GLOBAL TASK FORCE ON
CHOLERA CONTROL

REPORT OF THE

4TH MEETING OF THE GTFCC CASE MANAGEMENT WORKING GROUP

5-6 NOVEMBER 2019 | NEW DELHI, INDIA

Contents

Abbreviations

ALIMA	Alliance for International Medical Action
AMR	Antimicrobial resistance
AWD	Acute watery diarrhea
CATI	Case area targeted intervention
CDC US	Centers for Disease Control and Prevention
CFR	Case fatality rate
CHW	Community health worker
CTC	Cholera treatment centre
CTI	Comprehensive targeted intervention
DFID	Department for International Development
Gavi	Gavi, the Vaccine Alliance
GTFCC	Global Task Force on Cholera Control
icddr,b	International Centre for Diarrheal Disease Research, Bangladesh
IDCF	Intensified diarrhea control fortnight
IFRC	International Federation of Red Cross and Red Crescent Societies
IPC	Infection prevention and control
JHU	John Hopkins University
M&E	Monitoring and evaluation
MoH	Ministry of health
MSF	Médecins Sans Frontières
NAPHS	National action plan for health security
NCCP	National cholera control plan
NGO	Nongovernmental organization
NICED	National institute of Cholera & enteric diseases
OCV	Oral cholera vaccine
ORP	Oral rehydration point
ORS	Oral rehydration solution
ORT	Oral Rehydration Therapy
RDT	Rapid diagnostic test
RRT	Rapid response team
SAM	Severe acute malnutrition
SOP	Standard Operating Procedures
UNICEF	United Nations Children's Fund
WASH	Water, sanitation and hygiene
WG	Working group
WHO	World Health Organization

Executive summary

The Ending Cholera: A Global Roadmap to 2030 launched in October 2017 paved a path towards a world in which cholera is no longer a threat to public health. It sets out a target 90% reduction in cholera deaths and elimination of cholera in 20 countries by 2030.
Initial results of implementing the Global Roadmap can already be seen, with dramatic reduction of burden in countries such as South Sudan and rapid containment of outbreaks of potentially devastating and protracted outbreaks such as in Zimbabwe and Mozambique.
Despite available preventive actions and curative treatments, some countries, including Cameroon and Chad report very high case fatality rates (CFR) - up to 6.2%. The GTFCC Case Management Working Group addressed this issue at its 4th annual meeting on 5th and 6th November 2019 in New Delhi.

The objectives of the meeting were to:

- Look at the evolution of cholera mortality over time and identify risk factors;
- Critically review the strategies and tools available to treat patients in health facilities and at community level to identify key bottlenecks and best practices;
- Review the evidence and identify new tools and strategies and if appropriate, subjects for advocacy that can contribute to reducing cholera mortality;
- Based on the above, identify a research agenda for the case management working group, including specific research questions.

Risk factors for and potential strategies to prevent cholera mortality

To provide concrete country perspectives, the meeting began with presentations from Nepal, Cameroon, Somalia and DRC. Each country highlighted the national cholera situation and identified risk factors. Despite diverse geography and epidemiology of cholera a number of common themes were identified including: limited access to treatment for geographic or financial reasons, limited community knowledge of cholera leading to delays in care seeking and inadequate adoption of preventive measures and poor knowledge of treatment of cholera outside specialised treatment centres.

Following these presentations, GTFCC-partners presented their experiences and strategies to respond to cholera both in the community and at health facility levels. Examples of existing non-cholera specific diarrhoeal disease programmes were also shared. The potential to expand the use of antibiotics in a global context of concern about antimicrobial resistance was also discussed. Key challenges and opportunities were identified:

- Increasing awareness of and access to treatment in the community
- The importance of reducing secondary attack rates within household and neighbours
- The importance of continuing to document and evaluate targeted approaches in order to define the most effective strategies
- The importance of ensuring all health care personnel can treat cholera appropriate to help reduce mortality while cholera specific emergency programmes are established or for where they are not available
- The need to improve treatment for specific vulnerable groups
- Many countries are strengthening diarrhoeal disease control using community health workers, but few include cholera. There may be opportunities to integrate cholera in these programmes.
- An example of a specific educational programme prior to the diarrhoea season was given from India, this type of programme could also be considered for cholera.

- It may be beneficial to develop a community package that can be shared with governments to help show how cholera control can be integrated into existing diarrhoeal disease control programmes
- To ensure good monitoring of antimicrobial resistance in cholera, laboratory thresholds to measure resistance need to be established
- Use of prophylactic antibiotics should be documented and the impact evaluated.

The following global areas of work were identified: 1) improving integration with existing diarrhoeal disease programmes with a focus on community health education and treatment, and 2) ensuring guidance is disseminated and used by those who need it most including those not traditionally targeted for cholera training.

The final group of presentations was on current research projects following which the group worked to define priority research questions relating to case management. Based on the previous day's discussion four main topics were identified: 1) Expanding the use of antibiotics 2) Improving interventions in the community 3) Identification of risk factors for mortality and 4) Improving diagnosis and treatment of cholera in vulnerable populations.

At the end of the meeting a provisional agenda of work aiming to address the identified priority areas was developed.

Introduction and objectives of the meeting

The Ending Cholera: A Global Roadmap to 2030 launched in October 2017 was the first step in operationalizing the new global strategy for cholera control. It sets out a path toward a world in which cholera is no longer a threat to public health, targeting a 90% reduction in cholera deaths and elimination of cholera in 20 countries by 2030.

Initial results of implementing the Global Roadmap can already be seen, with dramatic reduction of burden in countries such as South Sudan and Nigeria. We have also seen rapid containment of outbreaks in places such as Zimbabwe and Mozambique that previously would have risked becoming protracted and difficult to control.

However, in some countries, case fatality rates are still unacceptably high – as much as 6% - at a time when both preventive actions and curative treatments exist and should be widely available. During this meeting the GTFCC Case Management Working Group will work to define its role and strategies to achieve a 90% reduction in cholera deaths by 2030.

