a low-resource setting and the applicability of parameters for predicting full-thickness (FT) necrosis and mortality.

METHODS

A retrospective analysis of a prospective corrosive injury registry (1st March 2017 – 31st October 2023) was performed to include all adult patients with acute corrosive ingestion managed at a single, academic referral centre in Cape Town, South Africa. Patient demographics, corrosive ingestion details, initial investigations, management, and short-term outcomes were described using simple descriptive statistics while univariate analyses with receiver operator characteristic area under the curve (ROC AUC) were used to identify factors predictive of FT necrosis and short-term mortality on admission. CT (grade III corrosive CT grading), endoscopy (Zargar IIIB), and blood gas findings were specifically analysed for FT necrosis prediction performance.

RESULTS

A total of 100 patients were included, with a mean age of 32 years (SD: 11.2 years) and a male predominance (65.0%). The majority (73.0%) were intentional suicide attempts. Endoscopy on admission was the most frequent initial investigation performed (95 patients), while only 17 were assessed with CT. A chest X-ray (CXR) was performed in 82 patients and only one patient was initially assessed using a contrast swallow examination. Neither CXR nor early contrast swallow findings directly influenced the management in any of these cases. Twenty patients required acute surgery with 17 having full thickness necrosis at surgery, of which eleven underwent emergency resection and six were palliated. Five patients underwent oesophagogastrectomy and five total gastrectomy, with two requiring extended resections (pancreas-preserving duodenectomy and proximal jejunal resection). Thirty-day mortality was 14,0% and morbidity 27,0%. Patients with full thickness necrosis at surgery and those with an established perforation had a 30-day mortality of 58.8% and 91,0%, respectively. Full thickness necrosis was associated with a cumulative survival of 17.6% at 2 years. Univariate analyses with ROC AUC showed admission endoscopy findings, CT findings, and blood gas findings, specifically pH, base excess, and lactate, to all have significant predictive value for full thickness necrosis, with endoscopy proving to have the best predictive value (AUC 0.850). CT and endoscopy findings were the only factors predictive of early mortality, with CT performing better than endoscopy (AUC 0.798 vs 0.759).

CONCLUSION

Intentional corrosive injuries result in devastating morbidity and mortality. Locally, early endoscopy remains the mainstay of severity assessment, but referral for CT imaging should be considered especially when blood gas findings are abnormal.

Key words: corrosive injuries; caustic injuries; adult; short-term survival

Core tip:

Management of acute adult corrosive injuries remains internationally under-reported, but specifically in sub-Saharan Africa. This large series of 100 patients highlights the high rates of morbidity and mortality, especially when full thickness necrosis is established. Predicting necrosis on admission is challenging, with international guidelines proposing CT as the investigation of choice. With limited availability of CT, endoscopy still performs well in our setting. CT should be considered in patients with suspected severe corrosive injury with abnormal findings on blood gas (pH, base excess, and lactate) serving as accurate and practical markers of severity in a low-resource setting.

BACKGROUND

Corrosive ingestion injuries remain a global problem with significant rates of associated morbidity and mortality[1]. A bimodal distribution, which includes paediatric injuries (which are mostly accidental) and adult injuries (which are mostly intentional) result in injuries of differing severity[2]. Management focuses on both the acute emergency management of these injuries, but equally on the long-term sequelae in those surviving the acute period, with oesophageal strictures being the most frequent chronic complication. The most concerning acute complication remains full thickness foregut necrosis with perforation resulting in significant mortality[1]. Outcomes may be improved with early identification of full thickness necrosis allowing for timeous surgical resection of any necrotic organs, prior to perforation occurring. Early endoscopic assessment using the Zargar classification[3], has been the cornerstone of severity assessment for over three decades, but has been replaced in most contemporary centres by computed tomography (CT) grading[4, 5]. CT grading out-performs endoscopy in selecting patients for acute resection, as the axial imaging allows for more accurate assessment of necrosis depth, compared to the purely luminal assessment of endoscopy[4, 5]. International data also suggest that serum blood tests, including raised white cell count, C-reactive protein, acidosis (with high lactate and low pH), deranged liver function tests and low platelet count, may aid in identifying full thickness necrosis[1].

Data on corrosive injuries from sub-Saharan Africa (SSA) is limited and focuses predominantly on the management of paediatric injuries and chronic oesophageal strictures[6-12]. Management of acute adult injuries is almost completely undescribed in SSA, although some papers from Nigeria, Ghana and Tunisia include some data on adult patients[13-15]. The only recent paper including a sizeable adult cohort coming from South Africa comes from Pietermaritzburg[16]. This paper highlights the significant challenges these injuries pose in a low resource setting, with a predominantly young, male demographic with intentional ingestion and limited use of CT imaging for acute assessment.

This study was performed to review the severity, management, and outcomes of acute corrosive ingestion injuries in a low resource SSA setting and to identify predictive factors of full thickness necrosis and short-term mortality.

METHODS

All adult patients managed for corrosive ingestion-related gastrointestinal injuries at Groote Schuur Hospital by the Upper Gastrointestinal Surgery Unit between 1st March 2017 – 31st October 2023 were analysed for inclusion. Exclusions included patients managed during this period for only the chronic sequelae of corrosive ingestion and those where acute management data was lacking (e.g. managed initially at another institution). Data were retrospectively analysed from an ethically approved prospectively maintained corrosive injury registry (HREC REF:R009/2022) with study approval by the University of Cape Town Human Research Ethics Committee (HREC REF:347/2022)

All patients presenting after an acute corrosive ingestion are assessed and managed as per the Advanced Trauma Life Support principles[17]. Assessment of injury severity is by either endoscopy or computed tomography (this is decided by imaging availability and by the initial treating physician). Early contrast swallow assessments are not advocated in our service. Patients with suspected full thickness necrosis are expedited to theatre for operative assessment. Suspecting full thickness necrosis is challenging and the decision to operate is made based on either endoscopic findings or CT findings (if a CT has been performed) and rarely, in cases of haemodynamic instability on initial assessment, the patient may be taken to theatre based on clinical findings prior to special investigations. In patients assessed by endoscopy and found to have severe injury, but not necessitating surgical resection, the opportunity is used to place an endoscopic nasojejunal feeding tube to allow for early enteral feeding. Less severe injuries are allowed to eat orally.

