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We are all members of the WHO Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations. We declare no competing interests.

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New WHO guidelines on emergency triage assessment and treatment

For many decades WHO has provided invaluable guidelines for the health care of children in low-income and middle-income countries where resources are limited. The principles behind these guidelines are that they use a minimum number of clinical signs to identify the condition in question and classify its severity, are simple to understand and implement, use essential medicines and appropriate technology, and are fit for the context for which they are designed. Historically, the most successful clinical guidelines have been on the use of simple interventions for common diseases, including oral rehydration salts for dehydration from gastroenteritis and antibiotics for pneumonia.[1,2]

Much has changed in the 40 years since the first WHO guidelines for low-income settings. National economies and health-care systems are now more dynamic, heterogeneous, and ambitious. Clinical guidelines are recognised as having an important role in maintaining quality of care in richer nations as well as in low-income countries. And many agencies and professional groups have developed their own guidelines that are easy to access on the internet. Diseases and our understanding of pathophysiology have changed too: pneumonia epidemiology, for example, is developing with the introduction of conjugate vaccines and the increasing prominence of viral syndromes; antimicrobial resistance has emerged for pathogens which cause neonatal sepsis, meningitis, tuberculosis, and malaria; and the International Classification of Diseases 10th Revision now includes more than 69 000 separate diagnoses. These changes to health in the 21st century have led to the development of guidelines for more complex

disease processes. Such guidelines are usually based on imperfect evidence.

An example is the WHO guideline for fluid boluses in shock and emergency care. WHO developed guidelines for Emergency Triage Assessment and Treatment (ETAT) in 2005. In field trials of ETAT, improvements in quality of emergency care reduced early mortality in hospitals in Africa and South America.[3,4] However, emergency cases are inherently more complex than a child with gastroenteritis and dehydration or pneumonia, for whom a simple guideline is suitable. In the early 2000s, most research available to guide the initial ETAT guidelines on shock was from high-income countries, particularly the USA, and the research on fluid management in shock was restricted to small comparative observational studies in highly resourced contexts.[5,6] During this time, the tide of emergency care consensus guidelines, such as Paediatric Advanced Life Support (PALS), was in favour of giving fluid boluses to children in shock. In the earliest version of ETAT, WHO aligned fluid guidelines for shock with PALS, recommending boluses of 20 mL/kg, repeated to a total of 60 mL/kg. This was the volume that, in the earliest observational studies, was associated with better outcomes in North American children with shock in highly resourced hospitals with facilities for intensive monitoring, mechanical ventilation, and inotropic support.[5,6] However, the clinical diagnosis of cardiovascular shock is not nearly as specific as the diagnoses of dehydration in a child with gastroenteritis, or pneumonia in a child with cough, difficulty breathing, and tachypnoea. WHO specified that cardiovascular shock required the presence of three signs: fast and weak pulse, cold extremities, and capillary refill longer than 3 s.[7,8] All three signs had to be simultaneously present to fulfil the WHO classification.

The FEAST trial, which extended this therapy to children with any one or more sign of shock, tested up to 40 mL/kg bolus fluid in febrile children in Africa.[9] Only 2% of enrolled children were in shock according to WHO criteria. In a context where pathophysiology was heterogeneous and very different from that in North America, and where there was no capacity to provide a differentiated response to different types of shock or to provide intensive-care support, bolus fluid therapy that had apparently saved lives in North America led to an increased risk of death in Africa.[9]

Shock is not a single entity and is caused by many diseases with varying pathophysiology: bacterial sepsis, systemic viral infections such as dengue or influenza, malaria, anaemia, envenomation or toxins, heart disease, abdominal surgical emergencies, or other causes of systemic inflammation. Shock can be hypovolaemic, euvolaemic, or hypervolaemic. Cardiac function can be normal, increased, or decreased,[10] and the vasculature can be dilated, constricted, leaking plasma, or normal. Shock can be accompanied by comorbidities, such as pneumonia, coma, or severe malnutrition, which affect the fluid response and influence the development of secondary consequences which can include cerebral, pulmonary, and tissue oedema. Furthermore, the expected responses to fluid therapy and the secondary consequences differ at different stages of the disease.[10]

After publication of the FEAST trial and related publications, WHO reviewed the ETAT guidelines. In 2013, a WHO Guideline Development Group identified topic areas and specific recommendations that should be updated in light of this and other new evidence. Three areas were prioritised: management of convulsions; oxygen therapy; and fluid management of children who present with shock. A WHO Steering Committee and a 21-member Guideline Development Group of experts were convened. Systematic reviews were done and a consensus expert meeting held in late 2014. The FEAST trial provided detailed data that informed and guided the recommendations; as the only relevant randomised controlled trial (RCT) it provided high quality evidence, particularly for the population without shock as defined by WHO.

