



Paediatric Association of Nigeria (PAN) Immunization Guidelines: An Update (2023)

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Background

Immunisation is one of the cost-effective public health interventions targeted to prevent up to four million deaths annually.^{1,2} Despite the achievements that accrue to immunisation, many children do not receive their requisite vaccinations. Therefore, vaccine-preventable diseases remain a major cause of morbidity and mortality in children. In Nigeria, pneumonia,

diarrhoea, meningitis, measles and pertussis contributed to 40% of under-five mortality in 2019.³ Of 5.2million global under-five deaths in 2021, Nigeria contributed the largest number of fatalities - 850,000.⁴ Although Nigeria has made some progress in the reduction of under-five, infant and neonatal mortalities, these statistics do not compare favourably with global, African and indeed the Sustainable Development Goal target for 2030 (Table I).

Table I: Comparison of U5MR, IMR and NMR between Nigeria, Africa and the World*

	Under-five mortality rate				Infant mortality rate		Neonatal mortality rate			
	1990	2000	2021	2030 ^β	1990	2021	1990	2000	2021	2030 ^β
Global	93	76	38	25	65	28	37	31	18	12
Africa	178	151	73		107	50	45	40	27	
Nigeria	209	182	111	-	124	71	50	46	35	

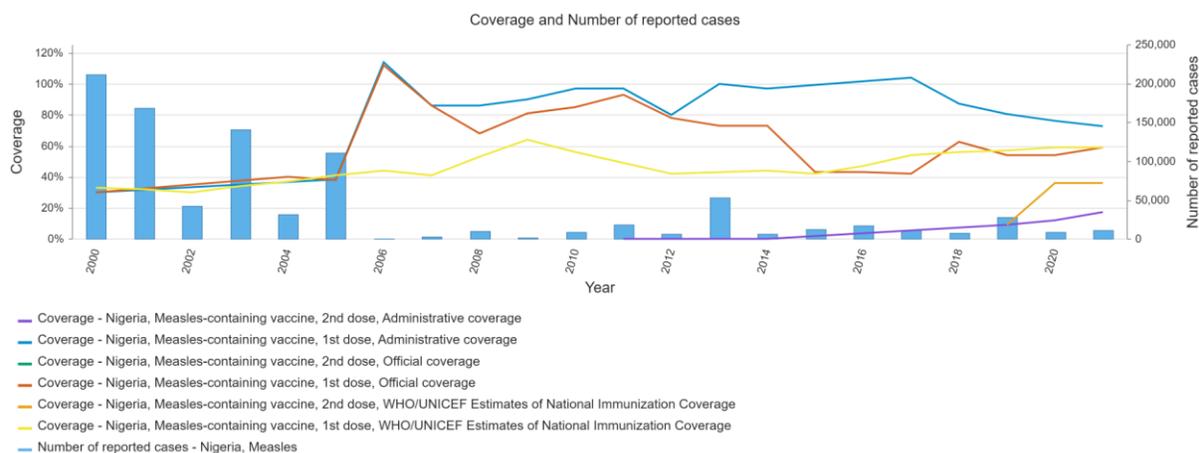
*Data is from State of the World's Children 2023⁴ ^βSustainable Development Goal target for 2030

A review of the immunisation landscape in Nigeria shows that the country's formal immunisation programme started in 1974 with the Expanded Programme on Immunization, which targeted six diseases.⁵ Over the years, there have been additions to the programme. Currently,

13 diseases (Tuberculosis, Poliomyelitis, Hepatitis B, Diphtheria, Pertussis, Tetanus, Haemophilus influenzae type B infections, Pneumococcal infections, Rotavirus diarrhoea, Measles, Yellow Fever, Meningococcal infections and the recently included Human

Papillomavirus infections) are targeted.⁶ Nigeria has had challenges with achieving high immunisation coverage. This necessitated a new approach with a high thrust for universal child immunisation, resulting in 80% coverage for all antigens between 1988 and 1990.⁷ This coverage was not maintained and has continued to fluctuate. It is, however, pertinent to note that despite the suboptimal coverage levels, immunisation has contributed to reductions in the

prevalence of target diseases, as shown in Figure 1.⁸ The reductions and increase in the prevalence of measles mirror the increase and reduction in immunisation coverage emphasises the fact that immunisation makes an impact on vaccine-preventable diseases. Thus, improving performance in the immunisation space in Nigeria is likely to contribute to achieving the SDG for under-five, infant and neonatal mortalities.



Source: WHO Immunization Data portal
 Date of export: 11/17/2022
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Figure 1: Measles vaccine coverage and reported cases of measles⁸

The Paediatric Association of Nigeria (PAN) guidelines for childhood immunisation were first published in 2012 (See Table II) as a follow-up to a position paper submitted to the Nigerian government in 2008.⁹ These guidelines are long overdue for updating since their lifespan has exceeded the recommended five years. New evidence and information have accrued, and new vaccines have emerged to prevent old and new diseases. The updated guidelines, while ensuring compliance with international best practices, are intended to guide the use of vaccines in the country as a whole (both within the national

guidelines and outside the national guidelines) as well as ensure that the use of vaccines is timely, comprehensive and in tandem with empirical evidence.

The updated guideline is intended for use by the Federal Ministry of Health, the Nigerian Immunization Technical Advisory Group (NITAG), the National Primary Health Care Development Agency (NPHCDA), Paediatricians and other healthcare workers in private and public

institutions, parents, other key policymakers and vaccine funders.

