The cost-effectiveness of delivering vaccines through a controlled temperature chain (CTC)

Anna-Lea Kahn (WHO)

Mercy Mvundura (PATH)

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Shaping a resilient and adaptive immunization program

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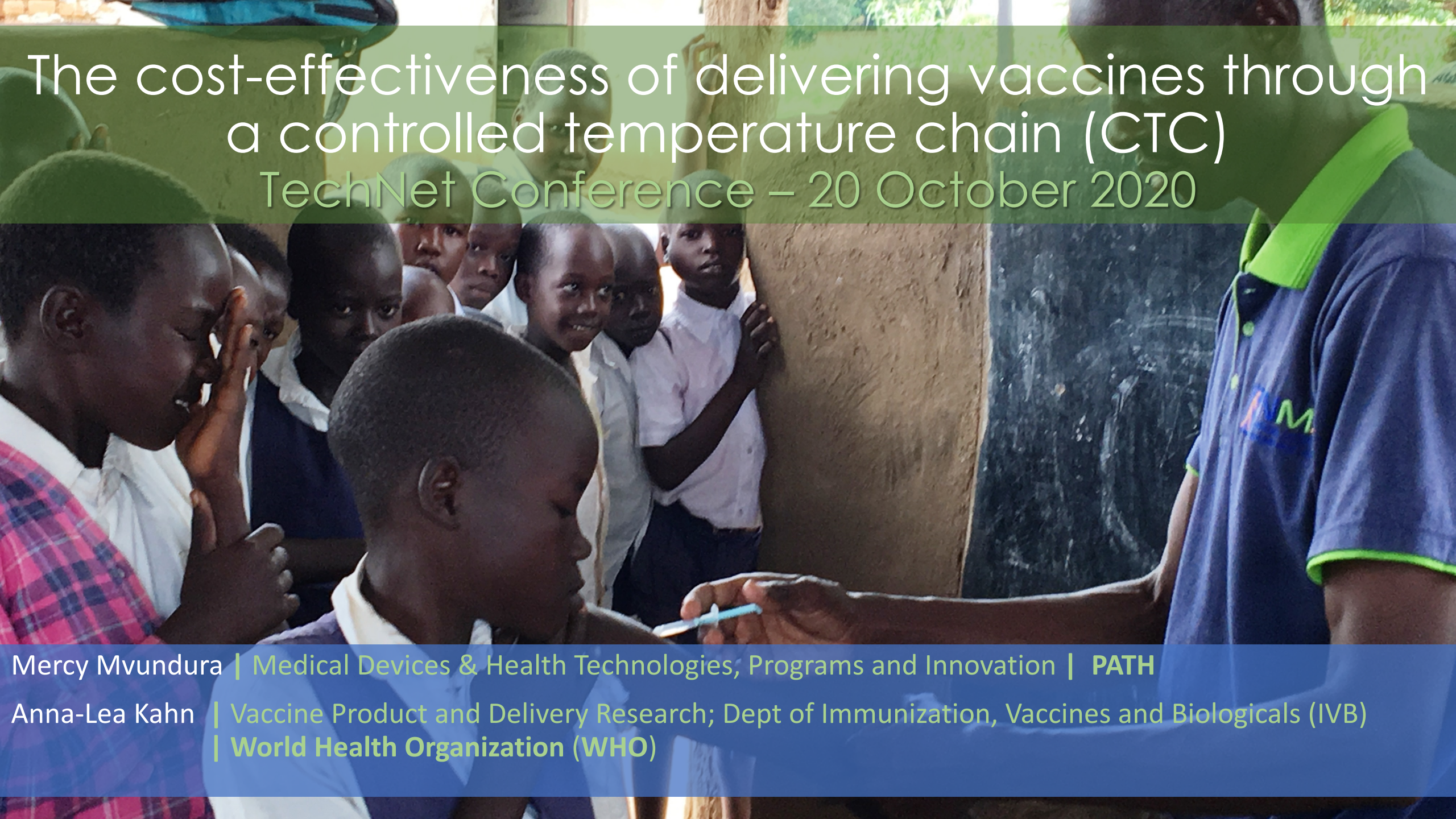


Mercy Mvundura | Medical Devices & Health Technologies, Programs and Innovation | **PATH**

