CONCEPT NOTE

Grading the risk of a serotype 2 vaccine-derived polio virus (VDPV2) outbreak in Tier 3 and 4 countries

Background

In its recent meeting of April 2017, SAGE discussed the evidence on the role of IPV in stopping transmission of WPV/VDPV2. Because IPV primarily offers a complementary benefit in stopping poliovirus WPV/cVDPV transmission, the primary vaccine of choice to eliminate WPVs and respond to cVDPVs remains OPV - in any of its two current formulations, bOPV and mOPV2. However, in countries using bOPV for routine immunization, IPV has a significant role in protecting children against poliomyelitis caused bycVDPV2 through routine immunization. This use of IPV in routine immunization is especially important as population immunity for type 2 continues to decrease in the period post-switch.

After the globally synchronized switch from trivalent to bivalent OPV conducted in April 2016, Sabin virus type 2 appears to have disappeared from the both the environment and in AFP samples, outside countries with mOPV2 use. However, Nigeria detected several VDPV2 in the environment in Bauchi, Gombe and Sokoto in 2017. As a consequence, SAGE expressed concern over the ongoing circulation of VDPV2 in Nigeria.

Related to the use of IPV and the medium-term availability of vaccine for low risk countries, as defined by tier 3 and 4 criteria, the SAGE concluded:

1. IPV supply should be prioritized for use in routine immunization (especially in Tier 1 and 2 countries); and
2. WHO should review its tier classification of countries with respect to prioritization of IPV to take into account the size of the population with no IPV protection and the recent type 2 VDPV events.

Risk assessment methodology

Following the request from the SAGE, an analysis of the risk of a serotype 2 vaccine-derived poliovirus (VDPV2) outbreak was assessed in all tier 3 and 4 countries based on the following four risk factors:

1. Estimated number of children under 5 years old susceptible to type 2 poliovirus

Serotype 2 population immunity, the size of the birth cohort and routine immunization coverage were strongly correlated with cVDPV2 emergence and spread in Nigeria. In Tier 3 and 4 countries, routine immunization with a serotype 2 containing vaccine stopped in April 2016, and so routine immunization with polio vaccine is irrelevant from this point in time. The number of children under 5 years old without serotype 2 immunity in April 2017 was therefore estimated based on average serotype 2 population immunity levels in April 2016 in this age group (estimated using vaccination coverage data from children with AFP and campaign data), the number of children under 5 years old and the size of the birth cohort in each country.

2. Child mortality rate as a proxy for poliovirus transmission efficiency (reproduction number)

Some populations have historically been less likely to suffer large polio outbreaks. In Africa, a good predictor of (WPV) polio outbreaks is the under-five mortality rate, alongside other variables such as population immunity and exposure to migrants from endemic countries. This variable is likely to correlate with health care access and socioeconomic status of the population, and so is included as proxy for poliovirus transmissibility.

3. Migration from countries with circulating VDPV2 (Nigeria, Pakistan, DRC and Syria in 2016-17)

Travel to and from countries with cVDPV2 represents a risk of imported cVDPV2. Based on data from the UN Population Division, the number of permanent migrants by origin and destination (UN Population Division) can indicate the international spread of polio better than data on air travelers and tourists and other non-permanent movement (gravity models). In this model, the flow of migrants from Nigeria, Pakistan, DRC and Syria are classified as a risk for imported cVDPV2.

4. Reported number of people with primary immunodeficiency shedding vaccine-derived poliovirus (iVDPV) during 2000-2012.

Countries were scored for risk from iVDPV2 shedding using data from the WHO database on iVDPVs reported between January 2000 and April 2017.

Scoring and outputs

Based on the above framework, countries were assigned a score for each risk factor based on their rank: top quartile scored 2 points, within the inter-quartile range scored 1, bottom quartile scored 0 points.

In the case of risk from iVDPV, scores were calculated differently: countries reporting an iVDPV case (any serotype) who continued to shed poliovirus were given a score of 2; those reporting iVDPV who had ceased shedding, died or whose status was unknown were given a score of 1; and all other countries were given a score of 0.

A total risk score was calculated by summing these scores, weighting the first risk factor (estimated number of children under 5 years old susceptible to type 2 poliovirus) more heavily by a factor of 3. Different weightings of the scores can change the overall ranking of a country.

Based on the above methodology, countries among the Tier 3 and Tier 4 that are graded at highest risk of a serotype 2 vaccine-derived poliovirus (VDPV2) outbreak are, in order of priority: Iran, Egypt, Tanzania and Sudan. These countries would benefit from immunization with IPV sooner than later, either through the routine programme or in a catch up[1] campaign if they are able to do fIPV.

