STUDY PROTOCOL:

"FEASIBILITY STUDY OF AN ENTERAL RESUSCITATION BUNDLE FOR MODERATE-SIZED BURN INJURIES (20-40% TOTAL BODY SURFACE AREA) IN NEPAL"

Protocol Version and Date: Version 3.0; February 28, 2022

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Introduction

1. **Title**
   Implementation of an enteral resuscitation bundle for moderate-sized burn injuries (15-40% total body surface area) in Nepal

2. **Trial Registration**
   This trial was registered with the U.S. National Library of Medicine ClinicalTrials.gov on February 1, 2021 (Identifier: NCT04732624).

3. **Clinical Protocol**
   Protocol Number and Title
   Enteral Resus Nepal V002: Implementation of an enteral resuscitation bundle for moderate-sized burn injuries (15-40% total body surface area) in Nepal

   Protocol Version Number and Date
   Version 2.0; February 28, 2022,

4. **Funding**
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Introduction

6. Background and Rationale

Nepal and the South Asian sub-continent carry some of the highest rates of burn injury globally, with an associated high morbidity and mortality. Nepal currently has one major center equipped for burn care, in Kirtipur, Nepal and receives referred patients from around the country. At presentation, most patients with major burns have had minimal to no resuscitation on arrival, often hours to days after the burn injury was sustained.

Timely fluid resuscitation, initiated as soon as possible after major burn injury, is the main tenet of acute burn care. Lack of adequate resuscitation in major burn injuries leads to kidney injury, progression of burn injury, sepsis, burn shock, and death. The current standard of care for major burn resuscitation is intravenous fluid resuscitation. In Nepal, however, adequately trained and equipped hospitals for treatment of burn care are not available (for a variety of reasons). Additionally, there is not a systematic emergency medical transport system available for provision of medical care and resuscitation during transport. Enteral-based resuscitation with substances like the WHO Oral Rehydration Solution (ORS) is recommended by burn experts and the professional burn societies when resources and access to intravenous fluid resuscitation are not available in resource-constrained settings such as rural areas, low- and middle-income countries, and military battlefield scenarios. Studies have previously demonstrated the efficacy and safety of enteral-based resuscitation in controlled, high-resource settings, however there have not been real-world effectiveness trials in austere settings. Therefore, we seek to ultimately address the problem of pre-hospital and pre-burn center admission resuscitation by studying the feasibility and effectiveness of enteral resuscitation with Oral Rehydration Solution (ORS) in preventing burn shock. An attachment has been provided with a more detailed literature review of enteral-based resuscitation research for burn injuries with references for further information on this topic **(Appendix)**.

Additionally, enteral-based resuscitation with ORS has been widely applied in other pathologies resulting in massive dehydration and ultimate death, such as diarrheal illnesses. ORS is a mixture of salts and sugar dissolved in water, created and modified in the 1940's-1970s. Use of ORS demonstrated a significant reduction in mortality from dehydration and multisystem organ failure during the cholera epidemic, and is used around the world in the setting of diarrheal illnesses. Given similar principles of rapid dehydration in the setting of burn injuries as well as the multiple studies demonstrating efficacy and safety of enteral-based resuscitation for moderate sized burn injuries, we plan to study the effectiveness of enteral resuscitation with ORS for burn resuscitation in Nepal.

The current project seeks to address gaps in our understanding of logistical and cultural barriers to protocolized enteral-based resuscitation (either drinking by mouth or via a nasogastric tube), and feasibility of protocolized intravenous resuscitation. The current project will also retrospectively review epidemiologic registry data, perform geospatial analysis and inform anticipated larger studies of multi-site enteral resuscitation trials.

7. Objectives

Many patients in low- and middle-income countries (LMICs) do not receive appropriate fluid resuscitation after sustaining a potentially survivable burn injury due to lack of resources or expertise. This population encompasses 90% of the 9 million people burned annually around the globe. Given current safety and efficacy data, burn care experts recommend enteral resuscitation (i.e., oral rehydration solution administered by mouth or nasal-enteric tube) instead of solely intravenous resuscitation, particularly when resources for acute burn care are scarce. However, there have been no studies to determine the real-world effectiveness and feasibility, acceptability,

facilitators and barriers for sustainability of enteral resuscitation for burn injuries in austere settings. In our initial studies, we have demonstrated feasibility of implementing the enteral resuscitation bundle, as well as feasibility of research study.

8. Trial Design

The study design is a mixed-methods implementation-effectiveness trial consisting of randomization of eligible participants into protocoled enteral-based resuscitation vs protocoled intravenous resuscitation (standard of care) arms to assess feasibility of protocol and randomization. The qualitative component entails semi-structured focus group interviews for involved healthcare providers assessing compliance, acceptability, feasibility, facilitators and barriers to sustainability of interventions.

9. Study Setting

The study will take place at the Nepal Cleft and Burn Center at Kirtipur Hospital (phect-NEPAL) in Kirtipur, Nepal which is the major tertiary burn care center in Nepal.

Nepal Cleft and Burn Center is an ideal to study burn resuscitation in austere settings given a very high incidence of serious burn injuries, frequent delays in resuscitation, and critically limited resources. By studying an enteral-based resuscitation bundle in this population, we can assess feasibility of the bundle within a realistic resource-limited context where a need exists.

10. Eligibility Criteria

Intervention:

Inclusion Criteria

Male or female; adults aged ≥18 years who present with moderate-sized burn injuries [15 – 40% total body surface areas (TBSA)] to the Nepal Cleft and Burn Center within 24 hours of injury.

Exclusion Criteria

Patients with electrical and chemical burns will be excluded, as will those with serious inhalation injury requiring treatment to maintain oxygen saturation. Patients in overt shock (defined as serum lactate >2.5, or hypotension and altered mental status), Pregnant patients, psychiatrically unstable patients will be excluded.

Patients with oropharyngeal defects and/or previously known diagnoses leading to high risk of aspiration, and/or precluding safe nasal-enteric access will be excluded. Patients will history of chronic nausea and/or vomiting, including those with a diagnosis of gastroparesis due to diabetes mellitus will be excluded.

Patients with a Baux score of over 100 (age + TBSA), patients with declared palliative intent on admission, and patients for whom clinicians have high level of clinical concern based on clinical judgement will also be excluded.

Qualitative Component:

Inclusion Criteria

Healthcare workers (physicians, nurses, nursing assistants) who are anticipated to or have provided care to eligible patients in the enteral resuscitation arm of the study.

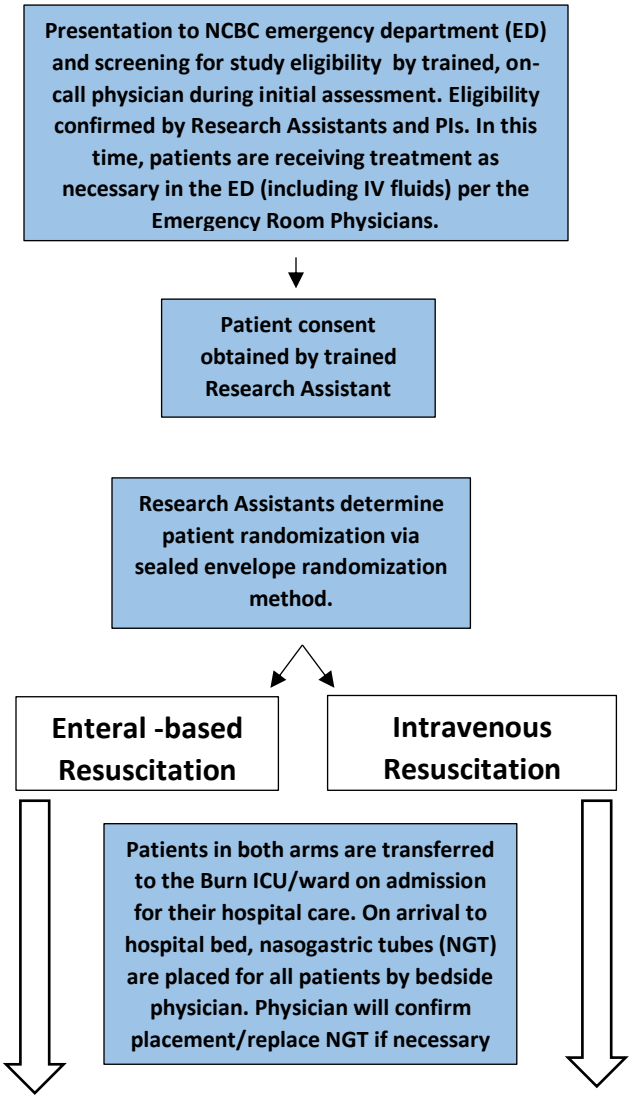
Exclusion Criteria

Exclusion criteria include co-PIs and co-investigators in this study to avoid bias.

