Drug Pricing and Value in Oncology vs. Other Areas in Medicine

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Value in Economics

- Maximizing value gained from resources used (economic efficiency) requires

- Value per $ spent is equalized across all uses

    - Health care vs. other goods and services

        - Within health: oncology vs. other conditions

- Creating consistent incentives and measures of value matters
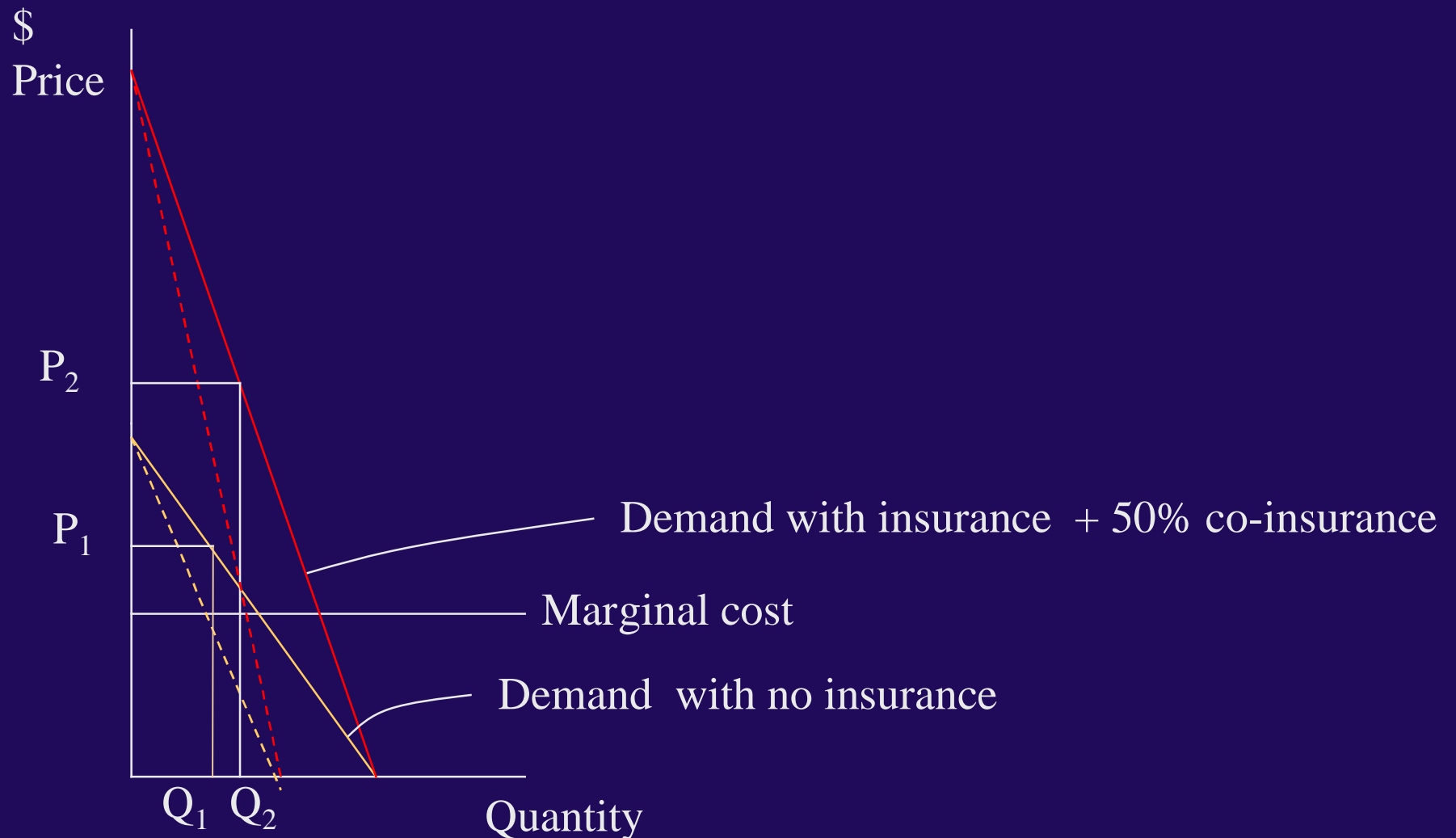
In Most Markets, Prices act as the "Invisible Hand" that Drives Efficient Resource Allocation

