

# Seeking the balance between harm & benefit: the role of pharmacosurveillance in choosing what drugs we should take

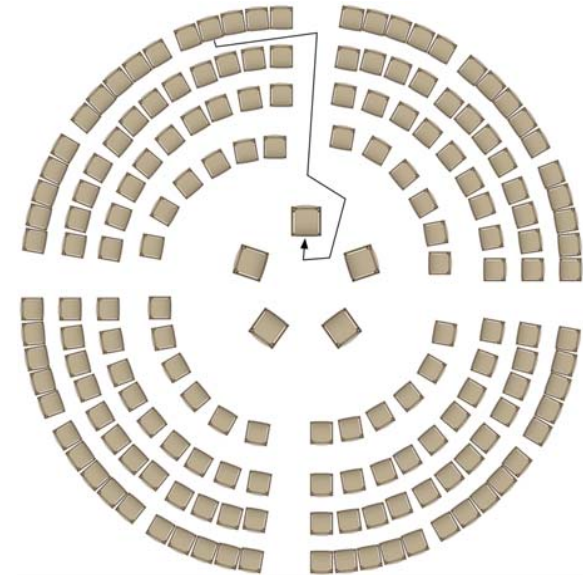
Colleen Metge (Chair)  
Ingrid Sketris  
Silvia Alessi-Severini

# Begin with the End in Mind

## Drug Safety & Effectiveness Network (DSEN)

# Fishbowl Conversation

Four to five chairs are arranged in an inner circle. This is the fishbowl. The remaining chairs are arranged in concentric circles outside the fishbowl. In an **open fishbowl**, one chair is left empty. The moderator introduces the topic and the participants start discussing the topic. The audience outside the fishbowl listen in on the discussion.



# Discussion Questions

(the group as policy/decision makers and healthcare manager discussants)

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- In light of DSEN's development, now might be a good time to discuss if we have done a good job at providing knowledge support to decisions about the effectiveness of prescription drugs and their use
  - *If yes, why do we perceive that the knowledge not been used?*

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- Both Lomas and Lavis (2005) made compelling arguments for moving away from researcher-driven knowledge translation towards co-production of knowledge (DSEN is set up to do just this) in order to use “better” evidence to make decisions
  - *They called for the establishment of “partnerships” between managers/policy makers and researchers so that a more comprehensive picture of the evidence might be available for the decisions to be made. How successful have you been at doing this?*

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- Finally, at the heart of the debate about informing policy making and management is a paradox:  
*“The more we attempt to make knowledge useable and context specific, the more difficult it becomes to draw on a repertoire of reviews or a stock of knowledge.”*
- Essentially, local partnerships, critical dialogues and reinterpretation in context will make a difference in the world of healthcare management & policy making.
  - *Who in the room operates in an environment like this?  
Please tell us your story!*

# Pharmacosurveillance

- Regular monitoring of medications in real clinical practice for benefits & harms
- MCHP's role has been to advance our knowledge about the benefits, harms and costs of medication
- How have we done?

# A model of a quality of care framework for examining a population's use of pharmaceuticals

## Donabedian's Model on Measures of Health Care Quality

Structure	Process	Outcome
Professional & organizational resources associated with the provision of care	Things done to and for the patient in the course of treatment	Desired states resulting from care, including a decrease in morbidity / mortality & an increase in QOL

## Proposed Model on measures of the Quality of the Population's Use of Pharmaceuticals

Utilization	Appropriateness	Effectiveness
Quantitative data on the access, extent, variability, and cost of the use of pharmaceuticals	Determination of whether the right drug was prescribed to the right person at the right time and dose	Outcomes or the net of benefit and harm* when a pharmaceutical is prescribed, dispensed, & taken under real-life circumstances