Methods

The members of the Child Health Watch Committee (a standing committee of PAN) were requested to update the PAN-recommended guideline on immunisation. The committee comprises general paediatricians, paediatric infectious diseases experts, neonatologists and neurologists. The extant guideline was scoped to identify potential areas for updating. WHO immunisation guidelines and the American Academy of Pediatrics and Canadian immunisation guidelines were reviewed.^{10,11,12}

The Nigerian immunisation landscape was reviewed, including historical perspectives, trends in immunisation coverage, child mortality and vaccine-preventable diseases. Key questions (PICO questions) were then formulated (Appendix 1). Evidence, which included systematic reviews and meta-analysis (where available), narrative reviews, original articles, and case reports/reviews, were searched for from different databases (Pubmed, Medline, Cochrane, Google Scholar, Scopus, EBSCO and Web of Science). Evidence summaries were prepared. The evidence available was then graded using the criteria set out in Table III.¹³ Following the grading of the evidence, recommendations were made. Where evidence was not available, consensus agreements were made. Recommendations were also made based on international best practices and WHO recommendations. The updated guidelines were sent to experts for external review.

PAN Updated Immunization Guidelines

The updated PAN immunisation recommendations (Table II) are based on the

principles of vaccinology, which include that the recommendations be based on the epidemiology of the disease, the age-specific morbidity and mortality, risk of adverse events, the efficacy and effectiveness of the vaccine, cost-effectiveness and age of recommended health care visits.¹⁴ The current guidelines, based on empirical evidence, recommended a longer, minimal interval of eight weeks between vaccines with multiple doses, specifically, the Pentavalent vaccine and pneumococcal conjugate vaccine.¹⁰ It was noted that there was a shortage of studies on immunogenicity in the Nigerian population to establish the non-inferiority or otherwise of the schedule with four weeks intervals being utilised in the national programme vis-a-vis adequacy of immune response and duration of protection/ the need for boosters. While recognising the need for a delicate balance between utilising schedules that generate maximum responses and completing the schedule before exposure to the risk of disease, it is imperative to note that many countries operate schedules with shorter intervals with good outcomes.¹⁵ Data from Nigeria also suggest adequate protection in infancy, but the waning of immunity in the second year of life indicates a need for boosters at this age.¹⁶ This is also the case for schedules with longer intervals.¹⁷ The new recommendation is for shorter intervals and boosters in the second year of life.

We recommend using two doses of inactivated polio vaccine and three doses of oral polio vaccine in addition to a birth dose, as this regimen offers better protection against the Type 2 poliovirus. We also recommend three doses of the Rotavirus vaccine instead of two in tandem with WHO recommendations based on the choice of *the Rotavac*® vaccine used in the national programme.¹¹

Child Health Watch Subcommittee of PAN & Others

Table II: PAN Immunization Guidelines showing old and updated recommendations

Recommended Age	Recommended vaccine(s)	Dose(route)	Guidance	Recommendation
Birth	Bacille Calmette Guerin (BCG)	0.05ml for 0-11 months 0.1ml for ≥12 months (Intradermal)	Test for evidence of tuberculosis infection (Mantoux test or Interferon-gamma) before giving if the child is older than six months.	Old
	Oral Polio Vaccine (OPV 0)	Two drops (Oral)	Skip if older than two weeks	Old
	Hepatitis B Vaccine	0.5ml (Intramuscular or Subcutaneous)*	Give at birth or within 24 hours of birth	New
6 weeks	OPV1	Two drops (Oral)		Old
	Rota 1	5 drops (Oral)	Skip if older than 23 months	New
	IPV 1	0.5ml (Intramuscular or Subcutaneous)*		New
	Penta 1	0.5ml (Intramuscular or Subcutaneous)*		Old
	PCV 1	0.5ml (Intramuscular or Subcutaneous)*		Old
Ten weeks	OPV2	Two drops (Oral)		Old
	Rota 2	5 drops (Oral)		Old
	Penta 2	0.5ml (Intramuscular or Subcutaneous)*	Time interval between Penta 1 and 2 reduced from 8 weeks to 4 weeks	New
	PCV 2	0.5ml (Intramuscular or Subcutaneous)*	Time interval between PCV 1 and 2 was reduced from 8 weeks to 4 weeks	New
14 weeks	OPV3	Two drops (Oral)		Old
	Rota 3	5 drops (Oral)		New
	IPV 2	0.5ml (Intramuscular or Subcutaneous)*		New
	Penta 3	0.5ml (Intramuscular or Subcutaneous)*	Time interval between Penta 2 and 3 reduced from 8 weeks to 4 weeks	New
	PCV 3	0.5ml (Intramuscular or Subcutaneous)*	Time interval between PCV 2 and 3 reduced from 8 weeks to 4 weeks	New
9 months to 12 months	MCV 1(MMR or MR)	0.5ml (Intramuscular or Subcutaneous)*		Old
	YF	0.5ml (Intramuscular or Subcutaneous)*	No boosters required	New
	Multivalent Meningococcal vaccine	0.5ml (Intramuscular or Subcutaneous)*		New
15 months	MCV 2(MMR or MMR+V or Measles + V)	0.5ml (Intramuscular or Subcutaneous)*		Old
	DTaP booster or DTwP	0.5ml (Intramuscular or Subcutaneous)*		Old
18 months	Hepatitis A	0.5ml (Intramuscular or Subcutaneous)*		Old
2 years	Typhoid	0.5ml (Intramuscular or Subcutaneous)*		Old
5 years	OPV	Two drops (Oral)		Old
	DTap	0.5ml (Subcutaneous)*		Old
	MMR	0.5ml (Intramuscular or Subcutaneous)*		Old
9 – 14 years	HPV	0.5ml (Subcutaneous)*	For males and females	New
	Tdap	0.5ml (Subcutaneous)*		Old
≥15 years	Td	0.5ml (Subcutaneous)*	For all females and males who are receiving immunisation for the first time.	New

*Intramuscular injections should be given in the anterolateral aspect of the thigh if <2 years and subcutaneous in the deltoid muscle if ≥ 2 years. Bold entries represent new recommendations.

