Review Article

Novel Technologies for Intradermal Delivery of Fractional-Dose Inactivated Poliomyelitis Vaccine: A Review of Implementation Research and Implications for Equitable Vaccine Access

Garba Bello Bakunawa[1], Mortada El-Shabrawi[2], Rana Muhammad Safdar[3], Asmatullah Arab[3], Catherine Daly[4], Paul LaBarre[4]

1. National Primary Health Care Development Agency, Abuja, Nigeria; 2. Cairo University, Egypt; 3. Independent researcher; 4. PharmaJet (United States), Golden, United States

Introduction: Recent trends in intradermal (ID) vaccination, as seen in the Global Polio Eradication Initiative and in the 2022 monkeypox (mpox) pandemic, are a reminder that vaccine administration to the dermis is a valuable alternative to the traditional routes of parenteral delivery. Despite favorable policy toward ID fractional inactivated polio vaccine (fIPV) in anticipation of oral polio vaccine (OPV) cessation, and despite WHO's emergency-use authorization of fractional ID mpox vaccine in response to the 2024 mpox public health emergency of international concern, ID delivery remains an underutilized strategy with the potential for broader impact, including improved coverage and cost savings. We aim to provide a comprehensive review of the published implementation research on novel ID delivery methods used for fIPV immunization to better understand the available ID delivery options, their implementation challenges, benefits, and opportunities for broader use for ID delivery of other vaccines, including rabies, malaria, and mpox.

Methods: A literature search was conducted using PubMed to identify literature in any language, published between January 2015 and July 2024 with the terms "inactivated polio vaccine" and "intradermal delivery". We identified studies that included implementation research on novel alternatives to needle and syringe (NS) ID delivery of fIPV.

Results: Of the 59 publications identified in the search, 14 met the criteria as original studies on human subjects using novel delivery methods for ID administration of commercial fIPV vaccines. Six novel

 doi.org/10.32388/CLBYI9.2

technologies were identified. In general, novel ID delivery technologies compared favorably against NS delivery. Benefits of individual technologies include high acceptance among both healthcare workers and caregivers, improved coverage rates, and cost savings. Two alternative ID delivery technologies are commercially available. The needle-free technology, Tropis-ID® (PharmaJet), has the most extensive body of implementation research among the alternatives reviewed and is the only technology in this review to achieve WHO prequalification.

Conclusion: Novel technologies for ID delivery of fIPV are viable and, in some cases, offer advantages over ID delivery with NS. Commercially available needle-free ID delivery has been thoroughly researched for campaign use and shown to reduce costs and increase coverage for polio immunization programs. ID delivery using novel alternatives to NS can be a valuable strategy for increasing equitable access to vaccines and for addressing vaccine shortages during campaigns and pandemic response. Commercially available needle-free ID delivery can increase campaign reach, enable effective strategies such as house-to-house campaigns, and potentially empower personnel without formal health training to administer vaccines. These results also suggest alternative ID delivery methods should be evaluated in new vaccine development.

Corresponding author: Paul LaBarre, Paul.LaBarre@PharmaJet.com

Summary

- What is already known on this topic: ID delivery of vaccines has well-established immunological benefits. Strategies for ID delivery have been developed to reduce immunization costs and to extend limited vaccine stocks. Novel ID delivery technologies have been assessed individually and compared with other novel technologies and to the standard Mantoux technique in studies that include implementation research.
- What this study adds: Commercially available, novel, needle-free ID delivery technologies can increase campaign reach, enable effective strategies such as house-to-house campaigns, and potentially empower personnel without formal health training to administer vaccines.
- How this study might affect research, practice or policy: As coverage, acceptability, and cost-savings are prized benefits of ID delivery, novel ID delivery methods should be implemented with fIPV and further evaluated with other vaccines that have been validated for ID delivery such as post-exposure rabies vaccine and mpox.

Strengths and limitations of this study

- This is the most comprehensive review of the implementation research conducted on novel technologies for ID delivery of fIPV.
- The findings in this review are applicable to ID delivery of additional vaccines of public health and global health interest.
- Due to the inconsistent implementation research methods applied across the identified publications, statistical analysis of the findings was not possible.

1. Introduction

Polio vaccines: The World Health Assembly committed to the goal of polio eradication in 1988.[1] Since then, the number of polio cases has decreased by 99.9%.[2] Wild poliovirus types 2 and 3 (WPV2 and WPV3) have been eradicated[3] due to the Global Polio Eradication Initiative (GPEI), which has delivered polio vaccines to over 2.5 billion children since 1990.[4] However, many countries, including Nigeria, Somalia, and the Democratic Republic of Congo (DRC) are still affected by type 1 and type 2 circulating vaccine-derived poliovirus (cVDPV)[5] and wild type 1 (WPV1) remains endemic in Afghanistan and Pakistan.[6] In these countries, the number of paralytic cases[7] as well as the genetic lineages[8] of WPV1 have decreased over the past five years. Transmission has become increasingly isolated to austere settings characterized by political insecurity, poor healthcare infrastructure, vaccine resistance, and difficult-to-access geographies. Concurrently, there have been recent cases in regions that previously eliminated polio, including Gaza,[9] Malawi,[10] and Israel,[11] and evidence of circulating poliovirus in wastewater in Canada, Great Britain,[12] and New York City.[13]

Two main types of poliovirus vaccines, oral and injectable, have been widely used to prevent polio transmission and disease. Sabin oral poliovirus vaccines (OPVs) have enabled monumental gains in the eradication of polio and have many benefits, including ease of administration, low cost, and high primary intestinal mucosal immunity, which prevents viral shedding and further transmission. However, as a live attenuated vaccine, OPV can lose its genetic attenuations and, on rare occasions, become neurovirulent and cause vaccine-associated paralytic poliomyelitis (VAPP) in individuals. Vaccine-derived polioviruses (VDPVs), originating from OPV, are also transmissible and can cause outbreaks of circulating VDPV (cVDPV) and paralysis.[5] In areas with persistently low vaccine coverage rates, cVDPV can result in sustained person-to-person transmission. In 2016, in response to the risk of cVDPV2 after the

transmission of WPV2 was successfully interrupted, GPEI began a phased OPV withdrawal plan towards eventual OPV cessation with a switch from trivalent OPV to Type 1/3 bivalent OPV in routine immunization (RI) programs. Molodecky and Sutter (2024) recently co-authored an in-depth review of this "2016 switch".[14] According to World Health Organization (WHO) recommendations, use of all OPV in RI programs will be replaced by inactivated polio vaccine (IPV) following WPV1 eradication.[15][16]

Over the last few years, there have been significantly more cases of cVDPV than WPV.[5],[15] To mitigate cVDPV, novel OPV (nOPV) types have been designed to be more stable than Sabin OPV. Since 2020, nOPV-2 has been used extensively in the African region with an approximately 80%[17] reduced risk for cVDPV compared with OPV. Nonetheless, from January 1, 2024, to December 31, 2024, there were 234 confirmed acute flaccid paralysis cases of cVDPV globally, with ten cases of cVDPV1, 221 cases of cVDPV2, and 3 cases of cVDPV3.[7] During that same period, only 84 WPV1 cases were confirmed,[7] illustrating a 2.8:1 ratio of vaccine-derived cases for each wild-type case.

IPV is an injectable alternative to OPV that has been used widely in supplementary immunization activities (SIAs) and in outbreak response to mitigate the risk of wild and vaccine-derived poliovirus among children who have previously received OPV.[18] A recently published article (Sutter, 2024) highlights the challenges and opportunities of IPV with a review of the evidence base and gaps.[19] While IPV is more difficult to administer, more expensive, and less effective at inducing intestinal mucosal immunity compared with OPV, it is a valuable immunization tool. IPV produces protective antibodies in the blood and boosts intestinal mucosal immunity in OPV-vaccinated individuals.[18],[20][21][22][23] When sufficient coverage is achieved, exclusive IPV administration can break the seeding cycle propagated by OPV. All countries have introduced at least one dose of IPV (IPV1) into their RI schedules, and the WHO recommends a second dose of IPV (IPV2).[3] WHO guidance indicates that countries should fully transition to IPV for RI when poliovirus transmission is sufficiently low and regions have achieved high homogeneous coverage and good sanitation. Despite these recommendations, many countries continue to lag in adoption of IPV2 due to affordability and health system capacity.[24] A standard (full) 0.5 ml dose of IPV vaccine costs about 15 times as much as a dose of OPV.[25][26] This puts a financial strain on already overburdened health systems and poses a challenge to OPV withdrawal. Additionally, progress toward achieving high IPV coverage rates has been impeded by global vaccine hesitancy,[27] interruptions to immunization processes caused by the COVID-19 pandemic,[28] and international and regional supply shortages triggered by the increased global demand for additional doses of IPV.[29][30]

