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The utilisation of vaccines in humanitarian crises, 2015–2019: A review of practice

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ABSTRACT

Background: The risk factors that emerge with the onset and protraction of humanitarian crises leave populations at a heightened risk of excess morbidity and mortality from vaccine-preventable diseases (VPDs). There is currently little clarity on which vaccines are being used in crises throughout the world, and whether vaccination decisions correspond to local disease threats. This review aimed to collect and analyse such information.

Methods: We reviewed vaccination services from January 2015 to June 2019 across all 25 humanitarian responses that had an activated coordination mechanism during this period. A range of online sources and informants within the humanitarian sector were consulted to compile data on which vaccines were provided in each crisis, and the modality and timing of vaccine provision. The package of vaccination services since the start of each crisis was then compared with local disease burden (baseline + excess due to crisis-emergent risk factors).

Results: The range of vaccines used in humanitarian crises appears limited. When offered, vaccines were primarily delivered through the pre-existing routine schedule, with few supplementary actions taken in recognition of the need for rapidly enhancing population immunity. Vaccine packages mostly did not address the actual range of VPDs that likely accounted for substantial disease risk.

Conclusions: This review suggests inconsistencies and inequities in vaccine provision to crisis-affected populations. A consistent, standardised and broader approach to vaccine use in crises is needed.

1. Introduction

1.1. Background

Humanitarian needs throughout the world are alarmingly high. An estimated 235 million crisis-affected people required assistance in 2021, a near 40% increase on 2020, largely attributed to COVID-19 [1]. Typically characterised by displacement, violence, food insecurity, overcrowding and inadequate water, sanitation and hygiene [2], these crises largely occur amid populations with a high baseline burden of infectious diseases [3]. These crisis-emergent risk factors, compounded by insufficient access to curative and preventive health services and the vicious cycle of disease and acute malnutrition, increase susceptibility to, transmissibility and severity of vaccine preventable diseases (VPDs), which may occur in both endemic and epidemic pattern [4]. To prevent excess morbidity and mortality in such crises, a fast-moving, context-appropriate public health response is required.

A standardised approach to vaccine provision in humanitarian crises has been proposed [2], yet in practice it is left to 'decision-makers' within each crisis to select which vaccines to use, when and how [5]. A World Health Organization (WHO) Strategic Advisory Group of Experts on Immunisation (SAGE) decision-making framework for emergencies (hereafter 'SAGE Framework') is available, but its application to date is unclear [6].

Abbreviations: ARI, Acute respiratory infection; AWD, Acute watery diarrhoea; BCG, Bacillus Calmette–Guérin vaccine (for tuberculosis); CAR, Central African Republic; DD, Diarrhoeal disease; DPT, Diphtheria, pertussis, tetanus; DRC, Democratic Republic of Congo; GAVI, Global Alliance for Vaccines and Immunisation; EPI, Expanded Programme on Immunisation; Hib, Haemophilus influenzae Type B; HPV, Human papillomavirus; IPV, Inactivated poliovirus vaccine; MMR, Measles, mumps, rubella vaccine; MR, Measles, rubella vaccine; MSF, Médecins sans Frontières; OCV, Oral cholera vaccine; OPV, Oral poliovirus vaccine; Penta, Pentavalent vaccine (Diphtheria, Pertussis, Tetanus, Hep B, Hib); PCV, Pneumococcal conjugate vaccine; Td, Tetanus-diphtheria vaccine; UNICEF, United Nations Children's Fund; UN OCHA, United Nations Office for Coordination of Humanitarian Affairs; VPD, Vaccine Preventable Disease; WHO, World Health Organisation.

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Of the 19.7 M children under 5y old that had received zero doses of vaccine, 14 M were estimated to live in the African continent and in countries affected by conflict, as of 2019 [7]. Estimated coverage of vaccines included in the Expanded Programme for Immunisation (EPI) is under 75% for most crisis-affected countries, below herd immunity thresholds for some VPDs [8]. Challenges to vaccination in crisis settings are well-recognised and can impact decision making. These include organisational bureaucracy [6], vaccine stock-outs [9], cold-chain needs and management [4], contextual restrictions and ethical considerations [10] high cost [4], and population movement [3]. Solutions may include reduced or single-dose schedules, e.g. for measles, oral cholera vaccine (OCV), haemophilus influenzae B (Hib) and pneumococcal conjugate vaccine (PCV) [5,2,11], combinations of mass-delivered and routine vaccination modalities, as well as procurement of vaccines through the low-cost Humanitarian Mechanism [12] and other vaccine-specific stockpiles.

