ChiAC

Learning Curve: Increasing Benefit of HAART According to Year of Initiation in a Middle-Income Country

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Abstract

Background: HAART with its well know benefits is under application for a decade. Evolution of the outcomes in resource-limited countries have not been fully evaluated. Chile, one of these countries, implemented expanded access program (EAP) to HAART in 2001 with significant decrease in HIV associated mortality and morbidity. The objective is to present the evolution of the impact of the EAP in the public health system according to year of HAART initiation.

Methods: Prospective follow up (f/u) of a national cohort that includes 90% of patients (pts) initiating HAART from 2001 to 2005, with f/u until 8/2007. Survival curves estimates (Kaplan Meier) were used for groups initiating HAART each year, comparing results with chi-square test. Global death relative risks were calculated for each group and then adjusted according to baseline CD4 count and to the most common HAART regimen (zidovudine/lamivudine [Z/L] plus efavirenz [E]) (Cox proportional Hazard Ratio).

Results: 3625 pts from ChiAC (84% men), baseline (BL) median CD4 count of 91 cells/ml, 41.3% in CDC stage C were included. Global mortality at 24 months was 8.0%, but it varied from 13.8%, 9.8%, 8.6%, 5.0% and 4.1% for the groups initiating HAART each year from 2001 (n=141), 2002 (n= 1090), 2003 (n=1020), 2004 (n=647) to 2005 (n=733) respectively ($p <0.05$ between each year). Unadjusted death hazard ratio (DHR) between pts from 2005 compared to 2002 was 0.366 (CI 95%: 0.239-0.565). CD4 count adjusted DHR was 0.376 (CI 95%: 0.245-0.576). In 1502 pts initiating Z/L and E, 24 months mortality was 10.3%, 5.5%, 5,5% and 2.2% for the initiating years of 2002, 2003, 2004 and 2005, respectively; (2002-2005 $p<0.001$). Unadjusted DHR was 0.186 (CI 95%: 0.091-0-380), CD4 count adjusted DHR was 0.191 (CI 95%:0.093-0.390) between the same 2 periods.

Conclusions: In pts initiating HAART with advanced disease in a middle-income country, global results have been comparable with those of developed countries. There has been a constant and progressive improvement in these outcomes, despite similar baseline conditions and HAART regimens used. A beneficial learning curved seems to be the cause

Objectives

- To measure the impact of the EAP in the Public Health System according to year of initiation of the therapeutic regimen in previously treatment naïve patients in gross mortality and death hazard ratio
- To evaluate these outcomes with a similar HAART regimen according to year of initiation of HAART
- To evaluate the role of baseline CD4 in the outcomes of therapy according to year of initiation of HAART
- To evaluate the existence of a "learning curve process" explaining an eventual variation in outcome

Methods

Prospective follow up (f/u) of a national cohort (ChiAC) that includes >90% of patients (pts) initiating HAART in the public health system from 2001 to 2005, with f/u until 8/2007. Survival curves estimates (Kaplan Meier) were used for groups initiating HAART each year; chi square test was used to compare results. Global death relative risks were calculated for each group and then adjusted according to baseline CD4 count and to the most common HAART regimen (zidovudine/lamivudine [Z/L] plus efavirenz [E]) using Cox proportional Hazard Ratio method.

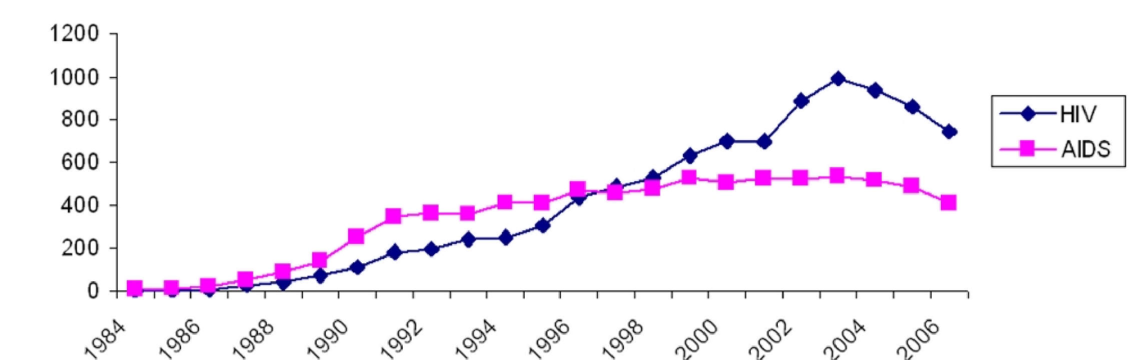
Background:

HAART with its well know benefits is under application for a decade. Evolution of the outcomes in resource-limited countries have not been fully evaluated. Chile, one of these countries, implemented expanded access program (EAP) to HAART in 2001 with significant decrease in HIV associated mortality and morbidity. The Chilean AIDS cohort (ChiAC) has enrolled most of the public health system patients under HAART for a prospective follow up and for evaluation of the impact of the EAP

Country characteristics

Population: 16,6 millions
Income: upper - middle- income (GNI per cápita, PPA US$ 13,588)
Population under line of poverty: 13% (from 45% 20 earlier)
Life expectancy: 75 years (men); 81 years (women)
Human development Index: 40th (3rd in the American continent, excluded USA and Canada)
HIV-AIDS prevalence: 0,2 % (estimate of 35.000 people living with HIV-AIDS)

HIV and AIDS: new cases, Chile 1984-2006



Results

3625 pts from ChiAC (84% men), baseline (BL) median CD4 count of 91 cells/ml, 41.3% in CDC stage C were included. Global mortality at 24 months was 8.0%, but it varied from 13.8%, 9.8%, 8.6%, 5.0% and 4.1% for the groups initiating HAART each year from 2001 (n=141), 2002 (n= 1090), 2003 (n=1020), 2004 (n=647) to 2005 (n=733) respectively ($p <0.05$ between each year) Figure 1. Kaplan Meier survival is shown in Figure 2. Unadjusted death hazard ratio (DHR) between pts from 2005 compared to 2002 was 0.366 (CI 95%: 0.239-0.565). CD4 count adjusted DHR was 0.376 (CI 95%: 0.245-0.576) Figure 3. In 1502 pts initiating Z/L and E, 24 months mortality was 10.3%, 5.5%, 5,5% and 2.2% for the initiating years of 2002, 2003, 2004 and 2005, respectively; (2002-2005 $p<0.001$) Figure 4. Unadjusted DHR was 0.186 (CI 95%: 0.091-0-380), CD4 count adjusted DHR was 0.191 (CI 95%:0.093-0.390) in 2005 compared with 2002. Figure 3.

Figure 1. Global mortality at 24 months of HAART according to year of initiation of therapy