Intradermal delivery of fractional IPV: While the standard dose of IPV is delivered to the intramuscular (IM) compartment, delivery of IPV to the ID space offers several advantages. The dermis and epidermis of human skin are rich in the diversity and density of antigen-presenting cells. Smaller (fractional) quantities of many vaccines delivered intradermally can achieve high levels of safety and effectiveness.[31] ID delivery of a fractional, 0.1 ml (20% dose) of IPV (fIPV) has been investigated since 1953.[32] Studies in the 1990s established the immunogenicity of fIPV.[33] Increased reliance on IPV associated with the WHO OPV-withdrawal strategy, shortages resulting from IPV supply constraints, and high IPV prices catalyzed research on the fIPV immune response. Multiple studies have confirmed that seroconversion rates (defined for IPV response as a ≥4-fold increase over the expected decline in maternally derived antibody titers) following the complete, full-dose vaccination series were comparable between ID fIPV and IM full-dose IPV groups.[34][35][36][37][38] Two fIPV doses can achieve significantly higher seroconversion rates in older infants (nine to 13 months) than a single full dose of IPV.[39][40] A single fractional fIPV dose is as effective in boosting previously OPV-immunized adults as a full dose of IPV.[19] Additionally, an analysis of four fIPV immunogenicity studies concluded that two fractional doses are more immunogenic, achieving higher seroconversion and higher antibody titers, than one full dose.[41] A meta-analysis of ten studies found that the gap in seroconversion rates between fIPV and full-dose IPV rapidly declines with an increased number of doses such that three fractional doses of ID fIPV can achieve similar seroconversion to that induced by three full doses.[42] Experts have proposed replacing bivalent OPV with fIPV in countries moving to an IPV-only schedule, citing fIPV's safety record.[42] While a two-dose fIPV schedule administered at a younger age (e.g., six and ten weeks) evokes slightly lower seroconversion rates compared with two full IPV doses, these differences are minimized when two doses of fIPV are administered later (e.g., 14 and 36 weeks).[43] Several studies showed higher seroconversion rates with later-scheduled fIPV administration when compared with later-scheduled, full-dose, IPV administration.[35],[39],[44]

In addition to antigen-sparing benefits, fractional dosing of IPV can provide cost savings to countries. In a cost analysis of fIPV, researchers found that in RI and campaign settings, costs per child vaccinated with two doses of fIPV were lower than those with full-dose IPV delivery across all evaluated vial sizes and use scenarios.[45] Costs per fully vaccinated child were up to 48% lower in RI settings when fIPV was delivered with a needle and syringe (NS) compared with full-dose administration.[45] Implementation

studies in RI programs will further assess the coverage, costs, and feasibility of needle-free-delivered ID fIPV compared with NS-delivered IPV.[46][47]

Advancing ID fIPV policy: Beginning in 2016, WHO began to endorse fractional fIPV as a strategy that is safe, effective, cost-efficient, and has the ability to stretch constrained vaccine supplies.[48] The WHO Strategic Advisory Group of Experts (SAGE) began promoting fIPV dose-sparing by encouraging countries to evaluate the cost-benefits, trade-offs, and programmatic feasibility associated with a two-dose ID fIPV schedule.[49] Citing a deteriorating IPV supply situation and evidence supporting the high efficacy of two-dose ID fIPV, SAGE strongly recommended that countries start preparing for a two-dose fIPV schedule within RI and that IPV outbreak response campaigns should only be conducted with ID fIPV.[50][51] In 2017, SAGE strengthened this guidance to include a strong recommendation for RI use of fIPV.[52][53] That same year, the Pan American Health Organization (PAHO) Technical Advisory Group and the Africa Regional Immunization Technical Advisory Group (RITAG) both recommended the implementation of a two-dose fIPV schedule in their regions.[54] In 2018, SAGE reviewed the available data on fIPV and emphasized that two doses of ID fIPV are superior to one full IPV dose.[55] In 2019[56] and again in 2020[57], despite improved IPV supply, SAGE maintained existing fIPV recommendations enabling all countries to adopt a two-dose IPV schedule using either IM full-dose or ID fIPV. UNICEF and WHO published guidance indicating that countries can also achieve high levels of immunity against poliovirus types 1, 2, and 3 by providing two ID fIPV doses in RI programs.[58] In 2021, The Global Vaccine Alliance (GAVI) supported the use of fIPV-only schedules in countries in polio-free regions with high RI coverage.[59] The latest 2022 WHO position paper on polio vaccines indicates that the preferred IPV schedule, with the first dose administered at a minimum of 14 weeks of age and the second IPV dose given at least four months later, may be carried out using full-dose IPV or with ID fIPV without loss of immunogenicity.[3] In 2023, SAGE recommended that, in areas of persistent transmission, an additional IPV (full or fractional dose) campaign should be conducted alongside OPV to promote individual-level protection and reduce transmission by enhancing mucosal immunity.[60] Justifying the off-label nature of these recommendations, SAGE has emphasized that public health authorities such as SAGE and National Immunization Technical Advisory Groups (NITAGs) frequently make recommendations that differ from the labeled use, citing hepatitis A, human papillomavirus, influenza, pneumococcal, and yellow fever vaccines as examples.[50],[61]

ID delivery adoption: Despite this supportive global policy for ID fIPV, very few countries have adopted this delivery method. To date, only six countries (Bangladesh, Cuba, Ecuador, India, Nepal, and Sri Lanka) have adopted fIPV for RI. Several countries, such as Nigeria and Pakistan, have evaluated fIPV delivery with NS in campaigns but have not yet adopted an NS fIPV strategy. One explanation is that fIPV delivery has traditionally been administered with the Bacillus Calmette–Guérin NS that may not reliably target the ID layer.[62] This approach, known as the Mantoux technique, requires the insertion of a 27-gauge needle, bevel upwards, and at a shallow angle, nearly parallel to the skin. Injectate is slowly administered to raise a visible skin bleb.[63] Precise placement of the needle-tip in the outermost layer of the dermis is essential to ensure a correct immunological response and to prevent vaccine fluid leakage. Mantoux delivery, introduced by Charles Mantoux over 111 years ago, is technically difficult and requires extensive training to ensure high-fidelity dose and depth.[64] The Mantoux technique is known for poor consistency and vaccine wastage due to the large dead space in the syringe[65] and the requirement to purge air from the needle.[66] Painful injections are common, adverse event rates are unacceptably high, and refusals resulting in non-vaccination during fIPV campaigns using Mantoux have been attributed to needle injection fear[67] and hesitancy.[68] The feasibility of delivering ID injections with needles on a large scale is a persistent concern due to the lack of vaccinators trained in the ID technique.[62] In one campaign study, when vaccinators received a full day of training on Mantoux, nine percent reported the training was inadequate to prepare them for fIPV delivery with a needle.[67] In the same study, bleb formation, indicative of proper Mantoux technique, was absent in 20% of the fIPV injections delivered at outreach stations.[67] Difficulties with outreach and house-to-house administration of fIPV with needles have been identified due to the need for sharps waste management and vaccinator inexperience with the Mantoux technique.[67],[69] The Mantoux technique for fIPV administration also shares the disadvantages of NS use, including the risk of needlestick injuries and needle reuse. As a result, some researchers consider ID delivery with needles unsuitable for outbreak response campaigns.[70]

Recently, liquid ID vaccination has been simplified by the development of several novel ID delivery technologies, including needle-free injectors, microneedles, and needle adapters[71]. These devices, unlike microarray patches, have the advantage of compatibility with established vaccine vial presentations without the need for reformulation. To the best of our knowledge, these delivery systems have never been reviewed with an exclusive focus on fIPV implementation. This review is intended as a reference for polio immunization policy and procurement decision-makers evaluating their options for

efficient, safe, and effective ID fIPV delivery as well as an information source for practitioners looking for the latest evidence to guide their decision-making and work practices.

2. Methods

We searched PubMed to identify literature in any language, published between January 2015 and July 2024, with the terms "*inactivated polio vaccine*" and "*intradermal delivery*". Reference lists were used for additional publications. We selected studies that included human-use implementation research on alternative ID delivery technologies for fIPV delivery alone or compared with NS delivery (either IM or ID). Studies that included assessment of uptake, reach, feasibility, cost-effectiveness, sustainability, acceptability, equity, coverage, access, and compliance of ID delivery interventions were included. Studies that focused on health effects (e.g., safety and efficacy) without any implementation research were excluded. Animal studies were excluded. Additional relevant publications suggested by polio immunization experts that met the inclusion and exclusion criteria were also included. For this review, we evaluated the most reported and relevant implementation factors, including child's distress associated with injection; acceptability (preference) with vaccinators; acceptability (preference) with caregivers; immunization coverage; training requirements and adequacy; vaccine wastage; ergonomics; acceptability among adult recipients; and feasibility.

3. Results

Of the 59 publications identified in the search, 14 met the criteria as original research on human subjects using alternative delivery methods for the administration of commercial fIPV vaccines. Four studies reported only clinical and safety data and offered no implementation research findings and therefore were excluded from further evaluation. The remainder of these studies are summarized in Table 1. Five of the evaluated publications described randomized controlled studies (RCTs) with primary endpoints of safety and efficacy. For these, implementation research findings were secondary. Three of these RCTs evaluated alternative ID delivery interventions in a campaign setting with children four months to five years of age. One publication evaluated interventions in an RI setting with children six weeks to five years of age. One evaluated ID interventions with Human Immunodeficiency Virus (HIV)-infected adults. Five studies were pragmatic evaluations of pilot or actual campaign implementation, with one of these involving house-to-house fIPV administration.

