Title: What ARV regimen to start in children ≥3 years old? (TDF)

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1. PICO question

<table>
<thead>
<tr>
<th>What ARV regimen to start (TDF in children)</th>
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<tbody>
<tr>
<td><strong>P</strong> Infants and children living with HIV [include specific consideration of infants living with HIV whose mothers received TDF + 3TC(FTC) + EFV]</td>
</tr>
<tr>
<td><strong>I</strong> Use of TDF-containing regimens</td>
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<tr>
<td><strong>C</strong> Use of non-TDF-containing regimens: AZT-based, ABC-based, D4T-based</td>
</tr>
<tr>
<td><strong>O</strong> Mortality, morbidity, severe adverse effects, viral response, CD4 response, adherence, switching rate, care retention, tolerability, TB incidence</td>
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2. Search strategy

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
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<tbody>
<tr>
<td>#4</td>
<td>Search ((#1) AND #2) AND #3</td>
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3. Flow diagram of screening process

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
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638 records identified through database searching

273 duplicates removed

365 records screened

343 records excluded

22 full text articles assessed for eligibility

19 articles excluded after full text assessment

3 studies included in review

4. Evidence summaries

Randomized controlled trials

Switch to TDF + 3TC + EFV at baseline versus week 24

Outcome: morbidity (AIDS-defining events) (48 weeks)
In one trial (Vigano 2005) with 48 weeks of follow-up, there was no significant difference in AIDS-defining events (none reported in either group) among participants switched to TDF + 3TC + EFV at week 1 versus week 24. This quality of evidence was downgraded due to serious indirectness and very serious imprecision.

Outcome: viral response (<50 copies/ml at 48 weeks)
In one trial (Vigano 2005) with 48 weeks of follow-up, there was no significant difference in viral response (week 1: 14/14 versus week 24: 13/14) among participants switched to TDF + 3TC + EFV at
week 1 versus week 24. This quality of evidence was downgraded due to serious indirectness and very serious imprecision.

**Outcome: study retention (48 weeks)**
In one trial (Vigano 2005) with 48 weeks of follow-up, there was no significant difference in on treatment completion (week 1: 14/14 versus week 24: 13/14) among participants switched to TDF + 3TC + EFV at week 1 versus week 24. This quality of evidence was downgraded due to serious indirectness and very serious imprecision.

**Switch to TDF-based regimens versus maintained on AZT or d4T-based regimens among children 2–16 years old**

**Outcome: immune response (VL <50 copies/ml) (48 weeks)**
In one trial (Gilead2 2012) with 48 weeks of follow-up, there was no significant difference in immune response with 71% in the TDF-based regimens versus 86% in the AZT or d4T-based regimens with VL <50 copies/ml. This quality of evidence was downgraded due to serious indirectness and serious imprecision.

**Outcome: discontinuation (48 weeks)**
In one trial (Gilead2 2012) with 48 weeks of follow-up, there was no significant difference in discontinuations with 6.3% in the TDF-based regimens versus 4.1% in the AZT- or d4T-based regimens experiencing discontinuations. This quality of evidence was downgraded due to serious indirectness and very serious imprecision.

**Outcome: Study retention (48 weeks)**
In one trial (Gilead2 2012) with 48 weeks of follow-up, there was no significant difference in study retention with 92% in the TDF-based regimens versus 98% in the AZT- or d4T-based regimens retained in the study. This quality of evidence was downgraded due to serious indirectness and very serious imprecision.

**Switch to TDF-based regimens versus maintained on their current regimen among people 12–17 years old**

**Outcome: serious adverse event or death (48 weeks)**
In one trial (Gilead12 2012) with 48 weeks of follow-up, there was no significant difference in serious adverse events or death, with 2.2% in the TDF-based regimens versus 0% in the current regimen arm experiencing one of these events. The quality of evidence was downgraded due to serious indirectness and very serious imprecision.

**Outcome: viral response (48 weeks)**
In one trial (Gilead12 2012) with 48 weeks of follow-up, there was no significant difference in viral response, with 70% in the TDF-based regimens versus 75% in the current regimen arm with viral response. This quality of evidence was downgraded due to serious indirectness and very serious imprecision.

**Outcome: study retention (48 weeks)**
In one trial (Gilead12 2012) with 48 weeks of follow-up, there was no significant difference in study retention, with 59% in the TDF-based regimens versus 66% in the current regimen arm retained in the study. This quality of evidence was downgraded due to serious indirectness and very serious imprecision.

5. Bibliography of included studies

Initiation of ART in ART-naive children

Randomized controlled trials: none identified.
Observational studies: none identified.

Initiation of ART in children switched to once-daily TDF regimens

2. Gilead12 study 2012 – personal communication.

6. Excluded studies with reasons

   • Observational study, conducted in high-income countries, and included a mixture of ART-naïve and ART-experienced children without presenting data separately

   • Single-arm study with no comparator.

   • Single-arm study with no comparator.

   • No outcomes of interest.

   • No outcomes of interest.
   • No outcomes of interest.

   • Not relevant.

   • No outcomes of interest and single-arm study with no comparator.

   • No outcomes of interest and single-arm study with no comparator.

    • No outcomes of interest and single-arm study with no comparator.

    • No outcomes of interest and single-arm study with no comparator.

    • No outcomes of interest and single-arm study with no comparator.