Six steps to estimating the cost-effectiveness of ART

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Introduction

- Presentation covers selected methodological issues related to two cost-effectiveness analyses, and some issues related to a third scheduled to start later in the year
- Focus is on the specific methods and steps that we have used in these studies, rather than on providing details of the particular study question and setting

The Six Steps (1)

- Step One – establish the interventions under evaluation
- Step Two – calculate unit costs for each service
- Step Three – establish the utilization of services by patients
- Step Four – establish outcomes of each treatment arm
- Step Five – construct Markov Model (a necessary evil!)
- Step Six – estimate cost-effectiveness ratios and conduct sensitivity analysis

Step One – establishing the interventions under evaluation

- Khayelitsha cost-effectiveness analysis (Cleary, Boulle, McIntyre & Coetzee, 2004)
- Research question: Is ART technically efficient?

  – Treatment Arm 1 = **"ART"** = treatment and prophylaxis of opportunistic and HIV-related infections and events with antiretroviral treatment
  – Treatment Arm 2 = **"No ART"** = treatment and prophylaxis of opportunistic and HIV-related infections and events without antiretroviral treatment

Step One – establishing the interventions under evaluation

- CTAC cost-effectiveness analysis (with Motasim Badri and Robin Wood):
- Research question: When is the more technically efficient point to commence ART?
- All patients enter the model with CD4>350, but are randomised into one of the following:
  - Treatment Arm 1 = **Start ART CD4>350**
  - Treatment Arm 2 = **Start ART CD4 200-350**
  - Treatment Arm 3 = **Start ART CD4<200**
  - Treatment Arm 4 = **No ART**
- OR: All patients enter model with WHO Stage I/II, and are randomised as follows:
  - Treatment Arm 1 = **Start ART WHO Stage I/II**
  - Treatment Arm 2 = **Start ART WHO Stage III**
  - Treatment Arm 3 = **Start ART WHO Stage IV**
  - Treatment Arm 4 = **No ART**

Step One – establishing the interventions under evaluation

- CIPRA cost-effectiveness analysis (Debbie Muirhead is PI):
  - Treatment arm 1: **Nurse-based care, non-DOTS second-line**
  - Treatment arm 2: **Nurse-based care, DOTS second-line**
  - Treatment arm 3: **Doctor-based care, non-DOTS second-line**
  - Treatment arm 4: **Doctor-based care, DOTS second-line**

The Six Steps (2)

- Step One – establish the interventions under evaluation and the perspective
- Step Two – calculate unit costs for each service
- Step Three – establish the utilization of services by patients
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Step Two – calculating unit costs

- Calculating unit costs including:
  - Cost per clinic or outpatient department visit
  - Cost per inpatient day (secondary and tertiary)
  - Cost per tuberculosis treatment completed

Step Two – methods for unit costs

- Ingredients approach for:
  - Medicines
    - prophylactic drugs (bactrim, fluconazole etc)
    - curative drugs (antibiotics, antifungals etc)
  - Clinical staff (doctors, nurses)
- Step-down method for:
  - Other staff (social workers, dieticians, administrative staff, counsellors, etc)
  - Overheads (electricity, water, and other expenditure that cannot be related directly to patients' utilisation)
  - Capital (buildings, equipment and initial staff training)

Step Two – unit costs

	Clinic visit ART (Cleary, 2004)	Clinic visit No ART (Cleary, 2004)	OPD visit (Govender, 2000)	Level 3 hospital (Cleary, 2004 and Govender, 2000)	Level 2 hospital (Haile, 2000)	TB care (Sinanovic, 2003)
Human resources	71%	56%	71%	61%	56%	55%
Infrastructure & equipment	5%	6%	9%	21%	11%	8%
Training	1%	0.1%	-	-	-	-
Commodities & products	2%	2%		15%	24%	7%
Drugs	8%	21%	18%	2%	8%	15%
Planning & administration	13%	14%	2%	2%	1%	15%
Unit cost ($)	19	17	20	230	127	487

The Six Steps (3)

- Step One – establish the interventions under evaluation and the perspective
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Step Three – Establish the Utilization of Services

