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Vaccination in Acute Humanitarian Emergencies

A FRAMEWORK FOR DECISION MAKING

World Health Organization

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ABBREVIATIONS AND ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
BCG	Bacille Calmette-Guérin
CMR	Crude mortality rate
CE-DAT	Complex emergency database
CFR	Case fatality ratio
CRS	Congenital rubella syndrome
DHS	Demographic and Health Survey
Dt	Diphtheria toxoid
DTaP	Diphtheria, tetanus, acellular pertussis
DTP	Diphtheria-tetanus-pertussis
DTwP	Diphtheria, tetanus, whole cell pertussis
EMA	European Medicines Agency
EPI	Expanded Programme on Immunization
EWARN	Early Warning Alert and Response Network
FEWS	Famine early warning systems
GAM	Global acute malnutrition
HAART	Highly-active antiretroviral therapy
HAV	Hepatitis A virus
HEV	Hepatitis E virus
HbsAG	Hepatitis B surface antigen
HCW	Health-care worker
HepB	Hepatitis B
HeRAMS	Health Resources Availability Mapping System
Hib	Haemophilus influenzae type b
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
ICG	International Coordinating Group
IFRC	International Federation of Red Cross and Red Crescent Societies

IPV	Inactivated polio vaccine
JE	Japanese encephalitis
MICS	Multiple Indicator Cluster Survey
MMR	Measles– mumps–rubella
MSF	Médecins Sans Frontières
NGO	Nongovernmental organization
NRA	National regulatory authority
OMP	Outer–membrane protein
OPV	Oral polio vaccine
PCV	Pneumococcal conjugate vaccine
ProMED	Program for Monitoring Emerging Diseases
PRP	Polyribosylribitol phosphate
RCT	Randomized controlled trial
SAGE	Strategic Advisory Group of Experts on Immunization
SAM	Severe acute malnutrition
SIA	Supplementary immunization activity
TB	Tuberculosis
TT	Tetanus toxoid
U5DR	Under 5 death rate
UN NICS	United Nations National Influenza Centres
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
VC	Vaccination coverage
VPD	Vaccine–preventable disease
VVM	Vaccine vial monitor
WHO	World Health Organization
YF	Yellow fever

EXECUTIVE SUMMARY

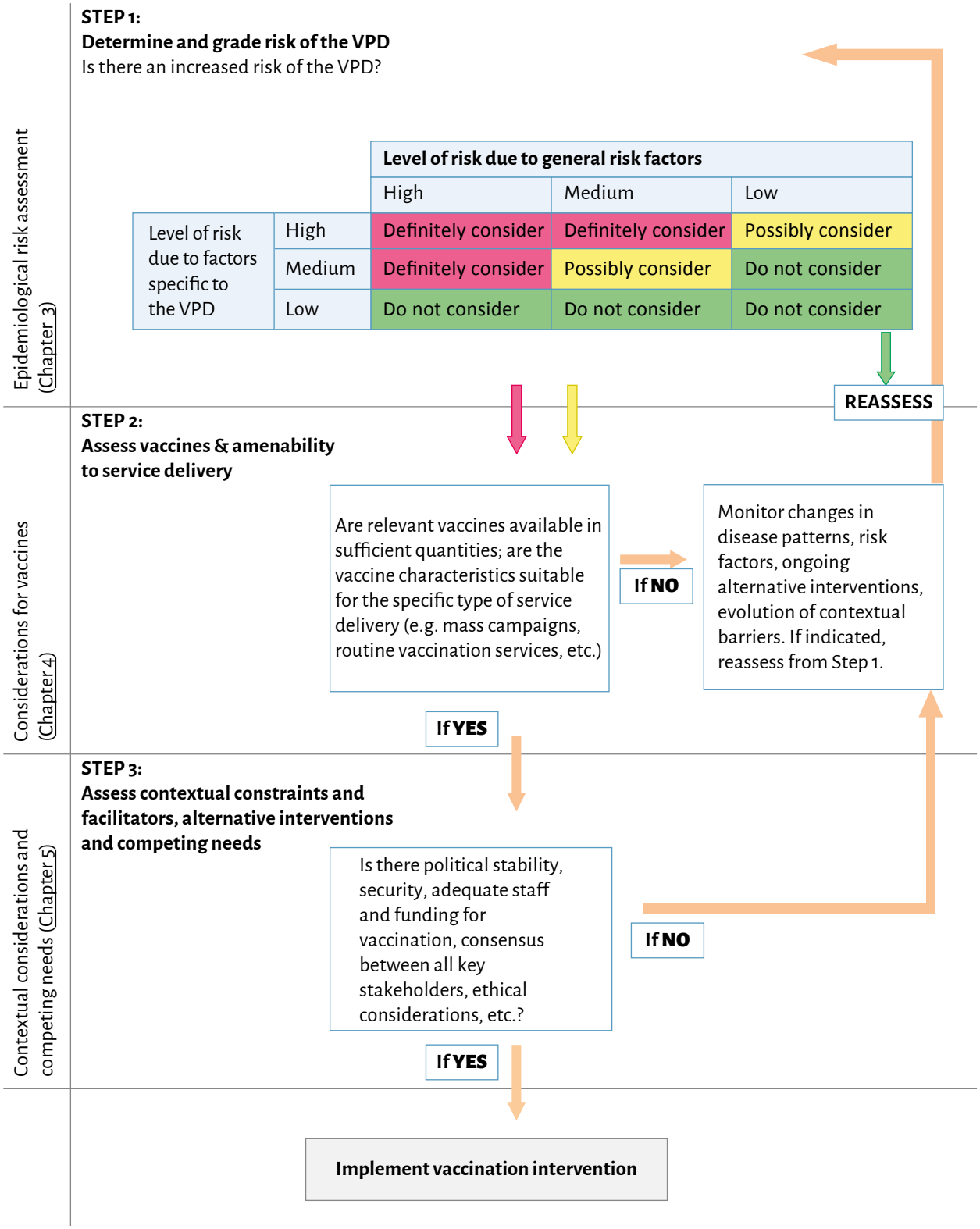
Humanitarian emergencies, regardless of type and cause, have a number of common risk factors for communicable diseases inextricably linked to excess risk of morbidity and mortality which can come from vaccine–preventable diseases (VPDs). The reduction of VPDs is a significant aim of public-health interventions during crises.

The WHO Strategic Advisory Group of Experts (SAGE) on Immunization carried out a comprehensive review of evidence on vaccination decision-making processes and considerations in humanitarian emergencies. This review resulted with decision-making framework which provides a transparent, evidence-based, and rigorous methodology for deciding on vaccination options in acute humanitarian emergencies. It consists of three essential steps: 1) assessing the local epidemiological risks of VPDs among the affected population, 2) vaccine selection and characteristics to consider, and 3) local contextual constraints that further assist in effective and timely decisions. The diagram below provides a schematic representation of this three-step approach in decision-making process.

This framework is intended to guide decision making on vaccination interventions immediately after the onset or during planning in anticipation of a possible or likely acute emergency. It may be applied in emerging humanitarian emergencies, or crisis of short duration, and in long-standing crisis and conflicts resulting in protracted humanitarian emergencies. The concept of "acute" emergency does not imply that the emergency in itself is short-lived, as in a protracted crisis situations can emerge and be considered as "acute". An acute emergency signifies a situation meeting one or more of the following conditions: sudden unplanned displacement of a large proportion of the population, direct exposure of the civilian population to new or exacerbated and sustained episodes of armed conflict, impending or already occurred sudden deterioration of nutritional status, natural or industrial disasters, and/or sudden breakdown of critical administrative and management functions which result in large-scale disruption of public health and related services.

This decision-making framework is intended for senior-level government and partner organization officials who are expected to work together to reach a decision regarding the need of vaccine antigen(s) in a given humanitarian emergency. It makes part of a package which also includes "Vaccination in Humanitarian Emergencies Implementation Guide". Both documents are supported with electronic versions to ensure that the most up-to-date vaccine and disease-specific data, and references to additional information and guidance are provided.

Fig. 1 Decision-making steps on vaccine use in acute humanitarian emergencies



I. INTRODUCTION

1. Background

Humanitarian emergencies, regardless of type or cause, have a number of common risk factors for communicable diseases. These include mass population movement and resettlement in temporary locations, overcrowding, economic and environmental degradation, impoverishment, scarcity of safe water, poor sanitation and waste management, absence of shelter, poor nutritional status as a result of food shortages, and limited access to health care. These risk factors are inextricably linked to excess risk of morbidity and mortality which can come from vaccine–preventable diseases (VPD). The reduction of VPDs is a significant aim of public-health interventions during crises.

1.1 Purpose and scope of this framework

This decision-making framework provides a transparent, evidence-based, and rigorous methodology for deciding on vaccination options in acute humanitarian emergencies. It provides a clear and consistent approach to 1) assessing the local epidemiological risk of VPDs among the affected population, 2) vaccine selection and characteristics to consider, and 3) local contextual constraints that further assist in effective and timely decisions. This framework is intended to guide decision making on vaccination interventions immediately after the onset or during planning in anticipation of a possible or likely acute emergency. It may also be applied in emerging humanitarian emergencies, or crisis of short duration, as well as in long-standing crisis and conflicts resulting in protracted humanitarian emergencies.

The ultimate aim of this document is to assist the user to thoughtfully, deliberately, ethically, and rationally determine whether or not the delivery of one or more vaccines to specific target populations during the acute phase of an emergency would result in an overall saving of lives, a reduction in the population burden of disease, and generally more favourable outcomes than would otherwise be the case.

This decision-making framework is intended for senior-level government and partner agency officials. They may deliberate in a small group (e.g. Immunization Task Force) to decide whether or not to use one or more vaccines in a given humanitarian emergency. In general, vaccination interventions should be agreed upon and this framework is meant to guide the discussions toward a consensus.

The final decisions should normally lie with appropriately designated officials of the Member State in which the emergency is occurring. In case of an emergency affecting more than one country, the final decision should be taken jointly by the designated officials of the Member States affected by the emergency.

In the recent past it has frequently been the case that emergencies unfold in countries with weak or poorly-functioning governments. In these cases, those in charge of coordinating humanitarian response (e.g. Health Cluster/ Immunization Task Force without governmental involvement) can apply the framework. However, this framework is not intended to be used by community-level health workers. More information on the establishment of an Immunization Task Force can be found in the Implementation Guide.

1.2 Evidence review: basis for the framework

In 2011, Strategic Advisory Group of Experts (SAGE) on Immunization formed the Working Group on Vaccination in Humanitarian Emergencies to review evidence on vaccination decision-making processes and considerations to identify current gaps and propose draft recommendations. The Working Group carried out a comprehensive review of literature[1] to collate existing guidelines, ethical considerations and documented experiences of use of vaccines in humanitarian emergencies in order to analyse key factors and methods involved in the consideration of vaccination during emergencies. The review was complemented by six case studies, conducted by the Working Group, with the aim of capturing the multifaceted and complex contextual and political considerations involved in such decisions. The information was gained through the recounting of experiences by organizations which participated in such decisions in affected countries. The Working Group prepared a document that was approved by SAGE in November 2012[2].

1.3 Guiding principles

General principles considered during the development of this framework are the following.

- Humanitarian emergencies pose specific challenges, to which guidelines developed for use in non-emergency settings need not apply. For example, emergencies may result in sudden changes in the burden of VPDs, either in their incidence or their case-fatality ratio, or both, as well as in an increased risk of epidemics and changes in usual geo-distribution patterns.
- Humanitarian emergencies may cause major disruptions in the delivery of all routine health services, including routine vaccination programmes. Thus, many of these services need to be addressed on an emergency basis and re-established as quickly as possible (details can be found in the Implementation Guide). Further, adequate case management should not be neglected which is particularly important in a protracted crisis.
- Security and logistics issues are more challenging during a humanitarian emergency, and have important implications for population access to health services and for access of health providers to the population. This may result with an inability to deliver full series of vaccinations and may prompt consideration of viable alternatives.
- Priority should be given to rapidly reduce the risk from a disease in order to protect the population during a period of extreme vulnerability. Strategies such as mass vaccination campaigns, expanded target age groups, and reduced courses for certain vaccines warrant greater consideration than they might in other circumstances, whether or not routine vaccination services remain functional.
- This framework is not intended to supersede or contradict existing WHO guidance on vaccination or any other acknowledged and validated guidance from WHO or partner organizations.

[1] WHO (2012). Vaccination in Humanitarian Emergencies: Literature Review and Case Studies. (http://www.who.int/immunization/sage/meetings/2012/april/2_SAGE_WGVHE_SG1__Lit_Review_CaseStudies.pdf, accessed 7 November 2016).

[2] WHO (2013). Meeting of the Strategic Advisory Group of Experts on immunization, November 2012 – conclusions and recommendations. Weekly Epidemiological Record 88:1-16 (http://www.who.int/wer/2013/wer8801.pdf, accessed 16 December 2016).

1.4 Ethical considerations

The following core ethical principles should be carefully considered during decision-making process (adapted from Guidance for managing ethical issues in infectious disease outbreaks, WHO, 2016[3]).

- **Justice**, or fairness, encompasses two different concepts:
  - **a. *Equity*** refers to fairness in the distribution of resources, opportunities and outcomes. Key elements include:
    - treating like cases alike
    - avoiding discrimination and exploitation
    - being sensitive to persons who are especially vulnerable to harm or injustice.
  - **b. *Procedural justice*** refers to a fair process for making important decisions. Key elements include:
    - due process (providing notice to interested persons and an opportunity to be heard);
    - transparency (providing clear and accurate information about the basis for decisions and the process by which they are made);
    - inclusiveness/community engagement (ensuring all relevant stakeholders are able to participate in decisions);
    - accountability (allocating and enforcing responsibility for decisions; and
    - oversight (ensuring appropriate mechanisms for monitoring and review).
- **Beneficence** refers to acts done for the benefit of others, such as efforts to relieve individuals' pain and suffering. In the public health context, the principle of beneficence underlies society's obligation to meet the basic needs of individuals and communities, particularly humanitarian needs such as nourishment, shelter, good health, and security.
- **Utility** as a principle states that actions are right insofar as they promote the well-being of individuals or communities. Efforts to maximize utility require consideration of proportionality (balancing the potential benefits of an activity against any risks of harm) and efficiency (achieving the greatest benefits at the lowest possible cost).
- **Respect for persons** refers to treating individuals in ways that are consistent to and are informed by recognition of our common humanity, dignity and inherent rights. Aspects of this principle are:
  - Respect for autonomy — requires letting individuals make their own choices based on their values and preferences. Informed consent[4] may be used to apply this concept. When individuals lack decision-making capacity, others may be charged to protect their interests.
  - Respect of values such as privacy and confidentiality, social, religious and cultural beliefs, and important relationships including family bonds.
  - Respect for transparency and truth-telling in the context of public health and research activities implementation.
- **Liberty** includes a broad range of social, religious and political freedoms, many of which are protected as fundamental human rights, such as freedom of movement, freedom of peaceful assembly, and freedom of speech.

[3] WHO (2016). Guidance For Managing Ethical Issues in Infectious Disease Outbreaks. Geneva: World Health Organization (http://apps.who.int/iris/bitstream/10665/250580/1/9789241549837-eng.pdf, accessed 16 December 2016).

[4] A process in which a competent individual authorizes a course of action based on sufficient relevant information, without coercion or undue inducement.

- **Reciprocity** consists of making a "fitting and proportional return"[5] for contributions that people have made. Policies that encourage reciprocity can be an important means of promoting the principle of justice, as they can correct unfair disparities in the distribution of the benefits and burdens of response efforts.
- **Solidarity** as a social relation in which a group, community, nation or, potentially, global community stands together, justifies collective action in the face of common threats, and supports efforts to overcome inequalities that undermine the welfare of minorities and groups that suffer from discrimination.

Practical applications of core ethical principles are outlined in Chapter 5.2.

1.5 Obligation to apply legitimate guidelines

National legal systems should guide the implementation of vaccination programmes, however, they frequently do not accommodate humanitarian emergencies. In instances where national legislative frameworks are absent or dysfunctional, international human rights law dictates a duty of care to protect those in need of assistance[6]. In these settings, implementation should ideally be guided by legitimate international health guidelines such as this framework and other guidance (e.g. WHO position papers on the use of specific vaccines available at http://www.who.int/immunization/policy/position_papers/en/), including this framework.

2. Key definitions and considerations

2.1 Definition of an acute humanitarian emergency

Several definitions of what constitutes an acute emergency have been proposed in the past, and different agencies employ varying classification and gravity benchmarking systems. For the purpose of this framework, a single definition is used in order to maintain global equity and consistency. The definition aims to capture any circumstances that are known to result in an increased risk of VPDs. The concept of "acute" emergency does not imply that the emergency in itself is short-lived, as even in a protracted crisis situations can emerge and be considered as "acute", in particular when the conditions deteriorate, risk factors accrue or the conditions evolve for a particular disease. The term "acute emergency" signifies a situation meeting any condition specified in the definition below. Accordingly, an acute emergency is defined as the occurrence of one or more of the following conditions, due to any reason (natural and/or man-made).

1. **Sudden unplanned displacement** of a large proportion of the population away from the community of habitual residence and into any settlement (e.g. refugee or internally displaced persons' camps, host community, urban areas, or uninhabited areas within the same country or across international borders).
2. Direct exposure of the civilian, non-combatant population to **new or exacerbated and sustained episodes of armed conflict** resulting in risk factors including disrupted access to health care, disrupted water and sanitation, food insecurity, etc.

[5] Becker, LC. (2005). Reciprocity, justice, and disability. Ethics:116(1):9–39.

[6] Resolution UNGA 217 A (III). Universal Declaration of Human Rights. Paris 10 December 1948. (http://www.ohchr.org/EN/UDHR/Documents/UDHR_Translations/eng.pdf, accessed 17 January 2017).

3. **Impending or already occurred sudden deterioration of nutritional status**, as evidenced by reliable food security and/or nutritional indicators, beyond and above known seasonal fluctuations or situations of chronic poor nutritional status and/or food insecurity.

4. **Natural or industrial disaster** resulting in temporary homelessness, disruption to critical public services (e.g. health care, water and sanitation, food deliveries, etc.), increased risk of injury and/or exposure to adverse weather conditions, famine, drought, environmental degradation for a large proportion of the population.

5. **Sudden breakdown of critical administrative and management functions** within the public and/or private sector, due to any reason, resulting in large-scale disruption of public health and related services (e.g. water and sanitation, housing).

The conditions included in the definition only aim to establish the need for application of this framework. The following remarks accompany the above definition.

a. **Size of affected population:** The size of the affected population is not a criterion for defining an acute emergency. Relatively small populations should equally receive appropriate consideration to ensure global equity and to maximize the potential impact of vaccination in all emergency-affected populations. However, the framework recognizes that scenarios in which large populations assemble within a given site (e.g. in a large camp) usually carry a higher risk of VPD epidemics, warranting more intense interventions.

b. **Duration of crisis:** Many acute emergencies occur in populations that are already affected by a long-lasting crisis due to protracted armed conflict or displacement, and/or other factors such as food insecurity, frequent natural disasters, environmental decay, etc. Whether an emergency does or does not occur against a long-lasting crisis is irrelevant for the purpose of the above definition. However, this circumstance is explicitly taken into consideration in the framework, as different vaccination interventions may be warranted (e.g. in a long-lasting crises, vaccination coverage is usually low).

c. **Excess population mortality:** In health terms, emergencies are frequently defined and their gravity benchmarked by estimates of excess population mortality. Accordingly, credible evidence may arise showing that over a recent period (e.g. within the last six months) the crude mortality rate (CMR), and/or deaths per person-time (e.g. per 10 000 people per day), and/or under five years death rate – deaths per person-time among children aged less than five years (U5DR), have greatly exceeded the non-emergency baseline. At least a doubling from the baseline is typically considered evidence of acute conditions. Scenarios featuring such elevations in mortality may also be classifiable as acute emergencies based on one or more of the conditions above. If the cause of the observed excess mortality is not immediately clear, urgent investigation should be carried out to ascertain whether the scenario meets one or more of the conditions 1–5 above. Plausible baseline figures should be extracted from a recent census or reputable health surveys, either within the population itself or, if unavailable, from neighbouring populations or countries with a similar demographic profile. In scenarios where the emergency is occurring in a crisis of long duration, mortality may already be elevated compared to the situation before the crisis. Comparison with the recent mortality levels observed in periods of chronic crisis is necessary to decide whether a sudden deterioration consistent with acute conditions has indeed occurred.

d. **Epidemic:** If any observed elevation in death rate is mostly attributable to a confirmed infectious disease epidemic, the epidemic should be accompanied by one or more of the conditions specified above in order for the scenario to be classifiable as an acute emergency. An epidemic alone is not sufficient to denote that an acute emergency is occurring.

e. **Pandemics:** Pandemics of influenza and HIV/AIDS, or possible future pandemics due to other diseases, are not within the scope of this framework unless they worsen underlying socio-economic and health conditions to an extent that the population begins to experience one or more of above conditions 1, 2, 3 or 5.

f. **Terrorism:** Terrorist attacks, defined as in UN Security Council Resolution 1566 (2004)[7] as "criminal acts, including against civilians, committed with the intent to cause death or serious bodily injury, or taking of hostages, with the purpose to provoke a state of terror in the general public or in a group of persons or particular persons, intimidate a population or compel a government or an international organization to do or to abstain from doing any act", are likewise outside the scope of this framework, unless they lead to one or more conditions listed above.

g. **Nutritional emergency:** A rapid deterioration in nutritional status may be detected based on food security indicators (e.g. staple prices, harvest sizes, household food consumption patterns) and/or on nutritional indicators (global [GAM] or severe [SAM] acute malnutrition prevalence). Food security indicators provide early warning of deteriorations while elevated SAM and GAM prevalence are typically seen only once a nutritional emergency is underway. Currently, prevalence estimates are typically computed among children aged 6–59 months based on the 2009 WHO Child Growth Standards and weight-for-height indices[8], although the use of middle upper-arm circumference, which may be less sensitive to regional body shape confounding, is increasingly advocated. For SAM and GAM specifically, various alert and emergency thresholds have been proposed. WHO considers the prevalence of ≥ 5% for SAM and ≥15% for GAM as indicative of a critical situation. However, a context-specific classification of gravity that considers underlying trends and concomitant disease risk factors is recommended. These chronic situations (such as alarming levels of malnutrition prevalence on a yearly basis noted in several regions of the world) require mostly long-term developmental solutions and do not fall within the scope of this framework. For the purpose of this definition, a rapid deterioration that occurs over a timeframe of weeks or a few months, above and beyond secular trends, is considered indicative of acute conditions.

h. **Availability of information:** In instances in which data and available information are imprecise, incomplete or controversial, application of the definition should err on the side of caution, i.e. it is preferable to assume that an emergency is taking place. The rationale for the decision should be documented carefully.

i. **End of crisis:** While it may be relatively straightforward to decide when an acute emergency has begun, it is often difficult to determine when it has ended. For the purpose of this framework, an acute emergency may be considered to have ended or to have moved into a chronic phase if conditions that resulted in a suddenly increased risk of VPDs have attenuated. This will typically occur when routine basic preventive and curative health services and other essential public services that impact public health, particularly water and sanitation provision, have been restored, food security has returned to pre-emergency levels and shelter conditions are acceptable. The transition from the acute to the chronic or recovery phase is gradual and subtle. Deciding whether acute conditions have ended, requires constant careful reassessment of epidemiological risk as the emergency evolves. Furthermore, chronic, long-duration crises may relapse into acute emergency conditions; this possibility should also be monitored vigilantly.

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[7] Resolution UN Security Council 1566. Terrorism, New York 8 October 2004. (http://www.un.org/en/ga/search/view_doc.asp?symbol=S/RES/1566(2004), accessed 17 January 2017).

[8] WHO (2009). WHO Child Growth Standards and the Identification of Severe Acute Malnutrition in Infants and Children: a Joint Statement by the World Health Organization and the United Nations Children's Fund. Geneva: World Health Organization (http://apps.who.int/iris/bitstream/10665/44129/1/9789241598163_eng.pdf, accessed 7 November 2016).

2.2 Beneficiary populations

Different population groups may require assistance during emergencies (e.g. groups living in urban or rural areas, displaced or in situ, sheltered in camps or living in unorganized settings). The epidemiological risks, the vaccine-specific characteristics, such as cold-chain availability, and the contextual setting may be different for each emergency-affected population. Accordingly, the framework may need to be applied separately to the different population groups. The decision to proceed with a specific vaccination may be different for different population groups and the details of any vaccination that is implemented may vary.

