Reference drug programs: Can we contain costs without harming patients?

Sebastian Schneeweiss, MD, ScD

BRIGHAM AND WOMEN'S HOSPITAL

Harvard Medical School

Division of Pharmacoepidemiology and Pharmacoeconomics,
Department of Medicine, Harvard Medical School,
Department of Epidemiology, Harvard School of Public Health

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Disclosure

- No stocks in pharmaceutical/biotech companies
- No consulting/speaker bureau for drug manufacturers
- Funded by grants from the US (AHRQ, NIA, NIMH)
- "Seed money" from BC PharmaCare in 1997 (<1% of $$)
- Research grants from Merck, Pfizer, and Pharmacia to study the safety of Coxibs and Dopamin receptor agonists
- Consulting/advisory boards: i3 Drug Safety, HealthCore, RTI, Adheris, ii4sm, FDA

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Effectiveness of RDP

- RDP
  - Mechanism
  - Clinical rationale
  - Economic rationale
  - RDP and prior authorization
- Evidence
  - British Columbia RDP experience
  - Selected other drug policies

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Mechanism: Drug plan perspective

- Plans identify *reference groups* of drugs that are therapeutically equivalent
- Plans establish a *reference price* within group
  - A) highest price of the 2 or 3 least expensive drugs
  - B) calculate an average price of the 2 or 3 least expensive drugs
- Plans reimburse only up to the reference price for all drugs within a reference group

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Mechanism: Drug plan perspective

- Therefore:
  - RDP is a reimbursement policy NOT a pricing policy!
    Calling the policy *reference pricing* is confusing
  - Alternative names:
    Maximum allowable costs (MAC) in the US
    Therapeutic substitution vs. generic substitution
    Therapeutic equivalence vs. bioequivalence

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Mechanism: Drug plan perspective

- Why do drug plans like RDP?
  - Savings are easily predictable
  - Savings are scaleable
    By expanding RDP to more reference groups
    By lowering reference prices
  - RDP is fair to low-income pats since no copay is required

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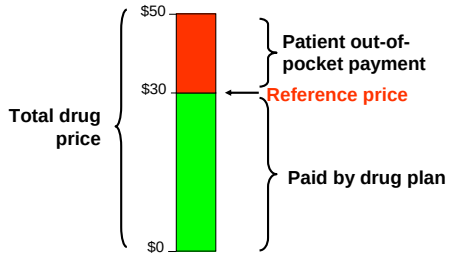
Mechanism: Patient Perspective



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Mechanism: Patient Perspective

- Patient reality:
  - Pats learn at the pharmacy of an increase in co-payment due to RDP
  - Pharmacists spend time to explain (if you are lucky)
  - Pats arranges a visit with physician to discuss alternatives and change prescription

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Clinical rationale of RDP: Therapeutic equivalence (1)

- RDP is based on therapeutic equivalence:
  - If 2 drugs are therapeutically equivalent, i.e. equally effective and non-toxic, why pay more for one when the other is more affordable?
  - If therapeutically equivalence can be documented then RDP provides full coverage for the specific reference group by substituting expensive drugs with less costly ones.
  - **RDP implicitly directs patients and physicians to one or several substitutes based on the best evidence.**
  - The latter is a critical difference to simple fiscal interventions, including fixed co-pays, co-insurance, deductibles

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Clinical rationale of RDP: Therapeutic equivalence (2)

Generating evidence of therapeutic equivalence:

- Head-to-head randomized clinical trials
  - No incentive for manufacturer to fund such trials ->
- Indirect comparison of several placebo controlled trials
  - Limited adjustment of unmeasured confounders
- RCTs in the population that uses most of the drugs
  - Most RCTs exclude elderly pats with multiple comorbidities

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High risk for manufacturer

- PROVE IT (Bristol-Myers Squibb):
  - Low-dose pravastatin vs. high-dose atorvastatin post MI
  - 16% higher rate of secondary MI in pravastatin (BMS drug)
- ENHANCE (Merck and Schering-Plough):
  - Ezetimibe+simvastatin (Vytorin) vs. simvastatin alone
  - No improvement in carotid wall thickness

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Clinical rationale of RDP: Therapeutic equivalence (2)

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- RCTs in the population that uses most of the drugs
  - Most RCTs exclude elderly pats with multiple comorbidities