The potential benefits for crisis-affected populations, and for global health generally, of more proactive, diverse and wider-reaching humanitarian vaccination services are increasingly recognised [13,14]. We wished to establish a baseline of current practice against which future policy and practice recommendations can be predicated. We thus sought to review vaccination strategies across all recent humanitarian responses and document their alignment with local VPD risk. Data were collected prior to the COVID-19 pandemic and should be considered within the pre-pandemic context; however, conclusions and recommendations are likely to still apply given that COVID-19 disruptions are mostly associated with additional constraints on vaccination and other humanitarian health services [15].

2. Methods

We reviewed vaccination strategies across all humanitarian responses with an activated health cluster (i.e. the main coordination mechanism for humanitarian response in the health sector), numbering 25 as of June 2019 [16] (Table 2). The Pacific Regional Cluster System was excluded as it covers 21 countries and territories and is a standing, rather than crisis-reactive mechanism, in addition to limited information being available online. Due to time constraints vaccination strategies for all crises were reviewed from 2015 onwards, or from the date of cluster activation if later.

2.1. Data collection

For information on each crisis, sources included Humanitarian Response Plans and Needs Overviews published by the United Nations Office for the Coordination of Humanitarian Affairs (UN OCHA) for each crisis [17,18], country planning and reporting documents available through the Gavi Country Hub [19], and the World Health Organisation (WHO)'s bulletin on weekly emergencies and outbreaks [20]. These sources were reviewed to capture information on approximate date of crisis onset, date of health cluster activation, occurrence of outbreaks, and presence of a systematic list of VPD risk factors (Table 4), drawn from the SAGE framework [5] and a Humanitarian Practice Network guide for public health assessment in crises [21]. Each factor was crudely considered present if specifically mentioned in the crisis' Humanitarian Response Plan. For data on vaccine services several data sources were reviewed: UNICEF's situation reports [22]; the International Coordinating Group's (ICG) dashboard on Cholera [23], Yellow Fever (YF) [24] and Meningitis [25]; MSF data (T. Ducomble

Table 1
Grading risk of excess morbidity and mortality for each VPD.

High Risk	One or more of the risk factors that are present in the crisis is highly relevant to the VPD in question
Moderate Risk	None of the general risk factors that are present in the crisis are highly relevant to the VPD, but at least one is moderately relevant
Low Risk	Low risk was assigned to all other circumstances or those crises in which the disease was not present.

Table 2
Overview of crises.

Crisis	Health cluster activated (year)	Key features of crisis	Estimated population affected (million)*
Zimbabwe	2019	Natural disaster (cyclone)	5.3
Mozambique	2019	Natural disaster (cyclone)	3
Cameroon	2018	Complex emergency; insecurity; influx of refugees (from CAR)	4.3
Bangladesh	2017	Influx of refugees (from Myanmar)	1.2
Nigeria	2016	Complex emergency; armed conflict; mass displacement; food crisis	7.1
Burundi	2015	Complex emergency; insecurity; mass displacement	1.8
Ethiopia	2015	Natural disaster (drought); food crisis	8.86
Libya	2015	Complex emergency; armed conflict; influx of refugees/ migrants (from sub-Saharan Africa and Middle East)	7.27
Syria (Regional)	2015	Armed conflict; mass displacement	13.1
Iraq	2014	Armed conflict; mass displacement	6.7
Ukraine	2014	Armed conflict	3.5
Mali	2012	Complex emergency; insecurity; mass displacement	3.2
Myanmar	2012	Insecurity (targeting of ethnic minorities); mass displacement; natural disaster (cyclone, flooding)	0.9
Yemen	2011	Complex emergency; armed conflict; mass displacement; food crisis	24.1
Colombia	2010	Armed conflict (internal); Influx of refugees (from Venezuela)	5.1
Niger	2010	Natural disaster (drought, desertification); Influx of refugees (from Nigeria)	2.3
South Sudan	2010	Complex emergency; armed conflict; mass displacement; food crisis	7.1
OPT	2009	Armed conflict	2.5
Sudan	2009	Complex emergency; armed conflict; mass displacement	5.5
Afghanistan	2007	Complex emergency; armed conflict; mass displacement; natural disaster (drought)	6.3
CAR	2007	Complex emergency; armed conflict; mass displacement	2.9
Chad	2007	Complex emergency; natural disaster (drought, flooding); food crisis	4.3
Pakistan	2007	Natural disaster (drought, flooding, cyclones); mass displacement; insecurity	3.2
DRC	2006	Complex emergency; armed conflict; mass displacement	12.8
Somalia	2006	Complex emergency; armed conflict; mass displacement; food crisis	4.2

* people in need as per most recent crises Humanitarian Response Plan[17].

Table 3
Risk factors associated with VPDs.

