LIBERIA EBOLA VIRUS DISEASE CLINICAL MANAGEMENT MANUAL

31 December 2014

Ministry of Health and Social Welfare

ACKNOWLEDGMENTS

This clinical management manual for Ebola Viral Disease in Liberia was developed after several ETUs were established in the country following the outbreak early this year. As the outbreak evolved, it became evident that different SOPs were being used by clinicians across these treatment facilities. As a result of discussions held by the National Case Management Committee of the Incident Management System, various stakeholders were brought together to contribute their time and expertise to the development of this manual.

The MOH is very pleased with the active participation of all of our partners who contributed in various ways to the development and finalization of this manual. We are especially grateful to our partners at the World Health Organization and the Clinton Health Access Initiative for providing technical guidance in working with our partners on the finalization of this manual.

We also specifically want to extend our appreciation to the following institutions and individuals:

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Finally, to all the clinicians in our treatment centers, let this manual be the cornerstone of the management of all EVD cases. Adherence to the protocol in this manual is necessary and critical to the management of all patients who will be admitted into ETUs across the country. It is our hope that as new evidence evolves on the management of EVD in Liberia and other settings, it will inform the continuous updating of this clinical manual.

We appreciate your continued support and commitment to the control and management of the EVD epidemic in Liberia.

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1. GLOSSARY AND DEFINITIONS

CT	Cycle threshold
DIC	Disseminated intravascular coagulation
ETU	Ebola Treatment Unit
EVD	Ebola Virus Disease
HCW	Health care worker
IMAM	Integrated Management of Acute Malnutrition
IV	Intravenous
MHC	Mental health clinician
MoHSW	Ministry of Health and Social Welfare
MPHSS	Mental health and psychosocial support
NGT	Nasogastric tube
NSAIDs	Non-steroidal anti-inflammatory drugs
ORS	Oral rehydration salts
PPE	Personal protective equipment
PPH	Postpartum hemorrhage
PO	Per oral
PR	Per rectum
RDT	Rapid diagnostic test
RUIF	Ready to use infant formula
RUSF	Ready to use supplementary food
RUTF	Ready to use therapeutic food
S/C	Subcutaneous route
SW	Social workers
WHO	World Health Organization

2. INTRODUCTION

Liberia is currently experiencing the first large-scale Ebola Virus Disease (EVD) outbreak. The Ministry of Health and Social Welfare (MOHSW) Ebola outbreak response includes EVD case identification, isolation, and clinical management at Ebola Treatment Units (ETUs). International partners have been actively supporting the MOHSW strategy by constructing and/or managing ETUs. This EVD clinical management manual has been developed to standardize clinical management of EVD patients and ensure best practices across all of Liberia.

Minor deviations from this protocol will be expected, given the variety of practitioners; major deviations will not be acceptable. Any partners or individuals using experimental drugs or practices (see Chapter 9) must complete an application to the National Health Science and Research Ethical Committee (NHSREC). In line with the gold standard of evidence based medicine, revisions of this manual will occur during the course of this outbreak and afterwards, as new evidence, treatment, or vaccines become available.

This document is divided into relevant EVD thematic patient care sections: EVD clinical management, nursing care for EVD patients, pregnancy and breast-feeding, paediatrics, mental health and psychosocial support, nutrition, experimental drugs and Ebola survivors. EVD case definition, admission criteria, and infection prevention and control practices are not addressed here, as these issues are addressed in other documents (e.g., medication dosages are available in the World Health Organization (WHO) manuals).[1]

2.1. GUIDELINE DEVELOPMENT PROCESS

In early 2014, the WHO published a pocket book on the Clinical Management of Patients with Viral Haemorrhagic Fever (VHF) for West African adaptation[2]. The development of this EVD clinical management manual has been coordinated by the MOHSW and draws upon the aforementioned WHO document, other relevant WHO guidelines[3] in addition to clinical expertise and best practice as it relates to the EVD response within Liberia.

The level of evidence currently available for the clinical management of EVD is minimal. Nonetheless, Liberian clinicians have some of the greatest experience with managing the disease. This document has been guided by that large experience-base. A methodical approach was adhered to in developing this manual; the MOHSW clinical guidelines subcommittee in collaboration with partners met, discussed the evidence and drafted the recommendations. These were recommendations mostly based on expert opinion consensus and aided by the current published literature in peer-review journals and/or WHO VHF pocket manual reference where applicable (the rationale of these discussions is found in appendix A). A clinical guidelines validation meeting was held on 11 November 2014 with representation from over 15 different organizations and 60 participants. Thematic areas were discussed and consensus achieved on clinical management approaches. If consensus could not be achieved an expert panel was solicited (appendix A). This manual is the product of that process.

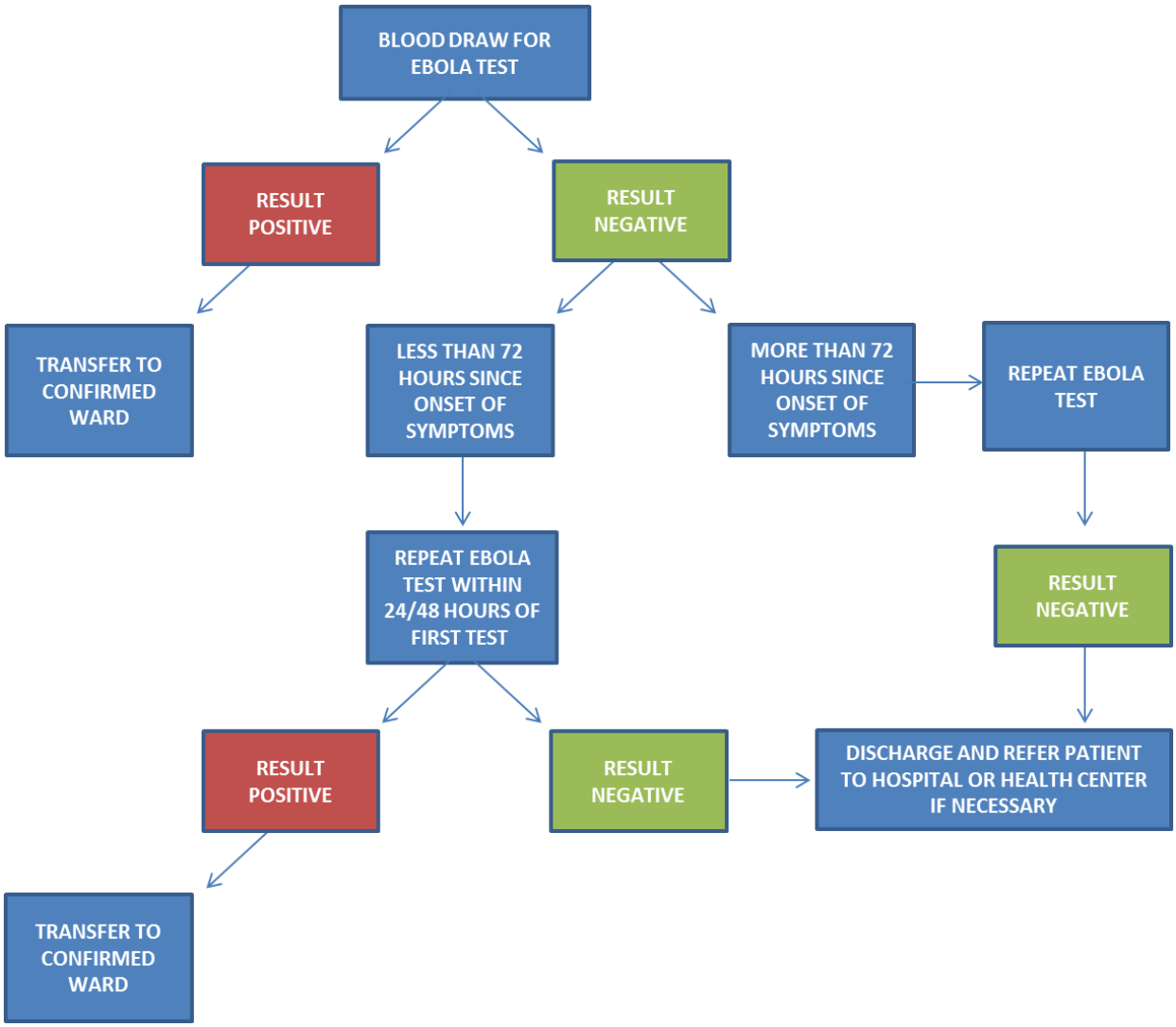
3. EBOLA DIAGNOSTIC ALGORITHM[4]

