**Poster 989**

**Cost and Cost-Effectiveness of Switching from Stavudine to Tenofovir in First-Line ARV Regimens in South Africa**

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**Abstract**

Background: Most first-line antiretroviral therapy (ART) regimens in Africa include stavudine (d4T) despite the high incidence of related toxicities. We estimated the cost and cost-effectiveness of switching from d4T to tenofovir (TDF) in South Africa, accounting for both the cost of switching and maintenance toxicities.

Methods: A Markov model was developed to estimate the proportions of patients in a hypothetical cohort beginning ART and, if d4T and TDF-related events and drug switches occur over the 2 years following initiation. Transition probabilities, event and drug costs, and utility losses for the d4T scenario were estimated from primary data from a large, public sector clinic; parameters for the TDF scenario were drawn from the literature. Outcomes included incremental budgetary cost, incremental cost-effectiveness ratio (ICER) per quality-adjusted life year (QALY) gained, and threshold prices for TDF.

Results: After 2 years, 82.5% of the d4T scenario cohort remained on d4T, 16.6% switched to d4T, 64.8% had, and 414 events not leading to a drug change occurred in the TDF scenario, 97.5% of the cohort remained on TDF and 2.5% switched to d4T. At a baseline cost of TDF of $317.00/month, the incremental cost of the TDF scenario was $128/patient/year and the ICER was $9,007/QALY gained. The change to TDF would be cost-neutral for the government at a price of $6.17/month and highly cost-effective at a price of $12.94/month. Attributing 20% of lost to follow up to d4T side effects would increase the highly cost-effective price of TDF to $15.91/month.

Conclusions: At a TDF price of $17.00/month, savings on d4T toxicity management would offset roughly 20% of the higher TDF price. The price of TDF would need to fall substantially to make the change cost-neutral in budgetary terms, but it would be highly cost-effective at a price only slightly less than what is currently available.

**Background and Objectives**

- Almost 70% of ART patients in resource-constrained countries start on d4T.
- d4T is effective and inexpensive.
- Almost 70% of ART patients in resource-constrained countries start on d4T.
- In Africa, d4T is associated with high rates of toxicities, including lactic acidosis, symptomatic hyperlactatemia, peripheral neuropathy, and lipodystrophy.
- Optimal costs for medical care, disease management, quality of life, cause drug discontinuations, and increased adherence and retention of ART patients.
- Tenofovir disoproxil fumarate (TDF) has been considered as a replacement for d4T.
- TDF is effective and safer but more expensive than d4T.
- The objectives of this analysis were to:
  - Estimate the incremental budgetary cost of switching from d4T to TDF in South Africa.
  - Estimate the incremental cost-effectiveness of switching from d4T to TDF in South Africa.
  - Determine the threshold prices of TDF at which the switch would become highly cost-effective and budget-neutral.

**Methods**

- **Methods**: 1. **Cost and cost-effectiveness of two scenarios**
  - d4T scenario (all patients initiated on d4T-3TC-EFV). 2. **TDF scenario** (all patients initiated on TDF-3TC-EFV). 3. **Used Markov model to estimate costs incurred and quality-adjusted life years (QALYs) gained**.
  - **Modeled a hypothetical cohort of 1000 adult patients for two years after initiation**.
  - **Computed the costs of ART and toxicity management only**.
  - **Toxicity management costs included lab tests, outpatient visits, and inpatient care**.
  - **Considered effect of d4T-related loss to follow up in sensitivity analyses**.