Risk Factors	Associated VPDs
Low population immunity	All
Intense rainy season/flooding	Diphtheria; cholera, Japanese encephalitis; rotavirus; yellow fever
Intense dry season/drought	Measles; cholera; meningococcal meningitis
Increased incidence of sexual and gender based violence	HPV; hepatitis B
Incidence of injuries or conflict	Tetanus
Low access to health services	Diphtheria; hib disease; measles; meningococcal meningitis; pertussis; pneumococcal disease; tuberculosis; cholera; rotavirus; Japanese encephalitis; hepatitis B; tetanus
High HIV/AIDS burden	Hib disease; measles; meningococcal meningitis; pneumococcal disease; tuberculosis; hepatitis B; HPV
High birth rate	Hib disease; measles; pertussis; pneumococcal disease; rotavirus; Japanese encephalitis; yellow fever; Hepatitis B; tetanus
Displacement	Diphtheria; hib disease; measles; meningococcal meningitis; pertussis; pneumococcal disease; tuberculosis; cholera; polio; rotavirus; hepatitis B
Overcrowding	Diphtheria; hib disease; measles; meningococcal meningitis; pertussis; pneumococcal disease; tuberculosis; cholera; polio; rotavirus; hepatitis B
Poor water supply and sanitation	Hib disease; measles; cholera; polio; rotavirus; Japanese encephalitis; yellow fever; hepatitis B
High prevalence of malnutrition	Diphtheria; Hib disease; measles; pertussis; Pneumococcal disease; tuberculosis; cholera; rotavirus; yellow fever

2019, personal communication, Aug 20th) on PCV campaigns conducted via the Humanitarian Mechanism; and WHO and UNICEF routine immunisation estimates by country [26]. We extracted information on vaccines offered, delivery modality (routine, mass campaign, other/hybrid approaches), dates of any vaccination campaigns, dosages and target age groups. Information on disease burden was obtained from online sources including the Centre for Disease Control and WHO or GAVI disease estimates [27–31].

All instances of the above sources published during the analysis period were reviewed. To complement online sources, an email request containing a standardised reporting form was sent to each UNICEF regional office via the Equity Reference Group for Immunisation [32]. Seven country offices (out of a possible 25 for each crisis) replied with complete data. This information was combined with that collected online to supplement and verify the results.

2.2. Analysis

A key objective of this review was to establish the extent to which crisis-specific packages of vaccination services aligned with actual or potential VPD burden (risk). We focussed on the risk of *excess* morbidity and mortality, i.e. disease burden attributable to the crisis that humanitarian vaccination services should have been designed and resourced to mitigate; in accordance with the SAGE Framework [5], however, we recognised that for many VPDs grading this excess risk requires information on crisis-emergent risk factors (e.g. overcrowding, malnutrition) as well as the baseline burden. For simplicity we restricted analysis to the leading 15 VPDs in terms of disability-adjusted life years lost [33]: measles, poliomyelitis, cholera, meningococcal meningitis, diphtheria, pertussis, tetanus, hepatitis B, haemophilus influenzae type B (Hib), pneumococcal disease, rotavirus, human papillomavirus (HPV), tuberculosis, yellow fever, and Japanese encephalitis.

The vector-borne diseases yellow fever and Japanese encephalitis are affected by similar risk factors yet are specific to certain regions, with yellow fever more common in sub-Saharan Africa and South America, and Japanese encephalitis more common in Asia. Given this limited geographic overlap (i.e. risk of both diseases occurring in the same crisis) we analysed them together. This study considers the impact of HPV and hepatitis B in the longer term. As per the WHO's SAGE Framework, equal value has been assigned to deaths in the present and deaths that will occur later in time, if both can be attributed to excess risk due to the crisis [5].

We developed a grading of high, moderate or low (Table 1) for each VPD and crisis as follows:

(i) We established the presence of each risk factor (e.g. high prevalence of malnutrition in Ethiopia; low HIV/AIDS burden in Syria).
(ii) If one of more of the risk factors present in each crisis has a high, moderate, or low relevance to the VPD in question they were graded as having a high, moderate or low risk of causing excess harm (Table 1). This level of relevance was benchmarked in the SAGE Framework's [5] 'general risk assessment table' and the 'disease specific risk assessment worksheets'., which, respectively, consider 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 or progression to disease; and VPD-specific risks (e.g. increased cholera transmission due to intense rainy season or flooding).
(iii) Lastly, we adjusted the grading in line with the baseline disease burden for each country (where required by the SAGE Framework for some VPDs), e.g. there is a high risk of meningococcal meningitis throughout the African meningitis belt.