◆ Consumers express their values/preferences through prices they pay => willingness to pay

◆ Prices (net of costs) attract producer investment and production decisions

◆ Market prices assure efficient resource allocation IF
  – consumers are well informed
  – consumers face full social costs (no externalities)
  – given the distribution of income

With Health Insurance, Prices are not Constrained by Consumer Willingness to Pay

♦ Health insurance protects patients from financial risk

♦ But insurance undermines patient price sensitivity
   => consumer "moral hazard" on volume and price

♦ Cost sharing can only partially mitigate consumer moral hazard
   – Co-insurance percents generally low and subject to stop-loss

♦ Insurance also affects producer pricing
   – less widely studied

Passive insurance => Producers Rationally Raise Prices and Volume Increases

$
Price

P_2

P_1

Demand with insurance + 50% co-insurance

Marginal cost

Demand with no insurance

Q_1 Q_2

Quantity

Insurance Coverage Rules Influence Customer Incentives and Hence Manufacturer Pricing

- Three key customers for pharmaceuticals

- Patients cost-sharing structure
  - Tiered co-payments or coinsurance; stop-loss or fully at risk

- Payers
  - Formulary design => leverage for manufacturer rebates
  - Stand-alone drug budget vs. cost offsets in other services

- Physicians
  - Financial stake in prescribing + reimbursement rules

- Insurance differs for physician-dispensed vs. pharmacy-dispensed drugs => may influence pricing for oncology vs. other drugs

Pharmacy-dispensed Drugs are Managed by Pharmacy Benefit Managers (PBMs/PDPs)

- ◆ 3-4 tiered formularies with tiered copayments e.g. $5/20/35

- ◆ PBMs negotiate discounts on manufacturer in return for 2nd tier status
  - – Less leverage if few close substitutes e.g. cancer vs. statins

- ◆ Medicare PDPs are required to cover (substantially) all cancer drugs

- ◆ Some are on 4th tier with significant cost-sharing or co-insurance
  - – If patients expect to hit stop-loss, their expected marginal out-of-pocket price is zero

Physician-Dispensed Drugs, Including Most Oncologics, are Covered by Medicare Part B or Medical Benefit

- ◆ Pre 2005:   Medicare paid physicians 95% x AWP (Average Wholesale Price)
  - – Firms discounted to physicians, to increase margin and gain share
  - – Incentives for firms to raise AWP (a list price)

- ◆ Post 2006: Medicare pays Average Sales Price (ASP) + 6%
  - – ASP = volume-weighted average sales price including all rebates

- ◆ ASP+   reimbursement also creates perverse pricing incentives

  - – Raising price increases physicians' reimbursement and margin (with a lag)

Patient Cost-Sharing May be a Weak Constraint on Pricing for Cancer

Pharmacy Dispensed Drugs

- Most private PBM plans have significant co-pays for 3rd/4th tiers, BUT
- Private patients usually have a stoploss
- Medicare Part D PDPs must have a stoploss
- Cost-sharing is mostly covered for low income patients

♦ Physician Dispensed Drugs

- 20% co-pay on Medicare Part B is significant, BUT
- Most patients have supplementary coverage
    - Medigap or Medicaid, to cover co-payments
- Or referrals to hospital
- Or co-pay may be forgiven

Implications

- Medicare Part B rules create no incentive for manufacturers to compete by lowering prices

  - Applies to most cancer drugs and some RA and MS drugs
  - May contribute to higher prices for cancer than most other diseases

- Part B effects may spillover to pricing of competing Part D drugs

Empirical Evidence on Prices for Cancer vs. Other Diseases is Problematic

- ◆ Valid price comparisons require
  - – Common health outcome metric
  - – Adjustment for relevant cost offsets

- ◆ Cost/QALY is the most widely used measure
  - – But is not systematically estimated/published in US

