HIV and Paediatrics in Central Europe

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I. Global status of HIV

II. Paediatric HIV epidemiology in Central Europe

III. HIV in children and adolescents in Romania

III. Current Paediatric Guidelines in Europe

IV. Key messages
I. Global status of HIV
Global AIDS Update Report
June 2016

• In June 2016, the United Nations General Assembly adopted a Fast-Track Strategy to put an end to AIDS epidemic by 2030.

• The main objectives are: the reduction of new HIV infections to less than 50,000 cases by 2020, decline in the AIDS-related deaths below 50,000 by 2020 and elimination of HIV-related stigma and discrimination by 2020.

• In this context, the Global AIDS Update Report released the status of HIV in 2015, enhancing both the progresses and the remaining barriers in achieving the abovementioned HIV/AIDS targets.

Source: Global AIDS Update. UNAIDS 2016, p.3
In 2015, approximately 33 million people were living with HIV/AIDS globally.

Of them, about 1.5 million persons were reported in Eastern Europe and Central Asia and 2.4 million in Western and Central Europe and in North America.

In terms of access to treatment, the evidence suggests 46% coverage worldwide, with 21% coverage in Eastern Europe and Central Asia and in Western and Central Europe and North America more than 50%.

From the standpoint of new infections, the figures suggest a total of 1.9 million new infections annually.

Source: Global AIDS Update. UNAIDS 2016
AIDS by the numbers
UNAIDS Report 2016

Adults and children estimated to be living with HIV | 2015

North America and western and central Europe
2.4 million
(2.3 million–2.7 million)

Eastern Europe and central Asia
1.5 million
(1.4 million–1.7 million)

Middle East and North Africa
230,000
(160,000–320,000)

Latin America and the Caribbean
2.0 million
(1.7 million–2.3 million)

Western and central Africa
6.5 million
(5.3 million–7.7 million)

Eastern and southern Africa
13.0 million
(12.7 million–13.5 million)

Asia and the Pacific
5.1 million
(4.4 million–5.9 million)

Total: 36.7 million [34.0 million–39.8 million]

AIDS by the numbers
UNAIDS Report 2016

Children (<15 years) estimated to be living with HIV | 2015

Total: 1.8 million [1.5 million–2.0 million]

Estimated number of children (<15 years) newly infected with HIV | 2015

Total: 150 000 [110 000–190 000]


* Estimates were unavailable at the time of publication.
Number of people living with HIV on antiretroviral therapy, global, 2010–2015

2010: 7.5 million
2011: 9.1 million
2012: 10.9 million
2013: 12.9 million
2014: 15.0 million
2015: 17.0 million

Sources: Global AIDS Response Progress Reporting (GARPR) 2016; UNAIDS 2016 estimates.

Antiretroviral therapy coverage among people living with HIV, by region, 2010–2015

Source: Global AIDS Update. UNAIDS 2016, p.2
## Regional antiretroviral therapy in 2015

<table>
<thead>
<tr>
<th>Region</th>
<th>Percentage of adults (aged 15+) living with HIV accessing antiretroviral therapy</th>
<th>Percentage of children (aged 0–14) living with HIV accessing antiretroviral therapy</th>
<th>Percentage of pregnant women accessing antiretroviral medicines to prevent mother-to-child transmission of HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern and southern Africa</td>
<td>53% [50–57%]</td>
<td>63% [56–71%]</td>
<td>30% [82–95%]</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>55% [47–64%]</td>
<td>64% [54–76%]</td>
<td>88% [77–95%]</td>
</tr>
<tr>
<td>Western and central Africa</td>
<td>29% [24–35%]</td>
<td>20% [16–25%]</td>
<td>48% [40–58%]</td>
</tr>
<tr>
<td>Asia and the Pacific</td>
<td>41% [35–47%]</td>
<td>41% [30–37%]</td>
<td>39% [34–44%]</td>
</tr>
<tr>
<td>Eastern Europe and central Asia</td>
<td>21% [19–22%]</td>
<td>...*</td>
<td>...*</td>
</tr>
<tr>
<td>Middle East and North Africa</td>
<td>16% [12–24%]</td>
<td>20% [16–25%]</td>
<td>12% [9–18%]</td>
</tr>
<tr>
<td>Western and central Europe and North America</td>
<td>59% [56–68%]</td>
<td>&gt;95% [92–95%]</td>
<td>92% [87–95%]</td>
</tr>
<tr>
<td>GLOBAL</td>
<td>46% [43–50%]</td>
<td>49% [42–55%]</td>
<td>77% [69–86%]</td>
</tr>
</tbody>
</table>

