Infant feeding and WASH interventions in children exposed to HIV in SHINE

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• No conflicts to disclose
Stunting is associated with reduced health, learning and human capital
Stunting has a complex underlying network of determinants

UNICEF Framework
Infections contribute to poor growth
Infections contribute to poor growth
Environmental enteric dysfunction
Could this be the answer to stunting?
Sanitation Hygiene Infant Nutrition Efficacy (SHINE) trial

- Two rural districts in Zimbabwe
- 5270 women enrolled
- Outcomes stratified by maternal HIV status (15% positive)
- Interventions from early pregnancy to 18mo of age
- **Primary outcomes:** Linear growth and haemoglobin at 18mo
- **Substudy at 24mo of age:** Early Child Development
The IYCF Intervention

- **Module 1**: Into to IYCF
  - Keep exclusively breastfeeding until 6 months
- **Module 2**: Thick porridge SQ-LNS
- **Module 3**: Process food
  - “A baby can eat anything adults eat”
- **Module 4**: Feeding baby during illness
- **Module 5**: Feed your baby from each food group

- **5 mo.**
- **6 mo.**
- **7 mo.**
- **8 mo.**
- **9 mo.**

*Small quantity lipid-based nutrient supplement (SQ-LNS) 18 mo.*
**The WASH Intervention**

**Module 1**
Put all feces in latrine. 
*Latrine constructed Tippy Taps installed*

**Module 2**
Handwashing with soap at key times
*Soap delivery*

**Module 3**
Protect child from feces and soil ingestion
*Play space and mat delivered*

**Module 4**
Treat drinking water especially for infant after EBF
*Water Guard delivery*

**Module 5**
Prepare Hygienic complementary food

- **20-24 wk gest**
- **29 wk gest**
- **Birth**
- **2 mo.**
- **4 mo.**
- **5 mo.**

- **Use latrine**
- **Soap delivered monthly**
- **Water chlorination**
Trial flow to 18 months of age

726 HIV-positive women

SOC (control)  
166 live births (46 clusters)

IYCF  
158 live births (48 clusters)

WASH  
205 live births (44 clusters)

IYCF+WASH  
209 live births (47 clusters)

Evaluated at 18 months

147 (46 clusters)

147 (48 clusters)

184 (44 clusters)

190 (47 clusters)

HIV status at 18 months

136 CHEU  
2 HIV positive  
9 HIV unknown

135 CHEU  
3 HIV positive  
9 HIV unknown

163 CHEU  
9 HIV positive  
12 HIV unknown

160 CHEU  
8 HIV positive  
22 HIV unknown

738 HIV-exposed live births

51 deaths  
18 lost to follow-up  
1 exit

668 evaluated at 18 months
## Baseline characteristics

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<td>28%</td>
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<tr>
<td>Improved source of drinking water</td>
<td>62%</td>
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<tr>
<td>Household meets minimum dietary diversity</td>
<td>37%</td>
<td>41%</td>
<td>36%</td>
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<tr>
<td>Maternal age, years; mean (SD)</td>
<td>29.7 (6.0)</td>
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<td>29.6 (5.7)</td>
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<td>Completed schooling, years (SD)</td>
<td>9.4 (1.8)</td>
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<td>CD4 count in pregnancy, cells/μL; mean (SD)</td>
<td>503 (215)</td>
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<td>Sex of infant (% female)</td>
<td>48%</td>
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<td>Mean birth weight, kg; mean (SD)</td>
<td>3.00 (0.50)</td>
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High uptake of SQ-LNS and improved infant diet in the IYCF arms

Consumed SQ-LNS past 24h

Dietary quality

Prendergast AJ et al., Lancet Child Adolesc Health 2019
Sanitation and hygiene behaviours changed with WASH intervention

Prendergast AJ et al., Lancet Child Adolesc Health 2019
Effects of IYCF on stunting and anaemia at 18 months of age

Children HIV-exposed

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<tr>
<th>% Stunted</th>
<th>No IYCF</th>
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<td>50</td>
<td>40</td>
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<th>% Anemic</th>
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<tr>
<td>14</td>
<td>10.5</td>
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RR (95%CI)

