Immunization Newsletter

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The Immunization Program in the Context of the COVID-19 Pandemic*

(30 March 2020)

Objective

- Provide guidance regarding the operation of immunization programs in the context of the COVID-19 pandemic.

Key Considerations

- In December 2019, a new coronavirus (SARS-CoV-2) was identified as the causative agent of a severe acute respiratory disease (COVID-19) in Wuhan, China.[1,2] The virus spread to different countries and the World Health Organization (WHO) declared a pandemic on 11 March 2020.[3]
- There are still some uncertainties in the natural history of SARS-CoV-2, including sources, transmission mechanisms, and persistence of the virus in the environment. Person-to-person transmission has been documented, with an incubation period of 2 to 14 days.
- There is currently no vaccine available against SARS-CoV-2. WHO has launched a project[4], which aims to coordinate and accelerate the development of this vaccine. As of 26 March, there are 2 candidate vaccines that have already started clinical trials and 52 that are in the preclinical phase.[5]
- Meanwhile, in the context of the COVID-19 pandemic, health systems are facing a rapid increase in demand. When health systems are overwhelmed, both direct outbreak mortality and indirect mortality from preventable and treatable conditions, such as vaccination, increase dramatically. In fact, an analysis of the 2014-2015 Ebola epidemic suggests that the increase in the number of deaths caused by measles, malaria, HIV/AIDS, and tuberculosis attributable to health system failures outnumbered deaths from Ebola.[6]
- Therefore, WHO recommends that vaccination should be considered an essential health service that should not be interrupted.

Recommendations

- The following are recommendations on vaccination and epidemiological surveillance for vaccine-preventable diseases (VPDs) in the context of the COVID-19 pandemic in the Region of the Americas, which were consulted on by members of PAHO's Technical Advisory Group (TAG) on Vaccine-preventable Diseases, and are aligned with recommendations from WHO's Strategic Advisory Group of Experts (SAGE) on immunization.[7]
- These recommendations are preliminary and are subject to review as new evidence becomes available.[8]

[1] Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020.

[2] [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi. 2020;41(2):145-51.

[3] World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 Geneva2020 [Available at: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020.

[4] World Health Organization. 2019 Novel Coronavirus. Global Research and Innovation Forum: Towards a Research Roadmap/report. [Available at: https://www.who.int/blueprint/priority-diseases/keyaction/Global_Research_Forum_FINAL_VERSION_for_web_14_feb_2020.pdf?ua=1]

[5] World Health Organization. DRAFT landscape of COVID-19 candidate vaccines – 26 March 2020. [Available at: https://www.who.int/blueprint/priority-diseases/key-action/Novel_Coronavirus_Landscape_nCoV_Mar26.PDF?ua=1]

[6] Elston, J. W. T., Cartwright, C., Ndumbi, P., & Wright, J. (2017). The health impact of the 2014–15 Ebola outbreak. Public Health, 143, 60-70.

[7] World Health Organization. Coronavirus disease (COVID-19) technical guidance: Maintaining Essential Health Services and Systems. Guiding principles for immunization activities during the COVID-19 pandemic. March 2020. [Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/maintaining-essential-health-services-and-systems]

[8] Updated information on COVID-19 is available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019

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IN THIS EDITION

What I Have Learned...

by Robert Steinglass

I have read each hard copy of the PAHO Immunization Newsletter since 1979. When I resided overseas, early issues of the Newsletter arrived like a breath of fresh air with the promise of new learning from the Americas. But I am getting ahead of myself…

My wife, new baby, and I were eating in a Georgetown, Washington, DC restaurant in 1977 when Dr. Ciro de Quadros walked past on the street. Newly graduated from The Johns Hopkins School of Hygiene and Public Health, I hadn't seen Ciro for years, since we worked in Ethiopia on smallpox eradication. He was excited about a new initiative called the Expanded Program on Immunization (EPI). He also mentioned vacancies for WHO smallpox surveillance officers.

I soon started a one-year assignment as WHO Technical Officer in North Yemen to collect evidence for the International Commission for the Certification of Smallpox Eradication. I was then appointed as WHO Technical Officer in the newly created EPI in North Yemen, where I remained for three more years as part of the first wave of WHO staff providing technical support initially to a handful of countries.

In those early EPI days, WHO had very few technical resource materials on building nationwide immunization programs in resource-poor countries. WHO gave me a blue, vinyl-covered, 2-volume set with a little guidance and also a box of 120 academic articles, most from the 1960's and even 1950's, primarily about vaccine-preventable diseases and vaccines in wide use (BCG, OPV, DTP, and measles). To a lesser extent,

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Announcement for Readers of the Immunization Newsletter

Dear Reader,

We would like to reduce printing quantities for the Immunization Newsletter. If you currently receive a printed copy and would like to receive it electronically instead, please email Octavia Silva at silvao@paho.org.

