Comparing tiered formularies and reference pricing policies: A systematic review

Introduction

Most community-based spending on prescription drugs in Canada is financed through provincial (40%) and private (35%) drug plans.[1] From 1997 to 2007, spending under provincial drug plans grew from $3.1 billion to $9.2 billion and spending under private plans grew from $2.8 billion to $7.8 billion. Under such financial pressures, it is possible that reference pricing and/or tiered formularies will be adopted by growing numbers of public and private insurers in Canada. Because these policies are similar in intent but slightly different in structure, we sought to review and compare evidence concerning the impact of reference pricing policies and tiered formularies. This work is intended to complement reviews focusing more specifically on reference pricing policies.[2,3]

Under reference pricing policies, a drug plan will generally cover low-cost options within given drug categories and require patients to pay any price differences if they are prescribed higher-cost products. Categories may include only chemically equivalent drugs (generic reference pricing); or they may include chemically distinct products with comparable therapeutic effects (therapeutic reference pricing). Public and private insurers in Canada and abroad use generic reference pricing extensively. The province of British Columbia and several countries abroad have applied therapeutic reference pricing.[4,5]

Under a tiered formulary, patients generally face incrementally higher co-payments for different treatment options: a relatively low co-payment applies to 'preferred' drugs within class (e.g., $5 for generics); a higher co-payment for 2nd tier products within class (e.g., $10 for 'preferred brands' with whom the insurer has negotiated a rebate); and an even higher co-payment for other drugs on formulary (e.g., $25 for other brands within a drug class). Tiered

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formularies are used most extensively in the US. As of 2007, 91% of American workers with employer-sponsored drug coverage faced at least two cost-sharing tiers for prescription drugs and 75% faced at least three tiers.[6]

As reference pricing and tiered formularies are already commonly used to decrease drug plan expenditures, it is important to understand the implications of these policies on both drug costs, use of medicines and patient health outcomes. This paper synthesizes and contrasts comparable quality evidence from published literature regarding the outcomes of these two policies.

Methods

We sought English-language studies published from 1986 to 2007 that assessed the effects of tiered formularies or therapeutic reference pricing of prescription drugs in markets comparable to Canada's (Appendix 1 contains complete search details). We searched fifteen electronic databases, performed web-based and repository searches for grey literature, traced citations to and from relevant articles, hand-searched core journals from which several citations were found electronically, and searched personal libraries for additional articles. We searched databases for terms clustered around the concepts of prescription drugs and the interventions of interest (various synonyms for co-payments, tiers, and reference pricing).

Our inclusion criteria were chosen to select quantitative studies that employed reasonable methods in their analysis of the impact of tiered formularies or reference pricing. Studies had to use patient-level data in an acceptable research design such as: randomized controlled policy trials, pre/post studies with nonrandomized comparison groups, interrupted time series analysis with comparison groups, interrupted time series without comparison groups, or pre/post studies

without a comparison group. We excluded analyses based on post-only or cross-sectional designs; analyses using aggregated drug utilization and/or cost data; and analyses pertaining to policies in developing countries.

Results

Searches identified a total of 2,964 potentially relevant citations. These were screened through a sequence of title, abstract and full-text review — QUOROM chart in Table 1. Title review eliminated 2,491 citations (primarily drug specific clinical studies). Two authors then reviewed remaining abstracts and eliminated all but 86 articles. An additional 13 articles were identified through citation tracing, and one article was found to be unavailable because it was under peer review. After full text screening by two authors (or three authors in cases of disagreement), 12 articles representing 11 studies were deemed eligible for inclusion in our review.