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Clinical rationale of RDP: Therapeutic equivalence (3)

- Database studies on *comparative effectiveness* in the target population
  - Difficult to adjust confounding by indication
  - Delay in availability of sufficient data
- In practice it will be a mix of all the above
- Ideally, evidence will be updated regularly

- US: Evidence-based Practice Centers
  DEcIDE Research Network

Click here for a 2h lecture on Comparative Effectiveness Research

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Clinical rationale of RDP: Breadth of reference group

- How broad can therapeutically equivalent reference groups be?
  - **Narrow** definitions, e.g. dhp-CCBs
    Often relatively clear evidence but limited economic effects if prices are homogeneous within group
  - **Broad** definitions, e.g. `antihypertensives`
    Potentially huge savings, but harder to establish therapeutic equivalence -> many exemption rules depending on severity and comorbidities (JNC7)

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Economic rationale for RDP: Balanced incentives

- Incentive for patients to be prescribed fully covered RDP drugs.
- Incentive for manufacturers to lower prices to the reference price
- Incentive for manufacturers to market true innovations since they can reach higher margins outside of RDP
  - Huskamp et al. called RDP „incentive pricing“

- Disincentive for manufacturers to lower prices below reference price

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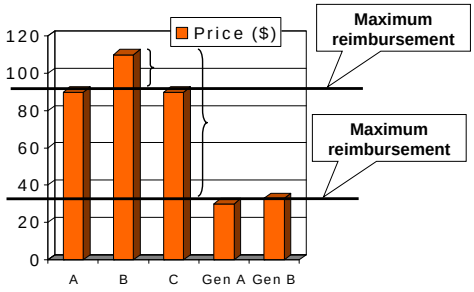
Economic rationale for RDP: Economics of RDP

- Plan savings from RP is a function of price variability and volume.



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Economic rationale for RDP: Economics of RDP

- Different perspectives, different issues:
- Drug plan
  - Savings = f(price difference*, utilization)
- Drug market
  - Savings = f(manufacturer price, utilization changes)
- Health care system
  - Net savings = f(drug savings, increased services, admin)

* Price difference = manufacturer price – reference price

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Economic rationale for RDP: RDP in a market-driven HC system

- Most savings realized by direct price negotiations -> rebates
- 3 tier copay systems very popular
  - Similar to RDP they assume therapeutic equivalence
  - The success of the price negotiations determines the tier allocation of drugs
- Often a highly segmented market so that increases in health services are irrelevant for drug plans (except HMOs)

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Economic rationale for RDP: Limits and synergies

- RDP can cover only markets with several alternative medications within reference group
- Single drug markets (highly innovative drugs) cannot be addressed by RDP and should not!
- For innovative drugs ***prior authorization*** can act as a gatekeeper to assure access for those with a medical need.

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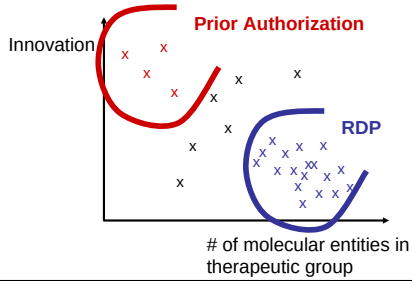
RDP + Prior Authorization Progs

- ***Prior authorization:*** evidence-based rules that identify patients who will benefit most from an innovative (expensive) medication.



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Now…

Empirical evidence

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Reference Pricing in British Columbia

- RDP for ACE inhibitors in 1997
  - Captopril, Quinapril, and Ramipril fully covered
  - Enalapril required cost-sharing by patients
- RDP for dhp-CCBs also in 1997
  - Felodipine fully covered
  - Nifedipine, amlodipine, nicardipine required cost-sharing by patients
- Generous RDP exemption rules

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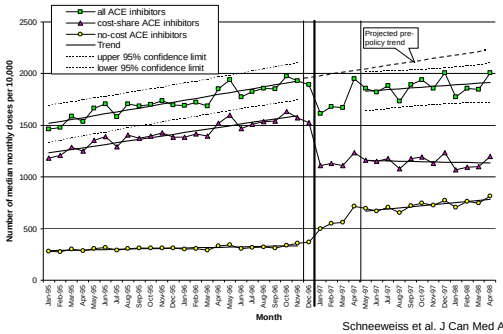
Changes in ACE inhibitor Utilization