Thank you very much,

Cuauhtémoc Ruiz Matus, Octavia Silva, Martha Velandia

** The information in this article will continue to be updated as more evidence becomes available. Please visit https://www.paho.org/en/topics/immunization for the most updated information.*

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1. Routine Vaccination during the COVID-19 Pandemic

- Involve the National Immunization Technical Advisory Group (NITAG) in making decisions about continuing vaccination services.
- The decision to maintain immunization services will be determined by national guidelines on social distancing, the health system situation, the burden of VPDs, the context of local SARS-CoV-2 transmission (without cases, sporadic cases, conglomerates or community transmission), as well as other factors, such as demographic data and the availability of vaccines and supplies. Possible scenarios to consider are the following:

Scenario	Recommendation
1. If the capacity of the health system is intact and the provision of essential health services continues	Vaccination should be conducted through fixed posts, mobile posts, and coverage extension activities, guaranteeing fulfillment of the recommended measures for infection prevention and control[9,10] and safe vaccination. The population should be informed on the continuation of vaccination services, and the importance of attending scheduled vaccination appointments.
2. When only limited service provision is available	Prioritize vaccination of vulnerable populations with the highest risk of morbidity and mortality from VPDs (for example, older adults, people with chronic diseases, health personnel, pregnant women, children under 5 years of age, communities with active outbreaks of measles, diphtheria, yellow fever).
3. If vaccination cannot be performed safely, and the risk of SARS-CoV-2 transmission increases	Suspend vaccination activities until the risk of SARS-CoV-2 transmission has been reduced and the capacity of the health system has recovered sufficiently to resume these activities.

- In scenarios 1 and 2, vaccination against influenza and measles should be prioritized:
  - ***Influenza:*** The recommendation to vaccinate against influenza applies primarily to countries that, following WHO recommendations for the southern hemisphere, will apply the flu vaccine in the coming months. Vaccination of health personnel, older adults, people with chronic diseases, and pregnant women should be prioritized.
  - ***Measles:*** Consider applying the zero-dose strategy for children aged 6-11 months in municipalities with active outbreaks.
- In health establishments where vaccination activities are to be carried out, it is essential that health professionals be alert to signs and symptoms of respiratory illnesses and offer patients with flu symptoms a surgical mask and refer them for medical evaluation according to local protocols for initial approach to patients with suspected COVID-19.
- Routine use of medical masks by health professionals in the context of routine vaccination during the COVID-19 pandemic is not recommended.
- As institutional births will continue, vaccination of newborns must remain a priority in all settings.
- Countries with pneumococcal vaccination programs for older adults and people with high-risk conditions should maintain these programs whenever the administration of this vaccine is possible.

2. Vaccinating People Diagnosed with COVID-19 and their contacts

- Although there are currently no known medical contraindications to vaccinating a person with COVID-19, it is recommended to defer all vaccination until complete recovery, according to established criteria.
- Although there are currently no known medical contraindications to vaccinating a person who has had contact with a COVID-19 case, it is recommended to defer vaccination until quarantine has been completed (14 days after the last exposure).

3. Conducting Vaccination Campaigns

- Based on current knowledge of SARS-CoV-2 transmission, and recommended prevention measures for social distancing, it is recommended to temporarily suspend mass vaccination campaigns due to the risk of strengthening transmission in the community and in health establishments.
- If a VPD outbreak occurs, the risk-benefit of conducting outbreak response vaccination should be evaluated while considering the health system's ability to safely carry out this activity in the context of the current COVID-19 pandemic. This evaluation should assess the risk of a late response against the associated risks of an immediate response, both in terms of VPD morbidity and mortality, and the potential impact of increased SARS-CoV-2 transmission. If the decision to conduct a vaccination campaign is made, strict measures must be followed to protect health workers, safeguard the population, and ensure solid waste management. If the decision is to delay the outbreak response vaccination campaign, a periodic assessment of VPD morbidity and mortality will be required and the risk of further delaying a response will be considered.
- The countries that had planned this year to conduct follow-up campaigns against measles, rubella or human papillomavirus (HPV) should continue the micro-planning phase and postpone the implementation phase until conditions permit.

4. Guidance for Vaccination Posts

- Conduct vaccination sessions in well-ventilated areas that are frequently disinfected.[11]
- Ensure the availability of hand sanitizer or a hand washing station with chlorinated water for use by users at the entrance of the health facility.[11]
- Limit the number of family members accompanying the person to be vaccinated (one companion).
- Perform triage of persons presenting respiratory symptoms before admission to the vaccination posts to prevent the spread of SARS-CoV-2. If patient presents respiratory symptoms, offer medical mask, do not vaccinate, and refer to service for evaluation.
- Avoid crowded waiting rooms. Some strategies for this could include:
  - Scheduled times for vaccination appointments;
  - Integrate vaccination activities with other essential preventive health services, as appropriate;
  - Carry out small and frequent vaccination sessions;
  - Utilize outdoor spaces and adhere to the recommendation of social distance within the facility, or vaccination post;
  - Establish exclusive vaccination sessions for older people and people with pre-existing medical conditions (such as high blood pressure, heart disease, respiratory disease, or diabetes).
- Whenever possible, the vaccination post must be separate from healing services (i.e., different hours, different spaces);