Four of the included papers, representing 3 studies, assessed the impact of reference pricing. All of these studies examined the implementation of reference pricing during the mid 1990s under BC's PharmaCare program for senior citizens.[7-10] Eight studies included in our review assessed the impact of changes in tiered formularies. Seven of these looked at the effect of tiered formularies for non-elderly enrolees of employment-related private insurance in the US.[11-17] One included study assessed the impact of tiered formularies on child dependents of enrolees of employment-related private insurance plans in the US.[18]

Impacts of reference pricing policies

The associations found in the studies of reference pricing included in this review are summarised in Table 1. These studies assessed the impact of reference pricing for three

categories of drug treatment: nitrate drugs, ACE-inhibitors, and calcium channel blockers (CCBs). Studies by Schneeweiss and colleagues and the study by Grootendorst and colleagues found that between 9% and 34% of patients switched to fully covered (reference) products after reference pricing was implemented.[7-10] Grootendorst and colleagues found that overall use of CCBs declined upon implementation of reference pricing whereas Schneeweiss and colleagues found that reduced overall use of CCBs was not statistically significant after adjusting for pre-policy trends.[10,7] The reverse is true for these authors' findings with respect to the use of ACE-inhibitors.[7,9]

Schneeweiss and colleagues found that the changes in utilization associated with reference pricing resulted in drug plan savings ranging from 12% to 19% ($1.67 million to $7.7 million per year) of plan spending on related medicines.[9,10] Partially offsetting savings in drug costs to the insurer, both sets of researchers found that reference pricing in BC was associated with increased physician services during first 2 or 4 months following policy change.[7-10] Research groups found different results with respect to longer-term use of physician services: Schneeweiss and colleagues found no such association while Grootendorst found evidence of increased use of physician services beyond 4 months for two of the three categories studied (CCBs and ACE-inhibitors).[7-10] Schneeweiss and colleagues estimated that the net savings after accounting for medical care expenses were between $1.62 million to $6 million a year.[9,10]

In two of the three drug categories investigated (CCBs and ACE-inhibitors), Schneeweiss and colleagues and Grootendorst and colleagues found that reference pricing was not associated with any change in the use of hospital services.[7,8,10] In the one study that investigated the impact of reference pricing for nitrate drugs, Grootendorst and colleagues found that reference pricing was associated with increased long-term probability of bypass or revascularization.[7]

Impacts of tiered formularies

The associations found in the studies of tiered formularies included in this review are summarised in Table 1. Despite differences in the populations and drug categories studied, studies of the impact of tiered formularies included in our review yielded a number of consistent findings. Most studies assessing such associations found that adding tiers to copayments for prescription drugs in the US private insurance market was associated with reduced total spending (decreases of 5%-20%).[15,13,18,17] The studies by Nair and colleagues and Fairman and colleagues did not find statistically significant associations between adding tiers to formularies and changes in total spending.[14,12] Where they were observed, reductions in total spending were the result of three common findings across studies and drug classes investigated: adding tiers to co-payment structures was associated with increased switching within drug classes in all 8 included studies (switching toward 'preferred' drugs on formulary occurred in 2% to 49.4% of patients);[15,13,18,17,16,11] decreased overall utilization of affected medicines;[12,15,13,18,16,11] and either no change[18] or an increase in the rate of discontinuation with prescribed drug treatments.[12-14,16,11]

When the distribution of costs was investigated, most studies found that employing tiered formularies was associated with reduced spending by the drug plan,[13,18,17,11] and increased spending by patients.[13,18,17,16,11] In the study by Nair and colleagues, changes in spending by the plan and patients were consistent with the findings of other studies but not statistically significant.[14]

None of the studies of tiered formularies included in our review had assessed potential health outcomes resulting from the policy. However, two studies found that moving from a 2-tier formulary to a 3-tier formulary was not associated with increased use of medical or hospital services.[12,11]

The one study of the effects of tiered formularies on medicine use by children was the only study not to find an association between the policy and medical discontinuation.[18] The one study that assessed the differences in policy impact on treatments for acute versus chronic conditions found greater relative reductions in the utilization of and persistence with acute condition treatments.[16]

Discussion

There are relatively few high-quality patient-level studies of the impact of reference pricing and tiered formularies and available evidence permits only limited comparisons between these policy tools due to differences in populations studied and health system context. However, the most common finding is that patients facing reference pricing or tiered formularies often switch toward medications with preferred coverage. Studies of reference pricing suggest that reference pricing is also associated with short term increases in the use of physician services, which may be interpreted as a transaction cost associated with switching medications. The balance of evidence found concerning health services use, hospitalization and death indicates that reference pricing (as implemented in BC) is not associated with adverse health impacts.

