Cognitive effects of HIV

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What do we know about HIV and brain?

- Over 60% adults with HIV show some cognitive effects (Fisher-Smith 2005)
- Before cART treatment almost all developed some brain pathology (Navia 2005)
- Cognitive effects even for those on treatment (Simioni 2009)

Grading system for HAND
HIV Associated Neurological Disorder

- **Asymptomatic neurocognitive impairment (ANI)**
  - Performance 1 SD below mean of normative scores in at least two cognitive areas (attention-information processing, language, abstraction-executive, complex perceptual motor skills, memory, learning and recall, simple motor skills or sensory perception
  - Asymptomatic
- **HIV-associated mild neurocognitive disorder (MND)**
  - Performance of at least 1 SD below demographically corrected norms on tests of at least two different cognitive domains
  - Interferes, at least mildly, with activities of daily living
- **HIV-associated dementia (HAD)**
  - Performance at least 2 SD below demographically corrected normative means in at least two different cognitive areas
  - Marked difficulty in ADLs due to the cognitive impairment

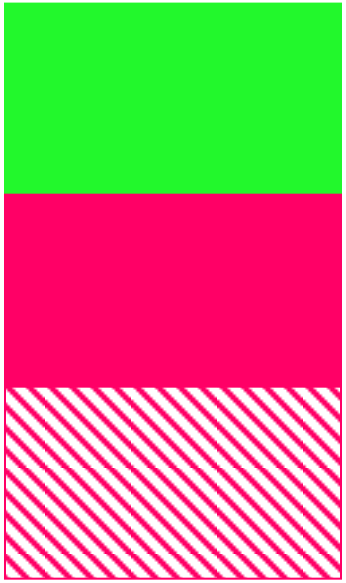
??????????Children???????????

HIV +ve Children

Cognitive effects

(2009 review Sherr et al, 2013 update 21 studies 18/21 deficit)

Overall effects found - key



Detrimental effect

No effect

Mixed effect

STUDY	PLACE	FINDINGS
Aylward et al (1992)	USA (n=96)	HIV positive children scored lower than negative or reverter children.
Bachanas P et al (2001)	USA (n=68)	25% HIV+ve clinically significant emotional or behaviour problems
Bell et al (1997)	Cote d Ivoire (n=153)	Low prevalence of HIV encephalitis - explained by comparatively early death
Belman et al (1996)	USA (n=247)	HIV+ve significantly more neurologic problems
Bisiacchi et al (2000)	Italy (n=42)	Executive function problems in all HIV+ve children
Blanchette et al (2001).	Canada (n=50)	HIV+ve significantly lower scores on mental scale and performance scale
Blanchette et al (2002)	Canada (n=25)	Subtle motor impairments in HIV+ve.
Bobat et al (2001)	South Africa (N=141)	HIV+ve children lowered length/weight for age
Boivin et al 1995	Zaire (n=50)	Motor and visual spatial deficits.
Bruck I et al (2001)	Brazil (n=150)	Significant neurodevelopmental delay in HIV+ve group

Buchacz (1997)	USA (n=983)	Immunosuppression associated with delayed pubertal onset.
Chase et al 1995	USA (n=51)	HIV associated with delayed motor and mental development
Cohen et al (1991)	USA (n=48)	Significant effects in school achievement.
Coplan et al (1998)	USA (n=78)	Language deterioration among HV+ve.
Corsi (1991)	Italy	Hyperactive
Coscia et al (2001)	USA (n=43)	Home and advanced disease factors.
Depas et al (1995)	France (n=8)	Functional abnormalities precede clinical symptoms
Esposito et al (1999)	Italy (n=117)	Children born to +ve mothers significantly higher depression and anxiety.
Fishkin et al (2000)	USA (n=80)	Overall ns. HIV+ve lower block design
Fowler et al (2000)	USA (n=595)	HIV associated with abnormal mental and motor growth, early and marked cognitive delays
Frank E et al (1997)	USA (n=27)	Visuomotor skills sensitive to stage of disease
Gay et al l(1995)	USA (n=126)	Mental and motor scores significantly lower in HIV+ve.
Havens J (1994)	USA (n=60)	High rates of disruptive/behavioural morbidity
Hilgartner (1993)	USA (n=333)	HIV+ve height decline, delays in sexual maturation. Lower scores