3.1. WHEN TO TEST

Laboratory Testing Protocol in the Ebola Treatment Setting: Material: 1 EDTA 3ml tube (purple cap) per patient.

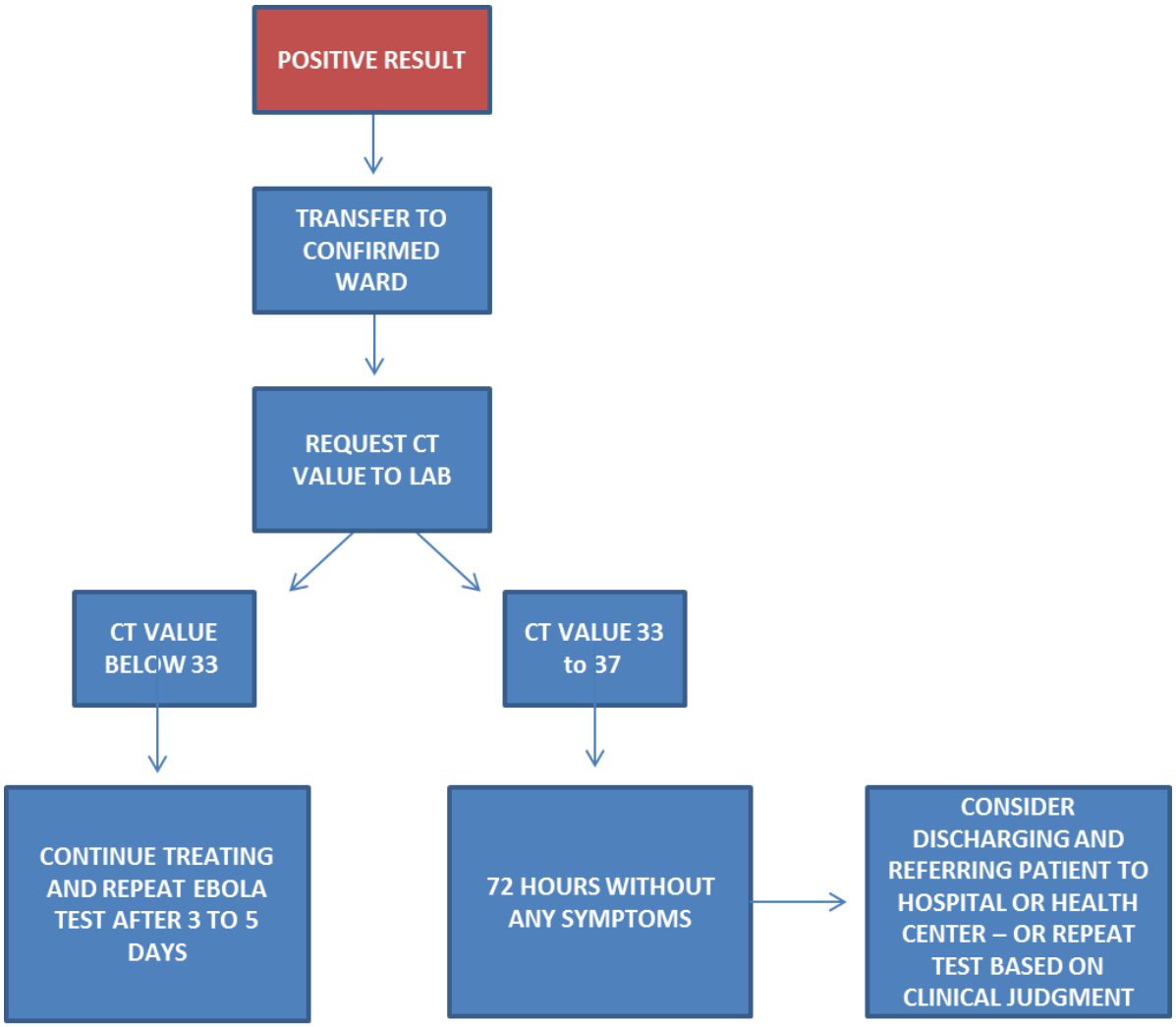
Golden Rule 1: DO NOT TEST ASYMPTOMATIC PATIENTS

At Admission to Suspect Ward – ETU, CCC or Hospital/Health Facility Holding Area



3.2. How to address a positive result

Golden Rule 2: DO NOT REPEAT TEST IF THE CLINICAL CONDITION IS IMPROVING



GOLDEN RULE 3: Do not repeat blood test after 24 hours (High chance to get a negative result).

For EBOLA TEST (Real Time PCR ASSAY) a positive reaction (Positive Result) is detected by accumulation of a fluorescent signal. The CT (cycle threshold) is defined as the number of cycles required for the signal to cross the threshold (i.e. exceeds background level). CT levels are inversely proportional to the amount of VIRUS in the sample (i.e. the lower the CT level, the greater the amount target nucleic acid in the sample).

4. EBOLA CLINICAL MANAGEMENT

This section addresses symptomatic care of EVD suspect, probable or confirmed cases (Table 1). It also reviews empirical therapy, fluid and electrolyte management, blood products and shock management. Additional information for children is found in Chapter 6. Chapter 4 addresses quality of care issues, including nursing care and patient engagement.

4.1. SYMPTOMATIC CARE OF EVD SUSPECT

The following table summarizes symptomatic care for adults and children unless otherwise indicated. In many situations, access to certain drugs is limited and will prevent delivery of recommended 1st line interventions and therefore 2nd or 3rd line options will apply. Careful monitoring and evaluation of patients should be carried out at all times with systematic reporting of any side effects.

Table 1 EVD symptomatic care

Symptom/sign	Interventions recommended by panel	Remarks and caveats
PAIN	1st line: **PARACETAMOL** PO, IV	***Caveat:*** *hepatotoxicity, hence max 4 gm/day in adult*
	2nd line: **TRAMADOL** PO, IV	Not all partners agree on its use; not on the WHO essential drugs list ***Caveat:*** *hepatotoxicity; do not administer together with ondansetron*
	Alternative 2nd line: Codeine PO	
	3rd line: **MORPHINE** PO, IV, S/C	**Can be used as 2nd line,** issue with availability and use (many people are not familiar with the use of morphine), requires doctor prescription, *important in terminally ill patients with excruciating pain* ***Caveat:*** *Respiratory depression*
	AVOID NSAIDs	**Strong recommendation**
FEVER (>38° C)	1st line: **PARACETAMOL** PO, IV	Concerns for convulsions in children ***Caveat:*** *max dose – 4 gm /day in adult or 75 mg/kg/day in children* Tepid sponging
	AVOID NSAIDs	**Strong recommendation**
DYSPEPSIA /STOMACH DISCOMFORT	1st line: **OMEPRAZOLE** PO, IV	
	2nd line: **MAGNESIUM TRISILICATE**	
	3rd line: **RANITIDINE**	(syrup)(based on availability)
	AVOID cimetidine	
CONFUSION /AGGRESSION	**DIAZEPAM** PO, IV; **HALDOL** PO, IM; **CHLORPROMAZINE** PO, IM	**Always reason with patient in a calm and non-aggressive fashion** *Transient 4-point restraints* to administer drugs (preferably oral or IM) is an option, need to have a clear plan to be discussed beforehand.