Publication location (reference)	Devices evaluated for delivery of ID fIPV (unless otherwise stated)	Study description	Time to vaccinate	Distress associated with injection	Acceptability with vaccinators	Acceptability with adult recipients	Acceptability with caregivers	Vaccine wastage	Training	Coverage	Ergonomics
Bashoran, 2022 The Gambia (70)	1. Needle-free injector, Tropis-ID® (PharmaJet) 2. Intradermal needle adapter, West IDA (West Pharmaceutical Services) with AD syringe 3. Standard BCG needle and syringe (BCG N&S)	• Non-inferiority RCT in a simulated campaign setting; • Children aged 4 months to 5 years	X	X				X	X		
Daly, 2020 Pakistan (73)	1. Needle-free injector, Tropis-ID® (PharmaJet) 2. Intramuscular full dose IPV with N&S (historical comparison)	• Operational research in a campaign setting • Children aged 4 months to 5 years	X	X	X		X		X	X	
Bullo, 2021 Pakistan (84)	1. Needle-free injector, Tropis-ID® (PharmaJet) 2. Full dose IPV with IM N&S	•Operational research in a campaign setting • Children aged 4 months to 5 years					X		X	X	
Yousavzai, 2017 Pakistan (74)	1. Needle-free injector, Tropis-ID® (PharmaJet)	• Operational research in a campaign setting • Children aged 4 months to 5 years	X	X				X	X		X
Resik, 2015 Cuba (81)	1. Needle-free injector, Tropis-ID® (PharmaJet) 2. Needle-free injector, B2000® (Bioject) 3. Needle-free injector, ID-Pen® (Bioject) 4. Standard BCG needle and syringe (N&S) 5. Full dose IPV with IM N&S	• Non-inferiority RCT in a campaign setting • Children aged 12–20 months			X						X
Saleem, 2017 Pakistan (75)	1. Intradermal needle adapter, West IDA (West Pharmaceutical Services) with AD syringe 2. Intradermal needle adapter, Star IDA (Star Syringe) with AD syringe 3. Standard BCG N&S	• Non-inferiority RCT in a campaign setting • Children aged 6-12 months	X	X	X			X	X		
Ahmad, 2022 India (76)	1. Intradermal needle adapter, West IDA (West Pharmaceutical Services) with AD syringe 2. Standard BCG N&S 3. Full dose IPV with N&S (intramuscular)	• Non-inferiority RCT in a routine immunization setting • Children aged 6-14 weeks	X								
Troy, 2015 USA (83)	1. Microneedle device (NanoPass MJ600) 2. Fractional dose with standard N&S (intramuscular)	• Non-inferiority RCT • HIV-infected adults				X					
Biya, 2023 Nigeria (82)	1. Needle-free injector, Tropis-ID® (PharmaJet)	• Operational research used to pilot house-to-house campaign • Children aged 3–59 months			X		X			X	
Nouh, 2024 Somalia (79)	1. Needle-free injector, Tropis-ID® (PharmaJet)	• Operational research used to pilot campaign • Children aged 4–59 months		X			X		X	X	

Table 1. Summary of the publications reviewed

Implementation categories that were addressed in these studies include:

1. Time to vaccinate (five studies)

doi.org/10.32388/CLBYI9.2

2. Child's distress associated with injection (five studies)
3. Acceptability (preference) with vaccinators (four studies)
4. Acceptability (preference) with caregivers (four studies)
5. Acceptability among adult recipients (one study)
6. Immunization coverage (four studies)
7. Training requirements and adequacy (six studies)
8. Vaccine wastage (three studies)
9. Ergonomics (two studies)
10. Feasibility (one study)

These characteristics are summarized in Table 3. Implementation research ranged from statistically relevant to quasi-scientific study designs, and the qualitative and quantitative methods of data generation varied widely to include surveys, government records, focus group discussions, interviews, and observations. A summary of the evaluated publications can be found in Table 1.

Six unique ID delivery technologies were identified in these studies:

1. Three needle-free injection technologies:
    1. Tropis-ID® (PharmaJet)
    2. B2000® (Bioject)
    3. ID Pen® (Bioject)
2. Two ID adapters used with commercial auto-disable NS
    1. West ID Adapter (West Pharmaceutical Services)
    2. Star ID Adapter (Star Syringe)
3. One microneedle device (MJ600, NanoPass).

Of these, two novel technologies, Tropis and MJ600, are commercially available with approvals or registrations with one or more stringent regulatory authorities. Tropis has received WHO prequalification.[72] A summary of the technologies can be found in Table 2.

doi.org/10.32388/CLBY1g.2

Type	Product	Publications	Commercially available	Stringent Regulatory Authority Approvals	WHO Prequalified?	Website
Needle-free injectors	Tropis-ID® (PharmaJet)	Bashoran et al., 2022 (70) Daly et al., 2020 (73) Bullo et al., (84) Resik et al., 2015 (81) Yousafzai et al., 2017 (74) Biya et al., 2023 (82) Nouh et al., 2024 (79)	Yes	CE Mark; Registered in Vietnam, Israel, India, Indonesia, Kenya, Ghana, Nigeria	Yes	https://pharmajet.com/tropis-id/
	B2000® (Bioject)	Resik et al., 2015 (93)	No	US 510(k)	No	None
	ID Pen® (Bioject)	Resik et al., 2015 (81)	No	None	No	None
Intradermal needle adapters with AD syringe)	Star IDA (Star Syringe)	Saleem et al., 2017 (75)	No	None	No	None
	West IDA (West Pharmaceutical Services)	Bashoran et al., 2022 (70) Saleem et al., 2017 (75) Ahmad et al., 2022 (76)	No	US 510(k)	No	None
Microneedle device	MJ600 (NanoPass)	Troy et al., 2015 (83)	Yes	CE mark; US 510(k); Registered in China, Brazil, Russia, Korea, Turkey	No	https://www.nanopass.com/micronjet-microneedle-device/

Table 2. Summary of the evaluated devices

doi.org/10.32388/CLBYI9.2

doi.org/10.32388/CLBY1g.2

ID delivery method	Needle-free injectors			Intradermal needle adapters		Microneedle
	Tropis	B2000	ID Pen	Star IDA	West IDA	MJ600
Images						
Time to vaccinate	• More vaccinators able to complete in less than 1 minute compared with West IDA and ID N&S (70) • Took more time than N&S IM (73) • Time decreased with experience to 38 sec after 30th child (74)	*not evaluated*	*not evaluated*	• Faster than N&S ID, 102 sec (75)	• Similar to N&S ID, fewer vaccinators able to complete in < 1 min compared with Tropis (70) • 152 sec (75) • Slower than N&S ID, 104 sec (76)	*not evaluated*
Child's distress associated with injection	• Less child crying before receiving an injection compared with West IDA and ID N&S (70) • Majority of vaccinators with preference for Tropis cited less child crying/discomfort with Tropis as reason for preference (73) • Vaccinators reported less child crying compared to previous experience with N&S IM (74) • 60.8% of caregivers cited no discomfort or pain experienced during injection as a benefit (79)	*not evaluated*	*not evaluated*	• Vaccinators reported less crying compared with West IDA and N&S ID (75)	• Vaccinators reported more crying compared with Star IDA (75)	*not evaluated*
Acceptability (preference) with vaccinators	• 97.6% preference compared with N&S (73) • Preferred over ID pen and ID N&S, less preferred than B2000 (81) • 93% preference compared with N&S IM (82)	• Most preferred over Tropis and ID pen and ID N&S (81)	• Least preferred of all 3 needle-free devices but preferred over ID N&S (81)	• Less preferred compared with West IDA and ID N&S (75)	• Preferred over Star IDA and ID N&S (75)	*not evaluated*
Acceptability (preference) with caregivers	• Most vaccinators with preference for Tropis cited caregiver acceptability with Tropis as reason for preference (73) • 94% preference compared with N&S IM (82) • 100% caregivers recommended for future campaigns (79)	*not evaluated*	*not evaluated*	*not evaluated*	*not evaluated*	*not evaluated*
Immunization coverage	• Coverage improved 18.4% over the preceding campaign involving full-dose IPV delivered with N&S (73) • 5.8% higher than similar areas in same campaign (84) • High coverage in house-to-house setting (82) • Achieved 96% coverage (79)	*not evaluated*	*not evaluated*	*not evaluated*	*not evaluated*	*not evaluated*
Training requirements and adequacy	• 2 hrs training (70) • Cascade starting with 2 day Master training and one day for field staff; 93.6% of vaccinators reported being satisfied with the training they received (73) • Several hours (74) • Half day training (79)	*not evaluated*	*not evaluated*	• 1 d (75)	• 2 hrs training (70) • 1 d (75)	*not evaluated*
Vaccine wastage	• 26% increase in usable vaccine (70) • No wastage (74)	*not evaluated*	*not evaluated*	• 33% wastage (75)	• 10% wastage (75)	*not evaluated*
Acceptability with adult recipients	*not evaluated*	*not evaluated*	*not evaluated*	*not evaluated*	*not evaluated*	• 54% preferred intradermal over IM with N&S (83)

Table 3. Summary of the ID delivery attributes

Time to vaccinate: Vaccination duration influences the amount of time the caregiver and child endure the invasive procedure and the potential throughput of a vaccinator in a clinic or campaign setting. The methods for measuring "time to vaccinate" varied substantially in the reviewed publications. Time to vaccinate for the Bioject needle-free devices and the NanoPass MJ600 device was not evaluated in any publications. Tropis needle-free delivery enabled faster administration than delivery with the West and Star ID adapters (IDAs). Citing RCT data, Bashoran (2022) found 54.6% of injections administered by Tropis were completed in under one minute compared with 32.7% by BCG NS and 33.6% by the West IDA.[70] Daly (2020) compared the median time taken to administer the vaccine recorded three times per vaccinator and found administration times with Tropis were 51.0 seconds for fIPV and 39.0 seconds for IM IPV with NS.[73] Two studies found that administration time for Tropis varied inversely with experience: In one study, the median jet injection time decreased from 57.2 seconds at the first visit to 43.2 seconds at the second visit.[73] In another study, the average Tropis application improved with experience, ranging from an average of 68 seconds for the first child to 38 seconds for the 30th child.[74] RCT administration times with NS methods of ID delivery were found to be substantially longer by Saleem (2017): The average times were 102 seconds for the Star IDA, 112 seconds for BCG NS, and 152 seconds for the West IDA.[75] These results are consistent with those found in the Ahmad (2022) RCT publication, which noted the average administration time was slightly more with the West IDA (104 seconds) compared to BCG NS (93 seconds).[76] The speed of use was cited as a reason for favoring Tropis needle-free delivery by 51.0% of those who favored needle-free over IM NS in the Daly (2020) study.[73]