- This involves calculating the utilization of clinic visits, tuberculosis treatment and hospital care by patients over time in each treatment arm
- Ultimately, stable utilization estimates require a fairly large number of patients in each treatment arm
- Furthermore, estimating utilization overtime requires long follow-up periods which are frequently unavailable at the time of the evaluation

Step Three – utilisation of services in Khayelitsha

	Clinic visit	Level 2 hospital IPD	Level 3 hospital IPD	TB incidence	Inpatient utilisation at death
No-ART, annually CD4 50-199	13.0	1.31	0.53	0.36	5.28
No-ART, annually CD4<50	13.0	1.87	1.03	0.56	7.13
ART first-line initial 6 months	11.7	0.46	0.19	0.07	4
ART annually thereafter	13.4	0.31	0.13	0.12	4
ART second-line initial 6 months	6.5	0.16	0.06	0.07	4
ART annually thereafter	13.4	0.31	0.13	0.12	4
Failing ART	13.0	1.87	1.03	0.56	7.13

The Six Steps (4)

- Step One – establish the interventions under evaluation and the perspective
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Step Four - Establish the outcomes of each treatment arm

- Khayelitsha, CTAC and CIPRA analyses all express outcomes as Quality Adjusted Life Years Gained and Life Years Gained
- Khayelitsha based on EQ5D, converted to QALYs using UK Time Trade Off values
- CTAC based on SF36, converted to QALYs using UK Standard Gamble values
- CIPRA – proposing to use QWB instrument

Step Four – QALY values for Khayelitsha and CTAC

	Khayelitsha	CTAC
Baseline / No ART	0.7	0.69
3-6 months	0.79	0.81

The Six Steps (4)

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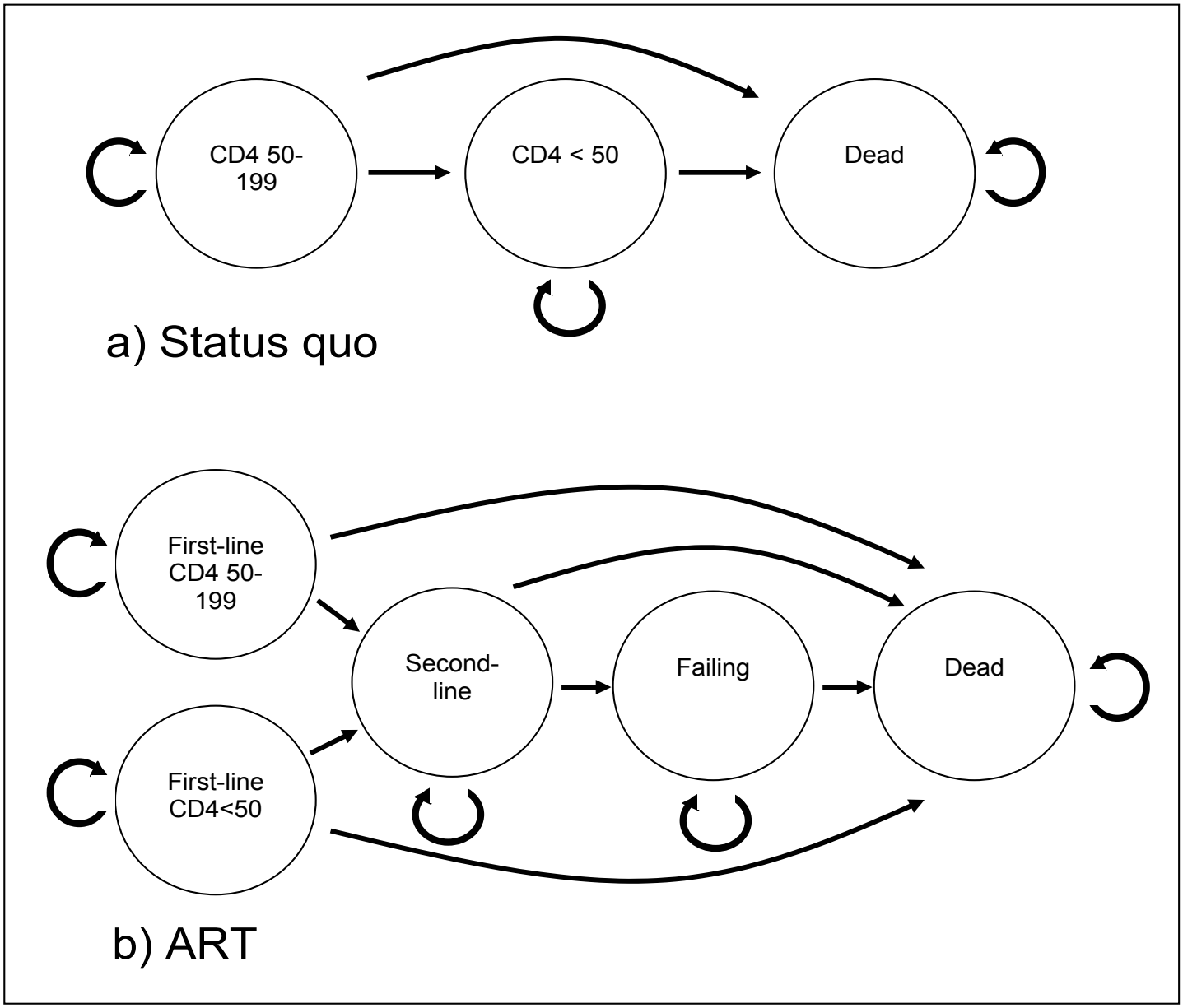
Step Five – construct Markov Model