Symptom/sign	Interventions recommended by panel	Remarks and caveats
		Constant physical constraints is not an option if patient left unmonitored
HICCUPS	**CHLORPROMAZINE**	*HALOPERIDOL : risk-benefit unclear because of lack of data. Metoclopramide may be an alternative.*
DIARRHEA	**FLUID REPLACEMENT PLUS POTASSIUM**	*Fluid replacement includes potassium, either IV or PO. Add IV calcium and magnesium, where electrolyte measurement is feasible*
	Panel split, no consensus on specific therapy (more research needed), see comments as follows:	
	Loperamide	*Risk-benefit unclear because of lack of data (see discussion in Appendix A)* ***Caveat:*** *if used, only with concomitant antibiotic therapy, under medical prescription, for short course, not in children.*
	Zinc	*No clear guidance, lack of data. More research required to determine benefit*
	Antibiotics	*These guidelines support the empiric use of antibiotics as needed*
VOMITING	1st line: **ONDANSETRON** 2nd line: METOCLOPRAMIDE or CHLORPROMAZINE (adults), PROMETHAZINE (children)	Preferred drug (based on availability) better safety profile, can be given to children (> 2 years). ***Caveat:*** Avoid in patients with arrhythmia; *do not administer together with tramadol* *Metoclopramide may be less effective*
SEIZURES	**DIAZEPAM** PR, IV **PHENOBARBITAL** IV	Approach patient with caution *Phenobarbital:* Increased mortality in children with cerebral malaria, difficult to administer (need a pump), can be given over 15 min in an ETU – (if resources available, then consider) ***Caveat:*** *Concern for respiratory depression in combination of diazepam and phenobarbital* Consider other causes of seizures: hypoglycaemia (in adults); high fever, hypoglycaemia, thiamine deficiency (in children)
ODYNOPHAGIA /ULCERS	1st line: **SALINE MOUTH WASH, LIDOCAINE RINSE**	If thrush, Nystatin oral suspension, USP 100,000 units/mL Consider "Magic mouthwash cocktail": This consists of an antihistamine, antifungal, antacid and an analgesic or local anesthetic, such as: (equal parts) Benadryl, nystatin oral suspension, Mylanta liquid and Lidocaine (bemylid) Patient must be able to spit. Preferably, mix the mouthwash in the green zone and bring it to the red zone. Alternatives/substitutions can be considered based on availability of other products. ***Caveat:*** Mylanta contains Aluminium compounds)

4.2. Co- infections and empiric therapies

4.3. Malaria

If a patient presents with malaria symptoms, then empiric treatment for uncomplicated malaria should be initiated based on the provider's discretion. Standard therapy is with oral artemether + lumefantrine. Severe malaria should be treated with intravenous (or rectal) artesunate (quinine in pregnant women in the 1st trimester). Empiric therapy might be considered especially if resources are limited, and there is a high patient load. Avoid the use of bed nets in ETUs.

4.4. Empiric antibiotics

Empiric therapy with cefixime or ceftriaxone should be administered to EVD patients with significant abdominal symptoms and risk of secondary bacterial infections. If symptoms progress to worsening GI complaints and/or bloody diarrhoea, metronidazole can be considered. Discontinuation of antibiotics should be at five days if symptoms improve. Consider changing from IV to PO antibiotics in patients who have been afebrile for more than 48 hours, if the patient is able to tolerate PO antibiotics. Preferred antibiotics: cefixime PO, ceftriaxone IV, metronidazole PO, IV. Bactrim PO or Cipro PO can be administered as alternatives to Cefixime.

4.5. Fluid and electrolytes management

Oral rehydration salts (ORS) solution is the first-line therapy for all EVD patients for rehydration. There should be a low threshold for IV cannula insertion for every patient, given the high likelihood of rapid deterioration and poor oral intake. Ringer's lactate is the intravenous fluid of choice. Oral and intravenous potassium replacement should be strongly considered for all patients with GI losses. Dextrose addition for the prevention and treatment of hypoglycaemia should be considered for all patients receiving intravenous rehydration. Routine monitoring for on-going losses should be routinely performed and integrated into care pathways. If electrolyte monitoring is available and easy to perform, it should be done on patients with significant fluid losses to ensure no significant hypokalemia, hypomagnesemia, sodium or calcium imbalances. For further detail, please refer to the *Clinical Management of Patients with Viral Haemorrhagic Fever Pocket Guide*.[5]

4.6. Blood products

Fresh whole blood transfusion, where available, can be considered for resuscitation in patients with hemodynamically compromising haemorrhage. Whole blood transfusion for diffuse coagulopathy or on-going disseminated intravascular coagulation (DIC) is not recommended. Use of convalescent plasma should be encouraged when necessary.

4.7. Shock

EVD shock is **LIKELY** due to a combination of septic and hypovolemic shock and will likely respond to aggressive fluid resuscitation. The management of EVD shock should be as per the WHO guidelines for fluid resuscitation[2], with IV Ringer's lactate as the preferred resuscitation fluid. Resuscitation targets include normalization of pulse, urine output, and other physical exam findings suggestive of improved tissue perfusion. These targets should be utilized to monitor response to fluid therapy and help to determine whether further fluid therapy is required.

Pulmonary oedema is a concern with over-aggressive fluid resuscitation. Monitoring for respiratory distress should be performed throughout resuscitation and upon its detection; fluid therapy should be titrated accordingly.

4.8. HIV/AIDS

Patients co-infected with EVD and HIV must continue their antiretroviral and other related medications.[6] Given liver and kidney involvement in EVD, awareness of drug metabolism and possible drug interactions for all drugs should be considered. Infants of mothers who are receiving ART should be given prophylaxis with daily nevirapine (NVP) (or twice daily zidovudine (AZT))[7].

4.9. GUIDANCE ON DISCHARGE OF PATIENTS

See Sections 3.1 and 3.2 for guidance on when to discharge and refer patients. At discharge, patients should be provided with abstinence counseling and also given a discharge package, which includes PPE, gloves, bucket, chlorine, mattress, soap, chloride, clothes for men and women, oil, a bag of rice, BP 100 (for children), mobile phone, condoms for adults and toys for children. Patients should be referred to a hospital or health facility for follow-up care as necessary. Also see section 8.4; nutritional care and support upon discharge.

5. NURSING CARE FOR EVD PATIENTS

5.1. GENERAL PATIENT NURSING CARE

Patients should receive bed baths, mouth care, regular turning and change of their linen and clothes. Weak patients require adequate rest and minimize movement therefore, as mentioned above, two buckets will be stationed by each bedside: one for stool and the other for vomitus. As a general principle, vomitus should be decontaminated with 0.5% chlorine before disposal. For bedridden patients, diapers or pampers will be used, which will be changed regularly. Staff should actively feed patients who are frail. Nasogastric tube (NGT) may be considered for feeding in certain circumstances (see nutrition section for cautions to be taken). Staff should take time to talk to the patient, to try and give them hope.