[9] Pan American Organization. Requirements and technical specifications of personal protective equipment (PPE) for the novel coronavirus (2019-ncov) in healthcare settings. February 2020 [Available at: https://www.paho.org/en/documents/requirements-and-technical-specifications-personal-protective-equipment-ppe-novel]

[10] World Health Organization. Rational use of personal protective equipment (PPE) for coronavirus disease (COVID-19). March 2020 [Available at: https://apps.who.int/iris/bitstream/handle/10665/331498/WHO-2019-nCoV-IPCPPE_use-2020.2-eng.pdf]

[11] World Health Organization. Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected. March 2020. [Available at: https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125]

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- Recommendations for vaccinators:
  - Frequently maintain hand hygiene as described in "My 5 Moments for Hand Hygiene": i) Before touching a patient; ii) Before clean or aseptic procedures; iii) After body fluid exposure/risk; iv) After touching a patient, and v) After touching patient surroundings.[12]
  - Hand hygiene consists of washing hands with soap and water or with a hand sanitizer that contains between 60% and 80% alcohol.
  - Comply with guidelines on clothing: i) Use a uniform, which should be not used outside the health facility; ii) Use closed shoes; iii) Do not use accessories (for example: earrings, rings, chains, watches).
  - Clean cell phones properly. Do not use cell phone while providing medical attention.
  - If you experience symptoms, such as cough or fever, you should not be working and should seek medical attention.

5. Reestablishing Vaccination Services

- Vaccination services should be restored when the risk of transmission of SARS-CoV-2 has been reduced and the capacity of the health system has recovered enough to resume these activities. There will probably still be some level of SARS-CoV-2 transmission when services resume. It is likely that stricter infection prevention and control measures and social distancing practices are still needed in the early stages of resuming vaccination services. The NITAG should advise the country on how to resume service and what populations to prioritize.
- Once health services go back to normal, countries should intensify vaccination as soon as possible, even if routine vaccination has continued throughout the entire pandemic, since it is possible that the service delivery level was not optimal or the population was unable or unwilling to access the service. Therefore, the intensification of vaccination services should be a priority. Furthermore, the mass vaccination campaigns that were suspended due to the pandemic should be prioritized. It may be necessary to adjust the target age groups of the campaigns to consider the largest number of age cohorts with low immunity. Where feasible, other vaccines and health interventions should be integrated to maximize health benefits, facilitate recovery and minimize the burden of multiple campaigns. Micro-planning will need to be reevaluated, especially if services were interrupted for an extended period.
- The decision to establish vaccination services should be communicated in a timely manner to health personnel and the population.

6. Cold Chain and Vaccine and Supply Stock

- It should be noted that interruption of flights and manufacturing of vaccines and supplies can affect delivery plans.
- Monitor the stocks of vaccines and supplies, as well as the functionality of the cold chain.
- The existing cold chain storage capacity may need to be expanded if excess vaccines exist due to anticipated shipments and/or low use due to an unexpected decline in vaccination services. Countries should maintain an updated list of all potential facilities (public and/or private) with a functional cold chain to expand capacity if necessary.

7. VPD Epidemiological Surveillance

- Surveillance systems should continue with early VPD detection and case management, at least for diseases with global surveillance mandates and elimination and eradication objectives: measles, rubella, neonatal tetanus, polio.
- Countries should also prioritize surveillance of VPDs with epidemic potential: influenza, meningococcus, yellow fever, measles, rubella, diphtheria, and polio.
- Routine surveillance for other VPDs should continue as long as possible. When laboratory testing is not possible, samples should be stored appropriately for confirmation when laboratory capacity allows. Countries should ensure enough sample storage capacity at the provincial and central levels and monitor it regularly. It is recommended to review the conservation conditions for samples, according to the type of sample and event.
- If it is not possible that VPD surveillance systems continue to function normally, identify and maintain critical functions, such as active acute flaccid paralysis (polio) surveillance, outbreak monitoring and sending of urgent samples and laboratory confirmation of priority VPDs. To reduce the risk of exposure to SARS-CoV-2, active surveillance for polio can continue in a limited number of priority hospitals, provided the surveillance officer uses the appropriate personal protective equipment (PPE). If this is not possible, active surveillance should be carried out remotely (for example, via internet, telephone) as much as possible.
- If epidemiological surveillance activities are temporarily suspended due to the COVID-19 pandemic, countries should implement necessary actions to ensure continuity of activities and plan recovery measures, if necessary (for example: active searches for suspected measles/rubella cases).
- Since the laboratories performing tests to detect VPDs may also be responsible for conducting SARS-CoV-2 tests, it is important that countries retain the ability to identify priority VPDs, although potentially at reduced levels, with a decreased frequency.
- Optimizing and prioritizing the use of laboratory tests will be essential to ensure the sustainability of laboratory surveillance during the time of the pandemic and in the months immediately following. There is a risk of limited availability of reagents and laboratory supplies due to an interruption or decrease in production, and limited capacity for their international transportation.■

