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Toronto Health Economics and
Technology Assessment Collaborative

New Methodologic Frontiers: Pharmacoeconomics

Murray Krahn MD MSc FRCPC

New Frontiers

- Better data
  - Costs
  - Utilities
- Better models
  - Policy models
  - Calibration and validation
  - Beyond Markov
- Role of health economics in social decision making
- Training:
  - Doers
  - Users

Using Administrative Data in HTA

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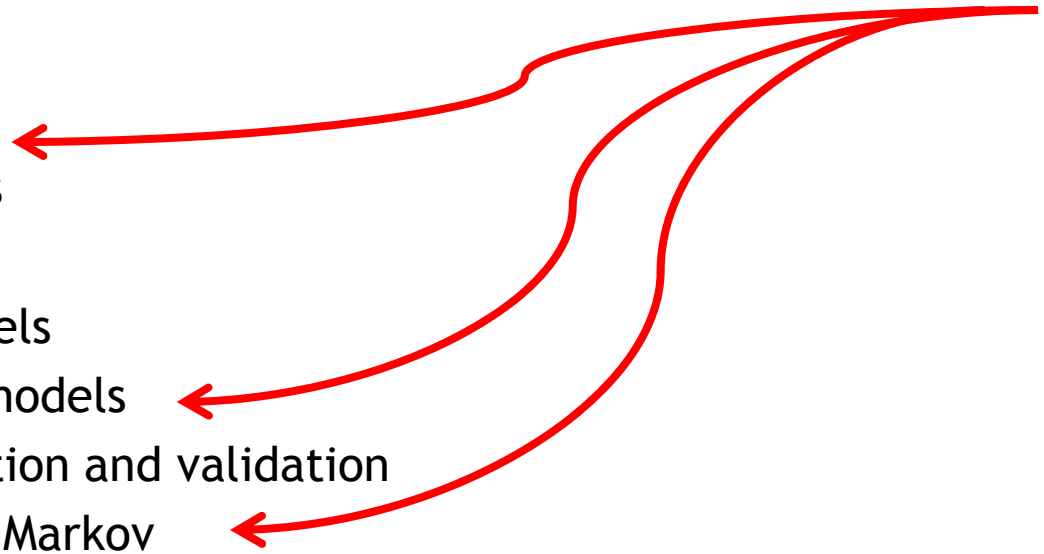

New Frontiers

- Better data
  - *Costs*
  - Utilities

- Better models
  - Policy models
  - Calibration and validation
  - Beyond Markov

- Role of health economics in social decision making

- Training:
  - Doers
  - Users

Predictors of Stage-specific Costs in Prostate Cancer

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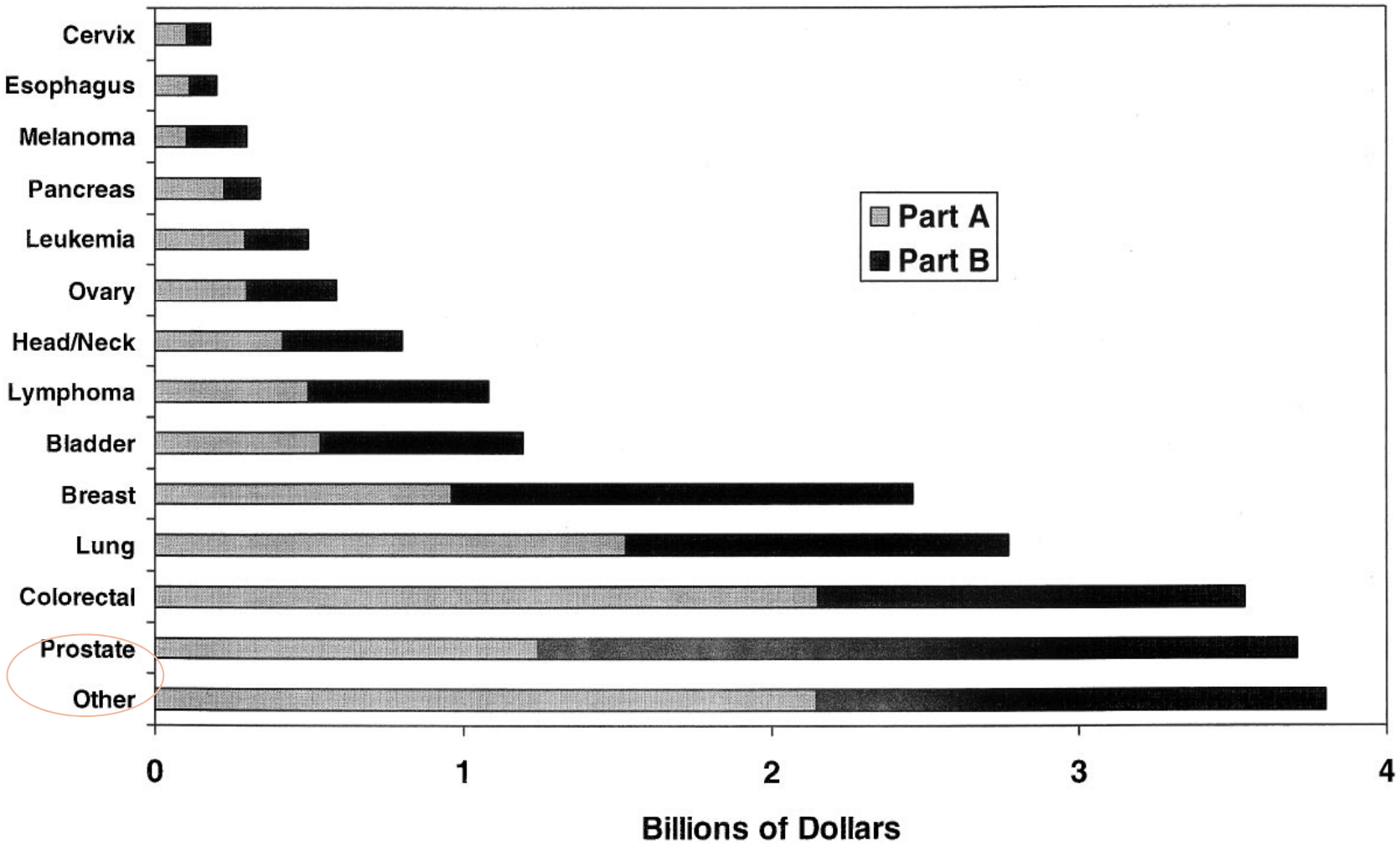
Cancer

- Leading cause of death in developed countries
- Accounts for
  - 2.9% of direct health care costs
  - 8.9% of indirect costs

Medicare expenditures in 1996



Brown et. Al. MEDICAL CARE
Volume 40, Number 8,
Supplement, pp IV-104-IV-117

Why study costs?

- Useful for policymakers and health researchers

- I) a measure of disease burden
- II) help in planning future programs in disease control
- III) help evaluate return on investment for research
- IV) patterns of care- reveal disparities in health access
- V) Useful in economic evaluation

Patients

- Ontario Cancer Registry
  - Population based cancer registry for Canada's largest province (n=12.5 million)
  - Registry data passively collected from: discharge summaries, path records, death certificates, and clinical records from regional cancer centers (n=8)

- Inclusion criteria:
  - (ICD) code 0 and topography code C61.9 (prostate)
  - 1/1/1995 - 4/30/2002

Patients

- Exclusion:
  - Missing histology codes
  - Diagnosis date same as death date
  - Female sex
  - Non-Ontario residents
  - PC code (billings, hospital discharges) etc. prior to 1/1/95

Study Design

- Phased approach- 5 phases

- Why- observation for all individuals is incomplete…need some way of putting together observation time

- Phase I- Prediagnostic- -6 months
- Phase II- Initial +12 months
- Phase III- Continuing care
- Phase IV- Pre-final –18months to –6 months
- Phase V- Final – 6 months

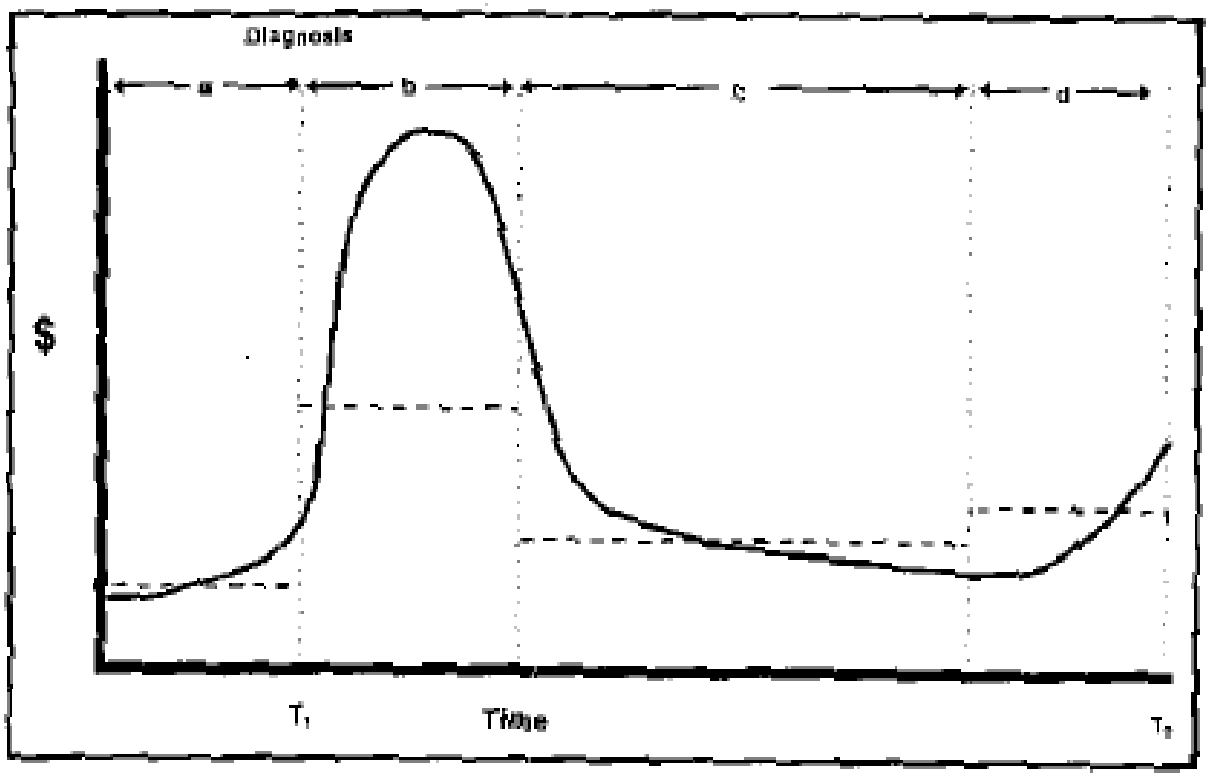
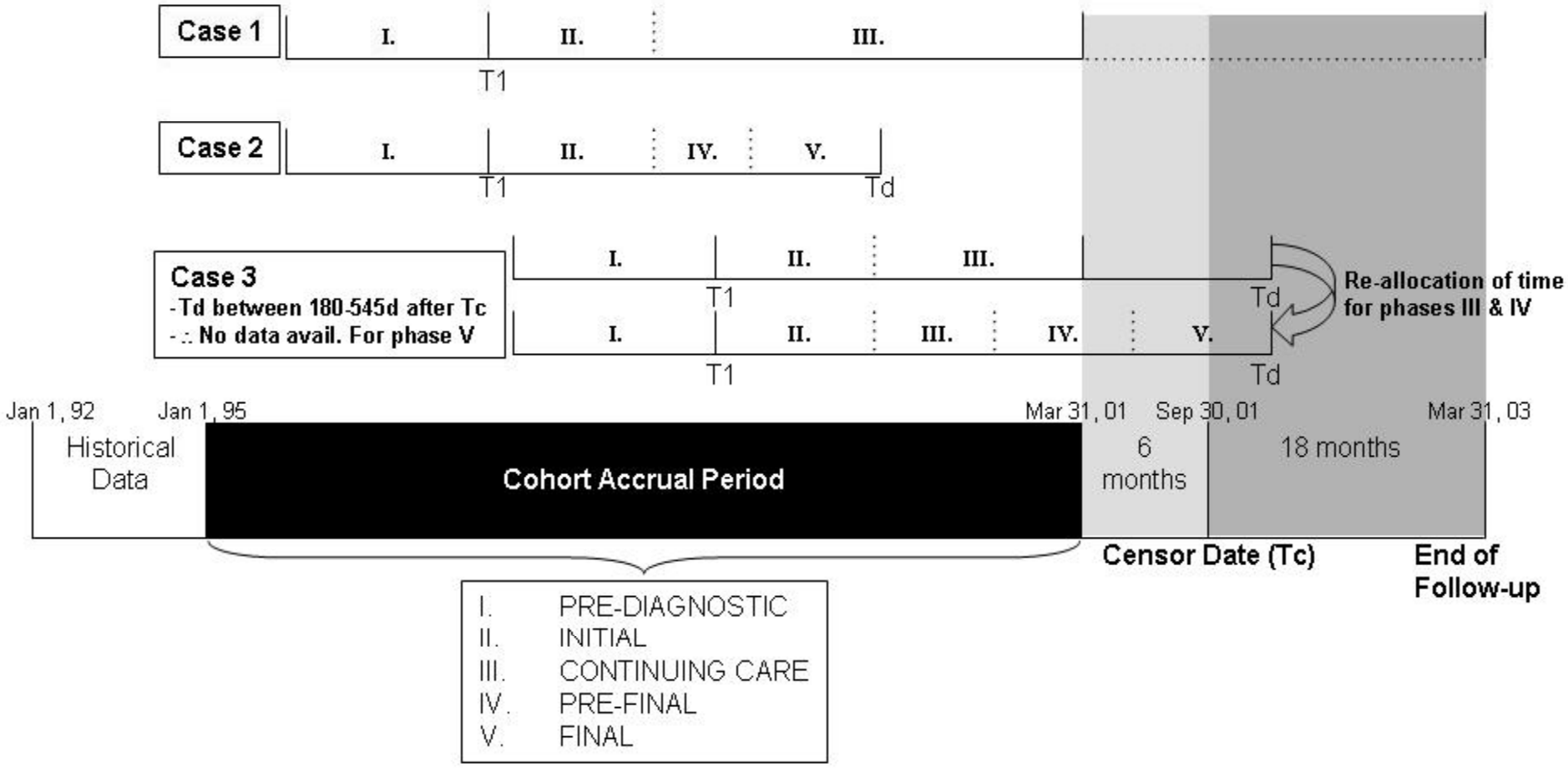