Child's distress associated with injection: Distress before, during, and after a vaccination session can lead to negative feelings about vaccination, needle phobia, and hesitancy.[77] Distress can impact the likelihood of a child returning to the clinic for subsequent injections.[78] The measurement of distress is very subjective. In the publications reviewed, children's distress was defined as reported by the vaccinators and caregivers and was often associated with the frequency of crying. Bashoran (2022) found that 83.0% of children injected with Tropis did not cry compared with those injected with BCG NS (46.6%) and the West IDA (44.9%).[70] Less discomfort/crying from the child was cited as a reason for favoring needle-free by 51.6% of vaccinators who favored needle-free in a campaign using Tropis.[73] In Somalia, Nouh (2024)

noted that 60.8% of caregivers surveyed cited their main motivation for recommending Tropis was that the children experienced no discomfort or pain during injection.[79] Yousafzai (2017) reported that all vaccinators claimed crying among children was less common with needle-free compared to their experience with NS.[74] In the evaluation of IDAs, Saleem (2017) noted that vaccinators reported crying among children was less common with the Star IDA compared to both the West IDA and BCG NS delivery methods.[75]

Acceptability (preference) with vaccinators: Vaccinator acceptability is an important factor that can impact novel technology demand and uptake.[80] Acceptability data were commonly collected by asking vaccinators their preferences through interviews and surveys. Daly (2020) reported that of the health workers with prior NS delivery experience in campaigns, 97.6% indicated a preference for the needle-free injectors. Ease of use was cited as a reason for favoring Tropis needle-free by 92.2% of those who favored needle-free.[73] Resik (2015) reported RCT data indicating a strong preference for needle-free delivery, with the B2000 device as the most-preferred method of fIPV delivery, followed by Tropis and then ID Pen (least preferred). BCG NS was the least preferred.[81] Reporting on Tropis use in a house-to-house campaign setting in Nigeria, Biya (2023) found 93% of health staff members preferred Tropis injections over the customary NS administration.[82] The IDAs were evaluated separately from needle-free technology; therefore, comparisons between these groups are not possible. Saleem (2017) found 67% of the vaccinators preferred the West IDA over the Star IDA and NS delivery methods. The Star IDA was the least preferred due to the cumbersome filling process and due to vaccine wastage. Vaccinator acceptability of the MJ600 was not evaluated.[75]

Acceptability (preference) among adult recipients: In the one publication that reported on adult fIPV administration, HIV-infected adults from the RCT reported ID administration with the NanoPass MJ600 microneedle device was preferred over IM NS by most subjects. The needle-free devices and IDAs were not evaluated for fIPV delivery to adults.[83]

Acceptability (preference) with caregivers: Like a child's distress, caregiver acceptability is linked with the likelihood of a child returning to the clinic for subsequent injections.[77],[78] Caregiver preferences were commonly assessed directly through interviews and surveys and indirectly through vaccinator perceptions. Daly (2020) noted that a positive caregiver response was a reason cited by 67.0% of vaccinators for their preference for Tropis needle-free over IM delivery with NS.[73] Bullo (2021) demonstrated that more children, 1.8%, were not vaccinated due to fear of injection in areas using full-

dose IPV as compared with only 0.7% in areas where ID fIPV was administered with Tropis needle-free.[84] Nouh (2024) noted that all 250 caregivers surveyed (100%) in areas where Tropis was deployed recommended the use of needle-free fIPV in the future.[79] Biya (2023) found 94% of caregivers preferred Tropis needle-free injections over the customary NS administration.[82]

Immunization coverage: There has been a growing interest in the potential of fIPV to enhance population immunity and campaign coverage, especially in the polio-endemic countries, Afghanistan and Pakistan.[85] In the reviewed publications, multiple methods were used to report on the coverage impact of fIPV delivery using Tropis needle-free administration. Daly (2020) compared administrative coverage across the same four towns of Karachi, Pakistan, between a 2019 SIA when Tropis was used for ID fIPV delivery and a 2018 SIA which used full-dose IPV administered with NS. In the 2019 campaign, fIPV was administered with Tropis in four towns and full IPV with NS was administered in six towns. In the areas where Tropis was used, an 18.4% higher mean coverage was achieved as compared with the previous year's SIA which administered full-dose IPV with NS.[73] Bullo (2021), citing cluster survey data from rapid convenience assessments, reported higher vaccination coverage in Tropis fIPV areas (85.3%) compared to areas where full-dose IPV was administered with NS (79.5%).[84] Reporting on a house-to-house vaccination campaign in Sokoto, Nigeria, and citing data from a modified cluster survey, Biya (2023) noted that administration in a house-to-house campaign with the Tropis needle-free injector device achieved high coverage (87%) within the target age group.[82] In Somalia, campaigns using Tropis achieved 96% coverage in each of two immunization rounds.[79] Coverage was not reported for the Bioject needle-free devices, the IDAs, or the NanoPass microneedle device.

Training requirements and adequacy: Adequate training is critical to the competency of vaccinators and to the quality of healthcare and immunizations.[86] Several reviewed publications reported on the injection experience of the vaccinators prior to training and on the training activities conducted but did not provide any assessment of training adequacy. Bashoran (2022), for example, reported that public health officers with NS ID immunization experience and nurses without experience received two hours of training on Tropis and the West IDA before the campaign.[70] In all reviewed cases, assessments of training adequacy were based on perceptions rather than on professional standards. Daly (2020) provided the most thorough description of training and assessment in describing a cascade training program for the Tropis device during which master trainers attended a two-day training session consisting of needle-free injection demonstrations and the opportunity to practice with the Tropis devices. One-day training

consisting of a demonstration/training video in the local language and a test injection practice session was cascaded to field staff prior to campaign implementation. During the subsequent survey, vaccinators were asked whether sufficient time was allotted for training components, the number of test injections administered, whether they reviewed the training video before or during the campaign, trainer preparedness, and whether they felt the training sufficiently prepared them to use the jet injectors in a campaign setting. Ninety-four percent of vaccinators reported being satisfied with the training they received. Seventy-four percent of vaccinators who received the training video reviewed it either before or during the campaign, highlighting its utility as a training resource. Of the 6.4% who felt the training was insufficient, the most common reason given by 38.4% was the need for more practice injections. [73] Yousafzai (2017) reported that training on Tropis needle-free injector use could be completed in several hours with vaccinators who do not have any formal health background or prior training in injection administration.[74] For the campaign in Somalia, Nouh (2024) reported that a half-day training on Tropis needle-free technique followed by cascade training was adequate and played an important role in the success of the pilot. After they were trained, most healthcare workers recognized Tropis was very user-friendly and could be used to vaccinate more children in a short time with minimal refusals.[79] For IDAs studied in Pakistan, community health workers received one day of training on each device. [75] Some authors did not provide additional detail on training, and thus the training requirements for the MJ600 Microneedle and Bioject devices are not described here.[81],[82]

Vaccine wastage: Vaccine wastage increases the total cost of immunization.[45] Methods of vaccine wastage measurement were not consistent among the publications. Thus, cross-publication comparisons are not possible. In their evaluation of the IDA, Saleem (2017) calculated wastage as the difference between the number of doses administered and the total number of doses available (represented by used vials) divided by the total number of doses available. The authors found vaccine wastage was highest for the Star IDA (37%) compared with 10% for the West IDA and 6% for the BCG NS.[75] Bashoran (2022) reported a mean of 63 fIPV doses were obtained from each 10-dose vial using Tropis needle-free compared with a mean of 50 using the NS, indicating that the very low dead space in needle-free syringes enables up to a 26% increase in usable vaccine.[70] Other authors found no wastage with the Tropis technology.[74] Wastage for the MJ600 Microneedle and Bioject devices is not described in the reviewed publications.[81],[82]

Ergonomics: Information about novel technology ergonomics may be useful for decision-makers when choosing ID injection devices to protect their workers from overuse-related injuries.[87] Resik (2015) evaluated health worker ergonomic preferences for three needle-free injectors to assess their suitability for programmatic use. Seven key ergonomic features were scored for each injector, including size, intuitive functionality, no pain, ease of filling, ease of managing air bubbles, ease of resetting, and noise level. All devices were scored high (mean score >80% as a percentage of maximum potential score) by healthcare workers on intuitive functionality, no pain, ease of filling, ease of managing air bubbles, and ease of resetting. The ID Pen scored lowest (mean score 64%) on size, and the B2000 scored lowest (mean score 69%) on perceived noise level.[81] In a campaign setting, 100% of vaccinators found that filling the Tropis needle-free syringe with the correct dosage, identifying and correcting air bubbles, and administering an injection was easy, while slightly fewer (90.9%) reported removing air bubbles was easy. None of the vaccinators reported significant ergonomic issues.[74]

4. Discussion

Novel ID delivery technologies present an alternative to the challenges of Mantoux ID delivery with NS. Benefits of individual technologies include high acceptance with both healthcare workers and caregivers, improved coverage rates, and cost savings. Two ID delivery technologies (NanoPass and Tropis) are commercially available, and one has achieved WHO prequalification. Among the technologies reviewed, the evidence base for the needle-free technology, Tropis, is the most developed; it is the only technology for which the reviewed literature assessed coverage and caregiver acceptability, and it is the only device in this review that has achieved WHO prequalification and WHO endorsement within polio eradication strategy.[42],[85]