Groote Schuur Hospital is one of two tertiary academic referral centres for several public regional hospitals in the Western Cape province, which has an estimated population of over 7 million[18]. The hospital also accepts self-referred patients who live within the surrounding suburbs of the hospitals. CT imaging facilities are available 24 hours a day at Groote Schuur Hospital but not at all the referring hospitals, while upper gastrointestinal endoscopy is generally available 24 hours a day at most referring centres.

Definitions:

Outcomes:

The main outcomes analysed were 30-day mortality and morbidity (i.e. 30 days from the corrosive ingestion incident).

Endoscopic and CT severity grading:

Endoscopic grading of acute corrosive injuries was performed using the modified Zargar classification[19]. CT grading was performed according to the CT grading published by Chirica et al.[1].

Statistical Analysis

Data analysis was performed using Microsoft Excel and IBM SPSS Statistics (version 29.0.0.0). Patient demographics, corrosive ingestion details, initial investigations, management, and short-term outcomes were described using simple descriptive statistics, with mean ± standard deviation for parametric data and median with inter-quartile range for non-parametric data. Survival data of those patients with full thickness necrosis and those without were compared and presented using Kaplan-Meier curves. Univariate analyses were performed to assess for any factors associated with full thickness necrosis and 30-day mortality using the Chi-squared test for univariate categorical data and Kruskal-Wallis test to allow for comparison of multiple groups with non-parametric data. Furthermore, post-hoc multiple comparison analyses using the Mann-Whitney U test were performed on any variables shown to be statistically significant. Performance of endoscopy, CT grading and blood gas parameters (pH, base excess, and lactate) were further analysed to assess specificity, sensitivity, and positive and negative predictive values for full thickness necrosis prediction. A p-value of <0.05 was considered statistically significant. Factors found to be statistically significantly associated with the tested outcome (necrosis or mortality) were then tested for predictive performance using the area under the curve (AUC) of receiver operator characteristic (ROC) curves. An AUC value of 0.700 – 0.800 was considered acceptable, while a value >0.800 was considered excellent for predictive performance.

RESULTS

During the 80-month study period a total of 126 patients with corrosive ingestion-related injuries were treated, of which 100 patients met the inclusion criteria. The mean age was 32 years SD: 11.2 years) with most being male (65.0%). Two-thirds had no known medical comorbidities, with 15% known with a prior psychiatric history. Forty-one patients reported substance use of which cigarette smoking was the most common (31.0%). Eleven patients had a prior suicide attempt, of which one was a corrosive ingestion and the others combinations of polypharmacy overdose, hanging and other unknown mechanisms. No patient in the study cohort was known with a prior accidental corrosive ingestion. *Table 1* outlines patient demographics at baseline.

Most of the ingested substances were alkaline solutions, with bleach (30%) being the most common (*Table 1*). Almost three quarters (73%) of patients ingested the corrosive in a suicide attempt, 20% were accidental ingestions while five patients were forced to drink corrosive ingestions during assaults. In 20 patients additional non-corrosive substances were ingested, which included toxins in 13 patients, painkillers, and medication in five patients, washing powder, and a non-corrosive cleaning agent. Ingested toxins included alcohol, rat poison, mercury, and organophosphate. When comparing acid vs alkali ingestion (in those patients where this was known), acid ingestions were more likely to cause gastric necrosis than alkali ingestion (32.3% vs 10.3%, p=0.012), while there was no difference between acids and alkalis in terms of oesophageal necrosis, need for emergency resuscitation on admission nor 30-day mortality.

Early endoscopy was the most prevalent investigation performed with 95 patients assessed at a median time of 24 (IQR 15-40) hours post ingestion (*Table 2*). In 7 patients (7.4%) the initial endoscopy was performed more than 72 hours post corrosive ingestion. There were no documented perforations occurring during endoscopy in our cohort. Only 17 patients were assessed using CT, of which 14 also had an endoscopy. In only three patients was the injury severity assessed on CT findings only. CT was performed at a median time of 28 (IQR 20-56) hours post ingestion. Only one of these patients had duodenal necrosis at subsequent surgery, but duodenal findings on the CT were not specifically reported on. A CXR was performed on admission in 82 patients with 78 (95.1%) being normal and the other four showing non-specific lung changes. No CXR showed features confirming a perforation and no CXR directly influenced the acute corrosive management. Only one patient underwent a contrast swallow study as part of the acute severity assessment, which was reported as normal.

Twenty-three patients (23.0%) required emergency resuscitation on initial presentation, nineteen of whom necessitated endotracheal intubation for a threatened airway (*Table 3*). Initial management prior to referral included prophylactic antibiotics in 7.0%, activated charcoal in four patients (of which only one had an actual concomitant toxin overdose warranting the use of activated charcoal). No patient was managed with a pH neutralizing agent. One-fifth (20 patients) required acute surgery, of which 17 were found to have full thickness necrosis. The remaining three patients included two patients needing surgical feeding access (gastrostomy or jejunostomy) and one patient with a negative laparotomy. Eleven underwent an emergency resection, while the remaining six patients had such extensive injuries that an intra-operative decision was made to palliate. Resections performed included oesophagogastrectomy in five patients and total gastrectomy in five. One patient had an oesophagectomy without gastrectomy. In two patients extended resections were performed (additional to gastric or oesophageal resections), in both patients pancreas-preserving duodenectomy and resection of proximal jejunum. Nine patients (of the 11 who underwent an acute resection) underwent reconstruction, with three immediate oesophagojejunal anastomoses following total gastrectomy, and six delayed reconstructions. Two resected patients had uncomplicated post-operative courses, while the remaining seven required repeat intervention and/or surgery resulting in major morbidity and/or death.

Thirty-day mortality was 14.0%, with 27.0% having a documented morbidity within 30 days of the corrosive ingestion (*Table 4*). Nosocomial pneumonia, acute kidney injury and unexpected cardiac arrest were the most common morbidities. One quarter (26.0%) of patients required intensive care admission within 30 days of the corrosive ingestion. One of these patients had a severe corrosive pneumonitis and was successfully managed with Extra-corporeal Membrane Oxygenation (ECMO) and ultimately survived. Patients found to have full thickness necrosis had a 30-day mortality of 58.8% (including patients selected for palliation) while those who underwent an acute resection had a 30-day mortality of 36.4%. Eleven patients were found to have an already-established perforation at surgery. Of these, 10 (91.0%) died, with the only survivor being a patient who initially had a reassuring CT with modified Zagar grade IIB caustic injury on endoscopy. Following increasing septic markers and pyrexia an oesophagectomy on day 7 after the ingestion was performed for delayed full-thickness perforation, with localized mediastinitis. Patients who underwent an acute resection had a median length of hospital stay for their primary admission of 28 (IQR 19-137.5) days. Kaplan-Meier survival curves show a significant survival difference between those patients with full thickness necrosis and those without. Full thickness necrosis was associated with a cumulative survival of only 17.6% at 2 years (*Figure 2*).