Specifically, the objectives of the meeting are to:

- Look at the evolution of cholera mortality over time and identify risk factors;
- Critically review the strategies and tools available to treat patients in health facilities and at community level to identify key bottlenecks and best practices;
- Review the evidence and identify new tools and strategies and if appropriate, subjects for advocacy that can contribute to reducing cholera mortality;
- Based on the above, identify a research agenda for the case management working group, including specific research questions.

Inaugural session & opening remarks

Dr Roderico Ofrin from the WHO Southeast Asia Regional Office (SEARO) welcomed the participants and opened the meeting.

Dr Poonam Khetrapal Singh, Regional Director, SEARO sent her regrets. Her message was shared by Dr Pem Namgyal, Director, Programme Management. In her message. Dr Singh observed that cholera is a major public health threat in the region. She noted that cholera is an indicator of inequality and social development requiring multisectoral approach for its control.

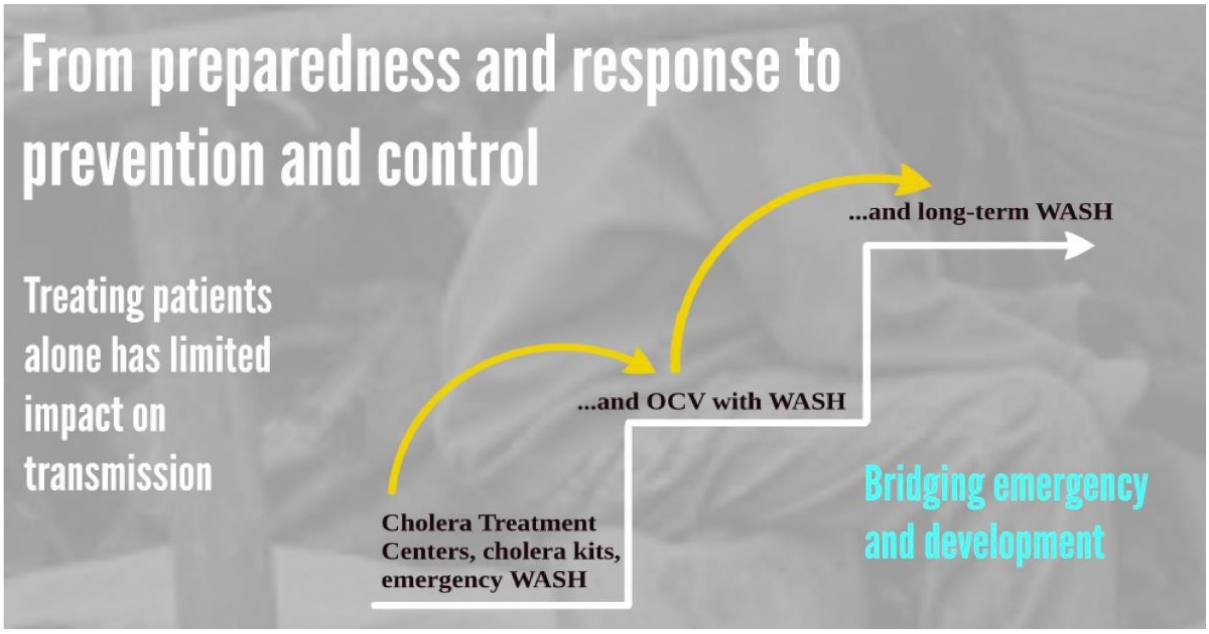
At the end of the message Dr Singh noted that the expertise gathered for the meeting were diverse; however, the commitment, to support the roll out of the road map for ending cholera by 2030 is common to all.

Session 1: Update from the GTFCC

Ending cholera – A Global Roadmap to 2030 – Dominique Legros

- Dominique Legros, Team Leader, GTFCC provided an overview of the principles of Roadmap. He noted that two years after the official launch of Roadmap (Figure 1) there has been unprecedented engagement of countries. He noted that Zambia and Zanzibar have launched their elimination plans. DRC, Nigeria, Somalia, South Sudan and Yemen are implementing large scale OCV campaigns. Bangladesh, Ethiopia and Sudan who had not reported cholera to WHO for many years have now all reported cholera. Bangladesh has taken a further step and has submitted a multi-sectoral cholera control plan to the GTFCC.
- Country engagement is supported by a broad range of partners and donors. Dominique Legros noted the encouraging increase in the number of development donors supporting sustainable WASH projects in hotspots.

Figure 1 – The ladder to reduce cholera cases



Update from the chair of case management WG – Md Iqbal Hossain

Md Iqbal Hossain shared the achievements of the working group since the successful GTFCC WG meeting in 2018 and presented the agenda and the objectives of the meeting. Key achievements included:

- the finalization of the Technical Note on the treatment of cholera in children with severe acute malnutrition,
- contributing to i) the Technical Note on IPC in cholera treatment structures, ii) the framework for the development of National Cholera Control Plans and iii) the Cholera Outbreak Manual that was completed this year and iv) the soon to be launched cholera app for field workers.

Dr Hossain also presented examples from published literature[12] showing of factors contributing to high case fatality rates from cholera. These include:

- difficulty to access care
- the time it takes to implement a response to a cholera outbreak and
- problems of the quality of care leading to death after discharge.

These were presented as some examples that should be kept in mind during the meeting in order to work towards finding solutions and reducing mortality from cholera.

Focus on the Cholera situation in the South East Asia Region – Dr Pushpa R Wijesinghe.

Cholera is endemic in the region but is under-reported and the burden is under-estimated. The need to strengthen surveillance to identify hotspots and prioritise areas for action was highlighted. Emphasis was also placed on how existing regional programmes and strategies can be used to support the implementation of the Cholera Roadmap in the region.