Table III: Criteria used for grading the evidence

Quality	Definition	Implication
High	The guideline development group is very confident that the true effect lies close to that of the estimate of effect.	Further research is very unlikely to change confidence in the estimate of the effect.
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Further research is likely to significantly impact confidence in the estimate of the effect and may change the estimate.
Low	Confidence in the effect estimate is limited: the true effect may differ substantially from the true effect's estimate.	Further research is very likely to have an important impact on confidence in the estimate of the effect and is likely to change the estimate.
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.	Any estimate of the effect is very uncertain.

A multivalent meningococcal vaccine is recommended for children and adolescents, having had the experience of vaccinating with monovalent meningococcal type A vaccine and a subsequent epidemic was due to serotype C, necessitating the use of a different vaccine to break the chain of transmission.¹⁸ The multivalent vaccines offer coverage over the commonest four serotypes (A, C, W and Y) or five serotypes (A, C, W, Y and X) causing disease.

Specific advisories for individual vaccines are presented below.

Bacille Calmette Guerin (BCG)

Nigeria is one of the highest-burden countries for tuberculosis, with an estimated prevalence of 467,000 cases in 2021, of which children contributed 15% (69,000 cases).¹⁹ BCG administration is one of the strategies for the prevention of tuberculosis. BCG is effective in preventing severe forms of tuberculosis in children. It is recommended to be given to every healthy newborn as soon after birth as possible. BCG may be given at any age subsequently, but it is recommended that Mantoux testing is done before its administration in children older than six

months to determine if the child is already exposed to the infection. If the Mantoux test is positive and the evaluation excludes tuberculosis disease, the child should receive tuberculosis preventive therapy.²⁰ (Old recommendation)

Polio

Nigeria was declared polio-free on 25th August 2020 but continues to record high numbers of paralysis caused by circulating vaccine-derived polioviruses due to low population immunity occasioned by low immunisation coverage.²¹ There are two types of polio vaccines: the oral polio vaccine, which has been instrumental in eradicating polio globally and in Nigeria, and the inactivated polio vaccine, which is given intramuscularly. While the deployment of oral polio vaccine in mass campaigns is easier with the added advantage of providing immunity at the gastrointestinal mucosa, it has been associated with the emergence of circulating vaccine-derived polioviruses, especially in areas with low population immunity due to low vaccination coverage.²¹ These circulating vaccine-derived polioviruses are now the major causes of polio-associated paralysis. Administering IPV before a

course of oral polio vaccine reduces the risk of vaccine-derived polio paralysis compared to oral polio vaccine alone.²²

PAN recommends achieving high coverage with the existing polio vaccines (birth dose of OPV, three doses of OPV at six, ten and 14 weeks and two doses of IPV at six and 14 weeks in tandem with WHO recommendations. (New recommendation)

Hepatitis B Vaccine

Nigeria is classified as endemic for Hepatitis B.²³ The hepatitis B vaccine was introduced twenty years ago, precisely in 2003.¹⁰ It is not known if the level of endemicity has reduced in addition to the fact that coverage with at least three doses of hepatitis B-containing vaccine has been suboptimal. The Hepatitis B vaccine should be given as soon after birth as possible (within 24 to 48 hours), which has been shown to reduce vertical transmission.²⁴ In the current guideline, this is extended up to two weeks.⁹ It is not known what the impact of this extended period of administration has on vertical transmission. This requires further interrogation in research. In a study on serological markers of Hepatitis B in Nigerian infants prior to receipt of their first immunisation, it was shown that a significant proportion (29.6%) had markers of Hepatitis B infection.²⁵ We recommend that the Hepatitis B vaccine be given at birth or within 24 hours. (Strong evidence and new recommendation)

Due to the low coverage of the third dose of hepatitis B-containing vaccine, many children grow into adolescence under-unimmunised. The World Health Organisation recommends a catch-up vaccination with three doses of the Hepatitis B vaccine, which is given using a 0-, 1-, and 6-month schedule.¹¹ (New recommendation)

Diphtheria, Pertussis, and Tetanus (DPT)-containing vaccine: Diphtheria remains endemic in Nigeria with recurrent epidemics.²⁶ Diphtheria

is a highly fatal infectious disease with a mortality rate of 5-10%. It is caused mainly by *Corynebacterium diphtheriae*. Diphtheria is vaccine-preventable, and Nigeria has been using the vaccine since 1974.⁵ The World Health Organization (WHO) recommends three doses of a diphtheria toxoid-containing vaccine as the primary series given within the first six months of life and three booster doses to be given in the second year of life, between four and seven years, and between nine and 12 years.¹¹ It is well documented that although the initial three doses generate adequate immunity, this wanes over periods depending on the epidemiological situation.²⁷ In developing countries with poor living conditions, overcrowding, and poor personal and environmental hygiene, natural boosting of immunity occurs, providing and maintaining immunity levels.²⁷