- Markov modelling is commonly used to evaluate CE of long-term interventions or chronic diseases
- Consists of a set of mutually exclusive health (Markov) states
- Transition probabilities describe movements between states
- Allows vital conclusions for policy purposes to be made although no final outcomes exist from primary data
- Sensitivity analysis uncovers any uncertainty in results

Step Five – Khayelitsha Markov Model



The Six Steps (4)

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Step Six – results for Khayelitsha and CTAC

Khayelitsha CEA	Lifetime Costs ($)	QALYs	Ave CER	Incr CER	
No ART	2,472.04	1.30	1,901.57	1,901.57	*
ART	7,520.49	4.30	1,748.95	1,682.82	
CTAC CEA					
No ART	4,201.67	3.39	1,239.43	1,239.43	*
Start ART CD4<200	5,450.71	5.37	1,015.03	630.83	
Start ART CD4 200-350	6,199.03	6.47	958.12	648.49	
Start ART CD4 >350	7,668.73	7.61	1,007.72	821.58	

No ART is assumed to be incremental on a zero cost zero effectiveness do-nothing approach

US$1 = R7.6; discount rate = 8%

Step Six – Sensitivity analysis

- Khayelitsha CEA used one-way sensitivity analysis
  - Involves varying key variables *cet par* to determine the impact on results
- CTAC CEA uses probabilistic sensitivity analysis,
  - Involves specifying a distribution on each variable (transition probabilities and costs), and allowing the model to sample from that distribution over a large number of iterations (Monte Carlo Simulation)
  - CE results are then specified as a mean with confidence intervals
  - Benefit is that sensitivity to all variables is assessed simultaneously
  - However, often will still need to do one-way sensitivity analysis together with probabilistic sensitivity analysis to examine impact of variables such as discount rate