- **Value**
  - **TDF scenario**
    - d4T: $3.62/patient/month
    - 3TC: $1,067,408
    - EFV: $24,000
    - AZT: $14,933
    - TDF: $17,000
  - **ARVs costs/patient/year**
    - d4T: $638
    - 3TC: $24
    - EFV: $14.93
    - AZT: $1,323,445
    - TDF: $6,170
  - **Total (ARV+event) costs/patient/year**
    - d4T: $662
    - 3TC-EFV: $7,999
    - AZT: $192
    - TDF: $12.94
  - **QALYs lost/event**
    - $130
  - **$/event**
    - 1a - severe peripheral neuropathy
    - 1b - moderate peripheral neuropathy
    - 1c - mild peripheral neuropathy
    - 2a - death from lactic acidosis
    - 2b - non-fatal lactic acidosis
    - 3a - non-acute lipodystrophy
    - 4a - severe renal toxicity
    - 4b - non-severe renal toxicity
    - 4c - lactate test only
    - 4d - lactate test only
    - 5a - severe peripheral neuropathy
    - 5b - moderate peripheral neuropathy
    - 5c - mild peripheral neuropathy
    - 5d - non-fatal lactic acidosis
    - 5e - severe symptomatic hyperlactatemia
    - 5f - mild symptomatic hyperlactatemia
    - 5g - lactate test only
    - 5h - lactate test only
    - 5i - severe peripheral neuropathy
    - 5j - moderate peripheral neuropathy
    - 5k - mild peripheral neuropathy
    - 5l - non-fatal lactic acidosis
    - 5m - severe symptomatic hyperlactatemia
    - 5n - mild symptomatic hyperlactatemia
    - 5o - lactate test only
    - 5p - lactate test only

- **Model and Events**
  - **Model setup**
    - A Markov model was developed to estimate the proportion of patients in a cohort entering model in 3-month cycles. In each cycle, each patient can remain in State 1 without an event, remain in State 1 with an event, or transition to States 2, 3, 4, or 5. Each state and event represent costs that are summed for the cohort after 8 cycles (24 months).
  - **Events defined for the analysis**
    - d4T scenario
      - 1a - severe peripheral neuropathy: change to AZT without interruption (State 3)
      - 1b - moderate peripheral neuropathy: change to AZT without interruption (State 3)
      - 1c - mild peripheral neuropathy: remain on d4T (State 1)
      - 2a - death from lactic acidosis: no new drug (State 5)
      - 2b - non-fatal lactic acidosis: change to AZT with interruption (State 2)
      - 2c - severe symptomatic hyperlactatemia: change to AZT with interruption (State 2)
      - 2d - mild symptomatic hyperlactatemia: remain on d4T (State 1)
      - 3a - lactate test only: remain on d4T (State 1)
      - 3b - non-acute lipodystrophy: change to AZT without interruption (State 3)
    - TDF scenario
      - 1a - severe peripheral neuropathy
      - 1b - moderate peripheral neuropathy
      - 1c - mild peripheral neuropathy
      - 2a - death from lactic acidosis
      - 2b - non-fatal lactic acidosis
      - 3a - non-acute lipodystrophy
      - 4a - severe renal toxicity
      - 4b - non-severe renal toxicity
      - 4c - lactate test only
      - 4d - lactate test only
      - 5a - severe peripheral neuropathy
      - 5b - moderate peripheral neuropathy
      - 5c - mild peripheral neuropathy
      - 5d - non-fatal lactic acidosis
      - 5e - severe symptomatic hyperlactatemia
      - 5f - mild symptomatic hyperlactatemia
    - **Model set-up**
      - **Cohort ages through model in 3-month cycles. In each cycle, each patient can remain in State 1 without an event, remain in State 1 with an event, or transition to States 2, 3, 4, or 5. Each state and event represent costs that are summed for the cohort after 8 cycles (24 months).**
  - **Modeling assumptions**
    - **Parameters for d4T scenario estimated from patient database of Themb Memorial Clinic, Helen Joseph Hospital, Johannesburg (n=764).**
    - **Parameters for TDF scenario drawn from literature.**
    - **Resource costs based on actual prices paid by study site and published values.**
    - **QALY values drawn from literature.**

- **Data**
  - **Parameters for d4T scenario estimated from patient database of Themb Memorial Clinic, Helen Joseph Hospital, Johannesburg (n=764).**
  - **Parameters for TDF scenario drawn from literature.**
  - **Resource costs based on actual prices paid by study site and published values.**
  - **QALY values drawn from literature.**

**Results**

- **Baseline TDF price used in model**
  - $6.17/patient/month
  - **Cost-neutral price of TDF**
  - $6.17/patient/month
  - **Price of TDF at which switch is cost-neutral for government**
  - $12.94 patient/month

**Conclusions**

- A TDF price of $17.00/patient/month, savings on d4T toxicity management will offset roughly 20% of the higher TDF price. The price of TDF would need to fall substantially to make the change cost-neutral in budgetary terms, but it would be highly cost-effective at a price only slightly less than what is currently available.