Nigeria only gives three doses of a diphtheria-containing vaccine at six, ten and 14 weeks with no boosters. While epidemiologically, Nigeria had poor living conditions in the past, this has improved, at least in some parts of society, so natural boosting of immunity may have decreased.²⁸ Also, the introduction of immunisation is known to reduce the circulation of *C. diphtheriae*, reducing the opportunity for exposure and boosting immunity.²⁷ A recent study on a nationally representative sample of children confirmed waned immunity among children, with only infants (less than one year) having minimal protection of up to 80%.¹⁶ There is evidence of sustained immunity till 39 years and probably beyond with the six-dose regime.²⁹

Tetanus is endemic in Nigeria. It is caused by *Clostridium tetani*, whose toxin is highly fatal. Although some studies have shown that immunity remains adequate in under-fives, the national survey showed that there was low immunity, especially in the age group between two and five years of age, suggesting the need for

booster doses.^{16,30} Also, studies have shown that a significant proportion of those who develop post-neonatal tetanus were not immunised at all or were partially immunised, and up to 59% of cases occur in adolescents.³¹⁻³³ The World Health Organization recommends primary doses in infancy at six, ten and 14 weeks, followed by three booster doses, preferably given during the second year of life (12–23 months), between four and seven years of age, and between nine and 15 years of age.¹¹

Pertussis

Nigeria is also endemic for pertussis. Cases are under-reported mainly because of the difficulty in making a bacteriological diagnosis. It is caused by *Bordetella pertussis*, an organism requiring a special isolation medium. Studies have shown that immunity wanes following primary immunisation.³⁴ We recommend booster doses at 15 months, five years, and between nine and 14 years, followed by the three doses in infancy, which are given at six, 10, and 14 weeks. (Strong evidence) (New recommendation)

Haemophilus influenzae Vaccine: *Haemophilus influenzae type b* is one of the causes of invasive diseases such as sepsis, meningitis, and pneumonia, which are common causes of morbidity and mortality in Nigerian children. This vaccine is a component of the Pentavalent vaccine, and three doses are given at six, ten and 14 weeks. (New recommendation)

Pneumococcal conjugate vaccine

Streptococcus pneumoniae is the most common bacterial cause of pneumonia and is also associated with meningitis and sepsis. *S pneumoniae* also causes acute otitis media, sinusitis and bacteraemia. There are different types of pneumococcal conjugate vaccines, varying based on the number of serotypes covered. The ten-valent vaccine is used in the national schedule and offers cross-immunity with

the additional serotypes contained in the 13-valent vaccine. This vaccine is given at six, ten and 14 weeks. (New recommendation)

Rotavirus vaccine

Rotavirus-induced acute gastroenteritis (AGE) has been a major disease burden in Nigeria since it was first reported in 1985.³⁵ Prevalence rates have increased with severe public health consequences, particularly among children. The nationwide pooled prevalence of rotavirus infection among children below five years of age in Nigeria was 23% (CI 95%: 19–27).³⁶ The rotavirus vaccine is very safe, and it is effective at preventing rotavirus disease. Some studies suggest that rotavirus vaccination possibly causes a slight increase in the risk of intussusception, but this side effect is reportedly very rare.³⁵ The vaccine should be repeated if given during a diarrhoeal episode. Safety and effectiveness in infants with known primary or secondary immunodeficiencies, including infants with the Human Immunodeficiency Virus (HIV) infection, infants on immunosuppressive therapy, or infants with malignant neoplasms affecting the bone marrow or lymphatic system, have not been established so there is not enough evidence to make a recommendation for this group of children. We recommend three doses of rotavirus vaccine for all children younger than 23 months in tandem with WHO recommendations (New recommendation)

Measles Mumps Rubella vaccine

Measles remains a major cause of morbidity and mortality globally. Nigeria contributes a significant proportion of the global cases of measles.³⁷ The Majority of the cases of measles in Nigeria occur in children under the age of ten. Due to low immunity, the risk of mortality is higher in malnourished children, in war-torn areas, and in Internally Displaced Persons camps. Measles is caused by the highly contagious measles virus. High population immunity is

required to prevent outbreaks. Nigeria has continued to have recurrent outbreaks of measles.

Rubella, also known as three-day measles, is an infectious disease caused by the rubella virus. The disease affects males and females of all ages. The virus is transmitted through airborne droplets of infected people and is an acute but usually mild viral disease that commonly affects susceptible children and young adults worldwide. Rubella is significant because of the devastating teratogenic effect on the unborn foetus when pregnant women are infected. It results in Congenital Rubella Syndrome, which is a disease of major public health importance. Available data from Nigeria showed that the peak incidence of rubella occurs in the first four months of the year, with most of the cases occurring in those <15 years of age and cuts across rural and urban areas.³⁸

Mumps is a systemic disease caused by the mumps virus. Typically, it presents with swelling of one or more salivary glands, usually the parotid glands. Symptoms are milder, and complications are less common among vaccinated persons. Orchitis is the most frequently reported complication, with up to half of those affected developing testicular atrophy of the affected testicle.¹⁰ Other uncommon complications include oophoritis, encephalitis, pancreatitis, transverse myelitis and myocarditis. Mumps is preventable by immunisation.