In addition, populations not affected by an emergency but living in close proximity to those that are, whether they host displaced people or are exposed to a higher risk of VPD because the circumstances around them have changed, should be provided with the benefits of any public-health interventions that are designed for, and implemented in, emergency-affected populations, to the extent that this is possible financially, logistically and operationally. The guiding principle should always be: equitable access to vaccination for equal risk. The refugees should receive vaccines according to the host country's schedule, given that prolonged stay in host countries is more common than return to their home country.

2.3 Vaccine-preventable diseases against which vaccines should be considered within the scope of this framework

VPDs fall within the scope of the framework if they meet the first condition, the increase in the burden of disease due to an acute emergency, and if they fall under one of the subsequent two conditions.

1. Burden of the disease may increase because of an acute emergency.
2. A WHO prequalified vaccine exists that can provide at least some protection against the disease in an emergency setting.
3. In cases where a WHO prequalified vaccine[9] for the specific disease does not exist or is unavailable, one or more of the following additional criteria may be applied.
   - **a.** Manufacturers that are already WHO pre-qualified for at least one vaccine product will normally be considered.
   - **b.** The vaccine should be licensed by the national regulatory authority in the country of manufacture.
   - **c.** The product is subject to the firm acceptance of the vaccine and manufacturer by the recipient country.
   - **d.** A vaccine registered for use in well-regulated countries (such as EU, Japan or USA) is normally preferred.

Vaccines to be considered within the scope of this framework include:

- vaccines used in national routine immunization programmes;
- vaccines used for seasonal interventions (such as influenza vaccination and meningococcal meningitis vaccination mainly in the meningitis belt of Africa in countries where conjugate meningococcal vaccine has not been introduced); and
- new vaccines that may not be fully integrated into national routine immunization programmes.

[9] List of prequalified vaccines [website]. Geneva: World Health Organization; 2016 (http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/, accessed 16 December 2016).

All vaccine-preventable diseases listed in the Table 1 should be considered along with those for which vaccines are included in national routine immunization programmes. Additional vaccine-preventable diseases may be considered as new vaccines become available[10,11].

Table 1 Vaccine-preventable diseases to be considered within the scope of this framework

Cholera (worksheet A2.1)
Diphtheria (worksheet A2.2)
Hepatitis A (worksheet A2.3)
Hepatitis B (worksheet A2.4)
Hepatitis E (worksheet A2.5)
***Haemophilus influenzae* type b** (worksheet A2.6)
Human papillomavirus, HPV (worksheet A2.7)
Influenza (worksheet A2.8)
Japanese encephalitis (worksheet A2.9)
Measles (worksheet A2.10)
Meningococcal disease (conjugate or polysaccharide vaccine) (worksheet A2.11)
Mumps (worksheet A2.12)
Pertussis (worksheet A2.13)
Pneumococcal disease (worksheet A2.14)
Poliomyelitis (worksheet A2.15)
Rabies (worksheet A2.16)
Rubella (worksheet A2.18)
Rotavirus (worksheet A2.17)
Tetanus (worksheet A2.19)
Tuberculosis (worksheet A2.20)
Typhoid fever (worksheet A2.21)
Varicella (worksheet A2.22)
Yellow fever (worksheet A2.23)

The framework, while providing specific guidance for existing vaccines (see Annex 2), also provides a general approach that will be applicable to the use of any vaccine in an emergency, including new ones as they become available, e.g. Ebola or Zika vaccine.

2.4 Vaccine procurement

In acute emergencies necessary vaccines can be obtained through purchase (direct, through response mechanisms and from stockpiles) and by donations.

[10] A vaccine for malaria has been authorized as per Article 58 of the European Medicines Agency (EMA). SAGE is not recommending it for widespread use until further results from pilot implementation projects become available. More information can be found in: WHO (2016). Malaria vaccine. WHO Position Paper. Weekly Epidemiological Record 91(4):33–52 (http://www.who.int/wer/2016/wer9104.pdf?ua=1, accessed 7 November 2016).

[11] Vaccine against dengue is available and it is licensed in several countries. WHO recommends restricted use of the vaccine to settings where seroprevalence is already very high. More information can be found in: WHO (2016). Dengue vaccine. WHO Position Paper. Weekly Epidemiological Record 91(30):349–364 (http://www.who.int/wer/2016/wer9130.pdf?ua=1, accessed 7 November 2016).

PURCHASE, RESPONSE MECHANISMS AND STOCKPILES

Vaccine may be purchased directly from the manufacturer, through the United Nations Children's Fund (UNICEF) response mechanisms, through CSOs or through stockpiles. A mapping of the key stakeholders active in supply of vaccines in humanitarian emergencies can be found the Implementation Guide (Annex 1).

Depending on the level of funding available, the price of the vaccine and related supplies may play a role in the decision-making process. Currently, work is being done to enable timely access to affordable vaccines in response to humanitarian emergencies. A "Humanitarian Mechanism" was developed in partnership by WHO, UNICEF, Medicines Sans Frontiers and Save the Children, that enables timely access to affordable supply of vaccines for entities such as Civil Society Organizations, Governments or UN Agencies who are procuring on behalf of populations facing humanitarian emergencies who otherwise do not have access to affordable vaccines (http://www.who.int/immunization/programmes_systems/sustainability/en/). However, the mechanism currently covers only a few vaccines. Manufacturers are constantly encouraged to provide price offers under the mechanisms and other means for humanitarian emergencies. As an example, UNICEF solicits offers and establishs procurement arrangement for access to vaccines and timely response to vaccine requests in humanitarian crisis. When requested by governments or non-governmental organizations, UNICEF has worked with suppliers to ensure the rapid availability of vaccines to meet the needs of populations that have been affected by humanitarian crises.

The international donor community has established stockpiles for meningococcal, yellow fever and oral cholera vaccines. These stockpiles are managed through an International Coordinating Group on Vaccine Provision (ICG) made up of four member agencies: UNICEF, Médecins Sans Frontières (MSF), International Federation of the Red Cross (IFRC), and WHO. When a country requests vaccines as a response to outbreak, ICG reviews the request and comes to a decision within 48 hours. If approved, the vaccine is delivered within a maximum of seven days. The decision whether or not to approve a request is based on predetermined criteria, namely epidemiological evidence for an outbreak (includes laboratory confirmation), availability of an action plan for mass vaccination, adequate storage conditions, etc.

UNICEF has other contractual agreements for emergency response and/or stockpile which includes oral and inactivated polio vaccines (OPV and IPV) for outbreak response and campaigns, stockpile for monovalent type 2 oral polio vaccine (mOPV2) in support of Global Polio Eradication Initiative (GPEI), measles and measles–rubella vaccines under Measles & Rubella Initiative (MRI), and preventive Cholera vaccine through Global Task Force in Cholera Control (GTFCC).

These stockpiles are not the only recourse for vaccine, and their existence does not guarantee vaccine availability for intervention planning. The application process and procurement of vaccines through existing international stockpiles is a separate process and the specific procedure should be followed.[12]

DONATIONS

Donations may form part of the strategy for access to vaccines in emergencies. Although as per the WHO and UNICEF joint statement on Vaccine Donations[13] five criteria are required to achieve good donations practice (suitability, sustainability, informed key persons, supply, licensing), the joint statement recognizes that in exceptional circumstances, including emergency situations, these minimum requirements may not be met. For example vaccine specifications and/or presentation may vary from what is used in the routine programme, or the remaining shelf-life may be limited, or sustainability may not be a priority consideration or relevant in an emergency response context. The most important consideration is that the vaccine is suitable

[12] International Coordinating Group (ICG) on Vaccine Provision: http://www.who.int/csr/disease/icg/qa/en/, accessed Jan 2017

[13] WHO/IVB/10/09. http://www.who.int/immunization/hpv/plan/who_unicef_joint_statement_on_vaccine_donations_who_unicef_2011.pdf, accessed Jan 2017

to the population needs from a public–health perspective as determined by the senior-level government and partner agency officials tasked to work together to decide on appropriate vaccine use in a specific situation.

More information on existing mechanisms for the procurement and supply of vaccines can be found in the Implementation Guide (Chapter 4.3 and Annex 1).

II. THREE-STEP DECISION-MAKING FRAMEWORK

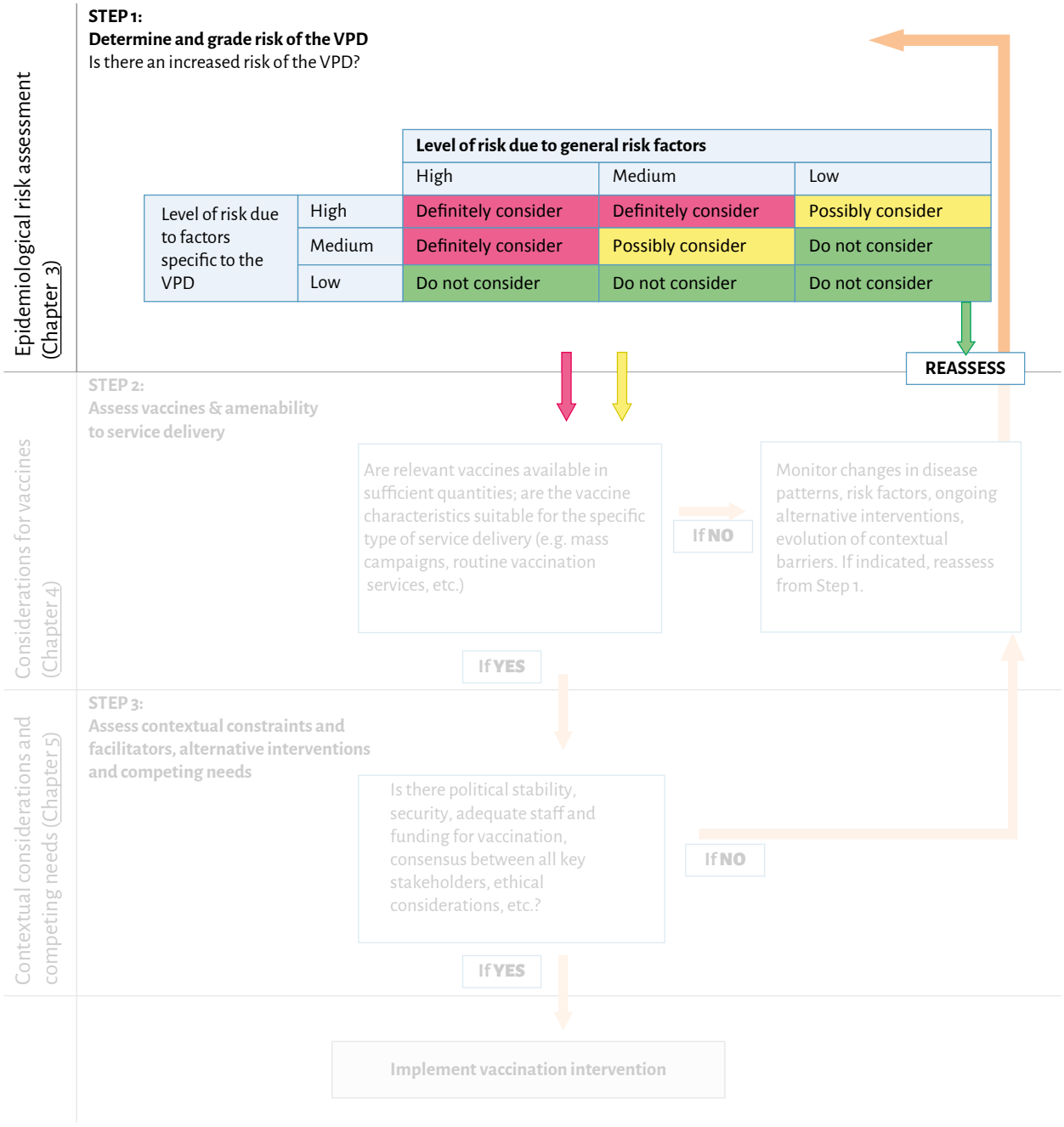
3. Step 1: Epidemiological risk assessment

In Step 1 you should carry out epidemiological risk assessment by completing the following tasks:

- Task 1: Grade the level of risk for the vaccine-preventable disease due to general risk factors.
- Task 2: Grade the level of risk due to factors specific to each vaccine-preventable disease.
- Task 3: Assess the overall risk of each VPD and characterize the expected risk for VPDs being considered further.

The output of Step 1 is classification of vaccine-preventable diseases within categories (definitely, possibly, and do not consider) to determine whether each vaccine-preventable disease will be further considered for intervention in the subsequent step of the framework.

Fig. 2 Step 1 of decision-making framework on vaccine use in acute humanitarian emergencies



3.1 General considerations

3.1.1 PURPOSE OF THE RISK ASSESSMENT

Before appraising different options for vaccination interventions, it is crucial to carry out a systematic epidemiological risk assessment for VPDs in an acute emergency in order to identify those for which specific vaccination interventions should be considered. This risk-assessment process should result in a shortlist of VPDs to be carried over into the subsequent step of the framework (Chapter 4). If carried out accurately and equitably, shortlisted VPDs should be those that carry the greatest epidemiological risk. A final determination

of whether to implement vaccination for these VPDs is only made after full consideration of all three steps in the framework process.

Risk assessment must be carried out systematically for every VPD within the scope of the framework to avoid personal bias or a priori considerations about which diseases are likely to be important and which vaccines appropriate. The suggested risk-assessment process may result in shortlisted VPDs for which vaccination has never or rarely been attempted in emergencies (e.g. pneumococcal disease), or for which vaccination is unlikely to be an appropriate choice of intervention (e.g. tuberculosis). However, in Step 1 it is important to let the classification of risk be guided solely by need (i.e. how much excess mortality could occur) and not by consideration of prior experiences in emergencies, or by feasibility, effectiveness, cost, and opportunity of providing a specific vaccine. All of these parameters are considered systematically in further steps of the framework.

3.1.2 THE MEANING OF RISK IN THE CONTEXT OF THE FRAMEWORK

Since mortality reduction is the primary aim of emergency public–health interventions, the main factor by which to assess the risk of VPDs is preventable deaths. For some diseases diminished pressure on curative health services (particularly inpatient facilities) as a result of a decreased disease incidence is also a desirable, albeit secondary, outcome of vaccination.

In certain emergency situations, excess risk for VPDs that are the focus of ongoing eradication and elimination programmes (e.g. **polio and measles**) may also be considered in terms of potential regional or global setbacks in the eradication/elimination effort, unless vaccination interventions are implemented. This factor should be considered secondary to that of excess mortality, however, the risk assessment suggests instances in which it could warrant prioritizing a given VPD. Note that WHO regional offices routinely carry out risk assessments for polio importation and outbreaks, and these should be consulted in the event of an emergency.

For specific VPDs (cervical cancer due to HPV, hepatitis B, tuberculosis), most excess risk will manifest well after the end of an acute emergency or in the next generation. For example, an armed conflict may result in a large number of female victims of sexual violence acquiring human papillomavirus (HPV), but the latency period of HPV-associated cancer means that these women will only experience excess disease and mortality later in life. For hepatitis B, a similar dynamic would occur and, in addition, women victims could transmit the virus during childbirth, resulting in further, future deaths among their children. The framework values these lag effects of acute emergencies on health. Balancing the value of preventing a death in the immediate period after the emergency's onset (e.g. by vaccinating against cholera) against the value of preventing a death later in life or among a second generation (e.g. by vaccinating against hepatitis B) is extremely difficult. It has epidemiological, economic and ethical dimensions, and would require more time and information than will be available for this risk assessment. To circumvent this complexity, the framework assigns an equal value to deaths in the present and deaths that will occur later in time, as long as both can be attributed to excess risk due to the emergency.

Lastly, it is important to note that the excess risks of VPDs may arise due to explosive epidemics, but also due to exacerbation in the baseline endemic pattern of disease resulting from increased incidence, increased probability of developing disease once infected, and/or higher case-fatality ratio (CFR). The framework process only distinguishes between these mechanisms to the extent that the threat of epidemics may require a particularly urgent vaccination response.

3.1.3 TIMING OF THE RISK ASSESSMENT

This risk assessment is intended to be a rapid, desk-based exercise to be completed within a few days as part of emergency preparedness, or during the first few days after the emergency begins. While assessing each VPD within the scope of the framework may appear time-consuming it is expected that a small team

of experienced assessors, having access to the country's disease surveillance and vaccination programme information, should be able to complete the risk assessment in a few days. As suggested in Annex 1, in nearly all scenarios some information will be unavailable or questionable. This should not delay the framework process and, if desk-based avenues to obtain this information are exhausted, best judgment assumptions should be used to fill information gaps. Nevertheless, a balance needs to be struck between the urgency to move forward with vaccination interventions as soon as possible and the minimal time required to complete a well-reasoned, informed and documented risk assessment.

Risk assessments should be an ongoing process due to the dynamics inherent in an emergency. A review of the risk assessment for each disease should be performed at least every three months, or as soon as possible if important, new information arises on any VPD, or if the general situation changes warranting immediate action (e.g. if disease surveillance systems indicate the onset of an epidemic or if the nutritional situation suddenly deteriorates). In practice, this review will be quicker than the original risk assessment, as the answers to relatively few questions are likely to change.

3.1.4 RISK ASSESSMENT FOR HOST POPULATIONS

In cases where a displaced population finds refuge within a host community (e.g. in a city or in a rural district), or where the two are in close proximity, it is important to assess risk for the latter population and to consider vaccination interventions accordingly. Political, policy, equity and communication issues may need to be addressed when considering extending or not extending vaccination to a host population.

Risk assessment for host populations should be done separately from that of the displaced population. It can be somewhat streamlined to consider the main potential threat, namely introduction or re-introduction of a VPD that is not circulating in the host population, but that may be carried by the displaced population. This is particularly relevant for diseases that are subject to an elimination or eradication programme, such as measles and polio, or that are known to cause explosive outbreaks such as cholera or meningococcal meningitis. A major factor to consider when assessing this threat is the immunity level of the host population (see Task 2), and whether this is likely to be high enough to prevent an epidemic (i.e. afford herd immunity) even after considering changes in population density due to the influx of the displaced (note that crowding increases the immunization coverage requirement for herd immunity), and the degree of mixing between the host and displaced populations.

3.2 The risk assessment process

3.2.1 OVERVIEW OF THE RISK ASSESSMENT

The risk assessment process should be conducted for each VPD. It consists of the following tasks:

1. **Task 1**: Grade the level of risk for VPDs due to general risk factors as “high”, “medium” or “low”, based on their occurrence and relevance to the given VPD.
   - **a.** Determine the presence of one or more general risk factors in the acute emergency situation, based on available information and by answering key questions (Table 3).
   - **b.** Use a priori knowledge (summarized in Table 4) on the expected effect of the general risk factors on the VPD to come up with a grading.
2. **Task 2:** Grade the level of risk due to factors specific to the given VPD as “high”, “medium” or “low”, based on available information.

3. **Task 3:** Come up with an overall classification by running each VPD through a two-dimensional matrix (Table 2).
   a. Decide whether the VPD should be considered further.
   b. Characterize the expected risk for VPDs to be considered further.

Fig. 3 Sequence of tasks for Step 1

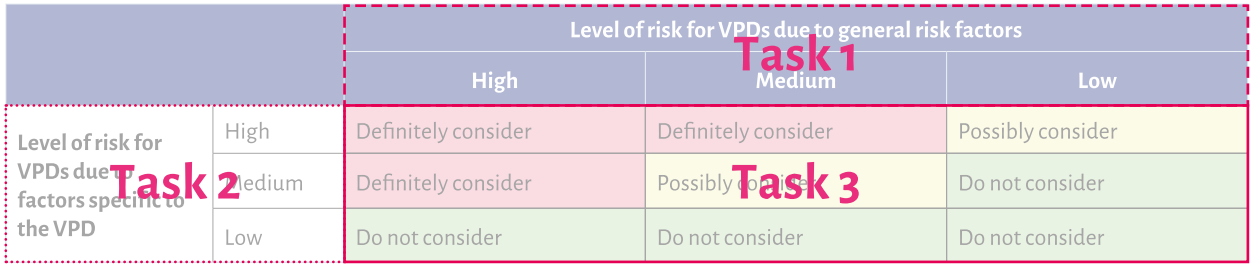


Table 2 Epidemiological risk assessment classification for any VPD

		Level of risk for VPDs due to general risk factors		
		High	**Medium**	**Low**
Level of risk for VPDs due to factors specific to the VPD	High	Definitely consider	Definitely consider	Possibly consider
	Medium	Definitely consider	Possibly consider	Do not consider
	Low	Do not consider	Do not consider	Do not consider

The two dimensions of the matrix are:

1. Level of the risk of the VPD assessed as a result of key general risk factors (see Table 3 and Table 4) that may or may not be present.
2. Level of the risk of the VPD assessed as a result of additional risk factors that are specific to the VPD in question (Table 5 and Annex 2).

For both dimensions, a simple "high", "medium", and "low" grading system is adopted. Both dimensions are equally weighted. The risk-assessment process will result in a classification from the matrix of each VPD in one of the following three categories.

- **Definitely consider:** the VPD has the potential to be one of the leading causes of mortality and/or to cause a major epidemic (thousands of cases, hundreds of deaths); thus, a specific vaccination intervention against this VPD should definitely be appraised in the next step.
- **Possibly consider:** the VPD is probably not a leading cause of mortality but could cause a considerable number of excess deaths and/or a large outbreak; thus, a vaccination intervention against this VPD could be considered in specific circumstances based on an assessment of competing priorities and other opportunities for control. In particular, vaccination against this VPD could be opportunistically coupled with that against VPDs falling in the above category, e.g. if dosage schedules and target age groups are compatible. Vaccination interventions against this VPD should be appraised in the next step.

- **Do not consider:** the VPD is unlikely to cause considerable excess mortality or an outbreak consisting of more than a handful of cases; thus, a vaccination intervention against this VPD should not be considered further in the framework unless a review of the risk assessment results in a change of classification.

Example

In a given acute emergency scenario, the presence of several general risk factors (e.g. overcrowding and insufficient water, sanitation and hygiene) could result in the risk of cholera being graded "high", the risk of Japanese encephalitis being graded "low", and the risk of diphtheria being graded "medium". Consideration of specific risk factors for each disease (e.g. levels of vaccination coverage and the location of the emergency) might result in a grading of "medium" for cholera, "high" for Japanese encephalitis, and "low" for diphtheria. The resulting classifications would therefore be: "definitely consider" for cholera, "possibly consider" for Japanese encephalitis, and "do not consider" for diphtheria.

3.2.2 TASK 1: GRADE THE LEVEL OF RISK FOR VPDs DUE TO GENERAL RISK FACTORS

Task 1a: Determine the presence of general risk factors

In acute emergencies excess burden of mortality and morbidity due to VPDs is often attributable to a few key general risk factors that:

- have a biological, behavioural or environmental basis;
- have a proximate causal relationship with disease;
- may already be present before the emergency or may become exacerbated as a result of the emergency; and
- can affect the risk of transmission, progression to disease or CFR for a variety of VPDs.

While, in reality, the intensity and effects of these risk factors can range from negligible to very high, for simplicity this framework only classifies them as present or not. The assessors should go through the general risk-factor table (Table 3) systematically and answer key questions to determine the presence of these factors.

