

Neurodevelopment of Ugandan and Malawian PROMISE exposed and unexposed uninfected children at 12 and 24 months of age

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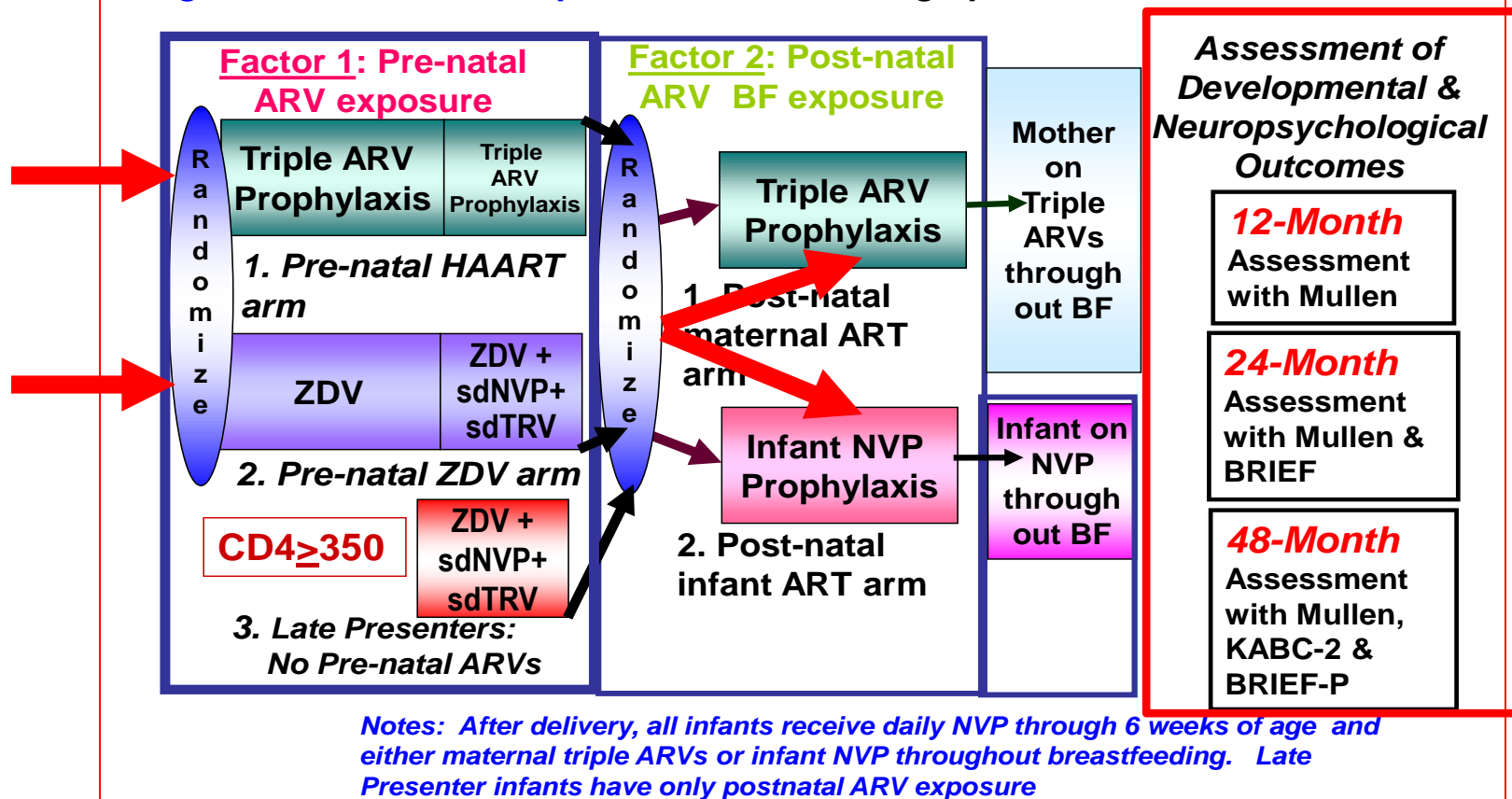
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Assessing Developmental Outcomes among ARV exposed Uninfected Infants in PROMISE 1077 BF Using a 2-Factor Design: Factor 1: Prenatal triple ARV regimens, or ZDV; Factor 2: Post-natal maternal triple ARVs or Infant NVP