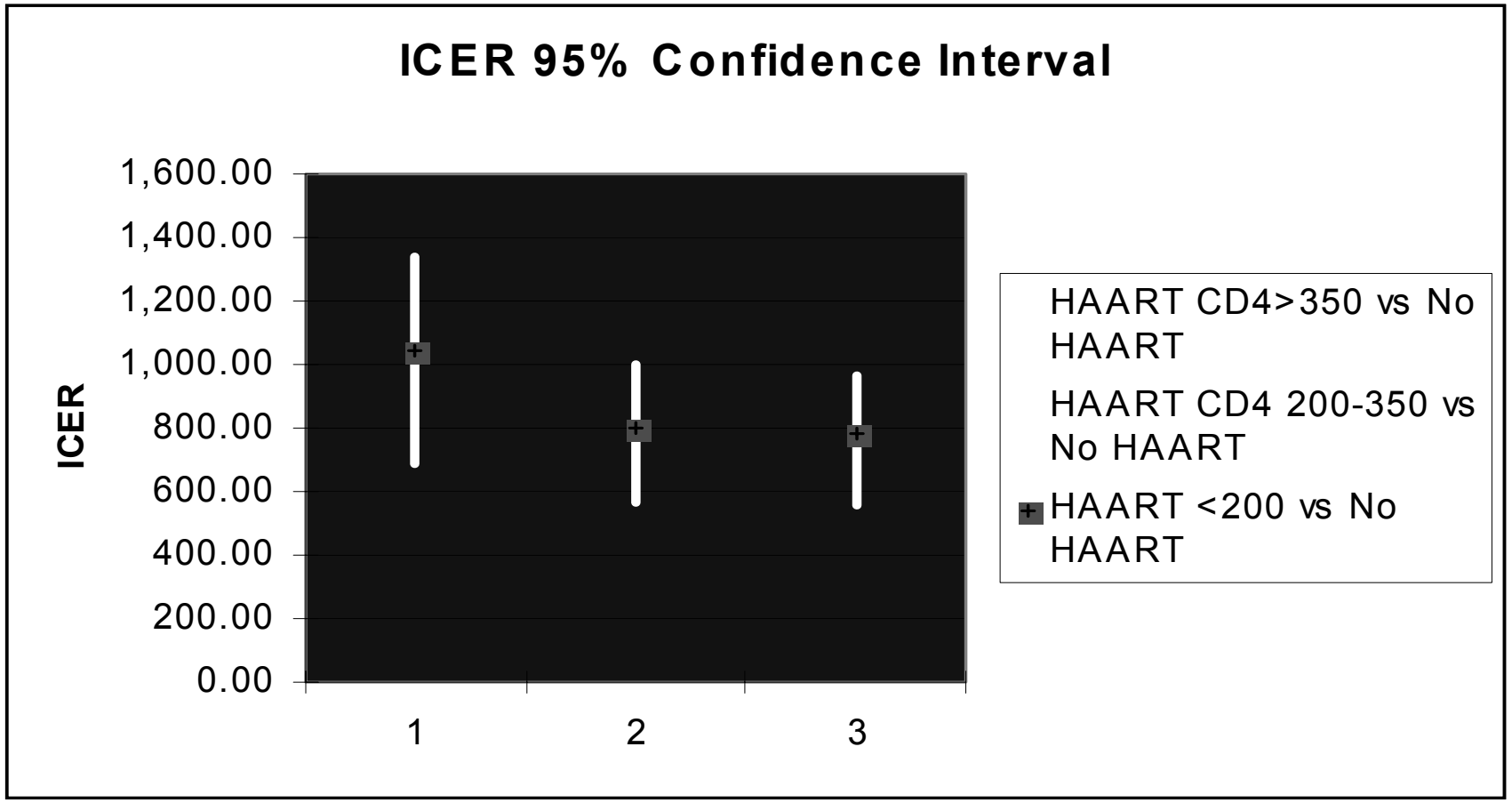
Step Six – Khayelitsha sensitivity analysis

Incremental cost-effectiveness and sensitivity analysis

Scenario	QALYs gained	Incr. cost (US$)	Incr. Cost per QALY gained	% change from baseline
Base case (8% discount rate)	3.02	4,596	1,522	
3% discount rate	4.16	6,563	1,578	+ 3.7
0% discount rate	5.20	8,364	1,608	+ 5.7
Patented medicines only	3.02	5,677	1,880	+ 23.5
15% uniform reduction in medicine prices	3.02	4,058	1,344	- 11.7
Viral loads excluded	3.02	4,016	1,330	- 12.6
15% reduction in mortality probabilities	3.50	5,340	1,526	+ 0.3
15% increase in mortality probabilities	2.68	4,132	1,542	+ 1.3
Additional 4% p.a. of patients defaulting	2.63	3,856	1,466	- 3.6
50-50 split in sequential regimen benefit	3.02	4,838	1,602	+ 5.3
70-30 split in sequential regimen benefit	3.02	4,192	1,388	- 8.8

Results were fairly stable - ART remained the most cost-effective intervention under all sensitivity analyses

Step Six – CTAC Sensitivity Analysis



Results are fairly sensitive, indicating a similar cost-effectiveness between starting ART with CD4<200 or CD4 200-350.

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