Key points raised during the discussion included:

- There is a continual need to engage the countries not yet on board and to strengthen the advocacy efforts to do this.
- Countries should be supported to better implement the Roadmap to reduce mortality by 90%, to reinforce surveillance activities to identify hot spots and to support efforts to bridge OCV with long term WASH activities
- Further development of the GTFCC operational model and the establishment of the Country Support Platform should help address this support issue.
- It is important to ensure strategic vaccine supply that is tailored to country needs and used in a strategic / preventive manner. A mechanism needs to be developed to use the stockpile balancing emergency and preventive requirements and the manufacturers' constraints.
- Countries should develop evidence-based cholera control programmes aligned to National Action Plans for Health Security (NAPHS). Leveraging this initiative could be constructive for all.
- In the Southeast Asia Region, the Delhi Declaration and Four 'I' initiative for Emergency Preparedness (identification, investment, implementation and interlinking) can also be used to support the roll out of the Ending Cholera Roadmap.

[1] BMC Public Health. 2019 Jan 25;19(1):112. doi: 10.1186/s12889-018-6299-3. **A cholera outbreak in a rural north central Nigerian community: an unmatched case-control study.**
Dan-Nwafor CC[1], Ogbonna U[2], Onyiah P[2], Gidado S[2,3], Adebobola B[2,3], Nguku P[2,3], Nsubuga P[4].

[2] Emerg Infect Dis. 2017 Dec;23(13). doi: 10.3201/eid2313.170529.
Cholera Mortality during Urban Epidemic, Dar es Salaam, Tanzania, August 16, 2015-January 16, 2016[1].
McCrickard LS, Massay AE, Narra R, Mghamba J, Mohamed AA, Kishimba RS, Urio LJ, Rusibayamila N, Magembe G, Bakari M, Gibson JJ, Eidex RB, Quick RE

Session 2: Cholera mortality assessments: risk factors and evolution over time

Reuben Samuel, WHO Country Office, Nepal

- Nepal has a marked seasonal trend of cholera cases. Although there are some issues with existing data sources for cholera mortality and morbidity, efforts are being made to strengthen surveillance and laboratory confirmation. One of the control strategies being tested in Nepal to reduce morbidity and mortality during outbreaks is comprehensive targeted interventions (CATI) which include household investigation, water quality monitoring, WASH interventions and health education in the neighbourhood of patients with confirmed cholera. This strategy has shown some positive results in terms of knowledge of cholera.

Alain Etoundi, Ministry of Health, Cameroon

- The national data reflected a high cholera case fatality rate (CFR), over 5.8% in 2018 and 4.4% in 2019. Difficulty to access health care was highlighted a risk factor for cholera deaths. Lack of financial, human and logistics resources were identified as elements restricting health access. Improving case management and community engagement were highlighted to decrease deaths.

Ahmed Discipline Mohamed, Ministry of Health, Somalia

- Following a large epidemic in 2017, the number of cholera cases and deaths has been declining. No deaths have been recorded in 2019 to date. Only facility level deaths are captured in reported data. Lack of knowledge in the community and lack of access to health facilities were noted as factors contributing to mortality during the peak of the epidemic. Need for community access to Oral Rehydration Solutions (ORS) and training of community volunteers were highlighted.

Placide Okitayemba, PNECHOL-MD, Democratic Republic of Congo

- Deaths from cholera occur more in epidemic areas and especially early in the epidemic. Knowledge of cholera and the importance of rapid treatment by the community, lack of knowledge of cholera by health staff and the delay to implement emergency interventions once an outbreak is detected were key elements contributing to cholera related mortality. Rapid response teams and targeted community interventions are key strategies being used to decrease cholera deaths

Key discussion points

- As surveillance is focused on health structures, resulting in under reporting from community which may lead to underestimates of the number of cases. Strengthening and integrating community surveillance is important.
- Poor knowledge of cholera in the community has been identified as a risk factor for cholera mortality, there should be more focus on increasing understanding of cholera in communities.

- Community engagement and strengthening links with existing community based programmes (e.g. volunteers, community health workers) could help address poor community knowledge of cholera and to increase treatment with ORS at the community level.
- There is a need to improve knowledge on cholera treatment at non-cholera specific health care centers as these are often the first point of care for patients with suspected cholera.

Session 3: Reducing mortality using existing tools

At community level

- Community case management model - Chris Brewer, IFRC [via WebEx]
    - A multi-level approach to improve access to ORS in the community was presented. The approach includes both long term provision of ORS via IFRC volunteers in cholera hotspots and surge capacity during outbreaks.
    - The difference between levels depends on the skill and expertise of the individuals. The programme is currently being piloted and training programmes for each level are being developed.

- Case-area targeted interventions – Monica Ramos, UNICEF
    - Experience from Haiti, Yemen, Zimbabwe and Mozambique was shared. Analysis of data from Haiti is promising, but more work need to be done to define components and to estimate impact, which is planned. Examples of the integration of health activities in CATI were presented.

- Community engagement during outbreaks to strengthen care seeking behaviour – Supriya Bezbaruah, WHO
    - The important role of the community to shape an outbreak was emphasized. How messages are shared with a community can have an impact. Local assessment was recommended as one step to ensure good communication with the community and to help ensure positive change and trust which is crucial in communication.

At health facility level

Panel 1: At Health facility level

- Experience from Bangladesh – Tahmeed Ahmed, icddr,b
    - The clinical experience and challenges at the icddr,b hospital were presented. Particular emphasis was placed on the experience of managing a large influx of patients in April 2018 and adaptations made. Recommendations to help manage future epidemics included strengthening links with the community and training government medical staff.

- Experience from Africa - Eric Sainte de Barte, ALIMA
    - The experience of emergency cholera response in Africa was shared. The delay in set up time and the lack of integration were identified as limitations as was the limited medical scope of classic cholera treatment facilities. Alima are exploring better targeted interventions, improving and extending medical care and raised the idea of integrated diarrhoeal treatment structures.

- Experience from Yemen – Louise Logre, Premiere Urgence Internationale [via WebEx]
    - The experience shared was from a remote area of Yemen. In addition to problems of access to care, cultural practices limited women's access to care. One element of the programme was the establishment of ORS points and transport for patients referred to a cholera treatment structure was highlighted as a limitation that could increase mortality Recommendations included ensuring diagnosis, infection prevention and control and waste management are included in training for treatment centre staff.