Are we speaking the same language? an argument for the consistent use of terminology and definitions for childhood vaccination indicators

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Effective communication is contingent on a shared use and understanding of language. This is no less true in the communication of research findings. In this commentary, we identify commonly used vaccination indicators and highlight inconsistencies in how childhood vaccine researchers use and define these terms. We propose the use of more standardized language to promote effective communication of research findings. For the purpose of this commentary, we define 'vaccination' as the administration of a vaccine to an individual, recognizing that vaccination and immunization are often used interchangeably in the literature.

What are vaccination indicators?

A 'health indicator' is a variable that can be directly measured to reflect the state of health of persons or a community and helps quantify the achievement of a result.[1,2] Establishing and monitoring health indicators enables effective surveillance of health states and program success, detection of public health risks, and identification of the need for policy or program improvements. Health indicators related to vaccination (e.g. vaccine coverage, up-to-date

[12] World Health Organization. My 5 Moments for Hand Hygiene [Available at: https://www.who.int/infection-prevention/campaigns/clean-hands/5moments/en/]

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vaccination) are critical public health indicators that permit ascertainment of individual and population protection from disease and monitor the effectiveness of vaccination programs. Vaccination researchers, as well as public health practitioners and policy-makers, commonly use vaccination indicators to measure and report vaccination targets and outcomes. Using clear and consistently defined terminology is essential to ensure that indicators can be compared between different time points, settings, and populations.

Commonly used vaccination indicators

The most frequently used vaccination indicators in the research literature include: vaccine coverage, uptake, and rate; vaccination status, initiation, and completion; and up-to-date, timely, partial, and incomplete vaccination. How these terms are used and defined varies throughout the research literature.

Vaccine coverage

The most common vaccination indicator is *vaccine coverage*. In the research literature, this term is typically used to report a proportion, specifically the proportion of a defined population that received a specific number of doses of a particular vaccine(s).[3–7] The Centers for Disease Control and Prevention (CDC) in the USA defines childhood vaccine coverage as the percentage of those children in the target population who received a dose of a recommended vaccine.[8]

The *numerator* in the coverage calculation differs across studies. In most, it is (as the CDC defines it) the number of children in the target age group who received a dose of a recommended vaccine[9-13], while in others it is the number of vaccine doses prescribed or dispensed,[14,15] with the assumption that every vaccine dose prescribed/dispensed equates to one person vaccinated. The numerator may report on (a) a specific number of doses of a vaccine, such as one dose of varicella vaccine[16] or the third dose of HPV vaccine[13]; or (b) a range of doses, such as children receiving ≥ 1 dose of HPV or influenza vaccine[9,17]; or (c) the number of children completing the vaccine series.[12,18]

The target population in the coverage *denominator* typically includes persons who are eligible for a specific vaccination program because they are considered at risk for disease, perhaps due to age, gender, or a pre-existing health condition, and are either residing in the jurisdiction of interest or are affiliated with a particular health centre/health insurance plan.[19,20] In some studies, the denominator is defined quite broadly, without consideration for whether the child is truly at risk for disease. For example, in annual coverage assessments of early childhood vaccines conducted by the CDC, the target population is defined as children aged 19-36 months[21]; and in a study by Jeannot, Sudre et al.,[19] the target population to be vaccinated with HPV vaccine was defined as 11-19 year old girls living in Geneva. Here, the assumption is made that all children in the denominator are actually eligible to receive the vaccine and/or at risk from the disease. Other studies explicitly limit the denominator to children who are susceptible to the disease. For instance, in studies by Giammanco et al. 2009[20] and Streng 2010,[16] the denominator only includes children susceptible to varicella (i.e. without history of having had varicella disease).

The choice of denominator and the ability to restrict it to children truly at risk is often driven by the availability and completeness of data sources. Thus, in practice, the target population is actually limited to the *accessible population*, which has implications for accuracy and bias in coverage calculations. For instance, a national/state population registry or census data can provide a fairly complete and unbiased denominator,[19,20,22,23] whereas a mail or phone survey of a sample of parents may be less so.[16,24]

While many studies explicitly define "coverage", including the numerator and denominator, in other cases, the definition is only implied. Most commonly, this is seen when the authors report coverage as a percentage without clearly articulating the numerator and/or denominator.[6,24–27] While in some cases, it is possible for the reader to deduce what is intended, the lack of definition leaves open the potential for misinterpretation of findings and makes comparison between studies/settings challenging.