Fig. 1. Cost of care for an individual cancer case patient. a = prediagnostic period; b = initial care (6 months); c = continuing care (variable length); d = terminal care (6 months); — = hypothetical costs care for an individual; : = endpoints of each phase; - - - - = average cost of care during the period; T_1 = diagnosis; T_2 = death.

[J Natl Cancer Inst 87:417-426, 1995]

Study Design

- Period allocation hierarchy used to assign observation time



Costing methods

- “NET (or Attributable) Costs”
  - Costs in cases less costs in controls
  - Match cases with controls
  - 2004 CDN dollars
  - Inflation: Health Care component of the Statistics Canada Consumer Price index

Identifying Resources

- Linked data at ICES (Institute for Clinical Evaluative Sciences)
  - Physician and laboratory billings:
    - Claims history database, Ontario Health Insurance Plan
  - Hospital admissions-
    - CIHI- DAD (discharge abstract database)
  - Ambulatory care and ER visits
    - NACRS (national ambulatory care reporting system)
  - Drugs
    - Ontario Drug Benefit Plan (>65 only)
  - Long-term care
    - LTC flag in ODB
  - Home care
    - OHCAS- Ontario Home Care Administrative System

Selecting Controls

- Registered persons database (n=12 000 000)
- Randomly assign index date of cases to potential controls
  - (males > 28 years)

- For each potential control, calculate
  - Charlson
  - RIO
  - ACG
  - Income quintile

  - Propensity score- likelihood of having prostate cancer
  - Then hard match on age (+/-2), index month/year, Charlson, propensity score

Matching

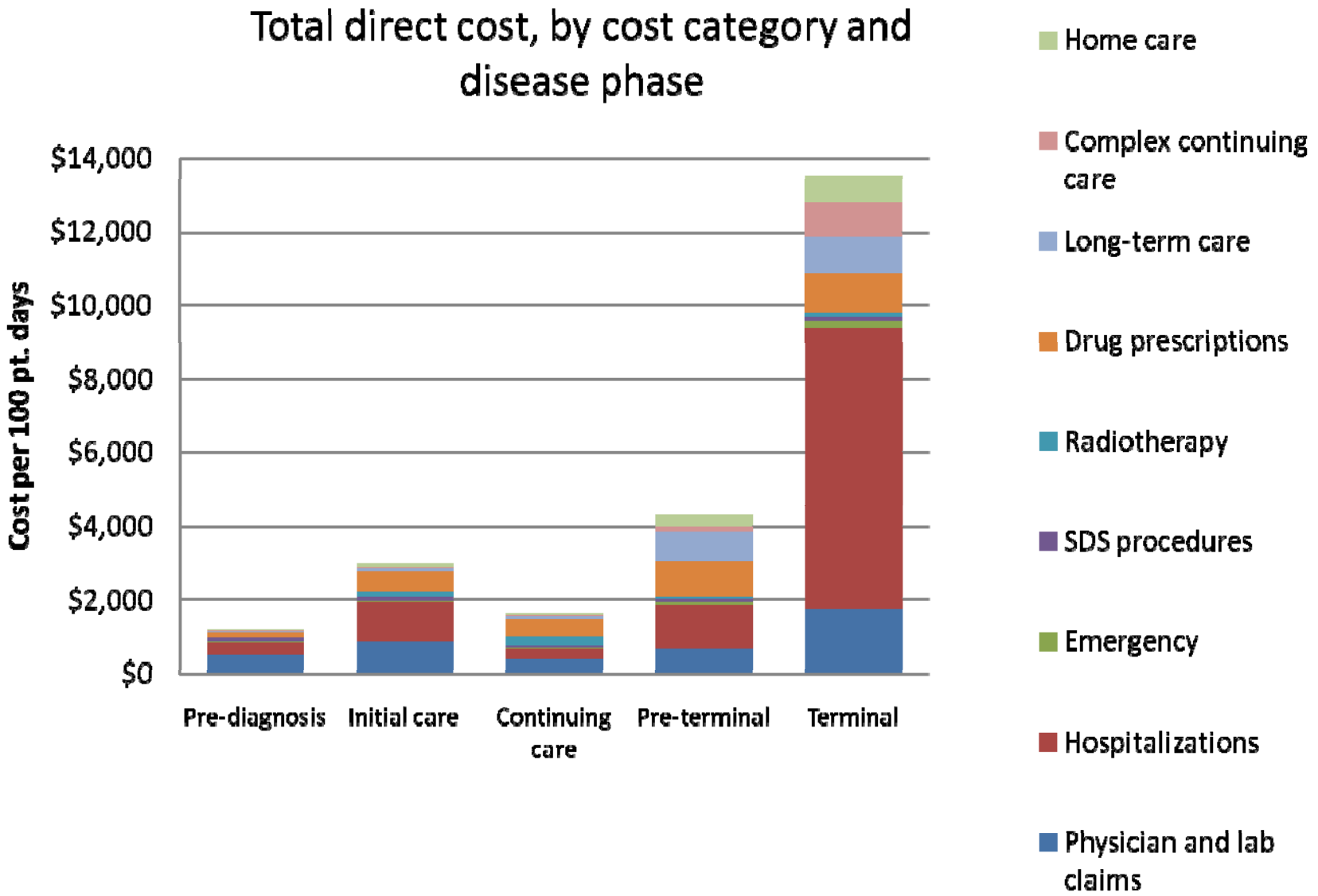
Variable	Value	Cases (N=42484)	Controls (N=42484)
Age at index	Mean ± SD	69.02 ± 8.68	69.02 ± 8.68
	Median (IQR)	69 (63-75)	69 (63-75)
RIO	Mean ± SD	20.26 ± 20.32	20.04 ± 20.43
	Median (IQR)	9 (6-34)	8 (6-33)
Charlson comorbidity	0 (%)	80.1	80.1
	1 (%)	8.5	8.5
	≥2 (%)	11.5	11.5
Rural/small town	%	17.2	17.3
Neighbourhood income quintile code	1 (%)	15.5	15.5
	2 (%)	18.5	18.7
	3 (%)	19.9	20.1
	4 (%)	21.0	20.9
	5 (%)	24.3	24.1
Long term care	%	0.5	0.5
Collapsed ACG	acute minor (%)	54.6	54.6
	acute major (%)	51.5	51.7
	likely to recur (%)	49.1	49.1
	asthma (%)	4.1	4.0
	chronic medical unstable (%)	40.1	40.1
	chronic medical stable (%)	59.9	60.3
	chronic specialty unstable (%)	10.5	10.2
	chronic specialty stable (%)	5.2	5.2
	eye, dental (%)	15.8	15.7
	psychosocial (%)	18.3	18.2

Total Cost (per 100 patient days)

Resource	Phase and range of days				
	I Pre-diagnosis (180 days)	II Initial (0-365 days)	III Continuing care (0-2451 days)	IV Pre-final (0-365 days)	V Final (0-180 days)
Cost per 100 patient days					
Physician and lab claims	$477	$846	$360	$655	$1,727
Hospitalizations	$334	$1,069	$296	$1,197	$7,632
SDS procedures	$103	$106	$61	$81	$115
RT- palliative	$0	$1	$1	$14	$56
RT- curative	$0	$138	$231	$53	$58
Drug prescriptions	$158	$557	$464	$954	$1,079
Drug prescriptions for <65 year-olds)	$4	$17	$14	$40	$77
Deductible drug costs, all	$23	$31	$40	$64	$64
Deductible drug costs for <65 year-olds)	$1	$2	$2	$2	$2
Long term care (MOH)	$44	$87	$119	$807	$996
Long term care (patient)	$19	$37	$50	$341	$420
Complex continuing care	$6	$40	$16	$166	$913
Emergency room	$31	$36	$23	$63	$190
Home care	$30	$85	$50	$300	$744
Total cost (per 100d)	$1,211	$2,994	$1,661	$4,353	$13,574
Bootstrapped 95% CI	$1,192-$1,231	$2,957-$3,030	$1,630-$1,690	$4,227-$4,486	$13,265-$13,886
Total cost (per Phase)	$2180	$10,928	-	$15,888	$24,433

Net Cost

Net cost (patients minus controls) per 100 patient-days					
Physician and lab claims	$196	$566	$83	$67	$384
Hospitalizations	$41	$783	$23	-$61	$1338
SDS procedures	$63	$63	$16	$4	$7
RT- palliative	$0	$1	$1	$6	$16
RT- curative	-$6	$137	$233	$19	$22
Drug prescriptions	$3	$380	$248	$493	$536
Drug prescriptions for those <65 year-olds)	-$2	$10	$8	$7	$13
Deductible drug costs	$3	$7	$5	$5	$3
Deductible drug costs for <65 year-olds)	$0	$1	$1	$0	$0
Long term care (MOH)	-$8	$6	-$14	-$248	-$84
Long term care (patient)	-$3	$2	-$6	-$104	-$35
Complex continuing care	-$14	-$14	1	$34	$333
Emergency room	$12	$16	$3	$6	$33
Home care	-$20	$31	$2	-$4	$134
Total cost (per 100d)	$269	$2003	$601	$321	$2722
Bootstrapped 95% CI	$240-$299	$1963-$2047	$433-$498	-$82-$738	$1925-$3501
Total cost (per Phase)	$484	$7311	-	$1172	$4900


Total direct cost, by cost category and disease phase
Cost per 100 pt. days
$14,000
$12,000
$10,000
$8,000
$6,000
$4,000
$2,000
$0
Pre-diagnosis
Initial care
Continuing care
Pre-terminal
Terminal
Home care
Complex continuing care
Long-term care
Drug prescriptions
Radiotherapy
SDS procedures
Emergency
Hospitalizations
Physician and lab claims

Characteristic		I Pre-diagnosis	II Initial Care	III Continuing care	IV Pre-final	V Final
Stage at diagnosis	Advanced	**1.16**	**1.89**	**1.46**	**1.39**	**1.70**
	Localized	1.00	1.00	1.00	1.00	1.00
Age (years)	≤59	**0.76**	**0.95**	**0.47**	**0.63**	**0.91**
	60-69	1.00	1.00	1.00	1.00	1.00
	70-79	**1.38**	**0.96**	**1.63**	**1.23**	**1.13**
	≥80	**1.75**	**1.16**	**2.1**	**1.54**	**1.36**
Charlson co-morbidity	0	1.00	1.00	1.00	1.00	1.00
	1	**2.05**	**1.23**	**1.67**	**1.23**	**1.16**
	≥2	**4.24**	**1.14**	**1.52**	**1.21**	**1.16**
Income quintile	1 (low)	**1.12**	1.01	**1.10**	1.01	**1.09**
	2	**1.09**	**1.03**	**1.12**	0.96	1.04
	3	**1.06**	1.01	**1.06**	0.92	1.03
	4	**1.04**	1.02	1.01	0.95	0.98
	5 (high)	1.00	1.00	1.00	1.00	1.00
Rurality	1 (urban)	1.00	1.00	1.00	1.00	1.00
	2	1.01	1.02	**1.05**	1.01	**0.91**
	3	**0.95**	0.98	**1.06**	0.92	**0.92**
	4	**0.93**	0.97	1.04	0.99	0.92
	5 (rural)	**0.87**	1.00	1.10	1.08	0.95
Index year	1995	1.00	1.00	1.00	1.00	1.00
	1996	**0.92**	**0.94**	0.95	0.95	0.98
	1997	**0.90**	0.99	**0.94**	0.96	0.97
	1998	**0.94**	0.99	**0.92**	1.02	0.95
	1999	**0.90**	**1.04**	**0.90**	0.99	1.00
	2000	**0.90**	1.03	**0.84**	**0.79**	0.97
	2001	**0.93**	**1.11**	**0.58**	**0.66**	**0.81**
	2002	0.95	1.06	-	-	**0.71**