There are several limitations to our review. The greatest hindrance to our assessment of the novel ID delivery technologies was the lack of standardized methodology across all the characteristics reviewed. For example, five publications evaluated the time to vaccinate, each using unique methods. This made it challenging to compare novel technologies that were not assessed within the same study. Furthermore, none of the reviewed studies accounted for the time it took to calm a child prior to injection, which may be the most time-consuming factor during immunization. Similarly, assessments of distress and acceptability, which rely on subjective interpretations, were not consistent across the reviewed publications. Another constraint is that no single characteristic was evaluated for all devices. In fact, several characteristics were assessed for only a few, or just a single, device. Wastage was assessed only for

the IDAs and Tropis. Caregiver acceptability and coverage were assessed only for Tropis. Two needle-free devices, the B2000 and the ID Pen, were evaluated only for vaccinator preference. The microneedle device, MJ600, was evaluated only for acceptability with adult recipients. Table 3 shows that the only WHO-prequalified device, Tropis, was the most thoroughly evaluated device, with data across seven of the eight characteristics. While this review revealed many gaps in the available data and the difficulties in comparing data between studies, it is also reassuring to see that the only commercial technology with WHO prequalification, Tropis, was also the most thoroughly reviewed, as evidenced by seven separate studies (Table 3).

Training requirements and adequacy were assessed only for Tropis and both IDAs. Nonetheless, there are some clear observations that can be derived from the six studies that included training. The training programs varied widely, even for a single technology. For example, Tropis vaccinator training programs ranged from two hours to a full day. One publication correlated experience using the novel technology with time to vaccinate, and another highlighted a dissatisfied vaccinator's desire for more practice injections. These observations highlight the need for more standardized training programs, the importance of supervised practice sessions, and competency standards when novel technologies for immunization are introduced.

Implications for polio eradication: To eradicate polio, WHO has committed to ensuring all children are fully vaccinated against polio. To achieve this, every country should seek to achieve and maintain high levels of polio vaccine coverage.[3] While countries continue to navigate a combined OPV/IPV solution, policy and implementation should leverage the strengths of each individual vaccine and minimize each vaccine's shortcomings. OPV induces mucosal immunity, but even improved "novel" OPV versions continue to seed live, mutated, or recombined viruses into communities, resulting in new endemic and epidemic transmission. Immunization with IPV eliminates the risk of seeding new transmission and is known to boost mucosal immunity in children previously immunized with OPV. However, IPV alone has a limited ability to induce intestinal mucosal immunity, is more expensive than OPV, and historically has been associated with all the challenges of NS delivery: needle reuse, needlestick injuries, sharps waste management, and incompatibility with house-to-house campaigns. High vaccination coverage is critical to transitioning to an IPV-only schedule in polio-free regions with strong sanitation and a very low risk of importation.[3]

Recently, SAGE recommended that IPV campaigns be considered to improve vaccination coverage in consequential geographies, including Northern Nigeria, eastern Democratic Republic of the Congo (DRC),

Somalia, Pakistan, and Yemen.[60] Evidence reviewed in this paper suggests high coverage is possible using a dose-sparing fIPV strategy with one of the alternative ID delivery tools. Needle-free ID delivery of fIPV, using WHO-prequalified Tropis, has been shown to increase coverage,[73],[79],[82] to decrease total immunization costs,[45][45] and to be highly acceptable to healthcare workers,[73],[75],[81],[82] caregivers, [73],[79],[82],[84] and children[70],[73],[74],[75] while eliminating sharps hazards. Targeted use of needle-free ID delivery of fIPV in consequential geographies for supplemental IPV house-to-house immunization outreach has the potential to achieve greater geographic reach, higher coverage, and lower costs compared to full-dose delivery with NS. Middle-income countries and those transitioning from Gavi support may consider needle-free delivery of fIPV, for both RI and campaigns, as a cost-saving strategy that can shift the vaccination paradigm from persistent NS hesitancy to increased immunization coverage.

Total immunization cost is a critical dimension for decision-makers in countries navigating their IPV delivery options. Unfortunately, comparative costs were not included in any of the publications reviewed. fIPV enables the vaccination of more children with less vaccine, and dose-sparing inherently reduces the contributed cost of the vaccine dose by 80%, not accounting for differences in vaccine wastage. Studies have reported 0% vaccine loss and 26% more doses obtained from each ten-dose vial administered with needle-free Tropis as compared to NS methods.[70],[74] Though the incremental cost of a needle-free syringe may be higher than that of a standard auto-disable syringe, this cost is offset by the reduced dose required for ID delivery.[71] Even when the incremental cost of novel ID delivery technologies like Tropis is considered, ID delivery of fIPV can reduce costs per vaccinated child compared with full-dose IPV. In RI setting models, vaccinating a child with two doses of fIPV intradermally can cost 15–48% less than vaccinating a child with a standard full-dose delivery.[45]

Analysis of the Only WHO-Prequalified Needle-Free ID Delivery Technology: As the only commercialized, WHO-prequalified ID technology evaluated, Tropis is commercially available and has been used in the administration of over ten million immunizations supporting GPEI campaigns. Unlike high-profile microarray patches, Tropis has the advantage of compatibility with established vaccine vial presentations without the need for reformulation. In reference to endemic country use, WHO has noted that the use of fIPV is well-supported in specific areas where the deployment of jet injectors can improve vaccine demand, increase the number of registered children, and enhance overall coverage with both OPV and IPV.[85]

Through implementation research of Tropis, scientists have studied and reported results on critical factors that influence feasibility, scalability, and sustainability. Tropis is highly effective at triggering the immune response compared with NS.[34] In the seven publications which included implementation research on Tropis, the needle-free innovation has been shown to be highly acceptable to health workers and caregivers; require minimum training; decrease child discomfort; decrease wastage; and improve coverage. Use of Tropis has been shown to be successful in vaccinating a high proportion of the target population in house-to-house campaigns, and Tropis has been tested in a randomized controlled trial of RI in 22 facilities in Oyo and Kano states in Nigeria.[46],[88] One published model[45] and unpublished data[47] confirm cost savings with Tropis. Given these findings and the existence of a WHO-endorsed technology,[60],[85] needle-free ID fIPV delivery represents a viable option for consideration by country immunization programs to increase equitable vaccine access and decrease total immunization costs. Tropis needle-free has also been used in preclinical and clinical studies for a wide range of both vaccines and treatments, including rabies[89] and immuno-oncology.[90][91][92]

Intradermal Delivery Beyond IPV: The COVID-19 pandemic highlighted the need for innovation in vaccine delivery and created an opportunity for a parenteral-delivery paradigm shift. Many vaccine and therapeutic development programs now include needle-free ID delivery using needle-free Tropis.[93] [94] [95] Successful development programs at Zydus Pharmaceuticals and Gennova Biopharmaceuticals Ltd. have resulted in emergency use authorization and commercialization of the novel, thermostable nucleic acid (NA) vaccines, ZyCoV-D®[96], the first approved DNA vaccine for humans, and GEMCOVAC® -OM, a lyophilized, self-amplifying mRNA vaccine.[97] PharmaJet's Tropis was selected as the exclusive delivery system for the first commercially available plasmid DNA human vaccine product (ZyCoV-D) after preclinical and Phase 1 trials showed high levels of immunogenicity with Tropis delivery compared with the NS method.[95] Building on this momentum toward ID delivery, Tropis, NanoPass, and other near-commercial-stage novel ID methods should be considered for new vaccine development and clinically evaluated for dose-sparing of supply-constrained vaccines for eradication efforts and during public health emergencies of international concern, such as the mpox outbreak in 2024.[98] Novel ID delivery methods should be evaluated and implemented with vaccines that have been validated for ID delivery, such as post-exposure rabies vaccine[99] and mpox.[100]

Conclusion: ID delivery of vaccines, including fIPV, is possible using novel, commercially available, non-NS solutions. fIPV has benefits inherent to the ID compartment, such as dose-sparing and cost savings.

There are additional benefits that are unique to commercialized delivery methods, such as improved acceptability and coverage. This review demonstrates that several alternative ID delivery technologies compared favorably against NS delivery. Of the technologies reviewed in this article, two, NanoPass MJ600 and PharmaJet Tropis, are commercially available. The existence of a WHO-prequalified technology demonstrates the maturity of this delivery approach for potential large-scale implementation.

As coverage, acceptability, and cost-savings are highly sought characteristics, novel ID delivery methods should be evaluated and implemented with other vaccines that have been validated for ID delivery such as post-exposure rabies vaccine and mpox. Donors and pharmaceutical companies should consider integrating novel ID delivery into early-stage pipeline development projects. Priority should be given to evaluating novel ID delivery of pandemic vaccines and vaccines used for eradication programs where the benefits of dose-sparing, ease of implementation in house-to-house campaigns, and high coverage would be valuable.

Statements and Declarations

Funding

Funding for this study was provided by PharmaJet.

Conflicts of Interest

B.G.B., M.E.S., R.M.S., and A.A. were provided with a small stipend remuneration for their time spent writing and editing the manuscript. C.D. is a PharmaJet consultant; P.L. is a PharmaJet employee.

Author Contributions

P.L. proposed the original idea and wrote the initial manuscript draft. P.L. and C.D. conducted the research and analysis. All authors contributed equally to the editing and conclusions. All authors have read and agreed to the published version of the manuscript.