- ◆ Medicare ASPs and IMS price data are per dose
  - – Not comparable across diseases

Canadian Coordinated Drug Review of Cancer vs. Non-Cancer Drugs, 5/2004-12/2008

	Cancer	Non-Cancer
# Drug Indications Reviewed*	10	100
# Drugs with Cost/QALY reported	**5****	**20**
Maximum	$126,500	$363,516
Mean	$73,900	$78,099
Median	$71,000	$61,000
Minimum	$36,000	$9,225
Recommendation		
Do not list	2	8
List	0	0
List in similar manner	0	1
List with criteria/condition	3	11
# Drugs without Cost/QALY	**5**	**80**
Do not list	3	39
List	0	4
List in similar manner	1	11
List with criteria/condition	1	26

* Including all final (most recent) recommendations from the CCDR for a given indication of a drug.

**Two analyses measured outcomes in life-years gained, not QALYs

Conclusions and Caveats on CCDR Data

- ◆ Weak evidence that cancer drugs are higher priced
  - Median cost/QALY slightly higher (but small sample)
  - Do-not-list rate slightly higher if no Cost/Qaly reported

- ◆ CCDR frequently questions cost/QALY estimates
  - Assumptions or lack of sensitivity analysis (one case)

- ◆ CCDR also considers effectiveness and price separately

- ◆ Cost/QALY data are frequently missing for various reasons
  - No analysis submitted
  - Manufacturer requested cost/QALY results not be published