11. Intervention

Please see schematic below for Intervention workflow. Specific goal-directed resuscitation protocols for IV fluid resuscitation and Enteral-based resuscitation in **Appendix** including details regarding modifications to allocated interventions based on response, patient request and improving/worsening disease.

Intervention Workflow Overview



Patient treatment per assigned resuscitation protocol will begin (Detailed protocols: Appendix A and B). Placement of NGT and start of resuscitation protocol may begin in ED if there is prolonged delay in transfer to hospital bed. Patient care will occur per appropriate COVID-19 precautions with physical distancing, hand hygiene and PPE use by staff per hospital policy. Patients who are COVID-19 positive will be excluded from the study and transferred to another hospital, per hospital policy.

Protocol will be followed as able for the duration of the acute resuscitation, typically 24-72 hours. Patients will be assessed at least every 2 hours with clinical markers such as vital signs, urine output, GI symptoms documented by bedside providers on the Resuscitation Documentation Flowsheet (Appendix C). Laboratory assessment will occur every 8 hours and will be documented.

General Resuscitation Protocol for Intravenous and Enteral-based Resuscitation

Resuscitation Timeline	Fluid Protocol	Clinical Assessment	Laboratory Assessment*	Additional Interventions
Hour 1	**See Appendices A and B** Administer Lactated Ringer's (LR) or Oral Rehydration Solution + LR according to calculated Parkland formula** Add or subtract fluid volume by every 2 hours based on urine output goal of at least 0.5 mL/kg/hr. IV Metoclopramide to be administered if GI symptoms such as bloating, nausea, discomfort, vomiting.	Measure and record vital signs every two hours or more frequently as needed. (Temperature, blood pressure, heart rate, respirations, oxygen saturation), urine output, physical signs of overt shock	CBC, BMP, Lactate, PT/PTT/INR (15 mL)	Additional interventions such as colloid or blood product transfusion, vasoactive agents, escharotomy/ faschiotomy, intubation as deemed necessary by clinical care team will be noted throughout this time period.
Hours 2-7				
Hour 8			CBC, BMP, Lactate (10 mL)	
Hours 9-15				
Hour 16			CBC, BMP, Lactate (10 mL)	
Hours 16+			CBC, BMP, Lactate every 8 hours, and PT/PTT/INR every 24 hours until resuscitation complete.	

* CBC=Complete blood count; BMP=Basic metabolic panel; PT=Prothrombin time; PTT=Partial Thromboplastin time; INR=international normalized ratio

**Parkland formula= 4cc * % Total Body Surface Area burned(TBSA) * weight(kg) = 24 hour fluid volume
Total resuscitation volume divided by 2, then divided by 8 to determine the starting resuscitation volume.

12. Outcomes

Goals

The overarching goals are to understand challenges and facilitators of enteral-based resuscitation and understand the effectiveness of the technique compared to standard of care (intravenous resuscitation).

Specific Aim 1: Determine the frequency of adherence to the enteral-based and IV fluid resuscitation protocols, and determine frequency of successful resuscitation.

Hypothesis 1: With goal-directed resuscitation, the primary outcomes of goal average urine output and successful resuscitation will be achieved in the majority of patients (over 50%). Protocol adherence will be at least 50%.

Specific Aim 2: Describe the challenges and facilitators to enteral and IV resuscitation protocol acceptance, implementation, compliance and sustainability.
Hypothesis 2: Enteral resuscitation will have logistical advantages over IV resuscitation, reduce delays in the initiation of resuscitation, have fewer interruptions, and will be easier to implement.

Primary endpoints
For the quantitative aspect, study variables will include measures of implementation and adherence to the enteral resuscitation protocol with variables such as: percent of resuscitation conducted enterally, proportion of protocol laboratory and clinical assessments completed, completeness of bedside documentation, number of inappropriate adjustments of resuscitation fluid rates based on urine output.

For the qualitative aspect, study variables and themes will be assessed to include the acceptability of the intervention for healthcare workers, acceptability of the intervention for patients, burden of the intervention and protocol for healthcare workers, acceptance of the protocol, perceived knowledge gaps, comfort level with the intervention protocol, concerns with the intervention, favored aspects of the intervention. These study variables will be ascertained from the interview guides, developed using the Consolidated Frameworks for Implementation Research (CFIR).

13. Participant Timeline

Patient screening and enrollment will occur after patient assessment in the Emergency Department at Kirtipur Hospital. After consent and enrollment, randomization to the intervention bundle will occur within the ED.

Treatment will commence per intervention assignment. The patient's clinical status and specific clinical metrics will be assessed every 2 hours during the acute resuscitation period, with laboratory marker measured every 8 hours. The acute resuscitation period typically lasts 24-72 hours.

Within 2 days of completing resuscitation, each patient will undergo a 10-15 minute semi-structured interview with a research assistant regarding their experience and opinion of the resuscitation bundle.

Patients data will be followed for the duration of their inpatient hospitalization in order to track hospital course, and outcomes such as survival and disposition. All communication with the patient and their families will be in person. If the patient and their family opt to do so, they can be contacted after the conclusion of the study with notification of the study results.

14. Sample Size

We would like to update the target patient enrollment to 240 patients. The sample size calculations are demonstrated below, with a necessary sample size of 212 and a 14% increase in target enrollment to account for missing data/dropouts. We assumed an absolute difference in the prevalence of the primary outcome (24-hour UOP within target range) of 20% between the exposed and unexposed, based off of available literature. This is non-probability-based convenience sampling of patients who present with acute burn injuries to Kirtipur Hospital.

Alpha: 0.05 (95% Confidence Level)
Power: 80%
Ratio of unexposed/exposed in sample: 1
Percent of unexposed with outcome: 35%

Percent of exposed with outcome:	Prevalence Difference vs. unexposed	Odds Ratio	Necessary Sample Size
55	20%	2.3	212

15. Recruitment

Patients will be screened by research study team members for eligibility in the Emergency Department at Kirtipur Hospital. All recruitment and screening will occur in the Emergency Department and inpatient setting on admission. No outside recruitment will occur. The study will aim to enroll over the winter season, as this is the timeframe with the highest incidence rate of burn injuries in Nepal.

Methods

16. Allocation

The patient treatment allocation sequence will be generated using the sealed envelope technique. The sealed envelopes for each sequentially numbered enrolled patient (e.g. Patient 1, Patient 2, Patient 3, etc) will contain a pre-assigned intervention arm that will be unknown to the research team prior to each patient's enrollment. Each sealed envelope will only be opened after patient enrollment is complete to reveal patient intervention arm allocation.

17. Blinding

This study is not blinded to the patients or providers.

18. Data Collection Methods

Intervention:

In order to ensure a contextually appropriate intervention and increase engagement, data collection tools have been adapted from the validated Joint Trauma System Burn Care Clinical Practice Guideline 12 (JTS Burn Care CPG 12) burn worksheet and resuscitation flowsheet with feedback from stakeholders at the Nepal Cleft and Burn Center. Please see attached documents (Resuscitation Flowchart and Documentation Chart) for the latest versions developed by the research and clinician team, to be further adapted for ease of use as needed.

Clinical data pertaining to the resuscitation interventions will be collected and documented by the bedside nurses and clinicians on the adapted Documentation Chart, with documentation of i) brief history and physical exam ii) two-hourly assessments of vitals, intake, output, and symptoms and iii) 8 hourly laboratory test results. This data will subsequently be transcribed into a secure electronic format by research assistants utilizing the RedCAP data collection system.

Post-resuscitation patient interview answers will be recorded on the RedCAP data collection system.