Hooper S et al (1993)	USA (n=38)	No significant differences
Hooper et al (1997)	USA (n=58)	No differences between HIV+ve and –ve
Knight et al (2000)	USA (n=50)	HIV+ve significantly lower baseline and f/up
Levenson et al (1992)	USA (n=49)	44% scoring low on the inventory. HIV+ve significantly worse than seroreverters.
Llorente et al (2003)	USA (n=157)	greater mortality in those scoring in lower quartile.
Macmillan et al (2001)	USA (n=1094)	lower for HIV+ve children, persisted at 24 months
McKinney & Robertson J (1993)	USA (n=170)	HIV +ve smaller weight for age and length for age
Mellins & Ehrardt (1994)	USA (n=25)	Loss and separation particular problems. Sibling anger high burden from caregiving
Mellins et al (2003)	USA (n=307)	High level of behaviour probs. No HIV effect
Mialky et al (2001)	USA (n=85)	53% special services. 25% not in appropriate class
Msellati et al 1993	Rwanda (n=436)	Motor problems 31% at 1 yr, 40% at 1.5 years
Ndugwe et al (1997)	Uganda (n=436)	HIV+ve greater deficits in motor development and neurologic abnormalities
Nozyce et al 1994	USA (n=181)	HIV+ve symptomatic significantly lower. HIV+ve well children similar to controls.

Piazza et al (1995)	Italy (n=138)	CS 36% for symptomatic HIV
Pilowsky et al (2001)	USA (n=73)	Children of depressed parents at higher risk
Pollack et al (1996)	USA (n=65)	HIV+ve infants impaired
Scafidi et al (1997)	USA (n=48)	Infants of HIV+ve mothers had more orienting problems and abnormal reflexes
Smith et al (2000)	USA (N=114)	Early HIV infection increased risk of poor neurdevelopmental functioning
Tardieu et al 1995	France (n=33)	29% affective disorders, 67% normal school achievement, 54% abnormal visual-spatial and time orientation, 44% speech/language delay
Watkins et al (2000)	USA (N=173)	Attention span affected in HIV +ve children
Whitt et al (1993)	USA (n=63)	No differences – but subtle deficits when compared to age norms.

2009-2013 Update

Van Rie et al. (2009)	Democratic Republic of Congo, N = 160)	HIV+ had significantly lower developmental scores
Van Rie et al. (2008)	Democratic Republic of Congo, (N = 160)	HIV+ had significantly more motor and language expression delay
Abubakar et al. (2009)	Kenya, (N = 367)	HIV has a detrimental effect on psychomotor development
Koekkoeka et al (2008)	Holland (N=22)	HIV+ performed significantly poorer on neuropsychological tests compared to norms
Brackis-Cott et al. (2009)	USA, (N = 325)	HIV+ significantly impaired receptive language ability and word recognition
Lowick et al. (2012)	South Africa, (N = 60)	HIV+ had significantly increased likelihood of severe neurodevelopmental delay
Jelsma et al. (2011)	South Africa, (N = 44)	HIV+ performed significantly worse on the Peabody developmental motor scales
Baillieu et al. (2008)	South Africa, (N = 80)	HIV+ children had significantly delayed cognitive and motor development.
Ferguson et al. (2009)	South Africa, (N = 86)	HIV+ children had significantly delayed motor development.