As an example, in Nigeria the risk of excess morbidity and mortality from rotavirus is high due to the country's low population immunity and poor water supply and sanitation. In Ethiopia, diphtheria risk was considered moderate as there is a high prevalence of malnutrition, low population immunity and limited access to health services since crisis onset. In Syria, yellow fever and Japanese encephalitis presented low risk, as even though risk factors are present such as poor water and sanitation, they are not endemic to the country. When grading risk of excess morbidity and mortality, both general and disease-specific risk factors were considered.

Lastly, we compiled vaccine information for each crisis, including which vaccines were provided, the modality of this provision (mass campaign or routine), whether any campaign was preventive or reactive (i.e. following an outbreak) and campaign timeliness, quantified in months and years following the activation of the health cluster (Table 6). We compared this information with the expected burden of each VPD targeted by the vaccine.

3. Results

Table 2 presents a brief description of each emergency, highlighting that most of the crises are severely protracted, and due to armed conflict or insecurity.

Table 4
Risk factors within each crisis (years indicate the date of health cluster activation).

Crisis (activation year)	Low population immunity*	Intense rainy season/ flooding	Intense dry season / drought	Increased incidence of sexual and gender based violence	Incidence of injuries or conflict	Low access to health services	High HIV/ AIDS burden**	High birth rate***	Displacement	Overcrowding	Poor water supply and sanitation	High prevalence of malnutrition****
Zimbabwe (2019)		x	x			x	x		x		x	
Mozambique (2019)	x	x	x	x	x	x	x	x	x		x	
Cameroon (2018)		x	x	x		x	x	x	x		x	
Bangladesh (2017)		x		x	x	x			x	x	x	x
Nigeria (2016)	x	x	x	x	x	x	x	x	x		x	x
Burundi (2015)	x	x	x	x		x		x	x		x	x
Ethiopia (2015)	x	x	x			x			x		x	x
Libya (2015)			x	x	x	x			x	x	x	
Syria (2015)				x	x	x			x		x	
Iraq (2014)	x	x	x	x	x	x		x	x		x	
Ukraine (2014)	x				x	x			x			
Mali (2012)	x	x	x	x	x	x		x	x		x	
Myanmar (2012)		x		x	x	x		x	x		x	
Yemen (2011)	x		x	x	x	x		x	x	x	x	x
Colombia (2010)		x	x	x	x	x			x	x	x	
Niger (2010)	x	x	x	x	x	x		x	x		x	x
South Sudan[1] (2010)	x	x	x	x	x	x	x	x	x		x	x
OPT (2009)				x	x	x		x	x	x		
Sudan (2009)	x	x	x	x	x	x		x	x		x	x
Afghanistan (2007)	x		x	x	x	x		x	x		x	x
Central African Republic[2] (2007)	x	x	x	x	x	x	x	x	x		x	
Chad (2007)	x	x	x	x	x	x		x	x		x	x
Pakistan (2007)	x	x		x		x		x	x		x	x
Democratic Republic of Congo[3] (2006)	x			x	x	x		x	x		x	x
Somalia (2006)	x	x	x	x	x	x		x	x		x	x

* Measles and DPT vaccines have below 75% coverage pre-crisis (used as proxy for complete immunisation coverage)[34,35].
** Defined as over 2% prevalence in 15–49 year olds[36].
*** Birth rate above average for country's region (children per woman)[37].
**** Over 10% prevalence of wasting, and 30% prevalence of stunting in children under-5; OR 40% prevalence of stunting in children under-5 only[38].
[1,2,3] Limited data available on nutrition status for CAR, South Sudan and Somalia. Given the context within each country, we assumed a high prevalence of malnutrition.

Table 5
Number of crises in which different VPDs were targeted by vaccines offered during the period of analysis, by VPD excess burden grading and modality of vaccine delivery.

VPD	Risk of excess morbidity/mortality	Number of crises	Vaccine offered in routine modality only	Vaccine offered through mass campaign	Vaccine not offered
Measles	Low	0	–	–	–
	Moderate	2	1	1	0
	High	23	3	20	0
Poliomyelitis	Low	11	3	8	0
	Moderate	11	1	10	0
	High	3	0	3	0
Cholera	Low	4	0	0	4
	Moderate	3	0	1	2
	High	18	0	11	7
Meningococcal meningitis	Low	10	1	1	8
	Moderate	3	0	0	3
	High	12	3	4	5
Diphtheria	Low	–	–	–	–
	Moderate	21	17	4	0
	High	4	1	3	0
Pertussis	Low	–	–	–	–
	Moderate	–	–	–	–
	High	25	20	5	0
Tetanus	Low	–	–	–	–
	Moderate	3	3	0	0
	High	22	16	6	0
Hepatitis B	Low	6	5	1	0
	Moderate	4	3	1	0
	High	15	12	3	0
Haemophilus influenzae Type B (Hib)	Low	5	5	0	0
	Moderate	10	7	3	0
	High	10	9	1	0
Pneumococcal disease	Low	–	–	–	–
	Moderate	2	1	0	1
	High	23	17	4	2
Rotavirus	Low	–	–	–	–
	Moderate	–	–	–	–
	High	25	13	1	11
Human Papillomavirus (HPV)	Low	1	0	0	1
	Moderate	10	1	0	9
	High	14	1	1	12
Tuberculosis	Low	–	–	–	–
	Moderate	–	–	–	–
	High	25	24	1	
Yellow Fever/Japanese Encephalitis	Low	9	0	0	9
	Moderate	1	0	0	1
	High	15	5	7	3