Anna-Lea Kahn | Vaccine Product and Delivery Research; Dept of Immunization, Vaccines and Biologicals (IVB) | **World Health Organization (WHO)**

Introduction to the Controlled Temperature Chain (CTC)

- **DEFINITION →** CTC use of vaccines allows for **removal of the vaccine from the standard cold chain into ambient temperatures** typically up to +40°C for a minimum of 3 days, for one permanent occasion prior to administration.
  - Heat-stable vaccines differ in the length of time they can be stored in a CTC and the maximum temperature they can endure while remaining stable and potent.
  - CTC qualification involves regulatory approval and prequalification by WHO.
  - Key time/temperature monitoring tools = VVM + Peak Threshold Temperature Indicator (PTTI)

- **NOTED BENEFITS OF CTC →** Increased vaccine delivery efficiencies, reduced burden on HCW, reduced delivery costs, increased vaccination coverage and equity
  → especially beneficial in campaign and special strategy contexts

- **IMPLEMENTATION OBJECTIVES →** Ensure high quality implementation effort which optimizes the flexibility and benefits offered by CTC and minimizes any associated risks.

Licensure and Prequalification status for CTC Vaccines

AVAILABLE

1. MenAfriVac® (2012)
   meningococcal A vaccine
   ➲ 4 days @ 40°C

2. Gardasil4™ (2016)
   human papillomavirus (HPV)
   ➲ 3 days @ 42°C

3. Shanchol™ (2018)
   oral cholera vaccine (OCV)
   ➲ 14 days @ 40°C

PIPELINE

1. Hepatitis B (birth dose)
2. Tetanus diphtheria vaccine
3. Typhoid conjugate vaccine
4. OCV
5. HPV

POTENTIAL

- Rabies vaccine

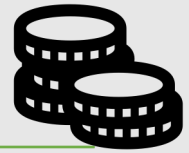
Prerequisites for CTC Labelling for Vaccines

An informed and willing vaccine manufacturer

A sufficiently heat stable product
(may need to increase initial potency)

Generation of stability data at one or two additional temperatures

Additional studies for some vaccines
(*preservative efficacy, post-reconstitution stability*)

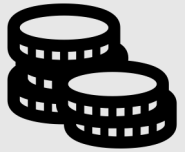


Inclusion of CTC storage information in the product insert

National regulatory approval

WHO prequalification approval

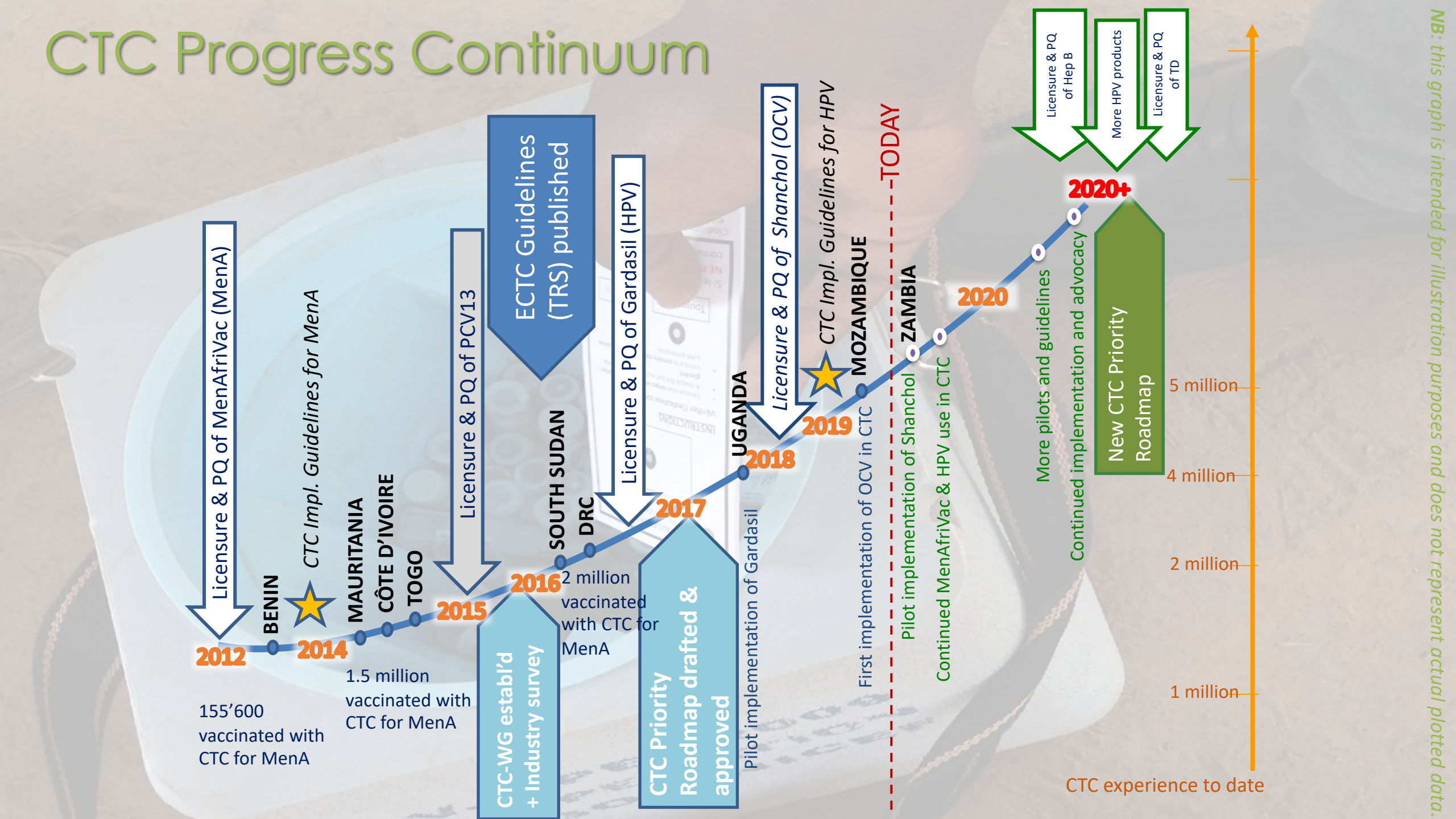
Potentially labeling primary containers with a VVM-TI rather than a VVM *(75% higher cost)*



