“Total Systems Effectiveness (TSE) is a holistic approach to prioritise or decide between products from a systems perspective, taking into consideration coverage, equity, programmatic implications and full systems cost.”
Immunization programmes have become more complex...

**Table 1: Summary of WHO Position Papers - Recommendations for Routine Immunization**

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Children</th>
<th>Adolescents</th>
<th>Adults</th>
<th>Considerations (see footnotes for details)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recombinant for all immunization programmes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCG</td>
<td>1 dose</td>
<td></td>
<td></td>
<td>Birth dose and HIV: Universal vs selective vaccination; Co-administration; Vaccination of older age groups</td>
</tr>
<tr>
<td>Hepatitis B2</td>
<td>3-4 doses (see footnote for schedule options)</td>
<td>3 doses (for high-risk groups if not previously immunized) (see footnote)</td>
<td></td>
<td>Birth dose; Premature and low birth weight; Co-administration and combination vaccine; Definition: high-risk</td>
</tr>
<tr>
<td>Polio</td>
<td>3-4 doses (at least one dose of IPV) with DTP/BCG</td>
<td></td>
<td></td>
<td>bOPV birth dose; Type of vaccine; Transmission and importation risk criteria</td>
</tr>
<tr>
<td>DTP-containing vaccine (DTPCV)*</td>
<td>3 doses</td>
<td>2 Boosters 12-23 months (DTPCV) and 4-7 years (Td)</td>
<td>1 Booster 9-15 yrs (Td)</td>
<td>Delayed/interrupted schedule; Combination vaccine; Maternal immunization</td>
</tr>
<tr>
<td>Haemophilus influenzae type b2</td>
<td>Option 1</td>
<td>3 doses, with DTPV</td>
<td></td>
<td>Single dose if &gt; 24 months of age; Not recommended for children &gt; 3 yrs old; Delayed/interrupted schedule; Co-administration and combination vaccine</td>
</tr>
<tr>
<td></td>
<td>Option 2</td>
<td>2 or 3 doses, with booster at least 6 months after last dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal (Conjugate)*</td>
<td>Option 1</td>
<td>3 doses, with DTPV</td>
<td></td>
<td>Vaccine options; Initiate before 6 months of age; Co-administration; HIV and prematurity neutropenia booster</td>
</tr>
<tr>
<td></td>
<td>Option 2</td>
<td>2 doses before 6 months of age, plus booster dose at 9-15 months of age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Rotarix: 2 doses with DTPCV</td>
<td>Rotarix: 2 doses with DTPCV</td>
<td></td>
<td>Vaccine options; Not recommended if &gt; 24 months old</td>
</tr>
<tr>
<td>Measles</td>
<td>2 doses</td>
<td></td>
<td></td>
<td>Combination vaccine; HIV early vaccination; Pregnancy</td>
</tr>
<tr>
<td>Rubella</td>
<td>1 dose (see footnote)</td>
<td>1 dose (adolescent girls and/or childbearing aged women if not previously vaccinated) (see footnote)</td>
<td></td>
<td>Achieve and sustain 90% coverage; Combination vaccine and Co-administration; Pregnancy</td>
</tr>
<tr>
<td>HPV16</td>
<td></td>
<td></td>
<td></td>
<td>Target 9-24 year old girls; Multi-age cohort vaccination; Pregnancy; Older age groups ≥ 15 years 3 doses; HIV and immunocompromised; 2 doses (females)</td>
</tr>
</tbody>
</table>
Increasing variety of new vaccines with different immunisation schedules...
Cost of immunizing a child has increased...
More people to vaccinate...
Need rapid response strategies...

Source: The Guardian, Sunday 18th March
We are struggling to reach coverage goals…
Hypothesis: we need new approaches to reach elimination targets
We already have differentiated products...

- Price
- No of doses
- Wastage
- Storage
- Cold chain footprint
And more in the pipeline...

Serum Institute of India Ltd., India

**MEASLES VACCINE LIVE ATTENUATED 1, 2, 5, 10 DOSES**

<table>
<thead>
<tr>
<th></th>
<th>1 DOSE</th>
<th>2 DOSE</th>
<th>5 DOSE</th>
<th>10 DOSE</th>
</tr>
</thead>
</table>

![Image of measles vaccine bottles and a hand applying a bandage]
TSE is a tool to articulate the public health value proposition of novel vaccines and delivery approaches.

(Direct / indirect) benefit of reducing vaccine preventable disease burden

Cost of development, procurement, delivery
# TSE vaccine product framework

<table>
<thead>
<tr>
<th>Equity is considered across all elements of the framework</th>
<th>TSE component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact</td>
<td>Health impact</td>
</tr>
<tr>
<td></td>
<td>Coverage</td>
</tr>
<tr>
<td></td>
<td>Safety</td>
</tr>
<tr>
<td>Cost</td>
<td>Commodity cost</td>
</tr>
<tr>
<td></td>
<td>Delivery cost</td>
</tr>
</tbody>
</table>
### Methodology overview

#### SAFETY
**Input:**
- AEFI incidence (P)
- Attributes affecting vaccine safety (P)
- Frequency of needlestick injury, contamination, etc (C)
- Number doses administered (C3)