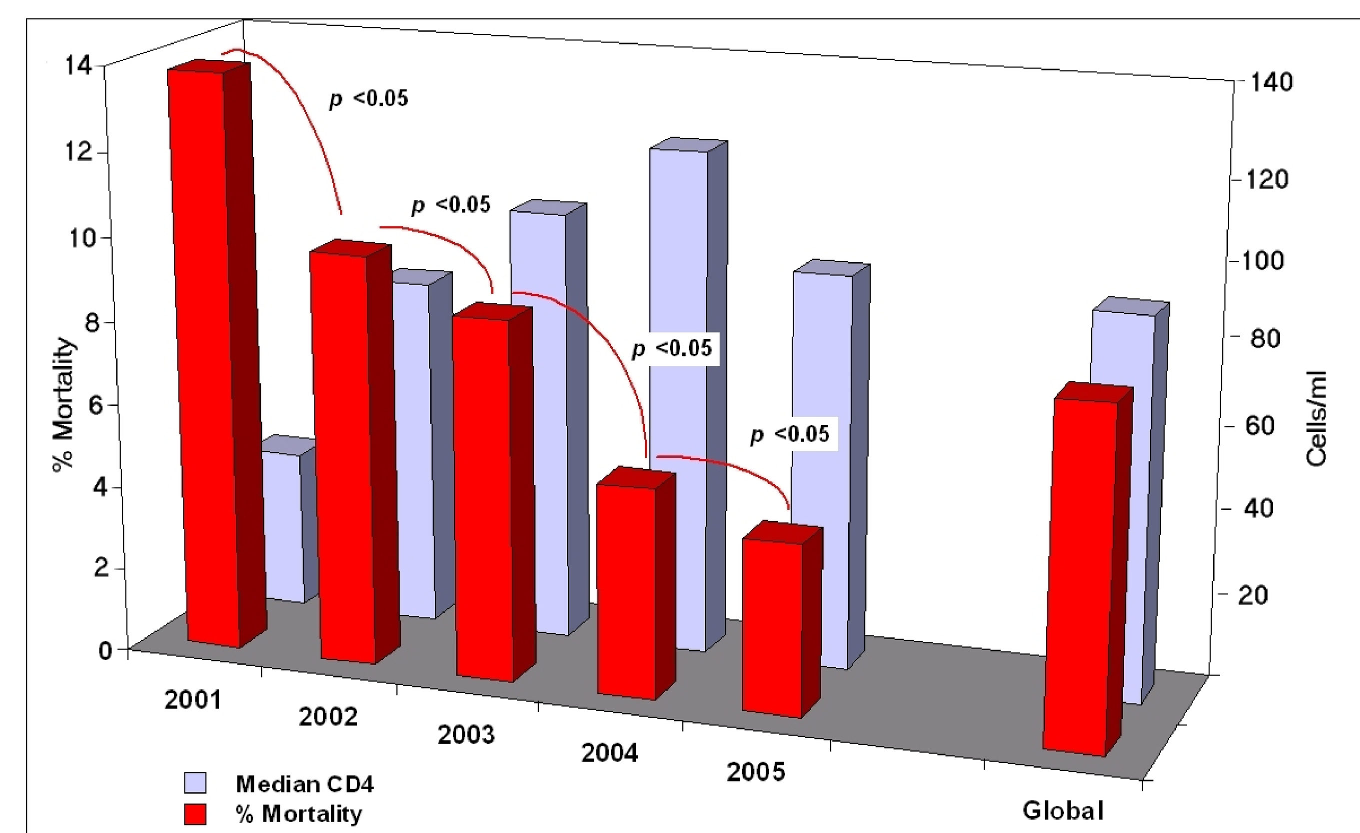


Figure 2. Kaplan Meier survival curve according to year of initiation of HAART

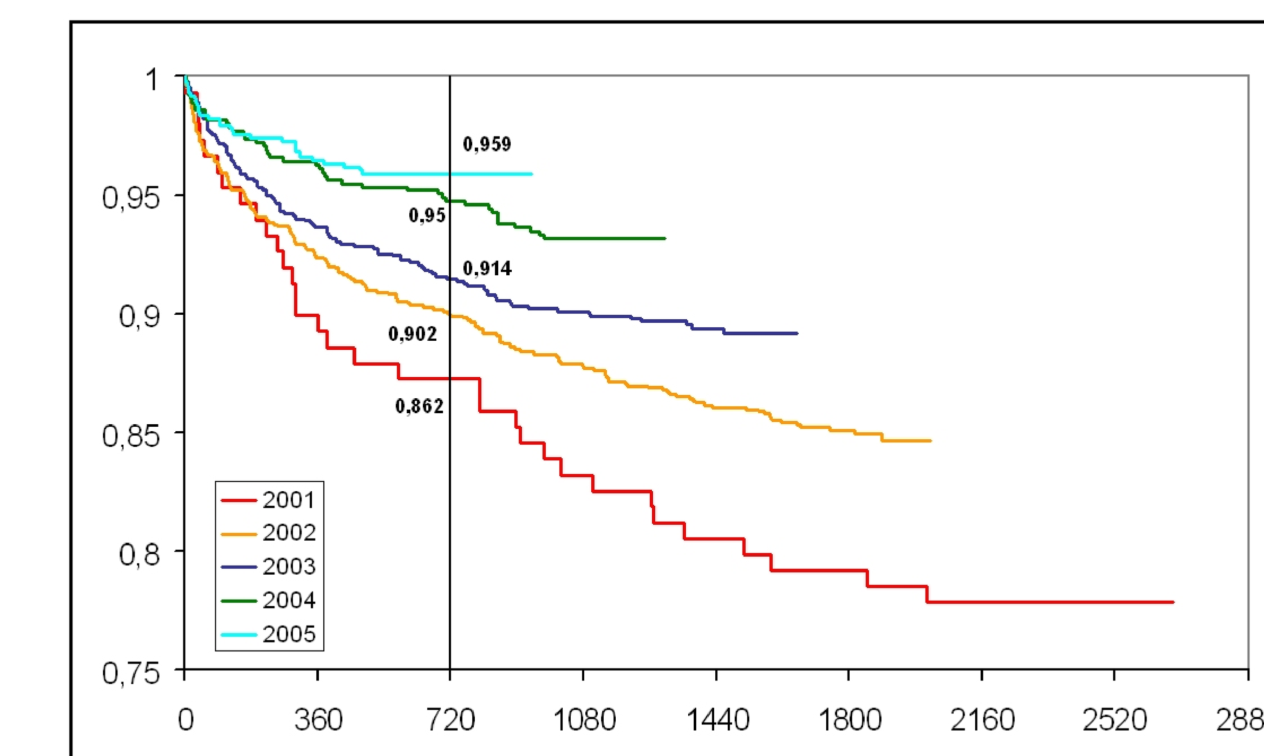
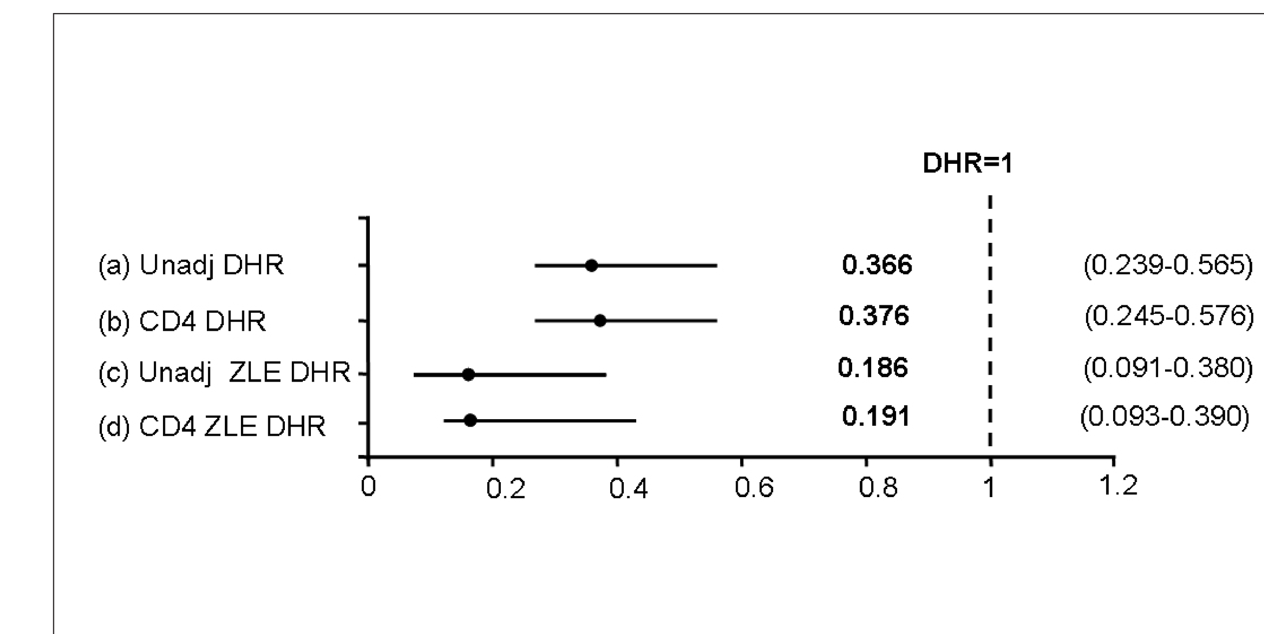
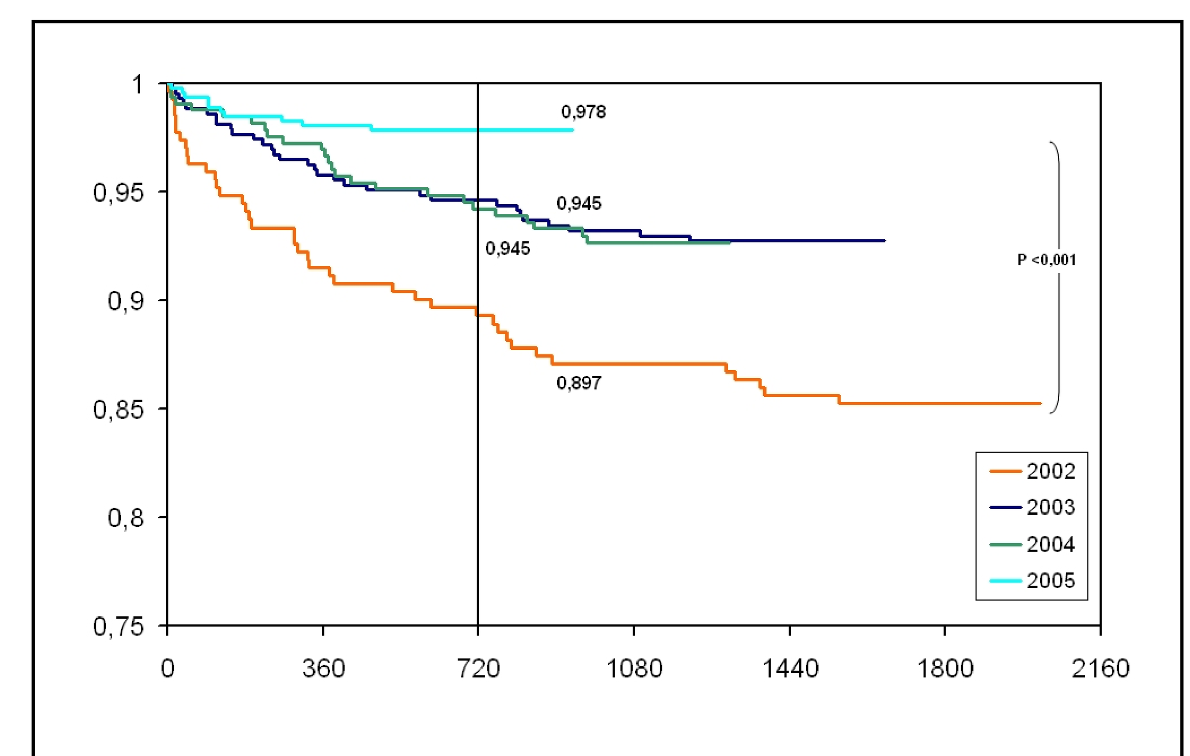


Figure 3. Death hazard ratio between 2002 (HR=1) and 2005 as years of initiation of HAART



Global unadjusted (a); global, adjusted for baseline CD4 (b); same HAART regimen, unadjusted (c) and same HAART regimen, adjusted for baseline CD4 (d)

Figure 4. Kaplan Meier survival curve between different years of initiation of same therapy (zidovudine, lamivudine and efavirenz)



Conclusions

- In Chile, a middle-income-country, most patients initiate HAART with advanced disease.
- Despite this, global results are comparable with those of developed countries.
- There has been a constant and progressive improvement in survival with therapy
- After adjustment for baseline conditions and HAART regimens used, this benefit continues to occur.
- A beneficial learning curve seems to be the explanation

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