Why CTC uptake might fail at programme level

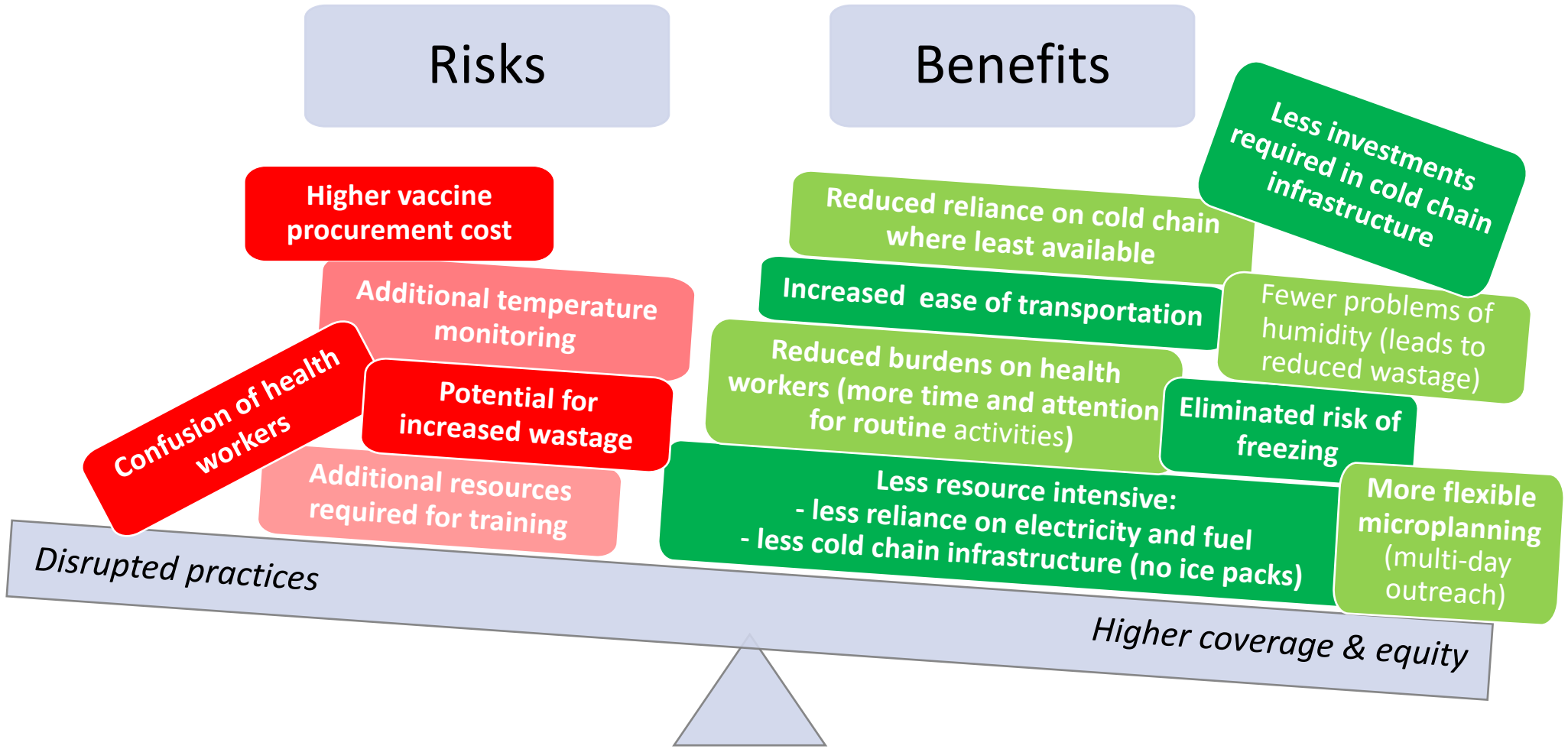
- Example 1: incompatible use case
  - PCV approved for CTC in 2015
  - Routine vaccine delivered with other vaccines requiring cold chain
- Example 2: unsuitable presentation
  - MSF Measles study demonstrated feasible stability
  - Single dose format not suitable for LMIC use because of higher vaccine price and larger cold chain volume / poor cost effectiveness
- Example 3: unsustainable price
  - CTC-compatible HepB-BD offered at potential 1 USD$ per dose price for single dose presentation
  - HepB-BD in Uniject™ (more expensive that single dose vials)