Baker et al. (2011)	USA, (N = 70)	HIV+ children scored lower than controls in the Peabody but was not significant
Gadow et al. (2012)	USA, (N = 525)	HIV+ had significantly more symptoms of psychiatric illness.
Mellins et al. (2009)	USA, (N = 340)	HIV+ significantly more likely to meet criteria for ADHD
Gadow et al. (2010)	USA & Puerto Rico, (N = 582)	HIV+ had significantly more severe somatization scores.
Maleea et al. (2011)	USA & Puerto Rico, (N = 416)	HIV+ had significantly more behavioural problems
Thomaidis et al. (2010)	Greece, (N = 60)	HIV+ neuro-imaging abnormalities <practical intelligence quotient scores and > abnormal emotional/ hyperactivity
Isaranurug et al. (2008)	Thailand, (N = 388)	HIV+ had significantly worse mean scores for self-control and quick recovery
Chernoff et al. (2009)	USA, (N = 575)	HIV+ children received >behavioural treatment.
Serchuck et al. (2010)	USA & Puerto Rico, (N = 576)	HIV+ youths self-reporting pain had significantly higher mean symptom severity for general anxiety disorder
Rice et al. (2012)	USA, (N = 437)	No significant differences in language impairment
Dobrova-Krol et al. (2010)	Ukraine, (N = 64)	No association between HIV status and attachment security
Ananworanich et al (2008)	Thailand, (N = 257)	No significant differences in CBCL

92.4% found at least some negative effects

50/66 studies significant detrimental effect of HIV

11/66 showed mixed

5/66 showed no differences

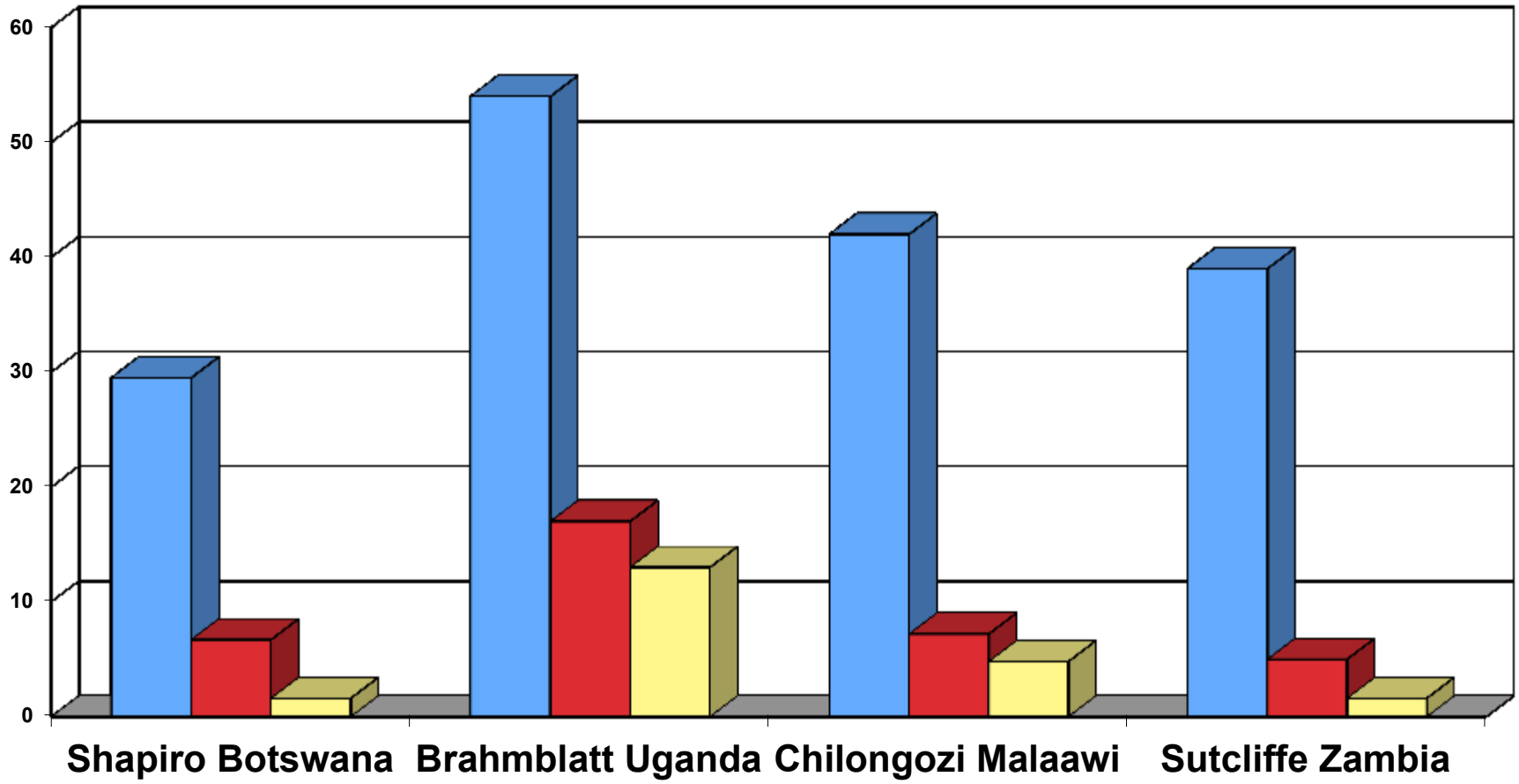
HIV Affected children – HIV-ve born to HIV+ve mothers