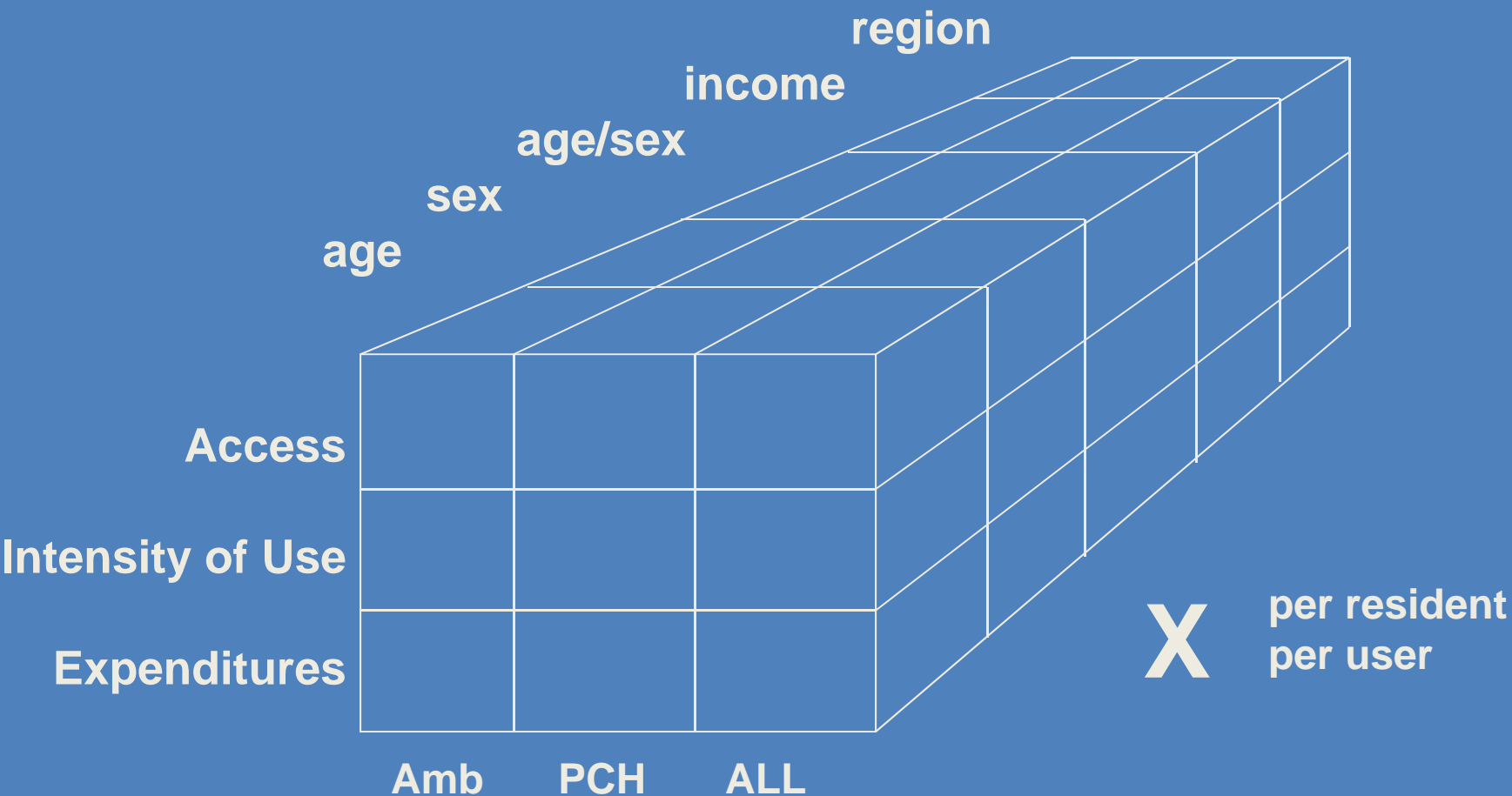
**Measures of outcome are often described as death, disease, disability, discomfort & dissatisfaction**