CTC Progress Continuum



NB: this graph is intended for illustration purposes and does not represent actual plotted data.

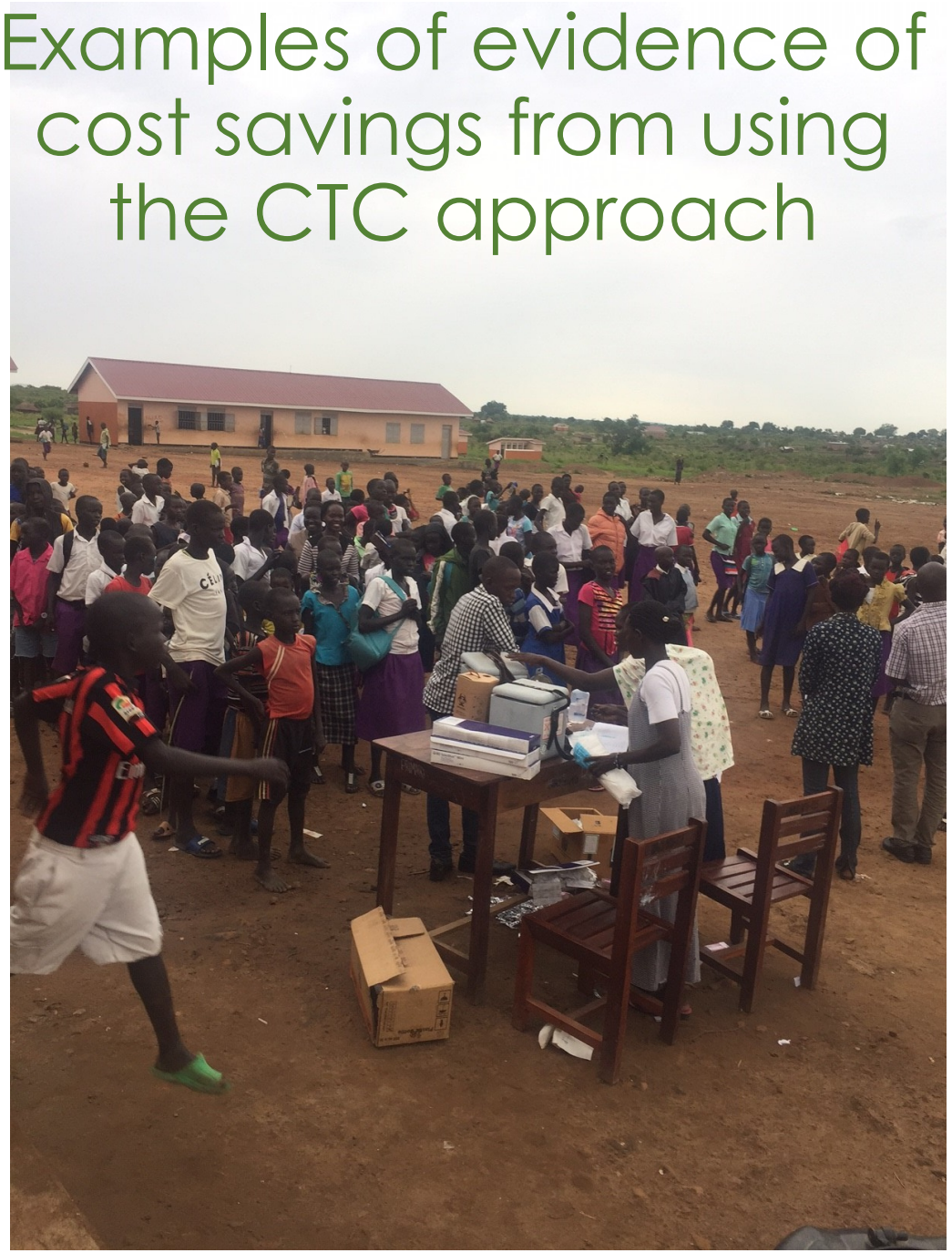
Risk/Benefit considerations when deciding on CTC