Qualitative Component:

Data collection tools include focus group interview guide which will serve to guide the semi-structured 1-hour discussions pre-enrollment, at 50% enrollment and after completion of enrollment with groups of doctors and nurses caring for the patients enrolled in the study. The

focus group interview guides are adapted for from the Consolidated Frameworks for Implementation Research (CFIR), a validated and widely used tool in Implementation Science research.

The focus group interviews will be audio-recorded, with audio files immediately transferred to a secure, password-protected data storage system. These audio files will subsequently transcribed and translated for thematic analysis.

19. Data Management

Personal patient information such as the collected demographic data and patient clinical outcomes data will be collected into a password protected, HIPPA compliant data storage system (REDCap®). The REDCap electronic data collection form will have built-in validation measures to ensure data quality and mitigate missing data (i.e; required entries, range checks, multiple choice single answer questions). When the data are downloaded for analysis, they will be downloaded in a de-identified manner. The physical charts with patient information such as the Documentation Chart will remain within the patient's medical record as a component of their records.

The majority of the patient in-depth interview guide will be adapted from validated tools to assess patient socioeconomic status, to assess household fire risk and safety, and cookstove safety. The interview will be audio-recorded, on two devices to ensure capture of the data in case of technical issues with the recording devices. The audio-files will be immediately transferred from the recording devices to a secure, password protected electronic data storage platform via a password protected device that is kept in a secure, locked location when not in use by the research assistants. The audio-files will be transcribed and translated, and a coded system will be utilized to de-identify the data. All qualitative analysis will take place using de-identified data. The datafiles will be retained for a minimum of 3-5 years after conclusion of the study per regulatory requirements.

Data downloaded for analysis will be de-identified. Data will be maintained in an electronic data storage platform (OneDrive for Business). The data will be managed by the University of Washington study team members. The co-Principle Investigators and co-Investigators (listed above) will have access to the final, de-identified data for purposes of data analysis. The Data Safety Management Board will also have access to the patient data for patient safety monitoring purposes.

20. Statistical Methods

We will perform descriptive and comparative statistics for both qualitative and quantitative implementation metrics. Qualitative analysis of the patient and focus group interviews will use a template analysis approach to code and organize data for cross-case analysis of patterns of challenges and facilitators for each component of the resuscitation bundle.

21. Data Monitoring

The research team will conduct weekly virtual meetings (increasing frequency of meetings as needed) to discuss progress and relevant issues. We will measure against our internal timelines of progress, including enrolling 10 patients per month after enrollment begins. Dr. Nakarmi, study PI, and Dr. Shankar Rai, study co-I, along with trained research assistants will be present for day to day monitoring, questions and problem solving. Dr. Kajal Mehta, U.S.- based PI will monitor all data submitted to RedCap for issues or patient safety concerns. Dr. Barclay Stewart, study co-I

and Assistant Professor of Surgery at University of Washington, will serve as a mentor for supervision and guidance on conducting the study.

Additionally, a Data Monitoring and Safety Board will be developed to monitor patient adverse events (AE) and serious adverse events (SAE). This is described below in section 22.

22. Harms

All patient clinical Adverse Events (AE) and Serious Adverse Events (SAE) will be monitored by study PIs. Furthermore, solicited or spontaneously reported adverse events will be reported to the study PIs. These will be investigated internally, in addition to reporting to the DSMB. All SAE will be reported to the DSMB within 1 working day of occurrence. All other AE and solicited or reported AE will be provided to the DSMB by study PI or Research Coordinator on a weekly basis.

Definitions:
Adverse Events (AE): are defined as those characterized as temporary in nature, mild symptomatology and no risk of long-term impact on morbidity and mortality, i.e. nausea/vomiting
Serious Adverse Event (SAE): those with risk of long-term impact on morbidity and mortality such as aspiration events, kidney injury requiring renal replacement therapy, and death.

Patients who experience serious adverse events attributed as a consequence of participation in the study may have costs of additional care (such as ventilation needs, renal replacement therapy needs) covered by the study.

23. Auditing

Trial conduct will be audited by the DSMB when it convenes to review serious adverse events. DMSB members will have access to the collected data to review. There will not be planned in-person audits unless requested by the DSMB members. The DSMB will be independent of study members.

Ethics and dissemination

24. Research Ethics Approval

The study is undergoing ongoing human subjects ethical review by the University of Washington Institutional Review Board and the Nepal National Health Research Council. Institutional approval has been obtained from the phect-NEPAL institutional ethical review board. The study team will work with the above ethical review boards to complete modifications as requested and amend the protocol.

25. Protocol Amendments

Important protocol modifications including changes to eligibility criteria, outcomes and analyses will be communicated to associated Institutional Review Boards (IRB) and trial registries. Outcomes and analyses will be presented to local and international burn care providers, and manuscripts reflecting the trial outcomes and analyses will be published in local and international journals.

26. Consent or assent

Intervention

Informed consent will be obtained from all patients and/or their authorized surrogate by our research team's trained research assistants after the patient has been identified as eligible for the study on screening and agrees to participate in the study. The consent form will be available in English and Nepali. Please see consent form (Appendix).

For patients who are functionally illiterate, consent will be obtained after understanding and agreement to participate in the study is confirmed by a witness. The patient to be enrolled will provide fingerprint signature, and the witness will sign in the designated area.

Qualitative Component:
Informed consent will be obtained from all participants (doctors, nurses) who participate in the Focus Group Interviews. The consent form will be available in English and Nepali.

All study participants including those from the Intervention and the Qualitative Component will be made aware of their ability to withdraw from the study at any time, and will be instructed in the channels to do so.

27. Confidentiality

Personal patient data will be collected and stored into a password protected, HIPPA compliant data storage system (REDCap®). If downloaded for analysis, the dataset will be downloaded in a de-identified manner in order to protect patient confidentiality during and after the trial. The DSMB and the PIs and Research Coordinator will have access to patient data with identifiers for patient safety monitoring purposes.

28. Declaration of Interests

The PIs and Co-Is have no financial or competing interests to declare for the trial of the study site at the Nepal Cleft and Burn Center.

29. Access to Data

Each of the study PI and Co-I (Dr. Kajal Mehta, Dr. Kiran Nakarmi, Dr. Shankar Rai), the Research Coordinator, Data analysts, and the DSMB members will have access to the final trial dataset.

30. Ancillary and Post-Trial care

The enrolled patients will continue to receive care per the standard of care after conclusion of the resuscitation portion of the study. The costs incurred for the remainder of standard of care (including operative management) will not be covered by the study.

31. Dissemination Policy

After conclusion of the study and data analysis, results will be presented to the healthcare providers at the study institution (Nepal Cleft and Burn Center at Kirtipur Hospital). Additionally, at the time of enrollment, patients will be asked if they would like to be contact in the future regarding study results. The patients who agree will also receive information regarding the results of the study.

The study analysis and results will be developed into manuscripts for publication as appropriate. The team will target both local and international journals, as well as local and international burn care conferences. PIs and Co-PIs, as well as research team members who contribute to the

study implementation and manuscript development will be included as co-authors in publications. The results are planned to be disseminated within 1 year of study conclusion.