References

1. ^*World Health Organization (2024). "Poliomyelitis – Fact Sheet." World Health Organization. https://www.who.int/news-room/fact-sheets/detail/poliomyelitis.*

2. ^Global Polio Eradication Initiative. "GPEI: Our Mission." Global Polio Eradication Initiative. https://polioeradication.org/who-we-are/.
3. a, b, c, d, eWorld Health Organization (2022). "Polio Vaccines: WHO Position Paper – June 2022." World Health Organization. https://www.who.int/publications-detail-redirect/WHO-WER9725-277-300.
4. ^Bandyopadhyay AS, Burke RM, Hawes KM (2024). "Polio Eradication: Status, Struggles and Strategies." Pediatr Infect Dis J. **43**(6):e207-e211.
5. a, b, cGlobal Polio Eradication Initiative. "Variant Poliovirus (cVDPV)." Global Polio Eradication Initiative. https://polioeradication.org/about-polio/the-virus/vaccine-derived-polioviruses/.
6. ^Global Polio Eradication Initiative. "Endemic Countries." Global Polio Eradication Initiative. https://polioeradication.org/where-we-work/polio-endemic-countries/.
7. a, b, cGlobal Polio Eradication Initiative (2024). "Global Wild AFP Cases and Environmental Samples 2018-2024." Global Polio Eradication Initiative. https://polioeradication.org/wild-poliovirus-count/.
8. ^World Health Organization (2023). "Poliomyelitis – Poliomyelitis Eradication: Report by the Director-General." World Health Organization. https://apps.who.int/gb/ebwha/pdf_files/WHA76/A76_13-en.pdf.
9. ^Zayed D, Ala'a B (2024). "Infectious Diseases Within a War-Torn Health System: The Re-Emergence of Polio in Gaza." New Microbes New Infect. **62**.
10. ^World Health Organization (2022). "Wild Poliovirus Type 1 - Malawi." World Health Organization. https://www.who.int/emergencies/disease-outbreak-news/item/wild-poliovirus-type-1-(WPV1)-malawi.
11. ^"Circulating Vaccine-Derived Poliovirus Type 3 – Israel." World Health Organization. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON366.
12. ^Klapsa D, Wilton T, Zealand A, Bujaki E, Saxentoff E, Troman C, Martin J (2022). "Sustained Detection of Type 2 Poliovirus in London Sewage Between February and July, 2022, by Enhanced Environmental Surveillance." Lancet. **400**(10362):1531-1538.
13. ^Link-Gelles R (2022). "Public Health Response to a Case of Paralytic Poliomyelitis in an Unvaccinated Person and Detection of Poliovirus in Wastewater—New York, June–August 2022." MMWR Morb Mortal Wkly Rep. **71**.
14. ^Molodecky N, Sutter R (2024). "Evaluation of the 2016 Switch From tOPV to bOPV." Global Polio Eradication Initiative. https://polioeradication.org/wp-content/uploads/2024/11/Switch-Report-20240930.pdf.
15. a, bGlobal Polio Eradication Initiative (2022). "GPEI Strategy 2022-2026." Global Polio Eradication Initiative. https://www.archive.polioeradication.org/gpei-strategy-2022-2026/.

16. ^Fahmy K, Hampton LM, Langar H, Patel M, Mir T, Soloman C, Teleb N (2017). "Introduction of Inactivated Polio Vaccine, Withdrawal of Type 2 Oral Polio Vaccine, and Routine Immunization Strengthening in the Eastern Mediterranean Region." J Infect Dis. **216**(suppl_1):S86-S93.

17. ^Peak CM, Lyons H, Voorman A, Gray EJ, Cooper LV, Blake IM, Bandyopadhyay AS (2024). "Monitoring the Risk of Type-2 Circulating Vaccine-Derived Poliovirus Emergence During Roll-Out of Type-2 Novel Oral Polio Vaccine." Vaccines. **12**(12):1308.

18. a, bJohn J, Giri S, Karthikeyan AS, Iturriza-Gomara M, Muliyil J, Abraham A, Kang G (2014). "Effect of a Single Inactivated Poliovirus Vaccine Dose on Intestinal Immunity Against Poliovirus in Children Previously Given Oral Vaccine: An Open-Label, Randomised Controlled Trial." Lancet. **384**(9953):1505-1512.

19. a, bSutter RW, Eisenhawer M, Molodecky NA, Verma H, Okayasu H (2024). "Inactivated Poliovirus Vaccine: Recent Developments and the Tortuous Path to Global Acceptance." Pathogens. **13**(3):224.

20. ^Parker EP, Molodecky NA, Pons-Salort M, O'Reilly KM, Grassly NC (2015). "Impact of Inactivated Poliovirus Vaccine on Mucosal Immunity: Implications for the Polio Eradication Endgame." Expert Rev Vaccines. **14**(8):1113-1123.

21. ^Macklin GR, Grassly NC, Sutter RW, Mach O, Bandyopadhyay AS, Edmunds WJ, O'Reilly KM (2019). "Vaccine Schedules and the Effect on Humoral and Intestinal Immunity Against Poliovirus: A Systematic Review and Network Meta-Analysis." Lancet Infect Dis. **19**(10):1121-1128.

22. ^Gamage D, Mach O, Ginige S, Weldon WC, Oberste MS, Jeyaseelan V, Sutter RW (2019). "Poliovirus Type 2 Seroprevalence Following Full-or Fractional-Dose Inactivated Poliovirus Vaccine in the Period After Sabin Type 2 Withdrawal in Sri Lanka." J Infect Dis. **219**(12):1887-1892.

23. ^Snider CJ, Zaman K, Wilkinson AL, Aziz AB, Yunus M, Haque W, Anand A (2023). "Poliovirus Type 1 Systemic Humoral and Intestinal Mucosal Immunity Induced by Monovalent Oral Poliovirus Vaccine, Fractional Inactivated Poliovirus Vaccine, and Bivalent Oral Poliovirus Vaccine: A Randomized Controlled Trial." Vaccine. **41**(41):6083-6092.

24. ^Global Polio Eradication Initiative. "OPV Cessation." Global Polio Eradication Initiative. https://polioeradication.org/polio-today/preparing-for-a-polio-free-world/opv-cessation/.

25. ^UNICEF Supply Division (2024). "Oral Polio Vaccine (OPV) Price Data." UNICEF Supply Division. https://www.unicef.org/supply/documents/oral-polio-vaccine-opv-price-data.

26. ^UNICEF Supply Division (2024). "Inactivated Polio Vaccine (IPV) Price Data." UNICEF Supply Division. https://www.unicef.org/supply/documents/inactivated-polio-vaccine-ipv-price-data.

27. ^Alfaro-Murillo JA, Ávila-Agüero ML, Fitzpatrick MC, Crystal CJ, Falleiros-Arlant LH, Galvani AP (2020). "The Case for Replacing Live Oral Polio Vaccine With Inactivated Vaccine in the Americas." Lancet. **395**(10230):1163-1166.

28. ^Basu S, Ashok G, Debroy R, Ramaiah S, Livingstone P, Anbarasu A (2023). "Impact of the COVID-19 Pandemic on Routine Vaccine Landscape: A Global Perspective." Hum Vaccin Immunother. **19**(1):2199656.

29. ^UNICEF Supply Division (2020). "Scaling Vaccine Procurement: Case Study IPV: The Fastest Introduction and Scale Up of a Vaccine Ever, But Not Without Challenges." UNICEF Supply Division. https://www.unicef.org/supply/stories/scaling-vaccine-procurement.

30. ^UNICEF (2023). "New Data Indicates Declining Confidence in Childhood Vaccines of Up to 44 Percentage Points in Some Countries During the COVID-19 Pandemic." UNICEF. https://www.unicef.org/rosa/press-releases/new-data-indicates-declining-confidence-childhood-vaccines-44-percentage-points-some.

31. ^Kupper TS, Fuhlbrigge RC (2004). "Immune Surveillance in the Skin: Mechanisms and Clinical Consequences." Nat Rev Immunol. **4**(3):211-222.

32. ^Salk JE (1953). "Recent Studies on Immunization Against Poliomyelitis." Pediatrics. **12**(5):471-482.

33. ^Samuel BU, Cherian T, Rajasingh J, Raghupathy P, John TJ (1992). "Immune Response of Infants to Inactivated Poliovirus Vaccine Injected Intradermally." Vaccine. **10**(2).

34. a, bResik S, Tejeda A, Mas Lago P, Diaz M, Carmenates A, Sarmiento L, Sutter RW (2010). "Randomized Controlled Clinical Trial of Fractional Doses of Inactivated Poliovirus Vaccine Administered Intradermally by Needle-Free Device in Cuba." J Infect Dis. **201**(9):1344-1352.

35. a, bResik S, Tejeda A, Sutter RW, Diaz M, Sarmiento L, Alemañi N, Aylward RB (2013). "Priming After a Fractional Dose of Inactivated Poliovirus Vaccine." N Engl J Med. **368**(5):416-424.

36. ^Mohammed AJ, AlAwaidy S, Bawikar S, Kurup PJ, Elamir E, Shaban MM, Sutter RW (2010). "Fractional Doses of Inactivated Poliovirus Vaccine in Oman." N Engl J Med. **362**(25):2351-2359.

37. ^Cadorna-Carlos J, Vidor E, Bonnet MC (2012). "Randomized Controlled Study of Fractional Doses of Inactivated Poliovirus Vaccine Administered Intradermally With a Needle in the Philippines." Int J Infect Dis. **16**(2):e110-e116.