Potential programmatic cost implications of CTC use vs cold chain excluding vaccine price

Cost categories	Examples of cost components	Likely change with CTC vs. cold chain
Supplies	• Peak threshold temperature indicators (assuming no VVM-TI).	↑
Training	• Training of vaccinators.	↑
Cold chain	• Capital costs for cold chain equipment; energy (electricity/gas) costs; costs for backup power sources for cold chain equipment.	↓
Transport	• Capital and fuel costs for vehicles used to collect or deliver vaccines (between district and health facility/vaccination sites). • Costs of trips to replenish ice packs during vaccination sessions.	↓
Human resources for logistics	• Per diems for trips to collect/deliver vaccines. • Time spent on freezing ice packs and cold chain–related activities.	↓
Human resources for service delivery and supervision	• Time spent on vaccine management at the end of vaccination sessions and supervision during sessions.	↑

Examples of evidence of cost savings from using the CTC approach



Men A vaccine campaign in Chad - Lydon et al (2014)

- A modeling study estimated that if the CTC approach had been used during a Men A vaccine campaign in Chad, logistics costs per dose would have been reduced by 50%.
- The study estimated a logistics costs saving of $0.12 per dose with CTC use.
- The largest share of savings with CTC use would have stemmed from elimination of the need to augment cold chain in districts that did not have adequate cold chain equipment to use during the campaign.

Men A vaccine campaign in Togo – Mvundura et al (2017)

- A study conducted during a Men A vaccine campaign in Togo estimated more modest savings from use of the CTC approach in districts where cold chain equipment was not augmented for the campaign.
- The study estimated that if the facilities without cold chain equipment had not used a CTC approach but had received daily deliveries of vaccines, the average cost per dose would have increased to $0.063 on average.
- Therefore CTC use reduced logistics costs per dose for these facilities by ~30%.

Key takeaways:

- CTC can result in savings in logistics costs, but the magnitude of the logistics cost savings depends on country / local context and how challenges with cold chain limitations are addressed.
- Estimated savings from CTC use from these two studies ranges from 30% to 50%.

Examples of evidence of CTC programmatic impact

Meningitis A campaign delivery with CTC

Sept-Nov 2014 *(Mauritania, Togo, Cote d'Ivoire)*

- High acceptance by HCW / No confusion reported
- #persons vaccinated using a CTC: 1,522,953
- Coverage rates: no difference
  (High coverage in all districts)
- No significant impact on wastage
- #vials discarded due to CTC excursion expiry: 60
- #vials discarded due to exposure >°40: 74
  (all in Mauritania/single vaccine carrier)

HPV School-based delivery with CTC

Oct 2017 *(Uganda: Districts of Adjumani and Luwero)*

- Confirmed reduction in burden on HCW/EPI Staff
- Improved coverage and access
- CTC might alleviate additional supply chain costs

Alternative storage arrangements had to be made in 3 of the districts because 17%-39% of HF did not have refrigerators or refrigerators were not working.