More research is required to examine the hypothesis that tiered formulary policies may result in increased use of physician services and potentially worse health outcomes. Surprisingly, only two of the eight studies of tiered formularies included in this review assessed such outcomes or surrogates thereof. This gap in knowledge is potentially critical given that seven of the eight tiered formulary studies found that tiered formularies were associated with reduced use of medicines, increased medicine discontinuation or both.

Conclusion

The rapid rise in tiered formularies among private insurance plans in the US may be a harbinger of the future trends in Canada: given rising medicine costs, it is likely that incentive structures for patient cost-sharing will be adopted more widely here in the future. Evidence suggests that patient incentives work insofar as they alter prescription drug use and save on drug costs. The available evidence does not clearly differentiate reference pricing and tiered formularies in terms of policy outcomes. Reference pricing has a slight evidentiary advantage given that patient health outcomes under tired formularies have not been well studied and that tiered formularies are associated with increased rates of medicine discontinuation.

When considering policy options in Canada, information and transaction costs for prescribers and patients should be taken into consideration. With dozens of potential formularies to consider for their patient rosters, US physicians may not have the time or resources necessary to know which drugs are on what 'tier' for each patient. High co-payment prescriptions may be prescribed unintentionally under such circumstances, potentially resulting in increased patient costs, strained physician-patient relationships, reduced adherence to treatments, and worse health outcomes. Such adverse policy outcomes may be minimized if patient cost-sharing, through reference pricing or tiered formularies, was harmonized across all payers within a province.

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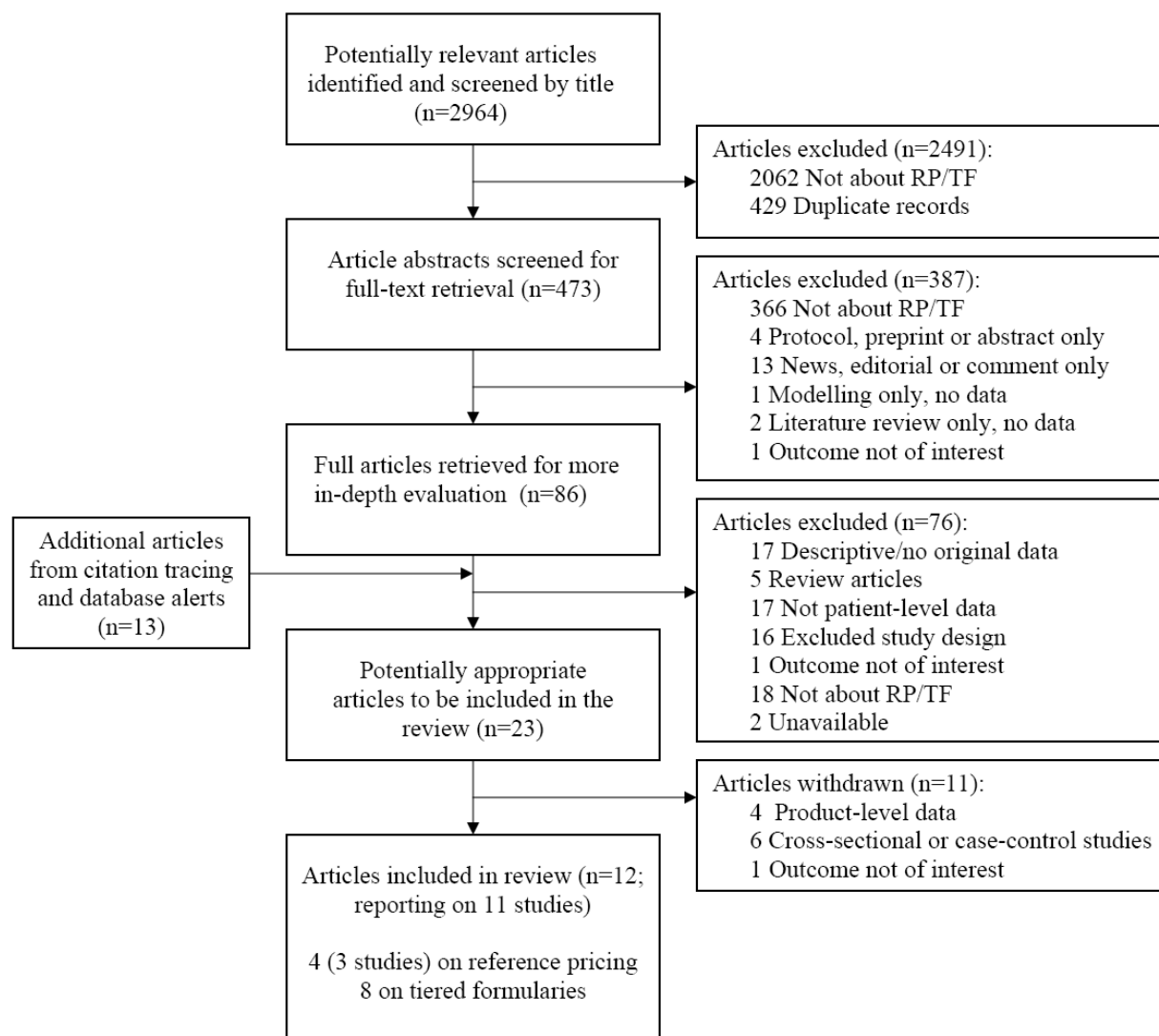
Table 1: QUOROM chart of search results