3.1. Presence of VPD risk factors

Table 3 presents the relevance of each risk factor to each vaccine preventable disease [5].

The assessed presence of different risk factors [5,21] within each crisis is summarised in Table 4.

Across several crises, such as CAR, South Sudan and Nigeria, all but one of the risk factors were present. Low access to health services was reported to be a consequence of all 25 crises, due to damaged infrastructure, restricted importation of medicines or often a lack of skilled staff due to insecurity. Pre-crisis routine vaccination coverage (and thus population immunity) was concerningly low in 17 countries, with measles and DPT coverage well below 75%. Coverage of DPT and measles vaccine was 13% and 20% for in South Sudan respectively, and 42% and 63% in the Ukraine, where the health system is relatively more robust [34,35].

3.2. Choice of vaccines and delivery modalities

Table 5 presents the number of crises that offered a vaccine targeting different VPDs, through routine or mass campaign modalities, and by graded risk of excess morbidity or mortality expected for each VPD. Only one response, Zimbabwe, appeared to vaccinate against all leading VPD threats (supplementary file). The vaccination strategies for the 24 other crises appeared to have significant gaps.

Fig. 1 presents, by crisis, the number of VPDs with a high or moderate excess disease risk grading, and the number of mass vaccination campaigns delivered (of any antigen) targeting VPDs with a high or moderate excess disease risk. For example, in Chad, all VPDs had a high or moderate excess disease risk but only two mass campaigns were delivered (for measles and polio).

The measles vaccine was offered in all crises. In 23 of the 25 crises there was a high risk that measles would cause excess morbidity and mortality; in 20 of these a mass campaign was conducted. Similarly, the polio vaccine (either injectable or oral) was offered in all crises, with a mass campaign conducted in 21/25 crises. The severity of risk for polio was low (11 crises) or moderate (11 crises). Polio campaigns were generally at national scale, with > 1 million children targeted per campaign [39], including in Afghanistan, Pakistan and Nigeria where polio remains endemic and the crisis context significantly heightens the risk of an outbreak.

Table 6
Timeliness of mass vaccination campaigns.

Crisis	Health cluster activated	Vaccine offered through a mass or catch up campaign	Timeliness of campaign (post cluster activation)
Zimbabwe	March 2019	OCV Penta; MR; rotavirus; HPV; PCV	1 month 2 months
Mozambique	March 2019	OCV MR; Polio*	1 month 2 months
Cameroon	January 2018	None	n/a
Bangladesh	September 2017	Polio*; MR OCV Penta; Td	1 month 2 months 4 months
Nigeria	January 2016	Polio* Meningitis Measles PCV OCV Yellow Fever	2 months 5 months 12 months 13 months 21 months 24 months
Burundi	2015	Measles	>48 months
Ethiopia	2015	Measles; OCV Polio*; Yellow Fever	>2 months >36 months
Libya	2015	Polio* MMR	>6 months >18 months
Syria	April 2015	Polio* MMR	Ongoing as cluster was activated 1 month

* Polio vaccine offered, limited data on which vaccine (OPV or IPV).

The remaining vaccines included were predominantly provided by routine modality. In 10 of the 25 crises Hib, a common cause of early childhood pneumonia and meningitis, was classed as a high risk for excess morbidity, but Hib vaccine was only provided through a mass campaign in in Bangladesh as part of the pentavalent vaccine.

PCV and rotavirus vaccine were predominantly offered through routine vaccination or not at all. In CAR, MSF supported the Ministry of Health to provide a catch-up campaign for all EPI vaccines. Prior to this, PCV coverage was estimated at 8% in 2011 and 23% in 2013. At the end of the 2-year campaign and again in 2018 coverage rates had increased to an estimated 47% [26]. We identified only a single rotavirus campaign (in Zimbabwe).

Among 12 crises in high-burden countries [31] (10 in the meningitis belt in Sub-Saharan Africa, plus Afghanistan and Pakistan), seven offered a meningococcus-targeting vaccine, while Cameroon, Ethiopia, Afghanistan, Pakistan and DRC did not.