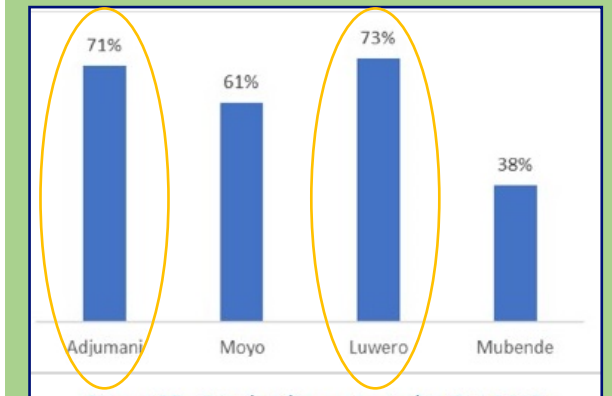


Figure 28 *- Total girls vaccinated in Oct 2017 (source: UNEPI)*

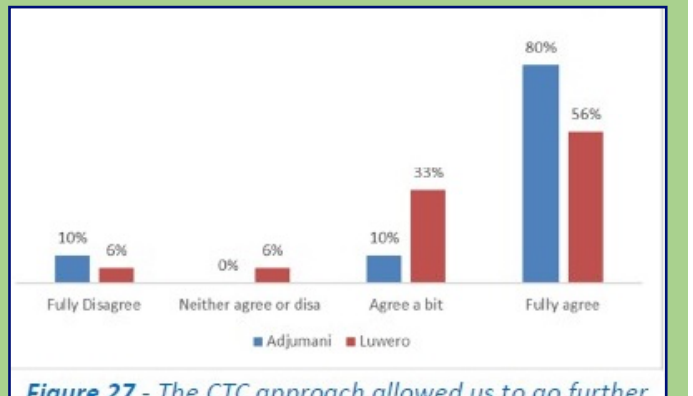


Figure 27 *- The CTC approach allowed us to go further with just a few vaccines to find more girls*

Example of evidence of cost-effectiveness of the CTC approach

Global modeling of Hep B birth dose vaccine delivery – Scott et al 2018

- The study modeled the potential cost-effectiveness of the CTC strategy for Hep B birth dose vaccine delivery.
- CTC use was assumed to result in:
  - a 10% increase in Hep B vaccine coverage in the baseline scenario.
  - the doubling of the delivery costs (compared to delivery costs when the cold chain approach was used). This is because of the added costs of community-based vaccination enabled by the CTC approach.
- The study found that a CTC strategy was cost-saving in 4 of the 6 WHO regions included in the model and highly cost effective in the other 2 regions.

