Directly observed therapy is associated with improved TB treatment outcomes, Thailand 2004-2006

Amornrat Anuwatnonthakate, et al.

TB Program

Thailand MOPH – U.S. CDC Collaboration

TB and Observed Therapy

- 8.8 million illnesses, 1.6 million deaths / year
- Treatment is a challenge
  - Duration at least 6 months
  - Patients take medications erratically or not at all
  - Non adherence decreases cure rate, increases relapse rate, selects for drug-resistant strains
- WHO endorses directly observed therapy
  - Trained person observes swallowing of medications
  - Randomized controlled trials have not shown a benefit to DOT

TB in Thailand

- Ranked 17th of 22 high-burden countries
- Adopted WHO DOTS in 1997
- Failure to control TB due to:
  - HIV epidemic
  - High death rates
  - High default rates

DOT in Thailand

- Patients receive different types of observer
  - DOT by health care worker (HCW)
  - DOT by family member (FAM)
  - No DOT (self-administered [SAT])
- DOT, if provided, usually only for 2 months

Study Questions

- Are patients receiving HCW or family DOT more likely to be on treatment at 2 months compared with patients receiving SAT?
- Are patients receiving HCW or family DOT more likely to successfully complete treatment compared with patients receiving SAT?

Thailand TB Active Surveillance Network

- All persons diagnosed with TB in public, private health care facilities
- Standard epidemiologic data at beginning and end of treatment
- Culture, susceptibility testing
- HIV counseling, testing

Note: Bangkok site includes Bamrasnaradura Institute

Patient Population

- Eligible
  - TB patients who initiated treatment from 10/2004 – 9/2006 in Thailand TB Active Surveillance Network
  - Pulmonary TB
  - Not previously treated for TB
  - Not known to have MDR TB
  - Data recorded about treatment observer
- Eligible, but excluded
  - Missing data about treatment status at 2 months
  - Missing data about end of treatment outcome

Definitions

- Standard WHO definitions for type of TB, and treatment outcome
  - Any death during TB treatment = death
  - Successful treatment = cured or completed
- Treatment observer
  - “Who observed treatment during the first two months of TB treatment?”
  - Classified as HCW, family, SAT, other
  - Recorded by surveillance staff

Data Analysis

- Treatment status at 2 months
  - On treatment vs. died or defaulted
  - On treatment vs. defaulted
- Treatment outcome
  - Successful vs. defaulted, died, or failed
  - Successful vs. defaulted

Data Analysis, cont.

- Create propensity score (probability for being on DOT) to control for differing baseline characteristics of exposure groups
- Perform multivariate logistic regression to analyze impact of HCW, family DOT or SAT on treatment outcome, adjusted for the propensity score

Propensity Score Analysis

- Used when baseline characteristics of exposure groups may be markedly different
- Examine factors associated with the intervention, combine factors into composite variable, adjust for composite variable in final analysis