- Unadjusted: 0.81 (0.68, 0.97)
- Adjusted: 0.83 (0.71, 0.99)

Prendergast AJ et al., Lancet Child Adolesc Health 2019
Effects of IYCF on stunting and anaemia at 18 months of age

Children HIV-exposed

- % Stunted
  - No IYCF: 50
  - IYCF: 40
  - RR (95%CI): Unadjusted 0.81 (0.68, 0.97), Adjusted 0.83 (0.71, 0.99)

- % Anemic
  - No IYCF: 14
  - IYCF: 10.5
  - RR (95%CI): Unadjusted 0.52 (0.34, 0.79), Adjusted 0.95 (0.90, 0.99)

Children HIV-unexposed

- % Stunted
  - No IYCF: 34.6
  - IYCF: 27.4
  - RR (95%CI): Unadjusted 0.79 (0.72, 0.87), Adjusted 0.81 (0.74, 0.88)

- % Anemic
  - No IYCF: 13.9
  - IYCF: 10.5
  - RR (95%CI): Unadjusted 0.75 (0.62, 0.90), Adjusted 0.76 (0.63, 0.92)

Prendergast AJ et al., Lancet Child Adolesc Health 2019

Humphrey JH et al., Lancet Glob Health 2019
Effects of WASH on stunting and anaemia at 18 months of age

Children HIV-exposed

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<thead>
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<th>% Stunted</th>
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<tr>
<td>No WASH</td>
<td>46</td>
</tr>
<tr>
<td>WASH</td>
<td>45</td>
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Unadjusted | 0.97 (0.81, 1.15)
Adjusted   | 0.95 (0.80, 1.12)

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<th>% Anemic</th>
<th>RR (95%CI)</th>
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<td>No WASH</td>
<td>8</td>
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<tr>
<td>WASH</td>
<td>13</td>
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Unadjusted | 1.42 (0.89, 2.27)
Adjusted   | 1.01 (0.96, 1.07)

Prendergast AJ et al., Lancet Child Adolesc Health 2019
Effects of WASH on stunting and anaemia at 18 months of age

Children HIV-exposed

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RR (95%CI)

- Unadjusted: 0.97 (0.81, 1.15)
- Adjusted: 0.95 (0.80, 1.12)

RR (95%CI)

- Unadjusted: 1.42 (0.89, 2.27)
- Adjusted: 1.01 (0.96, 1.07)

Children HIV-unexposed

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<th>% Anemic</th>
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<tr>
<td>No WASH</td>
<td>30.6</td>
<td>11.3</td>
</tr>
<tr>
<td>WASH</td>
<td>31.2</td>
<td>12.9</td>
</tr>
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RR (95%CI)

- Unadjusted: 1.03 (0.93, 1.13)
- Adjusted: 1.00 (0.91, 1.10)

RR (95%CI)

- Unadjusted: 1.14 (0.95, 1.36)
- Adjusted: 1.13 (0.92, 1.37)

Prendergast AJ et al., Lancet Child Adolesc Health 2019
Humphrey JH et al., Lancet Glob Health 2019
Summary 1

- Half of all children exposed to HIV were stunted at 18 months
- IYCF (improved complementary feeding plus SQ-LNS supplement from 6-18mo) reduced stunting by 20% (from 50% to 40%)
- WASH had no impact on stunting
- Findings similar in children exposed or unexposed to HIV
Early child development substudy

726 HIV-positive women

SOC (control) IYCF WASH IYCF+WASH

166 live births (46 clusters) 158 live births (48 clusters) 205 live births (44 clusters) 209 live births (47 clusters)

Evaluated at 18 months

147 (46 clusters) 147 (48 clusters) 184 (44 clusters) 190 (47 clusters)

Enrolled into early child development substudy

66 (31 clusters) 66 (40 clusters) 83 (33 clusters) 103 (38 clusters)