Summary

- PC costs are highest
  - Year following diagnosis- $11 000 ($7300 PC)
  - 6 months prior to death- $24 400 ($4900 PC)
- Attributable costs are much lower than total costs
  - 67% for phase II
  - 7-36% for other phases
- Attributable costs are affected by:
  - Age (??)
  - Comorbidity
  - Year of diagnosis
  - Stage at diagnosis
- But NOT by
  - Socioeconomic status
  - Rurality

Phase Based Costing in HCV

Table 4. Mean health care costs (2005 $CAD* per 100 days [%]) among cases and controls according to cost category and phase of disease

Cost Category	Phase of Disease					
	EARLY		LATE		PREDEATH	
	Cases n = 31,540 (% column total)	Controls n = 123,960 (% column total)	Cases n = 3,988 (% column total)	Controls n = 15,558 (% column total)	Cases n = 3,223 (% column total)	Controls n = 12,153 (% column total)
Outpatient prescription drugs	367 (28.0)	98 (19.5)	672 (17.3)	188 (17.9)	712 (5.2)	621 (6.2)
Acute inpatient services	364 (27.8)	144 (28.7)	1,757 (45.3)	330 (31.5)	9,254 (67.0)	6,135 (61.1)
Physician services	364 (27.8)	165 (32.9)	728 (18.8)	237 (22.6)	1,527 (11.1)	1,165 (11.6)
Nursing home services	58 (4.4)	29 (5.8)	221 (5.7)	145 (13.8)	777 (5.6)	906 (9.0)
Same-day surgery	49 (3.7)	23 (4.6)	147 (3.8)	34 (3.2)	130 (0.9)	81 (0.8)
Emergency department services	47 (3.6)	20 (4.0)	83 (2.1)	25 (2.4)	206 (1.5)	137 (1.4)
Home care services	37 (2.8)	15 (3.0)	190 (4.9)	47 (4.5)	577 (4.2)	508 (5.1)
Hospital-based long-term care services	24 (1.8)	9 (1.8)	77 (2.0)	42 (4.0)	634 (4.6)	495 (4.9)
Total	1,311	502	3,876	1,049	13,817	10,048

*2005 $1 CAD = $0.83 US

But….

- Attributable costs not really useful for CEA…except maybe screening/prevention

- Difficult to map phase-specific costs on to Markov states

Nested cohort- chart reviews

Table 1. Health States

	pers_dys			
	N	**Mean**	**Min**	**Max**
hs				
01-Local. WW	364	569.2	2	4,666
02-RT	274	463.84	109	548
03-RP	354	411.85	67	548
04-Hormone-Tx Local.	177	1173.14	29	4,566
05-Post-RT	244	1289.66	13	4,049
06-Post-RP	272	1399.56	6	4,239
07-Recurr./progression	185	1293.76	19	4,537
08-Refrac.progress local.	46	1026.74	3	3,770
09-Metast. Stable	133	492.59	2	2,658
10-Refrac.progress metast.	46	428.67	6	1,635
11-Death	286	205.53	67	209

Nested cohort- chart reviews

Mean Costs per 100d

	Health States										
	01-Local. WW	02-RT	03-RP	04-Hormone-Tx Local.	05-Post-RT	06-Post-RP	07-Recurr./progression	08-Refrac.progress local.	09-Metast. Stable	10-Refrac.progress metast.	11-Death
OHIP Diagnostic tests	$218	$112	$101	$108	$0	$0	$118	$0	$84	$0	$15
OHIP GP Services	$17	$47	$47	$74	$0	$0	$61	$0	$36	$0	$4
OHIP Specialists	$29	$122	$97	$107	$0	$0	$109	$0	$70	$0	$11
OHIP Other	$221	$148	$555	$342	$0	$0	$192	$0	$227	$0	$87
Inpatient stays	$2,375	$562	$3,062	$1,440	$561	$217	$624	$2,758	$1,396	$3,174	$8,230
same day surgery stays	$687	$84	$190	$90	$86	$67	$124	$49	$223	$104	$144
Drugs, ODB Paid	$601	$421	$137	$1,426	$421	$181	$586	$1,037	$1,296	$1,668	$1,012
Drugs, non-ODB	$41	$31	$15	$51	$46	$24	$48	$64	$60	$85	$76
LTC, Provincial Paid	$71	$0	$0	$43	$19	$0	$4	$0	$55	$147	$294
LTC, Patient Paid	$55	$0	$0	$34	$15	$0	$3	$0	$43	$115	$230
Complex Continuing Care	$13	$0	$0	$269	$18	$5	$1	$61	$485	$533	$3
ER visits	$61	$19	$27	$40	$17	$14	$26	$167	$48	$63	$167
Homecare services	$62	$51	$51	$138	$1	$0	$24	$3	$81	$4	$37
RT curative fractions	$1	$593	$32	$39	$0	$4	$61	$12	$14	$0	$0
RT palliative fractions	$0	$4	$0	$0	$2	$0	$0	$1	$41	$63	$24
Total Costs	$4,452	$2,194	$4,315	$4,201	$1,186	$512	$1,980	$4,152	$4,159	$5,956	$10,334

Summary

- Comprehensive costing (direct medical costs) is feasible with admin data

- Costs useful for CEA
  - Population based
  - Actual utilization
- But- not straightforward

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EXPLAINING CHANGES IN CORONARY HEART DISEASE MORTALITY IN ONTARIO 1994-2005

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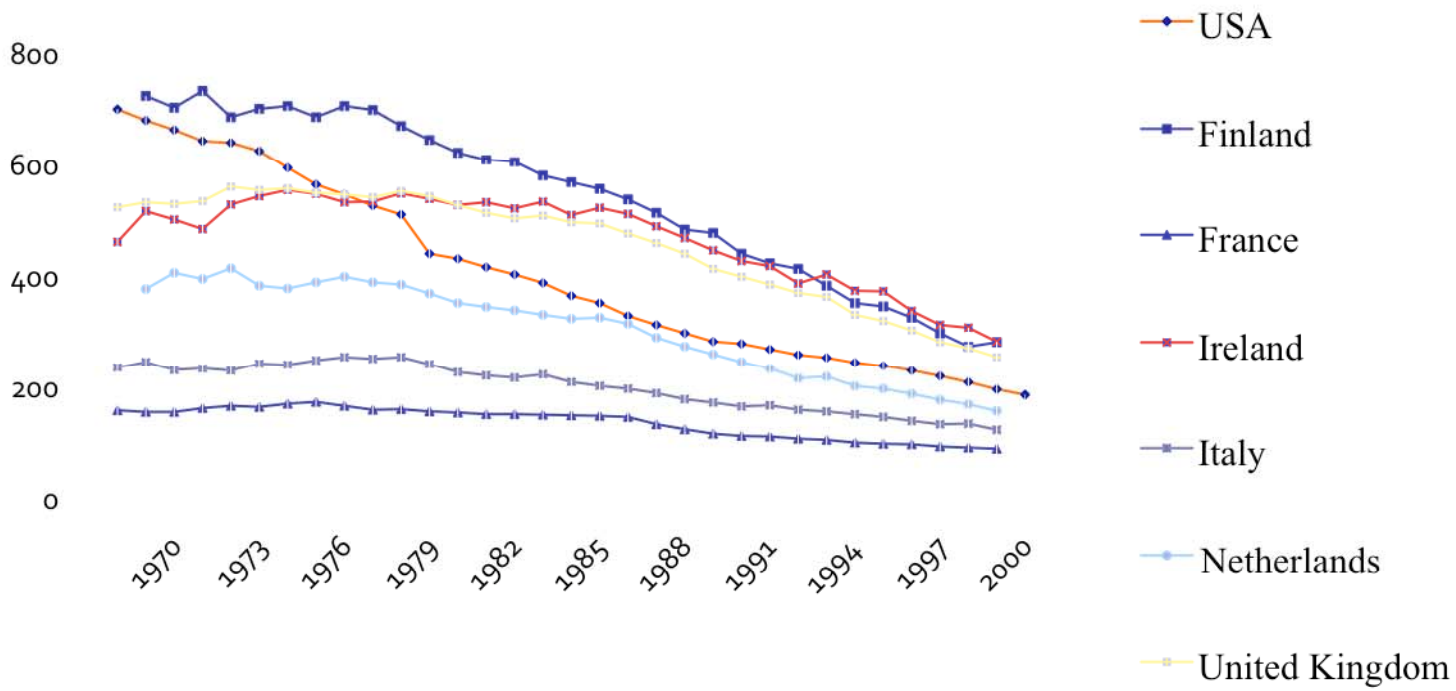
www.theta.utoronto.ca

Background

- Coronary heart disease (CHD) remains the leading cause of morbidity and mortality in Canada
- Despite an aging population, mortality has decreased



Objectives

- To determine the impact on mortality of changes in CHD risk factors and treatment strategies in Ontario, 1994-2005

- Develop a cardiovascular policy model for Ontario

Methods

- Adaptation of the IMPACT model to Ontario
  - Cell-based epidemiological model
  - Integrates population data on
    - CHD prevalence and cardiac-specific mortality, efficacy and uptake of specific treatments, and risk factors

IMPACT Methods

- 2 time points (1994 and 2005)
  - Cardiac specific mortality

- Main output:
  - Expected number of deaths in 2005 if 1994 age-gender mortality remained constant (adjusting for changes in population)
  - Difference between expected and observed deaths:
    - Number of deaths prevented or postponed (DPPs)

IMPACT Methods

- Determine the proportion of DPP attributable to temporal trends in risk factors and treatment:
  - Prevalence of 10 cardiac conditions
    - Myocardial infarction, unstable angina, heart failure etc
  - Utilization of selected treatments
    - Efficacy estimates from literature
  - Population trends in major cardiovascular risk factors
    - Associated impact on mortality

Methods

- Estimating the impact of treatment

  DPPs = A * B * C * D * E

  A: Number of eligible patients for a specific cardiology intervention

  B: Proportion receiving treatment

  C: Relative mortality reduction due to a specific intervention

  D: 1-Year case fatality rate

  E: Compliance rate

Methods

- Estimating the impact of risk factors
  - Regression approach:

$$\mathbf{DPPs = (1 - (e^{(\beta * Y)})*D}$$

ß: Coefficient associated a specific risk factor change

Y: Absolute changes in population mean risk factors from two different time points (e.g.,1994-2005)

D: CHD deaths in base year (e.g., 1994)

Methods

- Estimating the impact of risk factors
  - Population-attributable risk fraction (PARF) approach:

PARF = (P * (RR – 1)) / (1 + P * (RR – 1))

DPPs = C * D

Where,

P: The prevalence rate of each risk factor

RR: Relative risk for CHD mortality associated with that risk factor

C: CHD deaths in base year (e.g., 1994)

D: The relative PARF due to specific risk factor from two different time points (e.g.,1994-2005)

Impact Data Sources

Type of data*	Sources	Type of data (continued)	Sources (continued)
Population statistics		*Risk factors*	
Ontario residents	Statistics Canada	Alcohol consuption	CCHS, CHHS, NPHS,
CHD mortality		Diabetes	Southwestern Ontario
Mortality rate	Statistics Canada, CIHI DAD	Exercising	Database
CHD treatment uptake		Hyperlipidemia	
ACE inhibitors	EFFECT chart abstraction,	Hypertension	
Angioplasty	GRACE registry,	Obesity	
Aspirin	ACS II registry,	Smoking	
Beta blockers	GOALL registry,	*Diagnosis numbers*	
CABG	VP registry,	Angina pectoris (non-revascularized)	CIHI DAD, OHIP,
Gemfibrozil	Southwestern Ontario	CABG/PCI treated patients	Southwestern Ontario
PCI	database	Heart failure	Database
Sprinolactone		Hypertension/hyperlipidemia	
Statins		Myocardial infarction	
Warfarin		Unstable angina	

Results

- From 1994-2005, the overall CHD mortality rate in Ontario fell from 190.9 to 124.8 deaths per 100,000 inhabitants