Schneeweiss et al. J Can Med Assoc, 2002

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No increase in discontinuations

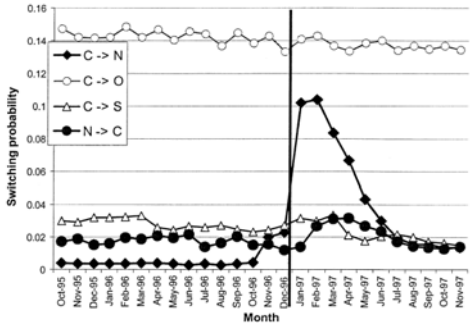

Fig. 5. Transition dynamics: plotted is the probability of switching medications once a patient enters the month as a cost-share drug recipient. (C = cost-share, N = no cost, O = any other antihypertensive medications, and S = stopping all antihypertensive medications).

Schneeweiss et al. J Clin Epi 2002

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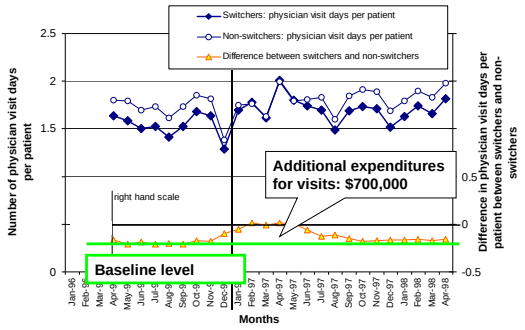
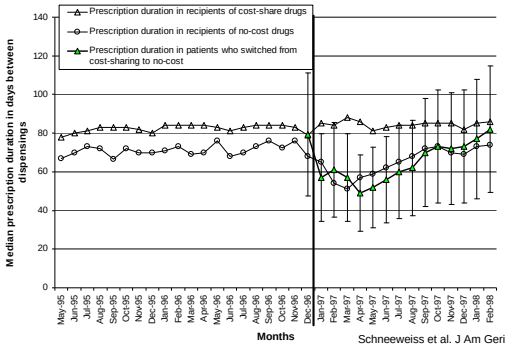
Additional visits in prevalent ACEI users



Reduced time between visits in patients who switched ACE inhibitors



Schneeweiss et al. J Am Geriatr Assoc 2002

No increase in Emergency hospitalizations due to RDP

TABLE 3. DIFFERENCES IN HEALTH CARE UTILIZATION AND ADMISSION TO LONG-TERM CARE FACILITIES IN 5353 SWITCHERS AS COMPARED WITH 27,938 NONSWITCHERS.*

OUTCOME	RELATIVE CHANGE IN RATE RATIOS BETWEEN SWITCHERS AND NONSWITCHERS AS COMPARED WITH BASE-LINE VALUES (95% CI)†		
	INITIATION PERIOD (1 MONTH BEFORE INDEX DATE)	EARLY PERIOD (1 TO 2 MONTHS AFTER INDEX DATE)	LATE PERIOD (3 TO 10 MONTHS AFTER INDEX DATE)
Visits to a physician	1.01 (0.97 to 1.05)	1.11 (1.07 to 1.15)	1.03 (1.00 to 1.06)
Hospital admissions through the emergency room	1.39 (1.20 to 1.61)	1.27 (1.07 to 1.51)	0.97 (0.86 to 1.09)
Nonemergency hospital admissions	1.17 (0.94 to 1.44)	1.05 (0.83 to 1.32)	0.90 (0.77 to 1.05)
Paid claims for physicians' services ($)‡	10.9 (4.4 to 17.4)	13.4 (7.3 to 19.6)	1.3 (−2.8 to 5.3)
Admissions to long-term care facilities	0.66 (0.39 to 1.15)	0.45 (0.26 to 0.80)	0.53 (0.35 to 0.82)