Table 3 Table for determining the presence of key general risk factors

Risk factor	Main effects on VPDs	Key questions to ask	Possible indicators to consider
High prevalence of malnutrition	Increased risk of infection, disease progression and case fatality	Is there evidence of a nutritional crisis, either already established or unfolding? Is there an unusually high prevalence of acute and/or chronic malnutrition, among young children or the general population (e.g. history or reports of specific micronutrient deficiencies especially vitamin A)?	• Prevalence of acute malnutrition among children aged 6–59 months, ≥15% or ≥2% measured within the last three months above and beyond seasonal levels • Average nutritional intake or food ration <2100 kcal per person per day • Deteriorating food security indicators (e.g. price of staple foods or livestock, yield of last harvest)
High burden of chronic diseases	Increased risk of infection, disease progression and case fatality	Is there unusually high burden of chronic diseases in the general population?	• Prevalence of chronic diseases including diabetes, cardiovascular, cancer, immunosuppressive drugs, and renal diseases in the general population
Young population and/or high birth rate	Greater pool of susceptible for VPDs mainly affecting children Higher herd immunity threshold	Are there a high number of children? Is there an increase in deliveries?	• Proportion of children aged under 5 years ≥15% • Crude birth rate ≥30 per 1000 people per year
High HIV/AIDS burden	Increased risk of infection, disease progression and case fatality	Do persons with HIV/AIDS make up a high proportion of the population? Is there a low access to highly-active antiretroviral therapy (HAART), or have HAART programmes been disrupted by the emergency?	• HIV sero-prevalence ≥15% and • HAART coverage <50% or probably falling due to the emergency
Low access to curative and supportive health services	Increased case fatality for all VPDs Increased risk of some vertically transmitted VPDs (neonatal tetanus, hepatitis B)	Has the emergency resulted in reduces access to quality outpatient and inpatient curative health services and if so, to what extent?	• <1 basic health unit per 10 000 people or <1 hospital per 250 000 people • High proportion of non-functional or inaccessible health facilities
Overcrowding	Increased transmissibility of airborne, droplet and faecal-oral VPDs	Does the population live in a large camp or a high-density urban community? How close together are residential structures?	• Size of camp >10 000 people • <3.5 m² covered floor area per person
Insufficient water, sanitation and hygiene	Increased transmissibility of faecal-oral diseases (mostly), vector-borne, airborne and droplet diseases	Does the population have inadequate access to water, sanitation and hygiene (e.g. soap, health promotion)? Camp settings near unprotected water sources (swamps or vector-breeding sources)?	• <15 l water available per person per day • >20 persons per latrine • <250 g of soap per person per month

While a few quantitative cut-off values (where possible, based on relevant indicators from the Sphere Project resources available at http://www.sphereproject.org/), are suggested in the table, **these are meant for guidance only**. Robust data may not always be available within the timeframe of the risk assessment to determine whether each risk factor is present. The risk assessment should not be delayed while data are obtained.

Therefore, the classification of each risk should primarily be qualitative, guided by judgment, consideration of available evidence, and understanding of the context.

Example

In some regions (e.g. South Asia), malnutrition exhibits a predictably seasonal pattern. Therefore, the period in which the emergency occurs should be considered (e.g. a flood occurring at the outset of the seasonal "hunger gap"), and a high prevalence of malnutrition should be classified as occurring if there is evidence of a deterioration above and beyond expected seasonal trends.

Annex 1 suggests possible sources of pre-emergency data to assess each general risk factor. Given that this framework can apply to diverse types of emergencies, not all general factors will be immediately relevant to all situations.

Task 1b: Produce a grading of risk for VPD due to general factors

Table 4 summarizes what is known about the relevance of each general risk factor to specific VPD irrespective of context and region of the world (i.e. all else being equal). The classification of relevance in Table 4 should be interpreted as follows.

- **High relevance**: Globally, a large proportion of the total disease burden due to the VPD is attributable (whether proximately or distally) to this risk factor. Removing the risk factor would result in a substantial decrease in the burden of this VPD. Obvious examples within this category are: insufficient water, sanitation, hygiene and cholera; high HIV/AIDS burden and tuberculosis; overcrowding and measles.
- **Moderate relevance**: Globally, a moderate proportion of the total disease burden is attributable to this risk factor. Addressing the risk factor is not among the top priorities to control the VPD, but its removal would probably bring about some decrease in burden (e.g. insufficient water, sanitation and hygiene and influenza).
- **Low relevance**: Globally, there is evidence that this risk factor has little or no effect on the burden of the VPD. Removing the risk factor would make a negligible difference to the attributable burden. For example, a high birth rate does not influence the burden of typhoid fever.
- **Unknown relevance:** There is insufficient evidence on the role that this risk factor plays in the global epidemiology of the VPD.

While Table 4 broadly reflects existing evidence, links between some risk factors and disease are tenuous or not yet investigated. In some cases, an attempt was made to grade the relevance using plausibility reasoning. For example, VPDs that are very similar in their interaction with the host and share the same route of transmission were assumed to have a similar link to certain risk factors. Low access to curative or supportive health services is almost always a risk factor for higher CFR, but its relevance was graded here according to the relative impact of treatment.

Contextual factors can heavily modulate these general associations. For example, the relevance of a young population to measles outbreaks would indeed be high in a setting with insufficient vaccination coverage, but less so where coverage is adequate. These factors are considered when assessing specific risk for each VPD (Task 2). The risk assessment is designed to ultimately produce a classification decision for each VPD that balances both general and specific risk factors.

Table 4 Relevance of each general risk factor to each VPD

	High prevalence of malnutrition	High prevalence of chronic diseases	Young population and/or high birth rate	High HIV/ AIDS burden	Low access to curative health services	Over-crowding	Insufficient water, sanitation and hygiene
AIRBORNE-DROPLET							
Diphtheria	Moderate	Low	Low	Unknown	Moderate	High	Low
Hib-disease	Moderate	Low	High	Moderate	High	Moderate	Moderate
Influenza	Unknown	Moderate	High	Moderate	Moderate	High	Unknown
Measles	High	Low	High	Moderate	High	High	Moderate
Meningococcal meningitis	Low	Low	Low	Moderate	High	High	Low
Mumps	Low	Low	High	Low	Low	Moderate	Low
Pertussis	High	Low	High	Low	Moderate	High	Low
Pneumococcal disease	High	High	High	High	High	High	Low
Rubella	Moderate	Low	High	Low	Moderate	Moderate	Low
Tuberculosis (meningitis and disseminated disease)	High	High	Low	High	High	High	Low
Varicella	Moderate	Low	Moderate	High	Low	High	Moderate
FAECAL-ORAL							
Cholera	Moderate	Low	Low	Unknown	High	High	High
Hepatitis A	Unknown	Low	Low[2]	Low	Low	Low	High
Hepatitis E	Unknown	Low	Low	Low	Low	Low	High
Polio	Low	Low	Low	Low	Low	High	High
Rotavirus	Moderate	Low	High	Low	High	Moderate	Low
Typhoid fever	High	Low	Low	Moderate	Moderate	Moderate	High
VECTOR-BORNE							
Japanese encephalitis	Unknown	Low	Moderate	Unknown	Moderate	Low	Moderate
Yellow fever	Moderate	Low	High	Unknown	Low	Low	Moderate
OTHER OR MIXED							
Hepatitis B	Unknown	Low	High	High	Moderate	Moderate	Moderate
HPV (cervical cancer)	Low	Low	Low	High	Low	Low	Low
Rabies	Low	Low	Moderate	Low	High	Low	Moderate
Tetanus[1]	Low	Low	High	Low	High	Low	High

[1] A high birth rate and low access to health services are relevant because they can result in a higher incidence of perinatally transmitted cases.

[2] In fact, in most settings, a young population and/or birth rate actually reduces disease burden, as infection tends to occur earlier in life when it is mostly asymptomatic or results in mild disease.

Determining overall grading of risk

Having graded the relevance of each general risk factor for each of the VPDs being analyzed, it is possible to determine an overall grading of risk for that VPD. To do this, simple categories of "high", "medium" and "low" risk are as follows:

- **high:** if one or more of the general risk factors that are present is highly relevant to the VPD in question, as determined in Table 4;
- **medium:** if none of the general risk factors that are present are highly relevant to the VPD, but at least one is moderately relevant;
- **low:** in all other situations.

Example

In the example of measles, if the emergency includes any of the general factors considered to be highly relevant to its epidemiology (high prevalence of malnutrition, high birth rate, low access to curative/ supportive care services, overcrowding), the general risk level would be "high". If the emergency includes only factors considered to be moderately relevant (high HIV/ AIDS burden or insufficient water, sanitation and hygiene), the general risk level would be "medium". Otherwise, the risk grade would be "low".

3.2.3 TASK 2: GRADE THE LEVEL OF RISK DUE TO FACTORS SPECIFIC TO EACH VPD

In Task 2, risk factors that are specific to VPDs are considered in detail for each VPD. These risk factors are examined separately as they are contextual and apply differently to each individual VPD. Specific factors that may be assessed along with key questions are shown in Table 5. However, not all factors are relevant to each VPD (e.g. climate and season are not known to influence the risk of HPV transmission or disease progression), and the importance of each varies disease-by-disease. For this reason, **VPD-specific worksheets** are provided in Annex 2. These contain guidance on how to grade risk arising from each specific risk factor relevant for the VPD based on the information available.

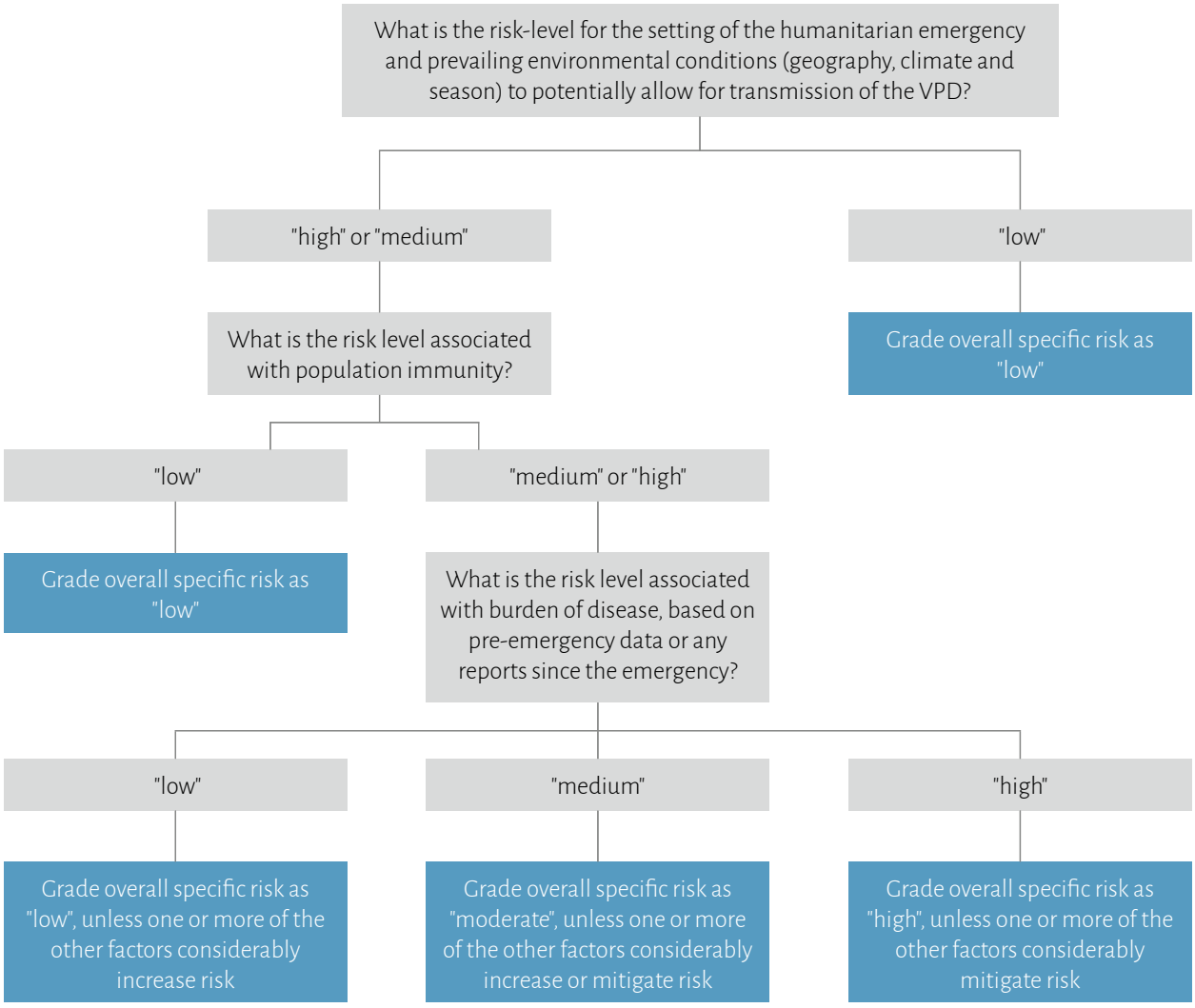
Table 5 Specific factors to be assessed for different VPDs

Factor	Relevance	Key questions to ask	Possible data to consider
Population immunity	Major determinant of individual and community risk of transmission	• Does a significant proportion of the population at risk have no adequate natural or vaccine-induced immunity? • Is the current vaccination coverage likely to afford herd immunity or a high level of individual protection? • Is there a risk of introduction or re-introduction of the VPD in naive or partly naive population?	• Latest vaccination coverage data (both routine and campaign) • Occurrence, size and mortality of past outbreaks in the population
Burden of disease	Indicates the importance of the VPD in the given setting either before or since the emergency	• Is the region within the known transmission boundaries of the VPD? • What is the (proportional) morbidity/mortality attributable to the disease in the country? • Have epidemics previously occurred? • Has an outbreak been confirmed since the emergency begun?	• Occurrence, size and mortality of past outbreaks in the population • Burden of disease estimates • Ongoing disease surveillance • Global disease-risk maps
Geography, climate and season	Certain VPDs only occur in given settlement zones (e.g. Japanese encephalitis mostly, although not exclusively, affects rural areas) or seasons (e.g. meningococcal disease), some carry a higher burden where people are exposed to cold (e.g. Hib disease) or dust and smoke.	• Does the setting where people live favour transmission? • Is the population exposed to cold temperatures? • Is the population exposed to indoor air pollution? • Will the acute emergency unfold during the high-transmission season?	• Climate data • Cooking fuel source
Level of sexual violence	High incidence of sexual violence can result in increased transmission of HPV and hepatitis B.	• Has the emergency resulted in a high incidence of sexual violence?	• Security reports • Hospital data
Incidence of injuries	A large number of untreated injuries entails a high risk of tetanus, particularly among males and if vaccination coverage is low	• Has the emergency resulted in a large number of people with injuries? • Is treatment available and prompt for these injuries?	• Field reports • Evidence from similar emergencies • Hospital data

Each VPD-specific worksheet should be completed as accurately as possible using the available information. An overall grade of "high", "medium" or "low" for the risk arising from specific factors should be determined for the VPD according to its worksheet.

Unlike for general risk, no clear-cut decision rule is suggested, recognizing that the various combinations of the different specific factors constitute too many scenarios to realistically capture in simple classification rules. Instead, a **qualitative** approach is recommended informed by all available evidence and sound, objective judgment. An algorithm to aid this qualitative decision is suggested in Figure 4.

Fig. 4 Algorithm for determining an overall grade of specific risk for a VPD



Examples

Risk assessment for Japanese encephalitis should consider whether the emergency is occurring in an area with known transmission of this virus. For typhoid fever, local evidence of previous outbreaks is an indication of higher risk. In the example of measles, three factors (population immunity, burden of disease, and geography/climate/season) are relevant for consideration. Criteria are provided for each disease based on assumed vaccination coverage, recent outbreaks and seasonality (Annex 2).

3.2.4 TASK 3: ASSESS THE OVERALL RISK OF EACH VPD

Task 3a: Decide whether the VPD should be considered further

Based on the result of Tasks 1 (general risk grading) and 2 (specific risk grading) a classification for each VPD should be reached using Table 2. The classification system should be considered as flexible and careful judgment, supported by all available evidence, should be exercised to occasionally deviate from it while erring on the side of caution when uncertainty precludes a clear decision. Written documentation of the rationale for each classification decision is essential to ensure transparency, buy-in from stakeholders, and for reference.

Task 3b: Characterize the expected risk for VPDs to be considered further

For VPDs that are carried over into the next step of the framework, a brief, qualitative description of the expected risk should be made in terms of the following parameters.

- **Type of threat:** Would excess mortality be mainly due to the endemic pattern of the VPD, to an epidemic, or could a mixture of the two occur? For some diseases this will be clear-cut, for example, in most parts of the world meningococcal meningitis presents mainly as an epidemic threat, while hepatitis A follows a very endemic (i.e. stable) pattern. For many diseases, however, a mix of endemic and epidemic patterns may occur depending on the setting. For example, typhoid fever cases presenting as part of the normal endemic pattern of the disease could experience excess mortality due to malnutrition or reduced access to health care, but a bona fide epidemic of typhoid fever could also occur due to water and sanitation problems.
- **Timeframe:** For each VPD, it should be indicated how quickly excess mortality could manifest itself, and/or the window of opportunity for intervening through preventive vaccination. Some general guidance is as follows.
  - Diseases that manifest in an endemic pattern may cause excess mortality from the very start of an emergency. For example, pneumococcal pneumonia mortality, already high in many countries before an emergency, will immediately increase if the emergency severely curtails access to health care or if nutritional status suddenly deteriorates.
  - An epidemic of faecal-oral, airborne, droplet and/or direct-contact spread diseases can occur as soon as the first two weeks following the onset of an acute emergency, particularly if immune status is low from the very beginning.
  - Provided the vector and pathogen are already present, an epidemic of a vector-borne VPD will usually take a few weeks longer to manifest (about one and a half months at least after the emergency), because of the time taken for vectors to breed and the latency periods of the pathogen in both vectors and humans to reach completion.
  - In protracted emergencies, epidemics of VPDs may become increasingly likely as existing vaccination programmes deteriorate and the pool of susceptible individuals increases, for example, measles or polio.
- **Age-specific burden:** Which age groups would be at the highest risk of infection and/or disease? Would the age range experiencing excess mortality due to the VPD be the same as the typical target age group for vaccination, or would additional age groups probably also experience excess mortality? Would leaving additional age groups unvaccinated cause an unacceptable risk of transmission to a high mortality group?

The disease-specific worksheets provide additional guidance on how to characterize the above parameters.

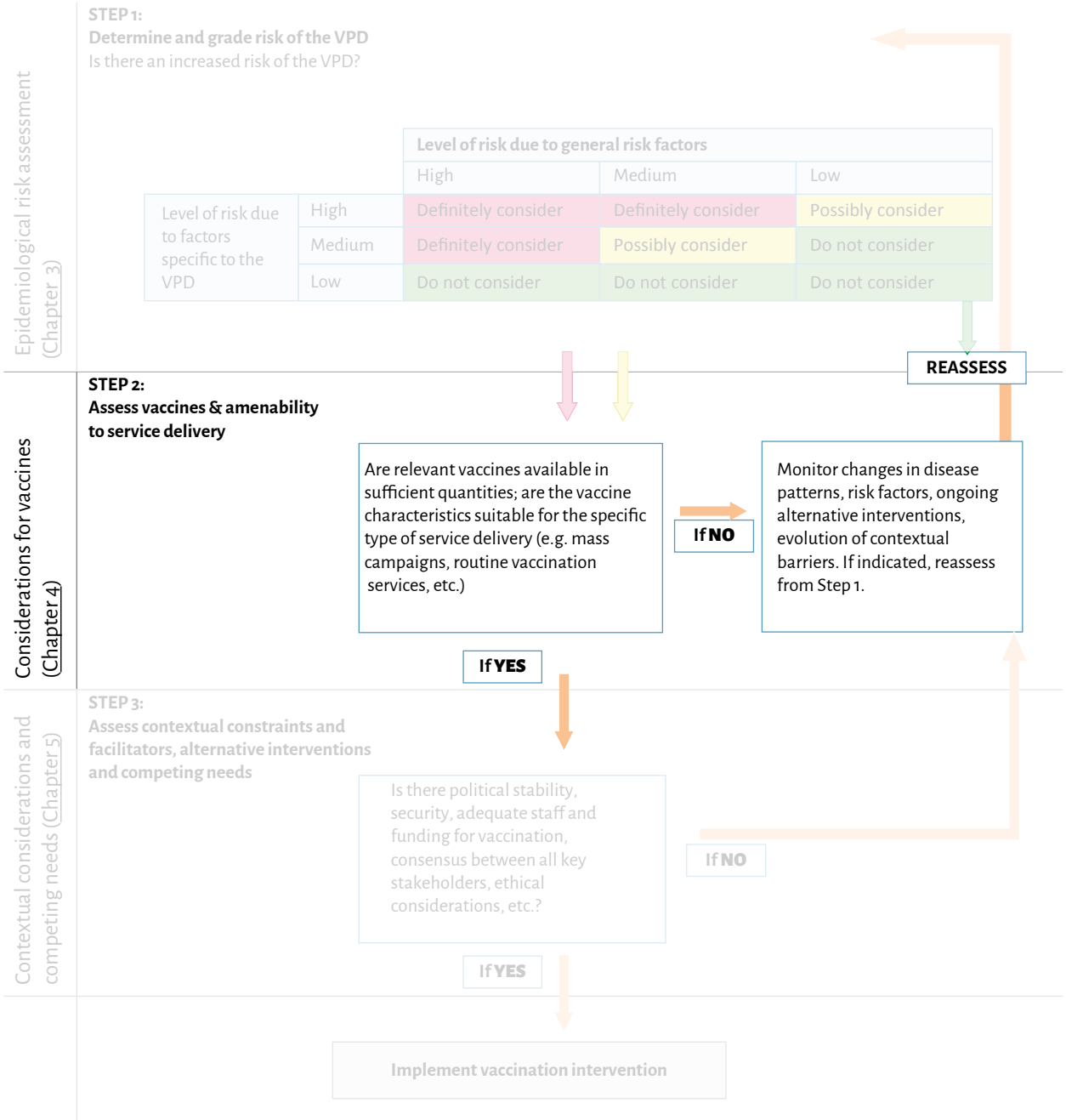
4. Step 2: Considerations for vaccines

In Step 2 you should assess relevant vaccines and their amenability for service delivery for each vaccine-preventable disease classified as definitely or possible to consider for intervention, by analyzing:

1. key vaccine characteristics
2. operational factors to ensure successful vaccination service.

The output of Step 2 is the shortlist of vaccine-preventable diseases for which vaccines are available and which are suitable for the specific type of service delivery.

Fig. 5 Step 2 of decision-making framework on vaccine use in acute humanitarian emergencies



4.1 General considerations

Vaccination poses specific challenges in humanitarian emergencies (e.g. mass vaccinations and/or area difficult to access). Epidemiological risk assessment may result in the recommendation for multiple-antigen campaign. Mass vaccination campaigns involve setting up vaccination sites in traditional or non-traditional health-care locations in order to reach a large number of people over a short period of time. This requires extensive planning and careful consideration of key vaccine and operational characteristics. Each situation is unique and it is impossible to determine one strategy valid for all situations, but common elements concerning vaccines themselves can be examined along with implementation considerations to determine their suitability for service delivery in humanitarian emergencies.

There are several different types of vaccines available, made using different processes. Two basic types of vaccines are live attenuated and inactivated. The characteristics of live and inactivated vaccines are different and they determine how the vaccine is used (see summary in Annex 3).

- Live attenuated vaccines are produced by modifying disease-causing (so-called wild) virus or bacteria in a laboratory. The resulting vaccine organism retains the ability to replicate and produce immunity. Live attenuated vaccines produce immunity in most recipients with one dose, except those administered orally. However, a small percentage of recipients do not develop immunity after the first dose of an injected live vaccine, or rarely, immunity wanes (such as measles, or measles–mumps–rubella vaccines). The second dose is recommended to provide another chance to develop immunity for the individual and high enough level of immunity in the population.
- Inactivated vaccines can be composed of either whole viruses or bacteria, or fractions of either:
  - Fractional vaccines are either protein-based or polysaccharide (carbohydrate) based.
  - Protein-based vaccines include toxoids (inactivated bacterial toxin) and subunit or subvirion products.
  - Most polysaccharide-based vaccines are composed of pure cell wall polysaccharide from bacteria.
  - Conjugate polysaccharide vaccines contain polysaccharide that is chemically linked to a protein. This linkage makes the polysaccharide a more potent vaccine.

These vaccines cannot cause disease from infection, even in an immunodeficient individual. Protection from a live, attenuated vaccine typically outlasts those provided by a killed or inactivated vaccine.

Live and inactivated vaccines both have advantages and disadvantages (see Table 6) that need to be considered in the decision-making process.

Table 6 Key advantages and disadvantages of live and inactivated vaccines

Type of vaccine	Advantages	Disadvantages
Live attenuated	• It does not cause infection as it contains modified/weakened live microbe. • Elicits strong cellular and antibody response and often confers long-lasting immunity with one or two doses.	• Careful assessment is required before administration of attenuated vaccines to individuals with impaired immunity such as those on chemotherapy or with HIV infection, or are pregnant. • Antibody from any source (e.g. transplacental) can interfere with replication of the vaccine organism and lead to poor or no response to the vaccine (also known as vaccine failure). • Live attenuated vaccines are sensitive and can be damaged or destroyed by heat and light. They must be handled and stored carefully. • Need to be refrigerated to stay potent.
Inactivated	• Can be easily stored and transported in a freeze-dried form.	• With a few exceptions, stimulate a weaker immune response than live vaccines. • Need several doses or periodic booster shots to maintain a person's immunity.

4.2 Vaccine characteristics

Vaccine characteristics are outlined in this section along with key definitions to help in assessing suitability for implementation. They are outlined in Table 7.