Due to the high burden of measles in Nigeria, we recommend the Measles, Mumps and Rubella (MMR) vaccine to be administered at nine months of age and a second dose at the age of 15 months. (Strong evidence and new recommendation)

The MMR vaccine prevents rubella virus infection. The MMR vaccine is safe, effective, and affordable, providing lifelong protection for most people. MMR vaccination is 97% effective against rubella, 97% effective against measles,

and 88% effective against mumps. The MMR vaccine is recommended to be administered at 12-15 months.³⁹

Yellow fever vaccine

Yellow fever is a viral haemorrhagic condition that can cause a high fever and multi-organ damage. The national case fatality rate reported during a two-year outbreak period (2018-2020) was 2.9%, and delays between outbreak confirmation and vaccination response made the size of the outbreak worse.⁴⁰ These delays in response to reported outbreaks significantly impact containing outbreaks rapidly. The yellow fever vaccine is a live attenuated vaccine. A single shot provides lifelong protection for most people, and it is recommended for those aged nine months or older. The vaccine is safe and highly effective. It can give immunity and lifelong protection against the disease. Adverse reactions or serious events from the vaccine itself are very rare. The vaccine provides immunity within ten days for 80–100% of people, and within 30 days, more than 99% of vaccinated people are immune.⁴¹ A single dose confers lifelong immunity, and no boosters are required.¹¹ (New recommendation)

Meningococcal vaccine

Neisseria meningitidis is a major cause of bacterial meningitis and septicaemia worldwide, with high case fatality rates and serious lifelong complications among survivors. Twelve serogroups are recognised, of which six (A, B, C, W, X and Y) are responsible for nearly all cases of invasive meningococcal disease (IMD).¹⁸ Nigeria is one of 26 countries in sub-Saharan Africa that constitutes the meningitis belt, which has witnessed repeated epidemics of meningococcal meningitis.¹⁸ The proportions of cases of IMD caused by the five common serotypes (A, B, C, Y, and W135) vary among different regions and within specific geographic locations.

The introduction of meningococcal C conjugate vaccines in the early 2000s was associated with a rapid decline in meningococcal C disease, whilst the implementation of a meningococcal A conjugate vaccine across the African meningitis belt led to near-elimination of meningococcal A disease. Consequently, other serogroups have become more important causes of IMD. In particular, the emergence of a hypervirulent meningococcal group W clone has led many countries to shift from monovalent meningococcal C to quadrivalent ACWY conjugate vaccines in their national immunisation programmes.

More recently, the WHO pre-qualified a pentavalent meningococcal vaccine that is effective against serotypes A, C, W, Y and X, while the Strategic Advisory Group of Experts have recommended that countries in the meningitis belt should recommend this vaccine as it is cheaper.⁴² Nigeria witnessed an epidemic due to the C serotype in 2016-2017 after the introduction of the Meningococcal A conjugate vaccine.¹⁸ Meningococcal vaccines are generally safe, but side effects, which are usually mild, can occur. These side effects include redness, pain/soreness or swelling at the site of injection, fever, fatigue, headache, muscle or joint pain, nausea or diarrhoea.

We recommend a multivalent Meningococcal vaccine for all Nigerian children at the age of nine months. (Strong evidence and new recommendation) The choice of the quadrivalent or the newer pentavalent vaccine will depend on the locale-specific efficacy and safety data.

Human papillomavirus vaccine

The human papillomavirus is the causative organism of over 95% of cervical cancer. It also causes vaginal cancer, oropharyngeal cancer, penile cancer, anal cancer and other conditions

like warts. The human papillomavirus is mainly transmitted sexually. Cervical cancer is the commonest gynaecologic cancer in Nigerian women.⁴³ There are currently bivalent, quadrivalent and nonavalent Human papillomavirus vaccines that have been licensed and are being used in many countries. Human papillomavirus vaccines are effective in preventing infection with the high-risk virus serotypes (16 and 18) known to cause over 70% of cervical cancers if given before sexual exposure. We recommend a single dose of the HPV vaccine to children aged nine to 14 years. (Strong evidence and new recommendation)

Varicella vaccine

Varicella is a highly contagious disease caused by the Varicella Zoster Virus (VZV). It is endemic in tropical countries and transmitted via airborne droplets, saliva, skin-to-skin contact, touching contaminated surfaces or by vertical transfers from mother to baby through pregnancy, labour or nursing. It causes self-limiting, itchy, blister rashes known as chickenpox but can be severe and even life-threatening in people with weakened immune systems. It is responsible for a lot of school days lost among children. A Nigerian study reported that 60% of children aged four to six years were seropositive for varicella antibodies.⁴⁴

One dose of varicella vaccine prevents 95% of moderate disease and 100% of severe disease. A two-dose schedule is recommended for vaccinating children against VZV at 12 to 15 months of age and four to six years of age, respectively (New recommendation). For children older than six years, including adolescents, we recommend two doses of the vaccine given three months apart for those aged six to 13 years and four to eight weeks apart for those older than 13 years.⁴⁵ (Old recommendation) If given to those who are not immune within five days of exposure to chickenpox, it prevents most cases of the disease.

The varicella vaccine is very safe and effective at preventing varicella. Most of the side effects of the vaccine are mild.