Individual Drug Results, Ranked by Cost/QALY

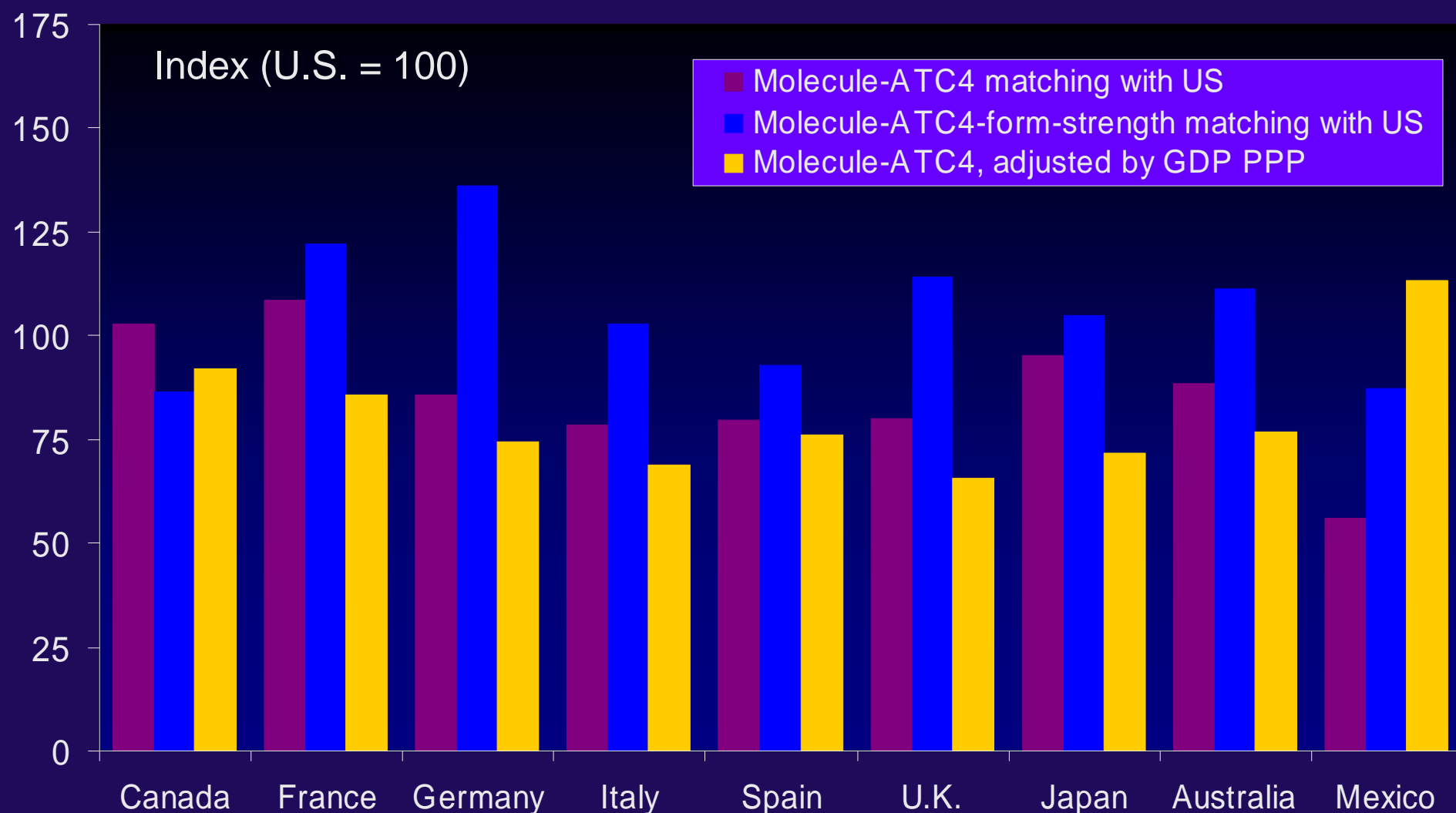| Chemical Name	Brand Name	Indication	Recommendation	Reason (effect)	Reason (price)	Cost/QALY (median)
Lumiracoxib	Prexige	Osteoarthritis (knee)	Do not list	Statistically significant improvements compared to placebo	Higher than generic forms; less than other therapies	$363,516 ($172,603)
Natalizumab	Tysabri	Multiple Sclerosis, relapsing-remitting	Do not list	No trials comparing with other drug therapy	More costly than other treatments	$185,000
Pegvisomant	Somavert	acromegaly	Do not list	Long-term benefits and risks are unknown	No comment	$137,000
Aprepitant	Emend	Chemotherapy induced nausea and vomiting	List with criteria/condition	Reduce number of patients experiencing emesis but not consistently shown to improve nausea	No comment	$126,500 ($52,750)
Adalimumab	Humira	Crohn's Disease	List with criteria/condition	Superior at inducing, maintaining remission compared to standard therapy	Higher than for standard therapies	$113,000
Telbivudine	Sebivo	Hepatitis B (chronic)	Do not list	While superior, relatively high proportion of patients will develop resistance	High cost compared to alternative therapy	$107,900 ($37,300)
Sunitinib	Sutent	Gastrointestinal stromal tumour (GIST)	List with criteria/condition	Statistically significant improvements compared to placebo	Costs more than alternative therapy	$80,000
Adalimumab	Humira	Ankylosing spondylitis (AS)	List with criteria/condition	Significantly more patients achieved improvement	No comment	$79,000
Adefovir dipivoxil	Hepsera	Hepatitis B	List with criteria/condition	Statistically significant improvements compared to other therapy	Much higher cost than other comparable therapy	$75,000
Erlotinib	Tarceva	Lung cancer, non-small cell	List with criteria/condition	Increased survival compared to survival for some indications of disease	No comment	$71,000 (per life-year gained)
Adalimumab	Humira	Arthritis, psoriatic	List with criteria/condition	Significantly more patients achieved improvement	Similar in price to other anti-TNF agents	$70,000
Deferasirox	Exjade	Iron overload	List with criteria/condition	Uncertain effectiveness compared with other therapy	Significantly greater than cost of alternative therapy	$67,595

Additional information, cont.