Vaccine uptake

In contrast to the term vaccine coverage, *vaccine uptake* is most commonly defined as the absolute number of people who received a specified vaccine dose(s), i.e. the numerator in the vaccine coverage calculation For example, vaccine uptake of influenza vaccine has been reported as the number of recipients of ≥1 dose of the vaccine during the influenza season,[4,28] whereas influenza vaccination coverage for that influenza season would be the proportion of the target population who had received the vaccine.[4,29,30] As with coverage, uptake may also refer to the number of *doses administered*, rather than number of people vaccinated. For instance, some studies report on the total number of doses administered to the targeted population,[9,13] or even the number of vaccine doses dispensed or sold, rather than administered.[19,31–33]

Although less common, some studies report vaccine uptake as a proportion, and use/define it similarly to how the term "coverage" is defined in other papers.[23,34–37] This is sometimes done implicitly, for instance "pandemic influenza vaccine uptake was low at 11.1%;"[24] and "vaccine uptake was higher in children (32%)".[26] In other cases it was explicitly defined as such. For instance, "uptake was defined as the proportion of girls who had received each dose at the end of the study period out of the total number of girls, who were still part of the study population at the end of the study period"[23]; and "vaccine uptake was expressed as the number of individuals receiving at least one dose of an influenza A/H1N1 vaccine over the number of individuals invited, according to the vaccination database".[33]

Some studies even use the terms "uptake" and "coverage" interchangeably within the same paper.[33,35,38,39] For example, one study stated "*uptake* was higher in younger women (25–44 years) compared to younger men (8.2% and 5.9% respectively, $p < 0.001$), and conversely older men (aged 45+ years) had better *coverage* than older women (8.2% and 6% respectively, $p < 0.001$)" [33] (italics added). Another stated that "the programme achieved overall coverage of 71.5%… (and) a study …in Manchester, UK found a similar vaccine *uptake* … to our study, of 70.6%"[38] (italics added).

Interestingly, we are aware of one national body that uses the indicators coverage and uptake to both mean proportions but defines them different. Uptake is the "initiation but not completion of the vaccine series", while coverage is defined as "completion of the vaccine series by the recommended age".[40]

Although rare, we did note some studies that explicitly differentiate between coverage and uptake.[9,13] In their study of the HPV vaccine, Schmidt and colleagues[9] defined vaccine uptake as the absolute number of vaccine doses given to eligible participants, while they defined single-dose vaccine coverage as the proportion of eligible participants who had ever received ≥1 vaccine doses. In Limia & Pachon,[13] they define uptake as "the total number of administered doses (reported by health care professionals) in the targeted female population" and defined coverage as "the proportion of the targeted population that received the first and the third doses of any HPV vaccine". However, even in this paper that explicitly defined uptake as an absolute number and coverage as a proportion, the terms were sometimes used contrary to these definitions, for instance, "a high level of vaccine uptake (80.1%) was achieved".[13]

Finally, it is noteworthy that while the term "uptake" is commonly used as an indicator, it is also often used as a *verb*, referring to the behavior of receiving a vaccine. For example, "uptake of seasonal influenza vaccine has been shown to be a strong predictor of vaccination intention"[24]; "uptake of these vaccines may differ by age and race"[41]; and "a steady uptake of the programme was observed".[20]

Vaccination rate

The indicator *vaccination rate* is often used interchangeably with vaccine coverage in the research literature, but is rarely explicitly defined.[9,20,26–28,32,38,41–44] It is usually synonymous with coverage, e.g. "the vaccination rates are calculated from the numbers of vaccinated persons over the respective populations"[7] or in a paper by Ernst et al.,[45] where they state that changes in vaccination coverage by region are reported as vaccination rate per 100,000 children. Rarely, vaccination rate is used in the technically correct sense, i.e. "a measure of the frequency with which an event occurs in a defined population in a defined time".[46] For instance Tennis[47] stated, the "vaccination rate was calculated by dividing the number of children vaccinated in a cohort by the total child-days of follow-up within a cohort"; or Lin[11] stated "to calculate vaccination coverage rate, we divided the total number of children who were … vaccinated by the latest Census population estimates in the area for the corresponding year".

Vaccination status

The term *vaccination status* is not usually explicitly defined in the literature but is generally used as an overarching term that encompasses various categories of vaccine receipt, including vaccine initiation, vaccine completion, up-to-date vaccination, timely vaccination, partial and incomplete vaccination, and non-vaccination, as described below. At the population-level, vaccination status appears to refer to the proportion of the population with a given status.[25]

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Vaccine initiation

The term vaccine initiation necessarily only applies to a multidose vaccine series,[31,48,49] referring to receipt of the first dose in a given vaccine series.[50–54] A number of studies assess vaccine initiation as receipt of ≥1 dose of a vaccine,[50–54] such as "HPV vaccine initiation (receipt of at least one dose based on healthcare provider records)"[37]; and "vaccine initiation (receiving ≥1 dose of HPV vaccine)".[55]