Hepatitis A Vaccine

Hepatitis A is a highly contagious liver infection caused by Hepatitis A virus and spreads through contaminated food or water or by contact with an infected person. It can cause mild to severe illness, does not cause chronic liver disease, but rarely causes acute liver failure. It occurs sporadically and in epidemics, especially in low- and middle-income countries. Hepatitis A infection can be prevented with an inactivated Hepatitis A virus vaccine administered intramuscularly in a single or two-dose regimen.⁴⁶ (Old recommendation)

The first dose is recommended at 12 to 23 months, and the second dose is given at least six months later. Older children and adolescents (2 - 18 years) without prior vaccination should be vaccinated. Live attenuated vaccines can be used for children 18 months and above as a single subcutaneous dose.⁴⁶ These vaccines offer 95% protection against the virus, and the protection lasts for at least twenty years or possibly for life.⁴⁶ The World Health Organization recommends including the Hepatitis A vaccine in national schedules for children ≥ 12 months if there is an increasing trend of acute Hepatitis A disease or a change in endemicity from high to intermediate and if it is cost-effective.⁴⁶

Vaccines for special situations

The following vaccines are given in specific epidemiologic situations and for particular groups of children.

Cholera Vaccine: Cholera is an infectious disease caused by the bacterium *Vibrio cholerae*, which is spread through ingesting food or water contaminated with the bacterium. It is a highly virulent disease that causes severe acute watery diarrhoea, dehydration and death within hours if

left untreated.⁴⁷ Cholera is a global threat to public health and remains endemic in many countries, including Nigeria.⁴⁷ A multifaceted approach is required to prevent cholera, including active surveillance, water, sanitation and hygiene, early treatment, and vaccination. The “Ending Cholera: A Roadmap to 2030”, an initiative launched in 2017, focuses on the use of oral cholera vaccine in cholera “hotspots” as one of the main strategies.⁴⁷

The oral cholera vaccine (OCV) provides acceptable protection in young children. It is recommended for individuals aged two to 64 years travelling to areas with current or recent cholera outbreaks.⁴⁸ Two doses are generally required, given seven days to six weeks apart. Children aged two to five years require a third dose.^{48,49} We recommend cholera vaccine for children at risk or traveling to “Cholera hotspots.” (Old recommendation)

Influenza vaccine: Influenza viruses are highly contagious and can cause an acute respiratory infection that may result in severe illness, especially in children with comorbidities such as asthma, neurological disorders and sickle cell anaemia. Influenza is a viral illness mainly affecting the nose, throat, bronchi, and, occasionally, the lungs. Influenza is known for its unique ability to cause recurrent epidemics and pandemics during which acute febrile respiratory illnesses occur in all age groups. In Nigeria, surveillance data suggest year-round activity of the virus.⁵⁰

Influenza vaccination is currently the most effective way of preventing both seasonal and pandemic influenza. The World Health Organization (WHO) has recommended vaccination against this virus for children aged six to 59 months, pregnant women, older adults, people with chronic diseases, and healthcare providers. There are two types of vaccines

available – live and inactivated, both of which can be used in children. The influenza vaccines have to be administered annually. The low prevalence of flu in Nigeria and other logistics, such as the ability of the national programme to reach every child yearly, preclude this recommendation. However, influenza poses significant health risks for those with comorbidities. We, therefore, recommend annual flu vaccination for children with comorbidities such as asthma, congenital heart diseases and neurological disorders. (Low evidence and new recommendation)

Pneumococcal Polysaccharide Vaccine: *S. pneumoniae* is known to cause severe invasive bacterial disease. Higher valent vaccine types, such as the 23-valent pneumococcal polysaccharide vaccine (PPSV23), have been recommended for children with certain special health situations or conditions who may be at increased risk. This is in addition to the pneumococcal conjugate vaccines used for the general population of children. These include children with sickle cell disease, post splenectomies, chronic conditions like chronic liver disease, post transplantations, cancer therapies and other immunodeficiency states. It is recommended that caregivers of eligible children be made aware of the benefits of this vaccine, and it should be made available for their use.⁵¹ In general, children aged two to 18 years with the aforementioned underlying medical conditions should receive PPSV23 at least eight weeks after completing all recommended doses of PCV13. Furthermore, an additional second dose (booster dose) of PPSV23 is recommended five years after the first dose of PPSV23.⁵¹

COVID-19 Vaccine: COVID-19 infection has been ravaging the world since 2020 and global data indicates that adults are predominantly affected.⁵² However, specific categories of children (usually older than five years) living in areas or regions with high COVID-19 endemicity,

as well as those with some chronic medical conditions or morbidities and immunocompromised conditions, are at risk of severe disease.⁵² Nevertheless, COVID-19 infections among children are reported to have less morbidity, severity and mortality compared with adults.⁵²⁻⁵⁴ WHO recommends three doses and two doses, respectively, for children aged six months and above with immunocompromised states (high priority) and children with severe obesity and other chronic health conditions that put them at COVID-19 risk (medium priority), while other children outside these two groups (low priority group) are to receive vaccine based on country public health policy.⁵²⁻⁵⁴

In Nigeria, little is known about the scope and burden of COVID-19 in children, as most research and interventions have been geared towards the adult population. However, available literature suggests a clinical disease mimicking most prevalent tropical diseases like severe malaria and sepsis with seemingly low mortality.⁵⁵ We, however, recommend (in keeping with the Nigeria National Primary Health Care Development Agency recommendations) COVID-19 vaccination for travel purpose or education purpose among children aged 12-17 years and above visiting regions of high COVID-19 endemicity.⁵⁶

Malaria vaccine: Nigeria accounted for 27% of global malaria cases in 2021 and also contributed significantly to deaths from malaria.⁵⁷ The Majority of the deaths occur among under-five children. The RTS, S, and R21 vaccines are malaria vaccines that have been shown to significantly reduce malaria cases among recipients.⁵⁸ Both malaria vaccines are administered in three doses. However, Nigeria will require a review of effectiveness and safety data in addition to the logistics of introducing the vaccine to determine the time and schedule of introduction.