1739 hits

54 reviewed in full

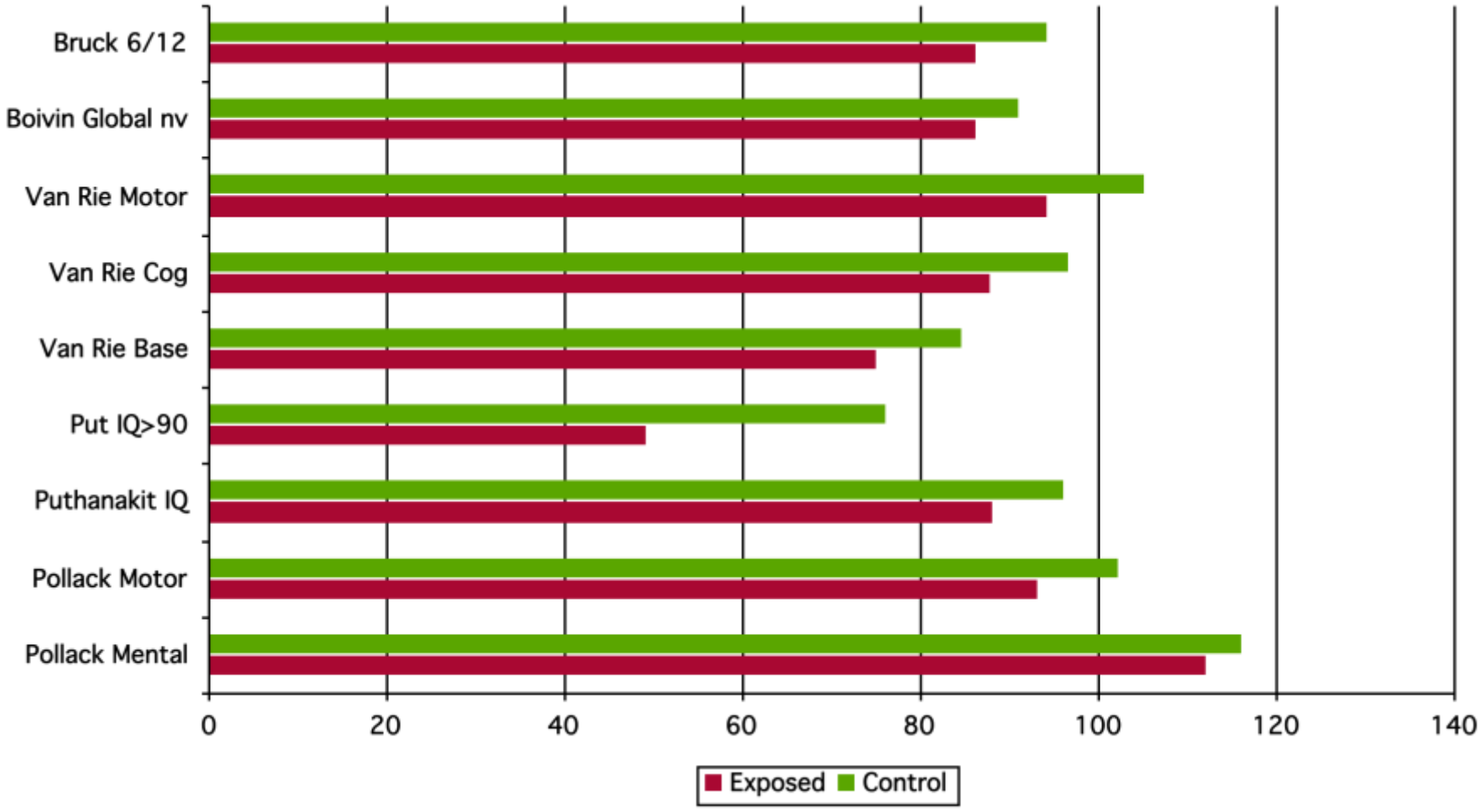
12 met inclusion criteria