38. ^Anand A, Zaman K, Estívariz CF, Yunus M, Gary HE, Weldon WC, Pallansch MA (2015). "Early Priming With Inactivated Poliovirus Vaccine (IPV) and Intradermal Fractional Dose IPV Administered by a Microneedle Device: A Randomized Controlled Trial." Vaccine. **33**(48):6816-6822.

39. a, bAziz AB, Verma H, Jeyaseelan V, Yunus M, Nowrin S, Moore DD, Zaman K (2022). "One Full or Two Fractional Doses of Inactivated Poliovirus Vaccine for Catch-Up Vaccination in Older Infants: A Randomized Clini

cal Trial in Bangladesh." J Infect Dis. ***226****(8):1319-1326.*

40. ^*Gamage D, Mach O, Palihawadana P, Zhang Y, Weldon WC, Oberste MS, Sutter RW (2018). "Boosting of Mucosal Immunity After Fractional-Dose Inactivated Poliovirus Vaccine." J Infect Dis.* ***218****(12):1876-1882.*

41. ^*Anand A, Molodecky NA, Pallansch MA, Sutter RW (2017). "Immunogenicity to Poliovirus Type 2 Following Two Doses of Fractional Intradermal Inactivated Poliovirus Vaccine: A Novel Dose Sparing Immunization Schedule." Vaccine.* ***35****(22):2993-2998.*

42. a, b, c*Mashunye TR, Ndwandwe DE, Dube KR, Shey M, Shelton M, Wiysonge CS (2021). "Fractional Dose Compared With Standard Dose Inactivated Poliovirus Vaccine in Children: A Systematic Review and Meta-Analysis." Lancet Infect Dis.* ***21****(8):1161-1174.*

43. ^*Saleem AF, Mach O, Yousafzai MT, Kazi Z, Baig A, Sajid M, Zaidi AK (2021). "One-Year Decline of Poliovirus Antibodies Following Fractional-Dose Inactivated Poliovirus Vaccine." J Infect Dis.* ***223****(7):1214-1221.*

44. ^*Bandyopadhyay AS, Gast C, Rivera L, Sáez-Llorens X, Oberste MS, Weldon WC, Rüttimann R (2021). "Safety and Immunogenicity of Inactivated Poliovirus Vaccine Schedules for the Post-Eradication Era: A Randomised Open-Label, Multicentre, Phase 3, Non-Inferiority Trial." Lancet Infect Dis.* ***21****(4):559-568.*

45. a, b, c, d, e, f, g*Mvundura M, Hsu JS, Frivold C, Kristensen D, Boyle S, Zehrung D, Jarrahian C (2019). "Evaluating the Cost Per Child Vaccinated With Full Versus Fractional-Dose Inactivated Poliovirus Vaccine." Vaccine X.* ***2****:100032.*

46. a, b*Pan African Clinical Trials Registry (2024). "Evaluating the Impact of an Intradermal Needle-Free Delivery Device on a Polio Routine Immunization Program." Pan African Clinical Trials Registry. pactr.samrc.ac.za/Search.aspx.*

47. a, b*BusinessWire (2024). "PharmaJet Announces Implementation Study Results: Increased Coverage, Cost Savings, and Preference for Routine Polio Immunization With Tropis® ID Needle-Free Delivery." BusinessWire. https://www.businesswire.com/news/home/20241024641989/en/PharmaJet-Announces-Implementation-Study-Results-Increased-Coverage-Cost-Savings-and-Preference-for-Routine-Polio-Immunization-with-Tropis%C2%AE-ID-Needle-free-Delivery.*

48. ^*World Health Organization (2016). "Polio Vaccines: WHO Position Paper – March 2016." World Health Organization. https://iris.who.int/bitstream/handle/10665/254399/WER9112 145-168.pdf?sequence=1.*

49. ^*Snider CJ, Zaman K, Estivariz CF, Yunus M, Weldon WC, Wannemuehler KA, Anand A (2019). "Immunogenicity of Full and Fractional Dose of Inactivated Poliovirus Vaccine for Use in Routine Immunisation and Outbreak Response: An Open-Label, Randomised Controlled Trial." Lancet.* ***393****(10191):2624-2634.*

50. ^a, ^b*World Health Organization (2016). "Meeting of the Strategic Advisory Group of Experts on Immunization, April 2016—Conclusions and Recommendations." Wkly Epidemiol Rec.* ***91****(21):266-284. https://www.who.int/publications/i/item/WER9121.*

51. ^*World Health Organization (2016). "Meeting of the Strategic Advisory Group of Experts on Immunization, October 2016—Conclusions and Recommendations." Wkly Epidemiol Rec.* ***91****(48):561-582. https://www.who.int/publications/i/item/WER9148.*

52. ^*World Health Organization (2017). "Meeting of the Strategic Advisory Group of Experts on Immunization, April 2017—Conclusions and Recommendations." Wkly Epidemiol Rec.* ***92****(48):729-747. https://www.who.int/publications/i/item/WER9222.*

53. ^*Global Polo Eradication Initiative (2017). "Use of Fractional Dose IPV in Routine Immunization Programmes: Considerations for Decision-Making." Global Polio Eradication Initiative. https://cdn.who.int/media/docs/default-source/immunization/tables/fipv-considerations-for-decision-making-april2017.pdf?sfvrsn=cff574f94.*

54. ^*World Health Organization (2017). "Meeting of the Strategic Advisory Group of Experts on Immunization, October 2017—Conclusions and Recommendations." Wkly Epidemiol Rec.* ***92****(22):301-320. https://www.who.int/publications/i/item/WER9247.*

55. ^*World Health Organization (2018). "Meeting of the Strategic Advisory Group of Experts on Immunization, April 2018—Conclusions and Recommendations." Wkly Epidemiol Rec.* ***93****(23):329-343. https://www.who.int/publications/i/item/WER9323.*

56. ^*World Health Organization (2019). "Meeting of the Strategic Advisory Group of Experts on Immunization, April 2019—Conclusions and Recommendations." Wkly Epidemiol Rec.* ***94****(22/23):261-279. https://www.who.int/publications/i/item/WER9422.*

57. ^*World Health Organization (2020). "Meeting of the Strategic Advisory Group of Experts on Immunization, 31 March-1 April 2020—Conclusions and Recommendations." Wkly Epidemiol Rec.* ***95****(22):241-255. https://iris.who.int/bitstream/handle/10665/332219/WER9522-241-255-eng-fre.pdf.*

58. ^*World Health Organization (2020). "Considerations for the Introduction of a Second Dose of Inactivated Polio Vaccine (IPV2) in Routine Immunization Programmes From 2021." World Health Organization. https://www.paho.org/sites/default/files/faqs_ipv2_eng_10_june_2020.pdf.*

59. ^*World Health Organization (2021). "Meeting of the Strategic Advisory Group of Experts on Immunization, October 2021 — Conclusions and Recommendations." World Health Organization. https://www.who.int/pub*

lications/i/item/who-wer9650-613-632#:~:text=The%20Strategic%20Advisory%20Group%20of,the%20discussions%2C%20conclusions%20and%20recommendations.

60. a, b, c World Health Organization (2023). "Meeting of the Strategic Advisory Group of Experts on Immunization, March 2023 – Conclusions and Recommendations." World Health Organization. https://www.who.int/publications/i/item/who-wer9822-239-256.

61. ^ Neels P, Southern J, Abramson J, Duclos P, Hombach J, Marti M, Hanquet G (2017). "Off-Label Use of Vaccines." Vaccine. **35**(18):2329-2337.

62. a, b Kim YC, Jarrahian C, Zehrung D, Mitragotri S, Prausnitz MR (2012). "Delivery Systems for Intradermal Vaccination." Intradermal Immunization. 77-112.

63. ^ Griep WA, Bleiker MA (1957). "The Injection Technique of the Mantoux Test."

64. ^ Lambert PH, Laurent PE (2008). "Intradermal Vaccine Delivery: Will New Delivery Systems Transform Vaccine Administration?" Vaccine. **26**(26):3197-3208.

65. ^ Flynn PM, Shenep JL, Mao L, Crawford R, Williams BF, Williams BG (1994). "Influence of Needle Gauge in Mantoux Skin Testing." Chest. **106**(5):1463-1465.

66. ^ Lambert PH, Laurent PE (2008). "Intradermal Vaccine Delivery: Will New Delivery Systems Transform Vaccine Administration?" Vaccine. **26**(26):3197-3208.

67. a, b, c, d Pervaiz A (2017). "Fractional-Dose Inactivated Poliovirus Vaccine Campaign—Sindh Province, Pakistan, 2016." MMWR Morb Mortal Wkly Rep. **66**.

68. ^ Bahl S (2016). "Fractional-Dose Inactivated Poliovirus Vaccine Immunization Campaign—Telangana State, India, June 2016." MMWR Morb Mortal Wkly Rep. **65**.

69. ^ Farag NH, Mansour Z, Torossian L, Said R, Snider CJ, Ehrhardt D (2018). "Feasibility of Jet Injector Use During Inactivated Poliovirus Vaccine House-to-House Vaccination Campaigns." Vaccine. **36**(32):4935-4938.

70. a, b, c, d, e, f, g Bashorun AO, Hydara MB, Adigweme I, Umesi A, Danso B, Johnson N, Clarke E (2022). "Intradermal Administration of Fractional Doses of the Inactivated Poliovirus Vaccine in a Campaign: A Pragmatic, Open-Label, Non-Inferiority Trial in The Gambia." Lancet Glob Health. **10**(2):e257-e268.