* Estimates were unavailable at the time of publication.
II. Paediatric HIV epidemiology in Central Europe
• At the end of 2014 as ECDC’ Surveillance Data Report reveals, Europe has registered the highest number of HIV infections, namely 142,000 cases, since the beginning of the reporting back in 1980s.
Geographical/epidemiological division of the WHO European Region

Figure A1: Geographical/epidemiological division of the WHO European Region

- West
- Centre
- East

The countries covered by the report are grouped as follows:


* Countries which constitute the European Union as of 1 July 2014.

Rate of new HIV diagnoses, by year of diagnosis, WHO European Region, 2005-2014

Data from Bosnia and Herzegovina, Turkmenistan and Uzbekistan excluded due to inconsistent reporting during the period.
Mother to child transmission in Western and Central Europe
Number of AIDS cases reported in 2005-2014

Source: HIV/AIDS surveillance in Europe 2014
Mother to child transmission in Eastern Europe 2005-2015
Number of AIDS cases reported in 2005-2014

Number of patients/year

Source: HIV/AIDS surveillance in Europe 2014
Mother to child transmission
Comparison by European Regions
Number of AIDS cases reported in 2005-2014

Source: HIV/AIDS surveillance in Europe 2014
Mother to child transmission
Comparison by European Regions
Number of AIDS cases reported in 2005-2014 (cont)

Source: HIV/AIDS surveillance in Europe 2014
At the end of 2013, 16 countries in EuroCoord reported 8,229 pHIV patients in follow-up in cohorts, compared with 5,160 cumulative diagnoses reported by the ECDC in the same area.

It is likely that the number of diagnoses of perinatal HIV reported to ECDC is an underestimate, although this varies by country. Further work is needed to refine estimates and encourage follow-up in adult HIV cohorts to investigate long-term outcomes and improve the care of the next generation of children with HIV.

Source: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21410
Number of perinatal patients in HIV cohorts in countries in the EU/EEA area, to end of 2013 (n = 8,229)

<table>
<thead>
<tr>
<th>Data source</th>
<th>EU/EEA country</th>
<th>Number of adult cohorts reporting MTCT patients&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Number of paediatric-only cohorts</th>
<th>Coverage of paediatric cohort</th>
<th>Number of MTCT patients in adult cohorts</th>
<th>Number of MTCT patients in paediatric cohorts</th>
<th>Total number of MTCT patients</th>
<th>Number of MTCT patients</th>
<th>Proportion of patients in EuroCoord/ECDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>14</td>
<td>14</td>
<td>NA</td>
<td>Single hospital</td>
<td>53</td>
<td>0</td>
<td>53</td>
<td>53</td>
<td>98%</td>
</tr>
<tr>
<td>Total</td>
<td>5,636</td>
<td>5,636</td>
<td>NA</td>
<td>Single hospital</td>
<td>2,439</td>
<td>5,790</td>
<td>8,229</td>
<td>5,636</td>
<td>NA</td>
</tr>
</tbody>
</table>

ECDC: European Centre for Disease Prevention and Control; EU/EEA: European Union and European Economic Area; HIV: human immunodeficiency virus; NA: not applicable.