Appendices

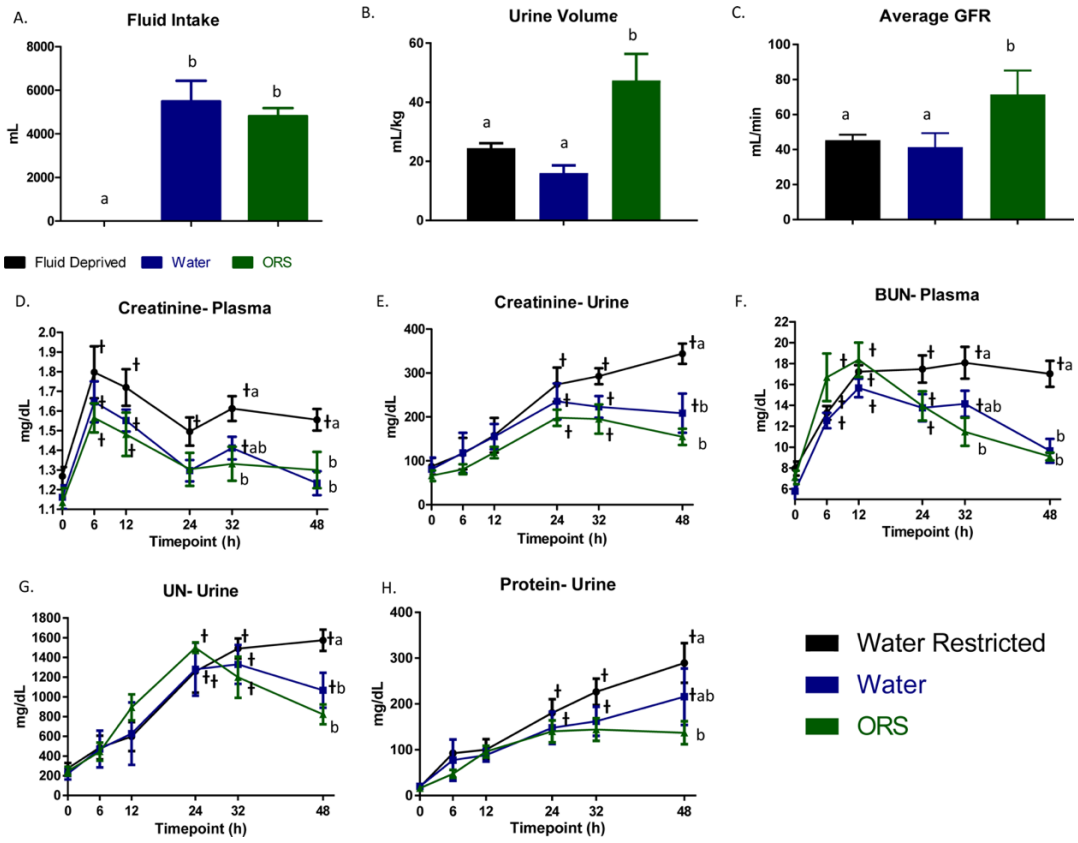
Appendix A: Enteral resuscitation literature review with references

Enteral resuscitation is efficacious and has unique physiological benefits in animal models. Multiple studies have demonstrated that sufficient volume repletion with enteral resuscitation can be achieved in burned animal models. Glucose-electrolyte solutions are well tolerated at rates commensurate with fluid resuscitation prediction formulas (i.e., evidence-based formulae that guides fluid resuscitation for burns, e.g., modified Brooke formula).[1]

A research team at The U.S. Army Institute for Surgical Research (USAISR**)** randomized 18 burned Yorkshire swine to three resuscitation groups: fluid deprivation, ad libitum oral water, or 70 mL/kg/day

WHO ORS.[2] ORS intake increased urine output and was associated with a lower plasma creatinine (i.e., a biomarker for acute kidney injury) compared to ad libitum or no water (Figure 1). The findings suggested that enteral resuscitation with WHO ORS rescues kidney function following burn injury.

Figure 1: World Health Organization (WHO) Oral Rehydration Solution (ORS) increases urine output positively influences burn-induced biomarkers compared in a porcine burn model[8]



Caption for Figure 1: Total fluid intake (A) urine output volume (B), and (C) Average glomerular filtration rate (GFR) throughout the duration of the study. Levels of creatinine (D, E) and urea nitrogen in the plasma (F) and the urine (G). Urinary protein (H). Means ± SEM with a different superscript are significantly different (P < 0.05) between treatments for indicated time point and a † indicates a significant (P < 0.05) difference from the BL value.

Enteral resuscitation also has unique physiological benefits that are not achieved by IV resuscitation, including maintenance of intestinal mucosal integrity and reduction in intestinal mucosal edema characteristic of capillary leak syndrome after burn.[3] Given that loss of intestinal mucosal integrity and bacterial byproduct translocation are hypothesized to contribute to multi-system organ failure, a common cause of death among burn patients, **enteral resuscitation may not only be a feasible and convenient complement to IV resuscitation, but may also be superior to IV resuscitation for patients with moderate-size burn injuries**.

Enteral resuscitation is safe and efficacious for burned humans in research settings. A recent systematic review of 12 studies examined the safety and efficacy of enteral resuscitation for patients with burn injuries.[4] **The authors reported that enteral resuscitation was**:

1. alone sufficient for most patients with 10-40% TBSA burns;
2. able to be administered at rates commensurate with fluid resuscitation prediction formulas;
3. associated with occasional gastrointestinal intolerance (e.g., nausea, vomiting), but not clinically significant aspiration;
4. not associated with atypical electrolyte derangements; and
5. ineffective and inappropriate for resuscitation in patients with cardiovascular collapse at presentation.

Given these findings, the American Burn Association, International Society for Burn Injuries, and International Committee of the Red Cross suggest considering enteral resuscitation for moderate-size burns, particularly when resources are limited.[5–8] However, there is insufficient prospective data regarding the effectiveness and implementation of enteral resuscitation in austere settings to inform guideline development.

References:

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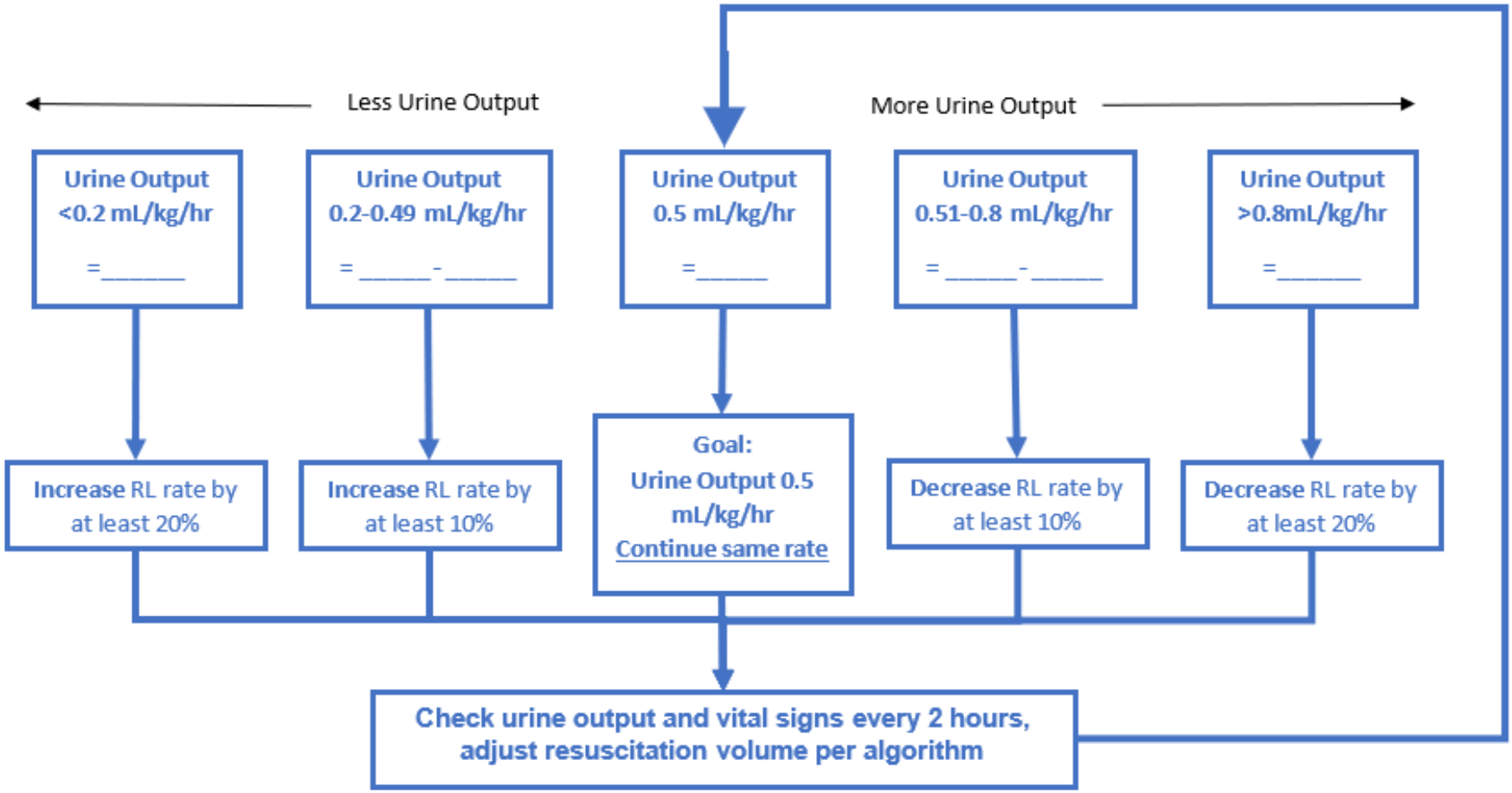
6. Peck, M., Jeng, J. & Moghazy, A. Burn Resuscitation in the Austere Environment. *Crit. Care Clin.* **32**, 561–565 (2016).
7. Burmeister, D. M. *et al.* Operational Advantages of Enteral Resuscitation Following Burn Injury in Resource-Poor Environments: Palatability of Commercially Available Solutions. *J. Spec. Oper. Med. Peer Rev. J. SOF Med. Prof.* **19**, 76–81 (2019).
8. ISBI Practice Guidelines Committee *et al.* ISBI Practice Guidelines for Burn Care. *Burns* **42**, 953–1021 (2016).