Univariate analysis with ROC AUC as predictive of necrosis and mortality, showed that Zargar IIIB findings, Grade 3 CT findings, pH, base excess, and lactate to all have good predictive performance for full thickness necrosis, with endoscopy proving to have the best predictive performance (AUC 0.850) (*Table 5*). CT and endoscopy findings were the only factors predictive of short-term mortality, with CT performing better than endoscopy (AUC 0.798 vs 0.759). Blood gas parameters (pH, base excess and lactate) were further analysed in the whole cohort, but also separately in patients without concomitant toxin ingestion (where blood gas findings may be falsely abnormal due to the toxin and not the corrosive substance). After excluding patients with additional toxin ingestion, both pH and base excess had a 100% negative predictive value for full thickness necrosis. In addition, an abnormal base excess (<2 mEq/l) had excellent predictive value for full thickness necrosis with a ROC AUC of 0.821 (*Table 6*).

DISCUSSION

Corrosive ingestion injuries remain a difficult clinical problem in our setting. Demographics in this series closely resemble those reported by Mthethwa et al[16] also from South Africa, with a low mean age and significant male predominance. Case series from Europe (United Kingdom and France) show a different demographic with a median age approximately10 years older than in the South African setting and a more equal gender distribution[2, 5, 20]. As seen in most studies on adult corrosive injuries, intentional suicide attempts remain the most common reason for the ingestion. The majority of patients in this series were not known with a prior psychiatric history, unlike results from international series, such as Challine et al. who reported 71.8% of patients having been known with a prior psychiatric history[20]. Five patients in our series were forced to drink a corrosive substance as part of an assault, one of which resulted in severe corrosive pneumonitis and the need ECMO. Corrosive assault is not well described and probably reflective of the high rates of interpersonal violence in South Africa which in general also occurs predominantly in young males [21]. Traditionally there has been much focus on differentiating between acid and alki ingestions, however in this case series, other than an increased rate of gastric necrosis, there was no difference between the two in terms of oesophageal injury nor mortality. We believe the type of substance ingestion should not influence investigation nor management choices.

Decision-making in the emergency setting revolves around the need for surgical resection. Patient selection is crucial and remains difficult. Delays to resection result in significantly worse outcomes, while unnecessary resections, especially oesophagectomy, carry a significant morbidity and even mortality. CT is now considered in many centres, and by international guidelines, to be superior in selecting patients for resection[1, 4, 22-24]. Some centres now rely on CT grading only in the emergency setting with endoscopy considered obsolete[5]. Management of severe corrosive injuries may require extended foregut resections and in patients with staged procedures technically demanding delayed reconstructions with high complication rates and poor eventual quality of life (QoL)[1]. Improving outcomes in these patients is best achieved by management in centralised high-volume centres with access to not only surgery but also minimally invasive interventions[2, 20].

CT utilisation in our study, as well as the study by Mthethwa *et al*., was low[16]. This is likely due to a combination of lack of emergency 24-hour access to CT imaging at the referral centres, but also a lack of awareness of the usefulness of CT grading for acute corrosives. Unfortunately, the data was unable to assess specifically why the CT utilisation was so low. It is not clear how many acute corrosive injures were seen within the drainage area during the study period in total, as minor cases have been managed at peripheral hospitals and are not included in this study. Most of these hospitals have 24-hour access to endoscopy but not CT imaging. Non-selective referrals of all corrosive ingestion patients will result in significant strain to an already overburdened tertiary facility. Selective referral of patients with suspected full thickness necrosis is crucial and should be expedited to allow resection before foregut perforation occurs. Perforation prior to surgery in our setting is invariably fatal.

Severity of oral and laryngeal injuries correlate poorly to severity of gastrointestinal injuries[1]. Although the data in this study did not include the reason for needing emergency endotracheal intubation, 19 patients did require emergency airway interventions. Only five of these patients (26.3%) however, actually had oesophageal or gastric necrosis.

Although plain radiography (CXR or lateral neck X-rays) and basic admission blood tests (full blood count and renal function with electrolytes) are routinely performed the results are of limited value in the acute management. Diagnostic laparoscopy may also have a diagnostic role, specifically in assessing transmural gastric necrosis where endoscopic and CT findings may be equivocal. There is surprisingly little written on the use of diagnostic laparoscopy in these patients, but Di Saverio *et al*, describe a case where laparoscopy was negative and allowed the avoidance of an unnecessary laparotomy[25]. We do feel whoever, there might be some drawbacks to using laparoscopy in this setting, not least of which in visualising the duodenum, as laparoscopic kocherisation does demand significant technical skill and patience, which may not always be available in the emergency setting.

Blood gas parameters (pH, base excess, and serum lactate) were the most useful blood tests to predict necrosis while endoscopy and CT both performed well as imaging modalities. Locally, a blood gas (which is relatively cheap, easy to perform and readily available at almost all emergency centres) can aid in selecting patients for referral for CT assessment. Although pH and base excess had an excellent negative predictive value (especially when the possible confounding effects of other toxin ingestion were excluded), we are cautious about implying that clinicians should rely solely on these findings. However, in a resource-limited environment where CT may not be readily available, a normal blood gas is at least partially reassuring and may allow for delay in transfer to a centre with a CT and rather allow for local investigation using endoscopy. We are also unable to comment on whether the timing of the blood gas influences the predictive performance, as this data was not available for analysis.