71. a, b Okayasu H, Sein C, Chang Blanc D, Gonzalez AR, Zehrung D, Jarrahian C, Sutter RW (2017). "Intradermal Administration of Fractional Doses of Inactivated Poliovirus Vaccine: A Dose-Sparing Option for Polio Immunization." J Infect Dis. **216**(suppl_1):S161-S167.

72. ^ World Health Organization (2018). "PharmaJet Tropis Prequalification, PQS Code E008/071, Single Use Auto-Disable Needle-Free Jet Injector." World Health Organization. https://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/categorypage.aspx?id_cat=37.

73. a, b, c, d, e, f, g, h, i, j, k, l Daly C, Molodecky NA, Sreevatsava M, Belayneh AD, Chandio SA, Partridge J, Maham ud A (2020). "Needle-Free Injectors for Mass Administration of Fractional Dose Inactivated Poliovirus Vacci ne in Karachi, Pakistan: A Survey of Caregiver and Vaccinator Acceptability." Vaccine. **38**(8):1893-1898.

74. a, b, c, d, e, f, g Yousafzai MT, Saleem AF, Mach O, Baig A, Sutter RW, Zaidi AK (2017). "Feasibility of Conductin g Intradermal Vaccination Campaign With Inactivated Poliovirus Vaccine Using Tropis Intradermal Needle Free Injection System, Karachi, Pakistan." Heliyon. **3**(8).

75. a, b, c, d, e, f, g Saleem AF, Mach O, Yousafzai MT, Khan A, Weldon WC, Oberste MS, Zaidi AK (2017). "Needle A dapters for Intradermal Administration of Fractional Dose of Inactivated Poliovirus Vaccine: Evaluation of I mmunogenicity and Programmatic Feasibility in Pakistan." Vaccine. **35**(24):3209-3214.

76. ^ Ahmad M, Verma H, Deshpande J, Kunwar A, Bavdekar A, Mahantashetti NS, Sutter RW (2022). "Immuno genicity of Fractional Dose Inactivated Poliovirus Vaccine in India." J Pediatr Infect Dis Soc. **11**(2):60-68.

77. a, b Alsbrooks K, Hoerauf K (2022). "Prevalence, Causes, Impacts, and Management of Needle Phobia: An Int ernational Survey of a General Adult Population." PLoS One. **17**(11):e0276814.

78. a, b Hasnan S, Tan NC (2021). "Multi-Domain Narrative Review of Vaccine Hesitancy in Childhood." Vaccine. **39**(14):1910-1920.

79. a, b, c, d, e, f Nouh K, Haga A, Sumaili K, Farid M, Alin M, Shube M, Bile A (2024). "Use of a Fractional Dose of I nactivated Polio Vaccine (fIPV) to Increase IPV Coverage Among Children Under 5 Years of Age in Somalia." BMC Glob Public Health. **2**(1):16.

80. ^ Frost LJ, Reich MR (2008). Access: How Do Good Health Technologies Get to Poor People in Poor Countrie s? xi+-245.

81. a, b, c, d, e Resik S, Tejeda A, Mach O, Sein C, Molodecky N, Jarrahian C, Sutter RW (2015). "Needle-Free Jet Inje ctor Intradermal Delivery of Fractional Dose Inactivated Poliovirus Vaccine: Association Between Injection Quality and Immunogenicity." Vaccine. **33**(43):5873-5877.

82. a, b, c, d, e, f, g, h Biya O (2023). "Notes From the Field: House-to-House Campaign Administration of Inactivat ed Poliovirus Vaccine—Sokoto State, Nigeria, November 2022." MMWR Morb Mortal Wkly Rep. **72**.

83. ^ Troy SB, Kouiavskaia D, Siik J, Kochba E, Beydoun H, Mirochnitchenko O, Maldonado Y (2015). "Compariso n of the Immunogenicity of Various Booster Doses of Inactivated Polio Vaccine Delivered Intradermally Vers us Intramuscularly to HIV-Infected Adults." J Infect Dis. **211**(12):1969-1976.

84. a, b, c Bullo UF, Mehraj J, Raza SM, Rasool S, Ansari NN, Shaikh AA, Chandio SA (2021). "An Experience of Ma ss Administration of Fractional Dose Inactivated Polio Vaccine Through Intradermal Needle-Free Injectors i n Karachi, Sindh, Pakistan." BMC Public Health. **21**:1-7.

85. ^ a, b, c, d World Health Organization (2024). "Report of the Sixteenth Meeting of the Technical Advisory Group on Poliomyelitis Eradication in Afghanistan and Pakistan (TAG), Doha, Qatar 22-25 May 2024." World Health Organization. https://reliefweb.int/report/afghanistan/report-sixteenth-meeting-technical-advisory-group-poliomyelitis-eradication-afghanistan-and-pakistan-tag-doha-qatar-22-25-may-2024.

86. ^ El-Hay A, Seham A, Abed Allah AK (2020). "Effect of Implementing Training Module on Competence of Internship Nursing Students Performance Regarding Needle Stick and Sharp Injuries Safety Issues." Tanta Sci Nurs J. **19**(1):152-180.

87. ^ Lara HJO (2013). "Quantifying the Ergonomic Impact on Healthcare Workers Using a Needle-Free Injector Device." University of South Florida.

88. ^ United States Agency for International Development (USAID) (2022). "Grant: PharmaJet, Evaluating the Impact of a Needle-Free Delivery Device on Polio Immunization." United States Agency for International Development (USAID). https://divportal.usaid.gov/s/project/a0gt0000001p7OyAAI/evaluating-the-impact-of-a-needlefree-delivery-device-on-polio-immunization.

89. ^ Armbruster N, Jasny E, Petsch B (2019). "Advances in RNA Vaccines for Preventive Indications: A Case Study of a Vaccine Against Rabies." Vaccines. **7**(4):132.

90. ^ Teixeira L, Medioni J, Garibal J, Adotevi O, Doucet L, Durey MAD, Langlade-Demoyen P (2020). "A First-in-Human Phase I Study of INVAC-1, an Optimized Human Telomerase DNA Vaccine in Patients With Advanced Solid Tumors." Clin Cancer Res. **26**(3):588-597.

91. ^ Thomas SK, Cha SC, Smith DL, Kim KH, Parshottam SR, Rao S, Kwak LW (2018). "Phase I Study of an Active Immunotherapy for Asymptomatic Phase Lymphoplasmacytic Lymphoma With DNA Vaccines Encoding Antigen-Chemokine Fusion: Study Protocol." BMC Cancer. **18**:1-9.

92. ^ Nelson EAS, Lam HS, Choi KC, Ho WC, Fung LE, Cheng FW, Chan PK (2013). "A Pilot Randomized Study to Assess Immunogenicity, Reactogenicity, Safety and Tolerability of Two Human Papillomavirus Vaccines Administered Intramuscularly and Intradermally to Females Aged 18–26 Years." Vaccine. **31**(34):3452-3460.

93. ^ Hernandez-Franco JF, Mosley YYC, Franco J, Ragland D, Yao Y, HogenEsch H (2021). "Effective and Safe Stimulation of Humoral and Cell-Mediated Immunity by Intradermal Immunization With a Cyclic Dinucleotide/Nanoparticle Combination Adjuvant." J Immunol. **206**(4):700-711.

94. ^ BusinessWire (2023). "First Human Clinical Study to Assess U.S. Department of Defense DNA Vaccine Candidate Against Venezuelan Equine Encephalitis Delivered With PharmaJet Precision Delivery Systems." BusinessWire. https://www.businesswire.com/news/home/20231116985895/en/First-Human-Clinical-Study-to-A

ssess-U.S.-Department-of-Defense-DNA-Vaccine-Candidate-against-Venezuelan-Equine-Encephalitis-Delivered-with-PharmaJet-Precision-Delivery-Systems.

95. ^a ^b Ledesma-Feliciano C, Chapman R, Hooper JW, Elma K, Zehrung D, Brennan MB, Spiegel EK (2023). "Improved DNA Vaccine Delivery With Needle-Free Injection Systems." Vaccines. **11**(2):280.
96. ^ Sheridan C (2021). "First COVID-19 DNA Vaccine Approved, Others in Hot Pursuit." Nat Biotechnol. **39**(12):1479-1482.
97. ^ Yadav PD, Kumar S, Agarwal K, Jain M, Patil DR, Maithal K, Abraham P (2021). "Assessment of Immunogenicity and Protective Efficacy of ZyCoV-D DNA Vaccine Candidates in Rhesus Macaques Against SARS-CoV-2 Infection." BioRxiv. 2021-02.
98. ^ Lee SS, Traore T, Zumla A (2024). "The WHO Mpox Public Health Emergency of International Concern Declaration: Need for Reprioritisation of Global Public Health Responses to Combat the MPXV Clade I Epidemic." Int J Infect Dis. **147**.
99. ^ World Health Organization (2018). "Rabies Vaccines: WHO Position Paper – April 2018." World Health Organization. https://www.who.int/publications/i/item/who-wer9316.
100. ^ Brooks JT, Marks P, Goldstein RH, Walensky RP (2022). "Intradermal Vaccination for Monkeypox—Benefits for Individual and Public Health." N Engl J Med. **387**(13):1151-1153.

Declarations

Funding: Funding for this study was provided by PharmaJet.

Potential competing interests: B.G.B., M.E.S., R.M.S., and A.A. were provided with a small stipend renumeration for their time spent writing and editing the manuscript. C.D. is a PharmaJet consultant, PL is a PharmaJet employee.