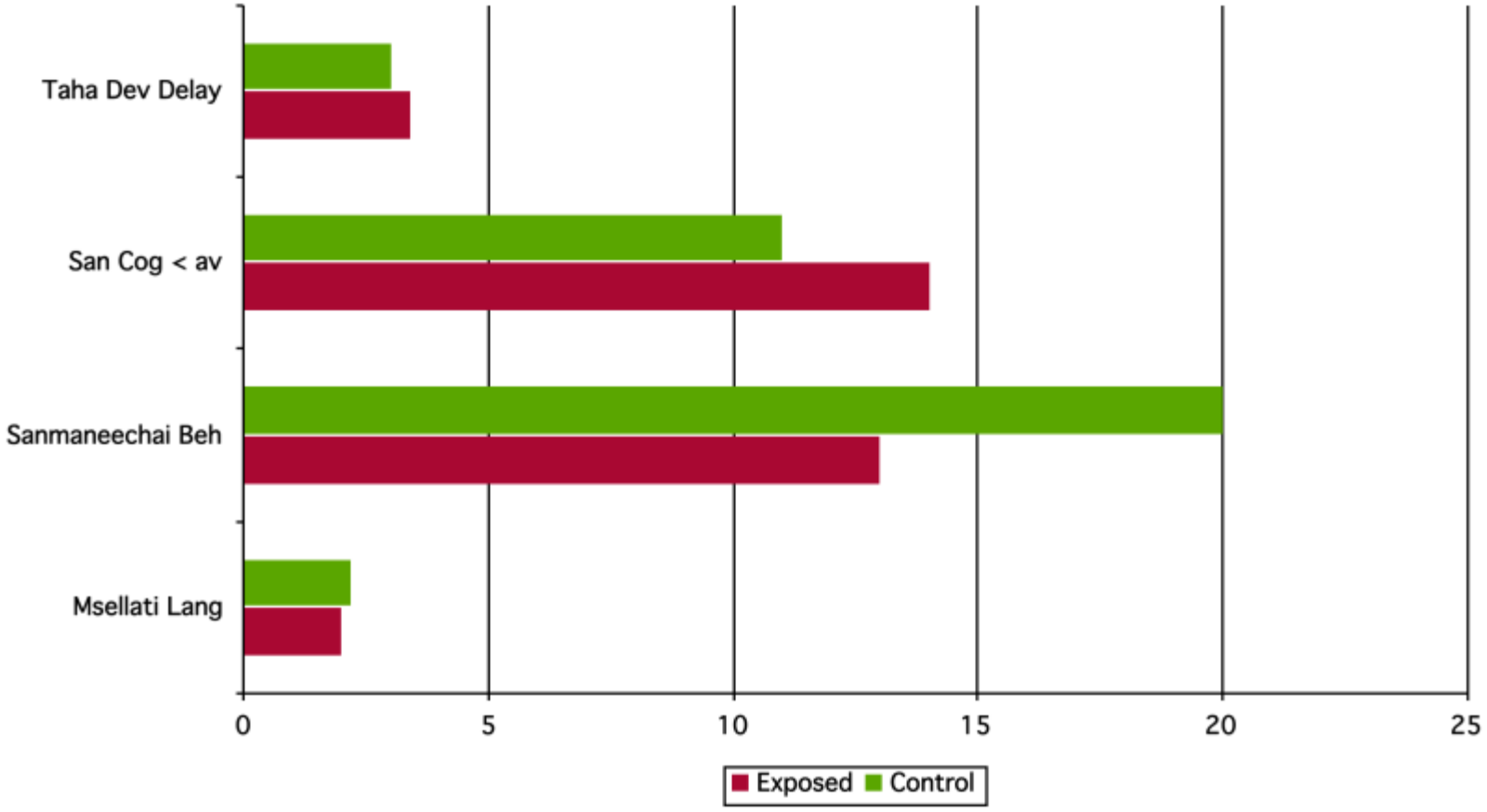
Clues from Overall Morality (Filtau et al 2010)