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┌─────────────────────────────────┐
│  Potentially relevant articles  │
│  identified and screened by title│        ┌──────────────────────────────────┐
│          (n=2964)               │────────▶│  Articles excluded (n=2491):     │
└─────────────────────────────────┘         │    2062 Not about RP/TF          │
                │                            │    429 Duplicate records         │
                ▼                            └──────────────────────────────────┘
┌─────────────────────────────────┐
│  Article abstracts screened for │         ┌──────────────────────────────────┐
│  full-text retrieval (n=473)    │         │  Articles excluded (n=387):      │
│                                 │         │    366 Not about RP/TF           │
└─────────────────────────────────┘────────▶│    4 Protocol, preprint or abstract only │
                │                            │    13 News, editorial or comment only │
                ▼                            │    1 Modelling only, no data     │
┌─────────────────────────────────┐         │    2 Literature review only, no data │
│  Full articles retrieved for more│        │    1 Outcome not of interest     │
│  in-depth evaluation (n=86)     │         └──────────────────────────────────┘
└─────────────────────────────────┘
                │                            ┌──────────────────────────────────┐
┌──────────────────┐    │                   │  Articles excluded (n=76):       │
│ Additional articles│   │                   │    17 Descriptive/no original data │
│ from citation tracing│─┤                   │    5 Review articles             │
│ and database alerts│   │                   │    17 Not patient-level data     │
│      (n=13)        │   │                   │    16 Excluded study design      │
└──────────────────┘    ▼                   │    1 Outcome not of interest     │
┌─────────────────────────────────┐────────▶│    18 Not about RP/TF            │
│  Potentially appropriate        │         │    2 Unavailable                 │
│  articles to be included in the │         └──────────────────────────────────┘
│  review (n=23)                  │
└─────────────────────────────────┘         ┌──────────────────────────────────┐
                │                   ────────▶│  Articles withdrawn (n=11):      │
                ▼                            │    4 Product-level data          │
┌─────────────────────────────────┐         │    6 Cross-sectional or case-control studies │
│ Articles included in review (n=12;│       │    1 Outcome not of interest     │
│  reporting on 11 studies)       │         └──────────────────────────────────┘
│                                 │
│  4 (3 studies) on reference pricing│
│     8 on tiered formularies     │
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Table 1: Summary of associations found in studies of reference pricing