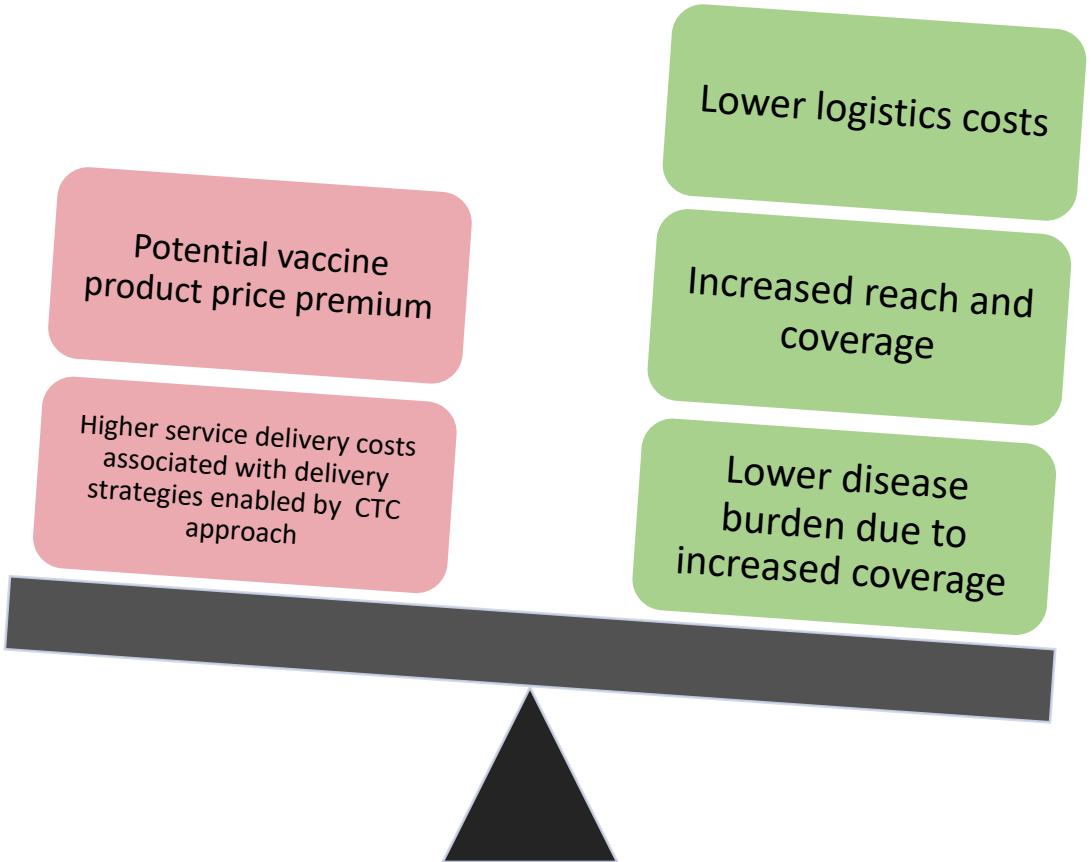
Key takeaway:

- Use of the CTC approach for Hep B birth dose vaccine delivery is likely to be cost saving or highly cost effective if coverage gains can be achieved due to expanding the reach of vaccines.

Adding up the evidence on the potential cost-effectiveness of the CTC approach

Potential cost increases with CTC approach

Potential savings with CTC approach



The CTC approach is likely to be cost effective even with a vaccine price premium associated with CTC labeling

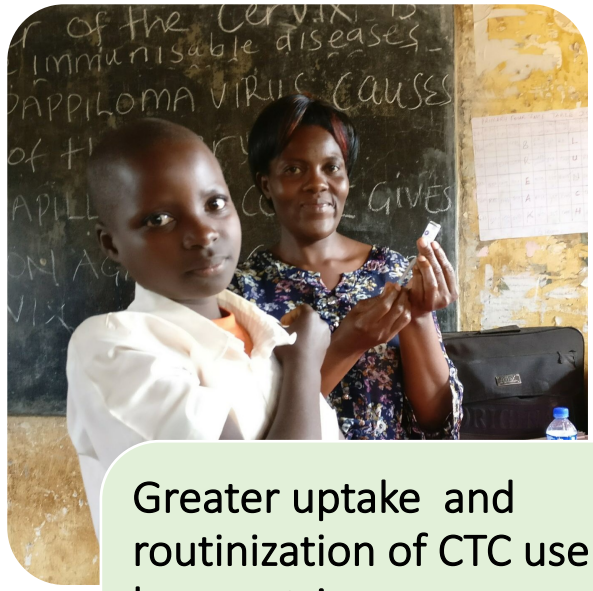
What needs to happen to continue to advance the CTC agenda given it's likely cost-effectiveness?

Increase the number of priority vaccines labeled for CTC use

- Manufacturers' awareness of country needs and priority vaccines - informing and spurring manufacturers' willingness to avail CTC labeled vaccines
- Market shaping for CTC labeled vaccines

Expand evidence based on programmatic implications of CTC use

- Additional evidence on cost implications of CTC use for other vaccines
- Programmatic evidence on impact of CTC use on reach and coverage



Greater uptake and routinization of CTC use by countries

- Adoption of CTC approach beyond pilots
- Multiple implementations of CTC approach for several vaccines in the same country

For more information, please contact:

Anna-Lea Kahn: kahna@who.int

Mercy Mvundura: mmvundura@path.org

To read more about CTC please consult the following pages of the WHO website:
https://www.who.int/immunization/programmes_systems/supply_chain/ctc/en/