Study	***Place***	***Sample***	***Lower mean scores for Affected Children vs Control (Y/N) (Significance reported)***
1. Boivin et al (1995)	Zaire	14 HIV+ve, 20 Affected, 16 Control	Yes*
2. Sanmaneechai et al	Thailand	30 affected, 35 control	Yes (sig)
3. Forehand et al 1998	USA	87 affected vs 149 control	Yes (sig)
4. Dorsey et al (1999) –	USA	87 affected, 149 control	Yes (sig)
5. Eposito et al (1999	Italy	39 Affected, 78 Controls	Yes (sig)
6. Van Rie et al (2008)	DCR	35 HIV+ve. 35 Affected, 90 Controls	Yes (Sig)
7. Van Rie et al (2009)	DCR	35 HIV+ve. 35 Affected, 90 Controls	Yes (Sig)
8. Isaranurug et al (2008)	Thailand	74 HIV+ve, 223 Affected, 91 control	unclear
9. Drotar et al (1998)	Uganda	61 HIV+ve, 234 Affected, 115 Control	No
10. Bagenda et al (2006)	Uganda	28 HIV+ve, 42 Affected, 37 Control	No
11. Msellati et al (1993)	Rwanda	43 HIV+ve, 133 Affected 193 Control	No
12. Mellins et al (1994)	USA	24 HIV+ve, 30 Affected, 23 Control	No