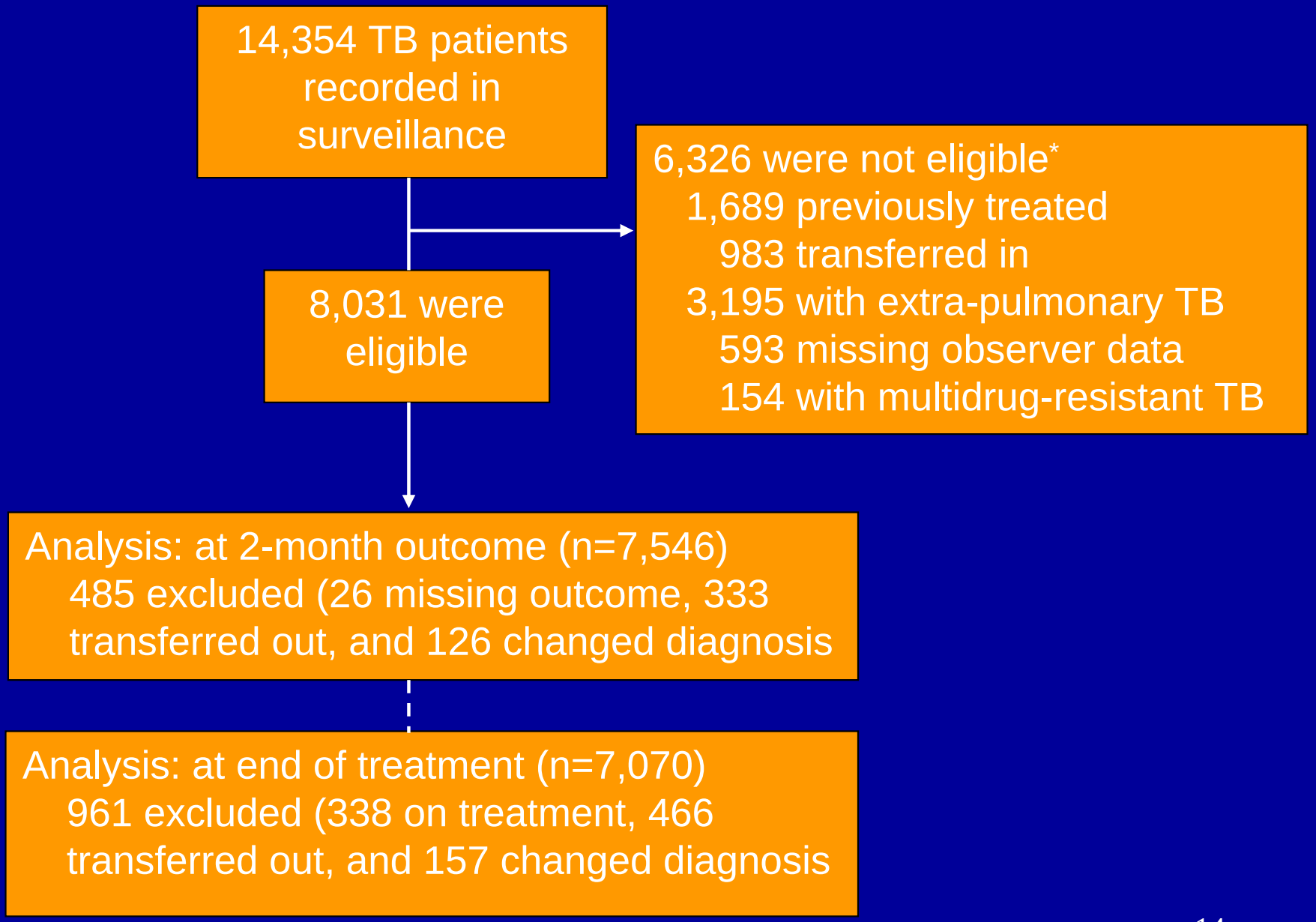
Propensity Score Example

- Patients who receive HCW DOT different than those that receive family DOT
- Do bivariate logistic regression to identify risk factors for receiving HCW DOT
- Do multivariate logistic regression to predict the probability of risk factors for receiving HCW DOT

Propensity Score Example

- Create propensity score (PS) from logistic regression - each patient assigned a PS measuring probability to receive HCW DOT
- Patient population divided into at least 5 strata based on PS score
- Analyze impact of HCW DOT on treatment outcome, adjusted for PS strata

Results



* Number do not sum, because patients may have been excluded for more than one reason.

Characteristics of Eligible Patients

(n=8,031)

- Most patients male, aged 15-44 years, married, from rural district
- Smear-positive TB: 63%
- HIV-infected: 21%
- DOT: 24% HCW, 59% family, 18% SAT
- 81% on treatment at 2 months
- 66% cured or completed treatment

On Treatment vs. Default or Death at 2 Months

Comparison between groups	No (%) on treatment			Propensity Score Risk Adjustment Odds ratio (95% confidence interval)
	HCW DOT	Family DOT	Self-Admin	
HCW vs. SAT	1605/1788 (90%)	—	1099/1319 (83%)	**1.3** (1.0-1.7)
Family vs. SAT	—	3805/4422 (86%)	1099/1319 (83%)	1.1 (0.9-1.4)
HCW vs. Family	1605/1788 (90%)	3805/4422 (86%)	—	1.1 (0.9-1.3)

On Treatment vs. Default at 2 Months

Comparison between groups	No (%) on treatment			Propensity Score Risk Adjustment Odds ratio (95% confidence interval)
	HCW DOT	Family DOT	Self-Admin	
HCW vs. SAT	1605/1640 (98%)	—	1099/1271 (86%)	**3.7** (2.3-6.0)
Family vs. SAT	—	3805/4010 (95%)	1099/1271 (86%)	2.0 (1.5-2.7)
HCW vs. Family	1605/1640 (98%)	3805/4010 (95%)	—	**2.1** (1.4-3.1)

Cured or Completed vs. Default, Death, Failure

Comparison between groups	No (%) cured or completed			Propensity Score Risk Adjustment Odds ratio (95% confidence interval)
	HCW DOT	Family DOT	Self-Admin	
HCW vs. SAT	1369/1716 (80%)	—	744/1154 (64%)	**1.6** (1.3-2.0)
Family vs. SAT	—	3130/4186 (75%)	744/1154 (64%)	**1.3** (1.1-1.5)
HCW vs. Family	1369/1716 (80%)	3130/4186 (75%)	—	1.1 (0.9-1.2)

Cured or Completed vs. Default

Comparison between groups	No (%) cured or completed			Propensity Score Risk Adjustment Odds ratio (95% confidence interval)
	HCW DOT	Family DOT	Self-Admin	
HCW vs. SAT	1369/1477 (93%)	—	744/1074 (69%)	**3.3** (2.4-4.5)
Family vs. SAT	—	3130/3529 (89%)	744/1074 (69%)	2.0 (1.6-2.4)
HCW vs. Family	1369/1477 (93%)	3130/3529 (89%)	—	**1.5** (1.2-1.9)

Conclusions

- Receiving 2 months of DOT is associated with improved TB treatment outcomes
  - HCW and family DOT beneficial, but greatest benefit from HCW
  - Impact primarily on reducing default, not on reducing death or failure
- Major strength
  - Largest epidemiologic study of DOT ever
  - Diverse patient population with large HIV burden

Limitations

- DOT classified by surveillance worker, not by independently verified observation
  - Would expect patients who were recorded as being on DOT to not actually receive DOT
  - This would bias study toward no association
- Data only about first 2 months of DOT; some sites may have provided DOT for longer
- Missing data

Recommendations

- Scale up use of DOT in Thailand, especially using HCWs
- Continue monitoring to measure impact on reducing default rates under routine program conditions

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Directly Observed Therapy and Improved Tuberculosis Treatment Outcomes in Thailand

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