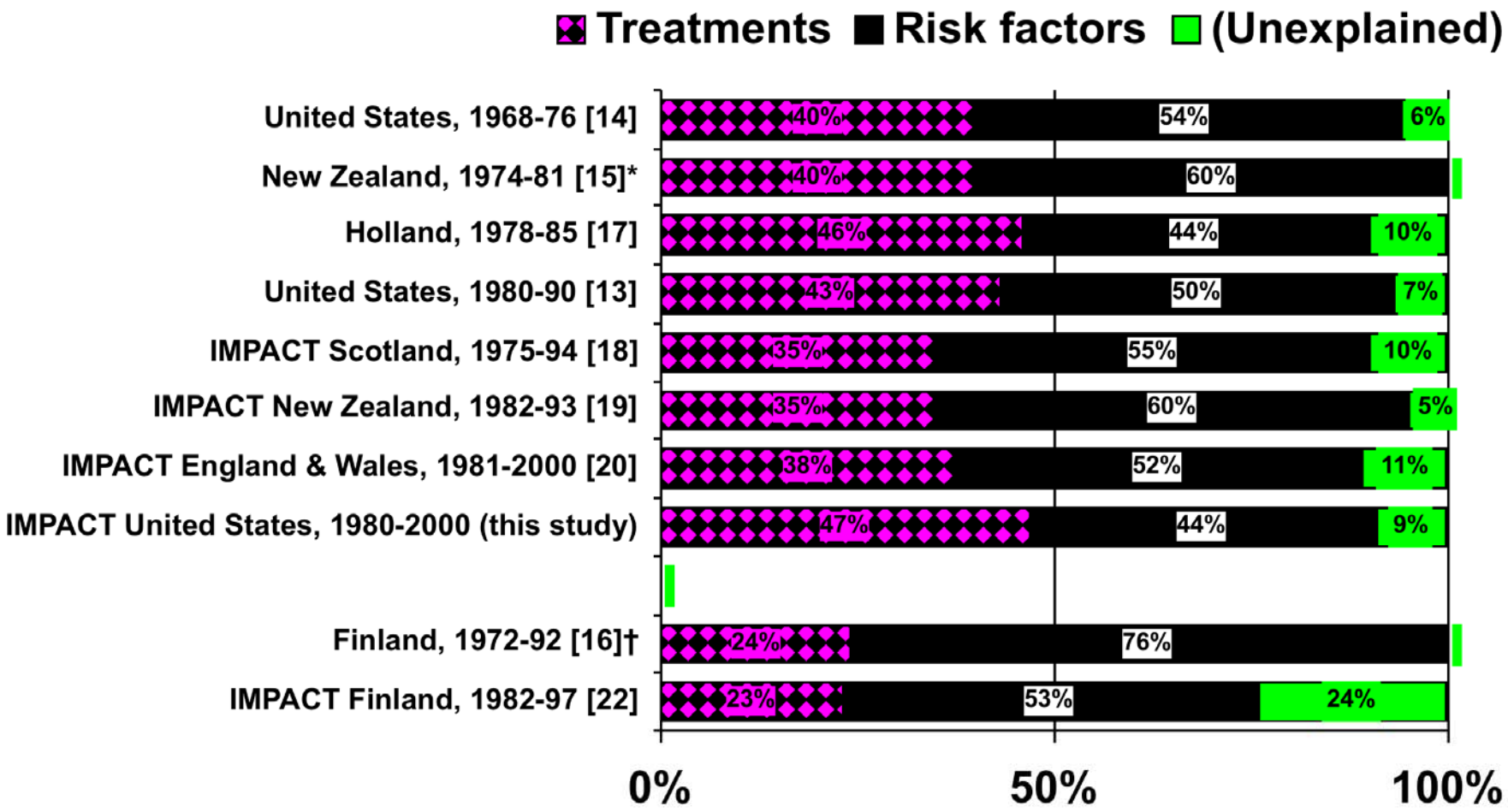
- **7585** deaths prevented/postponed

Risk factors	Changes in risk factors			Deaths prevented or postponed	
	Absolute	Relative	Changing factor	Mean	% overall
			RR		
Smoking prevalence (%)	-5%	-18%	2.52	345	4.5%
Diabetes prevalence (%)	1%	24%	1.93	-470	-6.2%
Physical inactivity (%)	-11%	-17%	1.27	310	4.1%
			β		
Systolic blood pressure (mmHg)	-1.39	-1%	-0.033	1465	19.3%
Total plasma cholesterol (mmol/L)	-0.05	-1%	-0.922	1525	20.1%
BMI (kg/m2)	0.37	1%	0.029	-180	-2.3%
Total risk factors				**2995**	**39.5%**

Intervention	Patients Eligible	Treatment Uptake (%)	DPP Mean	% overall DPP
Acute MI	**16640**		**530**	**7.0%**
Thrombolysis		31%	75	1.0%
Aspirin		94%	190	2.5%
Primary PTCA		52%	35	0.6%
Unstable Angina	**10180**		**30**	**0.4%**
2' Prev Post AMI	**37500**		**270**	**3.5%**
Chronic Angina and CHD	**292210**		**1960**	**18.8%**
Aspirin in community		44%	630	8.3%
Statins in community		73%	710	9.4%
Hospital Heart Failure	**1060**		**90**	**1.2%**
Community Heart Failure	**50440**		**1335**	**17.6%**
ACE inhibitor		53%	190	2.5%
Beta blocker		67%	785	10.4%
Hypertension Treatment	**459900**	**46%**	**130**	**1.7%**
Hyperlipidemia Treatment	**565295**		**155**	**2.1%**
Total Treatment			**3635**	**48.0%**

Comparisons with other studies:

% CHD mortality falls attributed to



Conclusion

- CHD mortality fall 1994-2005
  - 40% was attributable to improvements in risk factors (blood pressure, cholesterol)
  - 50% attributable to medical treatments (chronic angina, heart failure)
- Offset by adverse trends in obesity and diabetes

Applications

- Powerful method for estimating WHERE potential gains are-
  - Goal- by 2020 decrease CV deaths by 25%

- Project future trends in CHD burden
- Cost effectiveness analyses of CHD interventions

How to use for CEA?

- Directly within model?
- For new interventions…???

New Frontiers

- Better data
  - Costs
  - Utilities
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  - Beyond Markov
- Role of health economics in social decision making
- Training:
  - Doers
  - Users

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Toronto Health Economics and
Technology Assessment Collaborative

Cost-effectiveness of Multi-Disciplinary Community Based Care Clinics (MDCCC) for Patients with Heart Failure in Ontario

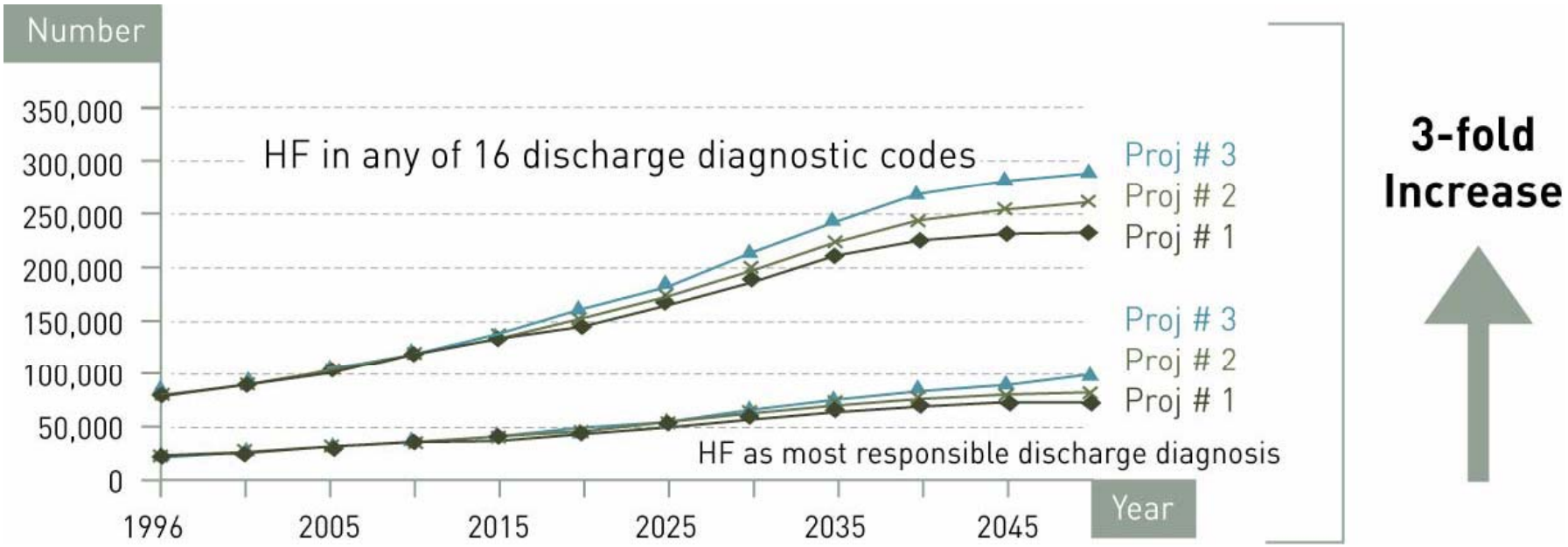
www.theta.utoronto.ca

Background

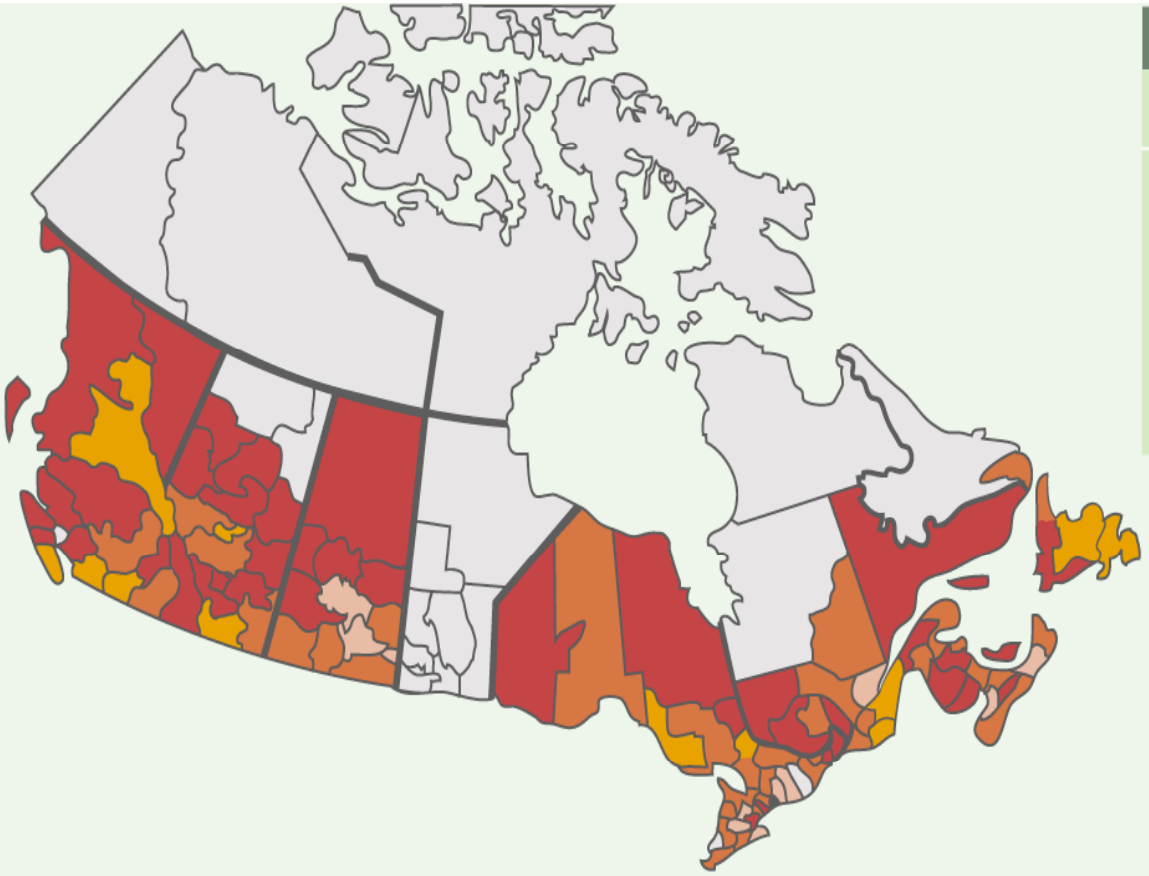
- Heart failure (HF) is a complex syndrome in which abnormal heart function results in clinical symptoms of low cardiac output and/or pulmonary or systemic congestion

Background

- HF is common and reduces quality of life, exercise tolerance and survival with an average 1-year mortality rate of 33%