Appendix B: Resuscitation Protocol Flowsheets and Documentation Chart

Enhanced Adult Burn Fluid Resuscitation Protocol for Intravenous Fluid Only Resuscitation

Use for Adults ≥18 years, not for pediatric patients, electrical/chemical burn patients or patients with suspected inhalation injury

- Baseline fluid calculation per Parkland Formula (4cc x %TBSA x weight (kg) = 24-hour fluid volume)
- Vital signs including Heart Rate (HR), Blood Pressure (BP), O2 saturation and Urine Output (UO) should be tracked every 1 to 2 hours, with fluid rate adjusted accordingly
- **Target Urine Output = 0.5 mL/kg/hr; HR < 120 bpm; Systolic BP >90 mmHg**
- If hypotensive with EITHER Intravenous of enteral-based resuscitation, give bolus of 10cc/kg IV fluids. Consider vasopressor or colloid augmentation.
- For all calculated hourly resuscitation volumes, please round to the nearest 10 (i.e., 74 =70ml, 76=80mL)



Adult Burn Fluid Resuscitation Protocol for Enteral-based Resuscitation

Use for Adults ≥18 years, not for pediatric patients, electrical/chemical burn patients or patients with suspected inhalation injury

- Vital signs including Heart Rate (HR), Blood Pressure (BP), O_2 saturation and Urine Output (UO) should be tracked every 1 to 2 hours, with fluid rate adjusted accordingly
- **Goal: UO=0.5 mL/kg/hr, HR < 120, Systolic BP >90**
- If hypotensive with EITHER resuscitation type, give bolus of 10cc/kg IV fluids. Consider vasopressor or colloid augmentation.
- ORS can be administered by drinking or administering the calculated volume via NGT every hour
- For all calculated hourly resuscitation volumes, please round to the nearest 10 (ie 76=80mL)

Abbreviations: IV= Intravenous, RL= Ringer's Lactate, ORS= Oral Rehydration Solution, NGT= Nasogastric Tube

Baseline Resuscitation Protocol for Enteral-based Resuscitation

Urine Output < 0.2 mL/kg/hr = _____ → Increase RL or ORS by at least 20%

Urine Output 0.2-0.49 mL/kg/hr = _____ → Increase RL or ORS by at least 10%

Urine Output 0.5 mL/kg/hr =_____ → Goal: Urine Output 0.5 mL/kg/hr Continue same rate

Urine Output 0.51-0.8 mL/kg/hr =_____ → Decrease RL or ORS by at least 10%

Urine Output >0.8mL/hr =_____ → Decrease RL or ORS by at least 20%

Enteral Resuscitation Pathway for low Urine Output

If using ORS and UO <0.5 mL/hr at check, **give additional 50% of calculated hourly resuscitation volume with RL**

If UO remains <0.5 mL/kg/hr at next check, then give additional **100% calculated hourly resuscitation volume with RL**

If UO remains <0.5mL/kg/hr, continue additional 100% IV LR resuscitation volume until improves

If UO improves to ≥ 0.5 mL/kg/hr at next check, then **down-titrate additional IV LR volume until back to only ORS** (i.e. next hour only 25% additional volume, and if maintains UO on next check, then no additional IV LR)

Enteral-based Resuscitation Intolerance Pathway

If patient receiving enteral resuscitation:

- If minor symptoms such as nausea, or discomfort: document and check on patient symptoms every 2 hours
- If any minor or major GI intolerance (nausea, discomfort, vomiting), then **start on scheduled metoclopramide**
- If two episodes of vomiting, then **transition to full RL IV fluid resuscitation**
- If patient unable to ingest the complete hourly volume requirement via ORS, then **give remaining volume via IV RL**

Today's Date: / / 2021	**Date and Time of Injury:** / / 2021; : AM/PM	**InPatient No:**
Name	**Admission Wt. (kg)**	**%TBSA** (Do not include superficial 1st degree burn)	**Burn Mechanism**

Parkland Formula: **Total Resuscitation Volume:** _____ % X _____ kg X 4ml = _____ in 24 hours (TBSA) (pt. weight)	**First 8 hours** (use 1/2 of total volume) _____ ÷ 8 hrs. **Starting Hourly Fluids =** _____ ml/hour	**Starting 2 Hourly I.V Fluid** **_____ ml**
Target Urine Output: _____ kg x 0.5 ml/kg/hr = **_____ per hour**	**Upper CutOff =** _____ kg x 0.8 ml/kg/hr = _____ per hr **Lower CutOff =** _____ kg x 0.2 ml/kg/hr = _____ per hr	**2 Hourly Urine** **Upper Cutoff: _____ml** **Target: _____ml** **Lower CutOff: _____ml**
Resuscitation Start time: _____:_____ AM / PM	**Time post Incident: _____Hrs _____ Mins**	

Resus. Hour	Planned total fluid rate	Amount of Fluids Given				Total fluids given (since last check)	**Urine Output (q 2hrs)**	Vitals			Symptoms: ✓ if yes				Comments on symptoms or issues	Calculated Resuscitation for **Next 2 Hrs.**
		Oral fluids		IV fluids	Additional fluids			Heart Rate	Blood Pressure	Oxygen Sat (%)	Nausea	Vomiting	Distention	Reflux		
		By mouth	By NG													
1 - 2							mL									
3 - 4							mL									
5 - 6							mL									
7 - 8							mL									
9 - 10							mL									
11 - 12							mL									

Lower Cutoff ← **Target Urine Output** → Upper Cutoff

↑↑ Fluid by 20% ↑ Fluid by 10% (continue same) ↓ Fluid by 10% ↓↓ Fluid by 20%

Resus. Hour	Planned total fluid rate	**AMOUNT OF FLUIDS GIVEN**				Total fluids given (since last check)	**Urine Output (q 2hrs)**	**VITALS**			**SYMPTOMS:** ✓ if yes				Comments on symptoms or issues	**CALCULATED RESUSCITATION RATE FOR NEXT 2 HRS.**
		Oral fluids		IV fluids	Additional fluids			Heart Rate	Blood Pressure	Oxygen Sat (%)	Nausea	Vomiting	Distention	Reflux		
		By mouth	By NG													
13 - 14							mL									
15 - 16							mL									
17 - 18							mL									
19 - 20							mL									
21 - 22							mL									
23 - 24							mL									

Resuscitation Laboratory Results

Time of Resuscitation	CBC	BMP	Arterial Blood Gas	Coagulation Markers (PT/PTT/INR)
Admission	WBC: Hgb: Hct: Plt:	Na: K: BUN: Creat:	**Lactate:** **Cl:** **HCO_3:**	PT: PTT: INR:
Hour 8	WBC: Hgb: Hct: Plt:	Na: K: BUN: Creat:		
Hour 16	WBC: Hgb: Hct: Plt:	Na: K: BUN: Creat:		
Hour 24	WBC: Hgb: Hct: Plt:	Na: K: BUN: Creat:	Lactate: Cl: HCO_3:	PT: PTT: INR:
Hour 32	WBC: Hgb: Hct: Plt:	Na: K: BUN: Creat:		
Hour 40	WBC: Hgb: Hct: Plt:	Na: K: BUN: Creat:		
Hour 48	WBC: Hgb: Hct: Plt:	Na: K: BUN: Creat:	Lactate: Cl: HCO_3:	PT: PTT: INR:

Appendix C: Post-Resuscitation Patient Interview Guide

Post-Resuscitation Patient Interview Guide

Interview to be administered by trained data collectors, responses will not be audio-recorded. Interview to last 10-15 minutes.