Cholera was the only VPD that no routine vaccination was provided for, even in endemic countries. In 18 of the 25 crises, a high risk of cholera was graded. In seven of these no vaccine was offered, with response strategies emphasising a curative approach and health promotion activities, including during outbreaks in Burundi and CAR, both in August 2016 [40,41]. In 11 crises a mass campaign was implemented, preventatively in five crises. The Rohingya refugee crisis in Bangladesh witnessed the largest of these campaigns, reaching over 712,000 by completion of the second dose round within 2 months of health cluster activation.

Human Papillomavirus was graded to have a high or moderate risk of causing excess morbidity across 24 crises, due primarily to increased levels of sexual and gender based violence (SGBV) or high HIV burden. The HPV vaccine was not offered in 21 of these crises but was offered through a catch-up campaign in Zimbabwe.

In five countries, the yellow fever (YF) vaccine was offered as a routine preventive measure due to its endemic nature, with coverage varying from 87% (Colombia) to 29% (Chad). Large-scale, high-coverage preventive mass campaigns were implemented in Nigeria (>26 million people reached [42]) and Sudan (>1.6 million people reached [43]). In four countries, the YF vaccine was offered in response to outbreaks. This included the DRC mass campaign, which followed a large outbreak emerging in Angola before spreading to DRC. Due to a global YF vaccine shortage and the risk of urban epidemics, WHO permitted the use of an innovative dose-fractioning strategy in which one fifth of a regular dose was provided to each person, estimated to provide immunity for a minimum of 12 months [44]. In a similar effort, a reactive Japanese Encephalitis campaign was implemented in Myanmar in November 2017 ahead of it being introduced as part of the routine schedule in January 2018 [45].

3.3. Timeliness of responses

Table 6 describes the variation in timing of vaccine campaigns between crises. For measles, timeliness ranged from 1 to

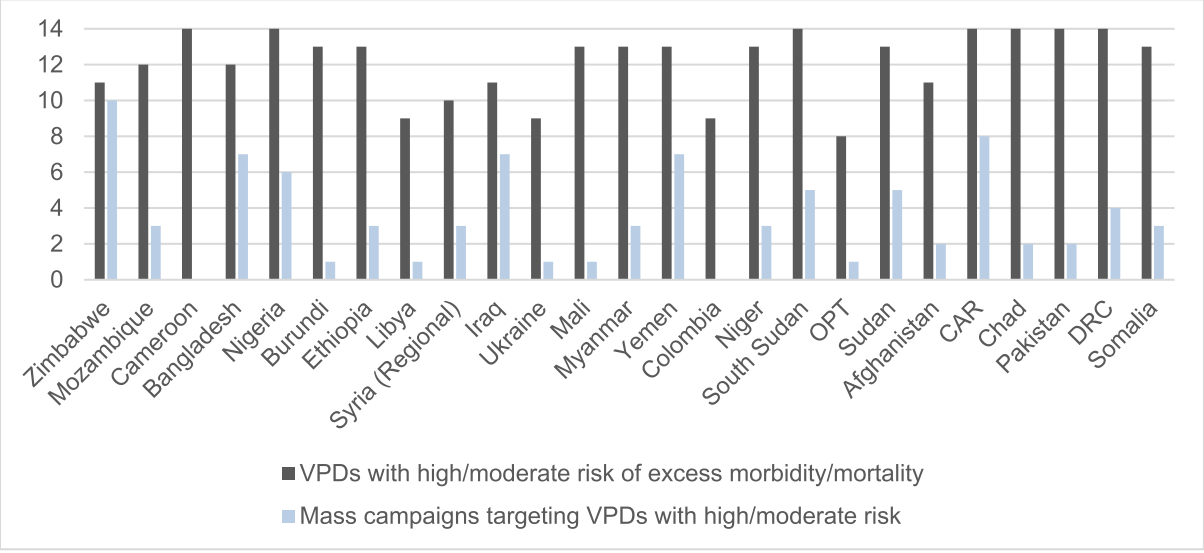

Fig. 1. Number of VPDs with a high or moderate excess disease risk grading, and the number of mass vaccination campaigns delivered targeting VPDs with a high or moderate excess disease risk.

48 months: in Nigeria a reactive campaign was conducted a year post health cluster activation, following 3,905 suspected cases of measles reported across four conflict-affected states. In Libya and Burundi measles campaign delays were 18 months and 48 months respectively.

For OCV, timeliness of the six reactive campaigns we identified ranged from one month (Cyclone Idai response in Mozambique, where over 500 cases of cholera were already reported in affected areas within two weeks of the disaster [46]) to 18 months in Yemen, during a countrywide epidemic that had begun 16 months earlier and led to 1.2 million recorded cases [47].