Table 7 Vaccine characteristics, definitions, and key questions

Characteristics	Definitions	Key questions
Availability	Assessment of vaccine supply and ability to procure vaccine(s).	• Is the supply of vaccines sufficient or can the vaccine be procured? • In case of vaccine supply constraints for certain vaccines, can a fractional dose be used?
Efficacy/effectiveness at full, less than full course, and at fractional dose use	Protection and duration of immunity assuming entire course is given. Efficacy of vaccine at less than full course. Protection and duration of immunity using a fractional vaccine dose.	• Of how many doses does the full schedule consist? • What is the time interval between doses? • Is the vaccine suitable for use in humanitarian emergency settings? • What is the efficacy at less than full course? • Is the level of protection optimal in particular with relation to the envisaged delivery strategy (particularly if mass campaigns are envisioned and/or necessary)? • What is the efficacy/effectiveness of a fractional vaccine dose?
Safety and inclusion/ exclusion criteria	WHO prequalification. Vaccines that are prequalified have an assurance of safety. Groups or ages for which the vaccine is contraindicated (e.g. children aged under one year, pregnant women or women of child-bearing age, immunocompromised). For pregnant or women of child-bearing age determination needs to be made based on the specifics of the humanitarian emergency and include factors such as the mortality in pregnant women and their fetus due to the disease versus the potential risk of the vaccine.	• Who should not be vaccinated due to safety concerns? • Is the vaccine WHO prequalified or licensed by a recognized regulatory authority (e.g. EMA) or NRA of a well-regulated country? • Should pregnant women be vaccinated after balancing the risks and benefits?
Administration schedule	Schedule of administration and age (e.g. the first dose at age 9 months and the second dose at 12 months of age or above).	• How many doses does the full course require? • What is the time interval between the doses? • Is the schedule feasible and/or adjustable (e.g. measles vaccine given at an earlier age in an outbreak setting) for a humanitarian emergency-affected population?
Composition and formulation	Combination vaccine (several active components – antigens included) Lyophilized, liquid formulation	• Is it a combination vaccine? • Is it a lyophilized vaccine? • Is it a liquid vaccine[1]?
Presentation and packaging	Single or multi-dose presentation (vial/ampoule, prefilled injection device, vial size) and volume (e.g. glass multi-dose vial at 11 cm^3).	• Is it a single or multi-dose presentation? • What is the volume?
Stability	Time during which a vaccine can be exposed to ambient temperature (e.g. one month at 37°C, outside labelled storage conditions). Vaccine vial monitors (VVM)[14 15] should be used as a guide.	• Can the vaccine withstand ambient temperature, outside labelled conditions, for a prolonged period of time?

Characteristics	Definitions	Key questions
Storage and cold chain	Temperature and conditions of storage (e.g. 2–8ºC in a dark room).	• Is cold-chain capacity for storage adequate and functional? • If not present, is there capacity to install cold-chain equipment in the affected area?
Cost	See V3P platform[16], UNICEF vaccine price data, PAHO revolving fund or Gavi listed prices for Gavi eligible countries.	• Is there adequate funding for procurement of vaccines and for vaccination implementation?

4.2.1 AVAILABILITY

Vaccine supply should ideally be regularly monitored to facilitate the assessment at the onset of a potential crisis. Manufacturers have different capacities for supply of vaccine and the lead time needed for the vaccine to be produced and delivered should be taken into account in the decision-making process. The shelf-life of the vaccine (i.e. time before the vaccine expires or can no longer be considered protective under ideal conditions) may play an important role in insecure contexts. This applies to situations where service delivery needs to be delayed or may occur in a "stop–start" manner, with the target population receiving vaccination at irregular intervals over a long period of time. If a vaccine is to be incorporated into an intervention, it is important to note the shelf-life by vaccine lots to be able to ensure delivery before expiration date. There are advantages to the use of vaccines in a country's routine immunization programme: the vaccine may already be present in the country and, health-care workers' and the populations' familiarity with the antigen can facilitate acceptance and implementation. The same is true for vaccines for seasonal diseases, such as meningococcal meningitis, where countries may have prior experience in conducting campaigns. Vaccines which are not in the routine immunization programme, such as oral cholera vaccines, may necessitate a different approach in terms of procurement and community acceptance. For more detail on vaccine procurement see Chapter 2.4, Table 7, and the Implementation Guide.

4.2.2 VACCINE EFFICACY AND EFFECTIVENESS (FULL OR PARTIAL COURSE)

Vaccine efficacy in preventing disease in the vaccinated population is obtained from controlled studies, where immunization is delivered under ideal conditions. Efficacy may vary depending on age, nutritional status, co-infections and other factors. Programmatic factors such as errors in vaccine storage, preparation or administration, which can affect the vaccine efficacy, may occur in the field. As a result, the efficacy of some vaccines is lower in "real world" than in clinical trial settings. Vaccine effectiveness is a different concept which describes how the vaccine reduces disease in a target population under programmatic conditions. Vaccine effectiveness is usually lower than vaccine efficacy.

Vaccine efficacy is determined by the number of doses of a recommended schedule or course of a vaccine that are administered. With population movements, or erratic access to populations due to security or logistic constraints, it may not be possible or realistic to deliver the full course of a recommended vaccine.

The decision to use a vaccine needs to consider known information about vaccine efficacy at full course and best available information about vaccine efficacy at less than the full course balanced against the potential benefits of vaccination for the target population. Delivery of less than a full-recommended course should be documented. It is important to note that, although additional vaccine doses may be administered (e.g. three doses instead of two in an individual with prior vaccination but undocumented vaccination status),

[14] WHO (2002). Getting started with vaccine vial monitors. Geneva: World Health Organization (WHO/V&B/02.35; http://apps.who.int/iris/bitstream/10665/67806/1/WHO_V-B_02.35_eng.pdf?ua=1, accessed 7 November 2016).

[15] For information on open vial guidance see WHO (2014). WHO Policy Statement: Multi-dose Vial Policy (MDVD). Geneva: World Health Organization (WHO/IVB/14.07; http://apps.who.int/iris/bitstream/10665/135972/1/WHO_IVB_14.07_eng.pdf?ua=1, accessed 7 November 2016).

[16] Vaccine Product, Price and Procurement (V3P) Web Platform [website]. Geneva: World Health Organization (http://www.who.int/immunization/programmes_systems/procurement/v3p/platform/en/, accessed 7 November 2016).

the effects of overdosing are minimal or absent. Further, it is important to determine if different possible schedules than the ones used in the routine programme exist for each specific antigen which would be better suited to accommodate the circumstances of the emergency (e.g. one dose under the age of one year and a booster dose later in life).

At times, administration of a smaller dose of a vaccine may be a solution to mitigate vaccine shortages. This measure, known as fractional dosing or dose sparing, is generally used in outbreak or emergency settings and only under certain circumstances proposed for routine immunization. Examples include the administration of a fractional dose of meningococcal vaccine[17], yellow fever vaccine[18], and inactivated poliovirus vaccine[19].

4.2.3 ADMINISTRATION

When multiple injectable vaccines are administered as part of the same intervention, separate syringes and different injection sites should be used. All inactivated vaccines can be administered concurrently. Live vaccines may also be administered concurrently but, if they are not administered at the same time an interval of at least four weeks should be allowed to ensure that a sufficient immune response is mounted without interference. The exception to this rule is OPV which may be given with other live vaccines and repeated at a shorter time interval (see Annex 3). When several doses of vaccine are required, similar vaccines produced by different manufacturers may be used interchangeably while considering differences in specified number of doses or contraindications.

4.2.4 TIME UNTIL PROTECTION

The time until protection is the time needed (days, weeks or months) for a vaccine (full or partial course) to induce the immune response that can be considered protective or partially protective. In addition, host-related factors such as age, pregnancy and any immune system-related disorders may alter the immune response and the time until protection.

Live vaccines require only one or two doses to elicit a protective response. The protection is generally considered to be conferred within a two-week window.

Few inactivated vaccines induce high and sustained responses after a single dose, even in healthy young adults. Inactivated vaccines usually require at least two doses, spaced three to four weeks apart. This means that there may be a delay of four weeks or longer from first vaccine dose to confer protection. Individuals who previously received one or more doses of the same vaccine need a shorter time to confer protective immunity (between 4–7 days). Table 7 provides definitions of vaccine characteristics and key questions to ask when appraising time until protection. Characteristics for each vaccine are summarized in Annex 3.

4.2.5 SAFETY

Vaccine safety is assessed in Phase I-III of clinical trials which inform licensure and/or WHO prequalification. Given the limited sample size and follow-up time, these trials may not always capture rare adverse events and events with long time to onset which may arise from post-licensure studies and surveillance data. Vaccines being considered should meet international standards of quality and safety and preferably have obtained WHO prequalification. However, under certain circumstances, non-prequalified vaccines may be approved

[17] WHO (2007). Use of fractional doses of meningococcal polysaccharide vaccines for the control of epidemic meningococcal disease in Africa in a context of vaccine shortage. Report of an Advisory Group of Experts. (http://www.who.int/immunization/sage/3._MEN_PS_control_menin_Africa.pdf, accessed 17 January 2017).

[18] WHO (2016). Fractional dose yellow fever vaccine as a dose-sparing option for outbreak response. WHO Secretariat information paper. (WHO/YF/SAGE/16.1; http://www.who.int/immunization/sage/meetings/2016/october/3_Fractional_dose_secretariat_report_full_version.pdf?ua=1, accessed 17 January 2017).

[19] Fractional dose IPV [website]. Geneva: World Health Organization (http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/inactivated_polio_vaccine/fractional_dose/en/, accessed 17 January 2017).

for use in a specific country. The decision to use such vaccines is a difficult and delicate one which necessitates expert advice. Information on safety needs to be assessed carefully, weighing the risks against the benefits of the vaccine. The risk-benefit ratio may vary among situations but, in emergencies, where morbidity and mortality is high, the expected benefits may far outweigh the risk of adverse events.

4.2.6 COMPOSITION AND FORMULATION

The formulation of the vaccine should be considered when assessing logistics, transportation and storage needs and the need for trained staff.

Vaccines are formulated with ingredients (additives or preservatives, sometimes adjuvants – commonly called excipients) that ensure the quality and potency of the vaccine over its shelf-life. Vaccines are usually formulated as liquids, but may be freeze-dried (lyophilized) and require reconstitution prior to administration. Preservatives may be added during the manufacturing process to prevent microbial contamination and in the final formulation to ensure sterility of the vaccine over the period of its shelf-life. Preservatives may be used to prevent contamination of multi-dose presentations. Most freeze-dried vaccines do not contain preservatives and after reconstitution, if not used, should be discarded within the recommended time.

Vaccines may contain more than one antigen. The administration of a combination vaccine should be considered to minimize the number of injections.

4.2.7 PRESENTATION AND PACKAGING

Vaccine presentation needs to be assessed when deciding on vaccines to use in emergency situations. It affects the needs for necessary storage and the staff needed for the intervention delivery. Table 7 provides definitions and key questions for this assessment.

4.2.8 STABILITY

Stability is the ability of a vaccine to retain its chemical, physical, microbiological and biological properties within specified limits throughout its shelf life. The VVM is an important means of registering cumulative heat exposure over time and is intended to detect vaccine exposure to different temperatures beyond the recommended ones. Vaccines prequalified and relabelled for extended controlled temperature conditions should be considered. Table 7 provides a definition and key question for this assessment.

4.2.9 STORAGE AND COLD-CHAIN CAPACITY

Cold-chain availability and storage capacity should be assessed, and solutions for adequate storage should be considered in case of a lack of functional cold-chain capacity/storage. Table 7 provides a definition and key question for this assessment.

4.2.10 COST

Adequate funding should be secured to ensure the procurement of the right amount of vaccines and their implementation (by taking into consideration factors that affect the total costs such as target population, strategy to be used, logistics and other operational factors). Allocation of funds should be prioritized according to the highest needs and current pricing should be taken into account. Table 7 provides a definition and key question for this assessment. Further information can be found in the Implementation Guide.

4.3 Implementation considerations

Implementation considerations for service delivery are outlined in this section along with key questions to help in assessing implementations factors. These are summarized in Table 8. Further information including budgeting and operational costs can be found in the Implementation Guide.

Table 8 Vaccination implementation considerations and key questions

Factor	Key questions
Geographical area	• Are there hard-to-reach areas? • Are there any specific geographical features that may impact on vaccination implementation?
Target population	• What is the target age group? • What is the estimated number of people targeted? • Are host communities included? • Is the number of people stable and well defined in a camp setting, or highly unstable with new arrivals and departures? • Are there special high-risk population groups in some areas? • Are there population displacements and/or nomadic populations?
Timing	• Can vaccination be delivered before the population begins to disperse/move on or back to their homes? • Can routine immunization services be maintained or established quickly?
Strategy	• What strategy is most appropriate: fixed, and/or mobile posts, or other?
Planning and logistics	• Are there sufficient and adequate human resources? • Are there sufficient and adequate material resources? • Are adequate and sufficient transportation means along with fuel available?
Social mobilization	• Can the population be adequately sensitized and informed about the importance of vaccination within a reasonable period of time?
Informed consent	• Can the population be well informed and their consent or refusal obtained?
Monitoring and evaluation	• Is there capacity to monitor implementation of the vaccination(s)? • Is there capacity to monitor adverse events following immunization?

4.3.1 GEOGRAPHICAL AREA

High-risk populations may be located in particular areas such as crowded sites or areas with no access to safe water or sanitation. Selection of specific geographic areas for vaccination needs to be balanced with ethical issues. Vaccination in only some geographic areas may create tension among the population and lead to the need to justify why certain groups are deemed eligible for vaccination while others are not.

4.3.2 TARGET POPULATION

Target population estimate should be obtained to determine the number of vaccine doses needed. Target populations vary by antigen, with some necessitating the vaccination of wide age ranges, and others a smaller subset. The target age range for vaccination should be based on the expected age distribution of cases, or if the outbreak has started, on the age profile of early cases. Although some guidance on how to determine target age groups for mass campaigns may be provided in the WHO vaccine position papers[20] e.g. on measles and on meningococcal meningitis , the target age range needs to be adapted based on both the epidemiologic risk and pragmatic issues. When different population figures are available, or the expected age distribution of cases

[20] Vaccine Position Papers. Geneva: World Health Organization (http://www.who.int/immunization/documents/positionpapers/en/, accessed 17 January 2017).

is not known, it is better to overestimate, rather than underestimate the target population for vaccination. This means that the highest number available should be used as a precautionary measure.

4.3.3 TIMING

All vaccination interventions should be implemented as soon as possible, and failure to deliver them on time represents a sub-optimal intervention. However, there may be logistical, political or ethical barriers to delivering all interventions simultaneously (see Chapter 5). In such cases, interventions should be prioritized by urgency (i.e. which interventions are most important to do first). Prioritizing vaccine interventions by urgency should be based on the epidemiological risk assessment (Step 1).

Example

In the example of measles and meningococcal disease, measles vaccine should be delivered immediately, due to the high risk of an epidemic. If the emergency occurs outside of the meningitis season, meningitis vaccination could be postponed until operational concerns are addressed, however in most cases vaccination will be considered an urgent need.

Should the use of this framework identify the need to administer more than one vaccine it is more efficient to deliver all vaccine interventions at the same time, rather than organizing individual campaigns for each antigen. Delivering multiple vaccines requires better organization in terms of campaign logistics and has the important advantage of maximizing the opportunities of delivering vaccine to individuals in one planned intervention.

4.3.4 STRATEGY

There are various strategies for immunization service delivery. Whenever possible, vaccination should remain a prerogative of routine immunization services, although in situations of high risk of outbreaks or high disease mortality, campaigns may more rapidly increase immunization coverage than routine service.

Two main strategies to be considered for vaccine delivery are fixed and mobile vaccination posts.

- **Fixed vaccination posts** can be located at permanent or temporary sites:
  - Permanent vaccination posts – located at permanent health facilities or community health posts. Vaccinations are provided at the facilities for at least the whole day, sometimes at night, for the duration of the campaign. These sites also serve as depots for storage and distribution of vaccine to temporary sites and mobile teams.
  - Temporary vaccination posts – additional outreach posts may be specifically constructed as semi-permanent structures if necessary, or may be located at schools, churches, mosques, bus depots, roadblocks, markets, village squares, etc. Villages and settlements with small populations may also be served through such temporary sites.

Fixed vaccination posts have the advantage that they can be designated in advance (schools, health facilities) or constructed in the form of temporary structures. Fixed posts have additional advantages in terms of providing a secure shelter for vaccination teams and an identifiable location for the population to participate in the intervention.

- **Mobile vaccination posts** or mobile vaccination teams move from community to community reaching population in hard-to-reach areas and/or nomadic populations which may not have access to a fixed vaccination post. The mobile teams set up a mobile vaccination post for the time needed to complete the task (for a few hours) before moving on to the next location. A mobile vaccination team may also vaccinate house-to-house or shelter-to-shelter, meaning that the vaccination teams bring the vaccine in

vaccine carriers and vaccinate individuals where they are located. Reaching hard-to-reach populations is a clear advantage of this strategy, however, additional resources may be needed as the teams can only visit a limited number of locations per day and concerns of security may limit their use.

In most situations, a combination of fixed and mobile vaccination posts is necessary. The appropriate strategy should be determined during the planning stage and may require creative solutions to provide sufficient opportunities for the target population to be reached. In large geographic areas, urban and densely-populated areas may best be served by fixed sites, ensuring that a large portion of the target population can be vaccinated quickly. In a rural area, mobile teams may be more appropriate to reach the target population.

In emergencies, it is essential to consider different, non-traditional places for vaccination. This may mean that sites are open during non-traditional hours and dispersed across the geographic area so that individuals can access a site. A classical programme-based strategy may not be the most appropriate. Opportunities such as vaccination at registration if the emergency entails refugees, or integration with other interventions, such as food distribution, should be considered. It is essential to remember that alternative vaccination strategies used in emergencies need to be carried out quickly and are not a replacement for routine programmes.

For more information on implementation strategies, see the Implementation Guide.

4.3.5 PLANNING AND LOGISTICS

Planning and logistics entail the activities associated with delivering the vaccines to the individuals in need. These include cold-chain storage facilities, adequate and safe transportation of the vaccine from the central store to vaccination posts, size of vaccination teams, planning for vaccination strategy implementation (fixed and/or mobile vaccination post, or other), and include information on how to calculate needs. This planning and logistic exercise should try to provide valid and realistic estimates of the resource needs, based on the target population and the reality on the ground concerning existing and locally available resources, both human and material.

4.3.6 SOCIAL MOBILIZATION

Providing information about upcoming vaccination(s) to target population is essential to ensure successful intervention. Social mobilization may be limited only to word-of-mouth but, when circumstances permit, it should include other formal and informal channels such as media or traditional or religious leaders. Social mobilization also serves to provide the population with important information about the risks and benefits of vaccination.

Social-mobilization activities should be planned to enlist support from the population and include mobilization of support by community and/or religious leaders, civil society organizations or nongovernmental organizations (NGOs) that may be operating in the area, and other informal support networks. Contact with individuals and groups should be made prior to vaccination to assess their views and solicit support to ensure acceptance. Leaders may be assigned specific tasks, which can include provision of human and other resources, and announcing the intervention within their communities both formally and through informal channels. Clear messages need to be designed, tested, and disseminated using suitable methods and activities. These activities will depend on each situation and may include walking though the community, radio messages, publicity by village, group or religious leaders, or town criers. Some countries have successfully utilized mobile-phones to inform and organize communities through the mass dissemination of text messages. Efforts should be tailored to reach underserved populations or special populations. These may include minority groups or marginalized populations, religious communities that may resist public-health interventions, nomadic/migratory groups and refugees and others. More information on social mobilization can be found in the Implementation Guide.

4.3.7 INFORMED CONSENT

Obtaining valid consent from individuals prior to offering medical intervention is an obligation guided by ethical principles (Section 1.4 Core ethical considerations).[21]

Under non-emergency circumstances, informed consent typically involves signed or witnessed affirmation that basic information about the intervention, and its potential risks and benefits are understood, and that the intervention can proceed based on the consent achieved. In some situations, the consent process may be implied (e.g. a parent bringing a child to a vaccination session with the expectation that the child will be immunized).

The nature of consent processes during a humanitarian emergency will often differ from those appropriate in a routine, non-emergency health setting. Given the range of challenging conditions during such emergencies, verbal informed consent – without the use of signed consent documents – may be warranted.

Further, the information provided in a consent process in an emergency context may need to be adapted or streamlined to minimize delays, especially when the health risk is acute. For example, group education prior to vaccination roll-out, or in the waiting space or line, using visual aids and other appropriate media, may assist in providing necessary information in a more time-efficient manner.

Regardless of the format of the consent transaction used in an emergency context, information on risks and benefits of the intervention, and information about the public health context in which it is being recommended (for example, a projected local outbreak of measles based on a regional epidemic) must be communicated to target populations in sufficient depth and with clarity, factoring language, cultural diversity, and varying health literacy levels.

Any questions raised should be adequately and accurately addressed directly by those involved in vaccinating, or referred to others with the requisite expertise. This obligation in the consent process will often involve some delay in launching a specific vaccination campaign, and advance preparations (for example, securing translators who can effectively present the relevant information to a specific target population, and able to effectively interact with medical staff to address questions and concerns) should be undertaken.

Depending on the setting, vaccination can be voluntary or mandated by the government. The refusal of vaccination (or other diagnostic, therapeutic, or preventive measures) is recognized as a right and a rational choice from the perspective of a mentally competent individual. If an individual is unwilling to accept vaccination in a programme proceeding from this guidance, the individual (or groups) should be engaged, wherever possible, in an open and respectful dialogue, paying careful attention to the concerns, perceptions, and situational needs.

These requirements may not always be feasible and should not prevent, or cause delays endangering health, of vaccination programme implementation under this guidance in an emergency setting.

In exceptional situations, there may be legitimate reasons to override an individual's refusal of vaccination implemented under this guidance. While isolation, restrictions of movement and other strategies involving such individuals to protect others from infection or other harm may be considered, this will typically not be practical or even possible in emergencies. Where there is an imminent threat of infectious disease that poses a significant risk of substantial harm to a large number of persons, individual liberties may be justifiably curtailed, and "compulsory vaccination" may be indicated.

Any such vaccination programme curtailing personal liberties must balance competing ethical principles, and countries which impose such actions must respect their obligations under international human rights

[21] Adapted from guidance issued in: Guidance for Managing Ethical Issues in Infectious Disease Outbreaks; Geneva: World Health Organization (2016).

agreements and international humanitarian law[22]. The "Siracusa Principles on the Limitation and Derogation Provisions in the International Covenant on Civil and Political Rights" (the Siracusa Principles)[23] are a widely-accepted framework for evaluating the appropriateness of limiting certain fundamental human rights in emergency situations.

The Siracusa Principles state that: "public health may be invoked as grounds for limiting certain rights allowing a State to take measures dealing with a serious threat to the health of the population or individual members of the population. These measures must be specifically aimed at preventing disease or injury or providing care for the sick and injured." Overall, any restrictions on rights or liberties must be carried out in accordance with the law and in pursuit of a legitimate objective of general interest. In addition, such restrictions must be strictly necessary and there must be no other, less intrusive means available to reach the same objective. Finally, any restrictions must be based on scientific evidence and not imposed in an arbitrary, unreasonable, or discriminatory manner.

In some humanitarian emergencies, relevant state institutions (such as Ministries of Health, etc.) may not be functioning at a level enabling effective and time-sensitive decision making which might invoke the Siracusa Principles. Where this is the case, it may fall to non-state actors – including international agencies, humanitarian NGOs, and others functioning as health clusters or otherwise – to recognize and assess the health threat using this guidance, and to deploy programmes which may involve some form of compulsory vaccination. This area of guidance is not well-developed at this point, and such action should be considered only in the most extraordinary of circumstances.

It is critically important to document the informed consent strategies employed in each vaccination programme implemented under this guidance, especially where the assessment of imminent threats to health or other factors result in decisions to abbreviate, limit or even forgo informed consent processes, or where the vaccination programme includes any form of compulsory vaccination.

The process of decision-making, who exercised authority in that process, and other relevant contextual information, should be captured as completely and as soon as practical. Further, especially where there has been some curtailment of rights or liberties in a vaccination programme, this decision-making information should be communicated to the target population as soon as conditions allow. In short, communication about such decisions to those affected is as much an obligation as striving to conduct robust consent processes and protecting their rights and liberties in principle.

4.3.8 MONITORING AND EVALUATION

Formal documentation of emergency response is often not a part of the standard operating procedure of many emergency organizations. Monitoring is essential to provide feedback on implementation and to identify potential problems and shortcomings. After immunization services have been implemented, evaluation in which successes and failures are documented is a critical step. The follow-up phase uses the experience to provide lessons learned and identify additional needs of the target population.