Study	Grootendorst[7]	Schneeweiss[9,8]	Schneeweiss[10]
Population studied	BC Seniors (65+) on medicines from the studied drug classes	BC Seniors (65+) who had received ACE-Is priced higher than the reference price in 1996	BC seniors (65+) who had received CCBs before the introduction of RP
Intervention studied	Reference pricing policy for nitrates (1995) Reference pricing policy for CCBs and ACE-Is (1997)	Reference pricing policy for ACE-Is (1997)	Reference pricing policy for CCBs (1997)
Drug classes studied	Nitrates, ACE-Is, CCBs	ACE inhibitors	CCBs
Total drug costs			
Insurer costs		[-] -19% = -$6.7 million/yr	[-] -12% = -$1.67 million/yr
Patient costs			
Net costs to insurer, including medical care		[-] -$6 million/yr	[-] -$1.62 million/yr
Prescription drug use	[-] Nitrates and CCBs [+] ACE-Is	[-] for ACE-Is [=] for antihypertensives	[=]
Switching to preferred (reference) drugs	[+] 21% to 34% of patients	[+] 18% of patients	[+] 9% of patients
Discontinuation of medicines in the drug classes studied			
Short term use of physician services (within 2 to 4 months of intervention)	[+] 0% to +5%	[+] +11% = +$0.7 million/yr	[+] +18% = +$0.05 million/yr
Long term use of physician services (4 months after intervention)	[+] + 0% to +11%	[=]	[=]
Hospital services	[+] Nitrate patients	[=]	[=]
Long-term care admissions	[=]	[=]	[=]
Mortality	[=]	[=]	

Note: [+] = statistically significant positive association between policy and specified outcome
[-] = statistically significant negative association between policy and specified outcome
[=] = no statistically significant association between policy and specified outcome
Blank = association between policy and specified outcome not tested in study
ACE-Is = ACE-inhibitors; and CCBs = calcium channel blockers

Table 1: Summary of associations found in studies of tiered formularies

Study	Motheral and Fairman[11]	Fairman et al[12]	Huskamp 2003[13]	Nair[14]	Gibson[15]	Landsman[16]	Landon et al[17]	Huskamp 2005[18]
Population studied	Enrolees in employment-sponsored insurance	Enrolees in employment-sponsored insurance	Enrolees and their dependents in employment-sponsored insurance	Enrolees in managed care plan	Enrolees in employment-sponsored insurance	Enrolees in employment-sponsored insurance	Enrolees in employment-sponsored insurance	Children of employees with employment-sponsored insurance
Intervention / comparison studied	2 to 3 tier vs. stable 2 tier	2 to 3 tier vs. stable 2 tier	1 to 3 tier and 2 to 3 tier vs. stable 2 tier	2 to 3 tier vs. stable 2 and 3 tier	1 to 2 tier vs. stable 3 tier	2 to 3 tier vs. stable 2 tier	Various tier increases vs. stable controls	1 to 3 tier vs. stable 2 tier
Drug classes studied	Antibiotics for otitis media; OCs, estrogens; anti-hypertensives; lipid drugs	All prescriptions; estrogens; OCs; antihypertensives; lipid drugs	ACE-Is, PPIs and statins	Medicines for hypertension, diabetes, dyslipidemia, GERD and arthritis	All prescriptions	NSAIDs, COX-2, TCAs, SSRIs, CCBs, ACE-Is and ARBs	All prescriptions	ADHD medications
Total drug costs	[-] -7% growth		[=]	[=]	[-] -$11 to -$16 per enrolee per quarter		[-] -5% to -15%	[-] -20%
Insurer costs	[-] -21% growth	[-] -26.6% growth	[-] 0% to -58%	[=]			[-] -20%	[-] -43%
Patient costs	[+] +34% growth	[+] +46.5% growth	[+] 0% to +148%	[=]		[+] +16% to +129%	[+] +20% to +100%	[+] +46%
Prescription drug use		[-] -4.2% growth, yr 1 No change, yr 2	[-] 0 to -34%	[=]	[-] -0.16 scripts per enrolee per quarter	[mixed] -6.8% to + 1.7%		[-] -17%
Switching to preferred drugs	[+] +2% growth ($)	[+] +30.5% growth ($)	[+] +17.6% to +49.4% of patients	[+] +5.6%	[+]	[+]	[+]	[+] +5% of patients