This month WHO published the revised ETAT guidelines,[11] and the new fluid guidelines for children with febrile illnesses without diarrhoea and dehydration are summarised in panel, with additional considerations on the management of shock. The guidelines emphasise the WHO definition of shock and a much more cautious approach to fluid administration, including not giving boluses to children with only one or two signs of poor perfusion. If a child does fulfil the WHO criteria for shock, the new guidelines recommend giving smaller volumes of fluid (10 mL/kg) over longer periods of infusion (30–60 min), and reassessment of the response each time. Even for children in shock there is a need to be careful about fluid management and

the risk of giving too much fluid. The most important recommendation in the guidelines is that, apart from children with diarrhoea and dehydration, if a child is not in shock, fluid boluses or too much intravenous fluid can be dangerous. Finally, the new WHO ETAT guidelines recognise the need for a differentiated response if initial therapies are not effective. That is, the need to understand the cause of shock and the underlying pathophysiology, and apply specific therapies where they exist. Children in cardiovascular shock that is poorly responsive to such intravenous fluid therapy could require an inotrope or vasoactive agent, more fluid, less fluid, a blood transfusion, a diuretic, positive pressure respiratory support (such as continuous positive airway pressure), hydrocortisone, adrenaline for anaphylaxis, antibiotics for bacterial sepsis, antivenom for snake bite, thiamine, or an echocardiograph to assess heart function and exclude tamponade.[10,12,13] A differentiated and often complex response is needed to a complex condition. There is a crucial need for review, clinical monitoring, and a second-round of decision making.

The revised ETAT guidelines were designed by weighing the best available clinical and pathophysiological evidence. A wide range of interpretations of the evidence from all continents was considered, and a consensus was reached.

It is not always optimum to evaluate the effectiveness of guidelines for complex therapies with the RCT method. Some RCT designs can be reductionist and separate technical interventions from the broader context. The FEAST trial investigators found that the implementation of their trial resulted in a lower than expected overall mortality.[9] There are several reasons for this finding; one is that the overall effect of improving triage and emergency treatment—the training, the structured approach, the prioritisation of treatment, the other aspects of supportive care—saves lives. If implementation of a guideline for fluid resuscitation of children with several possible causes and stages of shock is complex, then what is needed to improve quality of emergency care in resource-limited settings, and to make any individual therapy work, is even more complex. Crucially, health-care workers must be trained in how to review patients and use information about how children respond to initial treatments to guide the next treatment steps. Moreover, it is also

Panel: **Guidelines for management of children with signs of impaired circulation or shock, incorporating the new WHO fluid guidelines[11]***

1 Children who have some signs of circulatory impairment but do not have shock

1.1 Children with only one or two signs of impaired circulation, either cold extremities, or a weak and fast pulse, or capillary refill >3 s but who do not have the full clinical features of shock, ie, all three signs present together, should not receive any rapid infusions of fluids but should still receive maintenance fluids appropriate for age, weight, and disease process.

1.2 In the absence of shock, rapid intravenous infusions of fluids may be particularly harmful to children who have severe febrile illnesses, severe pneumonia, severe malaria, meningitis, severe acute malnutrition, severe anaemia, congestive heart failure with pulmonary oedema, congenital heart disease, or renal failure.

1.3 Children with any sign of impaired circulation, ie, cold extremities or weak and fast pulse or prolonged capillary refill, should be prioritised for full assessment and other treatments (treatment of the underlying cause and other possible treatments below in 2.1), and reassessed within 1 h.