5.2. PATIENT ENGAGEMENT

If feasible, patients should be engaged during triage, and the admission and treatment process should be explained. A client-centered approach to patient education and counseling is important. The patient should be involved in understanding their care – for example, the importance of infection and prevention control on the ward as well as continuous fluid and food intake.

6. PREGNANCY AND BREASTFEEDING

All female patients of reproductive age should be questioned, in confidence, regarding their pregnancy status and date of their last menstrual period, which should be noted on patient records and communicated to the relevant health care team/workers. The information must then be communicated to other health providers for continued care. Pregnancy testing should be made available to women of reproductive age at each ETU in order to stratify risk and provide clarity around pregnancy status if it is in question.

If a pregnant patient presents in an ETU, the provision of pregnancy-related services should occur within the ETU setting. If possible, ETUs should have skilled/professional obstetric providers (such as a midwife). The patient should be managed in a separate area of the confirmed ward with provisions for privacy.

If a suspect or probable case presents in labor at a hospital, then the patient should be isolated and precautions should be taken to prevent any infection amongst other patients or health workers. Health care workers (HCW) should use enhanced PPE in this setting.

Patients should be counseled on potential fetal and maternal outcomes. Patients discharged with intact pregnancy should be instructed to return to an ETU or maternity isolation ward for delivery or management of pregnancy complications.

6.1. ADMINISTRATION OF ANTIBIOTICS

For any pregnant woman admitted into an ETU, administer antibiotic prophylaxis and antimalarial treatment according to these guidelines, as well as ferrous sulfate/folic acid and multivitamins. Antibiotic prophylaxis should be considered especially for ruptured membranes; spontaneous abortion/incomplete abortion; obstetric hemorrhage; retained placenta or products of conception; and suspicion of pelvic inflammatory disease or tubo-ovarian abscess. Antibiotics may be considered following normal spontaneous vaginal delivery if there is concern for secondary infection.

6.2. LABOR AND DELIVERY

Pregnant patients with EVD may be more likely to have PPH and fetal demise/stillbirth. Allow patient to go through spontaneous labor with no interruption. Induction of labor should only be performed for maternal indications and by staff skilled in obstetric care.

If possible, plan and organize an extra person before performing any procedures. Early placement of peripheral IV is advised. A safe delivery kit – plastic umbilical cord clamps, blunt-nosed disposable scissors, absorbent drapes with plastic lining, menstrual pads, misoprostol for prevention of postpartum hemorrhage (PPH) – should be immediately available to mitigate risks around delivery. Long gloves should be worn and gloved hands should be washed between each patient, as HCW exposure to blood and other bodily fluids should be minimized.

Surgical intervention for complications cannot be safely performed in an ETU. Caesarean sections should *only* be performed in a controlled hospital setting. Avoid the use of instruments as much as possible i.e. no episiotomy, vacuum, or destructive delivery. Do not perform artificial rupture of

membranes, and limit the number of vaginal examinations. Oxytocin can be given for prolonged labor by experienced providers. Do not suture any tears; apply pressure to perineum with blue pads/adult diaper (underpads). There should be no manual removal of placenta.

If the baby is born alive, clamp the cord with 2 disposable cord clamps and cut with blunt-nosed disposable scissors. However, the observation from the 2014 outbreak is that almost all babies will be stillborn; if so there is no need to clamp and cut the cord, and cabergoline 1 mg PO may be administered to stop maternal milk production.

6.3. CORD CARE

7.1 per cent chlorhexidine should be applied to the umbilical cord immediately after delivery to prevent neonatal infection. WHO guidelines: Daily chlorhexidine (7.1 per cent chlorhexidine digluconate aqueous solution or gel, delivering 4 per cent chlorhexidine) application to the umbilical cord stump. *Appropriate infection prevention measures must be taken by health workers to avoid neonatal infection through cord care*.

6.4. PREVENTION AND TREATMENT OF PPH

For the prevention of PPH, provide a single dose of misoprostol 600 micrograms orally or 400 micrograms sublingually immediately after delivering the baby. After delivery *it is important to confirm that there is no undiagnosed second twin before giving the misoprostol. Note: the potential side effects of misoprostol include fever, chills, nausea vomiting and diarrhea, similar to Ebola symptoms. However, misoprostol related side effects are often self-limiting. Provide care accordingly*.

For the treatment of PPH, provide misoprostol, 800 micrograms sublingually[8]. If feasible, perform external uterine massage with protective covering (such as blue pads/adult diaper underpads) on the patient's abdomen, while standing on the side of the patient. To avoid exposure to blood and other body fluids, do not face the patient directly. If bleeding is excessive and clinical condition deteriorates further, consider intravenous fluid (preferably Ringers Lactate) and blood transfusion. The use of the non-pneumatic anti-shock garment as a temporizing measure may be considered.

6.5. POSTNATAL CARE

The mother should always be informed of the infant's prognosis. PCR-positive essential newborn care includes keeping the baby warm and dry, and early initiation of breastfeeding. Women should be encouraged to hold their baby skin-to-skin and breastfeed on demand. Babies who are born preterm or with low birth weight should be assessed and if required, provided with specialized care. Mothers of small babies can be supported to practice Kangaroo Mother Care that involves continuous, prolonged skin-to-skin contact with the baby on the mother's chest. Initiate Kangaroo care as soon as possible after birth, particularly in the absence of intensive neonatal care. Breastfeeding or cup feeding with expressed breast milk should be provided on schedule rather than on demand, as many premature babies have not yet developed the sucking reflex and may not wake up when they need to be fed. If breastfeeding is not possible, provide ready to use infant formula (RUIF).

6.6. BREASTFEEDING IN INFANTS

Virus is present in breast milk even after viraemia has ceased[9]. *Sudan Ebolavirus* has been cultured from breast milk samples collected both during and after viraemia. This data from two patients

suggests transmission *may* occur via breast milk.[10] All breastfeeding mothers admitted to an ETU with suspected Ebola should receive breastfeeding counseling, due to the potential EVD transmission risk for the breastfed infant of an Ebola-infected mother:

- Where the infant is asymptomatic, it is recommended that the infant is separated from the mother and referred to a social worker as well the nearest Integrated Management of Acute Malnutrition (IMAM) site to be assessed for malnutrition and supported with replacement feeding.
- Where the infant has developed Ebola or is a suspected Ebola case, if the mother is well enough to breastfeed, she should be supported to continue to do so. If the mother is too ill to breastfeed, then replacement feeding is needed.

The safest replacement feeding in the current context for infants aged less than 6 months is ready-to-use infant formula (RUIF). Wet nursing is not recommended. Children over 6 months and below 12 months can be given full cream liquid UHT milk, or it is not available, RUIF, and should commence adequate complementary food. (If in an ETU: Super Cereal, catered food (mashed or as soup) and RUTF (BP100 as a porridge); and upon confirmed negative discharge from an ETU, referred to a social worker and nearest IMAM site for continued fortnightly nutrition assessment, and provision of full cream liquid UHT milk/RUIF. The caregiver should be counseled on complementary feeding using locally available foods). The MoHSW guideline on nutritional care and support for EVD patients in treatment units and care centers (21 November 2014) provides more details on RUIF and infant feeding.

When abruptly stopping breastfeeding, the mother should express her milk to wean production using a handheld pump. The milk should be discarded, as other infectious waste is disposed in the latrine. Continue education efforts regarding breastfeeding so this is not stigmatized following current EVD epidemic.