4. Discussion

4.1. Summary of findings

Crises expose large populations to a high burden of VPDs. It is therefore critical that the full range of available vaccines, and an appropriate mix of delivery strategies, are considered as part of the armamentarium of disease control interventions in humanitarian responses. This review suggests that in most recent crises this has not happened. Instead, vaccines are primarily delivered on a routine basis as part of countries' EPI programmes, with few supplementary actions taken in recognition of the need for a higher and rapidly enhanced level of immunity. Mass campaigns that are implemented are primarily for measles or polio and do not reflect the range of high-burden VPDs that can occur in crisis contexts, nor are they implemented within a timeline consistent with prevention aims.

Vaccination through any modality was further impacted throughout 2020 and 2021, with health systems overwhelmed and compromised by the COVID-19 crisis. Essential health services and routine immunization programmes that were normally strengthened by supplementary immunization activities and national campaigns were severely affected. As of April 2021, 50 countries had at least one VPD campaign postponed during the pandemic, with additional delays to routine immunisations or campaigns due to the prioritisation of COVID-19 vaccine delivery. This left an estimated 228 million people, mostly children, exposed to the risk of VPDs [48].

4.2. Results in context

Within this broad overview, illustrative examples of campaigns and response strategies are worth highlighting.

In Zimbabwe, following Cyclone Idai, all vaccines included in the EPI schedule were included in a multi-antigen 'catch-up' campaign targeting the two affected districts. While the reach of the campaign was small (61,182 under-5 s and 31,553 girls aged 10–14 years [49]) it targeted those most vulnerable to the cyclone's impact within a relatively short timeframe. The first round of an OCV campaign was implemented within 1 month of the cyclone, [49]. With cholera endemic to Zimbabwe (a large-scale outbreak had occurred in September 2018 [50]), the need to mitigate against this risk was paramount. No such outbreak occurred after vaccination.

By contrast, in Cameroon an outbreak of cholera was declared in February 2019 but as of August 2019 there has been no vaccination campaign, despite 680,950 doses arriving in May 2019 according to the ICG dashboard [23]. The case fatality rate was high at over 5%, suggesting problems with case management [51].

A trend observed across multiple crises is that of vaccine strategies not reflecting the disease burden of the country and the crisis-specific risk factors. Among Rohingya refugees in Bangladesh, SGBV, forced prostitution and sex-trafficking are frequently reported [52]. Humanitarian stakeholders provide child protection programming, girl-friendly spaces and family planning support; however, to date no HPV vaccine campaign has been implemented. In 2015, 49% of global pneumonia deaths occurred in India, Nigeria, Pakistan, DRC and Ethiopia collectively (four of which are included within this review). While in recent years it has become possible for humanitarian actors to procure PCV at a substantially reduced price, the lack of specific PCV usage recommendations may be a key factor hindering uptake as a standard part of humanitarian responses. Evidence on practical, effective, and cost-effective ways to use PCV is critical for humanitarian actors to better evaluate the role of PCV in the vaccine portfolio for crises use [53]. Moreover, rotavirus-associated mortality is consistently highest in Sub-Saharan Africa, Southeast Asia and South Asia [54]. In DRC, 64% of diarrhoea deaths among under-5 s were attributable to rotavirus infection [54]. With low access to healthcare, a high birth rate [37] and poor water and sanitation the risk of rotavirus transmission is likely to be high in many crisis settings, suggesting the need for mass rotavirus campaigns at the outset of the crisis.

A similar trend is seen in relation to the modality in which vaccines are offered, which is predominantly on a routine basis. With already low pre-crisis coverage likely to have declined further with the breakdown of health services, displacement and insecurity, the need for catch-up campaigns or supplementary immunisation activities is critical to ensure herd immunity is achieved, though this approach needs to be articulated within a long-term strategy to restore EPI services and should be seen as a complement rather than a substitute to routine delivery.

4.3. Neglected vaccines

This review suggests that vaccines protecting against HPV, pneumococcal disease, Hib and rotavirus are considerably underutilised across crises. The effect of restrictive patents on vaccines has constrained market competition, resulting in high prices for countries not benefiting from Gavi support [55] and unable to afford establishing emergency vaccine stocks. Moreover, Gavi-subsidised prices have historically not been available to humanitarian actors, such as non-governmental organisations.