**Output:**
- S1: Number hospitalisations
- S2: Number deaths

#### COMMODITY COST
**Input:**
- Number of doses (C3)
- Number fully immunised (C1)
- Wastage (P)
- Commodity price/co-pay (P/C)
- Procurement cost (P)

**Output:**
- CC1: Number of each commodity procured
- CC2: Total financial cost (commodities)
- CC3: Financial cost per FIC

#### HEALTH SYSTEM CHANGES
**Input:**
- Social mobilisation/IEC intensity (P)
- Number of HW (C)
- Training/supervision intensity (P)
- Storage volume (P)
- Storage capacity (C)
- Quantity of each commodity procured (CC1)

**Output:**
- HS1: Additional HW required
- HS2: New storage required

#### DELIVERY COST
**Input:**
- Number each commodity (CC1)
- Waste disposal cost (C)
- Method of waste disposal (P)
- Transport cost (C)
- Change HW at each level (HS1)
- Change in storage (HS2)
- Time for administration (P)
- Cost of administration (C)

**Output:**
- DC1: Total financial cost (delivery)
- DC2: Financial cost per FIC

#### HEALTH IMPACT
**Input:**
- Effectiveness/efficacy (C/P)
- Duration of protection (P)
- Attributes affecting vaccine effectiveness (P)
- Proportion of ineffective vaccine doses administered (e.g. due to heatfreeze exposure) (C)
- Number fully/partially immunised (C1, C2)
- Disease epidemiology (number cases, deaths, hospitalisations) (C)

**Output:**
- H1: Number cases averted
- H2: Number hospitalisations averted
- H3: Number deaths averted

#### COVERAGE
**Input:**
- Target population (C)
- Vx product attributes that relate to coverage (P)
- Barriers to vaccination (C)

**Output:**
- C1: Number fully immunised
- C2: Number partially immunised
- C3: Number doses administered

#### FINANCIAL RISK PROTECTION
**Input:**
- OOP cost for vaccination (C)
- Number doses administered (C2)
- OOP for RV illness (C)
- Health impact (H1, H2, H3)

**Output:**
- F1: Change in OOP cost per capita
- F2: Catastrophic health expenditure cases averted

**Key**
- P = product attribute
- C = country attribute
- C1/S2/etc = output from other TSE component
How will methodology from existing tools be incorporated?

**TSE Lite** (WDI): estimates increased coverage by the extent to which product attributes address country barriers to vaccination

**UNIVAC** (PAHO/LSHTM): includes estimate for cases averted, with global data

**V-TIA** (PATH): projects costs for multiple products using Tanzania as a reference

**C4P**: includes methodology for introduction costs

Next steps:
- Map assumptions in existing tools
- To what extent can existing tools pre-populate the TSE model?
- How can we adapt existing methodology to align with TSE (e.g. incorporate equity lens, multiple products, etc)
How is TSE intended to help?

Downstream: the uptake conundrum

Countries lack tools to evaluate trade-offs of differentiated products.

Upstream: innovation conundrum

Without clarity on preferred attributes and demand, vaccine manufacturers and funders are challenged in developing appropriate products.
What does TSE do?

**Downstream: the uptake conundrum**
Countries lack tools for product selection that show trade-offs and support differentiated procurement. **TSE strengthens multi-criteria decision-making for coverage and equity**

**Upstream: innovation conundrum**
Without clarity on attributes and demand, vaccine manufacturers are challenged in developing appropriate products. **TSE communicates country priorities and preferences for procurement and R&D**
### Accelerating Availability & Access to Vaccine Innovation in LMICs

<table>
<thead>
<tr>
<th>TSE approach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Country needs</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Traditional approach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>R&amp;D</strong></td>
</tr>
</tbody>
</table>

TSE promotes a change in the product development paradigm, so that **country demand informs product development**

.... And creates a ‘pull’ for new products that meet LMIC preferences and reduces the timeline between licensure and uptake
**Country use case**

*Stakeholders:* MOH, NITAG, MOF

TSE informs selection of product that fit country-specific contexts

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**Global use case**

*Stakeholders:* global health policy, donors and procurers

TSE prioritises vaccine products and attributes that meet country needs through policymaking, investment and market shaping

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**R&D use case**

*Stakeholders:* vaccine manufacturers, product developers

TSE aligns value propositions, TPPs and investment with country demand
Adapting TSE to align with existing guidance
Work so far

☑ Country pilots in Indonesia and Thailand:

ITAGI, EPI and MOH, WHO Country Office, University of Indonesia, Padjajaran University, Muhammadiyah University, Gadjah Mada University
Planning Bureau, NRA, NITAG SEA Indonesia, Gavi

☑ Country pilots in Mali and Rwanda planned

☑ Transitioning from country use case to global use case....
Looking ahead

Completing in country pilot study: data end of 2018

Grant planning for 2019 – 2021 focusing on global use case: how does data from countries inform the types of products that we need in the pipeline?
How are TSE and market shaping related?

Objective: better tools, approaches, innovations to reach coverage and equity goals

- Barriers assessment & TSE country use case
- Define preferred product attributes & identifies selection criteria
  - Pipeline vaccines
  - More of an existing vaccine
  - New presentation or delivery technology