Monitoring keeps track of intervention progress and also provides an opportunity to adjust plans if needed. This includes both quantitative and qualitative aspects of campaigns.

- The quantitative component of monitoring ensures that careful tallying and recording of doses administered, vials utilized, doses wasted, plus reviewing of the number of doses administered against the expected-to-be-delivered is carried out on a daily basis. Monitoring of adverse events following

[22] Resolution UNGA 217 A (III). Universal Declaration of Human Rights. Paris 10 December 1948. (http://www.ohchr.org/EN/UDHR/Documents/UDHR_Translations/eng.pdf, accessed 17 January 2017).

[23] International Commission of Jurists. Siracusa Principles. Siracusa 1984. (http://icj.wpengine.netdna-cdn.com/wp-content/uploads/1984/07/Siracusa-principles-ICCPR-legal-submission-1985-eng.pdf, accessed 17 January 2017).

immunization should be conducted whenever feasible, ideally not by those who implemented the intervention.

- The qualitative component addresses observation of vaccination teams in action, with specific emphasis on the cold chain and handling of vaccines, and safe injection practices.

More information on monitoring and evaluation can be found in the Implementation Guide.

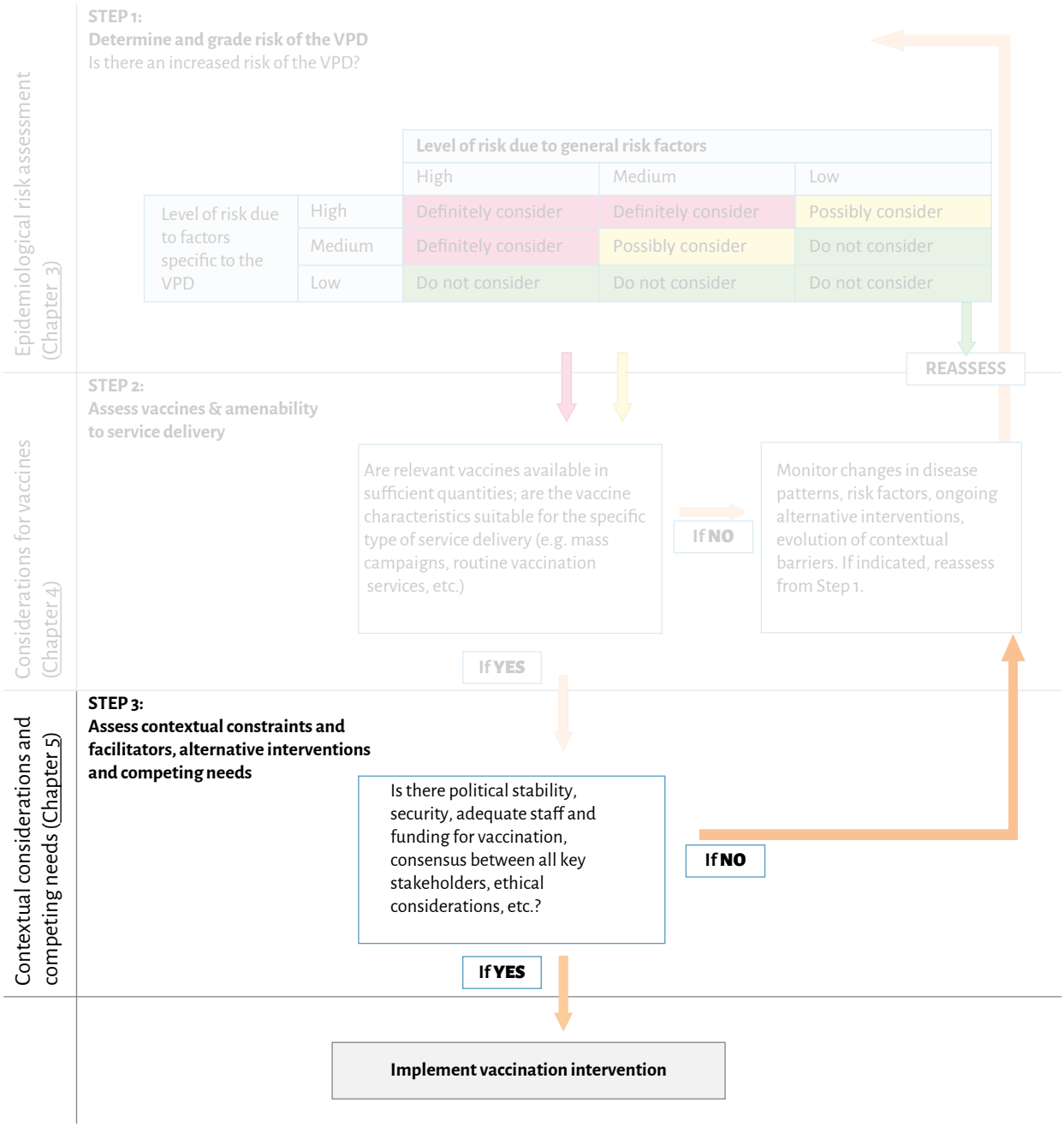
5. Step 3: Contextual considerations and competing needs

In Step 3 you should complete the decision-making framework by assessing contextual factors in which the emergency is developing through analyzing:

- ethical considerations
- political considerations
- security concerns
- economic, logistic and other constraints.

The output of Step 3 is a final determination on implementation of the vaccination intervention for each selected vaccine-preventable disease.

Fig. 6 Step 3 of decision-making framework on vaccine use in acute humanitarian emergencies



5.1 Overview of the assessment of contextual considerations

The final decision on whether to include a vaccination intervention in an emergency response will be influenced both by the political and social context in which the emergency is unfolding, and by ethical considerations, all to be assessed in Step 3. Like the preceding steps, this one does not provide definitive answers, but it does suggest that decision-makers need to consider a broad array of evidence from non-vaccine areas of the health sector, and from other areas as well, in order to reach a decision that will result in the best possible outcome for the emergency-affected population.

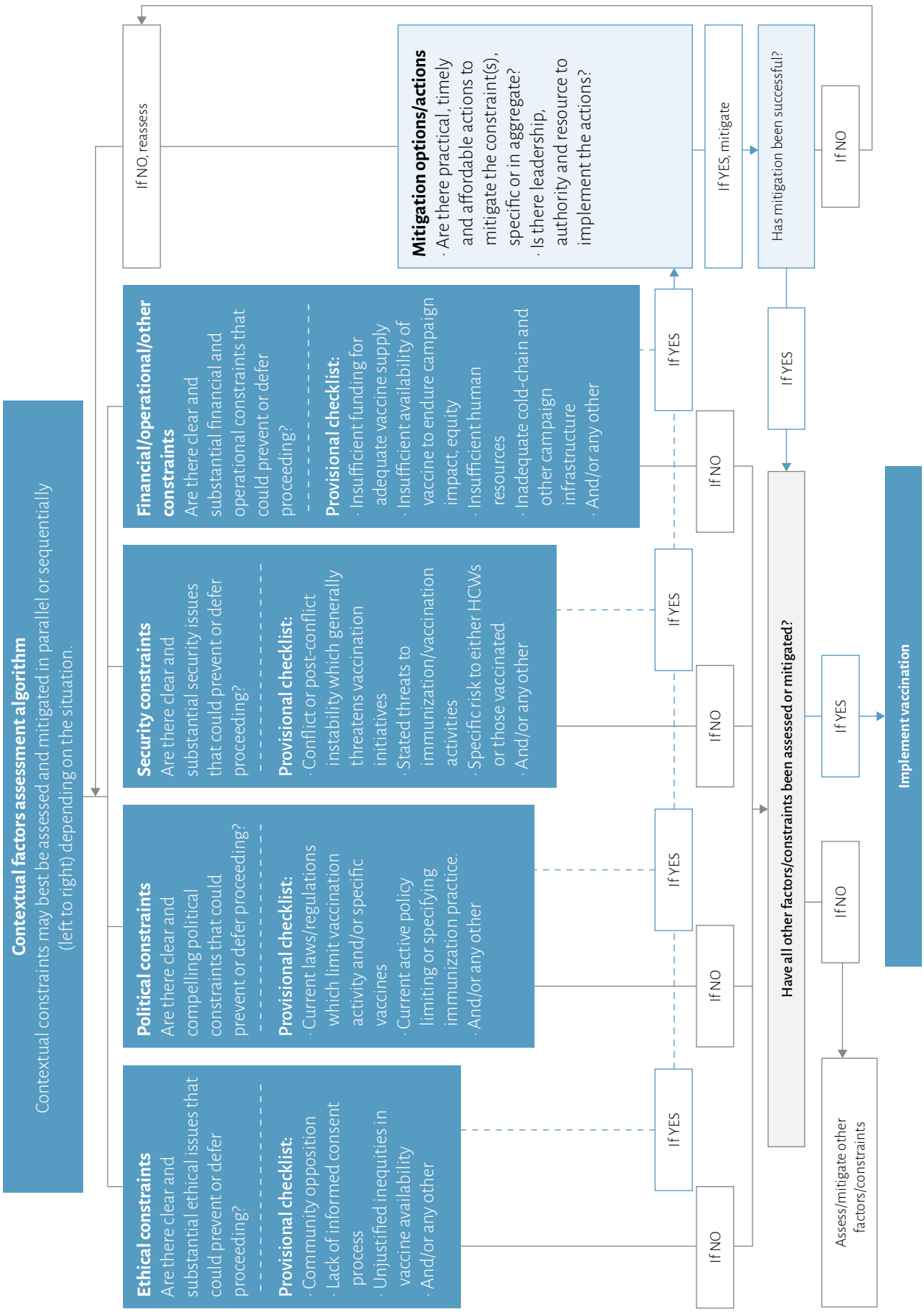
Specific contextual factors that should be examined include:

- ethical considerations
- political considerations
- security concerns
- human resources availability
- financial considerations
- alternative and competing interventions
- size of target population
- add-on interventions.

Every emergency setting is unique and what applies in one will not necessarily be appropriate to another. Any one of the contextual factors and competing needs may be debated by decision-makers to approve or defer immediate action, or decline vaccination intervention altogether. Such deferral or decline could relate to a specific vaccine or could function as a "blanket decision" about immunization in general. It is therefore particularly important to document decisions where immunization is clearly indicated, as a result of Steps 1 and 2 but deferred or declined at Step 3.

If changes in contextual factors result in a suspension or cessation of an intervention already underway, these instances and the supporting evidence driving decision making should be documented. Overall, such documentation will be critical to further refinement of the framework, and should, therefore, be shared transparently with the humanitarian and public-health community. Figure 7 provides the algorithm for assessment of contextual factors.

Fig. 7 Contextual factors assessment algorithm in acute humanitarian emergencies



5.2 Ethical considerations – practical application

The application of ethical principles (for core ethical principles see Chapter 1.4) should be informed by evidence as far as it is available. For example, in determining whether a particular action contributes to utility, decision-makers should be guided by any available scientific evidence about the action's expected benefits and harms. The more intrusive the proposed action, the greater the need for robust evidence that what is being proposed is likely to achieve its desired aim. When specific evidence is not available, decisions should be based on reasoned, substantive arguments and informed by evidence from analogous situations, to the extent possible.

Community engagement is emerging as a practical application of many of these core ethical considerations, both in health interventions such as vaccination in humanitarian crises as well in research about such interventions.

The Sphere Project (http://www.sphereproject.org/), along with the Core Humanitarian Standard on Quality and Accountability (CHS) Alliance (https://www.corehumanitarianstandard.org/the-standard) and Groupe urgence, rehabilitation, développement (URD, http://www.urd.org/), encourage the involvement of beneficiaries in the planning and implementation of aid programmes, codes of conduct for responding agencies, technical standards, and the use of performance indicators and impact assessments.

Example

Some of the core ethical principals' relevance to acute humanitarian emergencies is provided below.

1. **The ethical principle of non-maleficence (avoiding or minimizing harm)**. In acute humanitarian emergencies, this principle means that the potential risks of proven vaccines, however minor and unlikely, should be reduced to the lowest amount possible and monitored. Potential harms should be considered in relation to the likely benefits for individuals who may be directly protected against specific diseases, and the likely benefit to un-immunized others who may be protected by 'herd immunity'.
2. **The ethical principle of beneficence (doing good)**. In acute humanitarian emergencies, this principle means that effective vaccinations against disease threats should be available to those at risk. In addition, the rule of rescue also applies ("the imperative that people feel to rescue identifiable individuals facing avoidable death"[24]). How beneficence is applied depends on the severity of consequences if nothing is done, the ability to prevent such severe consequences, and any sacrifice required by the responding individual or agency.
3. **The ethical principle of distributive justice (fair allocation)**. In acute humanitarian emergencies, this principle means that limited vaccines be allocated as fairly as possible (given that information may be imperfect), and in a non-discriminatory way. For example, vaccine may be allocated to groups who are most at risk of infection, or most at risk of transmission.
4. **The ethical principle of procedural justice (transparent and accountable decision making)**. In acute humanitarian emergencies, this principle means that decisions about the vaccine programme (planning, implementation) be made transparently and with the participation of affected communities and potential beneficiaries. Decision-makers should document their decision-making process, including how ethical principles impacted their decisions to proceed with, defer on, decline, or suspend a vaccination intervention.
5. **The ethical principle of respect for autonomy.** In acute humanitarian emergencies, this principle means that efforts should be made to facilitate an informed decision on accepting a vaccination, bearing in mind the urgency of the threat, and decision-making vulnerabilities (such as presence of several distractions, the potential low literacy levels of vaccine-recipients, amongst others).

[24] McKie J, Richardson J. (2003). The Rule of Rescue. Social Science & Medicine 56(12):2407–2419

Ethical considerations also underpin much of the discussion around political, security, financial and other contextual factors, although they may not be overtly identified as "ethical" per se.

For example, in humanitarian emergencies, there are frequently resource limitations, including of qualified personnel (e.g. programme managers, drivers) for whom various programs may compete. In such emergencies, health authorities also experience shortages of qualified personnel who can provide care to the sick or wounded.

- Decision-makers must consider whether such personnel are best deployed toward a vaccination campaign versus other life-saving interventions. Decision-makers should consider the need to achieve maximal benefits in terms of aggregate wellbeing, i.e. achieving "the greatest good for the greatest number", along with other considerations. This ethical principle is certainly broadly accepted in many cultural contexts, but may not be the most relevant or compelling factor in final decision making.
- Vaccine program organizers should liaise closely with national and sub-national health authorities from whom many skilled personnel are recruited.
- They should support health authorities to enable difficult choices about allocation of scarce personnel to preventive versus curative and care measures.

Immunization decisions which may be supported after completing Steps 1 and 2 of the framework may still be burdened by significant ethical challenges. When that occurs, strategies to resolve or mitigate those challenges should be identified and undertaken by decision-makers before proceeding with, or in orderly parallel to, vaccination campaigns. Without specific action to successfully resolve ethical challenges, the vaccination decision process can be considered to have "failed" Step 3 contextual consideration. If mitigating actions to address such ethical challenges in parallel with a campaign are unsuccessful, then a specific decision to suspend vaccination activity at a predefined milestone should be engaged.

Furthermore, this framework anticipates that, in some emergency situations, decision-makers on the ground will encounter vigorous assertions that the duty of care and rule of rescue (beneficence) should outweigh all other contextual considerations and competing needs and that vaccination campaigns should proceed. While such advocacy is understandable and, indeed, informs humanitarian response at its most fundamental level, this framework recognizes that other contextual factors must and will play a crucial role in decision making.

5.3 Political considerations

Many emergencies are associated with highly charged, unstable political conditions. Tensions may exist between a ruling government and parts of its population, or between local authorities and the international relief community, or between any other combination of actors, making both the delivery and the acceptance of humanitarian assistance of any kind problematic due to suspicion and mistrust. In these circumstances, vaccination interventions have been politicized and become the subject of contention.

Where relevant, authorities in charge of emergency relief must decide whether to advocate with noncompliant or slow-moving civilian and/or military authorities for proceeding with vaccination when indicated, or to postpone this intervention, at least temporarily, in order to be able to deliver other forms of assistance more rapidly and effectively. Bypassing local authorities, or proceeding without their approval, can lead to significant problems.

Such political problems must be weighed against the benefits lost to those in need of an indicated vaccination intervention. If a decision to vaccinate has moved through Steps 1 and 2, any rejection, postponement, or suspension of indicated immunization action for political considerations should be based on clear evidence that there is clear benefit for those in need, and should be well documented.

5.4 Security concerns

The most serious potential impediment to vaccination is the insecure environment that often characterizes humanitarian emergencies. Violence, or even the threat of violence, can have important adverse consequences for health interventions of any kind but mass vaccination campaigns are especially vulnerable. Experience has shown that large gatherings are desirable targets for those intent on social disruption, especially if the population consists largely of unarmed women and children. In addition, access of the population to organized services can be severely affected if insecurity affects travel and communications. Even where access is possible, the real fear of violence takes a toll on the rate of utilization of available services. People who are concerned for their physical safety may not risk travelling by themselves, or with their children, to places where vaccination is offered. Even if vaccination is offered in as many individual communities as possible, the risk of violence directed toward health workers is real. The probability of delivering high quality vaccination services is clearly higher if security concerns have been adequately addressed. A choice must be made, therefore, between pushing ahead with a vaccination campaign that is entirely justified on public-health grounds or foregoing vaccination until the security situation becomes more stable, whether it is based on a negotiated, temporary truce between warring parties or a longer-term settlement.

This consideration has led some to argue that addressing the security situation in an emergency setting is a higher priority than initiating public-health interventions. Of course, what should specifically be done in any particular setting concerning the relative priorities of action in different sectors, such as protection and health, is entirely dependent on the local context, and only a careful analysis of the local situation by those working closest to it will result in the adoption of the best course-of-action.

5.5 Human resources availability

While political instability and physical insecurity are not prominent features of all emergencies, resource limitations are. The needs of emergency-affected populations may exceed the ability of national, regional, or international relief efforts to deliver appropriate and effective relief in a timely manner. Qualified public-health personnel are consistently in short supply, especially at the onset of an emergency. Programme managers, logisticians, public-health workers, drivers and translators, among others, are all needed for the successful implementation of vaccination programmes. However, these same people with the same skills are also needed for other health and non health-sector interventions that could be of great benefit to the same populations. Deploying them for days or weeks to a vaccination campaign could adversely affect the relief effort and hamper other life-saving interventions, such as health service delivery. The competition between priority programmes for individuals with these qualifications can be fierce. Strong and respected leadership is critical to ensuring that any intervention programme undertaken in an emergency is adequately staffed in order to maximize its chances of succeeding. It requires close collaboration with national and sub-national health authorities, as in most cases, qualified health workers and supervisors required for campaigns are recruited from the existing national health-system.

Utilitarian considerations require that allocation decisions achieve maximal benefits in terms of aggregate wellbeing, i.e. achieving "the greatest good for the greatest number"; although, in some situations, this principle may not be a prime factor for various reasons.

5.6 Financial considerations

As with other interventions, financing of any vaccination programme must be assured prior to implementation. Nevertheless, the distribution of funds between the many priorities that need to be met

during an emergency is a serious concern. Different mechanisms exist for procuring necessary funding — through the Central Emergency Response Fund or in response to the Consolidated Appeals Process of the United Nations Office for the Coordination of Humanitarian Affairs, or through the grants of regional or bilateral donors. All of these are competitive mechanisms and even though some VPDs are widely recognized as among as the highest of priorities for vaccination, the case for vaccination must be made when applying to each of these mechanisms.(this is true even though vaccination against, at least, some VPDs is widely recognized as among the highest of priorities). In some cases, when emergency campaigns overlap with planned or delayed development/elimination or preventive/control campaigns. In such cases, it is necessary to be clear about the urgency of vaccinating areas, which are either at high risk, or are experiencing confirmed outbreaks. This is important, in order to avoid delays due to confusion over whether or not a particular campaign should be funded from emergency or development budgets, and who the appropriate implementing partners might be.

5.7 Alternative and competing interventions to vaccination

Concerning competition between interventions, there is no algorithm that can determine the relative value of one intervention versus another and no mathematical formula that can be applied. The balance between the potential benefits and adverse consequences of implementing vaccination services during the acute phase of an emergency, compared to those of other interventions, is specific to each setting. Good judgment, based on a careful and systematic consideration of a variety of contextual and ethical factors, is the key to arriving at an appropriate solution to what might seem to be an intractable problem.

Ultimately, the decision as to whether or not to proceed with a vaccination campaign, should take into account the degree to which vaccination, weighed against other interventions, and assuming that not all interventions can be implemented, will result in reduced morbidity and mortality in the population. In any event, even if delivery of vaccination is delayed, while other interventions in the health sector or in other sectors (such as food distribution, water and sanitation, and shelter) are being implemented, the planning and preparation for a vaccination campaign should still proceed.

Within the health sector, the prioritization of specific services should be carefully considered. The distribution of human and financial resources between activities that provide immediate clinical care to the sick or wounded who are in grave danger of dying or of suffering severe disability, needs to be weighed against the value of preventive interventions such as vaccination, that may not have an immediate visible impact but which, if implemented in a timely manner, may save more lives in the longer term. Health authorities should never have to choose between offering clinical and preventive services — it is obvious that both are necessary to maintain the health of any population. However, emergencies such as those being considered in this framework influence heavily on the health status of a population, and the sad reality is that this choice often has to be made.

Whether the decision to implement one or more vaccination interventions is positive or not, due consideration should always be given to adequate case-management and consideration of water, sanitation and hygiene (WASH).[25]

5.8 Size of target population

The size of the target population for vaccination interventions must also be taken into account. In many emergencies, especially those in which displacement of large populations is a prominent feature, the risk of a VPD affecting the host population may be increased. Furthermore, especially where international emergency

[25] Water, Sanitation and Hygiene [website]. UNICEF. (https://www.unicef.org/wash/, accessed 6 December 2016).

relief is provided, the level of services, including vaccination, available to the emergency-affected population may, in fact, surpass that which is available on a routine basis to the surrounding communities. This can result in heightened tensions in the area and can, at times, complicate the relief effort. For these reasons, it has become standard practice to try to include these communities in health interventions. Doing so means resources must also be devoted to those not directly affected by the emergency, perhaps at the expense of providing more services to the affected population. The epidemiological, ethical and political consequences of this decision are additional context-specific factors that must also be taken into consideration.

5.9 Add-on interventions

In many cases, the vaccination intervention may also be used as a vehicle to add on other distributions, be it another vaccine, or other drugs and commodities such as vitamin A, soap, jerry cans, shovels, mosquito nets, blankets, etc. The demand for certain products and interventions for the target population needs to be assessed and be given due consideration. In instances where for example nutrition is the utmost priority for a population, this needs to be addressed in conjunction with the delivery of immunization services. Nevertheless, depending on the context, the addition of each additional item to vaccination delivery should be approached cautiously, as the risk of overwhelming limited human and logistical resources is real. Of course, specific situations may argue that add-on interventions may be both justified and the most practical means to ensure that indicated interventions actually reach the targeted populations in a timely manner.

5.10 Research

The acute emergency setting presents a unique opportunity to conduct research that can be extremely beneficial in providing a better understanding of the health and humanitarian consequences of emergencies, in establishing the safest and most effective health interventions, and in evaluating service-delivery models for specific disaster settings. The decision to conduct research may only be considered when it would not impact the emergency response and should not have any effect on decision-making process regarding vaccination intervention. With this in mind, collection of data should be done whenever possible and feasible in as systematic way as possible so it can be used retrospectively to answer operational research questions. Ideally, those doing the research should not be the same as those providing care to the people affected by the emergency. It is imperative that medical care and service delivery take precedence over research in resource-limited settings during an acute humanitarian emergency.

A local research ethics committee should verify that care needs are being met before personnel are permitted to conduct research. Consideration should be given to developing regional or international ethical review boards to assist where there is no appropriate local expertise. Research should obtain the permission of key gatekeepers, such as community leaders, where possible, and where possible the input of affected groups should be obtained. In countries where research governance structures are not functioning, researchers must use credible international ethics review boards.

The principle of justice dictates that communities which carry the burden of research must stand to benefit. Research protocols should be relevant and methodologically sound, and should make explicit the benefits or potential harms for participants. Potential risks and burdens to participants should be sufficiently minimized and sufficiently offset by the value of the knowledge to be gained. They should also contain clear plans for returning results to participants, recognizing that they may relocate in the months following the humanitarian crisis.