Progress has been made since WHO's recommendation that HPV be included in national EPI schedules, and in 2013 Gavi negotiated a cost of $4.50 per HPV vaccine dose for the poorest countries [56]. However, MSF argue that in reality this could still be significantly lower at $0.50–0.60 for a single dose [55]. The WHO estimates that cervical cancer will kill>443,000 women per year worldwide by 2030, nearly 90% of which in sub-Saharan Africa [57]. The HPV vaccine is being increasingly rolled out as part of EPI schedules, but the need for humanitarian use through campaigns should not be overlooked. The risk of excess morbidity and mortality from HPV may be exacerbated in crises due to increased levels of SGBV. An appropriate vaccine strategy should counter this risk by rapidly protecting girls from a young age, while also potentially extending the target age group depending on the patterns of SGBV.

In 2017, WHO, UNICEF, MSF and Save the Children established the Humanitarian Mechanism to facilitate efficient access of affordable vaccines by humanitarian actors [58]. As of September 2021, PCV and rotavirus vaccines were available through the mechanism, but partners were advocating for the mechanism to extend to all available vaccines.

In addition to access constraints, low and unsystematic use of vaccines may also reflect lack of technical expertise, evidence gaps on appropriate humanitarian vaccination strategies [2,53]. insufficient governance around decision-making, and low and declining levels of humanitarian funding per capita, all of which may disincentivise coordination mechanisms and individual actors from

adopting appropriate vaccination strategies. A rigorous, global study of barriers and facilitators to adoption of vaccines in humanitarian responses is warranted.

4.4. Limitations

This review has important limitations. Data collection was primarily restricted to online sources published by UNICEF, WHO, international NGOs, ReliefWeb or others. With no single or consistent source of information there are likely to be some discrepancies or omissions. Unpublished data provided by UNICEF for 7 of the 25 crises, did, however, broadly match the data sourced online, suggesting that the search strategy was sensitive and yielded reasonably accurate results. Available information was too sparse to extract detailed information on campaign strategies, for example whether a campaign was preventive or reactive, target age groups and dosages. Similarly, gauging the coverage of mass vaccination campaigns in relation to the population in need was mostly not possible. We only reviewed vaccination strategies from 2015 onwards due to limited time and resources. Therefore, the results for all crises that began prior to 2015 may be skewed, and longer-term trends obscured.

The risk factors included operate at different levels of causality, for example a proximate factor causing AWD or cholera could be poor water supply and sanitation, yet a more distal factor could be seasonal weather shocks or flash flooding. For the purpose of this paper the risk factors were considered as equally impactful, despite their varying causal proximity. Reliance on crude, secondary sources will also have resulted in some inaccuracy in the classification of risk factors. Moreover, the binary nature of our risk factor classification does not reflect the gradation occurring in reality, for example, displacement occurs in almost all crises, but is extremely common in some, such as South Sudan. More nuanced conceptual frameworks for risk factors can be developed and would be useful for more refined analyses.

There is a possibility of observer bias within the grading of VPDs per crisis. To mitigate against this, a published algorithm was used; however subjective analysis based on a personal understanding of the various contexts may have impacted the grading in some instances.

5. Conclusions

This review provides evidence that vaccine use in humanitarian crises is insufficient and may not align with disease burden. Humanitarian actors and relevant stakeholders should progress to a more consistent, broader and appropriate approach to vaccine provision.

As a potential general blueprint, we suggest that within the first weeks into a rapid-onset crisis, where possible, a standardised vaccination package consisting of measles, OCV, PCV, rotavirus and the pentavalent vaccine should be systematically offered, with potential adaptations (target age ranges, selection of vaccines) based on a small set of pre-defined crisis typologies (e.g. mass displacement) and broad epidemiologic settings (e.g. risk of cholera transmission). This package could be delivered through an initial, multi-antigen mass campaign unless robust evidence exists that immunity levels are sufficient to avert excess mortality. In accordance with the SAGE Framework [5], single- or reduced-dose regimens should be considered to increase operational feasibility, for vaccines that offer reasonable effectiveness even below the recommended regimen. In the weeks following crisis onset, a HPV campaign targeting all girls aged 9–14 years at a minimum should also be conducted, extended to older age groups if high levels of SGBV are suspected or predicted.

Beyond this initial response (i.e. in the crisis' protracted phase), a vaccination working group composed of technical and operational experts should be established, under the umbrella of the coordination mechanism. The group should be tasked with systematically completing the decision-making exercise laid out by the SAGE Framework [5], refine the initial package to include any other vaccines, set out a maintenance strategy consisting of an appropriate mix of routine and mass campaign modalities, and regularly review the vaccination package for appropriateness (i.e. responsiveness to disease burden) and performance (coverage, equity, efficiency).

To enable this more proactive and systematic approach, the Humanitarian Mechanism should be strengthened to include all available vaccines, and dedicated, rapid-release, flexible funding should be made available to support vaccination actors, including emergency preparedness and standing capacity. Advocacy for the development and licensing of more affordable vaccines also remains paramount to ensure children and adults have permanent, equitable access to vaccination.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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