Topic areas to cover:

- Experience and understanding of resuscitation (both IV and enteral)
- Palatability of enteral resuscitation
- Prior experience with oral rehydration solution (ORS)
- Challenges with resuscitation (both IV and enteral)
- Positives of resuscitation (both IV and enteral)

Appendix D: Healthcare Worker Focus Group Interview Guides

Focus Group In-Depth Interview Guides

The following templates outline the anticipated questions that will be used in semi-structured focus group interviews with involved healthcare providers. Based on responses, additional probes and questions may be asked to fully explore the responses.

Physician Focus Group

- Have you previously heard of or personally used Oral Rehydration Solution (ORS)?
- How often do you recommend/prescribe ORS in your typical practice?
    - At Nepal Cleft and Burn Center (NCBC)?
    - In other clinical settings?
- What clinical or laboratory datapoints do you use in your practice to diagnose shock?
- What clinical or laboratory datapoints do you find most useful to assess a patient's resuscitation progress?
- What are challenges with implementation of a resuscitation protocol?
    - Thoughts on hourly check of vitals and urine output
    - Thoughts on hourly adjustments to resuscitation volume
- From your participation in this study and observations made, do you think ORS provides an adequate amount of resuscitation?
- Do you think ORS provides an effective method of resuscitation?
- What are advantages to the use of enteral resuscitation in this population?
- What are challenges in the use of enteral resuscitation in this population?
- Do you think it will be beneficial to implement a protocol for resuscitation?
- After participating in this study, will you plan to increase your use of ORS in your clinical practice with burn patients?
- Do you have additional comments, questions, ideas you would like to offer?
-

Nursing Staff Focus Group

- Have you previously heard of or personally used Oral Rehydration Solution (ORS)?
- How often is ORS used for patients with burn injury at NCBC?
- What signs do you typically first notice when a burn patient starts to get sick?
- What are challenges with implementation of a resuscitation protocol?
    - Thoughts on hourly check of vitals and urine output?
    - Thoughts on adjustments to resuscitation volume?
- From your participation in this study and observations made, do you think ORS provides an effective method of resuscitation?
- What are advantages to the use of enteral resuscitation in this population?
- What are barriers in the use of enteral resuscitation in this population?
- What were logistical difficulties with enteral resuscitation?
- Were there differences in children and adult attitudes towards enteral resuscitation?
- After participating in this study, do you think a protocol should be used more often?
    - Should ORS be used more often?
- Do you have additional comments, questions, ideas you would like to offer?

Appendix E: Consent Forms for Patients (Intervention)

Research Study Consent Form
Nepal Cleft and Burn Center - PHECT Nepal Hospital and University of Washington
"Testing the Usefulness of Burn Resuscitation Protocols with IV Fluids and Oral Fluids"

Lead Researcher: Dr. Kiran Nakarmi, WhatsApp no.: +977 985-106-1490 email: knakarmi@gmail.com
Lead Researcher: Dr. Kajal Mehta, WhatsApp no.: +1-979-824-5064, email: kajalm@uw.edu
Researcher: Dr. Shankar Rai, WhatsApp no.: ph: +977 984-129-5062, email: shankarrai1956@gmail.com
Advisor: Dr. Barclay Stewart, email: barclays@uw.edu
(All phone numbers are monitored 24 hours a day)

We are asking you to be in a research study. This form gives you information to help you decide whether or not to be in the study. Being in the study is voluntary. Please read this carefully. You may ask any questions about the study. Then you can decide whether or not you want to be in the study.

KEY STUDY INFORMATION

This research study will trial a new protocol for treating patients with burn injuries, using two different methods of to restore fluids after a serious burn injury. Major burn injuries cause significant damage to the skin and causes the body to lose fluid quickly – which is why burn patients need to get treated with lots of fluids immediately. Burn patients usually receive fluids through an IV in their vein, once they reach the hospital. If they do not receive treatment, they can become very dehydrated and suffer major complications. That is why we are studying different methods of getting fluids to patients as quickly and effectively as possible.

We are inviting you to take part in this study because you have recently suffered a major burn injury. This page is to give you key information to help you decide whether or not to participate. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHY ARE WE DOING THIS STUDY AND WHAT WILL YOU BE ASKED TO DO IF YOU PARTICIPATE?

Both Intravenous Fluids (IVF) and oral fluids can be used for rehydration in burns. Oral fluids are not used as commonly, and there are not many tests to show that it can be used for burns in a setting like Nepal where it is hard to reach a hospital or burn center for some people. By doing this study, we hope to learn if it is possible for the hospitals around Nepal to learn this treatment method before sending patients to NCBC, and potentially save those patients lives. If you agree to participate:

- You will receive either Intravenous Fluids or Oral Fluids (using Oral Rehydration Solution) ± Intravenous Fluids (as needed). The study doctor will not pick which type of fluids you will take. We will use a computer to randomly place you in one of two study groups. One group will receive Intravenous Fluids only, the other group will receive Oral fluids plus Intravenous fluids as needed. The computer picks the group for you is by chance, like a flip of a coin. You will have an equal chance (50%/50%)of being in either group.
- Once the group is chosen, you will receive those fluids for the first 24-36 hours of your hospital stay, until you are stabilized. During this time, your vital signs like blood pressure and heart rate will be checked every hour, and we will measure how much urine you make every hour to check your hydration.
- You will have blood drawn 3 times in the first day to check your electrolytes and your organ function.
- The study team will check in on your progress and take note of the outcome of your injury.
- The type of fluid you receive will not affect your treatment options for your burns.

During the study, your team of doctors can share your lab results with you as you receive care.

WHY MIGHT YOU NOT WANT TO BE IN THIS STUDY?

If you are in this study, you will receive fluid treatment for your burn injury with an accepted fluid, but you and your doctor will not get to choose which one. It will be randomly chosen which fluid type you receive instead of a doctor choosing. If you already have a preference for either fluid type, then you might not want to participate in this study. The Detailed Consent provides a list of possible risks for the study fluids. You do not have to participate in the study to receive fluids to treat your burns. Currently, either Intravenous fluids or oral fluids are the two fluid rehydration treatment options, but they can be available to you in a different protocol outside of the study. If you decide not to be in the study, your burn doctor will choose a fluid treatment option and schedule of labs that he/she thinks is best for you.

WHY MIGHT YOU WANT TO BE IN THIS STUDY?

Both medicines used in this study have been used to rehydrate patients after burn injuries. No matter which fluid option you are assigned to, you will receive the medically necessary amount of fluid. The study provides the fluids and additional laboratory tests to you at no cost. The research team will monitor your progress closely. If your condition gets worse, or if you have any concerns, we can remove you from the study. Your hospital team can treat you per the hospital standards for burn care. If you are in this study, you will contribute to our understanding of how to treat burn patients better in the future.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. If you decide not to take part, you will not lose any services, benefits, or rights you would normally have. You will still receive treatment for your burn injury. You can choose to withdraw at any time during the study.

WHAT IF YOU WANT MORE INFORMATION?

The rest of this document gives you more information about the study, like:

- What will be done at the research visits
- The risks of the fluids
- Who will pay for treatment if you are injured from the study procedures
- How we will protect your privacy
- Who to talk to if you have problems, suggestions or concerns

DETAILED PURPOSE OF THE STUDY

The purpose of this study is to help decide if oral rehydration in large burn injuries will help decrease the serious complications from burns. Timely hydration is extremely important and lifesaving in severe burns. Given the difficulty of accessing medical attention equipped to treat burns in Nepal, the purpose of this study is to help determine if oral rehydration using a widely available Oral Rehydration Solution (ORS) can help provide timely rehydration in the setting of major burn injuries. We will be studying an oral rehydration protocol as well as an intravenous rehydration protocol with randomization of patients into either protocol. There will be approximately 120 patients each fluid group and 240 patients total.