ANNEX 1. Sources of information for the risk assessment

1a General guidance

In many emergency scenarios, reliable field data needed to quantify the parameters of the risk assessment (e.g. the burden of a given disease, the prevalence of acute malnutrition, the number of litres of water per person per day) will be missing during the time frame of the initial risk assessment. Some assumptions will need to be made about what is happening on the ground, supplemented by knowledge of the typical profile of given typologies of emergency. **The risk assessment should not be delayed until sufficient field data become available to accurately answer each question as this could take weeks or months.** You should, however, be prepared to update the risk assessment later if new data warrant a revision.

Risk assessment should, nonetheless, be carried out in close contact with field agencies. Any available information, including personal impressions of experienced field staff, situation reports and rapid assessments, should be sought and reviewed to "ground-truth" any assumptions made.

In many situations, only national data may be available, while only a specific region or population group may be affected by the emergency. If specific information on the emergency-affected population is not easily obtained, plausible assumptions may need to be made based on available information on the extent to which the emergency-affected population is likely to differ from the national average in terms of all the factors considered. For example, if the affected population clearly has lower socioeconomic status than the national average, an appropriate adjustment should be made to the expected occurrence of risk factors.

1b Sources of information to assess general risk factors

In addition to direct contact with agencies present on the ground, which may be facilitated by the Health Cluster, Nutrition Cluster, WASH Cluster, or other coordinating bodies, useful published information and assessments will typically be found on one of the main humanitarian information portals, such as ReliefWeb (http://reliefweb.int/) and AlertNet (http://www.reuters.com/subjects/AlertNet).

Table A1.1 provides other suggested sources that can be consulted when assessing the presence of general risk factors.

Table A1.1 Suggested sources of information on the occurrence of key general risk factors

Risk factor	Suggested sources
High prevalence of malnutrition	• For baseline levels of malnutrition prevalence, see latest Demographic and Health Survey (DHS) and/or Multiple Indicator Cluster Survey (MICS) results (http://dhsprogram.com/What-We-Do/Survey-Types/DHS.cfm, https://www.unicef.org/statistics/index_24302.html, accessed January 2017), more recent, site specific data may be found in the Complex emergency database (CE-DAT) and United Nations National Influenza Centres (UN NICS) databases (http://www.cedat.be/, https://www.unscn.org/,accessed January 2017) • Food security information may be available from surveillance systems that cover the region, e.g. Famine early warning systems (FEWS) (https://www.fews.net/, accessed January 2017) • Information on food access and nutritional intake since the emergency may be found in assessments published since the emergency, e.g. by the UN World Food Programme (http://www.wfp.org/, accessed January 2017)
Young population and/or high birth rate	• UN World Population Prospects (https://esa.un.org/unpd/wpp/, accessed January 2017)
High HIV/AIDS burden	• Prevalence estimates may be found on the Joint United Nations Programme on HIV/AIDS (UNAIDS) website (http://www.unaids.org/en/regionscountries/countries, accessed January 2017) • HAART coverage figures may be found on the WHO website (http://www.who.int/hiv/data/en/, accessed January 2017) • Information on disruption to curative health services may be taken as a proxy of disruption to HAART access
Low access to curative health services	• Health Resources Availability Mapping System (HeRAMS) assessment reports, if available (http://www.who.int/hac/herams/en/, accessed January 2017) • Initial rapid assessments, Health Cluster situation reports, damage reports and anecdotal information from the ground, if available
Overcrowding	• Initial rapid assessments, if available • Satellite imagery of the camp or the city, if available (e.g. https://www.unitar.org/unosat/maps, accessed January 2017)
Insufficient water, sanitation and hygiene	• For baseline information, see latest census, DHS and/or MICS results (http://dhsprogram.com/What-We-Do/Survey-Types/DHS.cfm, https://www.unicef.org/statistics/index_24302.html accessed January 2017) • Initial rapid assessments and anecdotal information from the ground, if available

1c Sources of information to assess VPD-specific risk factors

As suggested in Table A1.1, most of the information on specific risk factors will be found in any available rapid assessments or ground reports from agencies.

Information on **vaccination coverage** may be found in the most recent DHS or MICS survey reports, as well as in site-specific surveys reported on in the Complex Emergency (CE-DAT) database (http://www.cedat.be/) . In some countries the Ministry of Health also maintains online information on administrative vaccination coverage (i.e. derived from health-facility reports or the *Health management information system*). Obtaining the most up-to-date information for each vaccine used in the country, however, is paramount before undertaking the risk assessment. This will usually be readily available from the Ministry of Health and the country WHO and UNICEF offices, and from the WHO online database (http://apps.who.int/immunization_monitoring/globalsummary). Unfortunately, in many countries survey-based estimates are not up-to-date and may not reflect recent developments (e.g. deteriorations or improvements in routine vaccination, mass campaigns such as Child Health Days or Supplementary Immunization Activities). When survey estimates are out-of-date (e.g. not reflecting the situation in the last two years, or obtained before implementation of immunization services), they should be adjusted by considering the following:

- any information regarding coverage;
- evidence of recent changes in the performance of the routine vaccination programme, e.g. reduced funding levels, disruption due to insecurity, cold chain problems, etc.

Information on burden of disease requires a somewhat more sophisticated and VPD- specific analysis. In high-resource settings disease surveillance is nearly exhaustive, and fairly reliable incidence and mortality data for each VPD are usually publicly available on the internet, for example, from a country's national public health agency website. However, in most of the world this is currently not the case. For some diseases information is likely to be so sparse that proxy variables need to be considered instead, including vaccine coverage itself.

One or more of the following types of sources should be consulted for each VPD.

1. **Surveillance and epidemic reports**

Nearly all countries have a surveillance system designed to detect and respond to outbreaks, although the coverage and effectiveness of such systems may be limited. It is always useful to review information generated by such systems to gain an overview of which epidemic-prone VPDs have been observed most frequently in the past, and how large any outbreaks associated with these diseases have been. This may not be publically available, but can be obtained by contacting Ministries of Health or the WHO regional office. Any surveillance or Early Warning Alert and Response Network (EWARN) system established since the emergency may also have detected an ongoing outbreak.

Reports of past or ongoing epidemics in the country should also be identified, e.g. by consulting the archives of ProMED-mail (http://www.promedmail.org/) and WHO Disease Outbreak News (http://www.who.int/csr/don/en/), searching the internet through a standard search engine, and consulting scientific abstracts (https://www.ncbi.nlm.nih.gov/pubmed).

Information from disease surveillance and previous outbreak reports should be interpreted with caution. Evidence of high burden due to a given VPD (e.g. repeated outbreaks of measles during the past few years) is useful, but absence of evidence does not necessarily mean low burden, mainly for the following two reasons:

i. These sources tend to focus on epidemic-prone threats and may not be designed to quantify the risk of VPDs that usually manifest in a more endemic pattern (e.g. pneumococcal and Hib disease, other childhood cluster diseases).

ii. Some diseases (rotavirus, pertussis and seasonal influenza in particular) are hard to detect, even if they occur in an epidemic fashion, due to their non-specific presentation and challenges in laboratory confirmation in many low-resource settings. Thus, they may be subject to severe under-reporting.

2. **Burden of disease estimates**

This data are particularly useful for diseases that exhibit a fairly stable, endemic incidence pattern. More information on disease burden can be found in the WHO Global Health Estimates (http://www.who.int/healthinfo/global_burden_disease/en/) and the Global Burden of Disease (GBD) estimates (http://www.healthdata.org/GBD).

3. **Proxy variables**

For certain childhood cluster diseases that have an endemic as well as epidemic pattern, burden is often severely underestimated by surveillance (see above), but is reasonably well predicted by the child mortality ratio (i.e. probability of dying before reaching age five years per 1000 live births). As the above VPDs (pneumococcal and Hib disease as well as rotavirus-related diarrhoea) account for a majority of post-neonatal deaths under five years worldwide, a high child mortality ratio (e.g. > 100 deaths per 1000 live births) indicates that their burden should be assumed to be high, unless there is strong evidence to the contrary (e.g. a very high routine vaccine coverage or very reliable surveillance data).

Table A1.2 suggests which sources of information, if applicable, should be consulted to review the burden of each VPD in settings where national surveillance cannot be fully relied upon.

Table A1.2 Suggested sources of information to assess local burden of disease attributable to given VPDs

Disease	Surveillance and epidemic reports	Burden of disease estimates	Proxy variables	Other specific sources	Additional factors to consider
Cholera	X				
Diphtheria	X	X			
Hepatitis A		X			Regions with highest transmission have the lowest burden, as infection is acquired early in life when the disease is mostly mild.
Hepatitis B		X			
Hepatitis E		X		Within EWARN as acute jaundice syndrome (http://www.who.int/diseasecontrol_emergencies/publications/who_hse_epr_dce_2012.1/en/, accessed January 2017)	History of outbreaks in young adults may be an indicator of HEV endemicity.
Hib-related disease	X	X	X		
HPV-related disease		X			
Influenza (seasonal)	X	X			Seasonality may be less pronounced in the tropics.
Japanese encephalitis	X				Regional, mostly rural disease, see recent risk maps.
Measles	X	X	X	Measles & Rubella Initiative (http://measlesrubellainitiative.org/, accessed January 2017)	Assume low burden at baseline, check local data for high season.
Meningococcal meningitis	X				Epidemic risk highest in the African meningitis belt.
Mumps	X		X		Assume low burden at baseline.
Pertussis	X	X	X		Pertussis epidemics generally indicate the tip of the iceberg.
Pneumococcal disease	X	X	X		
Polio	X			Global Polio Eradication Initiative (http://polioeradication.org/, accessed January 2017)	Assume low burden at baseline.
Rabies	X				
Rotavirus	X	X	X		
Rubella			X	Measles & Rubella Initiative, EWARN, national CRS surveillance data if available	Risk of congenital rubella probably higher if the country is not using the vaccine.
Tetanus		X (neonatal)	X (neonatal)	Assume low burden of non-neonatal tetanus at baseline.	

Disease	Surveillance and epidemic reports	Burden of disease estimates	Proxy variables	Other specific sources	Additional factors to consider
Tuberculosis		X		WHO country profiles (http://www.who.int/tb/country/data/profiles/en/, accessed January 2017)	
Typhoid fever	X		X		
Varicella	X	X			Assume low burden at baseline, except in parts of tropics where the disease occurs later in life.
Yellow fever	X			WHO website (http://www.who.int/topics/yellow_fever/en/, accessed January 2017)	Not found in Asia or north of Panama in Central America.

ANNEX 2. Disease-specific risk-assessment worksheets

2a Guidance for going through each worksheet

Although each worksheet differs, the overall procedure for going through each is similar.

- For each factor, the user should first consider whether the criteria suggested for the classification of "high" are met, if not, whether the criteria for the "medium" classification are met, if not, adopt a classification of "low". Thus, the column for "low" risk indicates absence of "high" or "medium" risk level factors, and is therefore the default for all situations not meeting "high" or "medium" risk level criteria.
- Unless otherwise specified, the user is asked to assess whether any of the criteria listed under the "high", "medium" or "low" categories, for any factor, are fulfilled (i.e. based on "and/or" logic). Note that for some criteria, statements are made instead (these are explicitly stated whenever used).
- Having completed the worksheet, the user can refer to the points below as the basis for advancing a summary classification of specific risk. Note that this flowchart (Figure 4 in Section 3.2.3) is to be interpreted qualitatively, and that some recursive logic will be needed. For example, having established that the level of population immunity is insufficient in the second level of the flowchart, it may be necessary to reconsider its contribution to overall risk when coming up with the overall grading after the third node.

Note also the following specific points.

- The criteria suggested to classify the level of risk due to population immunity are, as per all other criteria in these worksheets, arbitrary. As such, they may occasionally be superseded by best judgment and special considerations specific to the emergency in question. However, thresholds suggested for the classification of "low" risk broadly reflect existing evidence on what is required to ensure a level of immunity sufficient to likely confer either herd (community) protection or a high level of individual protection.
- The occurrence of a large outbreak, either current or in the past, is listed in some of the worksheets as a criterion for determining risk level, and a case definition of what constitutes a large outbreak (based on number of cases or deaths) is suggested where appropriate as a rough guide. Judgment should, however, be used to decide whether, in a given setting, an outbreak should be considered large or not (e.g. in a country where surveillance is known to be incomplete, it would be expected that the reported number of cases would be a considerable underestimate of the true number and an exception to the case definition could be made accordingly.
- "N/a" in any risk column indicates "not applicable", i.e. for the VPD and specific factor in question risk should never be classified at that level.
- Sources for all data reported are the latest relevant WHO position papers unless otherwise indicated.

2b Risk-assessment worksheets

Table A2. 1 Cholera disease-specific risk factors[1]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• Widespread flooding resulting in potential large-scale contamination of water supply with excreta, dry weather, difficult access to health care or poor health care infrastructure (i.e. CFR in the affected area(s)>1%, area(s) with slums or refugees/ IDP settlements, area(s) with important population movements (border, market hub, etc.), high population density in the affected area(s), and poor access to water, sanitation, and hygiene (WaSH).	• The population lives alongside and gets water from a large body of water (river, estuary, lake). • Warm surface water temperatures • Limited flooding	• Minimal contamination of water supply, good water and sanitation infrastructure, and good quality of health care.	
Population immunity	• The population does not experience year-round cholera transmission, and • no vaccination has taken place before, or • a vaccination campaign was conducted >3 years ago.	• A vaccination campaign was conducted ≤3 years ago but there are reasons to believe that there are still individuals at risk (consideration for the quality of the campaign, the vaccine coverage, and any population movements).	• All other situations, i.e. absence of criteria warranting "high" or "medium" classification	Current vaccines afford cumulative protective efficacy of 60% and effectiveness of 80% for at least 2 years and confer strong transmission reduction effects, even at low coverage. Most cholera vaccines require more than one dose and efficacy varies according to doses received.
Burden of disease	• The area has experienced one or more large outbreaks in the past 5 years. • An outbreak is currently ongoing.	• The area has experienced one or more outbreaks in the past 5 years, but none of them were large.	• Non-endemic area with no obvious mechanism of introduction	The area refers to where emergency-affected people are currently living, and could be a city or a district/ region. A large outbreak could consist of >100 cases.

Risk characterization

Type of threat: Epidemic, either in a setting with no prior transmission or superimposed on an endemic pattern of transmission.

[1] WHO (2010).Cholera vaccines. WHO Position Paper. Weekly Epidemiological Record 85(13):117–128 (http://www.who.int/wer/2010/wer8513.pdf?ua=1, accessed 7 November 2016).

Time frame: An outbreak could start within days of the onset of an acute emergency, particularly if sudden environmental change occurs (e.g. due to flooding) or there is mass displacement into a camp with poor or no water infrastructure. Risk would remain high as long as risk factors, particularly overcrowding and insufficient water, sanitation and hygiene, persist. Any outbreak would propagate very quickly in a camp or urban setting (with local peaks within a few days) and diffuse more slowly (peaking within weeks) in a rural setting.

Age-specific burden: All age groups are at risk, however, in a risk setting the death of an adult from acute water diarrhoea should raise alarm.

Table A2.2 Diphtheria disease-specific risk factors[2]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• High transmission in cold seasons	• High transmission season within the next 3–6 months	• Low transmission season	Perennial transmission in tropical countries Transmission increased during cold seasons in temperate countries
Population immunity	• Routine DPT3 coverage for children <1 year old is <50%	• Routine DPT3 coverage for children <1 year old is 50–79%	• Routine DPT3 coverage for children <1 year old is >79%	Herd immunity requires >85% coverage Infection is thought to provide long-lasting, possibly lifelong immunity. Booster doses are needed.
Burden of disease	• The area has experienced one or more large outbreaks in the past 5 years, and/or • An outbreak is currently ongoing	• The area has experienced one or more outbreaks in the past 5 years, but none of them large	• Low endemicity area	In 2014, 7321 cases reported globally CFR can range from <1% to 5–6% (especially in Africa, SE Asia); CFR >10% have occurred in refugee camps

Risk characterization

Type of threat: Diphtheria mainly occurs as sporadic cases or small outbreaks in endemic settings. Most cases are asymptomatic or have a mild clinical course (some fever, and diminished activity and irritability in some children). However, in severe cases, pseudo-membranes form in the throat and may cause airway obstruction. CFR from respiratory diphtheria is 5–10%.

Time frame: The incubation period for diphtheria is typically 1–5 days. Onset is relatively slow and characterized by moderate fever and mild exudative pharyngitis. Communicability is generally <2 weeks and rarely >4 weeks for respiratory diphtheria. Rare chronic cases of diphtheria may transmit for six or more months.

Age-specific burden: Preschool and school-age children are the most commonly affected by respiratory diphtheria in endemic settings. Diphtheria is generally rare both among infants (presumably due to the presence of maternal antibody) and adults as a result of acquired immunity.

[2] WHO (2006). Diphtheria vaccine. WHO Position Paper. Weekly Epidemiological Record 81(3):24–32 (http://www.who.int/wer/2006/wer8103.pdf?ua=1, accessed 7 November 2016).

Table A2.3 Hepatitis A disease-specific risk factors[3]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• Widespread flooding and destruction of sanitary infrastructure	• Limited flooding and damage to sanitary infrastructure	• All other situations	Even within regions of high transmission, seroprevalence may be low due to variable economic development and status of sanitary infrastructure within a country or a sub-region.
Population immunity	• Low transmission areas (see below) • Travel to (humanitarian relief workers) or displacement to high transmission areas (see below)	• Intermediate transmission areas (see below)	• High transmission areas (see below)	Vaccine is not currently used in routine immunization. Recommended as a 2-dose series. Infection is thought to induce lifelong immunity. In high transmission areas, lifetime risk of infection is >90%, occurs mainly in childhood and is asymptomatic; therefore, individual susceptibility, disease severity and thus burden of disease actually increase as transmission decreases.
Burden of disease	• Low transmission areas, such as Australia and New Zealand, Canada, Europe, Japan and the USA with <30% seroprevalence	• Intermediate transmission areas, such as North Africa, South America, Central Asia and the Middle East with 30–70% seroprevalence	• High transmission areas, such as Sub-Saharan Africa, Central America and the Indian sub-continent with >70% seroprevalence	Global burden is 1.4 million cases per year.

Risk characterization

Type of threat: Not epidemic prone except in areas with low transmission rate and vaccine coverage, although time-space clusters of cases could occur following poor hygienic and sanitary conditions in acute humanitarian emergencies. The estimated case-fatality ratio of hepatitis A varies with age and ranges from 0.1% among children <15 years of age to 0.3% among persons 15–39 years of age, and 2.1% among adults aged ≥40 years. No chronic infection is known to occur. Disease severity generally increases with age, but complete recovery without recurrence is the rule.

Timeframe: The average incubation period is around 14-28 days (up to 50 days). Increase in incidence would mirror access to inadequate water and sanitation facilities in acute humanitarian emergencies in areas with low endemic transmission.

Age-specific burden: Age-specific profiles of anti-hepatitis A virus prevalence and disease incidence are endemicity-dependent. In highly endemic areas, most infections occur in early childhood (<5 years) and are asymptomatic. In intermediate endemicity countries, most cases occur in late childhood and early adulthood. In areas of low endemicity, hepatitis A occurs mainly in adolescents and adults in high-risk groups such as injecting-drug users, men who have sex with men, people travelling to areas of high endemicity, and in isolated populations, such as closed religious communities.

[3] WHO (2012). Hepatitis A vaccines. WHO Position Paper. Weekly Epidemiological Record 87(28-29):261–276 (http://www.who.int/wer/2012/wer8728_29.pdf?ua=1, accessed 7 November 2016).

Table A2.4 Hepatitis B disease-specific factors[4]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Levels of sexual violence**	• High incidence of consultations or hospitalizations for sexual violence-related conditions • Consistent reports of sexual violence being used as a weapon of war or systematically occurring during/after battles and attacks in civilian areas	• Moderate incidence of consultations or hospitalizations for sexual violence-related conditions • Some reports of sexual violence occurring during/after battles and attacks in civilian areas	• Minimal incidence of sexual violence in humanitarian emergency settings	Sexual transmission possible, risk of transmission related to seroprevalence in the adult population
Population immunity	• Routine vaccination coverage for children <1 year old is <80%	• Routine vaccination coverage for children <1 year old is 80–90%	• Routine vaccination coverage for children <1 year old is >90%	Full schedule = birth dose + 2 or 3 doses of Hepatitis B virus (HBV)-containing vaccine
Burden of disease	• Most of Africa, the Amazon Basin, South-east Asia, China, most Pacific Islands • Seroprevalence (HBsAg) > 8%	• Middle East, other parts of Asia • Seroprevalence (HBsAg) 2–7%	• The Americas and Europe	Global burden estimated as 360 million chronic infections and 600 000 deaths per year

Risk characterization

Type of threat: Not epidemic prone, although time-space clusters of infections could occur following mass sexual violence events. Worldwide distribution, but prevalence of infection and patterns of transmission vary greatly by region and by country. The outcome of HBV infection is age-dependent and includes asymptomatic infection, acute hepatitis B, chronic HBV infection, cirrhosis, and hepatocellular carcinoma. Most infections in high prevalence zones are asymptomatic, with very little acute disease, but long-term sequelae. In these areas, most transmission is perinatal or person-to-person in early childhood. Fulminant hepatitis with CFR of 70% develops in 0.1–0.6% of acute hepatitis cases. Five percent of acute infections progress to chronic HBV infection with risk decreasing with age.

Timeframe: Incubation period of 30–180 days. Increases in transmission would mirror patterns in the incidence of sexual violence, but most disease manifestations would occur many years later.

Age-specific burden: Acute hepatitis B occurs in 1% of perinatal infections, 10% of early childhood (1–5 years), and 30% of late infections (people aged >5 years). Chronic hepatitis B infection develops in 80–90% of perinatal infections, 30% of children infected before age six, and <5% of adults.

[4] WHO (2009). Hepatitis B vaccines. WHO position paper. Weekly Epidemiological Record 84(40):405–420 (http://www.who.int/wer/2009/wer8440.pdf?ua=1, accessed 7 November 2016).

Table A2.5 Hepatitis E disease-specific factors[5]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• Widespread flooding and destruction of sanitary infrastructure	• Limited flooding and damage to sanitary infrastructure	• All other situations	Even within regions of high transmission, seroprevalence may be low due to variable economic development and status of sanitary infrastructure within a country or a sub-region.
Population immunity	• Low transmission areas (see below) • Travel to (humanitarian relief workers) or displacement to high transmission areas (see below)	• Intermediate transmission areas (see below)	• High transmission areas (see below)	In 2011, China has produced and licensed the first vaccine to prevent hepatitis E virus infection, although it is not yet available globally.
Burden of disease	• High transmission areas such as Sub-Saharan Africa, Central America and the Indian sub-continent with high seroprevalence	• Intermediate transmission areas, such as North Africa, South America, Central Asia and the Middle East with 30-moderate seroprevalence	• Low transmission areas, such as Australia and New Zealand, Canada, Europe, Japan and the USA with low seroprevalence	A global burden of disease study estimated that hepatitis E genotypes 1 and 2 account for approximately 20.1 million hepatitis E infections, 3.4 million symptomatic cases, 70 000 deaths, and 3000 stillbirths annually.

Risk characterization

Type of threat: Sporadic and epidemic viral hepatitis. Increased risk of outbreaks occurs in poor hygienic and sanitary conditions in acute humanitarian emergencies. In rare cases, acute hepatitis E can result in fulminant hepatitis (acute liver failure) and death, especially among pregnant women. Overall population mortality rates from hepatitis E range from 0.1– 4.0%. Fulminant hepatitis occurs more frequently during pregnancy. Pregnant women are at greater risk of obstetrical complications and mortality from hepatitis E, which can induce a mortality rate of 10–50% among pregnant women in their third trimester. It is an acute disease that never progresses to chronicity.

Time frame: The incubation period following exposure to the hepatitis E virus ranges from 15–60 days, with a mean of 40 days. Increase in incidence would mirror access to inadequate water and sanitation facilities in acute humanitarian emergencies.

Age-specific burden: The hepatitis E virus causes acute sporadic and epidemic viral hepatitis. Symptomatic infection is most common in young adults aged 15–40 years. Although infection is frequent in children, the disease is mostly asymptomatic or causes a very mild illness without jaundice (anicteric) that goes undiagnosed.

[5] WHO (2015). Hepatitis E vaccine. WHO Position Paper. Weekly Epidemiological Record 90(18):185–200 (http://www.who.int/wer/2015/wer9018.pdf?ua=1, accessed 7 November 2016).