Schneeweiss et al. N Engl J Med 2002

No effect on mortality

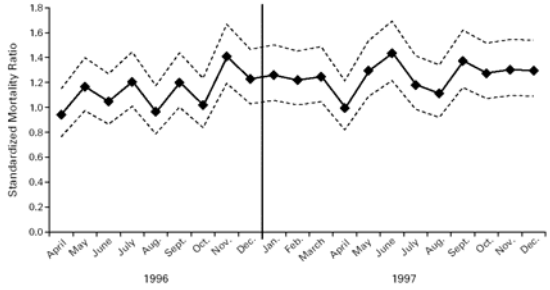
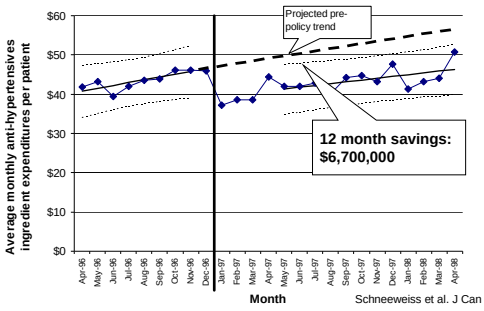


Figure 2. Standardized Mortality Ratios for the Study Cohort.
The dotted lines indicate the 95 percent confidence intervals. Standardized mortality ratios of over 1.00 indicate that the corresponding cohort has a higher mortality rate than the population in British Columbia excluding the study cohort. Standardized mortality ratios were calculated by indirect standardization, with adjustment for sex and age.

Summary: Clinical

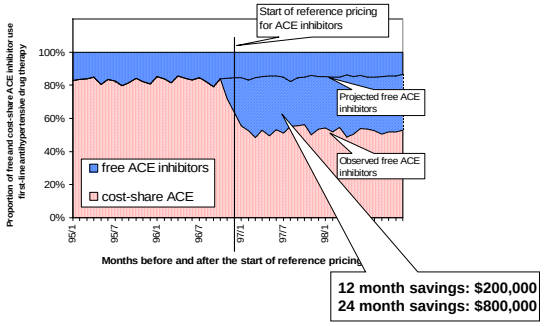
- No substitution with outside RDP drugs
- No increased discontinuation rates
- No (severe) adverse health outcomes
- Generous exemptions for clinical reasons smoothed transition

Pharmacy savings among prevalent ACE inhibitor users



Schneeweiss et al. J Can Med Assoc, 2002

Pharmacy savings among incident ACE inhibitor users

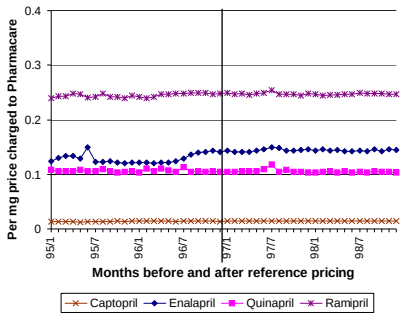


Schneeweiss, Dormuth, Grootendorst et al. Med Care 2004

Administrative costs

	Annual fixed costs	Annual variable costs	One-time costs
Ongoing Special Authority Requests*			
Labor			
Pharmacist, support, consultant		$159,143	
Capital and Overhead			
Fax, phone, space etc.	$24,789		
Development and Implementation (one time costs)**			
Staff			$36,301
Communications Materials			$25,000
Claims Processing System:			
Upgrade and Testing			$175,000
Total	$24,789	$159,143	$236,301

ACE-I prices after Reference Pricing

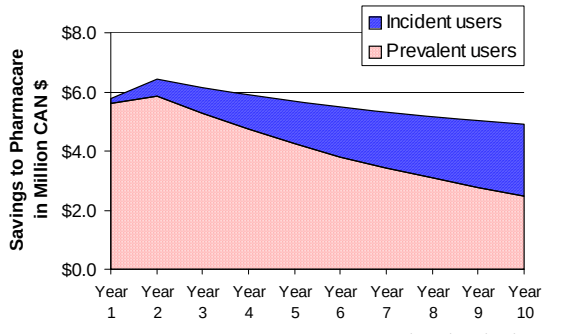


Net health care savings

Major spending component	Savings 1-year period	Savings 2-year period
(1) Prevalent users		
Savings in drug expenditures	$6.7M	$12.6M*
Expenditures for increased physician claims	-$0.7M	-$0.7M
(2) Incident users		
Savings in drug expenditures	$0.2M	$0.8M
(3) Administrative costs		
Cost for programming the central benefit server	-$0.24M	$0.00M
Expenditures for prior authorization process	-$0.18M	-$0.37M
(4) Price Component		
Savings through reduced drug price changes	$0.0	$0.0
Total	**$5.8M**	**$12.3M**