STUDY PROCEDURES

A mainstay of major burn injury is resuscitation – or rehydration. If you agree to participate in this study, you will be randomized to receive treatment either in the intravenous (IV) fluid treatment arm or the oral-

fluidbased treatment arm, which will follow the international guidelines for care in acute burns. This means there is a 50%/50% chance of receiving treatment in either the IV fluid treatment arm or the oral (enteral) fluid-based treatment arm.

During the fluid treatment portion of the study, you will be closely monitored. Your vital signs (heart rate, blood pressure, oxygen levels, breathing rate) and physical exam including signs of overt shock will be measured, monitored and recorded at least every 2 hours. We will also measure how much urine you are making every 2 hours, and adjust how much fluid you are getting to keep your urine at an appropriate level.

You will undergo treatment with fluids either by IV or a combination of taking fluids by mouth using Oral Rehydration Solution (ORS) plus IV fluids as needed to meet the fluid goals for every hour. This will continue for 24-36 hours after you come to hospital with your injury. Using IV fluids based on the size of your burn, and your weight is standard treatment for burns. Our study is seeing whether fluids by mouth (using ORS) similarly based on the size of your burn and your weight is possible here in Nepal.. Please be aware that if you are in the oral fluids-based treatment with ORS, if you are unable to drink or tolerate the amount of ORS that is needed, that is not a problem. You will receive the amount of fluid that you could not take by mouth, through an IV using IV fluids. You will not be penalized or punished for not being able to tolerate the ORS, if that happens.

The ORS which will be used in this study is F.D.A. approved for use in severe dehydration (from diarrheal illnesses), but is not currently F.D.A -approved for rehydration after major burn injuries. Despite this, ORS has been used and is recommended for use in certain settings when IV fluids are not available for major burn injuries.

You will have standard labs drawn on admission, at 8 hours, 16 hours, 24 hours and every 8 hours beyond while you are getting continuous fluids. This will help assess your progress. The labs taken on admission and every 24 hours will be a 15 mL blood draw. The labs taken at 8 hours, 16 hours and every 8 hours beyond 24 hours will each be a 10mL blood draw. A maximum of 50 mL of blood will be collected per day. You are able to refuse treatment at any time.

Once your fluid resuscitation is complete, the study team will continue to examine your medical records while you are admitted to the hospital to understand your hospital course, understand what complications you might have, and to see the outcome of your treatment including if and when you are able to leave the hospital. If you are randomized to the oral fluid-based treatment, after your fluid resuscitation is complete, 1-2 research team members will do a brief interview with you to understand your experience with the oral fluid method. The interview will last about 15 minutes, and will ask questions like how your found the fluid treatment, if you had any symptoms with the fluid treatment, and what you liked about the fluid treatment.

RISKS, STRESS, OR DISCOMFORT

Research-related risks to the study are limited, but most commonly may include abdominal discomfort, nausea and/or vomiting related to the consumption of Oral Rehydration Solution (ORS). Less common but potentially severe risks include the risk of aspiration with vomiting of ORS, and the risk of harmful electrolyte changes. All patients will be monitored for these side effects and risks, which will be immediately treated as able (ie. anti-nausea medication, oral rehydration stopped, oxygen therapy, etc). As part of the study and your burn treatment, you may receive IV fluids such as Ringer's Lactate. This fluid has very small risks of causing harmful changes to your electrolytes; we will be monitoring your blood electrolyte levels in order to recognize and treat these problems if they occur. Additionally, you may receive IV metoclopramide, which is an anti-nausea medication. This may rarely cause you to experience temporary drowsiness or change in how you taste food.

There are psycho-social risks for stress, anxiety and depression, as well as significant pain and discomfort associated with major burn injuries. If and when identified by study team members, these will be addressed by the treatment team as able with pain medications, anxiolytics, and/or psycho-social support.

ALTERNATIVES TO TAKING PART IN THIS STUDY

If you choose not to participate in the study, you will receive treatment for your burn according to the standard of care at the Nepal Cleft and Burn Center. There will be no penalty for not taking part in the study

BENEFITS OF THE STUDY

This study will help determine if oral rehydration can be used on a larger scale, and ultimately save lives of those injured with major burn injuries. As a participant in this study, you may benefit from increased frequency of monitoring and increased frequency of laboratory assessment which can be used to help direct your medical care. Additionally, you will not incur any of the costs of the medications, supplies and laboratory tests used for your resuscitation treatment during the study.

SOURCE OF FUNDING

The Nepal Cleft and Burn Center and the University of Washington study team is receiving financial support for the study from the United States National Institutes of Health (NIH). Additional financial support is from the University of Washington Department of Surgery.

CONFIDENTIALITY OF RESEARCH INFORMATION

The study teams at the Nepal Cleft and Burn Center and the University of Washington will have access to the confidential data associated with this study. The link between your identifiers and the research data will be destroyed after the records retention period required by law. Prior to analysis, any identifying information will be removed. Your personal lab results will be released to you and discussed with you as part of your clinical care. A copy of the consent form (both in Nepali and English) will be placed in your medical record.

Government or university staff sometimes review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

Certificate of Confidentiality

We have a Certificate of Confidentiality from the United States National Institutes of Health. These protections only apply to data held in the United States.

This helps us protect your privacy. The certificate means that we do not have to give out information, documents, or samples that could identify you even if we are asked to by a court of law in the United States. We will use the Certificate to resist any demands for identifying information.

We can't use the Certificate to withhold your research information if you give your written consent to give it to an insurer, employer, other person. Also, you or a member of your family can share information about yourself or your part in this research if you wish.

There are some limits to this protection. We will voluntarily provide the information to:

a member of the United States government who needs it in order to audit or evaluate the research;

individuals at the institution(s) conducting the research, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly;

individuals who want to conduct secondary research if allowed by federal regulations and according to your consent for future research use as described in this form;

to relevant authorities as required by other Federal, State, or local laws.

The Certificate expires when the NIH funding for this study ends. Currently this is July 1, 2022. Any data collected after expiration is <u>not</u> protected as described above. Data collected prior to expiration will continue to be protected."

USE OF INFORMATION AND SPECIMENS

Commercial Profit

The specimens collected as part of this research will NOT be used for commercial profit.

Genetic Sequencing

Any biospecimens obtained will not be used for genome sequencing

Returning Results to You

There will be multiple sets of laboratory data that will be obtained from you, and these results will be shared as part of your treatment, if desired. You can request your care team and the study team to not share the results.

Using Your Data in Future Research
The information and/or specimens that we obtain from you for this study might be used for future studies. We may remove anything that might identify you from the information and specimens. If we do so, that information and specimens may then be used for future research studies or given to another investigator without getting additional permission from you.

OTHER INFORMATION
You may refuse to participate and you are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. If you wish to withdraw, please contact the researchers listed at the top of page 1 of this consent form.

A description of this clinical trial will be available on https://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

RESEARCH-RELATED INJURY
If you think you have a medical problem or illness related to this research, contact Dr. Kiran Nakarmi (ph: +977 985-106-1490) or Dr. Shankar Rai (ph: +977 984-129-5062). They will treat you or refer you for treatment.

If you have any questions regarding your rights as a research participant, you can also contact the Nepal Health Research Council by phone (ph +977 1-425-4220), email (nhrc@nhrc.np.gov) or through the website (http://nhrc.gov.np/contact/). You will be directed to members of the NHRC board.

There are very limited risks to participation in the study, but if you are harmed from being in this study, medical care is available to you at the Nepal Cleft and Burn Center at Kirtipur Hospital. It is important that you promptly tell the researchers if you believe that you have been injured or harmed because of taking part in this study. You can tell the researcher in person or call him/her at the number(s) listed at the top of this form. This number is monitored 24 hours a day. The costs of the treatment may be billed to you or your health insurance similar to other medical costs, and there is typically not compensation available – however this will be reviewed on a case-by-case basis. By signing this consent form, you do not waive any right to seek payment.

_____

Printed name of study staff obtaining consent Signature Date

Subject's statement
This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

_____

Printed name of subject Signature of subject Date

When subject is not able to provide informed consent:

_____

Printed name of representative Signature of representative Date

Relationship of representative to subject

When subject is unable to read and/or write, they may provide their consent to participate in the study via fingerprint in the designated area after the research team and a witness have confirmed comprehension of the study and willingness to participate. A witness must sign after confirming the subject's understanding and agreement to participate in the study:

☐ Participant fingerprint denoting consent to participate in the study.