Tier 3

	Susceptibility	*Transmission*	*Exposure*	*iVDPV*	*Total score from 12 (weighting susceptibility x3)*
Iran	2	0	2	2	**10**
Egypt	2	0	2	1	**9**
Sudan	2	1	1	0	**8**
Côte d'Ivoire	1	2	2	0	**7**
Burkina Faso	1	2	1	0	**6**
Burundi	1	1	2	0	**6**
Senegal	1	1	1	0	**5**
Eritrea	1	1	1	0	**5**
Nepal	1	0	1	0	**4**
Sierra Leone	0	2	1	0	**3**
Guinea-Bissau	0	2	0	0	**2**
Tajikistan	0	1	0	0	**1**
Turkmenistan	0	1	0	0	**1**

Tier 4

	Susceptibility score	*Transmission score*	*Exposure score*	*iVDPV score*	*Total score from 12 (weighting susceptibility x3)*
Tanzania	2	1	2	0	**9**
Viet Nam	2	0	1	0	**7**
Ghana	1	1	2	0	**6**
Rwanda	1	1	2	0	**6**
Togo	1	1	2	0	**6**
Zambia	1	1	1	0	**5**

[1] Catch up is defined as the immunization activity designed to reach and immunize with IPV those children that did not receive a type 2 containing vaccine since the switch date (globally considered as the 1 May 2016). If a country introduce in RI but does not conduct the catch up simultaneously, the cohort for the future catch up activity would be the cohort between 1 May 2016 until the day of national introduction in RI.

Malawi	1	1	1	0	**5**
Zimbabwe	1	1	0	0	**4**
Uzbekistan	1	1	0	0	**4**
DPR Korea	1	0	0	0	**3**
Lesotho	0	2	0	0	**2**
Swaziland	0	1	0	0	**1**
Sao Tome and Principe	0	1	0	0	**1**
Comoros	0	1	0	0	**1**
Djibouti	0	1	0	0	**1**
Gambia	0	1	0	0	**1**
Cape Verde	0	0	1	0	**1**
Bhutan	0	0	0	0	**0**
Kyrgyzstan	0	0	0	0	**0**
Mongolia	0	0	0	0	**0**
Moldova	0	0	0	0	**0**

Note on Tier 4 country analysis: immunity estimates were only available for Tanzania, Malawi, Gambia and Zambia. For all, other countries it was assumed that immunity is 50% and applied that to the under-5 population. Therefore, some countries that appear in the higher risk score may move to lower risk after estimation of true immunity which is expected to be higher than 50%

PAHO countries and countries that have currently vaccine have not been included in the above tables. For a full list of countries in each tier, see Annex 1

Recommendations

1. The risk assessment model that has been used for slotting tentative timelines for supply allocation to countries. Countries at the highest risk are recommended for RI introduction as soon as supply is available. Countries are encouraged to consider fractional dose implementation and if so, supply could be slightly advanced in time.

2. The timelines are the based on the "maximum supply requirement", this is, that is based on all countries using full dose and therefore, not conducting catch up campaigns at this time as there is not enough supply to cover routine introductions and catch up with full dose. Catch up can only be considered at present if conducted by fractional dose, due to the supply constraints mentioned.

3. Full dose catch ups will not be possible until 2019 (exact timelines to be confirmed during 2018). The SAGE WG, meeting in Geneva in September 2017, will discuss on this issue and might make additional recommendations on the catch up activities.

4. WHO and UNICEF should prepare clear communications to relevant countries to share the revised timelines and global plans and to guarantee that countries will be prepared to introduce when vaccine becomes available.

Annex 1: Complete lists of Tier 3 and 4 countries

Tier 3

Bangladesh	SEAR
Burkina Faso	AFR
Burundi	AFR
Cote d'Ivoire	AFR
Egypt	EMR
Eritrea	AFR
Guinea-Bissau	AFR
Iran	EMR
Nepal	SEAR
Senegal	AFR
Sierra Leone	AFR
Sudan (the)	EMR
Tajikistan	EUR
Turkmenistan	EUR
Thailand	SEAR

Tier 4

Albania	EUR	Maldives	SEAR
Algeria	AFR	Mauritius	AFR
Antigua and Barbuda	AMR	Mongolia	WPR
Argentina	AMR	Morocco	EMR
Bahamas (the)	AMR	Namibia	AFR
Barbados	AMR	Nauru	WPR
Belize	AMR	Nicaragua	AMR
Bhutan	SEAR	Panama	AMR
Bolivia	AMR	Paraguay	AMR
Botswana	AFR	Peru	AMR
Cabo Verde	AFR	Republic of Moldova	EUR
Chile	AMR	Rwanda	AFR
Colombia	AMR	Saint Kitts and Nevis	AMR
Comoros (the)	AFR	Saint Lucia	AMR
Cook Islands	WPR	Saint Vincent and the Grenadines	AMR
Cuba	AMR	Samoa	WPR
Djibouti	EMR	Sao Tome and Principe	AFR
Dominica	AMR	Serbia	EUR
DPR Korea	SEAR	Seychelles	AFR
Ecuador	AMR	Solomon Islands	WPR
El Salvador	AMR	Sri Lanka	SEAR
Fiji	WPR	Suriname	AMR
Gambia (the)	AFR	Swaziland	AFR
Georgia	EUR	Macedonia	EUR
Ghana	AFR	Togo	AFR
Grenada	AMR	Tonga	WPR
Guatemala	AMR	Trinidad and Tobago	AMR
Guyana	AMR	Tunisia	EMR
Honduras	AMR	Tuvalu	WPR
Jamaica	AMR	Tanzania	AFR
Kazakhstan	EUR	Uzbekistan	EUR
Kiribati	WPR	Vanuatu	WPR
Kyrgyzstan	EUR	Venezuela	AMR
Lesotho	AFR	Viet Nam	WPR
Libya	EMR	Zambia	AFR
Malawi	AFR	Zimbabwe	AFR