Although not used for the acute injury severity assessment in some international centres, we still consider endoscopy to be a very useful investigation (especially in patients without necrosis). We recommend that early endoscopy should be considered in all patients who do not have evidence of full thickness necrosis on CT. We also find that endoscopy remains a useful investigation in patients with grade 2 or 1 injuries on CT, as it does allow for direct mucosal visualisation and if significant ulceration is found, this poses an opportunity for the placement of an endoscopically-placed nasojejunal feeding tube. It must be highlighted that initial reassuring CT and endoscopic findings in severe corrosive cases do not replace close clinical observation, as delayed perforation can still occur, as was evident in one patient in our series who had an oesophageal perforation diagnosed one week after the ingestion incident and where both CT and endoscopy were not suggestive of full thickness necrosis. Repeat investigations should be obtained in cases where there is clinical deterioration and development of delayed necrosis or delayed perforation are suspected. CT is recommended as the repeat investigation of choice, as per the World Society of Emergency Surgery guidelines on oesophageal emergencies, but there is limited data to support this recommendation[4].

The limitations of this study include the retrospective nature of the data analysis and the low patient numbers who had CT imaging compared to endoscopy which may have compromised the accuracy of ROC curves and predictive models for CT grading. Lack of data on these injuries in SSA hampers preventive health strategies and even in our setting it is unclear how many of these injuries are seen within the catchment area, but outside of our centre. Further research with multi-centre collaboration would generate larger patient numbers and give a more robust assessment of the full extent of this problem.

CONCLUSION

Acute corrosive ingestion in adults may result in devastating injuries and remains a condition poorly described in SSA. Acute management success hinges on accurate and timeous identification of full thickness necrosis and early surgical resection. CT is the most accurate tool to achieve this, but in resource-constrained environments is not readily available. Endoscopy thus remains an important and invaluable tool. We propose using blood gas findings to select patients who should be acutely referred to an academic centre for emergency CT imaging and assessment for surgical resection, but do suggest caution in cases where these tests are performed soon after the injury, as the blood gas may be falsely reassuring.

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FIGURES AND TABLES

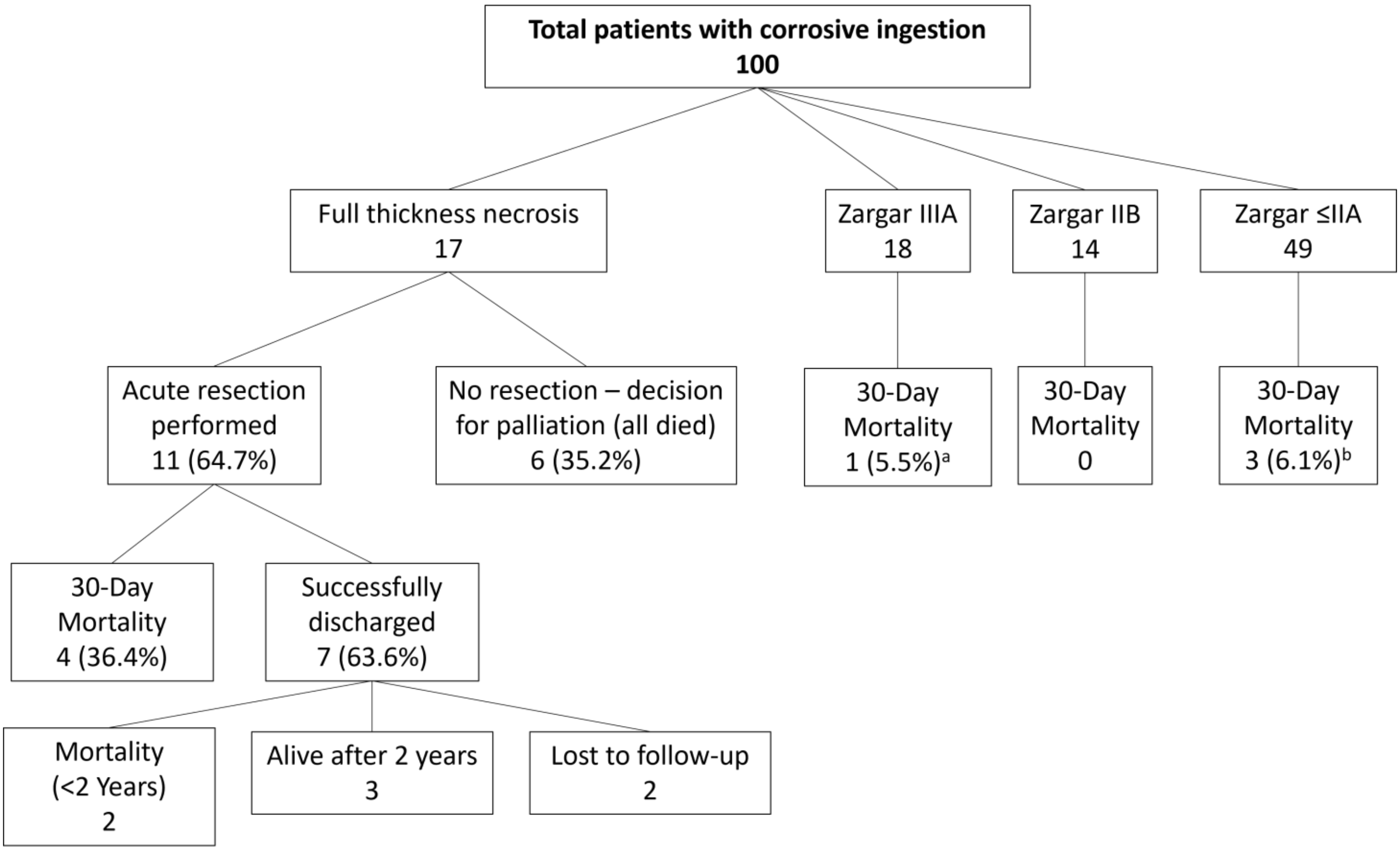

Figure 1. Flow diagram of patient outcomes. [a]One patient initially assessed as Zargar IIIa later developed oesophageal necrosis with tracheo-oesophageal fistula and died, [b]All three patients with minor corrosive