Typhoid vaccine: Typhoid fever is caused by *Salmonella* species and is a common cause of morbidity and mortality in sub-Saharan Africa. The disease is associated with poor socioeconomic amenities and food and water sanitation. It is thought to be endemic in Nigeria and is more common in children than speculated.^{59,60} WHO recommends vaccination from six months to 45 years in areas where typhoid fever is endemic.

The typhoid conjugate and the Vi polysaccharide vaccines have been pre-qualified by WHO. Live attenuated Ty21 and Vi capsular polysaccharide vaccines targeted at *S. typhi* are not very effective in young children against other forms of salmonella in areas where the burden of invasive *Salmonella* disease is highest.⁶¹ This is because typhoid fever accounts for less than half of the burden of salmonella disease as the non-typhi species are also common in these places.⁶² However, due to the prevalence of multi-drug resistant strain of *Salmonella typhi* in children, it is recommended to give conjugate vaccine as it has been found to protect against drug-resistant *S. typhi*.⁶³⁻⁶⁶

- The inactivated typhoid vaccine is administered as an injection. It may be administered to children aged two years and older. One dose is recommended at least two weeks before travel. Repeated doses are recommended every two years for people who remain at risk.
- Live typhoid vaccine is administered orally. It may be given to people aged six years and older. Four doses are taken as a capsule every other day. The last dose should be taken at least one week before travel. Each capsule should be swallowed whole (not chewed) about an hour before meals with cold or lukewarm water. A

booster vaccine is needed every five years for people who remain at risk.

Cautious use of vaccines in children

The vaccination of children with the following conditions should be approached with caution:

Inborn errors of immune deficiency - Vaccination in these conditions can increase adverse reactions or cause the disease itself; hence, it should be avoided until the type of immune deficiency is determined. Generally, live or bacteria vaccines should not be given and should be avoided in children with severe combined immune deficiency (SCID), but toxoid or inactivated vaccines can be given. Other vaccines should be prioritised based on benefit versus risk considerations. Both the patient and the caregivers should be vaccinated. Killed, inactivated, mRNA, or subcomponent vaccines can be used.^{67,68} Live vaccines, like oral polio vaccines, should be avoided. Other vaccines like rotavirus, Bacille Calmette-Guérin (BCG), varicella vaccines, and measles vaccine should be used with caution and avoided if the immune deficiency is severe. Caregivers who received live vaccines should avoid close contact with these groups of children for some period.^{67,68}

For patients with immune deficiencies, antibody levels should be checked often as they may require more frequent booster doses for *Haemophilus influenzae* type b (Hib), PCV, tetanus toxoid or acellular pertussis than children without inborn errors of immune deficiency. This monitoring can be done following the administration of pneumococcal vaccine, acellular pertussis vaccine and diphtheria toxoid.^{67,68}

HIV-infected children - Children with Human Immunodeficiency Virus (HIV) infection should be vaccinated according to the immunisation schedule, but live vaccines should be avoided if the disease has progressed to AIDS.^{69,70}

Preterm infants - Preterm infants who weigh more than 1500gm should be vaccinated as they can mount up immune responses appropriately. Not vaccinating preterm infants can be devastating as they are equally prone to bacterial and viral infections. Vaccination is relatively safe for these children.⁷⁰⁻⁷⁴

Children with malignancies - Children with malignancies may be revaccinated before the commencement of chemotherapy if they are seronegative to any of the common childhood infections. However, live vaccines should be avoided.⁷⁵

Combination vaccines

These are single-product antigens that prevent multiple diseases or multiple strains of the same infectious agent. Their use is attractive for various reasons, including reducing the number of injections a child receives, reducing the cost of stocking and administration, reducing the cost of extra health care visits, improving vaccine coverage and timeliness, reducing drop-out rates and introducing new vaccines. With children receiving three injections at six and ten weeks and possibly four vaccines, with the potential introduction of a malaria vaccine, it is expedient to consider using the hexavalent vaccine instead of the current pentavalent vaccine. The hexavalent vaccine will, in addition to the current content of the pentavalent vaccine, include the inactivated polio vaccine. However, efficacy, effectiveness, and safety studies of the Nigerian population will be required.

Catch-up Vaccination

Catch-up vaccination is regarded as evidence of a strong immunisation programme, and the WHO recommends that national programs have catch-up vaccination regimens.⁷⁶ Catch-up vaccination refers to the act of vaccinating an individual who missed or has not received doses of vaccines for

which they are eligible.⁷⁶ In Nigeria, the need for catch-up vaccination is evident with perennially low vaccine coverage levels. This suggests that many children become susceptible to vaccine-preventable diseases in adolescence and adulthood. Many studies also show that a significant proportion of cases of vaccine-preventable diseases occur in older children and adolescents who were under-vaccinated as children.³⁰⁻³² Catch-up vaccinations serve as opportunities to complete the vaccination of those who missed some of their vaccines in infancy while also providing vaccination for those who did not receive any vaccination in infancy.