Key discussion points

- Improving access to treatment in the community was a common theme with work necessary both to increase community awareness and increase the rapidity of health seeking, but also to ensure adequate treatment is available when patients present to any structure.
- The delay to set up cholera specific structures once an outbreak is identified was raised multiple times – the need for diagnostic confirmation, authorization, train staff, set up structures, find supplies etc all play a role. A more integrated approach could help bridge this gap and overcome other obstacles to care such as insecurity, distance and cultural barriers.
- The importance of secondary attack rates in household and the close community is not fully addressed in many contexts. Further documentation will help identify the most at risk groups and prioritise interventions.
- CATIs are designed to target this secondary transmission, but more studies are necessary to prove effectiveness and impact and to look into integration for sustainability
- Potential roles for case management when integrated into CATI include use of antibiotics, active case finding and investigation and Standard Operating Procedures (SOP) for case management engagement
- Treatment of specific, fragile populations including malnourished children, the elderly and those with co-morbidities was raised.
- Increasing training to increase awareness of treatment of cholera outside cholera specific structures may also reduce deaths.

Session 4: New tools or renewed strategies to reduce mortality

Access to Oral Rehydration Solution

The objective of the session was to raise awareness of existing diarrhoeal control programmes that could be built upon for cholera control.

Regional strategies for the control of childhood diarrhoea - Rajesh Mehta, WHO SEARO

- Rajesh provided an overview of the burden of childhood diarrhoea in SEAR and existing programmes to prevent and treat childhood diarrhoea.
- Despite significant progress in the reduction of under-five mortality, diarrhoea remains the second cause of under-five mortality in the region.
- The region has an integrated, multi sectoral protect, prevent and treat strategy to reduce diarrhoea. Community health workers play an important role in the continuum of care.
- Use of ORS has increased significantly in the period 2005-2016, but use of zinc lags behind.

- The example of India's Intensive Diarrhoeal Control Fortnight, implemented before the anticipated diarrhoeal season was given and may be a potential model for cholera, especially in identified hotspots.

Access to Health Care at the community level in Somalia – Ahmed Discipline Mohamed, Ministry of Health, Somalia

- The focus of this presentation was on rural areas of Somalia.
- Although there are few health structures, there are more than 2000 community health workers who are active in the community but are attached to a health structure. The CHW programme is not standardized and responsibilities vary depending on the sponsoring Non-Governmental Organization (NGO). Distribution of ORS is common to all CHW. Access to ORS in the community is expanding with a World Bank sponsored Lady Health Worker programme. Each Lady Health Workers covers 200 households for vital statistics registration, distribution of ORS and referral to health structures. There are currently nearly 1500, the programme is expected to expand to 8000 Lady Health Workers.
- ORPs are only set up during diarrhoeal outbreaks.

Suman Kanungo and Debjit Chakrabarti - National Institute of Cholera and Enteric Diseases (NICED), India

- The primary health care system in Kolkata, a highly endemic area for cholera was presented.
- Kolkata has a comprehensive primary health care approach which includes the principles of universality, outreach to the most vulnerable and a focus on prevention.
- CHW distribute ORS packets during home visits and UHND (urban health nutrition day) with support from an ORS corner which exist at all urban public health centres.

Key points

- An integrated & continuum approach to manage diarrhea (and pneumonia) is being used in SEAR and could be a useful approach to overcome some of the above barriers.
- The potential role of community health workers or volunteers was emphasized with a potential to expand beyond the current childhood focus. Although distribution of zinc by CHW is not authorized in all countries, all distribute ORS.
- Expanding the use of antibiotics via community health care workers was discussed. In many countries this is not authorized, but with specific protocols it could be explored in specific contexts.
- Other community interventions could be identified and integrated into existing government programmes and structures – the idea of a 'package' to share with governments was raised.
- There is a need to strengthen primary health care in the endemic areas for cholera to boost the ORS treatment in the community and close to the beneficiaries.

Prophylactic use of antibiotics

- Global policy on Antimicrobial Resistance (AMR) – Sirenda Vong, WHO SEARO
    - Sirenda presented the global context of antimicrobial resistance and the global and national actions plans that are being developed. These provide the backdrop for expanding the use of antibiotics for cholera, including prophylactic use.
    - Although the antimicrobials recommended for cholera are not priorities for the global antimicrobial resistance agenda, the same principles of stewardship should be promoted and the GTFCC should ensure surveillance of antimicrobial resistance in recommended antibiotics and monitor effectiveness of strategies implemented.

- Antimicrobial resistance in the context of Cholera – Thanadavarayan Ramamurthy, Translational Health Science and Technology Institute (THSTI)

- Thanadavarayan presented the history of antimicrobial resistance in *V. cholerae* from the 1970s to the present.
- Currently break points are defined for clinical proposed and not to detect resistance.
- Limitations to surveillance of AMR for cholera include that susceptible, intermediate and resistant levels (SIR) are not standardized for azithromycin and doxycycline, establishing these should be a priority
- A guidance document for AMR testing should be developed.

- Example of a planned use of prophylactic use of antibiotics – Iza Ciglenecki, MSF Geneva [via WebEx]
  - Iza Ciglenecki presented an example of a highly insecure context in northeastern Nigeria where access to care was limited.
  - MSF had planned to introduce prophylactic antibiotic use to contacts of patients as part of an overall response that was to include giving antibiotics to suspected patients presenting to an ORS point as well as household contacts as part of a package including hygiene promotion and WASH during home visits
  - In reality, the outbreak was very short and home visits were never established. Antibiotics were only given to suspected cases over the age of 12 presenting to ORS points.
  - This experience highlights some of the practical challenges to implement this type of programme if it is not integrated into plans prior to outbreak occurrence.