Cognitive development



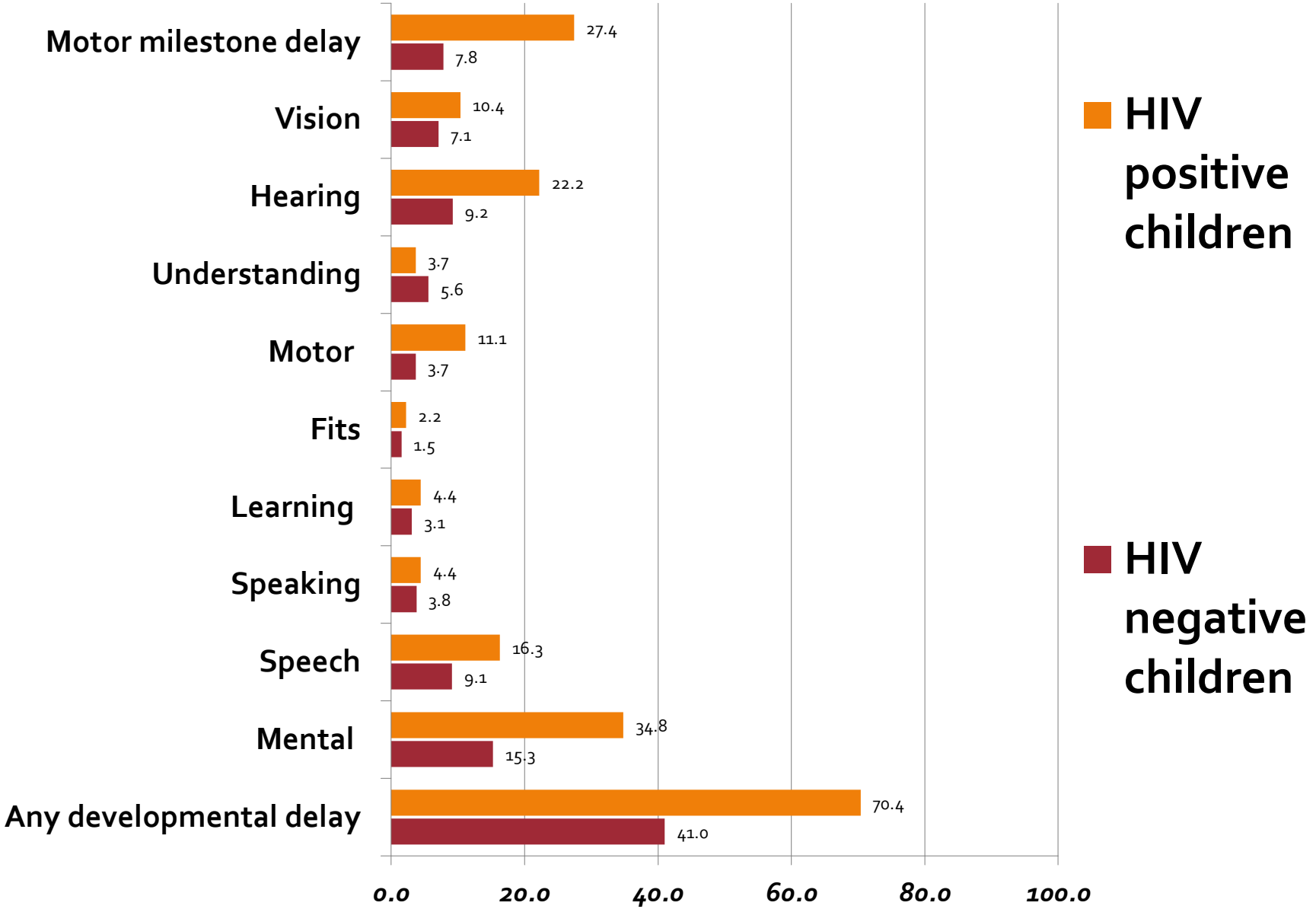

Taha Dev Delay
San Cog < av
Sanmaneechai Beh
Msellati Lang
0
5
10
15
20
25
Exposed
Control

Interventions

Table of Interventions

Community Cohort study

- 989 pairs
- 135 HIV+ve comparison group n=844
- South Africa Malawi
- Parental report, child report, Study cognitive measures
- No differences on mental health
- Significant difference on Cognitive
- HIV+ children twice as likely to present with developmental difficulties,
- But significantly less likely enrolled in child development programmes


Motor milestone delay
27.4
7.8
Vision
10.4
7.1
Hearing
22.2
9.2
Understanding
3.7
5.6
Motor
11.1
3.7
Fits
2.2
1.5
Learning
4.4
3.1
Speaking
4.4
3.8
Speech
16.3
9.1
Mental
34.8
15.3
Any developmental delay
70.4
41.0
0.0
20.0
40.0
60.0
80.0
100.0
HIV positive children
HIV negative children