Vaccine completion

Vaccine completion was defined in various ways in the literature. In some studies, it referred to receipt of all recommended doses for a particular vaccine series divided by the vaccine eligible population.[37,44,54,55] In others, it was defined as completion of the vaccine series among those who initiated the series (i.e. the denominator only included initiators, not the entire eligible population.[9,56] For example, Pathela et al.[56] defined completion as "the proportion of adolescents who received ≥3 doses among those who had ≥1 HPV vaccine dose". In both cases, the indicator could be more accurately referred to as vaccine series completion, but the choice of denominator should be clearly stated. In other studies, completion referred to the receipt of the requisite number of doses of *all vaccines in the recommended schedule*,[42,57] and was sometimes referred to as being *fully vaccinated*.[43,58] For example, Hull et al.[58] define fully vaccinated as the number of children who were completely vaccinated with the vaccines of interest by the designated age divided by the total number of children in the age cohort. When referring to "recommended doses" or "recommended schedule", it is important for researchers to identify the recommending body and the recommended series/schedule, as these recommendations vary between jurisdictions and over time. For instance, in February 2015, Canada's National Advisory Committee on Immunization changed their recommendation from 3 to 2 doses of HPV vaccine for immunocompetent individuals 9-14 years of age, but implementation of this change is not occurring simultaneously in the various jurisdictions across the country.[59] Thus, "series completion" may mean 2 doses in one jurisdiction, but 3 doses in another.

Up-to-date vaccination

The indicator *up-to-date vaccination* is generally used to describe individuals that have received recommended vaccines by a certain age or age range, or by a specific point in time, such as school-entry.[60–65] For example, "those (children) who received all 16 doses by 19 months of age";[65] and "received all of the vaccine doses required for school entry".[66] As noted in regard to vaccine series completion, the type, dose number, and timing of recommended/required vaccines are determined based on jurisdiction/country specific vaccination guidelines and thus should be specified in the report. An example of such reporting is from Dummer's study,[42] in which they present the Nova Scotia immunization schedule for children under two years of age at the time of the study and then specify that "a dose was up-to-date if it was administered according to the schedule, defined as within 1 month at ages 2, 4, 6, 12 or 18 months".

Timeliness/timely vaccination

Timely vaccination, also referred to as *age-appropriate vaccination*, is sometimes used interchangeably with up-to-date vaccination, to mean receipt of specified vaccines by a certain age or date.[57,67,68] For example, in Hug et al.,[57] timely vaccination is defined as "administration of ≥1 dose of MMR before 24 months (≥730 days) of age", while in Smith et al.[67] they define timely vaccination as "receipt of at least the recommended number of doses of each vaccine by age 19 months". However, it is most commonly used to refer to receipt of specified vaccines within a very limited and specified time period following the age at which the vaccines are due.[42,58,63,65,69] Common measure of timeliness are within 30 days,[58] 31 days,[65,69] 4 weeks,[12] or a month[42,63] of the recommended age. If children received a recommended childhood vaccine within the specified timeframe then they were considered to have received that vaccine in a timely manner.[67,68] Vaccination before that age is considered *early vaccination* and those given after the specified interval are *late vaccination*.[12,42] It should be noted that the cut-points for determining timeliness have an impact on the calculation of coverage rates. While there may be circumstances that dictate that only timely vaccines will be counted, there are other instances in which exclusion of doses administered after a very short lag (e.g. 1 month) will artificially lower the coverage. Thus, in some instances, calculation of timely vaccination should be accompanied by a calculation of coverage with a more lenient lag time.

Partial vaccination and incomplete vaccination

Partial vaccination and *incomplete vaccination* are two indicators that appear to have the same meaning, with some authors seemingly having a preference for one versus the other. Some authors use the term *partial vaccination* to refer to vaccination status that was not complete.[70–73] For instance, in Pabst et al.,[70] *partial vaccination* was defined as having received only one influenza vaccine dose when the child was recommended to receive two doses that season; and Moran et al.[72] considered children under the age of 9 years who only received 1 lifetime dose of influenza vaccine as partially vaccinated, compared to the required 2 lifetime doses to be considered completely vaccinated. Alternatively, other researchers[43,44,66,74] used the term incomplete vaccination to refer to people who were not completely vaccinated (i.e. they had not received all required vaccine doses for a vaccine series). The only study that we are aware of that distinguished between the two terms was Bell et al.,[75] who defined partial vaccination as receiving less than the recommended doses for at least one vaccine in the vaccine schedule, but having received some doses for any vaccine. Partial vaccination was then subdivided into *selective vaccination* (having received no doses of ≥1 vaccine while completing other vaccine series) and *incomplete vaccination* (having received ≥1 doses(s) of a multi-dose vaccine, but did not complete the series). While the definitions present a somewhat nuanced distinction, it was a useful method of operationalizing the categories of vaccine status in their study. The choice of term, partial versus incomplete, is not as important as ensuring that researchers define what is meant by the term chosen.