Recommendations and discussion points

- Standardized laboratory manuals for antimicrobial testing should be developed for the antimicrobials used for V. cholerae: azithromycin and doxycycline
- Work should be done to fix epidemiological cut off values for antibiotics especially used in cholera cases
- Study to do investment case versus co benefits and our focus should be on implementation research to help member states to know the way to optimize implementation for rapid uptake and scale up new tools
- GTFCC should promote and guide surveillance for Azithromycin in cholera effected countries.
- The prophylactic use of antibiotics should be scientific documented, and impact evaluated.

Session 5 and 6: Moving forward: defining the strategies of the WG to achieve 90% reduction in cholera mortality

Following a summary of the key points raised during the previous sessions, the group was divided into two to help define priority strategies: 1) How can we improve tools that are currently being used for cholera control to reduce cholera mortality and 2) Are there other tools that should be used to reduce cholera mortality. The combined recommendations are presented below.

Improved integration with existing programmes

- It is important to identify what elements would be necessary to add to current diarrhoeal disease control programmes in order to address cholera, especially in endemic areas. There could be relatively small additions that could improve emergency response.
- Significant efforts are being made to address childhood diarrhoea via community programmes (Community Health Workers/Health Volunteers) how can these resources be leveraged to include cholera response? How can diagnostic and reference quality be integrated/improved?
- Surveillance – are there additional indicators that should be added to existing platforms to improve cholera control e.g. data on antimicrobial resistance, risk factors (to be shared with Surveillance WG)
- Surveillance and RRTs – these exist, how can this immediate intervention be strengthened to address cholera outbreaks?
- Ensure that response capacity and all training linked to response capacity target district levels where they are most needed.
- The first point of consultation may be the private sector, what tools can be developed to ensure they are equipped to treat cholera patients (particularly around provision of ORS)?
- As delays to implement programmes are often linked to delays in laboratory confirmation, in endemic areas could rapid diagnostic tests be used to trigger intervention?

Improving implementation of existing guidance

- Train human resources on cholera treatment – all health staff need to know how to treat cholera patients as the first point of care is frequently not a cholera specific treatment centre
- Are materials available to the people who need them in the best format?
- Considering that countries engage best when they have been involved in the development of guidance, it is recommended that implementation research be included in each National Cholera Control Plan – this will strengthen how recommendations are implemented in each context (e.g. implementation strategies for cholera infection control)

Session 7: Ongoing research

Funding cholera research and the global research agenda for cholera

Elizabeth Klemm and Helen Groves Elizabeth and Helen provided an overview of the Wellcome Trust funding model and where cholera sits within that framework.

- They also provided an overview of the outcome of the targeted funding call for cholera. The results from the selected projects are expected at the end of 2021 or early 2022. One project related to case management was selected.
- To ensure that future research funding provides evidence to develop strategies to treat and reduce mortality from cholera
- With this objective, Wellcome Trust have developed a Steering Committee for cholera research and have issued an request for proposals for independent groups to develop a global cholera research agenda which should be publicly communicated in 2021

Identifying clinical risk factors for cholera in children – Iqbal Hossain, icddr,b

- This retrospective analysis was carried out on data from the icddr,b hospital in Dhaka to identify clinical signs that could help differentiate between cholera and non-cholera diarrhoea in children.

- Factors that were significantly associated with cholera vs non-cholera diarrhoea were: age over 12 months, high stool frequency (great than 10 per 24 hours), showing signs of some or severe dehydration, patient presenting in warmer months (April-September in Dhaka) and having a working mother.
- Factors that were negatively associated with a diagnosis of cholera vs non-cholera included: absence of abdominal pain and the child being predominantly breast fed during first six months of life.
- Relatively more children with cholera needed admission and IV fluids as compared to other watery diarrhea diseases.

Research into Infection Prevention and Control – Monica Ramos, UNICEF for the GTFCC WASH WG

- IPC in cholera treatment centres is critical to reducing transmission.
- Recent and ongoing reviews by the London School of Hygiene and Tropical Medicine have shown that many of the existing recommendations on IPC are not evidence based. This work will guide research on the subject.
- Subjects that are evidence based include the disposal of cholera effluent, hand hygiene and hand washing, hygiene promotion packages in households of patients in specific contexts, and cleaning and disinfection.
- Monica presented an outlined how the WASH WG has worked to identify knowledge gaps and are building a research agenda based on this analysis.

Case fatality during cholera outbreaks in DRC higher in adults and in non-hotspot zone - Marianne Van der Sande, Institute of Tropical Medicine, Antwerp [via WebEx]

- Marianne presented results of a retrospective analysis of surveillance data collected from 2008 to 2017.
- Analyses were carried out comparing three profiles: 1) Health zones identified as hotspots 2) Health zones in hotspot provinces, but not identified as hotspot zones and 3) Other health zones.
- Analyses showed the case fatality is highest in non-hotspot provinces followed by non-hot-spot health zones in hot spot provinces and finally hotspot health zones. Only half the cases, but ¾ of deaths are reported in these areas.
- In all zones CFR was higher in patients 5 and over as compared to patients under 5 years. When broken down further, CFR increased with age with highest CFR in the over 50 age group.
- CFR was highest at the beginning of outbreaks.

Gastroenteritis aggressive versus slow treatment for rehydration - Kathryn Maitland, Imperial College/KEMRI [via WebEx]

- Kath presented an overview of the ongoing research to improve rehydration protocols for children with severe acute malnutrition (SAM) and dehydrating gastroenteritis.
- Although rehydration protocols are widely accepted, some studies suggest they can be improved (doi: 10.1186/s12916-019-1356-z).
- Current recommendations for children with SAM and diarrhoea leading to severe dehydration and very conservative (only if signs of decompensatory shock) due to concerns about overhydration and heart failure.
- Current research does not support these concerns).
- A new three arm randomized clinical trial GASTRO-SAM is in progress for children with SAM and diarrhoea. For children with some or severe dehydration the three arms are: current WHO protocols for severe dehydration (standard treatment), a slower arm with no specific treatment for shock and oral rehydration only following current WHO guidelines for children with SAM and shock. Children with shock are treated accordingly to the respective guidance.