6.7. TREATMENT OF INCOMPLETE ABORTION/MISCARRIAGE

Pregnant patients with EVD are at increased risk for spontaneous abortion. Considering the concern of needle use and other instrumental procedures, misoprostol should be used for treatment of incomplete abortion.

If uterine size at the time of treatment is equivalent to a pregnancy of gestational age 13 weeks or less, provide a single dose of misoprostol 400 micrograms sublingually [11]. If bleeding is excessive and clinical condition deteriorates further consider intravenous fluid (preferably Ringers Lactate), blood transfusion and/or manual vacuum aspiration.

If uterine size at the time of treatment is equivalent to a pregnancy of more than gestational age 13 weeks,[i] provide misoprostol 400 micrograms sublingually. This dose may be repeated every 3-4 hours if necessary. If bleeding is excessive and clinical condition deteriorates further consider, intravenous fluid (preferably Ringers Lactate), blood transfusion and/or manual vacuum aspiration.

[i] There are no WHO recommendations for medical management of second trimester incomplete abortion, where the uterine size is greater than the size of a 13 week gestation. Experts recommend using first trimester regimen and then repeating the dose as needed. Larger doses of misoprostol may also be considered. If possible document and report outcomes.

6.8. POST ABORTION CARE

The patient should be advised to use contraception for a minimum 6-month interval in order to reduce the risks of adverse maternal and perinatal outcomes. She should also be advised to report any change (e.g: bleeding, faintness) that may occur.

6.9. EBOLA VIRUS IN SEMEN OF MEN WHO HAVE RECOVERED FROM EVD[12]

The Ebola virus is shed in bodily fluids such as blood, vomit, faeces, saliva, urine, tears, and vaginal and seminal fluids. There is evidence that seminal fluids of convalescing men can shed the Ebola virus for at least 82 days after onset of symptoms. Although the scientific evidence is limited, it is clear that semen is a potential source of infection and could therefore cause transmission of the virus through delivery of the infectious virus on a mucosal surface.

Key messages:

- Men who have recovered from EVD should be aware that seminal fluid may be infectious for as long as three months after onset of symptoms.
- Because of the potential to transmit the virus sexually during this time, they should maintain good personal hygiene after masturbation, and either abstain from sex (including oral sex) for three months after onset of symptoms, or use condoms if abstinence is not possible.
- WHO does not recommend isolation of male convalescent patients whose blood has been tested negative for EVD.

7. PAEDIATRICS

For the purpose of this brief, children are defined as age 14 years and younger. Children are commonly patients in the ETU and require special consideration in: protection and supervision, monitoring vital signs, medication dosages, and discharge.

All children should have a weight documented on ETU admission: preferably measured, and if that is not feasible, estimated by Braslow tape or similar tool, or estimated by calculation based on age (It is acknowledged these estimation techniques were validated in non-malnourished children and can pose a risk of under dosage).

Special monitoring requirements in children include:

- ***Oxygen saturation*** (if available): Oxygen saturations should be maintained >93%.
- ***Blood glucose:*** As children, and particularly infants are at particular risk for hypoglycemia, symptomatic children (lethargy, history of vomiting, decreased oral intake) should have their levels checked. Treatment should follow current WHO guidelines. Empiric treatment of suspected hypoglycemia in a symptomatic child in an ETU without access to blood glucose monitoring should proceed without delay.

Systematic antibiotics therapy on admission is not recommended. Empiric antibiotic therapy can be considered for EVD children with significant abdominal symptoms (e.g. vomiting and diarrhea) and risk of secondary bacterial infections.

Children without signs of severe illness	< 5 yrs. or <15 kg: **Amoxicillin** > 5 yrs. of > 15 kg: **Cefixime**
Children with signs of severe illness	With peripheral IV: **Ceftriaxone** Without peripheral IV: a. With signs of respiratory infection: **Amoxicillin** or **Cefixime** b. No signs of respiratory infection: **Cotrimoxazole**

Fluid resuscitation should be guided by WHO Guidelines for children with shock as described in the WHO VHF Pocket Guide[2].

It is suggested that children receive empiric treatment according to established MOHSW and WHO guidelines.

Early establishment of IV access is recommended due to technical difficulty in children with intravascular depletion. Rather than active fluid resuscitation, it is suggested that maintenance IV fluids are instituted with further resuscitation guided by clinical condition of the child.

The use of Loperamide is controversial (for expert panel discussion outcomes, see Appendix A). Limiting fluid loss to reduce dehydration as well as reducing staff exposure to body fluids is important. There is, however, an increased risk of ileus, discomfort, and bacteremia secondary to gut translocation.

Survivors are sometimes engaged for childcare in the ETU. These survivors should have their Ebola IgG and IgM measured prior to commencing work in the ETU. Survivors should wear basic PPE while in the ETU. All employees, including survivors, should have unfettered access to mental health care before, during, and after their employment.

It is important that all patients in the ETU receive directly observed medication administration, including children who may need additional assistance in taking medications.

Children admitted to an ETU should be referred immediately to the social worker, even if they arrive with parents or family. The nature of the outbreak and care in the ETU often leads to separation of families who must be followed closely by social work to facilitate reunion and post-discharge placement.

Children affected by EVD have significant and specific psychosocial needs – see MHPSS section for further details.

8. MENTAL HEALTH AND PSYCHOSOCIAL SUPPORT

Mental health is a key element of EVD care, especially in the context of family admissions. This section consists of two elements of mental health care: the minimum standard of care expected at each stage of ETU admission and the quality indicators to monitor this, as well as the clinical management of mental health conditions presenting in an ETU.

8.1. MINIMUM STANDARD OF MENTAL HEALTH CARE

Table 2: ETU stages of care

STAGE OF CARE	GUIDELINE	INDICATOR
GENERAL	▪ Dignified care ▪ Give hope ▪ Have daily ward routine up on a board ▪ Ward environment is positive and life affirming ***Children*** Children who test positive and who have a parent or relative who is also positive should be kept together but away from the General ward. There should be child friendly spaces in each treatment area and family visiting area.	➢ All ETU personnel have received some form of training in supportive communication ➢ All ETUs have mental health clinicians (MHCs) and social workers (SWs) dedicated to MHPSS work ➢ All patients will have access to mental health and psychosocial services (MHPSS) ➢ Every patient who needs it will get a brief mental state assessment ➢ ETU SW in collaboration with MHC informs the relatives about the medical evolution of the patient every day
TRIAGE	▪ Employ listening and questioning skills ▪ Allay anxiety through relaxation techniques such as deep breathing ▪ Perform a mental status examination: This involves ensuring that all patients know who they are, where they are, and approximately what time of day or night it is. They need to know what will happen next. This may involve a daily schedule on a whiteboard, a big enough clock that is well displayed on the ward etc. ***Children*** As far as possible, positive children with a positive significant other should be kept together. See the discharge guideline below on unaccompanied children.	➢ 80% of patients who are well enough to understand receive psychoeducation