Current Standard of Care



Percent of CHF Patients Treated by GP/FP		
	Percent Treated	Number of health regions in each category
	80 to 100	38
	60 to <80	39
	40 to <60	23
	20 to <40	9
	0 to <20	9
	missing/suppressed	21

Overall % of Canadian CHF patients treated by GPs/FPs = 50%

Multi-Disciplinary Community Based Clinics (MDCCC)

- Multidisciplinary, including physician, nurse practitioner, pharmacists, dietician, physiotherapist

All Cause Mortality

- 29% reduction in favor of HF clinics

HF-Specific Mortality

- A 58% RRR in HF-Specific mortality

Objective

- To determine the cost-effectiveness of MDCCC versus standard medical care in patients with HF from the perspective of MOHLTC

Methods (Life-Expectancy)

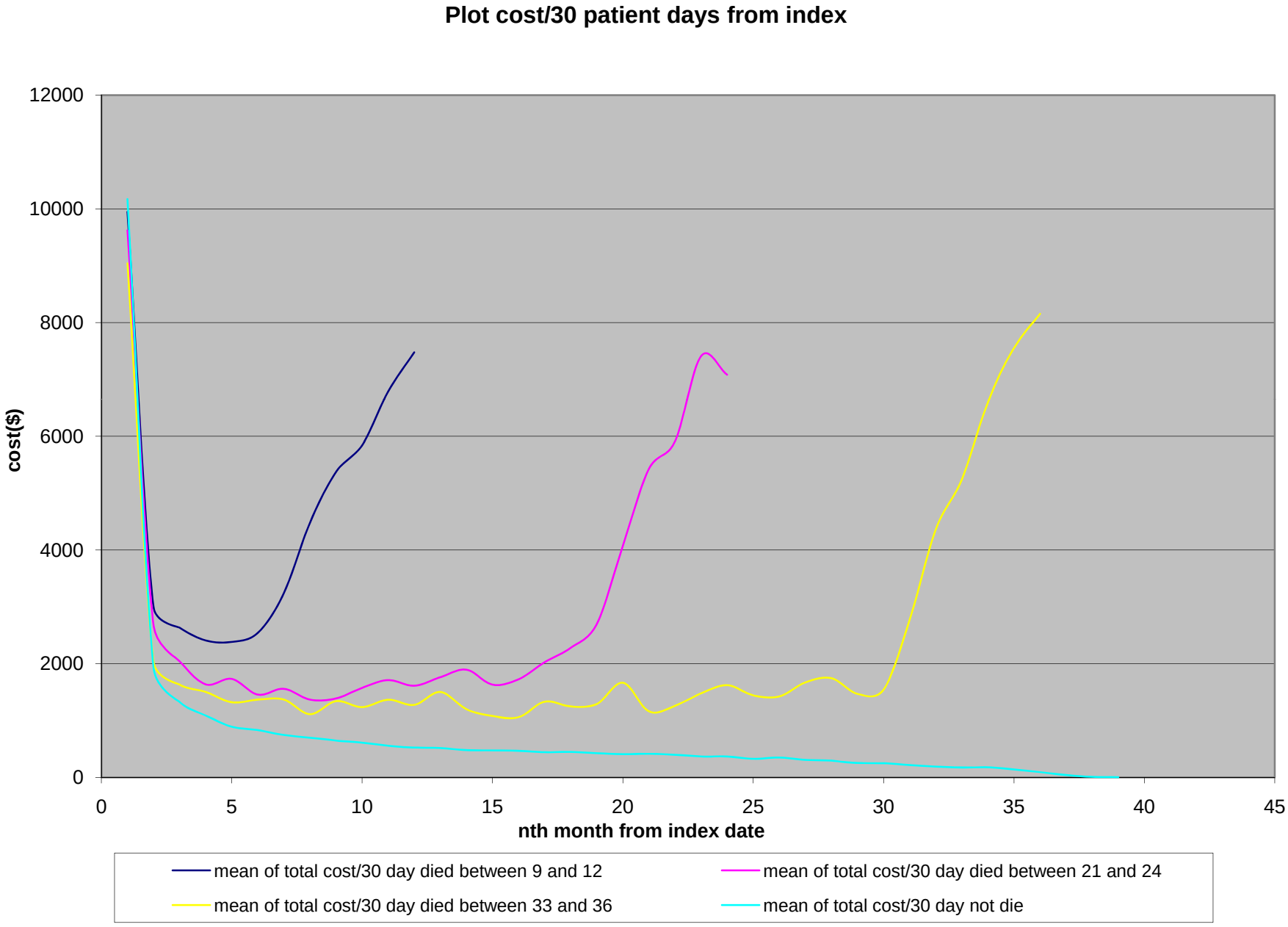
- Standard care cohort:
  - Life-tables over 12 year time horizon for patients with index HF hospitalization in Ontario
- MDCCC cohort:
  - Survival curves derived using efficacy estimate from systematic review.
  - Assume 10% of patients will leave clinic per year

HF Clinic (micro-costing)

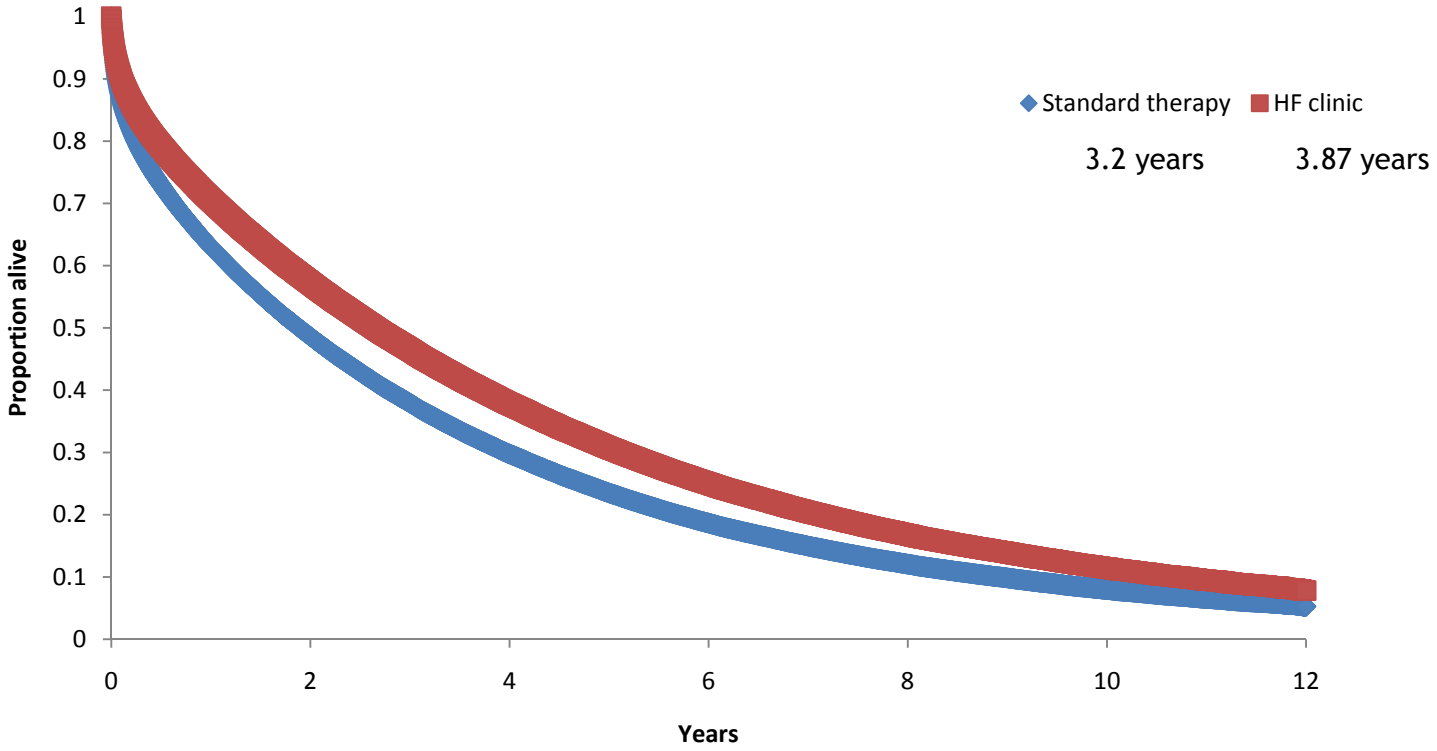
Staff	FTE	Cost / Year	Cost / 30 Patient-Days
Cardiac Technician	0.40	38,311.42	2.86
Cardiologist	n/a	176,735.00	13.20
Clerical (booking)	1.00	58,523.40	4.37
Clerical (charting, data entry)	0.30	17,135.94	1.28
Dietician	0.05	4,539.13	0.34
Kinesiologist	0.20	13,322.40	1.00
Nurse Practitioner	0.40	42,822.00	3.20
Pharmacist	0.08	9,325.68	0.70
Social Worker	0.03	2,731.33	0.20
Supplies, Op. Costs, Utilities		**Cost / Year**	**Cost / 30 Patient-Days**
Supplies, etc.	n/a		
Operating Costs	11.70	6,177.60	0.46
Utility Charge	4.29	2,265.12	0.17
Tests / Imaging		**Cost / Year**	**Cost / 30 Patient-Days**
Blood Work		35,255.00	2.63
EKG		32,455.50	2.42
Echo		255,860.00	19.11
		Total Cost / 30 patient-days =	**51.95**

Methods (Long Term Costs)

- For each HF patient in standard care cohort, obtain 30 patient-day costs for
  - 1. physician services (OHIP)
  - 2. inpatient care (CIHI DAD)
  - 3. ambulatory visits (NACRS)
  - 4. emergency room visits (NACRS)
  - 5. same day surgery (NACRS)
  - 6. home care (HCDB)
  - 7. medications (ODB)
  - 8. long term care (CCRS)


Plot cost/30 patient days from index
12000
10000
8000
6000
4000
2000
0
cost($)
0
5
10
15
20
25
30
35
40
45
nth month from index date
mean of total cost/30 day died between 9 and 12
mean of total cost/30 day died between 21 and 24
mean of total cost/30 day died between 33 and 36
mean of total cost/30 day not die

Results (Survival)



Results (CEA)

NON-DISCOUNTED		
	cost	survival
Current care	$61,475	3.8
HF clinics	$77,474	4.7
Delta	$15,999	0.9
ICER	**$17,443**	

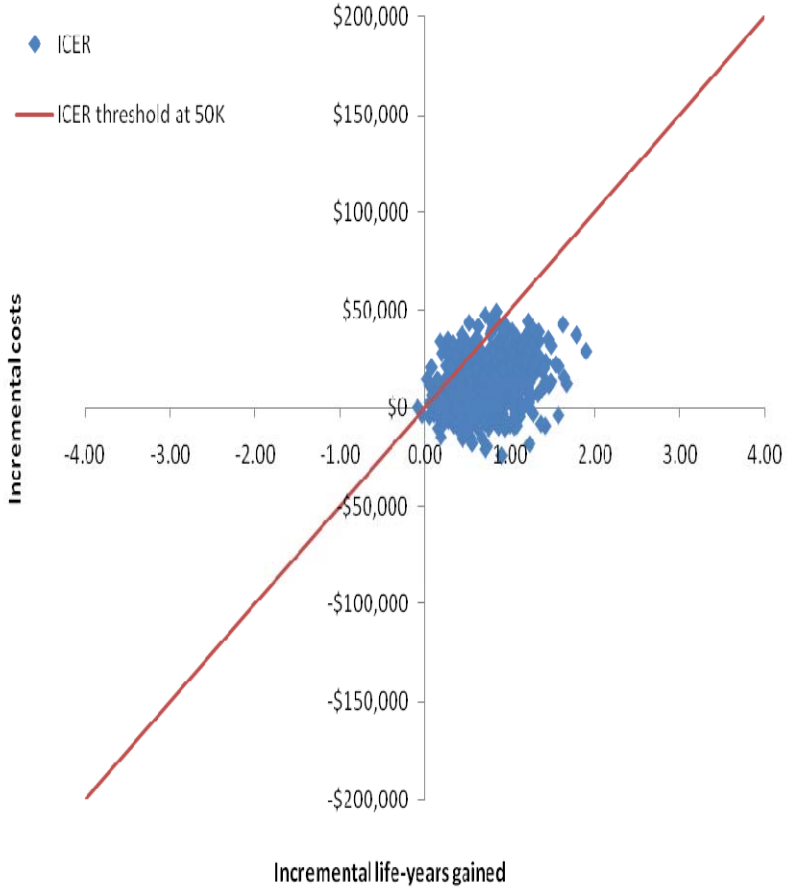
DISCOUNTED		
	cost	survival
Current care	$53,357	3.2
HF clinics	$66,250	3.9
Delta	$12,894	0.7
ICER	**$18,269**	