Chemical Name	Brand Name	Indication	Recommendation	Reason (effect)	Reason (price)	Cost/QALY (median)
Omalizumab	Xolair	Asthma, severe persistent	Do not list	No statistically significant improvement relative to placebo	No comment	$63,000
Pegaptanib sodium	Macugen	Macular degeneration, age-related	Do not list	Statistically significant improvements compared with placebo	No comment	$59,000
Sunitinib malate	Sutent	Metastatic renal cell carcinoma	Do not list	No data supporting the use of the drug in the group indicated	No comment	$56,000
Tipranavir	Aptivus	HIV infection	List with criteria/condition	Statistically significant improvement compared to other therapies	Significantly greater than cost of alternative therapy	$52,000
Rivaroxaban	Xarelto	Venous thromboembolism prevention	List with criteria/condition	Statistically significant improvements compared to other therapies	Lower than alternative therapy costs	$40,000
Ranibizumab	Lucentis	Macular degeneration, age-related	List with criteria/condition	Shown to be more effective	No comment	$38,150 ($16,975)
Sorafenib tablets	Nexavar	Renal cell carcinoma	Do not list	Differences not statistically significant compared to placebo	No comment	$36,000 (per life-year gained)
Insulin glargine (rDNA origin)	Lantus	Diabetes, Type 1 & 2	Do not list	No statistically significant differences compared to other therapy	Higher cost than for other comparable therapy	$32,200
Darunavir	Prezista	HIV infection	List with criteria/condition	Statistically significant improvements compared to other therapies	More than some therapies; less than one	$31,000
Rituximab	Rituxan	Arthritis, rheumatoid	List with criteria/condition	Significant improvements compared to other therapy	Cost significantly more than DMARDs; similar in cost to anti-TNF therapies	$18,400
Peginterferon alfa-2a and Ribavirin	Pegasys RBV	Hepatitis C, chronic	List in a similar manner to other drugs in class	Significantly higher positive outcomes compared to other therapy	Essentially identical to other therapy	$11,000
Entecavir	Baraclude	Hepatitis B (chronic)	List with criteria/condition	Statistically significant improvements compared to other therapy	Significantly greater than cost of alternative therapy	$10,000
Sitagliptin phosphate	Januvia	Diabetes Mellitus (Type 2)	Do not list	No trials comparing with other drug therapy	More costly than many alternative therapies	$9,225 ($4,307)