738 HIV-exposed live births

51 deaths
18 lost to follow-up
1 exit

668 evaluated at 18 months

193 were not eligible
152 were not enrolled

323 enrolled into ECD (6 HIV-positive)
### Malawi Developmental Assessment Tool

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Unadjusted difference (95% CI)</th>
<th>( P )</th>
<th>Adjusted difference (95% CI)</th>
<th>( P )</th>
</tr>
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<tbody>
<tr>
<td><strong>SOC</strong></td>
<td>90.9 (8.2)</td>
<td>0.0 (Reference)</td>
<td></td>
<td>0.0 (Reference)</td>
<td></td>
</tr>
<tr>
<td><strong>IYCF</strong></td>
<td>91.7 (8.8)</td>
<td>0.81 (-1.99, 3.61)</td>
<td>0.57</td>
<td>-0.91 (-3.40, 1.58)</td>
<td>0.48</td>
</tr>
<tr>
<td><strong>WASH</strong></td>
<td>89.6 (9.2)</td>
<td>-1.26 (-3.80, 1.28)</td>
<td>0.33</td>
<td>-1.63 (-4.26, 0.99)</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>IYCF+WASH</strong></td>
<td>95.3 (9.0)</td>
<td>4.57 (1.91, 7.23)</td>
<td>0.001</td>
<td>3.05 (0.86, 5.25)</td>
<td>0.006</td>
</tr>
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Ntozini R et al., CROI 2019
## MacArthur Bates test

<table>
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<th>Mean (SD)</th>
<th>Unadjusted difference (95% CI)</th>
<th>P</th>
<th>Adjusted difference (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SOC</strong></td>
<td>56.6 (18.5)</td>
<td>0.0 (Reference)</td>
<td></td>
<td>0.0 (Reference)</td>
<td></td>
</tr>
<tr>
<td><strong>IYCF</strong></td>
<td>57.6 (21.3)</td>
<td>1.00 (-5.74, 7.55)</td>
<td>0.77</td>
<td>-2.47 (-8.60, 3.67)</td>
<td>0.43</td>
</tr>
<tr>
<td><strong>WASH</strong></td>
<td>58.2 (20.1)</td>
<td>1.58 (-4.12, 7.29)</td>
<td>0.59</td>
<td>-2.27 (-8.14, 3.60)</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>IYCF+WASH</strong></td>
<td>65.1 (17.0)</td>
<td>8.50 (3.66, 13.33)</td>
<td>0.001</td>
<td>6.01 (1.14, 10.88)</td>
<td>0.015</td>
</tr>
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Ntozini R et al., CROI 2019
Other ECD outcomes

• **A-not-B test** (short-term memory and object permanence)
  • No evidence of differences between arms

• **Self-control task**
  • No evidence of differences between arms

Ntozini R et al., CROI 2019
Summary 2

• HEU children had ECD scores 0.1-0.2 standard deviations lower than HIV-unexposed children

• A combined IYCF + WASH intervention improved neurodevelopment across several domains at 2 years of age, by 0.4-0.5 standard deviations

• The combined intervention closed the developmental gap between CHEU and HIV-unexposed children
Discussion

• Improving IYCF may have particular benefits in high HIV prevalence areas
• IYCF + WASH had benefits for ECD
  • Pathways to stunting and ECD may differ
  • Pathways may differ in CHEU
• Findings need to be replicated elsewhere
• Children who are HEU may be responsive to packages of interventions
  • Nurturing Care Framework approach
Collaborators and donors

Zimbabwe Ministry of Health and Child Care
Goldberg Mangwadu, Ancikaria Chigumira, Cynthia Chasokela

Zvitambo Institute for Maternal and Child Health Research
Mduduzi Mbuya (currently GAIN), Robert Ntozini, Naume Tavengwa, Kuda Mutasa, Florence Majo, Bernard Chasekwa, Virginia Sauramba, Phillipa Rambanepasi

Johns Hopkins Bloomberg School of Public Health Jean Humphrey, Lawrence Moulton
Queen Mary University of London Andrew Prendergast, Ceri Evans
Cornell University Rebecca Stoltzfus
University of Liverpool Melissa Gladstone, Jaya Chandna
University of British Columbia Amee Manges
George Washington University James Tielsch
Middlebury College John Maluccio
University of Michigan Andrew Jones