Printed name of Witness | Signature of Witness | Date

Witness role/relationship (family member, friend, nurse, hospital assistant, etc.)

Copies to: Researcher
Subject
Subject's Medical Record (if applicable)

Appendix F: Consent Form for Healthcare Workers (Qualitative Component)

Research Study Consent Form
Nepal Cleft and Burn Center - PHECT Nepal Hospital and University of Washington
"Healthcare Worker Attitudes on the Feasibility of Burn Resuscitation Protocols with IV Fluids and Oral Fluids"

Lead Researcher: Dr. Kiran Nakarmi, WhatsApp no.: +977 985-106-1490 email: knakarmi@gmail.com

Lead Researcher: Dr. Kajal Mehta, WhatsApp no.: +1-979-824-5064, email: kajalm@uw.edu
Advisor: Dr. Barclay Stewart, email: barclays@uw.edu
(All phone numbers are monitored 24 hours a day)

We are asking you to be in a research study. This form gives you information to help you decide whether or not to be in the study. Being in the study is voluntary. Please read this carefully.

A description of this clinical trial will be available on https://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

DETAILED PURPOSE OF THE STUDY

The overall research study will trial a new protocol for treating patients with burn injuries, examining two methods to restore fluids after a serious burn injury. As you know, major burn injuries cause significant damage to the skin and causes severe dehydration. Patients with major burn injuries are typically treated with Intravenous (IV) fluids once they reach a hospital, however you have taken care of many patients who did not receive adequate or timely fluids after their injury. As you are aware, if patients do not receive treatment, they can become dehydrated and suffer major complications such as burn shock and death. Given this, the purpose of this study is to help determine if it is possible to use oral rehydration using a widely available Oral Rehydration Solution (ORS) can help provide timely rehydration in the setting of major burn injuries. We will be studying an oral rehydration protocol as well as an intravenous rehydration protocol with randomization of patients into either protocol. There will be approximately 120 patients in each of the rehydration protocols. You have been trained in these resuscitation protocols and are helping take care of patients who are enrolled as participants in the study.

The specific portion of the study you are being asked to participate in is a set of focus group interviews, in which the research team will talk with you and your colleagues to understand your experiences in administering the IV and oral fluid-based resuscitation protocols. You are able to provide key insights into your experience with implementing these protocols. This consent form will give you key information to help you decide whether or not to participate.

STUDY PROCEDURES

- You will be asked to participate in focus group meetings with the research team members. These are group discussions that the research team will lead. Each meeting will last about 1 hour.
- The focus group discussions will be amongst groups of healthcare providers caring for burn patients enrolled in this study (doctors, nurses).
- The focus group discussions will be focused on your experiences in understanding and using the resuscitation protocols. This includes challenges that you predict, are experiencing, and ideas for improvement. This also includes aspects of the protocols and methods that you think may be advantageous and easier.
- The meetings will be confidential, and in no way will you be penalized for your opinions or experiences that you share. Your opinions do not have any impact on your job security.
- The meetings will be voice-recorded so the recordings can be written out and translated for further examination. You will be not be associated with your words on the transcription. Once the work with the voice-recordings is complete, they will be destroyed. If you have concerns about the voice-recordings, you can ask to review specific parts during which you spoke, and you can request those be deleted.
- Tea and snacks will be available during the interviews.

RISKS, STRESS, OR DISCOMFORT

If you are in this study, you will be asked to share your experiences or opinions of the new protocols, which you may be uncomfortable for you. You may worry how others perceive your opinion, and this may

cause you stress. The goal is for an open and honest discussion as we seek to improve the care for our burn patients. There are minimal risks of participating in this study. The research team, including the senior surgeons, will not and cannot punish you for opinions you may share. These focus group discussions have no effect on your job status.

ALTERNATIVES TO TAKING PART IN THIS STUDY

If you choose not to participate in the study, that is entirely acceptable. There will be no penalty for not taking part in the study. You will continue to care for your assigned patients, whether enrolled in the study or not.

BENEFITS OF THE STUDY

As a healthcare provider, you see the severe complications of burn injuries and lack of access to treatment throughout your daily job. By participating in this study, you will provide crucial information for the research team to understand how to improve access to fluids for patients in a more timely manner. You will be able to personally contribute to the development of knowledge and improvement of care within your field of work. This can be fulfilling and rewarding. There may also be small benefits additional benefits such as tea and snacks provided during the focus group interviews. If at any time you feel uncomfortable sharing your opinion and experience, you can ask to be removed from the study.

This study will help determine if oral rehydration can be used on a larger scale, and ultimately save lives of those injured with major burn injuries. As a participant in this study and research, you will be able to provide valuable information to the research team and contribute to the science of oral fluid-based resuscitation.

SOURCE OF FUNDING

The Nepal Cleft and Burn Center at Kirtipur Hospital and the University of Washington study team is receiving financial support for the study from the United States National Institutes of Health (NIH). Additional financial support is from the University of Washington Department of Surgery.

CONFIDENTIALITY OF RESEARCH INFORMATION

The study teams at the Nepal Cleft and Burn Center and the University of Washington will have access to the confidential data associated with this study. The link between your identifiers and the research data will be destroyed after the records retention period required by law. Prior to analysis, any identifying information will be removed. A copy of your consent to participate will be kept on file, in a secure location.

Government or university staff sometimes review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

Certificate of Confidentiality

We have a Certificate of Confidentiality from the United States National Institutes of Health. These protections only apply to data held in the United States.

This helps us protect your privacy. The certificate means that we do not have to give out information, documents, or samples that could identify you even if we are asked to by a court of law in the United States. We will use the Certificate to resist any demands for identifying information.

We can't use the Certificate to withhold your research information if you give your written consent to give it to an insurer, employer, other person. Also, you or a member of your family can share information about yourself or your part in this research if you wish.

There are some limits to this protection. We will voluntarily provide the information to:

- a member of the United States government who needs it in order to audit or evaluate the research;
- individuals at the institution(s) conducting the research, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly;
- individuals who want to conduct secondary research if allowed by federal regulations and according to your consent for future research use as described in this form;
- to relevant authorities as required by other Federal, State, or local laws.

The Certificate expires when the NIH funding for this study ends. Currently this is **July 1, 2022**. Any data collected after expiration is not protected as described above. Data collected prior to expiration will continue to be protected.

USE OF INFORMATION AND SPECIMENS

Returning Results to You

The research team will present the findings of the research, including the important points learned from the focus group interviews to the hospital staff including physicians, nurses and others.

Using Your Data in Future Research

The information and/or specimens that we obtain from you for this study might be used for future studies. We may remove anything that might identify you from the information. If we do so, that information may then be used for future research studies or given to another investigator without getting additional permission from you.

OTHER INFORMATION

You may decline to participate and you are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. If you wish to withdraw, please contact the researchers listed at the top of page 1 of this consent form.

A copy of the consent form will be emailed to you at an email address that you provide. It will be a "PDF" document. Most computers already have PDF viewer software installed, which will allow you to open, read, or print the consent form. The email we send you will include a link to PDF viewer software (such as Adobe Acrobat Reader) in case your computer doesn't already have it. If you would prefer to receive a paper copy of the consent form at no cost to you, please contact the researcher listed on page 1 of this consent form.

A description of this clinical trial will be available on https://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

RESEARCH-RELATED INJURY

If you think you have an issue or question related to this research, contact Dr. Kiran Nakarmi (ph: +977 985-106-1490) or Dr. Shankar Rai (ph:+977 984-129-5062). They will help answer your questions.

If you have any questions regarding your rights as a research participant, you can also contact the Nepal Health Research Council by phone (ph +977 1-425-4220), email (nhrc@nhrc.np.gov) or through the website (http://nhrc.gov.np/contact/). You will be directed to members of the NHRC board.

There are very limited risks to participation in the study, but if you believe you are being harmed from participating, please let the research team know right away. Any concerns will remain confidential. You can tell the researcher in person or call him/her at the number(s) listed at the top of this form. This number is monitored 24 hours a day.

If you agree to participate in the study, please sign below:

Subject's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. I give permission to the researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

Printed name of subject	Signature of subject	Date

Printed name of study staff obtaining consent	Signature	Date

Copies to: Researcher

Subject