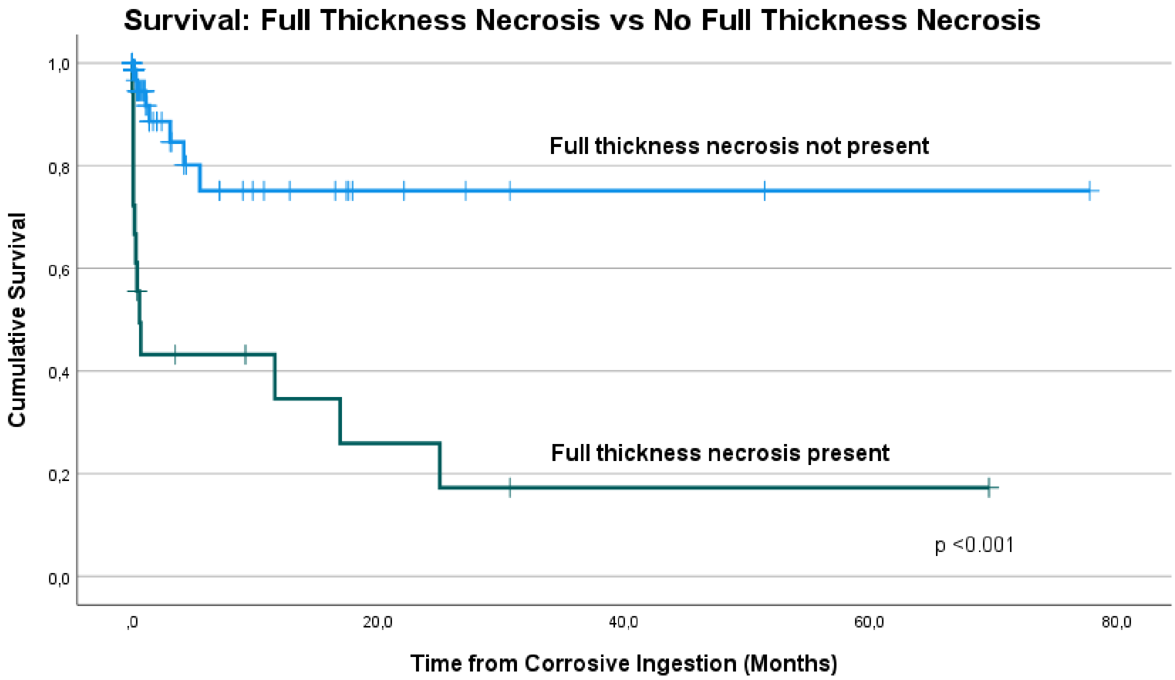

Figure 2. Kaplan-Meier survival curve comparing cumulative survival in patients with or without full thickness necrosis.

Table 1. Baseline demographics and details of the corrosive ingestion incident. [a]HIV = human immunodeficiency virus

Baseline demographics (n=100)	**n**	**%**
Gender		
Female	35	35.0%
Male	65	65.0%
Comorbidities		
No	67	67.0%
Yes	33	33.0%
Specified comorbidities		
Known psychiatric history	15	15.0%
HIV[a] positive	12	12.0%
Hypertension	2	2.0%
Obesity	3	3.0%
Diabetes mellitus	1	1.0%
Other comorbidity	7	7.0%
Substance use		
No	59	59.0%
Yes	41	41.0%
Substance use specified		
Smoking	31	31.0%
Alcohol - regular use	21	21.0%
Marijuana	10	10.0%
Methamphetamine	8	8.0%
Methaqualone	7	7.0%
Opioids	1	1.0%
Prior corrosive ingestion/suicide attempt		
Yes	11	11.0%
No	89	89.0%
Corrosive ingestion incident (n=100)		
Intentional/accidental		
Intentional (suicidal)	73	73.0%
Accidental	20	20.0%
Forced ingestion (assault)	5	5.0%
Unknown	2	2.0%
Substance ingested		
Acid	32	32.0%
Sulphuric acid	22	
Hydrochloric acid	3	
Other acid	7	
Alkali	58	58.0%
Sodium hypochlorite (bleach)	30	
Sodium hydroxide	27	
Other alkali	3	
Other corrosive substance	10	10.0%
Unknown corrosive substance	5	5.0%

Table 2. Imaging and endoscopy investigations performed on admission. [a]CT = computed tomography

Imaging/endoscopy during acute admission (n=100)	**n**	**%**				
Endoscopy	95	95.0%				
Chest X-ray	82	82.0%				
Lateral neck X-ray	31	31.0%				
CT[a]	17	17.0%				
Contrast swallow	1	1.0%				
None	1	1.0%				
Time to endoscopy (from ingestion)	24 (15-40) hours					
Time to CT (from ingestion)	28 (20-56) hours					
Endoscopy findings (n=95)	**n**	**%**	**n**	**%**	**n**	**%**
	Oesophagus		**Stomach**		**Duodenum**	
Not entered	1	1.1%	3	3.2%	32	33.7%
Zargar 0	23	24.2%	14	14.7%	42	44.2%
Zargar I	11	11.6%	25	26.3%	9	9.5%
Zargar IIA	20	21.1%	14	14.7%	7	7.4%
Zargar IIB	26	27.4%	8	8.4%	1	1.1%
Zargar IIIA	6	6.3%	16	16.8%	1	1.1%
Zargar IIIB	8	8.4%	14	14.7%	3	3.2%
Zargar IV	0	0.0%	1	1.1%	0	0.0%
CT findings (n=17)	**n**	**%**	**n**	**%**		
	Oesophagus		**Stomach**			
Grade 1 - Normal	2	11.8%	5	29.4%		
Grade 2 - Oedematous only	11	64.7%	8	47.1%		
Grade 3 - Lack of contrast enhancement						
Without perforation	3	17.6%	2	11.8%		
With perforation	1	5.9%	2	11.8%		

Table 3. Overview of acute management. [a]Other emergency resuscitation: atropine with methylene blue administration for bradycardia & methaemoglobinaemia and recurrent emergency potassium shifting for refractory hyperkalaemia. [b]Extended resections: oesophagogastrectomy/total gastrectomy with additional pancreas-preserving duodenectomy and proximal jejunal resection in two patients. [c]Gastrojejunostomy was performed in a patient with delay to theatre and evidence of early stricture formation of the distal stomach with anticipated obstruction developing.