Non-vaccination

Non-vaccination is typically used to indicate no receipt of specified vaccine(s). The indicator is rarely defined explicitly, but has been used to mean failure to receive any doses of a given vaccine[16,27,42] or of all the vaccines in the recommended schedule[42,75] by a specified point in time. The assumption is often made that non-vaccination equates to unwarranted refusal of the vaccine. There is typically little mention of the fact that there are situations when vaccination is not recommended, e.g. due to a medical contraindication. Inclusion of these individuals in the denominator for calculation of coverage is warranted if the goal is to determine herd immunity, but not recommended if the goal is measurement of program performance. Since the number of non-vaccinators is typically small, this may not have implications at a population level for large geographic areas, but may result in meaningful difference in results for small populations, such as neighbourhoods or schools.

Population versus individual indicators

Many of the indicators used in the literature can be used to refer to both individuals and populations. For instance, vaccine completion and up-to-date vaccination status were used in the literature to refer to both individuals and populations. At the individual level, the terms indicated that a person had completed the vaccine series (or had received the specified number of vaccine doses by a certain age), while at the population-level the term referred to the proportion of the target population that had done so.[3,34,54] Other terms, such as vaccine coverage or vaccine rate are exclusively used to refer to populations.

Summary and recommendations

Many vaccination indicators are not explicitly defined within published research studies and/or are used quite differently across studies. Although the term *coverage* is most commonly used to refer to a proportion, not all authors clearly state the numerator and denominator that contribute to the calculation. It is also not uncommon for the terms *vaccination rate* and *vaccine uptake* to be used interchangeably with *coverage*, although *uptake* is more commonly used to mean the numerator in the coverage proportion. Other indicators that are often used interchangeably are *timely* and *up-to-date* vaccination.

The choice of indicator in a given study is typically predicated by program or vaccine specific factors, such as the local vaccination program schedule, the type of vaccine, and/ or the necessary number of vaccine doses (i.e. single versus multi-dose vaccines). For instance, vaccine series completion or dose-specific uptake and coverage would only be relevant for reports on multi-dose vaccines, e.g. HPV vaccine.

The choice of indicator may also be constrained by the data sources available. For instance, if there is no way to confirm administration of vaccine doses, the numerator may necessarily be the number of vaccine doses dispensed. In jurisdictions that cannot determine accurate numbers for the target population (i.e. no denominator available), researchers would be limited to reporting vaccine uptake (i.e. only the numerator). The ability to assess timeliness of vaccination is commonly limited due to data that can only report vaccination by a given age or time point, for example school entry, rather than being able to identify the exact date of vaccine administration.

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Table 1. Proposed standardized definitions of vaccination indicators.

	Definition	
Terminology	**Referring to an individual**	**Referring to a population**
Vaccine coverage	N/A	The proportion of the target (or accessible) population that received the specified number of vaccine doses. It is important for researchers to specify the nature of the target population, e.g., all persons in a specific population who are in the age group, vs. only those persons in the age group who meet eligibility criteria according to the named and specific recommending body.
Vaccine uptake	The behavior of accepting a vaccine.	The number of people who received a specified vaccine dose(s).
Vaccination rate	N/A	The proportion of the target (or accessible) population that received the specified number of vaccine doses, within a specific timeframe
Vaccination status	Receipt of vaccines categorized as non-vaccinated, vaccine series initiated, vaccine series completed, partially or incompletely vaccinated.	The proportion of the target population that have achieved the designated category.
Vaccine series initiation	Receipt of the first dose in a specified vaccine series. It is important to specify whether the denominator is all eligible individuals, or only those that initiated the series.	The proportion of the target population that have received the first dose in a specified vaccine series.
Vaccine series completion	Receipt of all recommended doses for a particular vaccine series (should specify who makes the recommendation and what the recommended series consists of).	The proportion of the target population that have received all recommended doses for a particular vaccine series.
Completely/Fully vaccinated	Receipt of all vaccines recommended by a certain age (should specify who makes the recommendation and what the recommended schedule consists of).	The proportion of the target population that have received all vaccines recommended by a certain age.
Up-to-date vaccination	Receipt of the recommended number of vaccine doses by a specified age, whether or not it was all doses required for series completion.	The proportion of the target population that have received the recommended number of vaccine doses by a specified age, whether or not it was all doses required for the series.
Timely vaccination	Receipt of specified vaccines within a time-limited period following the age at which it was due (most commonly, within 1 month of scheduled date). The age it is due and the lag time being applied should be specified.	The proportion of the target population that have received specified vaccines a time-limited period following the age at which it was due.
Partial vaccination or incomplete vaccination (there is no clear consensus on which term to use)	When referring to a multi-dose vaccine: Receipt of less than all required vaccine doses for a vaccine series. When referring to an entire vaccine schedule: Receipt of less than all required vaccine doses in the vaccine schedule.	The proportion of the target population that have received less than all required vaccine doses for a vaccine series or less than all required vaccine doses in the vaccine schedule.
Non-vaccination	No receipt of specified vaccine(s). If possible, researchers should specify if this includes individuals non-vaccinated for legitimate reasons, such as medical contraindication.	The proportion of the target population that have not received the specified vaccine(s).

