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

P_92

Michael J. Boivin[1,2], Limbika Maliwichi-Senganimalunje[3], Mary Nyakato[4], Alla Sikorskii[5], Lillian Wambuzi Ogwang[4], Rachel Kawalazira[6], MacPherson Mallewa[6], Itziar Familiar-Lopez[1], Horacio Ruiseñor-Escudero[1], Jim Aizire[7],Taha Taha[7], Mary Glenn Fowler[8]

[1]Department of Psychiatry, Michigan State University; [2]Department of Psychiatry, University of Michigan; [3]Department of Psychology, Chancellor College – University of Malawi; [4]Makerere University-Johns Hopkins University; [5]Department of Statistics & Probability, Michigan State University; [6]Malawi College of Medicine - Johns Hopkins University; [7]Department of Epidemiology, Johns Hopkins University; [8]Department of Pathology, Johns Hopkins University

BACKGROUND

- HIV exposed uninfected children (HEU) in Africa are developmentally at-risk both from the effects of HIV disease on the mother and fetus during gestation, and from pre- and postnatal (breast feeding) exposure to anti-retroviral treatments (ARTs).
- This study compares neurodevelopmental outcomes of co-enrolled PROMISE Malawian and Ugandan children, to age and gender-matched HIV uninfected unexposed (HUU) community controls.

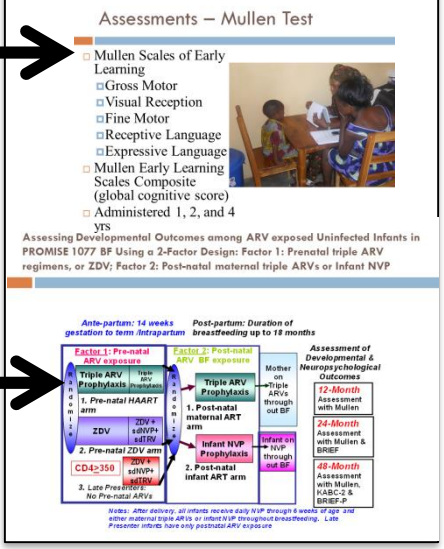
OBJECTIVES of PROMISE Neurodevelopmental Study

- To determine if the
  - developmental,
  - neuropsychological,
  - physical growth, and
  - haematological

  outcomes of HIV/ARV-exposed uninfected African children from Malawi and Uganda are similar to those of the control group of non-HIV/non-ARV-exposed children from comparable socioeconomic and cultural backgrounds.
- To determine if these outcomes are affected by duration of antenatal and postnatal exposure to HAART in the context of prevention of mother-to-child transmission of HIV.

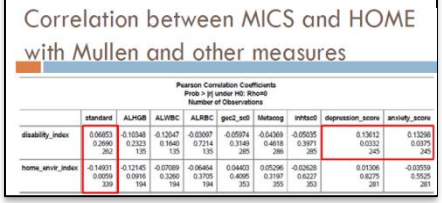
DESIGN/METHODS

- 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.



RESULTS

- In a repeated-measure (12 & 24 months) mixed models, HUU children had higher MSEL composite cognitive ability scores 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 ~1/2 *SD* (normative) is clinically meaningful in terms of developmental delay.
- HUU were better on Visual Reception at 12 mos in Malawi (group mean 51 vs 49, p<0.01), and 24 mos in Uganda, group mean 41 vs 39, p=0.01); 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 between-cohort differences were not significant for HUU and HEU groups.
- 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 or with maternal ART exposure in Uganda and Malawi were at greater overall neurodevelopmental risk than matched HUU children.
- This was even though the HEU children received monthly medical and nutritional monitoring and support through their follow up in the IMPAACT PROMISE study.
- MSEL test performance differences between study sites may be developmental differences, or they may be partly due to contextual differences in adaptation and administration of the MSEL.
- We are continuing MSEL and KABC-II (cognitive ability) evaluation of these cohorts at 4 yrs of age.

Funding: NIH RO1 HD073296 (PIs: Fowler, Boivin).
Special thanks to the Johns Hopkins University teams at Makerere University College of Health Sciences and the Malawi College of Medicine