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 drug prices and the cost of managing toxicities.

Methods: A Markov model was developed to estimate the proportion of patients in a hypothetical cohort experiencing d4T- and TDF-related events and drug switches over the 2 years following ART 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 AZT, 0.8% died, 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 AZT. At a baseline cost of TDF of $17.00/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 loss 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 will offset roughly 20% of the higher TDF price. The price of TDF would have 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.

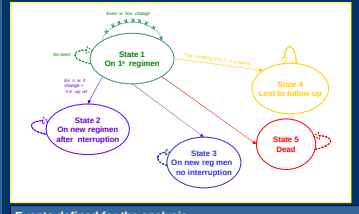
Background and Objectives

- Almost 70% of ART patients in resource-constrained countries start on d4T.
  - d4T is effective and inexpensive.
  - In Africa, d4T is associated with high rates of toxicities, including lactic acidosis and symptomatic hyperlactatemia, peripheral neuropathy, and lipodystrophy.
  - Side effects impose costs for medical care, diminish quality of life, cause drug switches, and may suppress adherence and retention of ART patients.
- Tenofovir disoproxil fumarate (TDF) is often considered as a replacement for d4T.
  - TDF is effective and safe but much 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's first line regimens at existing drug prices.
  - Estimate the incremental cost per quality-adjusted life year gained from the switch at existing drug prices.
  - Determine the threshold prices of TDF at which the switch would become highly cost-effective and budget-neutral.

Methods

- Compared the costs and cost-effectiveness of two scenarios
  - d4T scenario (all patients initiated on d4T-3TC-EFV)
  - TDF scenario (all patients initiated on TDF-3TC-EFV).
- 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.
- Included costs of ARVs 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 analysis.

Model and Events



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 State 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)
2e - Lactate test only; remain on d4T (State 1)
3a - Non-acute lipodystrophy; change to AZT without interruption (State 3)

TDF scenario

4a - Severe renal toxicity; change to AZT with interruption (State 2)
4b - Non-severe renal toxicity; change to AZT without interruption (State 3)

Data

- Parameters for d4T scenario estimated from patient database of Themba Lethu Clinic, Helen Joseph Hospital, Johannesburg (n 5,766)
- Parameters for TDF scenario drawn from literature.
- Resource utilization per event estimated from patient records and clinical judgment.
- Resource costs based on actual prices paid by study site and published values.
- QALY values drawn from literature.

Results

Unit cost and QALY estimates

ARVs	*$/patient/month*	
d4T	$3.62	
3TC	$6.98	
EFV	$26.05	
AZT	$14.93	
TDF	$17.00	
Events	***$/event***	***QALYs lost/event***
1a - severe peripheral neuropathy	$130	0.16
1b - moderate peripheral neuropathy	$130	0.06
1c - mild peripheral neuropathy	$92	0.02
2a - death from lactic acidosis	$2,502	0.96
2b - non-fatal lactic acidosis	$7,999	0.13
2c - severe symptomatic hyperlactatemia	$192	0.02
2d - mild symptomatic hyperlactatemia	$119	0.01
2e - lactate test only	$49	0.00
3a - non-acute lipodystrophy	$121	0.12
4a - severe renal toxicity	$8,477	0.09
4b - non-severe rental toxicity	$213	0.01

Cohort status after 24 months (8 cycles)	d4T scenario	TDF scenario
Still on original drug (State 1)	82.5%	97.5%
Changed to new drug after event (State 2 or 3)	16.6%	2.5%
Died (State 5)	0.8%	0.0%

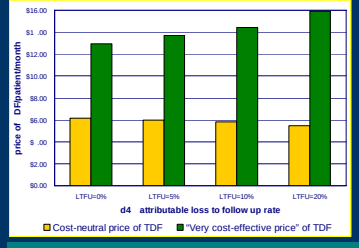
Number of events in 1000 patient cohort over 24 month period

d4T scenario	
1a - severe peripheral neuropathy	28
1b - moderate peripheral neuropathy	32
1c - mild peripheral neuropathy	75
2a - death from lactic acidosis	9
2b - non-fatal lactic acidosis	12
2c - severe symptomatic hyperlactatemia	39
2d - mild symptomatic hyperlactatemia	213
2e - lactate test only	126
3a - non-acute lipodystrophy	65
TDF scenario	
4a - severe renal toxicity	5
4b - non-severe renal toxicity	20

Budgetary cost and cost effectiveness

Value	*d4T scenario*	*TDF scenario*
Total cost of scenario (24 months, ARVs + toxicity events only, per 1000 patients initiated)	$1,067,408	$1,323,445
ARV costs/patient/year	$445	$638
Event costs/patient/year	$88	$24
Total (ARV+event) costs/patient/year	$534	$662
Incremental cost of TDF scenario/patient/year		$128
Incremental cost per QALY gained by TDF scenario		$9,007
Baseline TDF price used in model		$17.00/patient/month
TDF price at which switch is cost-neutral for government		$6.17/patient/month
TDF price at which switch can be considered "very cost effective" (average cost/QALY gained GDP/capita)		$12.94 patient/month

What if d4T is responsible for a proportion of observed loss to follow up?



As d4T-attributable loss to follow up increases, the cost-neutral price of TDF falls, because patients who discontinue treatment cease to incur costs. But the cost-effective price of TDF rises, because more QALYs are lost by patients who discontinue treatment. If 10-20% of observed loss to follow up results from d4T-related side effects, then TDF would be "very cost effective" at only slightly less than the modeled price of $17/patient/month.

Conclusions

- At a TDF price of $17/patient/month, reduced costs for managing d4T-related toxicities would offset about 20% of the higher price of TDF.
- For the switch to TDF in first-line regimens to be cost-neutral for the South African government, price of TDF will have to fall to approximately $6/patient/month.
- In terms of patient welfare (QALYs,) however, the switch w ll be highly cost-effective at a TDF price of $13/patient/month.
- If 10-20% of observed loss to follow up is attributable to d4T-related toxicities, then sw tching to TDF is very cost effective at currently available prices.
- Analysis was limited by data quality, model constraints, and time frame; assumptions used were conservative and likely underestimated the costs of d4T-related toxicities.
- Full manuscript is available from authors on request.

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