A comparison of the association of current CD4 cell count with the short-term risk of AIDS and death in HIV-infected children and adults

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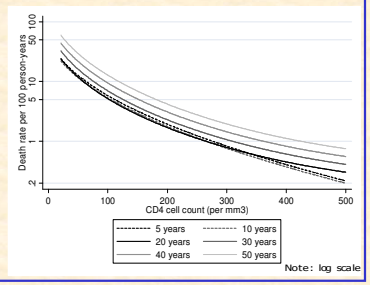
Background

- Short-term risk of disease progression in absence of effective ART is an important consideration in the decision whether to initiate ART. The key prognostic marker used to quantify this risk is the number of CD4 cells (absolute count or percent).
- Separate estimates of this risk have recently been published for adults and children, which have informed treatment guidelines.
- A direct comparison of these estimates would help inform whether adult treatment guidelines are applicable to children/adolescents.

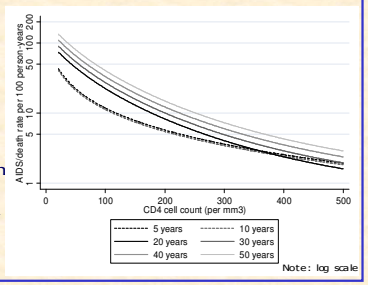
Progression to death

- Sharp increase in mortality when CD4 falls below 100-150 cells/mm^3
- Strong gradient in adults but not in (older) children
- Children >5 years experience similar mortality rate to adult aged ~20 years



Recurrent bacterial infection

- RBI most common AIDS diagnosis in children >5 years
- Occurs at relatively high CD4 counts, and more restrictive case definition in adults
- If ***exclude*** RBI, children have similar or lower progression rates than adults (cf. mortality)

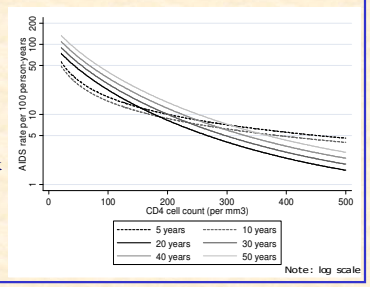


Methods

- A joint, standard analysis of data from two large studies of vertically-infected children (HPPMCS) and adult seroconverter cohorts (CASCADE).
- Follow-up was censored at earliest of (1) end-1995 i.e. prior to widespread use of dual antiretroviral therapy (2) next measurement (3) 12 months after current measurement.
- AIDS/death and death incidence rates were estimated according to age and *most recent* CD4 count using fractional polynomial Poisson regression models.

Progression to AIDS/death

- Age effects similar to those for mortality
- Incidence in children in same (broad) range as adults for CD4= 150-300 cells/mm^3
- Children at lower risk below, and higher risk above, this range



Conclusions

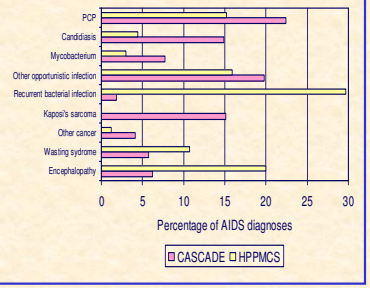
- Our results suggest that similar CD4 count criteria for starting antiretroviral therapy can be applied to adults and children >5 years.
- Question of CD4 criteria for younger children is more problematic; still uncertain if CD4 count or percent is the more appropriate marker in this age group.
- Inclusion of older children could enhance the generalisability of a "when-to-start" trial, if one is undertaken.
- Relatively favourable prognosis in children may be partly explained by survivorship effects.

Results

- 3244 children (7790 person-years FU) from HPPMCS and 3497 adults (12710 person-years FU) from CASCADE included.
- 595/665 deaths and 949/945 AIDS/death endpoints observed from HPPMCS/CASCADE respectively.
- Wide range of ages covered (birth to 60+ years), with gap at adolescent ages.
- Children <5 years experienced much higher rates of disease progression than older children and adults; ***further analysis limited to children >5 years.***

AIDS-defining illnesses

- Previous analysis requires careful interpretation as different spectrum of AIDS-defining illnesses in children and adults
- Reason partly biological, partly due to variation in AIDS case definition



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