Cholera and severe acute malnutrition – Tahmeed Ahmed, icddr,b

- Tahmeed provided an overview of the clinical signs and treatment of children with SAM and shock
- He then presented a clinical trial that is to be funded by the Wellcome Trust that should begin later this year on the treatment of children with SAM and cholera or other dehydrating diarrhoea and shock.
- The trial is planned as an open 2-arm trial comparing the standard protocol with blood transfusion vs the use of dopamine which is considered easier to administer in the field.

Estimating cholera incidence in Bangladesh - Sonia Hegde, JHU

- Sonia described a project modelling the number of cholera cases in Bangladesh. The project uses existing data from MoH general surveillance and sentinel cholera surveillance that helps estimate the cholera positive rate by age to model the number of cholera cases, the incidence and seasonality in a 5x5 km grid. This work helps identify high risk areas to prioritise intervention.
- There are limitations to the work as it is based on those accessing care and further work will be required to identify the most vulnerable groups.

Key discussion points

- Secondary attack rates in families was a discussion – improving measurement and identifying key contributing risk factors in different context could be useful to adapt interventions.
- Are there lessons to be learned, especially in the community from the current Ebola virus disease outbreak?
- Some guidance is aimed for partners with resources, but simplified versions are also needed e.g. recommendations for safe burials at the community
- There was discussion about the strengths and limitations of estimating burden based on sentinel data that does not include all treatment sites.

Session 8: Translating knowledge gaps into research questions

Developing a research agenda:

Based on the discussions throughout the meeting, four thematic areas of research were identified: 1) Expanding the use of antibiotics 2) Interventions in the community 3) Reducing mortality risk and 4) Treatment of vulnerable populations. The participants worked in small groups and developed a preliminary list of research questions relating to each of the four thematic areas. The questions listed below are a selection of the questions developed.

Expanding use of antibiotics

- What effect does treatment with antibiotics have on mild disease and this transmission route?
- What is the effect and duration of antibiotic prophylaxis on the magnitude, transmission and secondary attack rate of cholera outbreaks when given to:
    a). household contacts (main priority)
    b). mass prophylaxis in specific high-risk gatherings e.g. refugee camps, prisons (secondary priority)
- Is there a different effect on transmission if chemoprophylaxis is used in zones that are epidemic vs endemic for cholera?
- Are there synergies with other interventions such as WASH?

- How would antibiotic prophylaxis affect AMR in *V. cholerae* and other pathogens?
- Are there synergetic treatments (adjuvant) to enhance antibiotic efficacy when treating cholera? E.g. zinc
- Evidence review of use of antibiotics in cholera patients with no or some signs of dehydration and vulnerable populations.
- Is community level antibiotic treatment effective and feasible (comment that this would be via community health workforce)?
- What is the correct antibiotic susceptibility test/threshold for azithromycin and doxycycline for *V. cholerae*? (question for lab working group)
- What proportion of patients have already received antibiotics before presenting to a cholera treatment centre – does this have an effect on outcomes?
- Are standard antibiotic treatment protocols for cholera being followed by health care providers, and how does adherence to protocols affect mortality?

Interventions in the community

- How and where do people in the community seek treatment?
- What can be done to reduce delays to accessing treatment for cholera?
- Evaluation of system integration of community healthcare workers in treatment of cholera.
- Can a composite clinical score be used to improve diagnosis in the community (and replace RDT?).
- Could zinc or other agents play a role in reducing incidence/ severity/ deaths from cholera?
    - seasonal zinc prophylaxis in <5s
    - Zinc given to contacts of index case
- Can ORS be made available for use by community members (feasibility) at home apart from healthcare workers or ORS points?
- Can community members be trained as part of cholera management?
- How can transfer to a treatment centre be improved?
- What are high risk behaviours for cholera transmission in communities and how can they be addressed:
    - Burial a specific example, current guidance is not always feasible at community level.
- What is the efficacy of risk communication in communities?
- What are the cultural/behavioural barriers that affect (delay) health care seeking behavior.

Risk factors for mortality

- Will a comprehensive intervention package (including WASH, antibiotics, OCV, ORT) reduce cholera mortality in a specific epidemic context?
- Identify risk factors, including both proximal (more direct risks) and distal factors, for cholera mortality in communities. (example of funeral practices given - evidence may already exist on some practices in different contexts
- Examine availability and acceptability of antibiotics/ORT in hospitals and communities to determine relationship to mortality. (Desk review)
- How does OCV affect disease severity and associated-death during reinfection of cholera in the long term?

Treatment of Vulnerable Populations

- Identify valid and reliable hydration status assessment criteria in patients with cholera and severe acute malnutrition, in pregnant women and in the elderly.
- Identify treatment complications in vulnerable populations (sodium levels, rate of rehydration etc)
- Identify co morbidities /disease states (such as diabetes, hypertension, obesity, complex chronic disease, HIV) that increase risk of poor outcomes (e.g. mortality, increased length of stay) following cholera infection and how to adjust treatment accordingly.
- Is preventive vaccination or chemoprophylaxis in vulnerable populations during epidemics (e.g. the elderly and pregnant women) effective and feasible (linked to expanded use of antibiotics)?
- Quantify the risk of foetal loss in different contexts
- Quantify and identify risk factors for poor outcomes following cholera treatment (hydration, antibiotics) in SAM, Pregnant women, Elderly population

Session 9: Agenda of work for GTFCC WG

Agenda of work:

A preliminary agenda of work was developed based on the discussions held throughout the meeting and priorities identified.