Management		
Median (IQR) time from ingestion to first healthcare assessment	6 (2-13) hours	
Emergency resuscitation	**n**	**%**
Required emergency resuscitation	23	23.0%
Specified		
Endotracheal intubation	19	19.0%
Chest compressions	1	1.0%
Inotropes	3	3.0%
Other[a]	2	2.0%
Other management initiated in the emergency department		
Proton pump inhibitor (PPI) therapy	35	35.0%
Prophylactic antibiotics	7	7.0%
Therapeutic antibiotics	4	4.0%
Nasogastric tube insertion (for drainage, not feeding)	4	4.0%
Activated charcoal administration	4	4.0%
Steroids	1	1.0%
Neutralizing agent	0	0.0%
Surgery		
Required acute surgery	20	20.0%
Decision for needing surgery (n=20)		
Based on endoscopy findings	13	65.0%
Based on CT findings	5	25.0%
Based on clinical findings only	2	10.0%
Type of Surgery (n=20)		
Emergency resection performed	11	55.0%
Oesophagectomy only	1	
Oesophagogastrectomy	5	
Gastrectomy only	5	
Extended Resections[b]	2	
Exploration only - decision for palliation	6	30.0%
Feeding jejunostomy (only)	1	5.0%
Gastrojejunostomy[c] & gastrostomy	1	5.0%
Negative laparotomy	1	5.0%

Table 4. Outcomes for 30-days post corrosive ingestion. Acute admission outcomes. [a]ICU = intensive care unit

Outcomes (n=100)	**n**	**%**
30-day mortality	14	14,0%
30-day morbidity	27	27,0%
Required ICU management[a]	26	26,0%
Median (IQR) ICU stay	2.5 (2 - 3.25) days	
Median (IQR) length of hospital stay	6 (2 - 15.5) days	
Full-thickness Necrosis	17	17,0%
Underwent Surgical Resection	11	11,0%
Acute morbidities specified (n=39)		
Pneumonia (nosocomial)	7	17,9%
Acute kidney injury	5	12,8%
Cardiac arrest (unexpected)	4	10,3%
Refeeding syndrome	3	7,7%
Systemic sepsis	2	5,1%
Unplanned extubation	2	5,1%
Surgical site infection	2	5,1%
Other	14	35,9%

Table 5. Univariate analyses of numerous admission variables in predicting full thickness necrosis and short-term mortality. All numerical values expressed as median (inter-quartile range). [a]FT necrosis: full thickness necrosis. [b]ROC AUC: receiver operator characteristic curve area under the curve. [c]HIV: human immunodefiency virus. [d]CT: computed tomography. [e]BP: blood pressure. [f]WCC: white cell count

Variables			**Predicting full thickness necrosis**						**Predicting Acute Mortality**					
		Total n	**No FT necrosis[a]**		**FT necrosis**		**p-value**	**ROC AUC[b]**	**No mortality**		**Mortality**		**p-value**	**ROC AUC**
Gender	Female	35	31	88,6%	4	11,4%	0,279		28	80,0%	7	20,0%	0,207	
	Male	65	52	80,0%	13	20,0%			58	89,2%	7	10,8%		
At least one comorbidity	No	67	58	86,6%	9	13,4%	0,178		56	83,6%	11	16,4%	0,323	
	Yes	33	25	75,8%	8	24,2%			30	90,9%	3	9,1%		
Known psychiatric history	No	85	71	83,5%	14	16,5%	0,739		72	84,7%	13	15,3%	0,377	
	Yes	15	12	80,0%	3	20,0%			14	93,3%	1	6,7%		
Known HIV[c] positive	No	88	75	85,2%	13	14,8%	0,11		74	84,1%	14	15,9%	0,138	
	Yes	12	8	66,7%	4	33,3%			12	100,0%	0	0,0%		
Prior corrosive/suicide attempt	No	89	75	84,3%	14	15,7%	0,339		77	86,5%	12	13,5%	0,673	
	Yes	11	8	72,7%	3	27,3%			9	81,8%	2	18,2%		
Needing endotracheal intubation	No	82	71	86,6%	11	13,4%	**0,043**	0.604	69	84,1%	13	15,9%	0,257	
	Yes	18	12	66,7%	6	33,3%			17	94,4%	1	5,6%		
Needing chest compressions	No	99	83	83,8%	16	16,2%	**0,027**	0.529	85	85,9%	14	14,1%	0,687	
	Yes	1	0	0,0%	1	100,0%			1	100,0%	0	0,0%		
Needing inotropes/vasopressors	No	97	81	83,5%	16	16,5%	0,447		83	85,6%	14	14,4%	0,480	
	Yes	3	2	66,7%	1	33,3%			3	100,0%	0	0,0%		
≥Zargar IIIB endoscopic findings	No	79	75	94,9%	4	5,1%	**<0.001**	**0.850**	74	93,7%	5	6,3%	**<0.001**	**0.759**
	Yes	16	4	25,0%	12	75,0%			8	50,0%	8	50,0%		
Grade 3 CT[d] Findings	No	12	10	83,3%	2	16,7%	**0.016**	**0.788**	11	91,7%	1	8,3%	**0.026**	**0.798**
	Yes	5	1	20,0%	4	80,0%			2	40,0%	3	60,0%		
Age (years)		100	31 (24-38)		39 (30-50)		**0.015**	0.687	32 (24-40)		31 (25-40)		0,917	
Systolic BP[e] (mmHg)		48	134 (114-143)		129 (113-149)		0.926		130 (113-144)		134 (120-137)		0,919	
Diastolic BP (mmHg)		48	80 (73-90)		83 (75-97)		0.309		82 (73-90)		79 (64-91)		0,520	
Heart rate (beats per minute)		48	94 (79-109)		86 (72-105)		0.405		93 (76-110)		94 (82-107)		0,965	
Urea (mmol/L)		79	4.6 (3.3-5.9)		5.1 (2.7-7.1)		0.686		4.7 (3.2-6.5)		3.9 (3.4-5.4)		0,432	
Creatinine (umol/L)		88	70 (57-81)		84 (68-102)		**0.038**	0.666	72 (58-85)		72 (66-84)		0,892	
WCC[f] (x 10^9/L)		85	14.07 (9.58-18.31)		13.80 (9.76-19.16)		0.695		13.79 (9.59-18.31)		15.75 (10.63-20.50)		0,605	
Platelets (x 109/L)		81	253 (210-326)		206 (171-266)		**0.045**	0.666	245 (194-308)		263 (232-375)		0,142	
Calcium (mmol/L)		12	2.21 (2.00-2.35)		1.99 (199-1.99)		0.310		2.15 (1.99-2.35)		2.21 (2.21-2.21)		0,885	
pH		41	7.37 (7.31-7.42)		7.13 (7.07-7.35)		**0.003**	**0.823**	7.35 (7.17-7.40)		7.36 (7.27-7.43)		0,593	
Base excess (mEq/L)		40	*-0.50 (-5.50-2.10)		*-14.20 (-17.00- -4.60)		**0.004**	**0.819**	*-3.2 (-12.1-0.65)		2.45 (-0.58-5.38)		**0,020**	0.199
Lactate (mmol/L)		40	1.80 (1.20-3.30)		3.20 (2.60-4.45)		**0.026**	**0.746**	2.45 (1.20-3.55)		1.55 (1.18-3.48)		0,677	
Ingestion to first assessment (hours)		94	6.0 (2.5-14.5)		4.0 (2.0-8.5)		0.209		6.0 (3.0-15.5)		3.0 (1.5-6.5)		0,052	