STAGE OF CARE	GUIDELINE	INDICATOR
SUSPECT WARD	▪ Pre-PCR test counselling ▪ Post-PCR test counselling ▪ Begin stress management training including teaching relaxation techniques *Children* There has to be transitional quarantine for children who are negative who may have accompanied an adult who tests positive, linked to each ETU, which allows for cohorts to remain separated. Refer to Protocol for Children in the ETU.	➢ 80% of patients who are well enough to understand get pre- and post-test counseling and training in stress management techniques
POSITIVE WARD	▪ Supportive communication for every patient every day ▪ Patient is able to talk to the family ▪ ETU provides updates to the patients' families ▪ De-escalation techniques ▪ Medications management ▪ ETUs facilitates family visits if patients are well-enough *Children* ▪ "Child friendly" spaces in each ward with access to toys and other life affirming activities.	➢ Every patient receives counselling / psychoeducation at least once every day with a MHC/SW ➢ Every patient will have access to family members every day (Direct contact, family visit, patient-directed call, or provider facilitated call)
DISCHARGE	▪ 72 hour notice is given to the MHC and the SW ▪ Patients will not be compelled to go home after 2:00 pm ▪ Explanation of what is in the *discharge package* *Children* For every unaccompanied child with no next of kin contact information, tracing of the next of kin should begin as soon as the child is admitted so that by the time discharge and referral, the child can go home to the relatives, rather than to the orphanages	➢ For every patient who tests negative on the first test, ETU MHC or SW makes contact with Community SW and or MHC to prepare family and community for re-integration ➢ Number of patients who leave the ETU after 2:00 pm ➢ Proportion of children who are reunited with relatives
DEATH	▪ Immediate family members who wish to be provided options for honoring the dead relative will receive that information **Dignified dying, not dying alone.**	Proportion of family member who take advantage of options to honor their dead relative

8.2. CLINICAL MANAGEMENT OF MENTAL HEALTH CONDITIONS

Table 3 Mental health conditions and quality indicators

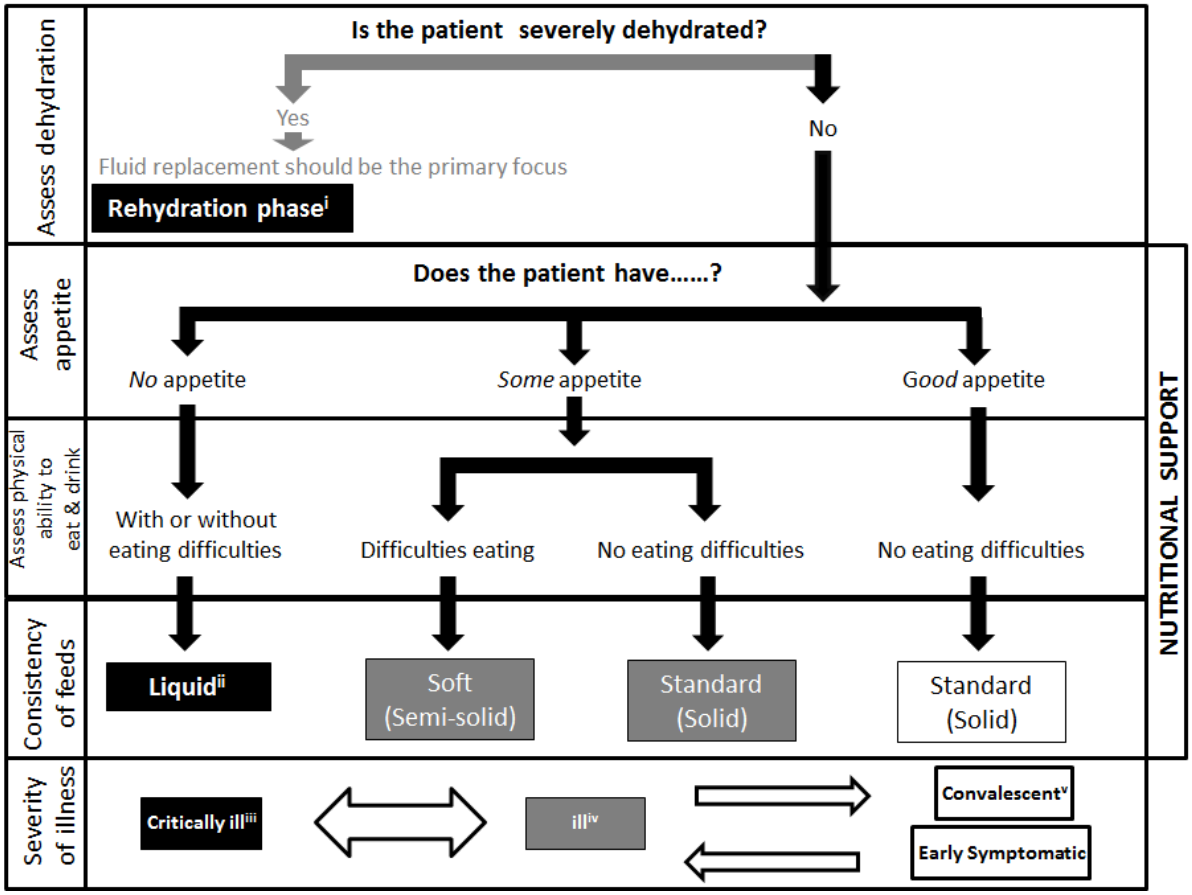
CONDITIONS	GUIDELINES	INDICATORS
ALL PATIENTS	▪ Engage patients in social/occupational activities	➢ Every patient on medications is referred to a MHC for follow up on discharge ➢ Every patient is offered the opportunity to engage in social and occupational activities according to their abilities
SUBSTANCE USE DISORDERS	▪ Assess for Substance Use Disorder if withdrawal is suspected ▪ Manage withdrawal signs and symptoms with diazepam	➢ Withdrawal symptoms in every patient with Substance Use Disorders is effectively managed ➢ Availability of Diazepam IV and Tabs
ANXIETY	▪ Listening and helping ▪ Relaxation techniques ▪ Medications – anxiolytics e.g. Diazepam	➢ Every patient who shows signs of anxiety is provided the appropriate level of care ➢ Availability of Diazepam
DEPRESSION	▪ Counseling ▪ Antidepressants ▪ Assess for suicide risk, 24 hour watch if indicated, place patient where there is frequent HCW traffic	➢ Availability of Fluoxetine ➢ Every patient who shows signs of depression is appropriately assessed and provided the appropriate level of care
PSYCHOTIC EPISODES/DELIRIUM *(CONFUSION/AGGRESSION)*	▪ De-escalation techniques ▪ Humane transient physical restraint if necessary to administer drugs (see Table 1) ▪ Consider the administration of Diazepam and/or Haloperidol or Chlorpromazine	➢ Availability of Diazepam, Haloperidol and Chlorpromazine
EPILEPSY/ SEIZURES/ CONVULSIONS	▪ If convulsions occur, determine if the person is a known patient with epilepsy or it is the first time ▪ If convulsion lasts 30 minutes, this is status epileptics, give diazepam (PR or IV) (see Table 1) ▪ If it is established that the person has had previous convulsions without a trigger, then initiate treatment with Carbamazepine ▪ For a child below 5 years of age, it could be febrile convulsions, so do tepid sponging, give Paracetamol, give Diazepam (pr or iv)	➢ No of patients who developed convulsions that were effectively managed

9. NUTRITION

Nutrition is vitally important for clinical improvement during EVD. Signs and symptoms that affect nutritional care in EVD patients include lack of appetite, sore throat, nausea[i], swallowing difficulties and breathing difficulties. Vomiting interferes with nutritional care and along with diarrhoea, causes additional nutritional stress through rapid loss of electrolytes, protein, other essential nutrients and fluid.

The MoHSW guideline on nutritional care and support for EVD patients in treatment units and care centers (21 November 2014)[13] is adapted from the WHO/UNICEF/WFP interim guideline on nutritional care of children and adults with EVD in treatment centres[14]. In summary, the nutritional needs and the approach to nutritional care is determined by the patients preceding nutritional status, age and clinical condition; and is assessed by severity of dehydration, presence of appetite and physical ability to eat (see Figure 1).