Schneeweiss et al. Med Care, 2004

Net Health Plan Savings



Schneeweiss et al. Med Care 2004

Summary: Economics

- RDP for ACE inhibitors provided $5.8 million net savings during the first year (6%!)
- RDP for dhp CCBs provided net savings of $1.6 million Schneeweiss et al. CPT 2004
- All savings from the perspective of a comprehensive health insurance
- 1/6 cost-shifting to patients
  - Is cost shifting to patients bad?
- Similar findings for NSAIDs and H_2RAs

RDP for H2 receptor antagonists

Table 3: Mean monthly drug ingredient cost reimbursed by BC Pharmacare per defined daily dose of gastrointestinal drugs

Drug group	Time period; mean monthly cost per defined daily dose (and % of baseline), $									
	Historical comparator period (Jan 1993 to Aug 1994)		Baseline (Sept 1994 to Aug 1995)		Policy transition period (Sept to Dec 1995)		First 12 mo after policy change (Jan to Dec 1996)		Follow-up (Jan 1997 to May 1999)	
H_2RAs										
Restricted										
Ranitidine	1.14	(130)	0.88	(100)	0.72	(82)	0.68	(77)	0.65	(74)
Famotidine	1.57	(127)	1.24	(100)	1.03	(83)	1.05	(85)	1.06	(85)
Nizatidine	1.84	(100)	1.84	(100)	1.51	(82)	1.55	(84)	1.47	(80)
All restricted H_2RAs	1.24	(126)	0.98	(100)	0.80	(82)	0.76	(78)	0.72	(73)
Reference standard										
Cimetidine	0.32	(128)	0.25	(100)	0.25	(100)	0.25	(100)	0.25	(100)
All H_2RAs	1.06	(125)	0.85	(100)	0.46	(54)	0.40	(47)	0.41	(48)
PPIs										
Omoprazole	2.29	(100)	2.28	(100)	2.27	(100)	2.29	(100)	2.27	(100)
Lansoprazole	NA		NA		2.51	(NA)	2.62	(NA)	2.29	(NA)
Pantoprazole	NA		NA		NA		NA		2.03	(NA)
All PPIs	2.29	(100)	2.28	(100)	2.27	(100)	2.30	(101)	2.25	(99)

Grootendorst, CMAJ 2002

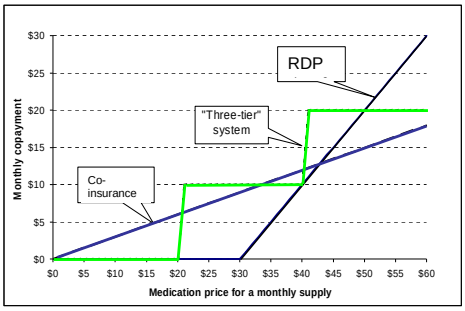
RDP for NSAIDs

Table 2: Average Pharmacare Expenditure per Day of Therapy Dispensed by Analgesic and Time Period

