Unfavorable Outcomes Associated with Genetic Screening of *HLA-B*13:01* for the Prevention of Co-Trimoxazole-Induced Severe Cutaneous Adverse Reactions among HIV-Infected Patients in Thailand: A Cost-Effectiveness Analysis

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Introduction

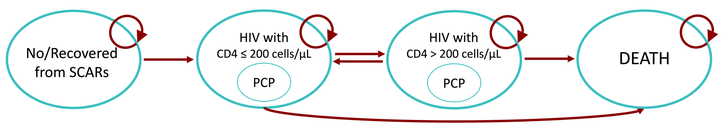
- Co-trimoxazole is an essential preventive therapy for pneumocystis pneumonia (PCP) and other infections in people living with HIV.[1]
- Besides its benefits, co-trimoxazole has been found to have a strong association with the occurrence of severe cutaneous adverse reactions (SCARs) among those who carry the *HLA-B*13:01* allele.[2,3]
- Genetic screening before initiation of co-trimoxazole is a potential strategy to reduce co-trimoxazole-induced SCARs cases. However, it bears additional costs of testing.

Objective

To evaluate the cost-effectiveness of *HLA-B*13:01* screening prior to initiation of co-trimoxazole in HIV-infected patients, from a societal perspective.

Methods

- A Markov model was employed to project lifetime costs and outcomes of two treatments treatment strategies: 1) *HLA-B*13:01* screening before co-trimoxazole initiation and 2) usual practice from societal perspective.



- Model assumptions:
  1) Patients with PCP infection would not have re-infection in the next cycle.
  2) Patients changing health state from "CD4 ≤ 200 cells/µL" to "CD4 > 200 cells/µL" would not be infected in the transition cycle.
  3) After receiving the treatment, we assumed they would either recover or die within one cycle.
  4) Full compliance from patients was also assumed.
- Alternative drugs are not considered because dapsone (the second-line drug) also presents a high risk of SCAR associated with *HLA-B*13:01*.[4]
- Input parameters were obtained from literature, government documents, and a part of the TREAR Asia HIV Observational Database (TAHOD).
- One-way sensitivity analyses and probabilistic analyses were performed to determine the robustness of the findings.
- All costs were adjusted and presented in the 2020-year value.

Results

Table 1. SCAR and PCP-related outcomes

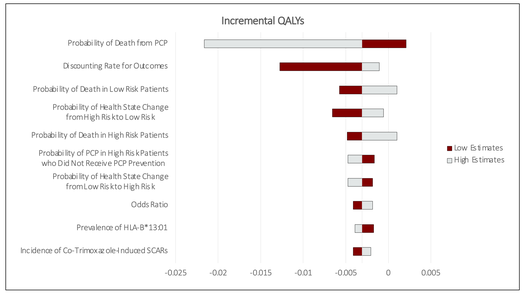
Strategy	Expected SCAR case*	Expected death from SCAR*	Patients who received co-trimoxazole (%)	Patients who did NOT receive co-trimoxazole (%)	Expected PCP cases	Expected deaths from PCP
Current practice	31.4	0.88	99.69	0.31	524.20	20.97
*HLA-B*13:01* screening	21.36	0.60	88.30	11.70	622.05	24.88

*per 10,000

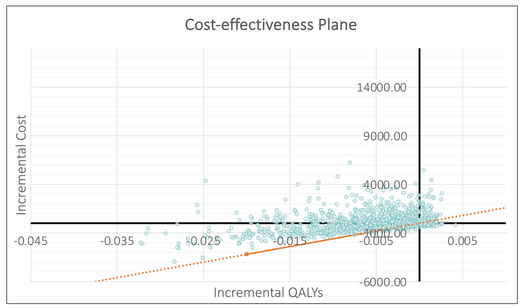
Table 2. Base case analysis

Strategy	Cost (THB/ USD)	Effectiveness		Incremental cost (ΔTHB/ ΔUSD)	Incremental effectiveness		ICER (ΔTHB/ ΔQALYs)
		QALYs	LYs		ΔQALYs	ΔLYs	
Current practice	1,387,356/ 44,333	19.377	22.702				
*HLA-B*13:01* screening	1,387,726/ 44,345	19.374	22.696	370/12	-0.0031	-0.0061	Dominated

- *HLA-B*13:01* screening resulted in 0.0061 quality-adjusted life years (QALYs) loss with an additional cost of 370 THB ($11.84).



- **Figure 1.** Tornado diagram showing a series of one-way sensitivity analysis



- **Figure 2.** Cost-effectiveness scatter plot
- At the cost-effectiveness threshold of 160,000 THB ($5,112.85),[4] the probability of the genetic screening strategy being cost-effective is 9.54%.

Discussion and Limitations

- The *HLA-B*13:01* allele screening before initiation of co-trimoxazole among HIV-infected patients is not cost-effective in Thailand because the benefit of preventing SCARs could not outweigh the risks from PCP.
- We derived health state transition from country-specific real-world data from TAHOD. Other model parameters were also country-specific, which resulted in context-specific findings.
- This study has limitations including:
  - The incidence of SCARs available in Thailand was collected from one tertiary hospital in Thailand.[5]
  - Data regarding PCP infection and deaths from PCP was obtained from literature where prophylactic and treatment agents are more varied.[6]
  - Due to the inexplicit pattern of SCARs, the long-term consequence was assumed to be only one condition (dry eye syndrome, 36.7% in Stevens–Johnson syndrome (SJS/TEN) patients).[7]

Conclusions

- This analysis demonstrated that *HLA-B*13:01* allele screening before initiating co-trimoxazole among people living with HIV is unlikely to be cost-effective in Thailand.
- It is necessary to have an alternative drug provided for those who are contraindicated for co-trimoxazole.
- Our findings will help policymakers make evidence-informed decision making.

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