- Conduct a desk review and potentially develop a policy paper on integration of treatment of cholera with existing diarrheal disease programmes. This work should focus on hotspot areas in affected countries.
- Linked with the above, conduct a desk review of the scope of work of Community Health Workers relating to cholera both during epidemics and outside epidemics. This would include identification of age groups treated and the role of CHW in surveillance, treatment, referral and health and hygiene promotion.
- Adapt existing recommendations for safe burial to community environments.
- Develop interim treatment protocol for treatment of pregnant women with cholera.
- Identify centres which have datasets in order to conduct retrospective data analysis for clinical signs for the diagnosis of cholera.
- Participate in the working group on CATI with a specific focus on the role of the community workforce including the distribution of ORS.
- Look for partners or opportunities in order to evaluate chemoprophylaxis to reduce transmission of cholera.
- Further develop the research agenda for case management

Annex 1: Meeting Agenda

GLOBAL TASK FORCE ON CHOLERA CONTROL

Fourth Meeting of the Global Task Force on Cholera Control (GTFCC) Working Group on Case Management

5-6 November 2019, New Delhi, India

Final Annotated Agenda

TUESDAY, 5 November 2019

Session	Content
08.30-09.00	**Registration and Welcome Coffee**
09.00-09.30	**Welcome notes –** Dr Roderico Ofrin, Regional Emergency Director, WHO SEARO **Keynote address** – Dr Poonam Khetrapal Singh, Regional Director, WHO SEARO **Group Photo**
09.30-10.00	**Session 1: Update from the GTFCC** *During this session the GTFCC secretariat and the WG chair will present the progress made since the last meeting of the working group. The Regional Office will present an overview of the situation in the region, including the role of WHO at regional level.* **Facilitator**: Iqbal Hossain **Presentations**: • Update from the GTFCC Secretariat – Dominique Legros • Update from the Chair of the Working Group – Iqbal Hossain, icddr,b • Focus on the Cholera situation in the South East Asia Region – Pushpa Wijesinghe, WHO SEARO
10.00-11.15	**Session 2: Review of cholera mortality** *This session will set the scene and present cholera mortality data over time in selected countries. It will highlight the different contexts in which cholera epidemics take place and areas where interventions could help reduce cholera related mortality.* **Facilitator**: Iqbal Hossain **Cholera mortality assessments: risk factors and evolution over time** • Reuben Samuel, WHO Country Office, Nepal • Placide Okitayemba, PNECHOL-MD, DRC • Alain Etoundi, Ministry of Health, Cameroon

	• Ahmed Discipline Mohamed, Ministry of Health, Somalia
11.15-11.30	**Coffee Break**
11.30-13.00	**Session 3: Reducing mortality using existing tools** **Panel discussion** - *During this session, participants will share experiences from the field and identify both best practices and challenges associated to the use of existing tools and strategies to manage cholera cases.* **Facilitator**: Sirenda Vong **Panel 1: In the communities** • Case-area targeted interventions – Monica Ramos, UNICEF • Community engagement during outbreaks - Supriya Bezbaruah, WHO • Community case management model - Chris Brewer, IFRC [via WebEx]
13.00-14.00	**Lunch Break**
14.00-15.30	**Panel 2: At Health facility level** • Experience from Bangladesh – Tahmeed Ahmed, Icddr,b • Experience from Africa - Eric Barte de Sainte Fare, ALIMA • Experience from Yemen – Louise Logre, PUI [via video] **Session 4: New tools or renewed strategies to reduce mortality** *During this session participants will explore new options to reduce the mortality associated to cholera. It will be an opportunity to learn the lessons from practitioners working in fields other than cholera.* **Facilitator**: Eric Barte de Sainte Fare **Panel 1: Access to Oral Rehydration Solution** • Regional situation on childhood diarrhoea – Rajesh Mehta, WHO SEARO • Access to health care in communities – rural setting - Ahmed Discipline Mohamed, Ministry of Health, Somalia • Access to health care in communities – urban setting – Dr Suman Kanungo and Dr Debjit Chakrabarti, NICED, India **Panel 2: Prophylactic use of antibiotics** • AMR in the context of cholera – Thandavarayan Ramamurthy, THSTI • Antimicrobial Resistance (AMR) Global Overview, Global & National Action Plans - Sirenda Vong, WHO SEARO • Example of targeted prophylaxis – Iza Ciglenecki, MSF [via WebEx]
15.30-16.00	**Coffee Break**
16.00-17.30	**Session 5: Moving forward: defining the strategies of the WG to achieve 90% reduction in cholera mortality** *Using the previous sessions as a base, this group work session will aim at identifying strategic areas of work, including research and advocacy, for the case management*

	working group moving forward. New or improved guidance, training or other documents can also be proposed **Group work** • Improving exist tools and renewing strategies – **Facilitator**: Sirenda Vong • Developing new tools and strategies – **Facilitator**: Eric Barte de Sainte Fare
17.30	**End of Day 1**
19.30	**Dinner**

WEDNESDAY, 6 November 2019

Session	Content
09.00-09.45	**Session 6: Summary of Day 1 and Feedback from the group work**
09.45-10.45	**Session 7: Ongoing Research** *During this session, ongoing research studies and operational projects that contribute to advancing the agenda of the case management working group will be presented.* **Facilitator**: Iqbal Hossain **Presentations:** • Burden and differential features of cholera and non-cholera watery diarrhea among under-five children: a case-control study in Bangladesh, Iqbal Hossain, icddr,b • Infection prevention and control, Monica Ramos, UNICEF
10.45-11.15	**Coffee Break**
11.15-12.00	**Session 7: Ongoing Research (continues)** *During this session, ongoing research studies and operational projects that contribute to advancing the agenda of the case management working group will be presented.* **Facilitator**: Iqbal Hossain **Presentations:** • Gastroenteritis aggressive versus slow treatment for rehydration, Kathryn Maitland, KEMRI [via WebEx] • Cholera and Severe Acute Malnutrition, Tahmeed Ahmed, icddr,b • Marianne Van der Sande, ITM [via WeBex] • Estimating cholera incidence in Bangladesh, Sonia Hegde, JHU
12.00-13.00	**Lunch Break**

13.00-13.30	**Introduction to the Global Research Agenda for Cholera** Presentation by Wellcome Trust
13.30-15.30	**Session 8: Translating knowledge gaps into research questions** *During this session participants will take stock of the presentations and discussions and will develop research questions on the key topics identified during the meeting and ultimately agree on a research agenda* **Group work** **Presentations and discussion**
15.30-16.00	**Coffee Break**
16.00-16.30	**Session 9: Agenda of work** *This session will present the agenda of work of the Case Management Working group for the next 12 months.*
16.30-17.00	**Meeting summary and next steps**