N/A: Not applicable.

It is also important to choose the indicator that best reflects the outcome of interest. For instance, the performance of a vaccination delivery program is often evaluated based on the achievement of high vaccination coverage or vaccine series completion. Indicators like coverage also play an important role in assessing herd immunity within a population, which is critical to ascertain in a disease outbreak scenario. Other indicators, such as partial vaccination and non-vaccination, are useful for the assessment of the vaccine behaviours of a population (e.g. assessing the proportion of the population that starts but fails to complete the vaccine series versus those that refuse all vaccines). In contrast, indicators like timeliness of vaccination could be useful for assessment of individual protection or, conversely, period of time at risk from disease.

It is important for researchers to thoughtfully consider the most appropriate vaccination indictor(s) to use in reporting their findings and to explicitly define those indicators. In **Table 1**, we list the most commonly used vaccination indicators,

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and propose some standardized definitions based on key reference sources (e.g. CDC, WHO) and common usage in the research literature.

Conclusion

Poorly defined and inconsistent use of indictor terminology in vaccination research limits the communication of study findings. It also decreases the ability to compare findings across settings and time periods, which is necessary when conducting comparative effectiveness research of vaccine programs and delivery systems. It is strongly recommended that researchers in this field consider adopting standardized terms and definitions. We have proposed such definitions here, but see this as an opportunity to open dialogue on this issue, rather than issuing an edict about the best choice. Regardless, we do emphatically encourage researchers to exercise transparency in reporting how vaccination indicators are defined, including the components, i.e. the numerator and denominator, of all indicators. ■

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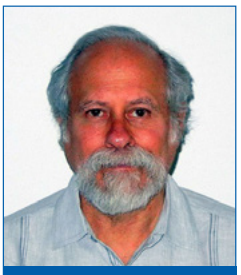
some operational aspects of immunization programs were included. For example, there were instructions on how to flame BCG needles between uses and boil used syringes and needles! What was largely missing from these resource materials was real-life experience implementing immunization programs in resource-poor countries, since such practical experience had rarely been compiled before EPI. Everything was new and field learning was prioritized; regional and global WHO offices were themselves eager to learn, since child vaccination coverage in most resource-poor countries was less than 10%.

After another six years with WHO technically supporting ministries of health (MOH) to establish the EPI in Oman and Nepal, I spent the next 30 years until my retirement last year leading an amazingly talented immunization team at John Snow Inc., (JSI) headquartered in Washington, DC, and in the field. We provided long- and short-term technical support to over 50 countries, mostly in Africa, Asia and the former Soviet Union, and to global partners like WHO, UNICEF and Gavi.

I especially enjoyed reading Newsletter articles on the experience of the Americas in government ownership, legislation, neonatal tetanus prevention, and the deliberations of advisory groups. I appreciated the voices of national managers bringing their field experience – the "HOW."



Robert Steinglass.

Early on, I recognized the need to tailor the rich Americas experience before exporting those lessons to other regions and countries, with extensive road networks and communications channels, educated cadres of health officials, relatively greater financial resources, committed national governments, active civil societies, etc.

I think the Americas experience of delivering services in urban slums – which governments sometimes don't even acknowledge exist, where social cohesion has been disrupted, and the MOH may not even have jurisdiction – could be shared better with the rest of the world. The EPI was designed 40 years ago based on a rural model. But the world is over half urban.

I also would have liked more practical information on operational issues such as preparing (beyond surveillance) for new vaccine introductions, sustaining political and community engagement for routine immunization, offering booster doses across the life course, reducing left-outs and drop-outs, using different vial size presentations (e.g., 5 dose MR vials), managing sharps waste disposal, engaging sectors beyond the MOH, and more about what other partners were doing in the Region. Over time, I came to wish that lessons learned elsewhere in the world on the above and other topics could be better captured in this regional Newsletter.

Over my long career, I have understood the importance of learning from the field and bringing the voice of front-line health workers to the attention of national, regional and global levels; and, conversely, the need to customize global, regional, and national policies/approaches at each successively lower level of the health system. I have learned that direct investment in and development of equitable and affordable routine immunization services must be done as an integral part of the wider health system (not as a byproduct of episodic campaigns), without which heavily donor-funded, vertical approaches have limited potential for sustainability. I have also learned that health workers are often under-supported and rely on those of us privileged to work at the top of the pyramid to advance approaches which can be most easily implemented at the bottom. ■

The objective of the "What I Have Learned…" column is to provide a space for immunization professionals from across the Americas to share their unique experiences and lessons learned. Individuals who are interested in authoring a column are encouraged to contact Octavia Silva at silvao@paho.org