Cancer Drugs with No Cost/QALY Data

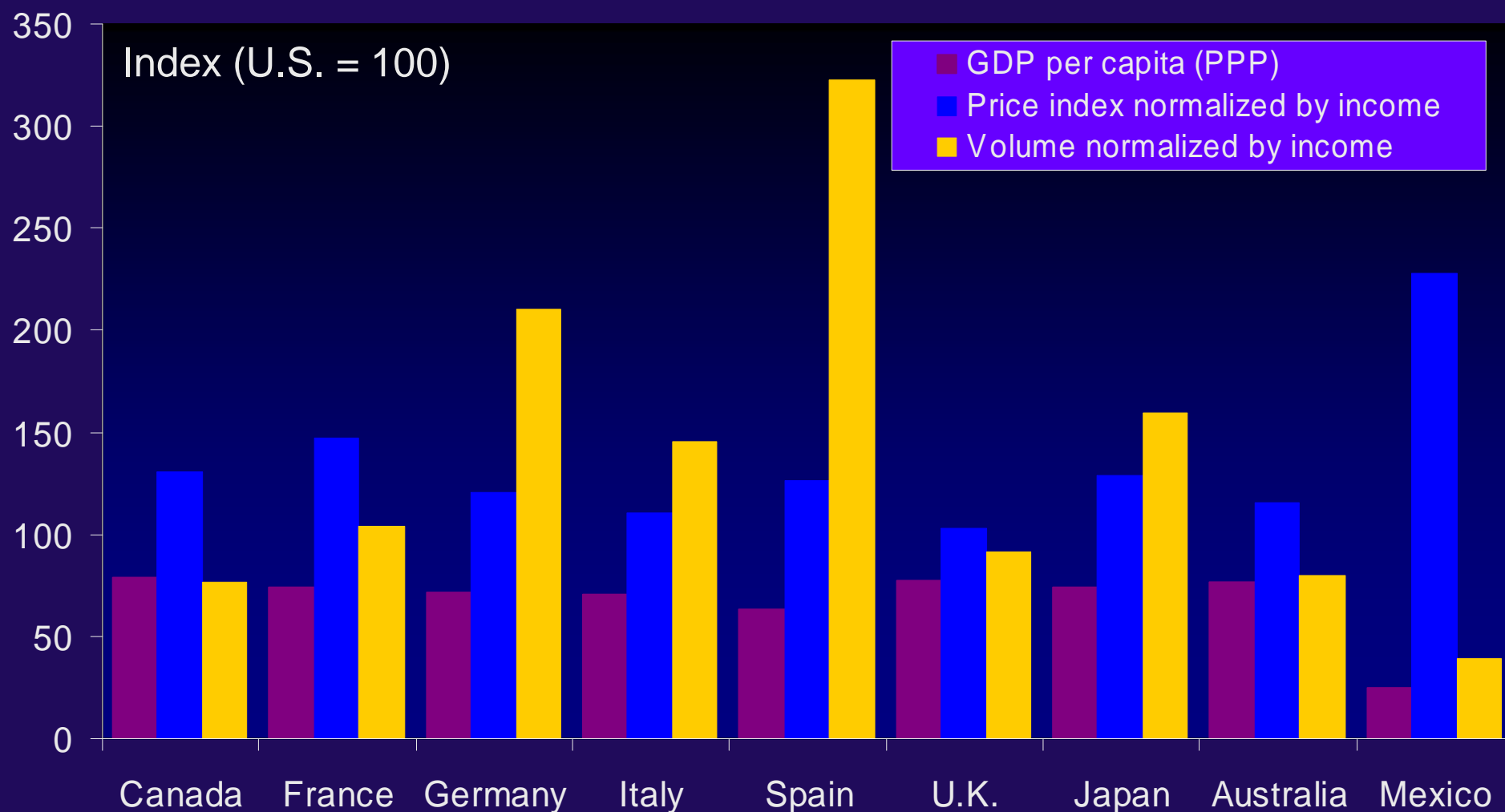| Chemical Name	Brand Name	Indication	Recommendation	Reason (effect)	Reason (price)
Delta-9-tetrahydrocannabinol / cannabidiol	Sativex	Cancer Pain (adjunctive analgesia to maximum tolerated strong opioids)	Do not list	Statistically significant improvement compared to placebo	Daily cost is higher than other agents
Gefitinib	Iressa	Lung cancer, non-small cell	Do not list	Effectiveness cannot be determined	No comment
Histrelin acetate	Vantas	Prostate cancer	Do not list	Lack of demonstrated therapeutic advantage over other therapies	Similar in cost or less costly than other therapies
Pegfilgrastim	Neulasta	Neutropenia	List with criteria/condition	No signifcant advantage compare to other therapy	On average, drug costs likely more than other therapy
Triptorelin pamoate	Trelstar	Prostate cancer	List in a similar manner to other drugs in class	No significant differences compared to other therapy	Similar to or less than other therapies

Biopharmaceutical Price Indexes, Relative to U.S. Prices (US=100)
All Biologics, Including Cancer

Index (U.S. = 100)

Legend:
- Molecule-ATC4 matching with US
- Molecule-ATC4-form-strength matching with US
- Molecule-ATC4, adjusted by GDP PPP

Countries: Canada, France, Germany, Italy, Spain, U.K., Japan, Australia, Mexico

Source: Danzon and Furukawa, *Health Affairs 2007.* Authors' calculations based on IMS MIDAS data, 2005

Biopharmaceutical Price and Volume Indexes, Relative to U.S. (US=100), Normalized by GDP Per Capita

Index (U.S. = 100)

Legend:
- GDP per capita (PPP)
- Price index normalized by income
- Volume normalized by income

Categories: Canada, France, Germany, Italy, Spain, U.K., Japan, Australia, Mexico

Conclusions: Comparing Prices Across Drugs/ Diseases Requires a Common Outcome Metric

♦ Lack of US data to compare cost/QALY across drugs is problematic for researchers

  – and presumably for physicians, payers and patients

♦ Insurance/reimbursement rules for physician-dispensed drugs, including cancer, may contribute to higher prices

♦ CCDR data provides some weak evidence that cancer drugs are higher priced

♦ Improving evidence on cost-effectiveness could improve choices in medical care and R&D investment