Table A2.6 Haemophilus influenzae type b (Hib) disease-specific factors[6]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting Geography, climate and season	• Most households have poor shelter and hygiene , lack of blankets and heating, and – Cold climate, or – High altitude with cold nights, or – Cold/wet season within the next three months.	• A substantial proportion of households have poor shelter and hygiene, lack of blankets and heating, and – Cold climate, or – High altitude with cold nights, or – Cold/wet season within the next three months.	• A substantial proportion of households have good shelter, hygiene and heating • Warm weather	
Population immunity	• Routine vaccination coverage for children 12–59 months old is <50%	• Routine vaccination coverage for children 12–59 months old is 50–79%	• Routine vaccination coverage for children 12–59 months old is >79%	Hib transmission has been shown to decrease to near zero, even at low vaccination coverage.
Burden of disease	• Child mortality ratio pre-emergency ≥100 per 1000 live births • Hib-attributable mortality rate among children 1–59 months old estimated at ≥100 per 100 000.	• Child mortality ratio pre-emergency 25–99 per 1000 live births • Hib-attributable mortality rate among children 1–59 months old estimated at 10–99 per 100 000	• Child mortality ratio pre-emergency <25 per 1000 live births • Hib-attributable mortality rate among children 1– 59 months old is estimated at <10 per 100 000.	Burden of Hib disease has declined significantly after nearly global introduction of Hib-containing vaccines, but local pockets of disease are common.

Risk characterization

Type of threat: Exacerbation of the endemic pattern of Hib disease (which includes pneumonia, meningitis and invasive bacterial disease) due to higher transmission, greater risk of progression to disease and higher CFR.

Time frame: As soon as the emergency starts, and for as long as emergency conditions persists.

Age-specific burden: Children under two years of age bear the highest burden.

[6] WHO (2013). Haemophilus influenzae type b (Hib) vaccination. WHO Position Paper. Weekly Epidemiological Record 88(39):413–428 (http://www.who.int/wer/2013/wer8839.pdf?ua=1, accessed 7 November 2016).

Table A2.7 Human papilloma virus (HPV) disease-specific factors[7]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting Levels of sexual violence	• High incidence of consultations or hospitalizations for sexual violence-related conditions • Consistent reports of sexual violence being used as a weapon of war or systematically occurring during/after battles and attacks in civilian areas	• Moderate incidence of consultations or hospitalizations for sexual violence-related conditions • Some reports of sexual violence occurring during/after battles and attacks in civilian areas	• Minimal incidence of sexual violence	Overcrowded conditions or armed conflict in acute or protracted humanitarian emergencies can increase the risk of sexual violence.
Population immunity	• No vaccination programme, or routine vaccination coverage for girls 9–13 years <50%	• Routine vaccination coverage for girls 9–13 years 50–79%	• Routine vaccination coverage for girls 9–13 years >79%	Two doses of HPV vaccine are recommended in girls aged 9–14 years.
Burden of disease	• Highest burden of cervical cancer in the developing world (sub-Saharan Africa, Latin America, south-central and south-East Asia, the Caribbean and Melanesia) due to restricted prevention, early detection and treatment options	• Intermediate burden of cervical cancer in transition economies, including eastern Europe (not all countries may have adequate prevention, early detection and treatment options set in place)	• Low burden of cervical cancer in developed countries with prevention, early detection and treatment options set in place	A large majority (>80%) of cervical cancer cases occur in the less developed regions, where it accounts for almost 12% of all female cancers. 528 000 new cervical cancer cases and 266 000 related deaths per year worldwide in 2012, of which >80% in the developing world.

Risk characterization

Type of threat: Not epidemic prone, may manifest up to 10 years or later in form of cervical cancer among infected women. Time–space distribution of cervical cancer cases may follow patterns of sexual abuse in humanitarian emergencies.

Time frame: In most cases, HPV infections are asymptomatic and clear spontaneously within 1–2 years. The interval between the acquisition of HPV infection and progression to invasive carcinoma is usually about 10 years or longer.

Age-specific burden: HPV prevalence in populations peaks in young women after the onset (<25 years) of sexual debut and gradually decreases with age, although a second lower prevalence plateau at middle-ages. Up to 70% of sexually active young women will acquire infection within the first five years after sexual debut, about half of which are of high-risk genotype. In many developed countries, there is a steady rise in cervical cancer incidence from mid-20s to mid-40s, after which rates become relatively constant. Most cervical cancer cases are diagnosed in women >40 years.

[7] WHO (2014). Human papillomavirus vaccines. WHO Position Paper. Weekly Epidemiological Record 89(43):465–492 (http://www.who.int/wer/2014/wer8943.pdf?ua=1, accessed 7 November 2016).

Table A2.8 Influenza (seasonal) disease-specific factors

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• Within two months of high transmission season	• Within 3–4 months of high transmission season	• Low transmission season	High in winter months of temperate countries All year-round transmission in some tropical countries, with two peaks each year

Risk characterization

Type of threat: Influenza A virus can cause large epidemics with moderate to high mortality. Malnutrition and poor access to health care in acute humanitarian emergencies contribute to higher rates of complications and death. Clinical attack rates during annual epidemics range from 5%–20% and may exceed 20% in crowded camp settings during humanitarian emergencies. The highest CFRs are observed among infants <6 months and the elderly.

Time frame: The average incubation period for influenza is two days (range: 1–4 days). Epidemics or outbreaks typically last 6–8 weeks or longer.

Age-specific burden: Rates of serious disease and complications are highest among children <2 years, adults >64 years, and persons of all ages with certain chronic medical conditions. Pregnant women may also experience increased severity of disease, especially after the first trimester. Over 90% of influenza deaths occur among those aged 65 and older.

Table A2.9 Japanese encephalitis disease-specific factors[8]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting Geography, climate and season	• High season currently or within the next 3 months, and • Rural area, and • Widespread flooding	• High season within the next 3–6 months, and • Rural or peri-urban area, and • Small-scale flooding	• Low transmission season	Primarily in rural agricultural areas, but can occur in peri-urban centres—rare in urban areas. High transmission season is usually April to October in temperate climates; less seasonality in tropical climates but increases with rainy season. Flooding can result in vector proliferation.
Population immunity	• Routine vaccination coverage for at-risk population is <80%, and • SIA done >5 years ago, and • No large epidemic (1000s of cases) within last 5 years	• Routine vaccination coverage among at-risk population is 80–90%, and • SIA done 2–5 years ago, and • No large epidemic (1000s of cases) within last 5 years	• Routine vaccination coverage among at-risk population is >90% • Large epidemic within last 5 years affecting same population • SIA within last 2 years with coverage >80%	
Burden of disease	• South-East Asia, parts of China • Endemic area with known large epidemics within past 10 years • Annual incidence • 5–10+/100 000 within the susceptible age-range (typically those <14 years of age) • Evidence of ongoing outbreak	• East Asia (parts of China, Japan, Republic of Korea), northern Australia • Endemic area with known outbreaks (100s of cases) • Annual incidence of 3-5/100 000 within the susceptible age-range (typically those <14 years of age)	• Africa, the Americas, South Asia, Europe and the Middle East; urban settings. Annual incidence of <3/100 000 within the susceptible age-range (typically those <14 years of age)	Global burden of disease is estimated at 67 900 cases, with approximately 13 600 to 20 400 deaths.

Risk characterization

Type of threat: Hyper-endemic outbreaks in endemic areas (e.g. South-East Asia, Indonesia). Seasonal epidemics can be explosive with thousands of cases over a period of several months. About 1 in 250–500 infected individuals manifest clinical disease; of those with clinical disease, the CFR is 20%–30% and another 30% of the surviving patients experience severe sequelae. Outbreaks have occurred in several previously non-endemic regions.

Time frame: The incubation period is 4–14 days. Outbreaks can occur 1–2 months after a trigger event (e.g. flooding).

Age-specific burden: The vast majority of cases are <15 years old in endemic areas and <10 years in hyper-endemic areas. In areas with high routine JE vaccination coverage (VC), incidence declines and cases shift to older children and adults. Children <5 years old experience the highest morbidity and CFR, but in naive populations all age groups may be at risk.

[8] WHO (2015). Japanese Encephalitis Vaccines. WHO Position Paper. Weekly Epidemiological Record 90(9):69–88 (http://www.who.int/wer/2015/wer9009.pdf?ua=1, accessed 7 November 2016).

Table A2.10 Measles disease-specific factors[9]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting Geography, climate and season	• Sub-Saharan Africa • South and South-East Asia • High transmission season occurring currently or within the next 3 months	• High transmission season within the next 3–6 months	• Low transmission season • The Americas, Europe and the Middle East	Likely that seasonal climate patterns influence population density that, in turn, increases the transmission of measles. Strongest seasonal effect is in the Sahel, where cases peak in the dry season as people congregate in villages and towns. In other parts of Africa, cases peak in the cool rainy season. Local experts should be consulted on local seasonal changes.
Population immunity	• Routine vaccination coverage for children <18 months is <70%	• Routine vaccination coverage for children <18 months is 70–89%	• Routine vaccination coverage for children <18 months is >95% and routine immunization can be maintained.	Reaching all children with 2 doses of measles-containing vaccine should be the standard for all national immunization programmes. Infection is thought to provide long-lasting/lifelong immunity. Acute malnutrition and vitamin A deficiency increases measles mortality. Case management is very important in an outbreak.
Burden of disease	• The area has experienced one or more large outbreaks in the past 3 years, and/or • An outbreak is currently ongoing	• The area has experienced one or more outbreaks in the past 5 years, but none of them large	• The country has achieved elimination status	A large outbreak could consist of >100 cases or >10 deaths. Global burden estimated at 20 million cases/year; 114 900 measles deaths globally in 2014. CFR can range from <1% to 5–6% (higher in Africa, SE Asia); CFR >10% have occurred in refugee camps.

Risk characterization

Type of threat: Epidemics occur in population groups where the number of susceptibles becomes higher than the number of the birth cohort. Measles outbreaks can result in many deaths in unvaccinated individuals, especially among young, malnourished children. The risk of death is greatly reduced in people who are vaccinated; therefore, in areas with high vaccination coverage, the risk of death is also lower as most cases are in vaccinated individuals.

Time frame: Incubation period of 10–14 days. Measles is highly infectious. Outbreaks can occur rapidly (<1 month) in crowded settings with a high proportion of non-immune population.

Age-specific burden: Children <5 years are especially vulnerable; children 5–14 generally have lower rates of complications or death but should also be vaccinated. The risk of complications and death increases with age beginning around 15 years, and recent epidemics have featured considerable transmission in young adults, warranting consideration of these age groups for vaccination. Special efforts may be needed to mobilize older children and adolescents for vaccination.

[9] WHO (2017). Measles vaccines. WHO Position Paper. Weekly Epidemiological Record 17(92):205–228 (http://apps.who.int/iris/bitstream/10665/255149/1/WER9217.pdf?ua=1, accessed 8 May 2017).

Table A2.11 Meningococcal meningitis disease-specific factors[10]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• High transmission season occurring currently or within the next 2 months	• High transmission season within the next 3–4 months	• Low transmission season	Incidence is highest in dry season in the tropics especially in the meningitis belt; spring and winter seasons in temperate countries.
Population immunity	• Conjugate vaccine not in EPI programme or EPI VC <80%, and • SIA conjugate vaccine VC within the past 3 years <80%, and • No large outbreaks in the last 3 years	• VC of conjugate vaccine 80–89% through EPI or SIA in last 3 years	• VC of conjugate vaccine >89% through EPI	Meningococcal vaccines against all available serotypes should be considered. MenA conjugate vaccine[11] usually provided through SIA for age 9 months to 18 years (up to 29 years) followed by inclusion in EPI.
Burden of disease	• The area has experienced one or more large outbreaks in the past 5 years • An outbreak is currently ongoing • Incidence >10 cases/100 000 population	• The area has experienced one or more outbreaks in the past 5 years, but none of them large • Incidence 2–10 cases/100 000 population	• Non-endemic area	High burden in meningitis belt of Africa (26 countries): rates of sporadic infection 1–20 cases/100 000 and up to 1000 cases/100 000 during epidemics.

Risk characterization

Type of threat: Group A meningococcus is associated with large-scale epidemics, particularly in the 'meningitis belt' in sub-Saharan Africa, with regular epidemics every 8–12 years, observed incidence rates exceeding 1 000 cases per 100 000 and CFRs of 10–15%. Group B and W135 disease is more commonly observed in developed countries.

Time frame: Incubation period is typically 3–4 days (range: 2–10 days). Outbreaks of Group A can develop within two weeks among susceptible populations.

Age-specific burden: Infants (3–12 months) have the highest risk of meningococcal disease. Incidence rates decrease after infancy and then increase in adolescence and young adulthood. During epidemics, however, rates may rise in older children and young adults.

[10] WHO (2011). Meningococcal vaccines. WHO Position Paper. Weekly Epidemiological Record 86(47):521–540 (http://www.who.int/wer/2011/wer8647.pdf?ua=1, accessed 7 November 2016).

[11] WHO (2015). Meningococcal A conjugate vaccine: updated guidance. Weekly Epidemiological Record 90(8):57–62 (http://www.who.int/wer/2015/wer9008.pdf?ua=1, accessed 7 November 2016).

Table A2.12 Mumps disease-specific factors[12]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• n/a (see medium risk level)	• High transmission season occurring currently or within the next 3 months in temperate countries	• Low transmission season in temperate zones	Perennial transmission in tropical climates; in temperate zones, cases peak in late winter to early spring.
Population immunity	• Routine vaccination coverage for children <18 months old is <50%, and • No large outbreaks in the last 3 years	• Routine vaccination coverage for children <18 months old is 50–79%, and • No large outbreaks in the last 3 years	• Routine vaccination coverage for children <18 months old is ≥80%	Two doses of mumps-containing vaccine (MMR) is recommended in countries with a well-established, effective childhood vaccination programme, with the capacity to maintain high level vaccination coverage with measles and rubella vaccination, and where the reduction of mumps incidence is a public health priority. Infection is thought to provide long-lasting, possibly lifelong immunity. A large outbreak could feature > 100 cases.
Burden of disease	• n/a (see medium risk level)	• High child mortality ratio (≥100 deaths per 1000 live births) • The area has experienced one or more large outbreaks in the past 5 years • An outbreak is currently ongoing	• Very low incidence of the disease in the area	Annual incidence of mumps in the absence of vaccination is in the range of 100–1000 cases/100 000 population, with epidemic peaks every 2–5 years in most parts of the world. CFR is low (0.01%), but permanent sequelae, including paralysis, seizures, cranial nerve palsies and hydrocephalus can occur.

Risk characterization

Type of threat: Mostly an endemic disease, epidemics can occur but with low CFR.

Time frame: An outbreak could start within days or weeks after the onset of an acute emergency, in a situation of overcrowding. The incubation time averages 16–18 days (range: 12–25 days).

Age-specific burden: Mumps is predominantly a childhood disease, with peak incidence varying globally, but typically at 5–9 years. Mumps can also affect non-vaccinated adolescents and adults, in whom complications (including meningitis and orchitis) are more common.

[12] WHO (2007). Mumps virus vaccines. WHO Position Paper. Weekly Epidemiological Record 82(7):50–60 (http://www.who.int/wer/2007/wer8207.pdf?ua=1, accessed 7 November 2016).

Table A2.13 Pertussis disease-specific factors[13]

Factor	Risk level			Comments
	High	Medium	Low	
Population immunity	• Routine vaccination coverage for children <1 year old is <50%	• Routine vaccination coverage for children <1 year old is 50–79%	• Routine vaccination coverage for children <1 year old is >79%	Full schedule = at least 3 doses of DTwP- or DTaP- containing vaccine (DTP) as recommended in the routine immunization schedule. Natural infection does not confer long-term immunity. A shift in the age distribution of pertussis towards older age groups (adolescents and young adults) has been reported in recent years in some high income countries, in particular where aP vaccines have replaced wP vaccines for primary vaccination series.
Burden of disease	• High child mortality ratio (≥100 deaths per 1 000 live births) • The area has experienced one or more large outbreaks in the past 5 years • An outbreak is currently ongoing	• Moderate child mortality ratio (25–100 per 1 000 live births) • The area has experienced one or more outbreaks in the past 5 years, but none of them large	• Low endemicity area	Ongoing transmission in all countries. In 2013, approximately 63 000 deaths in children under 5 years of age from pertussis occurred globally. Naturally, cyclic patterns occur every 3–4 years. Some mainly aP using countries have reported a resurgence of pertussis. A large outbreak could feature >100 cases.

Risk characterization

Type of threat: Epidemic super-imposed onto existing pattern of transmission. An exacerbation of the existing burden could occur even without an epidemic, due to factors that increase the CFR, such as malnutrition and low access to curative health services. Epidemics have been observed in developing as well as in developed countries.

Time frame: An exacerbation of the typical burden of pertussis could occur immediately after the onset of the emergency. An outbreak could also start as soon as days or weeks after the emergency's onset if there is overcrowding, or a few months into the emergency if cohorts of unvaccinated infants accumulate due to disrupted routine vaccination. The typical incubation period for pertussis is 9–10 days (range: 6–20 days).

Age-specific burden: The highest incidence of pertussis is in children aged <5 years, particularly among infants <6 months. CFR in unimmunized children is 3–4% for children <1 year old and 1% for children 1–4 years old. Incidence, morbidity and mortality are higher in females than males. Mortality in populations with high VC is low, usually occurring in infants too young to have received the primary series.

[13] WHO (2015). Pertussis vaccines. WHO Position Paper. Weekly Epidemiological Record 90(35):433–460 (http://www.who.int/wer/2015/wer9035.pdf?ua=1, accessed 7 November 2016).

Table A2.14 Pneumococcal disease-specific factors[14]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• n/a (see medium risk level)	• Most households are exposed to outside temperatures due to poor shelter, lack of blankets, lack of heating etc., and – Cold climate, or – High altitude with cold nights, or – Cold/wet season within the next 3 months, or – Most households use fossil fuels	• Optimal shelter • Warm weather	Exposure to cold temperatures or indoor fuel smoke is known to increase the risk of disease progression to pneumonia.
Population immunity	• Routine vaccination coverage for children 12–59 months old is <50%	• Routine vaccination coverage for children 12–59 months old is 50–79%	• Routine vaccination coverage for children 12–59 months old >79%	Full schedule consists of at least 2 doses of pneumococcal conjugate vaccine by 12 months of age
Burden of disease	• Child mortality ratio pre-emergency ≥100 per 1 000 live births • Pneumococcus-attributable mortality rate among children 1–59 months old estimated at ≥100 per 100 000 • Local pneumonia etiology studies showing that vaccine-type pneumococcal serotypes, taken together, are the main causative agent.	• Child mortality ratio pre-emergency 25–99 per 1 000 live births • Pneumococcus-attributable mortality rate among children 1–59 months old estimated at 10–99 per 100 000 • Local pneumonia etiology studies showing that vaccine-type pneumococcal serotypes, taken together, are among the top three causative agents	• Child mortality ratio pre-emergency <25 per 1 000 live births; • Pneumococcus-attributable mortality rate among children 1–59m old estimated at <10 per 100 000	Most pneumococcal mortality is due to pneumonia, with the remainder attributable to meningitis or other invasive manifestations.

Risk characterization

Type of threat: Exacerbation of the endemic pattern of pneumococcal disease (which includes pneumonia, meningitis and invasive bacterial disease), due to higher transmission, greater risk of progression to disease and higher CFR. Overcrowding, malnutrition, insufficient health services, HIV infection and other factors listed above may cause this.

Time frame: As soon as the emergency starts, and for as long as the above risk factors remain highly prevalent.

Age-specific burden: Children under 5 years bear the highest burden. Old people are also at high risk and may partially be protected by pneumococcal polysaccharide vaccine, but this vaccine is only offered in very few, high-income countries. Old people can be protected indirectly by vaccinating children.

[14] WHO (2012). Pneumococcal vaccines. WHO Position Paper. Weekly Epidemiological Record 87(14):129–144 (http://www.who.int/wer/2012/wer8714.pdf?ua=1, accessed 7 November 2016).

Table A2.15 Poliomyelitis disease-specific factors[15]

Factor	Risk level			Comments
	High	Medium	Low	
Population immunity	• Reported routine vaccination coverage for children <23 months old is <80% • In endemic or countries at high risk of outbreaks following importation – The last SIA was done >6 months ago; or in the last 6 months but with VC <80%	• Reported routine vaccination coverage in children <23m is 80–89% • In endemic or countries at high risk of outbreaks following importation – The last SIA was done within the last 6months but with VC <90%	• Routine vaccination coverage in children <23 months is >89%	Many polio-free countries at high risk of outbreaks following virus importation or emergence of circulating vaccine-derived poliovirus also carry out regular SIAs
Burden of disease	• The country experiencing the emergency (or from which refugees have fled) has ongoing virus transmission, i.e. is either endemic for polio or is currently affected by transmission or shares borders with an infected country or area.	• The country experiencing the emergency or from which refugees have moved in, was recently infected (endemic or outbreak-related transmission), but no polio case has been reported for at least 12 months.	• No polio case for at least 3 years, with good surveillance	About <1% of poliovirus infections inchildren <5 years of age, varying with serotype and age results in paralysis. The case-fatality rates among paralytic cases range from 5 to 10% in children and from 15 to 30% in adolescents and adults. Wild poliovirus eradication certified regions are the Americas, European, South-East Asian, and the Western Pacific Regions. All polio-free areas remain at risk as long as any country remains endemic.

Risk characterization

Type of threat: Main threats are: renewed polio outbreaks in polio-free countries; in areas affected by emergencies, and in areas with low performing immunization systems following wild poliovirus importation from infected areas or emergence of circulating vaccine-derived poliovirus. New outbreaks in polio-free countries represent a major setback for the Global Polio Eradication Initiative.

Time frame: Reintroduction and/or a large outbreak could occur within weeks of the emergency's onset. The incubation period is 7–10 days; infectiousness lasts 3–6 weeks.

Age-specific burden: Cases usually occur in children <5 years, with highest burden among those <36 months; however, epidemics affecting adults have recently occurred where virus was imported into populations with past immunity gaps.

[15] WHO (2016). Polio vaccines. WHO Position Paper. Weekly Epidemiological Record 91(12):145–168 (http://www.who.int/wer/2016/wer9112.pdf?ua=1, accessed 7 November 2016).

Table A2.16 Rabies disease-specific factors[16]

Factor	Risk level			Comments
	High	Medium	Low	
Population immunity	No vaccination programme for humans set in place.	No vaccination programme for humans set in place.	Vaccination programme for humans set in place and high vaccination coverage achieved	By 2016, Peru, Philippines and Brazil are currently the only countries which had or have implemented human rabies immunization programmes in specific geographical areas.
Burden of disease	• Endemic regions (Sub-Saharan Africa, Latin America, South- East Asia and the Indian sub-continent) **and** – large number of stray dogs with poor vaccination programmes for canines; – increased number if stray dogs and contact with humans in an humanitarian emergency setting.	• Endemic regions **and** – good vaccination and control programme for stray dogs; – minimal contact between humans and canines in a humanitarian emergency setting.	• Non-endemic regions • Rabies-free country or region	Global burden of disease is estimated at 55 000 deaths, highest case-fatality rate of any illness known, at 99.99%. Although a number of carnivores and bat species serve as natural reservoirs, rabies in dogs is the source of 99% of human infections and poses a potential threat to >3.3 billion people. Vaccination programmes are available for canines and for humans in selected countries. Pre-exposure prophylaxis is available for individuals at increased risk of infection e.g. laboratory worker. Humans should receive post-exposure vaccination. No known immunity to rabies even though not all infected become symptomatic. Rabies can spread to rabies-free countries in regions where the disease is endemic.

Risk characterization

Type of threat: Not epidemic prone but direct body fluid contact with cases can cause disease. The percentage of bitten people developing rabies is highly variable, depending on the bite number/location, on rabies reporting (human and animal) as well as on animal rabies control. Available data indicates that an average of 19% of people bitten by a rabid dog will die without any post-exposure prophylaxis. There is a potential for high mortality in an endemic humanitarian emergency settings if access to proper care is compromised.

Time frame: Excess burden could occur from the very start of the emergency. The incubation period ranges from 7 days to several years, but is less than 60 days in 70% of the cases.

Age-specific burden: Shorter incubation periods and severe disease are commonly seen in children because they are likely to receive multiple, severe wounds of the head, which is richly innervated.

[16] WHO (2010). Rabies vaccines. WHO Position Paper. Weekly Epidemiological Record 85(32):309–320 (http://www.who.int/wer/2010/wer8532.pdf?ua=1, accessed 7 November 2016).