Discontinuation of medicines in the drug classes studied	[+] Estrogens	[+] +13% for oral contraceptives	[mixed] -7.5% to +32%	[+] +10%	[+] 2 to 8 times higher	[=]
Long term use of physician services (post 4 months)	[=]	[=]				
Hospital services	[=]	[=]				

Note: (+) = statistically significant positive association between policy and specified outcome
(-) = statistically significant negative association between policy and specified outcome
[=] = no statistically significant association between policy and specified outcome
[mixed] = mixed associations found between policy and specified outcome
% growth = percentage point difference in growth rates between intervention and comparison groups
No change = no statistically significant association between policy and specified outcome
Blank = association between policy and specified outcome not tested in study
OCs = oral contraceptives; ACE-Is = ACE-inhibitors; PPIs = proton pump inhibitors; GERD = gastroesophageal reflux disease; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants; CCBs = calcium channel blockers; ARBs = angiotensin receptor blockers; and ADHD = attention deficit hyperactivity disorder.

Appendix 1: Search Strategy, Search Terms and Inclusion Criteria

Search Strategy

Databases searched for systematic review

- ABI-Inform AND ProQuest Digital Dissertations
- CINAHL (1982 - Present) (EBSCOHost)
- Clinical Evidence (BMJ - few citations to formulary, UK)

- EBM Reviews (Ovid)
- ACP Journal Club (ACP)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Cochrane Database of Systematic Reviews (CDSR)
- Database of Abstracts of Reviews of Effectiveness (DARE)
- EconLit (1969 -) (EBSCOHost)
- EMBASE (1980 to present) (Ovid)
- International Pharmaceutical Abstracts (IPA) (Ovid)
- MEDLINE (1966 to Present with Daily Update) (Ovid)
- NLM Gateway (NLM – Includes what used to be HealthSTAR, NIHCSR)
- PAIS International and PAIS Archive (CSA)
- Web of Science (ISI)

Grey Literature Sources
- Theses/Dissertations
- Theses Canada Portal
- Proquest Digital Disserations
- Networked Digital Library of Theses and Dissertations (NDLTD)
- Google Canada and Google Scholar
- Scirus
- Yahoo
- PapersFirst
- ProceedingsFirst
- WHO main search page and regional sites and library catalogue
- WHO Statistical Information System (WHOSIS)

- INRUD http://www.inrud.org/RIS/RISWEB.ISA
- Key Canadian Websites:
    - Canadian Centre for Policy Alternatives
    - Canadian Evaluation Society (Grey Lit database)
    - Canadian Health Services Research Foundation
    - Canadian Institutes of Health Research
    - Health Canada
    - Index to Canadian Federal "Royal Commission Reports"
    - Public Health Agency of Canada
- Key US Websites:
    - GrayLIT Network (US Gov't publications)
    - GPO Locator Service

Search terms

We searched using search terms clustered around the concepts of: prescription drugs, intervention types, and methodologies (not applicable in some databases). Wherever possible, subject headings were utilized and exploded to include all relevant subheadings. Keywords for drugs included (Pharmaceutical* OR Prescription OR Prescription Drug* OR Drug* OR Medicine* OR Medication*). Keywords for interventions combined (Hierarchical OR Multilevel OR multi-level OR tiered OR differential) with (copay* OR co-pay* OR user charge* OR user-charge* OR charge* or fee* OR formular* or subsid* OR benefit*), various synonyms for reference pricing, interchange, substitution, user fees, copayments, reimbursement mechanisms, and subsidies. In databases where it was possible and useful, search filters for methodologies were applied, or keywords for impact, assessment, and outcomes were added.