Table 6. Admission endoscopy, CT and blood gas performance in predicting full thickness necrosis. [a]FT necrosis = full thickness necrosis; [b]PPV = positive predictive value; [c]NPV = negative predictive value; [d]ROC AUC = receiver operator characteristic area under the curve; [e]CT = computed tomography;

	Total	FT[a] necrosis	Not FT necrosis	Sensitivity	Specificity	PPV[b]	NPV[c]	p-value	ROC AUC[d]
Endoscopy performance (n=95)									
Zargar IIIB	16	12	4	75,0%	94,9%	75,0%	94,5%	**<0.001**	**0.850**
CT[e] performance (n=17)									
CT Grade 3	5	4	1	66,7%	90,9%	80,0%	83,3%	**0.026**	**0.788**
Blood gas performance (n=40)									
pH <7.35	20	7	13	77,8%	58,1%	35,0%	90,0%	0.062	0.679
BE <-2 mEq/L	18	7	11	77,8%	64,5%	38,9%	90,9%	**0.027**	**0.711**
Lactate >2.0 mmol/L	21	8	13	88,9%	58,1%	38,1%	94,7%	**0.014**	**0.735**
Blood gas performance (Patients with concomitant toxin ingestion removed) (n=35)									
pH <7.35	19	7	12	77,8%	58,1%	35,0%	100,0%	**0,007**	**0,786**
BE <-2 mEq/L	17	7	10	77,8%	58,1%	35,0%	100,0%	**0,003**	**0,821**
Lactate >2.0 mmol/L	18	6	12	77,8%	58,1%	35,0%	94,1%	**0,046**	**0,714**

SUPPLEMENTARY TABLE

Table 7. Classification systems for endoscopic and CT grading of acute corrosive injuries

Modified Zargar Endoscopic Grading[19]	
Grade 0	Normal
Grade I	Oedema and hyperaemia of mucosa
Grade IIA	Superficial localised ulcerations, friability and blisters
Grade IIB	Circumferential and deep ulcerations
Grade IIIA	Multiple and deep ulcerations and small, scattered areas of necrosis
Grade IIIB	Extensive necrosis
Grade IV	Perforation
CT Grading[1]	
Grade 1	Normal appearance
Grade 2	Wall and soft tissue oedema, increased wall enhancement
Grade 3	Transmural necrosis with absent wall enhancement (with or without perforation)

APPENDICES

Appendix A – Surgical Departmental Research Committee Approval

UNIVERSITY OF CAPE TOWN

Department of Surgery
Departmental Research Committee
A/Prof Maritz Laubscher
Groote Schuur Hospital
Observatory 7925
South Africa
Tel (021) 404 5108
Email: maritz.laubscher@uct.ac.za

19 Apr 2022

Dr M Scriba

Department of Surgery
University of Cape Town

Dear Dr Scriba

RE: Project 2022/039

PROJECT TITLE: An Overview Of Adult Corrosive Ingestion Injuries In A Sub-Saharan African Setting

The above protocol has been reviewed by the Department of Surgery Research Committee. I am pleased to inform you that the committee approved the scientific merit of the study, and endorse the protocol for submission to the relevant ethics committee.

Although this letter serves as confirmation that the above protocol has successfully passed through the surgical DRC, respective ethics committees still require DRC chair signature before submission.

Please use the above project number in all future correspondence,

Yours sincerely

A/PROF MARITZ LAUBSCHER
CHAIR SURGICAL DRC

"OUR MISSION is to be an outstanding teaching and research university, educating for life and addressing the challenges facing our society."

Appendix B – University of Cape Town Human Research Ethics Committee Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
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Website: www.health.uct.ac.za/fhs/research/humanethics/forms

23 June 2022

HREC REF: 347/2022

Dr G Chinnery
Division of Surgical Gastroenterology
E23 GIT Unit NGSH
Email: Galya.chinnery@uct.ac.za
Student: Matthias.scriba@gmail.com

Dear Dr Chinnery

PROJECT TITLE: **AN OVERVIEW OF ADULT CORROSIVE INGESTION INJURIES IN A SUB-SAHARAN AFRICAN SETTING-SUB-STUDY LINKED TO R009/2022 (MASTERS CANDIDATE-DR MATTHIAS SCRIBA)**

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19. Please refer to guidance letter dated 02 February 2022 on our website:
http://www.health.uct.ac.za/fhs/research/humanethics/forms

Approval is granted for one year until the 30 June 2023.

Please submit a progress form, using the standardised Annual Report Form (FHS016) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Matthias Scriba will also be involved in this study

Please quote the HREC REF 347/2022 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

APPENDIX C – Author Guidelines: World Journal of Gastroenterology

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First published:June 30, 2015

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1 FIRST SECTIONOFWRITING REQUIREMENTSYES or NO

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2.5Tables[ ]

2.6Notes in illustrations and tables[ ]

2.7Abbreviations[ ]

2.8Italics[ ]

2.9Acknowledgements[ ]

2.10References[ ]

3 ETHICS POLICIES/STATEMENTS YES or NO

3.1 Institutional review board[ ]

3.2Informed consent [ ]

3.3 Conflict-of-interest[ ]

4 LANGUAGE EDITING FOR MANUSCRIPTS SUBMITTED BY NON-NATIVE SPEAKERS OF ENGLISHYES or NO

5STEPS FOR SUBMITTING MANUSCRIPTSYES or NO3 / 26

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1FIRSTSECTIONOFWRITING REQUIREMENTS

All contributions should be written in English; the authors may use either UK or US English language, but the chosen English language usage must be consistent throughout the document. All articles must be prepared withWord-processing Software, using 12 ptBook Antiqua font and 1.5 line spacing with ample margins. Required information for each of the manuscript sections is as follows:

1.1Title.The title should be no more than 18 words. The title should summarize the core content of the manuscript, so that the reader may readily understand the key concepts and important findings presented within. This type of succinct and impactful statement will serve to catch readers' attention and stimulate their interest in reading the abstract and/or downloading the full paper. It is also strongly recommended that the title include one or two of the key words associated with the manuscript's topical content,to facilitate the paper being readily found by electronic searches of public databases, such as Google or PubMed. Finally, words such as 'exploration', 'research', 'analysis', 'observation', and 'investigation' are to be avoided. The title should not start with 'A', 'An', or 'The' and will not include any Arabic numbers or abbreviations.