<sup>a</sup> Adult cohorts may include paediatric patients while paediatric cohorts include children up to age 16 or 18 years or remaining in paediatric care.
From Dublin to Rome: 10 years of responding to HIV, in Europe and Central Asia

Figure 10. Proportion of PLHIV\(^5\) eligible for treatment and receiving it\(^6\) (2010–2013)

Number of children receiving antiretroviral therapy in low- and middle-income countries

http://www.who.int/hiv/topics/paediatric/data/en/index2.html

WHO Paediatric HIV data and statistics 2013

III. HIV in children and adolescents in Romania
Route of transmission
PLWHA
31 December 2015
14451/21479

- HETERO: 32%
- IDU: 7%
- MSM: 6%
- MTCT: 3%
- NOSO*: 20%
- TRANSFU*: 7%
- Unk*: 25%

*Romanian children’s cohort from the late 1980s (non-vertical transmission)
Age distribution in Romania
31 December 2015

Age at time of diagnosis/notification
Cumulative total 1985-2015

Age distribution of living patients

Source: Compartment for Monitoring and Evaluation of HIV/AIDS in Romania - INBI “Prof. Dr. M. Balș”
Tendencies in the routes of transmission
Romania 2007-2015

Source: Compartment for Monitoring and Evaluation of HIV/AIDS Infection in Romania INBI “Prof.Dr.M.Balş”
Age group distribution of HIV/AIDS infection cases, acquired through vertical transmission
31 December 2015

Source: Compartment for Monitoring and Evaluation of HIV/AIDS Infection in Romania INBI “Prof.Dr.M.Balș”
Children (0-14 years): number of schemes prior to the actual one
31 December 2015

Source: Compartment for Monitoring and Evaluation of HIV/AIDS Infection in Romania INBI “Prof.Dr.M.Balș”
Viral load values in children under antiretroviral treatment
31 December 2015

- Undetectable: 36%
- <50: 21%
- 51-100: 7%
- 1001-10000: 10%
- 10001-100000: 9%
- 100001-1000000: 3%
- >1000000: 1%

Source: Compartment for Monitoring and Evaluation of HIV/AIDS Infection in Romania INBI “Prof.Dr.M.Balș”
Young mothers, multi-experienced in ART
Mothers with unknown HIV status should be tested and treated for HIV.
New approach for management of perinatally exposed newborns.
National Registry of the Perinatally exposed child and HIV infected women

Almost all ARVs are registered in Romania
Universal access to treatment
Treatment regardless of CD4 values.
Treatment as prevention.
Sub-optimal regimen in early childhood.
Antiretroviral associated toxicities.
Special issues in ART in young women.

New psychoactive drugs
New approach for the case management of the adult and the newborn to HIV mothers who use new drugs.

PLWHA
MTCT
ART Use
IDUs
III. Current Paediatric Guidelines in Europe
Since the introduction of potent regimens, in the early 2000s, cART for children has improved gradually.

cART regimens include, at least, three therapeutic agents from a minimum of two classes, thus ensuring life expectancy by an improved quality of life.

On the other hand, there are many children who experience long and short term toxicity, with impact on their development as teenagers.

ART resistance in children develops more rapidly than in adults, mainly due to problems associated to resistance, sub optimal levels, followed by incomplete viral suppression.
Determining factors for therapeutic options:

- Age, especially young ages
- Stage of disease
- Drug formulations
- Complexity of medication that consists in both ART drugs and drugs for associated diseases
- Importance of the first therapeutic regime
- Co-morbidities, such as:
  - Tuberculosis
  - HBV, HCV
  - Chronic liver and kidney affections
- Adherence/compliance of the family or caregivers of the HIV infected child, to the care plan.
Steps to follow in order to reach essential ART objectives:

- Reducing HIV morbidity and mortality in children
- Virologic and immunologic success
- Prevention of ART resistance
- Reducing drug toxicity/metabolic changes
- Normal weight, height and neurocognitive development.
International guidelines’ recommendations for ART initiation in children
2016 update