Univariate Sensitivity Analysis

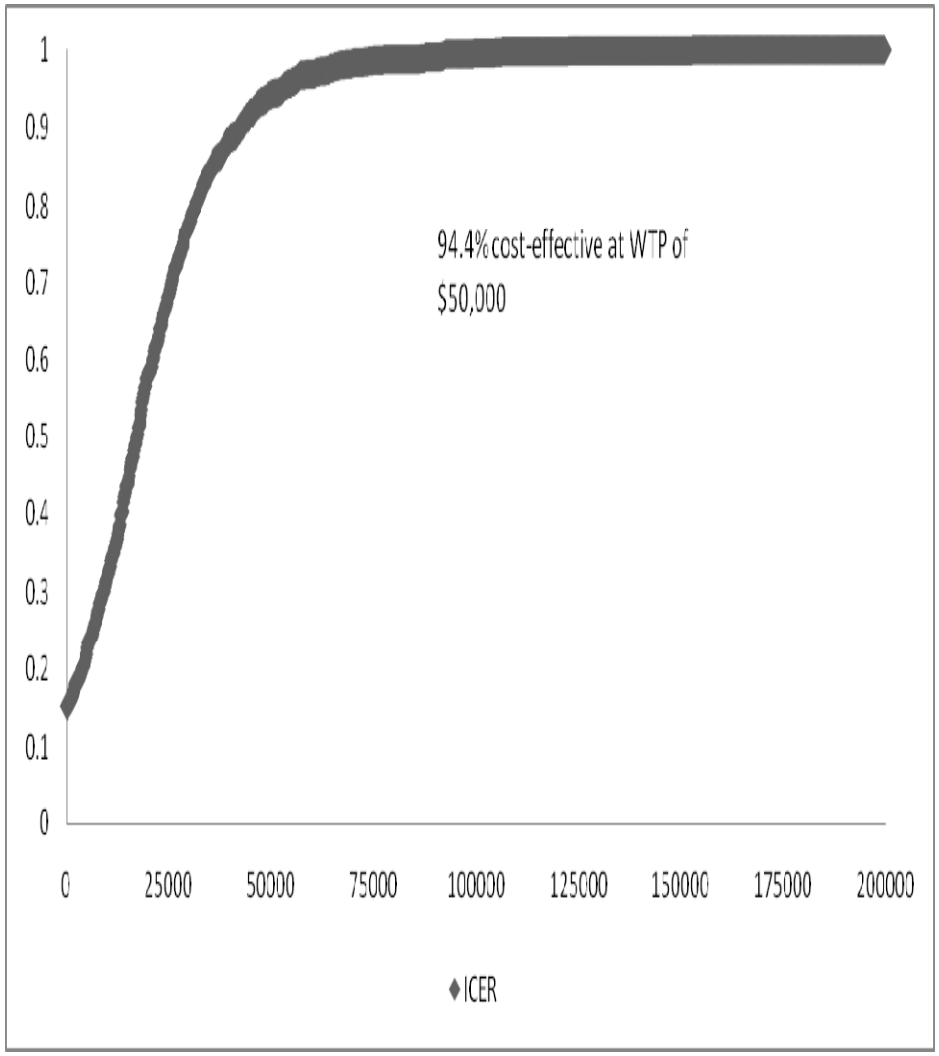
- Variation +/- 50% of base-case values
  - Costs
    - All <50,000 per LYG
  - Effects
    - Hospitalization, OHIP, ER, and SDS all <50,000 per LYG
    - All-cause mortality: RR threshold at 0.92 (base-case = 0.71, CI95% 0.56-0.91)

Probabilistic Sensitivity Analysis

ICER Scatterplot



Acceptability curve



Budget Impact Analysis

		2008*	2009	2010	2011	2012	2013
Prevalent cases		16147					
Year 1			12280	9805	9930	10054	10178
Year 2				10843	8658	8768	8878
Year 3					9734	7773	7872
Year 4						8850	7066
Year 5							8141
Incident cases	n/a		12893	13057	13221	13383	13546
Deaths†	n/a		3867	4525	5383	6098	6693
Eligible patients		16147	21306	29181	36160	42730	48988
Cost per 30-day patient	$	52	$ 50	$ 47	$ 45	$ 43	$ 41
Cost per patient per year	$	624	$ 594	$ 566	$ 539	$ 513	$ 489
Budget impact	**$**	**10,075,728**	**$ 12,661,845**	**$ 16,515,999**	**$ 19,491,434**	**$ 21,936,251**	**$ 23,951,034**

* Base case year

† In previous year

Conclusion

- Initial analysis showed MDCCC clinics to be cost-effective in Ontario
- Preliminary results were robust from a SA standpoint
- Implementation costs were estimated at an average CAD$ 17.5M per year

Conclusion

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Toronto Health Economics and
Technology Assessment Collaborative

The Cost-effectiveness of Cancer Drugs: Providing Evidence of Medicines in Delivering Expected Outcomes

J. Hoch, M. Krahn et. Al.

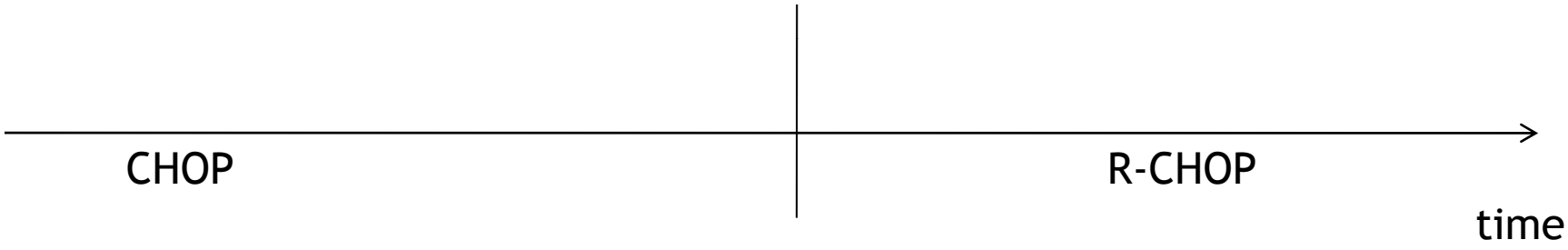
www.theta.utoronto.ca

Objectives

The main objectives of this project are to

1) Describe patterns of care for patients receiving study drugs in Ontario
2) Estimate lifetime costs, for patients on study drug and matched controls
3) Estimate survival for patients on study drug and matched controls
4) Estimate cost-effectiveness of study drugs as used in practice in Ontario

Main methodologic challenge



Drug funded

How to define cases and controls

- 1. receipt of drug
  - Problem- cancer care has changed
- 2. by period
  - Problem- not everyone in “period” got the “period” drug
- 3. both, with age stratification

Administrative datasets can be used to …

- Estimate costs…
  - By phase of disease
  - By Markov state
  - By time…including lifetime
- Perform full economic evaluations…
  - But methods still being worked out…

Improving Health Technology Assessment

- Science- not advocacy
  - Better data
    - Costs
    - Utilities
  - Better models
    - Policy models
    - Calibration and validation
    - Beyond Markov
- Role of health economics in social decision making
- Training:
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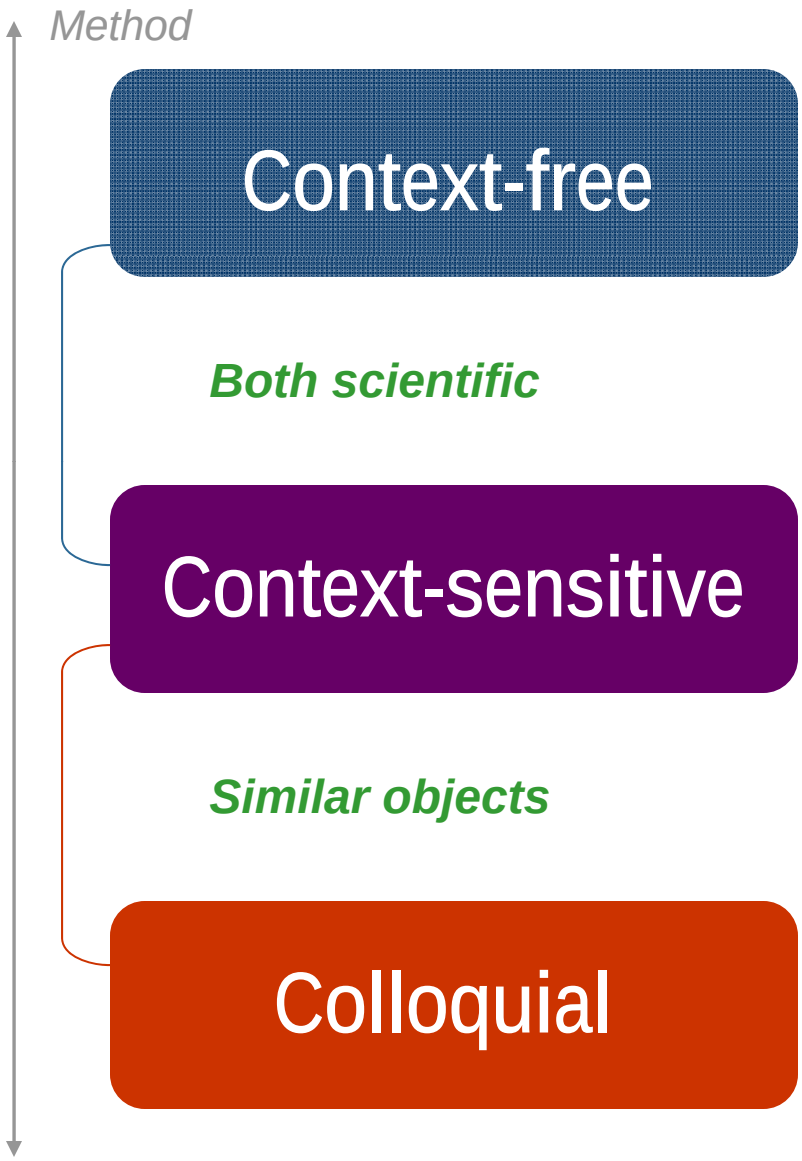
What is evidence? – A reminder

Evidence

1) Systematic reviews and meta-analyses
2) Randomised controlled trials with definitive results
3) Randomised controlled trials with non-definitive results
4) Cohort studies
5) Case-control studies
6) Cross sectional surveys
7) Case reports

(Pettigrew and Roberts 2003, 527).

Evidence Comes in Kinds

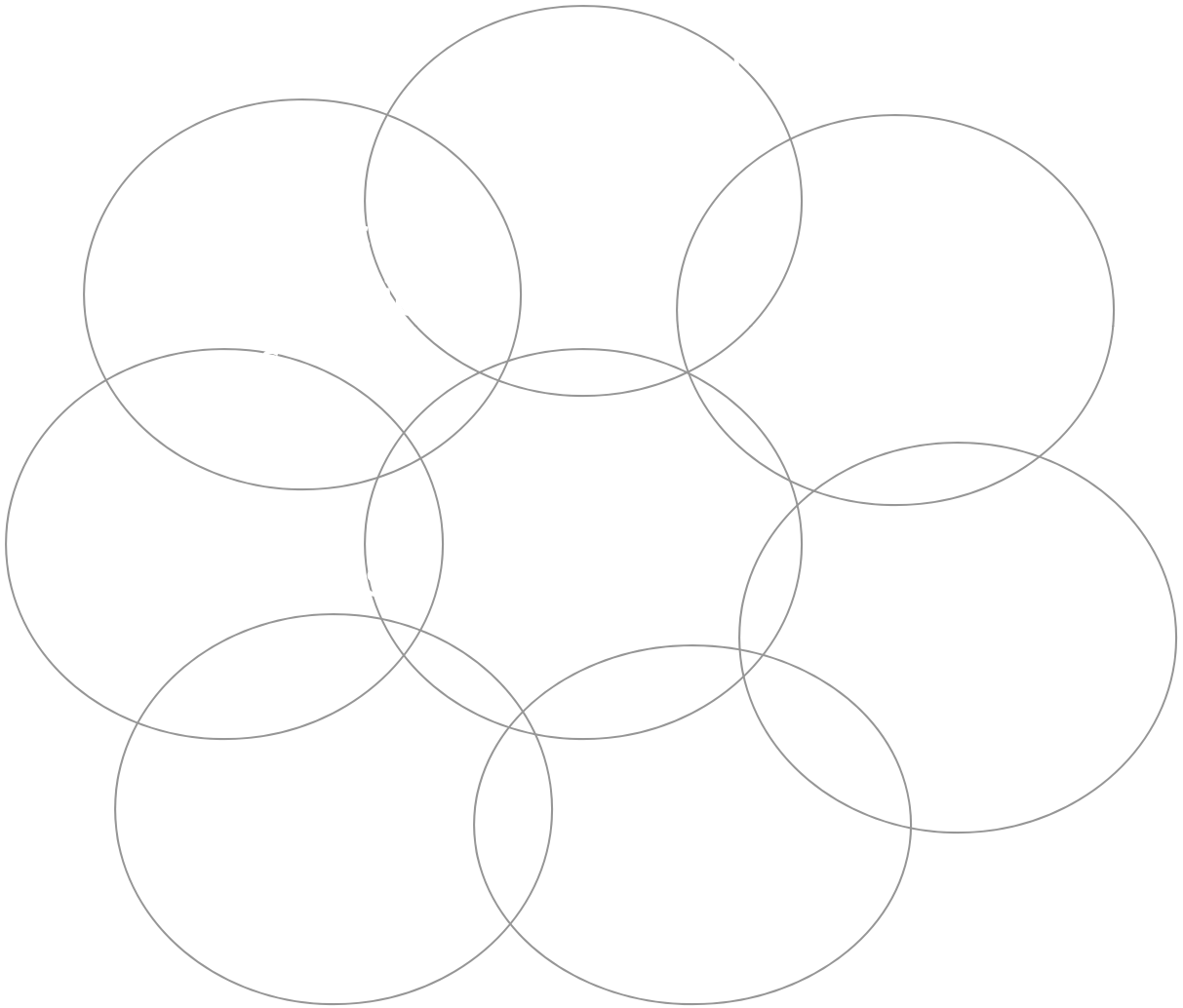


- "the *philosophical-normative* orientation towards what constitutes evidence is unconstrained by context" (Dobrow et al.)
- What works?