Annex 2: List of participants

GLOBAL TASK FORCE ON CHOLERA CONTROL

4th MEETING OF THE CASE MANAGEMENT WG
5 and 6 NOVEMBER 2019, NEW DEHLI, INDIA

LIST OF PARTICIPANTS

REPRESENTATIVES FROM COUNTRIES

CAMEROON

Georges Alain Etoundi Mballa, Director of Disease Control
Ministry of Public Health
Email: dretoundi@yahoo.fr

DEMOCRATIC REPUBLIC OF CONGO

Placide Welo Okitayemba, Director PNECHOL-MD
Ministry of Health
Email: pwelo2018@gmail.com

NEPAL

Ramakanta Duwadi, Deputy Director General, Department of Water Supply and Sewerage Management
Ministry of Water Supply
Email: duwadirk@gmail.com

SOMALIA

Ahmed Moallim Mohamed, National Emergency & Surveillance Coordinator and Technical Adviser
Federal Ministry of Health and Human Services
Email: ammohamed@moh.gov.so

GTFCC PARTNER INSTITUTIONS AND DONOR AGENCIES

ALIMA

Eric Barte de Sainte Fare, Programme Manager
Email: ebsf@alima.ngo

FONDATION MERIEUX

Marianne Gojon-Gerbelot, Conference Organizer
Email:marianne.gojon-gerbelot@fondation-merieux.org

IMPERIAL COLLEGE [via WebEx]

Kathryn Maitland, Professor of Paediatric Tropical Infectious Diseases Division of Medicine
Email**:** k.maitland@imperial.ac.uk

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH

Md Iqbal Hossain, Senior Scientist, Hospitals, Nutrition and Clinical Services Division
Email:ihossain@icddrb.org

Ashraful Islam Khan, Chief Physician and Head, Hospitals, Nutrition and Clinical Services Division
Email:ashrafk@icddrb.org

Tahmeed Ahmed, Senior Director, Nutrition & Clinical Services, Maternal and Childhood Malnutrition, Nutrition and Clinical Services Division
Email:tahmeed@icddrb.org

INSTITUTE OF TROPICAL MEDICINE ANTWERP [via WebEx]
Marianne van der Sande, Head Department Public Health, Professor Public Health
Email: mvandersande@itg.be

INTERNATIONAL FEDERATION OF RED CROSS AND RED CRESCENT SOCIETIES [via WebEx]
Christopher Brewer, Africa Cholera Coordinator
Email: christopher.brewer@ifrc.org

INTERNATIONAL VACCINE INSTITUTE
Jacqueline Lim, Research Scientist
Email: kalim@ivi.int

JOHNS HOPKINS UNIVERSITY
Sonia Hegde, Postdoctoral Fellow, Department of Epidemiology.
Email:shegde@jhu.edu

MEDECINS SANS FRONTIERES [via WebEx]
Iza Ciglenecki, Operational Research Coordinator
Email: Iza.Ciglenecki@geneva.msf.org

NATIONAL INSTITUTE OF CHOLERA AND ENTERIC DISEASES
Debjit Chakraborty, Scientist D
Email: drdebjitepi@gmail.com

Suman Kanungo, Scientist E
Email: sumankanungo@gmail.com

PATH
Sudhir Maknikar, Head maternal and child health
Email: smaknikar@path.org

PREMIERE URGENCE INTERNATIONALE [via WebEx]
Louise Logre, Head of Technical Department
E-mail : llogre@premiere-urgence.org

TRANSLATIONAL HEALTH SCIENCE INSTITUTE OF TECHNOLOGY
Thandavarayan Ramamurthy, National Chair, Head-chme
Email: tramu@thsti.res.in

UNICEF
Monica Ramos, Coordinator, GTFCC WASH Working Group

Email: monramos@unicef.org

US CENTERS FOR DISEASE CONTROL AND PREVENTION

Talia Pindyck, Medical Epidemiologist/Cholera SME, Waterborne Disease Prevention Branch Global Team
Email:nrb1@cdc.gov

WELLCOME TRUST

Helen Groves, Project Support Office
Email:h.groves@wellcome.ac.uk

Elizabeth Klemm, Postdoctoral Fellow
Email:e.klemm@wellcome.ac.uk

WORLD HEALTH ORGANISATION

WHO HEADQUARTERS - GTFCC SECRETARIAT

Kathryn Alberti, Technical Officer
Email: albertik@who.int

Dominique Legros, Team leader
Email: legrosd@who.int

Margot Nauleau, Technical Officer
Email: nauleaum@who.int

WHO REGIONAL OFFICE FOR SOUTH EAST ASIA

Supriya Bezbaruah, Technical Officer, Risk Communications
Email: bezbaruahs@who.int

Rajesh Mehta, Regional Adviser, Newborn, Child and Adolescent Health
Email: mehtara@who.int

Jennie Musto, Team Lead, Epidemiology
Email: mustoj@who.int

Roderico Ofrin, Regional Emergency Director
Email: ofrinr@who.int

Sirenda Vong, Area Manager
Email: vongs@who.int

Pushpa Ranjan Wijesinghe, Technical Officer, Epidemiologist
Email: wijesinghep@who.int

WHO COUNTRY OFFICE – BANGLADESH

Mohamed Hammam Hassan El Sakka, Team Leader, Health Security and Emergency Response
Email: elsakkam@who.int

WHO COUNTRY OFFICE – INDIA

Reuben Samuel, Team Leader, Health Security and Emergency Response
Email: samuelr@who.int

WHO COUNTRY OFFICE – NEPAL

Tran Minh Nhu Nguyen, Team Leader, Health Security and Emergency Response
Email: tranminhn@who.int

OTHERS

Mahtab Singh, Rapporteur
Email :drmahtab2013@gmail.com

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