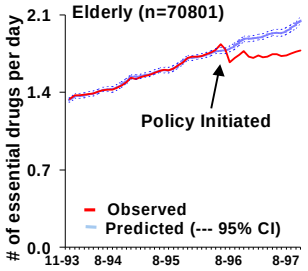
Analgesic Category	Time Period: Pre-RP Feb 93–Mar 94	Type 1 RP Apr 94–Oct 95	Type 2 RP Nov 95–Oct 96	Delistings Nov 96–Jun 0
NSAIDS				
Unrestricted				
ASA ect 650 mg tab	0.22 100	0.13 59	0.12 55	0.12 55
Ibuprofen tab	0.20 100	0.11 55	0.11 55	0.11 55
Naproxen tab	0.27 100	0.22 81	0.22 81	0.21 78
Subtotal	***0.23 100***	***0.16 71***	***0.19 82***	***0.19 82***
First line restricted				
Diclofenac	1.03 100	0.85 83	0.63 61	0.62 60
Diclofenac/misoprostol	1.24 100	1.23 99	1.00 81	0.90 72
Diflunisal	1.12 100	0.85 76	0.63 56	0.64 57
Fenoprofen	1.20 100	1.18 99	0.90 75	0.95 79
Flurbiprofen	1.23 100	0.84 69	0.61 50	0.61 49
Indometacin	0.49 100	0.43 88	0.41 84	0.35 71
Ketoprofen	0.89 100	0.55 62	0.46 52	0.41 46
Naproxen ect & sr	0.82 100	0.85 103	0.52 63	0.49 59
Salsalate	—	1.44 —	1.23 —	1.14 —
Subtotal	***0.96 100***	***0.87 91***	***0.66 69***	***0.62 65***
Second line restricted				
Sulindac	1.27 100	1.04 82	0.81 64	1.00 79
Nabumetone	—	1.49 —	1.22 —	1.26 —
Piroxicam cap	1.01 100	0.81 80	0.63 62	0.73 72
Tenoxicam	1.36 100	1.34 98	1.03 76	1.06 78
Tiaprofenic acid	1.46 100	1.23 84	0.78 53	0.93 64
Tolmetin	1.10 100	0.98 89	0.78 71	0.91 83
Subtotal	***1.29 100***	***1.19 92***	***0.93 72***	***1.06 82***
Delisted/special auth.	***1.38 100***	***1.32 95***	***0.97 70***	***1.08 78***
All NSAIDs	***0.83 100***	***0.79 95***	***0.47 57***	***0.39 47***

Grootendorst HSR 2005

Some alternative measures



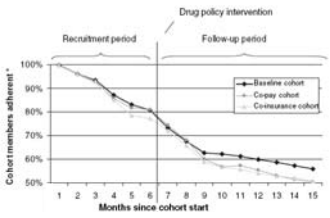
Negative effect of 25% co-insurance in Quebec on essential drug use



Tamblyn, JAMA 2000

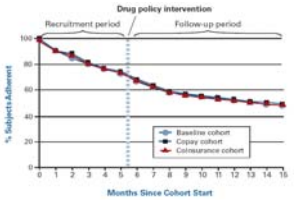
Negative effect of 30% co-insurance on adherence

Statins: -10%



Schneeweiss, Circulation 2007

Beta blocker: -0%



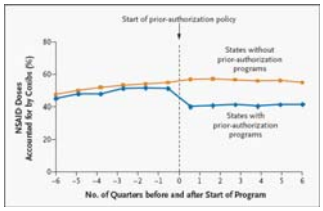
Schneeweiss Am J M Care 2007

3-tiered co-payment systems in the US

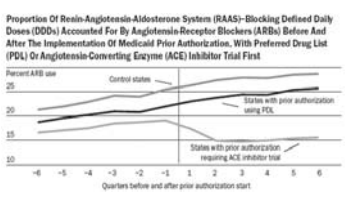
- Motheral & Fairman, 2001:
  - Reduced utilization, reduced spending
  - No increase in out-patient visits, ER visits
  - Slightly increased discontinuation in 1 of 4 drug groups

Medicaid experience with PA programs:

Selective Cox-2 inhibitors



Angiotensin receptor blockers



Safety of PA programs

- Not much evidence
- Implementation is highly variable
- Implementation is usually not transparent

What do we make out of all this?

- RDP has great philosophical appeal
- It has proven safe and effective in many jurisdictions, if
  - therapeutic equivalence can be established
  - exemptions for medical reasons are in place
- Most effective in combination with prior authorization
- It is fairly easy to implement

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Practical Issues when implementing RDP

- Generating evidence of therapeutic equivalence
  - Needs to be done very careful
  - Transparent process (EPC)
  - Needs to be regularly addressed
- Address single drug markets
  - Innovative drugs will not be included in RDP
  - Prior authorization directs use to those who need it
- Provide Information technologies
  - Requires a basic IT network for current reference price information

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Practical Issues when implementing RDP

- Information for physicians, patients, pharmacists
  - All stakeholder need to understand the functioning of RDP
  - Failure to provide good information can kill RDP (Norway)
  - Extra cost for explaining RDP needs to be acknowledged
- RDP exemptions for individual pats
  - In theory not necessary
  - In practice very useful in smoothing transitions
- Expect negative campaigns
  - Yes, you can bet on them to come
  - Need anticipatory media campaign
  - Proactive evaluation
- Plan for RDP maintenance
  - Reference groups and prices need regular updating -> budget

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Why not more RDP programs?

- Why no RDP in Ontario?

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