Concept A - Drugs:

- (Pharmaceutical* OR Prescription OR Prescription Drug* OR Drug* OR Medicine* OR Medication*)

Concept B – Intervention type:

- (Hierarchical OR Multilevel OR multi-level OR tiered OR differential) AND/SAME/ADJ (copay* OR co-pay* OR user charge* OR user-charge* OR charge* or fee* OR formular* or subsid* OR benefit*)
- (Hierarchical copay* OR Hierarchical co-pay* OR Hierarchical user charge* OR Hierarchical user-charge* OR Hierarchical charge* OR Hierarchical fee* OR Hierarchical formulary* OR Hierarchical subsid* OR Hierarchical benefit* OR multilevel copay* OR multilevel co-pay* OR multilevel user charge* OR multilevel user-charge* OR multilevel charge* OR multilevel fee* OR multilevel formulary* OR multilevel subsid* OR multilevel benefit* OR multi-level copay* OR multi-level co-pay* OR multi-level user charge* OR multi-level user-charge* OR multi-level charge* OR multi-level fee* OR multi-level formulary* OR multi-level subsid* OR multi-level benefit* OR tiered copay* OR tiered co-pay* OR tiered user charge* OR tiered user-charge* OR tiered charge* OR tiered fee* OR tiered formulary* OR tiered subsid* OR tiered benefit* OR differential copay* OR differential co-pay* OR differential user charge* OR differential user-charge* OR differential charge* OR differential fee* OR differential formulary* OR differential subsid* OR differential benefit*)
- (Reference drug* OR Reference pric* OR Reference based pric* OR Reference-based Pric*)
- (Therapeutic interchange* OR therapeutic substitut* OR drug interchange* OR drug substitut* OR product interchange* OR product substitut* OR generic interchange* OR generic substitut*)
- User fee
- User charge
- Co-payment OR Co-pay*
- Subsidy

Concept C – Search Filter (hedge) for Methodologies:

- "Randomized controlled trials" OR RCTs OR "Randomized controlled policy trials"
- (Pre OR Post) studies with nonrandomized comparison groups
- Comparative Study

- Time series*
- Interrupted time series analysis
- with comparison group*
- without comparison group*
- (Pre OR Post) studies without a comparison group
- "Post-only designs" OR "Nonrandomized post-only designs" OR Retrospective Studies
- Cross-sectional studies
- Longitudinal*
- longitudinal cohort
- longitudinal study
- Cohort studies
- Prospective Cohort
- Retrospective cohort
- Drug Utilization Review
- Concurrent Review
- Pragmatic trial
- Case-control
- Outcome
- Impact*
- Assessment*
- RCT* (apply prefab RCT filters)

In our search term brainstorming and collecting, we initially excluded or never came up with a few search terms that are used in the US context of predominantly private health care. These include:

- cost sharing
- formularies*
- health benefit plans/employee
- insurance, pharmaceutical services
- prescription fees

Inclusion/Exclusion criteria for search strategy

Inclusion criteria for systematic review
- Studies from 1986 to 2007
- English language
- Studies of countries with markets relatively similar to Canada
- Studies on the effects of drug benefit policies that utilized tiered or reference-based pricing
- Studies that employ patient-level data
- Studies that used designs from our list of acceptable methodologies
    - o randomized controlled policy trials,
    - o pre/post studies with nonrandomized comparison groups,
    - o interrupted time series analysis with comparison groups,
    - o interrupted time series without comparison groups, and
    - o pre/post studies without a comparison group
- Studies that measured outcomes from our list of identified outcomes
    - o health benefits and harms,
    - o changes in access to medicines,
    - o changes in use of other health care services,
    - o changes in drug costs,

- o changes in other costs,
- o changes in financial burden
- o OR other outcomes relevant to patient care and cost effectiveness

Exclusion criteria

- Qualitative studies such as focus groups
- Surveys of attitudes or opinions
- Articles containing only description, analysis, commentary, or opinion
- Studies using post-only or cross-sectional designs
- Studies that employ product-level data
- Studies of therapeutic interchange policies
- Studies of reference pricing of products other than prescription drugs
- Studies that focused on markets in developing countries