1.2Authorship. Authorship credit should be given in accordance with the standard proposed by the International Committee of Medical Journal Editors (ICMJE) (http://www.icmje.org/), specifically, authorship is merited by (1) substantial contributions to conception and design of the study, acquisition of data, or analysis and interpretation of data; (2) drafting the article ormaking critical revisions related to important intellectual content of the manuscript; and (3) final approval of the version of the article to be published. Authors should meet conditions 1, 2 and 3.

Designation of co-first authors and co-corresponding authors is not permitted.

Author names (unabbreviated) should be given as first name, middle name initial4 / 26

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(with no period) and family (sur) name, andtyped in bold with the first letter capitalized; a hyphen should be included between the syllables of Chinese names. For example,Jason Lamontagne, Laura F Steel,Paul V Harper Jr, Bo Yuan, and Wei-Hong Tang.

1.3Institution. Author names should be written out first (as first name, middle name initial (with no period) and family (sur)name; with a hyphen included between the syllables of Chinese names) and typed in bold, followed by a comma and the complete name of the affiliated institution, city, province/state, postcode and country typed in non-bold. For example:

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2.9Acknowledgements.Brief acknowledgements of persons who have made genuine contributions to the manuscript and who endorse the data and conclusions should be included. Authors are responsible for obtaining written permission to use any copyrighted text and/or illustrations.

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2 Zhang ZM, Deng H, Zhang C, Yu HW, Liu Z, Liu LM, Wan BJ, Zhu MW. Strategies for diagnosis and treatment of benign and malignant colorectal obstruction. *Shijie Huaren Xiaohua Zazhi*2017; 25: 2597-2604 [DOI: 10.11569/wcjd.v25.i29.2597]

In press articles:

3Sipos F, Constantinovits M, Valcz G, Tulassay Z, Műzes G. Association of hepatocyte-derived growth factor receptor/caudal type homeobox 2 co-expression with mucosal regeneration in active ulcerative colitis. *World J Gastroenterol*2015; In press

Organization as author:

4 Diabetes Prevention Program Research Group. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension*2002; 40: 679-686 [PMID: 12411462]

Both individual authors and an organization as author:

5 Vallancien G, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms.*J Urol*2003; 169: 2257-2261 [PMID: 12771764]16 / 26

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No author given:

6 21st century heart solution may have a sting in the tail. *BMJ*2002; 325: 184 [PMID: 12142303]

Volume with supplement:

7 Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short-and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache*2002; 42Suppl 2: S93-99 [PMID: 12028325]

Issue with no volume:

8 Banit DM, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res*2002; (401): 230-238 [PMID: 12151900]

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9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction*2002; 1-6 [PMID: 12154804]

BOOKS

Individual author(s):

10 Sherlock S, Dooley J. Diseases of the liver and biliarysystem. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors):

11 Lam SK. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-45017 / 26

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Author(s) and editor(s):

12 Breedlove GK, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

CONFERENCE-RELATED ARTICLES

Conference proceedings:

13 Harnden P, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference papers:

14 Christensen S, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

ELECTRONIC JOURNALS

Electronic journals(list all authors):

15 Huynen MMTE, Martens P, Hilderlink HBM. The health impacts of globalisation: a conceptual framework. Global Health. 2005; 1: 14. Available from: https://globalizationandhealth.biomedcentral.com/articles/10.1186/1744-8603-1-14

doi.org/10.1186/1744-8603-1-14 [PMID: 21501219 DOI: 10.1186/1744-8603-1-14]

PATENTS

Patents(list all authors):

16 Pagedas AC, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 18 / 26

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20020103498. 2002 Aug 1

CLINICAL TRIAL

17 Cannon R. Rilonacept to improve artery function in patients with atherosclerosis. [accessed 2015 Apr 25]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine. Available from: http://clinicaltrials.gov/show/NCT00417417 ClinicalTrials.gov Identifier: NCT00417417

DEPOSITED ARTICLES(preprints, e-prints, or arXiv)

18 Krick T,Shub DA,Verstraete N, Ferreiro DU, Alonso LG, Shub M, et al. Amino acid metabolism conflicts with protein diversity; 1991. Preprint. Available from: arXiv:1403.3301v1. Cited 17 March 2014.

PUBLISHED MEDIA(print or online newspapers and magazine articles)

19 Fountain H. For Already Vulnerable Penguins, Study Finds Climate Change Is Another Danger. The New York Times. 29 Jan 2014. Available from: http://www.nytimes.com/2014/01/30/science/earth/climate-change-taking-toll-on-penguins-study-finds.html Cited 17 March 2014.

NEW MEDIA(blogs, web sites, or other written works)

20 Allen L.Announcing PLOS Blogs. 2010 Sep 1 [cited 17 March 2014]. In: PLOS Blogs [Internet]. San Francisco: PLOS 2006 -. [about 2 screens]. Available from: http://blogs.plos.org/plos/2010/09/announcing-plos-blogs/.

MASTERS' THESES OR DOCTORAL DISSERTATIONS

21 Wells A. Exploring the development of the independent, electronic, scholarly journal. 19 / 26

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M.Sc. Thesis, The University of Sheffield. 1999. Available from: http://cumincad.scix.net/cgi-bin/works/Show?2e09

DATABASES AND REPOSITORIES (Figshare or arXiv)

22 Roberts SB. QPX Genome Browser Feature Tracks; 2013 [cited 2013 Oct 5]. Database: figshare [Internet]. Available from: http://figshare.com/articles/QPX_Genome_Browser_Feature_Tracks/701214

MULTIMEDIA(videos, movies, or TV shows)

23 Hitchcock A, producer and director. Rear Window [Film]; 1954. Los Angeles: MGM.

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