Ante-partum: 14 weeks gestation to term /Intrapartum **Post-partum: Duration of breastfeeding up to 18 months**



IMPAACT PROMISE Neurodevelopmental Study Methodology

Comparability of HEU and HUU children at both study sites

- 188 Malawian (Blantyre) and 208 Ugandan (Kampala) PROMISE HEU infants followed at two research sites were tested with the Mullen Scales of Early Learning (MSEL) at 12 months of age, along with 179 Malawian and 194 Ugandan age- and gender-matched HUU children.
- At 24 months, 214 Malawian and 219 Ugandan HEU children were tested, along with 202 Malawian and 213 Ugandan HUU children.
- Least-squared means for age/gender standardized scores were compared by exposure group (HUU, HEU) and by country site (Uganda, Malawi) for 12 and 24 months using the linear mixed models with interaction effects of time, site and HIV exposure status.
- HEU and HUU study children at both sites were comparable in terms of Caldwell HOME quality of caregiving, MICS4 Child Development Environment, maternal depression (HSCL-25), maternal anxiety (HSCL-25), and Durkin TQQ disability screening measures (MICS4).
- HEU mothers at both sites reported more Behavior Rating Inventory Executive Function (BRIEF) problems (GEC). Physical growth poorer for Uganda site only at 12 and 24 months (IAS Poster, Aizire et al. 2016)
- Caldwell HOME and MICS4 Child Development environment predicted MSEL Composite Standardized Cognitive Composite ($P = 0.006$)
- Maternal Depression ($P = 0.03$) and Anxiety ($P = 0.04$) predicted TQQ disability screening.

Results: Mullen Scales of Early Learning (MSEL) scores at 12 and 24 months of age by HIV+ARV exposure, and by study site

- In a repeated-measure (12 & 24 months) mixed models, HUU children had higher **MSEL composite cognitive** ability than the HEU cohort for the Malawi children at 12 months (group mean HUU vs HEU, 98 vs 94, $p=0.01$) and for the Ugandan children at 24 months (group mean HUU vs HEU, 90 vs 86, $p < 0.01$).
- This composite difference of $\sim 1/2$ SD (normative) is clinically meaningful.
- Significant MSEL differences also favoring HUU were obtained for **Visual Reception (visual spatial processing and working memory items)** at 12 mos in Malawi (group mean 51 vs 49, $p < 0.01$), and 24 mos in Uganda, group mean 41 vs 30, $p=0.01$).
- MSEL differences favoring HUU obtained in Uganda for **Fine Motor** at 12 months (group mean 51 vs 48, $p < 0.01$) and 24 months (group mean 46 vs 42, $p < 0.01$) as well as **Expressive Language** at 24 mos, (group mean 43 vs 41, $p=0.01$).
- *Receptive Language* differences were not significant for HUU and HEU groups in either country site.
- In a separate analysis comparing the combined HEU/HUU Ugandan and Malawian cohorts on MSEL scores, scores were generally significantly higher for the Malawian children on Visual Reception and Expressive Language; while the Ugandan children scored higher on Fine Motor and Receptive Language.

CONCLUSIONS



- HEU children on NVP prophylaxis with maternal ART exposure are at greater neurodevelopmental risk than matched HUU children.
- This was even though the HEU children received monthly medical and nutritional monitoring and support.
- MSEL test performance differences between study cohorts and sites may be developmental differences (see handout on Ugandan caregiver training intervention RCT study with HIV and HEU children 2 to 5 yrs of age).
- We are continuing MSEL and KABC-II (cognitive ability) evaluation of these cohorts at 4 yrs of age.
- We will evaluate the neurodevelopmental effects of PMTCT cARV (HAART) exposure duration on MSEL outcomes.