- "the *practical-operational* orientation to what constitutes evidence is context-based, with evidence defined with respect to a specific decision"
- Will it work here? Should it be done? How do we do it?

- "evidence is proxy for 'most up-to-date information' on a subject — nothing more, nothing less."
- "anything that establishes a fact or gives reason for believing something" (Oxford American Dictionary)

Colloquial evidence informs scientific evidence



Not really frontiers, not really pharmacoeconomics

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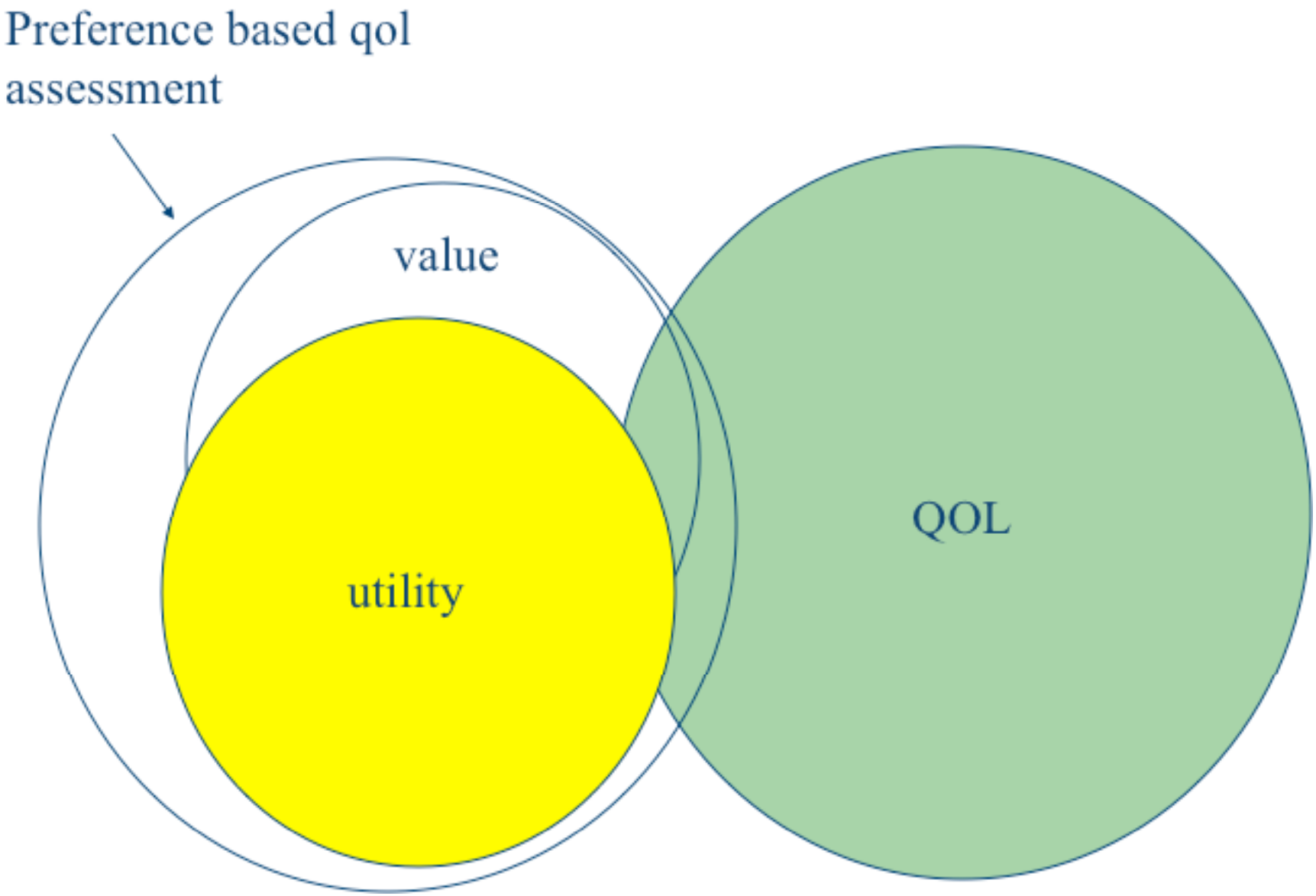

Preference based qol assessment
value
utility
QOL

Utilities can be derived

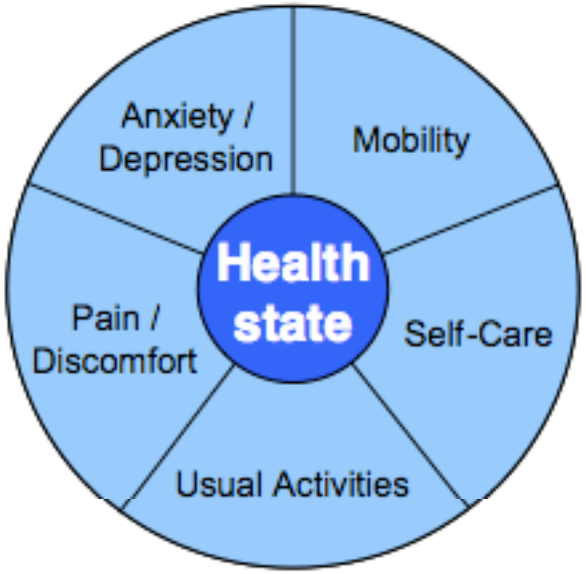
- Directly- using standard gamble, time tradeoff
- Indirectly- preference instruments
  - Attributes, levels

DIRECTLY measuring preferences

Response method	Question framing	
	Certainty (values)	Uncertainty (utilities)
Scaling	A RS, CS, VAS	B ?
Choice	C TTO Paired comparison Equivalence/ PTO	D SG

Indirect preference measurement

A unique health state is defined by combining 1 level from each of the 5 dimensions.



EQ-5D

Differences

- Direct-
  - Preferences elicited directly
  - Source- USUALLY patients
- Indirect
  - Instrument
  - Source of responses-USUALLY patients
  - Preference weights- members of the general public

Utilities and QOL Measurement compare and contrast

	Disciplinary origins	What is measured?	How?	Scores	Weights	Applications
Utility	Utilitarian-ism, economics	GLOBAL health status	Scaling/ choice methods	0-1 (some-times <1)	Prefer-ence weights	As follows
QOL	Social sciences	Selected attributes, occasionally overall QOL (profile)	Question naire	variable	Usually none	Assess outcomes in RCT, cohort studies etc.

Gold et. al. "Cost effectiveness in Health and Medicine"

- …the societal perspective is the appropriate one for decision making concerning health care resources in the public interest. A logical extension of that reasoning would suggest that the best articulation of society's preferences for particular health states would be gathered from a representative sample of fully informed members of the community. Only with preferences so gathered could we begin to scale the differences between "optimal health" and a large array of conditions on an interval scale.

ELSEVIER

Journal of Clinical Epidemiology 53 (2000) 920–930

Journal of Clinical Epidemiology

Construction of the Patient-Oriented Prostate Utility Scale (PORPUS): a multiattribute health state classification system for prostate cancer

Murray Krahn[a,b,h,*], Paul Ritvo[c,d,e,f,g,i,j], Jane Irvine[c,d,e], George Tomlinson[c], Andrea Bezjak[g,h],

ELSEVIER

Journal of Clinical Epidemiology 58 (2005) 466–474

Journal of Clinical Epidemiology

Reliability and validity of the PORPUS, a combined psychometric and utility-based quality-of-life instrument for prostate cancer

Paul Ritvo[a,b,c,d,e,f,*], Jane Irvine[a,d,e], Gary Naglie[d,e], George Tomlinson[e], Andrea Bezjak[b,c,d,e], Andrew Matthew[c,e], John Trachtenberg[b,c,d,e], Murray Krahn[c,d,e]

[a]*York University*
[b]*Ontario Cancer Institute*
[c]*Princess Margaret Hospital*
[d]*University Health Network*

unada

Medical Decision Making

Development and validation of a utility weighting function for the PORPUS- Patient Oriented Prostate Utility Scale

&PUS Health Classification System

1-3 and 5-10, please check the statement that comes closest to describing you in the last two weeks.

turbing Body Sensations (e.g., hot flashes, painful swelling of breasts, nausea)
› pain and no disturbing body sensations.
ild pain or disturbing body sensations that do not limit any activities (e.g., work, social, sexual, sleep).
oderate pain or disturbing body sensations that limit a few activities.
oderate to severe pain or disturbing body sensations that limit some activities.
vere pain or disturbing body sensations that limit many activities.

ery full of energy, lots of pep.
'airly energetic, no limitation of activities (for example: work, social, sexual).
Moderate reduction in energy or pep that limits a few activities.
enerally low energy or pep that limits some activities.
o energy or pep at all. I feel drained, and many activities are limited.

n Family and Friends
ost of the time feel supported by my spouse, family and friends.
fair amount of the time feel supported by my spouse, family and friends.
ccasionally feel supported by my spouse, family and friends.
urely feel supported by my spouse, family, and friends.

ion With Doctor (primary caregiver for prostate cancer, may be specialist or family doctor)
› statement that comes closest to describing you in the last two scheduled appointments
ways able to express my concerns to my Doctor and get all the information or advice I need.
ost the time, able to express my concerns to my Doctor and get all the information or advice I need.
me of the time, able to express my concerns to my Doctor and get all the information or advice I need.
urely able to express my concerns to my Doctor and get all the information or advice I need.

/ell-Being
enerally happy and free from worry, sadness, or frustration.
little worry, sadness, or frustration.
oderate worry, sadness, or frustration.
ite a bit of worry, sadness, or frustration.
treme worry, sadness, or frustration.

quency (need to pass urine frequently during the day or night) and Urgency (difficulty delaying urination s felt to urinate, ability to "hold it")
› urinary frequency or urgency.
little urinary frequency or urgency, does not interfere with sleep or other activities (e.g., work, social); no need to ahead.
me urinary frequency or urgency that interferes with sleep or other activities; may need to plan ahead.
ite a bit of urinary frequency or urgency; need to be near a bathroom most of the time.
treme urinary frequency or urgency; need to be near a bathroom always.

se/ Poor Bladder Control
ver, under any circumstances leak urine or lose bladder control.
rare occasions, leak urine or lose bladder control, does not interfere with any activities (for example: work, l, sexual, sleep).
ccasionally leak urine or lose bladder control, interferes with a few activities.
moderate amount of the time, leak urine or lose bladder control, interferes with some activities.
ost of the time, leak urine or have poor bladder control, interferes with many activities.
quire a clamp, catheter, or collecting bag because of leaking urine or poor bladder control.

ion (problems with achieving / maintaining an erection)
ll erections sufficient for intercourse.
ections sufficient for intercourse, but some reduction in firmness.
ections sufficient for masturbation or foreplay only.
ections, but not firm enough for any sexual activity.
› erections at all.

st / Drive
rmal amount of sexual drive and interest for you.
little decrease of sexual drive or interest for you.
oderate decrease of sexual drive or interest for you.
bstantial decrease of sexual drive or interest for you.
› sexual drive or interest.

lems: diarrhea, rectal discomfort (pain, burning or irritation) or constipation.
› diarrhea, rectal discomfort, or constipation.
ccasionally have diarrhea, rectal discomfort, or constipation.
equently have diarrhea, rectal discomfort, or constipation.
arly always have diarrhea, rectal discomfort, or constipation.