Table A2.17 Rotavirus disease-specific factors[17]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• High season currently or within the next 3 months in temperate climate	• High season within the next 3–6 months in temperate climate	• Low transmission season	In temperate climates, incidence peaks in the winter; in tropical settings, transmission is perennial.
Population immunity	• Routine vaccination coverage for children <1 year old is <50%	• Routine vaccination coverage for children <1 year old is 50–79%	• Routine vaccination coverage for children <1 year old is >79%	Full schedule, 2 or 3 doses dependent on vaccine. Vaccines are not as effective in low income settings. Prior infection does not lead to immunity, but reduces chances of severe disease in subsequent episodes.
Burden of disease	• Child mortality ratio pre-emergency ≥100 per 1 000 live births • Low and middle income countries in Sub-Saharan Africa and South Asia • Annual rotavirus-attributable mortality rate ≥100 deaths per 100 000 children <5 years • ≥15% of <5 year mortality is due to diarrhoea • Ongoing cluster of diarrhoea cases	• Child mortality ratio pre-emergency 25–99 per 1 000 live births • Low and middle income countries in Central and South America, Central Asia, and South-East Asia • Annual rotavirus-attributable mortality rate 50–99 deaths per 100 000 children <5 years • 10–14% of <5 year mortality is due to diarrhoea	• Child mortality ratio pre-emergency <25 per 1 000 live births • High income countries • Annual rotavirus-attributable mortality rate <50 deaths per 100 000 children <5 years • <10% of <5 year mortality is due to diarrhoeal disease	Global burden of disease in 2013, is estimated at approximately 215 000 (215 000–233 000) deaths. There is a wide clinical spectrum from mild to severe diarrhoea, but the first exposure is usually the most severe. Global CFR is <1%, but varies widely by country's development status; >80% of deaths occur in developing countries.

Risk characterization

Type of threat: Exacerbation of endemic disease pattern due to more intense transmission and/or increase in the CFR as a result of malnutrition and low access to health services. Not epidemic prone, but clusters of cases can occur.

Time frame: Excess burden could occur from the very start of the emergency or as soon as the season starts. The incubation period is <48 hours.

Age-specific burden: Severe rotavirus gastroenteritis (and mortality) is primarily limited to children 6–24 months; the initial episode in low-burden, after rotavirus vaccine introduction, the burden shifts to between 2–5 years.

[17] WHO (2013). Rotavirus vaccines. WHO Position Paper. Weekly Epidemiological Record 88(5):49–64 (http://www.who.int/wer/2013/wer8805.pdf?ua=1, accessed 7 November 2016).

Table A2.18 Rubella disease-specific factors[18]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• High season currently or within the next 3 months in temperate climate	• High season within the next 3–6 months in temperate climate	• Low season	In temperate climates, cases peak in late winter/early spring.
Population immunity	• Routine vaccination coverage for children <1 year old is <50%	• Routine vaccination coverage for children <1 year old is 50–79%	• Routine vaccination coverage for children <1 year old is >79%	One dose of rubella-containing vaccine should be given with measles. Good VC is important to avoid shifting the disease to older age-groups when women will be child bearing.
Burden of disease	• n/a (see medium risk level)	• The area has experienced one or more large outbreaks in the past 5 years	• Low transmission area	In the absence of vaccination, rubella occurred worldwide with epidemics every 5–9 years. It has been eliminated from the WHO Region of the Americas. A large outbreak could consist of >100 cases or >1% case fatality rate.

Risk characterization

Type of threat: Rubella is primarily a mild, self-limiting disease with low CFR (1/10 000 cases). Its public–health importance is related to effects on the fetus associated with Congenital Rubella Syndrome (CRS). Approximately 90% of infections in the first trimester of pregnancy result in congenital defects. Increased transmission would result in higher incidence of CRS. Large epidemics with hundreds or thousands of cases can occur, but their extent, ability to diagnosis (many times assumed measles) and periodicity is highly variable.

Time frame: An outbreak or increased transmission could occur within days or weeks of the emergency's onset. The incubation period is 12–23 days (average 14 days).

Age-specific burden: Primarily a childhood disease affecting those <5 years. In settings with high VC, age of susceptibility can increase.

[18] WHO (2011). Rubella vaccines. WHO Position Paper. Weekly Epidemiological Record 86(29):301–316 (http://www.who.int/wer/2011/wer8629.pdf?ua=1, accessed 7 November 2016).

Table A2.19 Tetanus disease-specific factors[19]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Incidence of injuries**	Non-neonatal tetanus: • Reports of a very large number (>10 000) of people with untreated, recently sustained injuries	Non-neonatal tetanus: • Reports of a considerable number (1 000–10 000) of people with untreated, recently sustained injuries	Non-neonatal tetanus: • Reports of a limited number (<1 000) of people with untreated, recently sustained injuries	
Population immunity	Neonatal tetanus: • Routine vaccination coverage <50% among pregnant women • Non-neonatal tetanus: • Routine vaccination coverage <50% VC among infants • Routine vaccination coverage <50% of age-appropriate booster doses among older children and adults	Neonatal tetanus: • Routine vaccination coverage 50–79% among pregnant women • Non-neonatal tetanus: • Routine vaccination coverage 50–79% among infants • Routine vaccination coverage 50–79% of age-appropriate booster doses among older children and adults	Neonatal tetanus: • Routine vaccination coverage >79% among pregnant women • Non-neonatal tetanus: • Routine vaccination coverage >79% among infants • Vaccination coverage >79% of age-appropriate booster doses among older children and adults	Vaccination coverage can be misleading primarily due to non-retention of vaccination cards and failure to record completed doses. As a result, areas that should ideally be classified as low-risk may end up being areas of high risk. Full schedule: All children worldwide should complete 3-dose primary series plus 3-booster doses by adolescence. Pregnant women who have received only 3 doses of DTP in early infancy should receive 2 doses of a TT-containing vaccine with a minimal interval of 4 weeks. Those who received 4 doses of tetanus vaccine during childhood need only 1 booster dose.
Burden of disease	Neonatal tetanus: • Child–mortality ratio pre-emergency ≥1 per 1 000 live births • Non-neonatal tetanus: • n/a	Neonatal tetanus: • Child–mortality ratio pre-emergency 0.1–0.9 per 1 000 live births • Non-neonatal tetanus: • n/a	Neonatal tetanus: • Child–mortality ratio pre-emergency <0.1 per 1 000 live births • Non-neonatal tetanus: • n/a	In 2015, a total 10 301 tetanus cases including 3 551 neonatal tetanus cases were reported. In the absence of medical intervention, the case-fatality rate approaches 100%.[20]

Risk characterization

Type of threat: Not epidemic prone, not a contagious disease. For neonatal tetanus, an exacerbation of the endemic pattern of disease, with more cases and higher CFR, may occur. Any increase in non-neonatal tetanus cases, due to mass injuries, will resemble an epidemic, even though there is no person-to-person transmission and cases will decrease without intervention. A case can be made for the vaccination of specific cohorts such as men involved in flood cleanup or reconstruction work.

Time frame: An increase in neonatal tetanus cases and deaths could occur immediately if there is a sudden disruption in obstetric care and safe births. In places with a well implemented immunization programme, a sudden disruption of antenatal care and obstetric practices is less likely to impact on neonatal tetanus cases. This is because the cohort that is being protected, those from 15-49 years, remain more or less protected during disruptions. It is only those becoming 15 years and joining the cohort that is a source of worry. However, a

[19] WHO (2017). Tetanus vaccines. WHO Position Paper. Weekly Epidemiological Record 6(92):53–76 (http://apps.who.int/iris/bitstream/10665/254582/1/WER9206.pdf?ua=, accessed 8 May 2017).

[20] Roper MH, Vandelaer JH, Gasse FL. (2007). Maternal and neonatal tetanus. Lancet:370(9603):1947–59

more progressive increase could occur if the emergency is protracted and routine vaccination/antenatal care deteriorates over time. The vast majority of non-neonatal cases will present within the first 2–3 weeks after a mass injury event.

Age-specific burden: Neonatal tetanus affects neonates, usually 3–14 days after birth. The largest proportion of non-neonatal cases in developing countries is among male older children and young adults, but the age and gender distribution may vary depending on who is at greatest risk of injuries in an emergency.

Table A2.20 Tuberculosis (meningitis, disseminated disease) disease-specific factors[21]

Factor	Risk level			Comments
	High	Medium	Low	
Population immunity	• Routine vaccination coverage for children <5 years old <50%	• Routine vaccination coverage for children <5 years old 50–79%	• Routine vaccination coverage for children <5 years old >79%	The vaccine should be administered as soon as possible after birth. Vaccination only protects against meningitis and disseminated disease. It does not prevent primary infection and, more importantly, does not prevent reactivation of latent pulmonary infection, the principal source of bacillary spread in the community.
Burden of disease	• n/a (refers only to tuberculosis meningitis and disseminated disease)	• TB period prevalence (all forms) ≥ 200 per 100 000 people (all ages)	• TB period prevalence (all forms) < 200 per 100 000 people (all ages)	Period prevalence of any TB may be considered a proxy of the burden of TB meningitis and disseminated disease in children (the latter condition is difficult to monitor through routine surveillance). TB meningitis and disseminated disease are fairly rare, but severe manifestations and their burden should never be considered high.

Risk characterization

Type of threat: An exacerbation of the endemic pattern of TB meningitis and disseminated disease cases.

Time frame: Excess cases could start occurring a few weeks/months after the emergency's onset if the risk of TB transmission increases straight away due to overcrowding, HIV/AIDS burden, malnutrition and other general risk factors. Generally, most cases of TB meningitis occur within a year of primary infection but, because infection may occur at various times during early life, most excess cases due to high transmission are likely to occur after the acute emergency, as the cohort of neonates that missed their BCG vaccination goes through the childhood years.

Age-specific burden: Mainly children <5 years old in settings with high TB transmission, and mainly adults in settings with low TB transmission. Globally, children account for most of the disease burden.

[21] WHO (2004). BCG Vaccine. WHO Position Paper. Weekly Epidemiological Record 79(4):27–38 (http://www.who.int/wer/2004/en/wer7904.pdf?ua=1, accessed 7 November 2016).

Table A2.21 Typhoid fever disease-specific factors[22]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• Widespread flooding or other event resulting in potential large-scale contamination of water supply and poor sanitary conditions	• Limited flooding or other event resulting in potential large-scale contamination of water supply and poor sanitary conditions	• Access to optimal water and sanitation • No flooding	
Burden of disease	• Endemic regions • The area has experienced one or more large outbreaks in the past 5 years • An outbreak is currently ongoing or not further specified diarrhea, constipation, high-grade fever (≥38°C) lasting 3 or more days, and jaundice outbreaks as proxy for an ongoing outbreak.	• The area has experienced one or more outbreaks in the past 5 years, but none of them large	• High endemicity area	Annual global incidence is 21 million cases. CFR is 1%–4%. Ninety percent of deaths occur in Asia. A large outbreak could consist of >100 cases or >10 deaths.

Risk characterization

Type of threat: Epidemic.

Time frame: An outbreak could occur days or weeks after major disruption to water supplies, and would remain a threat for as long as people are exposed to contaminated water. The incubation period is normally 8–14 days (range: 3–60 days). Around 10% of untreated patients remain infectious for 3 months after symptom onset.

Age-specific burden: Age-specific incidence is variable across different endemic regions and countries. Available epidemiological data suggest that in most endemic countries, there is low incidence in infants <1 year, low incidence in children 2–4 years (although this may be greater in some endemic countries), peak incidence in school-aged children (5–19 years), and low incidence in adults >35 years. CFR is 4% in children aged <5 years versus 0.4% in older children. Although infants may manifest severe clinical forms of typhoid fever, infection in children <2 years old is typically mild and nondescript.

[22] WHO (2008). Typhoid Vaccines. WHO Position Paper. Weekly Epidemiological Record 83(6):49–59 (http://www.who.int/wer/2008/wer8306.pdf?ua=1, accessed 7 November 2016).

Table A2.22 Varicella disease-specific factors[23]

Factor	Risk level			Comments
	High	Medium	Low	
Population immunity	• Routine vaccination coverage for children <10 years old is <50% and • <50% of children are infected before age 10 years (if known)	• Routine vaccination coverage for children <10 years old is 50–79% and • <50% of children are infected before age 10 years (if known)	• Routine vaccination coverage for children <10 years old is >79%	Vaccination (single dose to children) is offered in very few industrialized countries. Infection induces lifelong immunity.
Burden of disease	• n/a	• n/a	• n/a	In temperate high-income countries in the pre-vaccination era, >90% infections occurred before adolescence and <5% of adults remained susceptible. In many tropical settings, acquisition of infection occurs at older ages resulting in higher susceptibility among young adults. The disease is complicated by varicella-zoster virus-induced pneumonia or encephalitis, or herpes zoster later in life. Overall CFR is 2–3/100 000 cases. In children, CFR is approx. 1/100 000 cases, in adults, CFR is approx. 20–25/100 000 cases.

Risk characterization

Type of threat: Periodic large outbreaks may occur with an inter-epidemic cycle of 2–5 years and could manifest in an acute emergency if other factors, such as overcrowding, are present.

Time frame: An outbreak could occur weeks after the onset of an emergency in an overcrowded setting. The incubation period is usually 14–16 days (range: 10–21 days) and infectiousness lasts for 10–21 days following infection.

Age-specific burden: In temperate climates without immunization program, varicella affects at least 90% of the population by age 15 years. In tropical areas, a greater proportion of cases and deaths would be among adults.

[23] WHO (2014). Varicella and herpes zoster vaccines. WHO Position Paper. Weekly Epidemiological Record 89(25):265–288 (http://www.who.int/wer/2014/wer8925.pdf?ua=1, accessed 7 November 2016).

Table A2.23 Yellow fever disease-specific factors[24]

Factor	Risk level			Comments
	High	Medium	Low	
Risk level for the setting **Geography, climate and season**	• n/a	• Tropical regions of Africa and South America • Middle or end of the rainy season • Emergency is occurring in a jungle/ forest setting	• Temperate countries	
Population immunity	• Routine vaccination coverage for children <5 years old <60% • No previous vaccination campaigns or routine vaccination • Naive or unvaccinated population moving into endemic area	• Routine vaccination coverage for children <5 years old	• Routine vaccination coverage for children <5 years old >80%	Vaccination with a single dose should be administered with measles as part of routine schedules, or in campaigns. Vaccination confers lifelong immunity. The use of YF fractional dose of yellow fever vaccination can be considered in response to an emergency situation in which current vaccine supply is insufficient. Fractional dose vaccination should be used for vaccination campaigns in response to an outbreak or in settings where the extension of the outbreak is imminent and should not be used for routine immunization.[25]
Burden of disease	• n/a	• Outbreak in the area within the past 5 years	• Non-endemic areas	CFR among unvaccinated people is about 0.1% per infection. 90% of reported cases occur in Africa and 30 000 deaths are believed to occur annually.

Risk characterization

Type of threat: Epidemic.

Time frame: Difficult to predict, but likely to be concomitant with the rainy season. Incubation period is approximately 3–6 days.

Age-specific burden: Children are at greatest risk, given that the prevalence of natural immunity accumulates rapidly with age. High attack rates in children (>70%) typically may reflect areas where older individuals are protected by prior vaccination campaigns or natural immunity (majority of infections are asymptomatic). CFR is greatest among young children and the elderly.

[24] WHO (2013). Vaccines and vaccination against yellow feve. WHO Position Paper. Weekly Epidemiological Record 88(27):269–284 (http://www.who.int/wer/2013/wer8827.pdf?ua=1, accessed 7 November 2016).

[25] WHO (2016). Fractional dose yellow fever vaccine as a dose-sparing option for outbreak response. WHO Secretariat information paper. (WHO/YF/SAGE/16.1; http://www.who.int/immunization/sage/meetings/2016/october/3_Fractional_dose_secretariat_report_full_version.pdf?ua=1, accessed 7 November 2016).

Table A3.1 Characteristics of potential vaccines to be considered as part of the intervention[26,27]

Antigen[28]	Presentation[29]	Full course	Efficacy/ effectiveness at full course[30]	Efficacy/effectiveness at 1 dose	Efficacy/ effectiveness at 2 doses	Target age[31]	Packaging[32]	Stability	Cold-chain volume (cm³/dose) information
BCG	BCG	1[33]	50% all TB Fulminant TB in infancy >70%	50% all TB Fulminant TB in infancy >70%	n/a	Neonates	10, 20 dose vial	VVM 14–30	Multiple products available, more information here: PQ vaccine list
Cholera	Dukoral®	2–3 doses	~60% at 2 years	~80% at 1 year	~80% at 1 year	≥2 years	1 dose	-	Dukoral
	Shanchol®	2 doses[34]	-	-	-	≥1 year	1 dose	-	Shanchol
	Euvichol®			-				-	Euvichol
Diphtheria, Tetanus, Pertussis, Hib, and Hep B	DTP (liquid)	3	>90%	Varies with antigen. For the pertussis antigen a primary series of both whole–cell (wP) and acellular (aP) pertussis vaccines significantly decrease disease–related mortality in the first year of life, though the use of aP may result in resurgence after a number of years.	-	≥6 weeks to <7 years, pregnant	1, 10, 20 dose vial	Do not freeze	Multiple products available, for more information click on the vaccine commercial name here: PQ vaccine list
	DTP–Hep B–Hib (pentavalent liquid)	3	>90%	Varies with antigen. For pertussis component see above.	-	≥6 weeks to <7 years	1, 2, 5, 10 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
	DTP–Hep B–Hib (pentavalent lyophilized)	3	>90%	Varies with antigen. For pertussis component see above.	-	≥6 weeks to <7 years	1, 2, 10 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
	DTP–Hib (liquid)	3	>90%	Varies with antigen. For pertussis component see above.	-	≥6 weeks to <7 years	1, 10 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
	DTP–Hib (lyophilized)	3	≥95%	Varies with antigen. For pertussis component see above.	-	≥6 weeks to <2 years	1, 10 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list

[26] More information on vaccine specific considerations and WHO recommendations available at http://www.who.int/immunization/policy/position_papers/en/.
[27] More information on WHO prequalified vaccines available at http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/.

Antigen[28]	Presentation[29]	Full course	Efficacy/ effectiveness at full course[30]	Efficacy/effectiveness at 1 dose	Efficacy/ effectiveness at 2 doses	Target age[31]	Packaging[32]	Stability	Cold-chain volume (cm^3/dose) information
Diphtheria, Tetanus, Pertussis, Hib, and Hep B	Hep B	3	≥95%	~56% in adults, for children no information	-	Birth dose within 24 hours	1, 2, 6, 10, 20 dose vial and Uniject	Do not freeze, VVM 30	Multiple adult and paediatric products available, see: PQ vaccine list and Hep B Uniject
	TT	3+2	~90–99%	1 dose not protective	-	Infancy, adult	1, 10, 20 dose vial and Uniject	Do not freeze	Multiple products available, see: PQ vaccine list, and TT Uniject
	DT	3+2	~90–99%	1 dose not protective	-	Infancy and children <7 years	1, 10, 20 dose vial	-	Multiple products available, see: PQ vaccine list
	dT	2+1; 3	~90–99%	1 dose without primary DT not protective	-	≥7 years and adults	1, 10, 20 dose vial	-	Multiple products available, see: PQ vaccine list
Hepatitis A	Hepatitis A	1	94–100%	>90%	-	≥1 year	1 dose vial	Do not freeze	Hep A adult Hep A junior
Hepatitis E	Hepatitis E vaccine	3	≥95%	-	-	>16 years	1 dose vial	Do not freeze	1 dose: 100
HPV	HPV (Cervarix®)	2	~90–100%	-	~90–100%	9–13 years	1, 2 dose vials	-	Cervarix 1 Cervarix 2
	HPV (Gardasil®)	2	~90–100%	-	~90–100%	9–13 years	1 dose vial	-	Gardasil
Influenza	Influenza, seasonal inactivated	1–2	Varies	Varies	Varies	≥6 months	1, 10 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
	Influenza, seasonal live attenuated	1–2	~82%	Varies	Varies	2–49 years	1 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
Japanese encephalitis (JE)	JE (lyophilized, liquid)	2 doses, single dose, dependent on vaccine	~95%	-	-	≥6/8/9 months, dependent on vaccine	1, 4, 5 dose vial	Do not freeze	Multiple products for adults available: PQ vaccine list, and JE Pediatric

[28] Precautions and contraindications should be considered for all vaccines. These include previous anaphylaxis for all vaccines, immune-deficiency status for live vaccines, age group (e.g. rotavirus and yellow fever vaccines), and pregnancy.

[29] Not all combination vaccines are covered, only the ones most frequently used in developing countries

Antigen[28]	Presentation[29]	Full course	Efficacy/ effectiveness at full course[30]	Efficacy/effectiveness at 1 dose	Efficacy/ effectiveness at 2 doses	Target age[31]	Packaging[32]	Stability	Cold-chain volume (cm^3/dose) information
Measles, mumps and rubella	Measles	2	~90–100%	~85%	~90–100%	≥9 months, can be considered as of >6 months e.g. in outbreak settings.	1, 2, 5, 10, 20 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
	MR	2	~90–100%	~85%	~90–100%	≥9 months, can be considered as of <6 months	1, 2, 5, 10 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
	MMR	2	~90–100%, less for mumps component	~85%	~90–100%	≥9 months, can be considered as of <6 months	1, 2, 5, 10 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
Meningitis	MenA/C® (lyophilized)	1	85–99%	85–99%	n/a	1–29 years	10 dose vial	Do not freeze	Multiple products: PQ vaccine list
	MenAfriVac A®	1	~75–95%	~75–95%	n/a	1–29 years	10 dose vial	Do not freeze VVM 30	MenAfriVac MenA pediatric
PCV	PCV10&13	3	>90%, depending on serotype	~73%	~96%	6 weeks to 5 years	1, 2 dose vial	Do not freeze, VVM 30	Multiple products available, see: PQ vaccine list
Polio	IPV	At least 1 dose	Depending on serotype	-	-	≥14 weeks	1, 2, 5, 10 dose vial	Do not freeze	Multiple products available, see: PQ vaccine list
	bOPV	3 primary dose (+IPV)	High seroconversion	-	-	From birth	10, 20 dose vial	Store frozen, VVM 2	Multiple products available, see: PQ vaccine list
	mOPV	-	High seroconversion	-	-	-	10, 20 dose vial	Store frozen VVM 2	Multiple products available, see: PQ vaccine list

[30] Information on efficacy is based on current knowledge. The information is derived from published data. It is important to keep in mind that this information does not necessarily reflect the effectiveness of the vaccine in field conditions and is best viewed as an upper boundary. Further, the efficacy of vaccine varies by outcome and target population, therefore, the estimates provided need to be considered with caution.

[31] Target age group in emergency settings should be based on epidemiological considerations.

Antigen[28]	Presentation[29]	Full course	Efficacy/ effectiveness at full course[30]	Efficacy/effectiveness at 1 dose	Efficacy/ effectiveness at 2 doses	Target age[31]	Packaging[32]	Stability	Cold-chain volume (cm³/dose) information
Rabies	Rabies (lyophilized, liquid)	Pre-exposure: 3 dose regimen Post-exposure: 4 or 5 dose regimen	-	-	-	-	1 dose vial		Multiple products available, see: PQ vaccine list
Rota	Rotavirus (RotaTeq® liquid)	3	40-90%, varies by setting	-	-	6 weeks to 2 years	1 dose vial	Do not freeze	RotaTeq
	Rotavirus	2	40-90%, varies by setting	-	-	6 weeks to 2 years	1 dose vial	Do not freeze	Rotarix
	(Rotarix® liquid)	2	40-90%, varies by setting	-	-	6 weeks to 2 years	1 dose vial	-	-
Typhoid	Rotavirus (Rotarix® lyophilized)	1 dose (injectable), 3–4 doses capsular (oral)	Vi polysaccharide (ViPS): ~70%, Ty21a: 3–4 doses, efficacy 33–67%	-	-	≥ 2 years of age (ViPS) or ≥5 years of age (Ty21a)	1 dose vial	-	Typhoid ViPS
Varicella	V (lyophilized)	1 or 2	~95%	~95%	~95%	>9 months	1 dose vial	-	-
	MMRV (lyophilized)	1 or 2	~95%	~95%	~95%	>9 months	1 dose vial	-	-
Yellow Fever	YF	1	~99%	~99%	-	>9 months	5, 10, 20, 50 dose vial	-	Multiple products available, see: PQ vaccine list

[32] Packaging of WHO prequalified vaccines
[33] 2 doses given 2–6 weeks apart in individuals above 5 years of age, 3 doses for children 2–5 years
[34] 2 doses given 14 or 28 days apart