2 Children who have shock

2.1 Children who have shock, ie, who have all the following signs: cold extremities and a weak and fast pulse and capillary refill >3 s, should receive intravenous fluids and consideration for other treatment as follows:

- Give high-flow oxygen
- 10–20 mL/kg of isotonic crystalloid fluids over 30–60 min
- If severe anaemia (severe palmar or conjunctival pallor), give blood as soon as possible and do not give other boluses of intravenous fluid
- Monitor the effect of fluid,† fully assess to look for an underlying cause of shock
- If the child is still in shock after initial fluid therapy, then consider a further infusion of 10 mL/kg over 30 min, and at the same time assess the need for other emergency treatments.
  - Start inotrope (adrenaline, dopamine) or vasoactive agent (noradrenaline) if hypotensive or persistent shock
  - Give antibiotics for bacterial sepsis +/– antimalarial if in malaria endemic area
  - Diuretic (furosemide 1 mg/kg intravenous) if signs of fluid overload or heart failure
  - Positive pressure respiratory support (such as continuous positive airway pressure) if hypoxaemia or severe respiratory distress despite oxygen
  - Hydrocortisone if hypotensive despite inotrope or vasopressor
  - Adrenaline intravenous or intramuscular if any sign of anaphylaxis
  - Antivenom if signs of snake bite
  - Thiamine if beri beri is suspected, or if the child has severe malnutrition
  - Echocardiograph to assess heart function and exclude tamponade
  - Tranexamic acid and urgent blood transfusion if there is traumatic haemorrhage
  - Surgical review if abdominal emergency or trauma
- Reassess airway, breathing, circulation, monitor for the effects of emergency treatments, and further review the underlying cause of shock by history and examination.
- If shock has resolved, then provide fluids to maintain normal hydration status only (maintenance fluids).
- Decide on the best location of ongoing care and monitoring: intensive or high dependency area, paediatric ward. Order frequency of monitoring, reassessment, and other supportive care.

*These guidelines are not for fluid management of children with diarrhoea and dehydration, for which WHO has separate guidelines.[1,8] †If, at any time during fluid infusions, there are signs of fluid overload, cardiac failure, or neurological deterioration then the infusion of fluids should be stopped and no further intravenous infusions of fluids should be given until these signs resolve.

important to have adequate numbers of well trained and supervised staff with access to essential therapies and investigations; guidelines cannot compensate for weak health systems. Addressing issues in quality of care and supporting health systems is necessary to tackle the challenges of paediatric care in resource-limited settings in the era of the Sustainable Development Goals.

The WHO Hospital Care for Children guidelines, which includes the ETAT guidelines, are available in print[8] in many languages and in a new app (iOS and Android) that can be updated as new evidence becomes available and guidelines change.[14] There is, of course, still a need for simple guidelines for common conditions. The historical principles of WHO guidelines that are fit for context and based on the best available evidence, using where possible the minimum number of highly predictive clinical signs or laboratory tests, all remain relevant. The new ETAT guidelines will need to be evaluated, and the design of such research should reflect the broader context and recognise that these are not isolated simple interventions.

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Equal access to colorectal cancer screening

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See Articles page 751

Population-based screening is effective in reducing the burden of colorectal cancer, and organised screening programmes have been implemented in many European countries.[1] Maximum participation in screening is crucial to achieve the greatest health benefits at population level. As with most cancer screening programmes, however, there is a gradient in uptake of colorectal cancer screening by socioeconomic status, from the most to the least deprived.[2–4] Because colorectal cancer screening results in earlier diagnosis or primary prevention, inequalities in colorectal cancer outcomes between socioeconomic groups are expected to increase with wider implementation of screening programmes.[5]

The data on inequality in colorectal cancer screening are predominantly from the USA.[4] For Europe, analyses from the UK National Health Service Bowel Cancer Screening Programme, in which faecal occult blood testing is offered to individuals aged 60–74 years at no cost, have shown uptake of 35% in the lowest socioeconomic quintile compared with more than 60% in the highest quintile.[3] In *The Lancet*, Jane Wardle and colleagues[6] present the results of the ASCEND project, which involved various mailed interventions aimed at lessening socioeconomic inequality for participation in the Bowel Cancer Screening Programme in England. Wardle and colleagues did four cluster-randomised controlled trials in which eligible individuals received either standard information about the screening programme or supplemented information in different forms—a leaflet re-presenting the information in