Conclusion

Immunisation remains a vital resource for safeguarding population health. Immunisation recommendations are based on several considerations, including epidemiological profiles of diseases, vaccine efficacy, and safety profiles. Some of this crucial information is not available for many diseases in Nigeria. Systematic reviews and meta-analyses are important resources needed to develop or update guidelines. These were hardly available for many of the vaccines or diseases in Nigeria. Research on disease incidence at the national level, immunogenicity studies, duration of immunity and safety profiles for vaccines are required to fill the gaps. The conduct of systematic reviews also depends on the availability of these studies. The updated PAN immunisation recommendations are expected to guide the appropriate use of vaccines among Nigerian children to reduce morbidity, mortality and disability from vaccine-preventable diseases. This updated guideline will be disseminated to paediatricians, governmental agencies and other relevant stakeholders for advocacy and implementation.

The PAN-recommended catch-up vaccination schedule is depicted in Tables IV and V.

Table IV: Catch-up vaccination for children aged below five years

Clinical scenario	Guidance
Child aged <3 years no vaccination at all	Follow the schedule, omitting birth doses except for BCG. Observe caveats for the rotavirus vaccine.
Child aged <3 years incompletely vaccinated	Tuberculin Sensitivity Testing if older than six months. Observe caveats for rotavirus vaccine. Complete the schedule. Do not restart.
Child aged >3 years but <5years with no vaccination at all	Follow the schedule, omitting birth doses except for BCG. Do a tuberculin sensitivity testing if the child is older than six months. Observe caveats for rotavirus vaccine. Use Tdap-containing vaccine rather than DTaP
Child of uncertain immunisation status	Omit birth doses if older than two weeks. Check for BCG scar. If present, give all other vaccines according to schedule, except BCG. If absent, give all vaccines according to schedule but do Tuberculin Sensitivity Testing before giving BCG if the child is older than six months.

Table V: Catch up vaccination schedule for children aged 5-18 years who have never been vaccinated

Vaccine	Guidance	Recommendation
BCG	Do a TST and vaccinate if negative	Old
Hepatitis B	Three doses (Given at 0, 1 and 6 months)	New
Tdap	Three doses given at least four weeks apart	Old
Yellow Fever	One dose	New
Quadrivalent Meningococcal vaccine	One dose	New
HPV	One dose male and female from age nine years	New
Td	Five doses for male and female older than 15 years	New
Varicella	Two doses given three months apart in the age group 6-13 years and 4-8 weeks apart in those aged >13years	New

Plan for scheduled review and update

This guideline will be reviewed and updated in the next five years of completion of the final draft.

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Authorship role: The members of the Child Health Watch Subcommittee of the Paediatric Association of Nigeria and the others listed on this document participated in literature reviews, reviews and grading of evidence, drafting of the guidelines, and revision of the draft for sound intellectual content. They all approved the final version of the guideline draft. Therefore, all the individuals listed on this document (members of the Child Health Watch Subcommittee and others) are recognised as authors of these guidelines.

Conflict of Interests: Members of the Child health Watch Subcommittee and the other authors declare no conflict of interest.

Financial Supports: None.

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APPENDIX 1

PICO QUESTIONS FOR UPDATING PAN IMMUNISATION GUIDELINES

1) Do Nigerian children need booster doses to reduce the incidence of VPD?

P – Nigerian children

I – Booster doses

C – Compared to not having booster doses

O – Reduced incidence of vaccine-preventable disease

a) Are there sero-epidemiological studies that show that the titres in Nigerian children are lower after primary immunisation series or that they wane over time?

b) Are there epidemiological data that show increased vaccine preventable diseases amongst older children who were immunised in infancy thus suggesting waned immunity?

2) Are there new childhood vaccines that should be included in the Nigerian immunisation schedule?

P - Nigerian children

I - New vaccines

C - Compared to not receiving the new vaccines

O - Reduce incidence of the diseases prevented by the new vaccines

a) What is the epidemiological evidence that children are at significant risk to warrant these vaccines being included in the schedule?

b) What is the evidence that these vaccines are effective?

3) Do we need a catch-up immunisation schedule for Nigerian children who did not get/complete the primary immunisation schedule to protect them from vaccine-preventable diseases?

P - Nigerian children

I - Catch-up vaccination for those who missed/did not complete the primary immunisation schedule.

C - Compared to not receiving catch-up doses of vaccine

O - To reduce vaccine-preventable diseases

a) What is the evidence that those who did not get/did not complete the primary immunisation series are at increased risk for vaccine-preventable diseases at older ages?

b) What is the evidence that the use of a catch-up schedule improves vaccination coverage and reduces the incidence of vaccine-preventable diseases in general and in older age groups?

4) Do we need a vaccination schedule to protect Nigerian adolescents from vaccine-preventable diseases?

P – Nigerian adolescent

I – Immunisation

C – Compared to not receiving vaccines

O – Reduced vaccine-preventable diseases in this group

a) What is the evidence that supports an adolescent schedule, and what should be included in it?

b) Which vaccines are available for use in adolescents globally?

c) What evidence exists about the safety and effectiveness of these vaccines in adolescents?

5)

a) What other vaccine-preventable diseases present in the schedule are not being given universally?

b) What are the reasons for their restricted use?

c) Which target group(s) require(s) them?

d) Are there other guidelines that address the use of these vaccines in the targeted age groups?