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Construction of the Patient-Oriented Prostate Utility Scale (PORPUS): a multiattribute health state classification system for prostate cancer

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Fitting an MAU function

$$\bar{U}(\underline{P}) = \left\{ \prod_{i=1}^{10} \left[1 + cc_i \bar{u}_i(P_i) \right] - 1 \right\} \Big/ c \qquad \text{(Equation 1)}$$

$$\prod_{i=1}^{10} (1 + cc_i) - 1 = c \qquad \text{(Equation 2)}$$

Medical Decision Making

Development and validation of a utility weighting function for the PORPUS- Patient Oriented Prostate Utility Scale

Scoring the PORPUS

Table 4: Scoring the PORPUS

Item	Response to item (1 = Best; 6(plus) = Worst)					
	1	2	3	4	5	6
(1) Pain	1.38661	1.38644	1.38798	1.38516	1.37666	-
(2) Energy	1.38661	1.38817	1.38843	1.38787	1.38459	-
(3) Social support	1.38661	1.38856	1.38829	1.38522	-	-
(4) MD communication	1.38661	1.38879	1.38846	1.38748	-	-
(5) Emotional	1.38661	1.38891	1.38827	1.38709	1.3831	-
(6) Urinary frequency	1.38661	1.38853	1.38828	1.38719	1.38378	-
(7) Urinary leakage	1.38661	1.38840	1.38799	1.38723	1.38439	1.37796
(8) Sexual function	1.38661	1.38856	1.38841	1.38779	1.38607	-
(9) Sexual interest	1.38661	1.38857	1.38847	1.38798	1.3861	-
(10) Bowel problems	1.38661	1.38828	1.38821	1.38118	-	-

1) Look up the scores for the responses to each item in the table below. Call these scores Z_1 to Z_{10}. For example, someone who has the response 4 on all 10 items would have:

$Z_1 = 1.38516$
$Z_2 = 1.38787$
$Z_3 = 1.38622$
$Z_4 = 1.38749$
$Z_5 = 1.38709$
$Z_6 = 1.38719$
$Z_7 = 1.38723$
$Z_8 = 1.38779$
$Z_9 = 1.38798$
$Z_{10} = 1.38118$

2) The PORPUS-U score is found by subtracting 25.65658 from the product of the 10 scores. For the example response above:

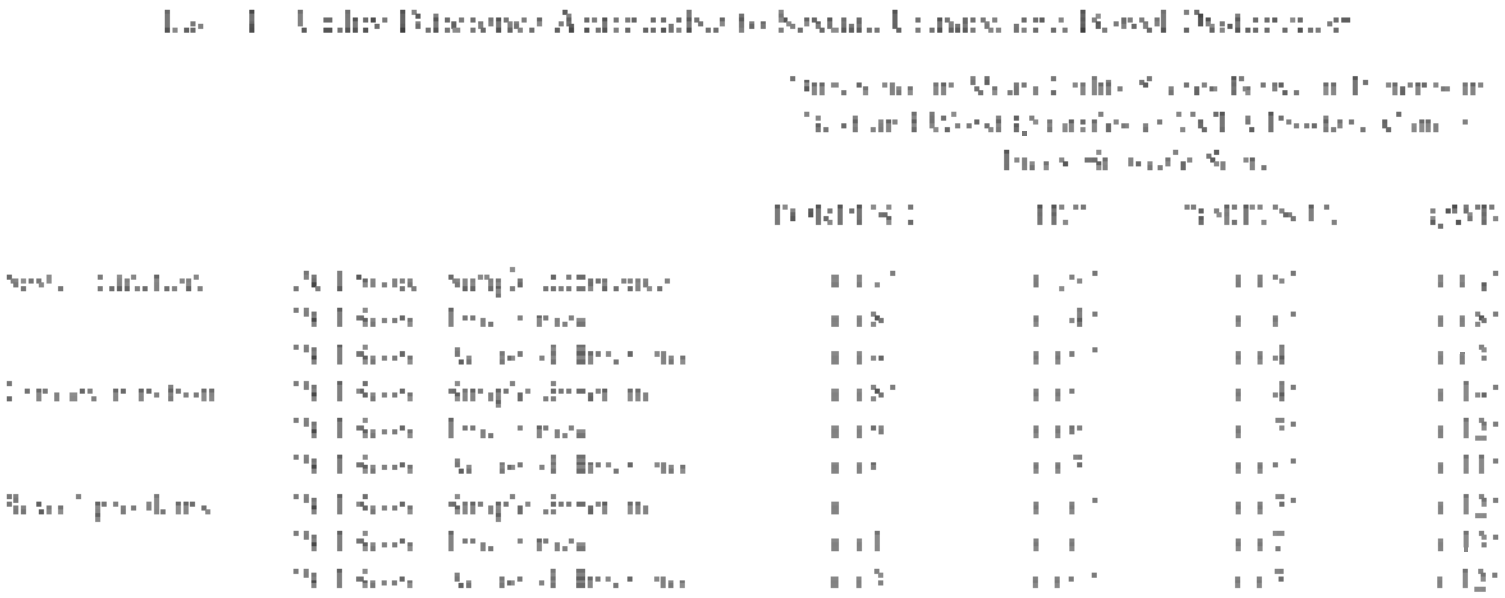
$$\text{PORPUS-U} = Z_1 \times Z_2 \times Z_3 \times Z_4 \times Z_5 \times Z_6 \times Z_7 \times Z_8 \times Z_9 \times Z_{10} - 25.65658$$

The PORPUS-U score for someone giving response 4 on all items is:

$$\text{PORPUS-U} = 26.27327 - 25.65658 = 0.61669$$

The PORPUS-U score generated using these formulas should be rounded to two

Disutility attributable to sexual, urinary, and bowel dysfunction



MEDICAL CARE
Volume 41, Number 1, pp 1-●●●

Quality of Life Research (2007) 16:509–522
DOI 10.1007/s11136-006-9132-x

Responsiveness of disease-specific and generic utility instruments in prostate cancer patients

Murray Krahn[1,2,8], Karen E. Bremner[1], George Tomlinson[1,4,5], Paul Ritvo[3,6], Jane Irvine[3,7] & Gary Naglie[1,5]

Table 5. Internal responsiveness, Cohort N only

	Standardized effect size		Standardized response mean	
	$\frac{Change}{SD_{pre}}$		$\frac{Change}{SD_{change}}$	
	T1–T2	T2–T3	T1–T2	T2–T3
Profile				
Instruments-EORTC				
QLQ-C30				
Physical function	−0.30	0.20	−0.46	0.24
Cognitive function	0.08	−0.11	0.10	−0.01
Emotional function	0.23	0.06	0.31	0.08
Social function	−0.32	0.35	−0.27	0.37
Role function	−0.32	0.06	−0.33	0.05
Global Health	−0.16	0.24	−0.17	0.27
PCI				
Sexual function	−1.07	0.35	−1.12	0.36
Urinary function	−1.99	0.44	−0.73	0.55
Bowel function	−1.04	0.46	−0.64	0.39
PORPUS-P	−0.99	0.41	−1.03	0.40
Utility– Disease Specific				
PORPUS-U_{RS}	−0.70	0.23	−0.56	0.22
PORPUS-U_{SG}	−0.69	0.08	−0.37	0.07
PORPUS-U_1	−1.25	0.37	−0.92	0.37
Utility-Generic				
HUI 2	0.01	−0.12	0.01	−0.12
HUI 3	−0.06	0.02	−0.06	0.02
QWB	−0.15	0.21	−0.14	0.24
EQ 5D	0.18	0.08	−0.14	0.07

In preference measurement

- Patients will become more important…
  - Theoretical grounds
    - Experienced utility vs “decision utility”
  - Measurement grounds
- Future of disease specific utility measurement ????

Why doesn’t pharmacoeconomics feel (very) scientific?

Bell et. al. BMJ 2006

Table 2 Characteristics of studies associated with favourable incremental cost effectiveness ratios according to three threshold values. Values are odds ratios (95% confidence intervals)

Study characteristic	Crude OR (95% CI)			Adjusted OR (95% CI)*		
	<$20 000/QALY	<$50 000/QALY	<$100 000/QALY	<$20 000/QALY	<$50 000/QALY	<$100 000/QALY
Publication year						
1976-91	1.6 (0.98 to 2.7)	1.4 (0.80 to 2.4)	1.2 (0.67 to 2.3)	1.6 (0.96 to 2.7)	1.3 (0.76 to 2.3)	1.2 (0.61 to 2.2)
1992-6	1.3 (0.94 to 1.9)	1.4 (0.93 to 2.3)	1.1 (0.68 to 1.6)	1.3 (0.87 to 1.8)	1.3 (0.87 to 1.9)	1.0 (0.64 to 1.6)
1997-2001	1.0	1.0	1.0	1.0	1.0	1.0
Journal impact factor†						
<2	1.0	1.0	1.0	1.0	1.0	1.0
2-4	0.62 (0.42 to 0.91)	0.62 (0.41 to 0.94)	0.59 (0.38 to 0.94)	0.75 (0.50 to 1.1)	0.82 (0.53 to 1.3)	0.77 (0.47 to 1.2)
>4	0.60 (0.42 to 0.86)	0.56 (0.38 to 0.82)	0.83 (0.53 to 1.3)	0.95 (0.63 to 1.4)	0.81 (0.52 to 1.3)	1.1 (0.66 to 1.9)
Disease category						
Cardiovascular	1.0	1.0	1.0	1.0	1.0	1.0
Endocrine	1.3 (0.68 to 2.6)	1.2 (0.58 to 2.5)	1.3 (0.58 to 3.0)	1.2 (0.56 to 2.4)	1.1 (0.52 to 2.3)	1.2 (0.53 to 2.7)
Infectious	1.1 (0.66 to 1.7)	0.79 (0.48 to 1.3)	0.74 (0.43 to 1.3)	1.0 (0.64 to 1.7)	0.75 (0.44 to 1.3)	0.71 (0.39 to 1.3)
Musculoskeletal	1.4 (0.60 to 3.3)	1.3 (0.51 to 3.1)	1.4 (0.50 to 3.7)	1.1 (0.43 to 2.7)	0.89 (0.34 to 2.3)	1.1 (0.37 to 3.1)
Neoplastic	0.91 (0.56 to 1.5)	0.79 (0.46 to 1.3)	0.77 (0.42 to 1.4)	0.78 (0.47 to 1.3)	0.64 (0.37 to 1.1)	0.69 (0.36 to 1.3)
Neurological/psychiatric	0.76 (0.40 to 1.5)	0.78 (0.40 to 1.5))	0.66 (0.31 to 1.4)	0.75 (0.39 to 1.4)	0.70 (0.34 to 1.4)	0.61 (0.27 to 1.4)
Other	1.2 (0.75 to 1.8)	0.67 (0.42 to 1.1)	0.52 (0.31 to 0.88)	1.0 (0.63 to 1.6)	0.53 (0.31 to 0.88)	0.49 (0.27 to 0.86)
Study funding source‡						
Non-industry	1.0	1.0	1.0	1.0	1.0	1.0
Industry	2.2 (1.4 to 3.4)	3.5 (2.0 to 6.1)	3.4 (1.6 to 7.0)	2.1 (1.3 to 3.3)	3.2 (1.8 to 5.7)	3.3 (1.6 to 6.8)
Not specified	1.3 (0.95 to 1.9)	1.5 (1.1 to 2.2)	1.4 (0.93 to 2.1)	1.3 (0.89 to 1.8)	1.5 (1.0 to 2.1)	1.5 (0.97 to 2.2)
Region of study						
Europe	0.50 (0.28 to 0.89)	0.43 (0.21 to 0.87)	0.46 (0.21 to 1.0)	0.59 (0.33 to 1.1)	0.42 (0.21 to 0.86)	0.43 (0.19 to 0.96)
United States	0.35 (0.21 to 0.57)	0.29 (0.16 to 0.55)	0.33 (0.16 to 0.66)	0.44 (0.26 to 0.76)	0.35 (0.18 to 0.67)	0.33 (0.16 to 0.68)
Other§	1.0	1.0	1.0	1.0	1.0	1.0
Methodological quality¶						
1.0-4.0	1.0	1.0	1.0	1.0	1.0	1.0
4.5-5.0	0.92 (0.64 to 1.3)	0.95 (0.64 to 1.4)	0.96 (0.62 to 1.5)	1.0 (0.70 to 1.5)	1.1 (0.70 to 1.6)	1.0 (0.63 to 1.6)
5.5-7.0	0.48 (0.33 to 0.70)	0.57 (0.39 to 0.83)	0.82 (0.52 to 1.3)	0.58 (0.37 to 0.91)	0.72 (0.45 to 1.2)	0.90 (0.51 to 1.6)