Figure 1: Decision Tree on Determining Appropriate Diet of an EVD Patient



[i]These patients would only have IV fluids and ORS solution if possible.

[ii]It is very important to maintain hydration with ORS solution, particularly in critically ill patients (liquid diet).

[iii]It is particularly important critically ill patients (liquid diet), only receive low osmolarity, low renal solute load options (i.e.: F75).

[iv]It is important that ill patients (soft and solid diet), receive low osmolarity, low renal solute load options.

[v]For convalescent patients do not limit the quantity of food and provide extra snacks.

[i] Likely due to bowel wall oedema.

In critically ill patients with severe dehydration, fluid replacement should be the primary focus. Nutritional support should not interfere with the strategies for volume and electrolyte repletion, as nutritional requirements will temporarily be of a lower priority. For patients requiring nutritional support, the foremost considerations in the selection of food commodities includes the **low osmolarity and renal solute load** of the diet; along with the consistency of food commodities. In addition patient preferences of familiar foods have been balanced against providing therapeutic foods. See protocol listed as Table 4; adapted from the MoHSW guideline on **nutritional care and support for EVD patients in treatment units and care centers** (21 November 2014).

The type of diet is categorized based on the consistency of the food suitable to the condition of the patient:

- Liquid diet (composed of clear liquid)
- Soft diet (composed of semi-solid foods)
- Standard diet (composed of mostly solid foods)

An example protocol of food commodities, consistency and quantities of those products that are suitable for adults in ETUs is presented in Table 4. Further tables for other age groups in ETUs and care centres are presented in the MoHSW guidelines. Note, for infants <6 months, RUIF is recommended.

9.1. ENTERAL FEEDING

The MoHSW guideline on **nutritional care and support for EVD patients in treatment units and care centers** (21 November 2014) cautions against the use of nasogastric tubes (NGTs) in under resourced, under staffed ETUs, due to the following:

- Verification of tube placement has barriers in the isolation setting
- Patients with sore throat or confusion may not tolerate the NGT and removal by the patient may create a contamination risk
- In patients who have haemorrhaging (<6%) or unexplained bleeding (<20%) placement of the tube may cause harm[15]
- Difficult to monitor if health staff has limited time

When patients support NGT placement, exceptions can be made for treatment centers that are fully equipped with sufficient and appropriate staff and material, good infection-prevention-control practice and good waste disposal management.

9.2. PARENTERAL NUTRITION

Critically ill EVD patients with severe dehydration will be in the rehydration phase (fluid management), whilst critically ill EVD patients *without* severe dehydration will be in the liquid consistency feed phase (F-75 and ORS solution). The MoHSW guideline on **nutritional care and support for EVD patients in treatment units and care centers** and the **WHO/UNICEF/WFP interim guideline on nutritional care of children and adults with EVD in treatment centres** do not discuss parenteral nutrition.

9.3. MICRONUTRIENTS

EVD patients should be provided with a minimum of the recommended daily allowance for each nutrient. Until further evidence is available, excess use of any micronutrient for EVD patients is currently not recommended, unless correcting for a specific micronutrient loss (e.g. treating hypokalaemia). There are multiple examples where excess micronutrients have caused harm with

various infectious diseases. Any use of excess micronutrients is viewed as experimental. For patients who receive adequate quantities of fortified ready-to-use-food, multivitamins are not required.

9.4. NUTRITIONAL CARE AND SUPPORT UPON DISCHARGE

EVD survivors will require immediate nutritional care and support upon discharge to ensure full recovery. A nutritional assessment of recovered patients should be taken at discharge as the presence or absence of malnutrition will determine the appropriate nutritional care, follow-up care, and referral to the facility providing IMAM services. See the MoHSW guideline on nutritional care and support for EVD patients in treatment units and care centers (21 November 2014) for details.[16]

Table 4: Nutritional Management of Adult EVD Patients in ETUs based on Assessment of Nutrition-Related Conditions

Adults in ETU		*Daily Recommended Energy and Nutrient Intake: 1,800kcal to 2,400kcal*						
Phases of Nutrition-Related Conditions of EVD Patients				**Management**				
Severity of Illness	**Presence or Absence of Severe Dehydration**	**Level of Appetite**	**Presence or Absence of Eating Difficulties**	**Diet and Consistency of Food**	**Food Commodities**	**Quantity per Day**	**Estimated Kcal**	**Fluid Intake**
Criticality ill	Severely dehydrated	**Rehydration using ORS solution is the first priority**. No nutrition intake during this phase. Nutritional support should not interfere with the strategies for volume and electrolytes repletion as meeting nutrition requirements will be temporarily be of a lower priority.						IV fluids, with ORS solution if possible
	Not severely dehydrated	No appetite	With/without difficulty eating	Liquid	F-75	80 - 100kcal/kg/day		ORS solution
Ill	Not severely dehydrated	Some appetite	Difficulty eating	Soft diet - Semi-solid	Catered mashed food/soup[i], **and**	3 meals (1 meal = 250 kcal)	750	*ORS solution *Water, *Low osmolarity beverages * RUTF/ RUSF should be given only to those who are able to drink sufficient water by themselves (a minimum ratio of 1ml of water for each kcal of the diet)
					RUTSF biscuit (as a porridge) **and**	1.5 sachet (1 sachet = 500 kcal)	750	
					Supercereal[ii]	1 serving (100g dry product)	380	
			No eating difficulties	Standard diet - Solid	Catered food[i]	3 meals (1 meal = 300 kcal)	900	
					RUTSF biscuit **and**	2 sachets (1 sachet = 500 kcal)	1,000	
					Supercereal	1.5 serving (150g dry product)	570	
Convalescent[iii] or early symptomatic	Not severely dehydrated	Good appetite	No eating difficulties	Standard diet - Solid	Catered food[i]; **and**	3 meals (1 meal = 300 kcal)	900	
					RUTSF biscuit **and**	2 sachets (1 sachet = 500 kcal)	1,000	
					Supercereal[ii]	1.5 serving (150g dry product)	570	

Note: If RUTF is not available, ready to use supplementary food (RUSF) can be used with the same quantity per day as for RUTF. All food commodities listed for each category should be offered to the patient, not either or.

Note: If RUSF is not available, RUTF can be used with the same quantity per day as for RUSF. All food commodities listed for each category should be offered to the patient, not either or

[i] Refer to catering section for the sample catered menu which includes use of WFP supplies

[ii] If Supercereal is not available, Supercereal Plus may be provided although it is a complementary food that is specifically recommended to the nutritional needs of the 6-24 months age group;

[iii] For patients who do not have vomiting and diarrhoea and are requesting high osmolarity beverages (such as commercial fruit juices or carbonated soft drinks) they may only be given in this phase. Note: Carbonated soft drinks are low in essential nutrients.

10. EXPERIMENTAL DRUGS

Experimental drugs and practices are defined as any drug or practices that deviate from the Liberian Ebola clinical management guidelines. Drugs currently being used in Liberia without the National Health Science and Research Ethical Committee (NHSREC) approval include: convalesce whole blood, antivirals e.g. Lamivudine. Experimental supportive treatments include selenium, and phyte exponent.

EVD experimental drugs must adhere to the same ethics review committee process as with any new drug. Hence a medical ethics application form must be completed for EVD: novel therapeutics, vaccines, novel diagnostics, and supportive care.