<table>
<thead>
<tr>
<th>WHO</th>
<th>PENTA</th>
<th>DHHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART in <em>all</em> children regardless of WHO stage and CD4 count(^1)</td>
<td>ART in <em>all</em> children.(^2) *For those with good CD4 count time can be taken in order to address: issues of adherence and psychological effects of treatment.(^2)</td>
<td>ART in <em>all</em> children regardless of CD4 count, clinical stage-asymptomatic or with mild symptoms.(^3)</td>
</tr>
<tr>
<td>Priority: infants and children &lt;3 years of age, to adolescents, and to children with symptoms and/or low age-specific CD4 counts.(^2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Stage</th>
<th>&lt;1 year</th>
<th>1-5 years</th>
<th>&gt;6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cell</td>
<td>%</td>
<td>Cell</td>
</tr>
<tr>
<td>1</td>
<td>≥1500</td>
<td>≥34</td>
<td>≥1000</td>
</tr>
<tr>
<td>2</td>
<td>750-1499</td>
<td>26-33</td>
<td>500-999</td>
</tr>
<tr>
<td>3</td>
<td>&lt;750</td>
<td>&lt;26</td>
<td>&lt;500</td>
</tr>
</tbody>
</table>

Source: MMWR/April 11, 2014/Vol.63/nr.3
Updates in PENTA Guidelines 2009/2015

• Initiate ART- *all* children 1-3 years

• ART in children >5 years, including in those with high CD4 values

• Clinical indication- severe HIV associated diseases in children- ART irrespective of age

• First therapeutic line- new protease and integrase inhibitors- third ART drug

• HBV, HCV, TB co-infections- irrespective of age

• Importance of adherence, especially in children < 1 year and 1-3 years who depend, completely, on their families or caregivers

Updates in PENTA Guidelines 2009/2015 (cont.)

• Accurate and complete history of the first therapeutic lines (if this is the case) for both children and mothers.

• The genotypic profile (documented at baseline)

• Viral load and CD4 levels should be carried out every 6 months

• For children with undetectable viral load, clinical assessment to be performed every 3-4 months.
IV. KEY MESSAGES
• Increase in the rate of survival of children with HIV in the context of UNAIDS’ Fast Track Targets entails:
Parenting issues

- Disclosure to children
- Confidentiality
- Guilt
- Fear of transmission
- Caring for a child with HIV
- Secrecy and religious beliefs
- Migration
- ‘Aftercare’ following death
- Parenting through own illness
- Adherence
- Stress

Source: Mardarescu M. East meets West. Management of Women Living with HIV. EACS Belgrade, 13 October 2011
• Adherence to ART, especially at the time of initiation, that has significant impact on the patient's quality of life.

• The younger an infant or child is, adherence directly depends on the socio-economic status of his family or caregivers as well as on their ability to understand the importance of treatment.

• The relatively limited number of paediatric drug formula, taste, high number of pills, frequency of doses administration, diet restrictions bare strong implications on adherence.
A country’s economic development generates:

- The possibility to provide all paediatric drug formulations (23 approved by FDA)
- Consistent management of HIV treatment and care for children.

New challenges for Eastern and Central European countries:

- Management of mother to child transmission in the context of:
  - Women who use drugs/i.v. drugs
  - Co-infections: HIV/HBV/HCV/TB/STDs
  - All paediatric formulations should be provided on a constant basis with universal access (!!!)
Management and prevention of opportunistic infections:

- Corroboration between opportunistic infections and ART treatment
Last but not least, please bear in mind Jean Piaget’s words

“A child is not a miniature adult”
References

• Global AIDS Update. UNAIDS 2016


• AIDS Info. *Guideline for the Use of Antiretroviral Agents in HIV Paediatric HIV Infection.*

• World Health Organization. *Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key populations. 2016 Update*
  <http://apps.who.int/iris/bitstream/10665/246200/1/9789241511124-eng.pdf?ua=1>