Application forms can be downloaded electronically from the MOHSW website and either sent as hard copies to: Liberian Institute of Biomedical Research/National Health Science Research Ethics committee Address: NHSREC/LIBR Charlesville, Margibi county or submitted electronically to: director.libr@gmail.com The review process is being expedited during this Ebola outbreak (it normally takes 6 weeks but can be completed currently in 2 weeks). Application outcomes will be either: approved, conditionally approved, or not approved.

Any investigator who does not comply with this process will have their experimental project terminated and legal action will be taken. Any institution which knowingly or unknowing conceals information on malpractice shall be liable as per the ethics committee regulations.

11. EBOLA SURVIVORS

Survivors have a significant role in ETU in-patient care. Due to their real life experience of surviving EVD in the ETU, they are well placed to provide physical, psychosocial and emotional support to patients. They may also have a useful role in coaching, encouraging, assisting patients early in their disease course who are capable of some self-care – e.g., assisting or encouraging oral rehydration. Care must be taken to ensure that Survivors have no mental health and psychosocial support consequences from their own experience before they are taken on to work in an ETU. Survivors should be prepared for the work in the ETU through training, as well as going through a one day Psychological First Aid orientation. Survivors can be used in different capacities:

11.1. CARETAKERS

Survivors can be used as orphan caretakers, to assist with feeding and basic daily activities including showering, etc. substituting the family role (if the family member is not admitted, or if the family member is too sick to look after their child).

11.2. PATIENT SAFETY/SECURITY

Survivors can be stationed on the ward (in PPE), to talk to patients, provide education and prevent confused patients from wandering to other wards.

11.3. FAMILY SUPPORT

Survivors can serve as important links between the patients and their families; patients can be informed about relatives' arrival for visits and can be assisted to the visitors pouch. Survivors can also facilitate communications for immobile patients by changing phone batteries, dialing relatives, etc.

11.4. PSYCHOSOCIAL/FAMILY SUPPORT

Survivors can fill the gap of a true friend or relative in the ETU; they can encourage conversations, play, read, and other activities that enhance survival chances.

11.5. CARE FOR CHILDREN

It is common to have an entire family admitted to the ETU. When such situations occur, the parents are often critical, are unable to care for their own children. Survivors can support families in these dire circumstances. Survivors also have a role to play in the Interim Care Centers (plan is to have one attached to each ETU). Survivors can help with the care of unaccompanied children, or children who have to wait 21 days before they can be re-integrated into families.

NB: It would be best if Survivors have completed 90 days post testing EVD negative, especially if they are going to work with patients in the suspects ward, or with children who may be negative.

APPENDICES

APPENDIX A: GOVERNMENT OF LIBERIA CLINICAL GUIDELINES EVD DISCUSSION DOCUMENT

Discussion	References
Use of loperamide The use of loperamide to slow diarrhea led to much discussion. Advocates stated that it reduced the infectious burden, made patient care easier, and had few side effects. Detractors made the contrary claim that it may lead to paralytic ileus and worsening colonic dilatation. Parallels with other infectious gastroenteritis where anti-motility agents are contra-indicated were raised. Advocates started loperamide at the first sign of diarrhea with good effect. There has not been any systematic examination of its safety and efficacy experience thus far in the outbreak.	[1][2][3][4]
Testing and treatment for malaria The prevalence of malaria ranges across the country, from 7% in Montserrado county to over 20% in Bomi county. The use of RDTs for malaria were not universally employed, due to concerns for HCW safety. Additionally, the diagnostic value was questioned, given that many units were systematically treating patients with anti-malarials regardless, given the minimal side-effect profile of standard medication regimens. The standard RDT available in Liberia was the pLDH/HRP2 combination assay. The preference for oral anti-malarial was artemether/lumafantrine, with atovaquone/proguanil as another option. Amodiaquine was not a preferred agent. Artesunate was the preferred intravenous agent. Incorporating multiplex PCR assays into standard Ebola testing was discussed as the next step in diagnostics.	[5][6]
Empiric Antibiotics	

Discussion	References
The role of oral, empiric antibiotics for all patients was discussed at length. Prophylaxis against gut translocation was the dominant theory for benefit, and many centers have started systematic coverage. Operational issues were also raised, stating that, given resource constraints, protocolizing antibiotics was safer. The counter-argument was made that there is little benefit and that there may be some harm with gut microbiota alterations and potential breeding of resistance for subsequent bacteremias. The oral antibiotics used included amoxicillin, ciprofloxacin, cefixime, doxycycline, or azithromycin. Microbiologic testing was not possible in any context to help guide therapy at this stage of the outbreak. Severely ill patients received intravenous antibiotics, typically with ceftriaxone and/or metronidazole. The use of oral antibiotics in Ebola virus has not been systematically examined in this outbreak. Hepatotoxicity was raised as a concern for medication administration, given known risk for elevated transaminase with Ebola infection.	
Fluid and electrolytes The routine placement of IVs in all patients with Ebola was discussed, and consensus was not achieved. Some advocated for IV placement due to the risk of rapid deterioration and safety purposes; the counter-argument was made that early IV insertion was not associated with improved outcomes, and that early IVs often come out anyway, reserving IV placement for those with progressive signs and symptoms. There was no significant concern for coagulopathy as a major limiting issue. HCW safety was brought up as a concern, although no one present documented a needle stick injury due to IV insertion. Ultimately, there was a consensus that IV placement was recommended in every patient with poor ambulation, nausea, or any signs of dehydration, and that it should be considered in all patients with Ebola infection. The type of fluid was generally consensus-driven, with RL as the fluid of choice for maintenance and bolus therapy. Normal saline was proposed, but many were less comfortable, given recent evidence of harm in critically ill patients. Many advocated for potassium supplementation, given the high rates of hypokalemia when tested, although the concern of impending renal failure was raised; urine output was discussed as the appropriate decision-tool. Adding dextrose into the intravenous fluid drip was considered as an option for patients who could not tolerate any oral feeding.	[7,8][9]

Discussion	References
Given shift schedules, a major limitation was having supervised fluid administration. Some advocated for short bolus therapy with capping IV off between shifts, while others were more comfortable with a constant, unsupervised infusion.	
Shock Considering shock in Ebola as a combination of hypovolemic shock and septic shock led most discussants to advocate for aggressive fluid resuscitation, guided by clinical parameters as outlined by the WHO. The endpoints of resuscitation were discussed, and standard septic shock endpoints were promoted. Ceasing fluid resuscitation was emphasized when hemodynamics had been restored to avoid complications of over-administration of fluid. The use of ultrasound in the management of shock was discussed and can be considered as an advanced care option. Dopamine was discussed as an option for fluid-refractory shock, although maintaining a constant infusion rate was discussed a major limitation. Lactate was considered as a guide to therapy, but its availability as a test was not universal. Fluid resuscitation in children, specifically under 5 years, was discussed. Concern about aggressive bolus resuscitation was raised in light of the FEAST trial, an RCT of E African children with severe infection who were randomized to receive saline bolus, albumin bolus, or no bolus in the setting of compensated shock. The children who received no boluses were more likely to survive. The group agreed that cautious fluid resuscitation with frequent monitoring and response was required. For adolescents, similar fluid strategies to those for adults were recommended.	[10][11] [12] [13]
Transfusion Transfusions were proposed to restore blood volume during hemorrhage. The complications of transfusions were raised, including allergic reactions, lung injury, and inflammation. Additionally, the risks of transfusing patients with presumed DIC was discussed. The availability of transfused blood was another limitation. Blood component therapy was not routinely available.	[14]

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