# Population-based rates of pharmaceutical use

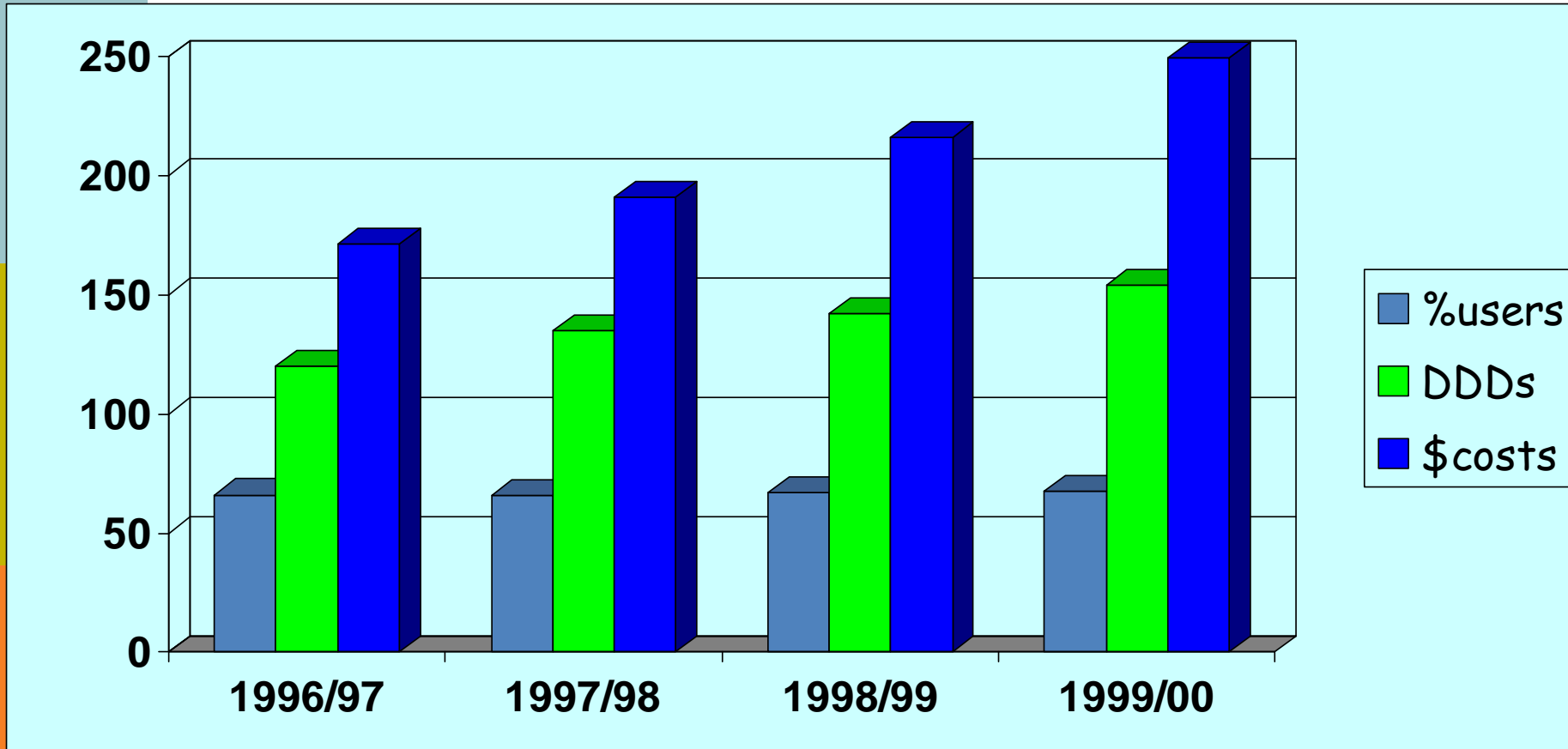
## Units of Analysis:

- **Access**: % Manitoba residents using at least one prescription (Rx) drug per year
- **Intensity of Use**:
  - # prescriptions (Rxs) dispensed per 1000 residents/pharmaceutical users (mean # Rxs/resident)
  - # different drugs dispensed/user (ATC Level 4)
  - # DDDs used per 1000 residents/users
- **Expenditures**: average cost/Rx, average cost/DDD, total expenditures by population characteristic

# Population-based rates of pharmaceutical use

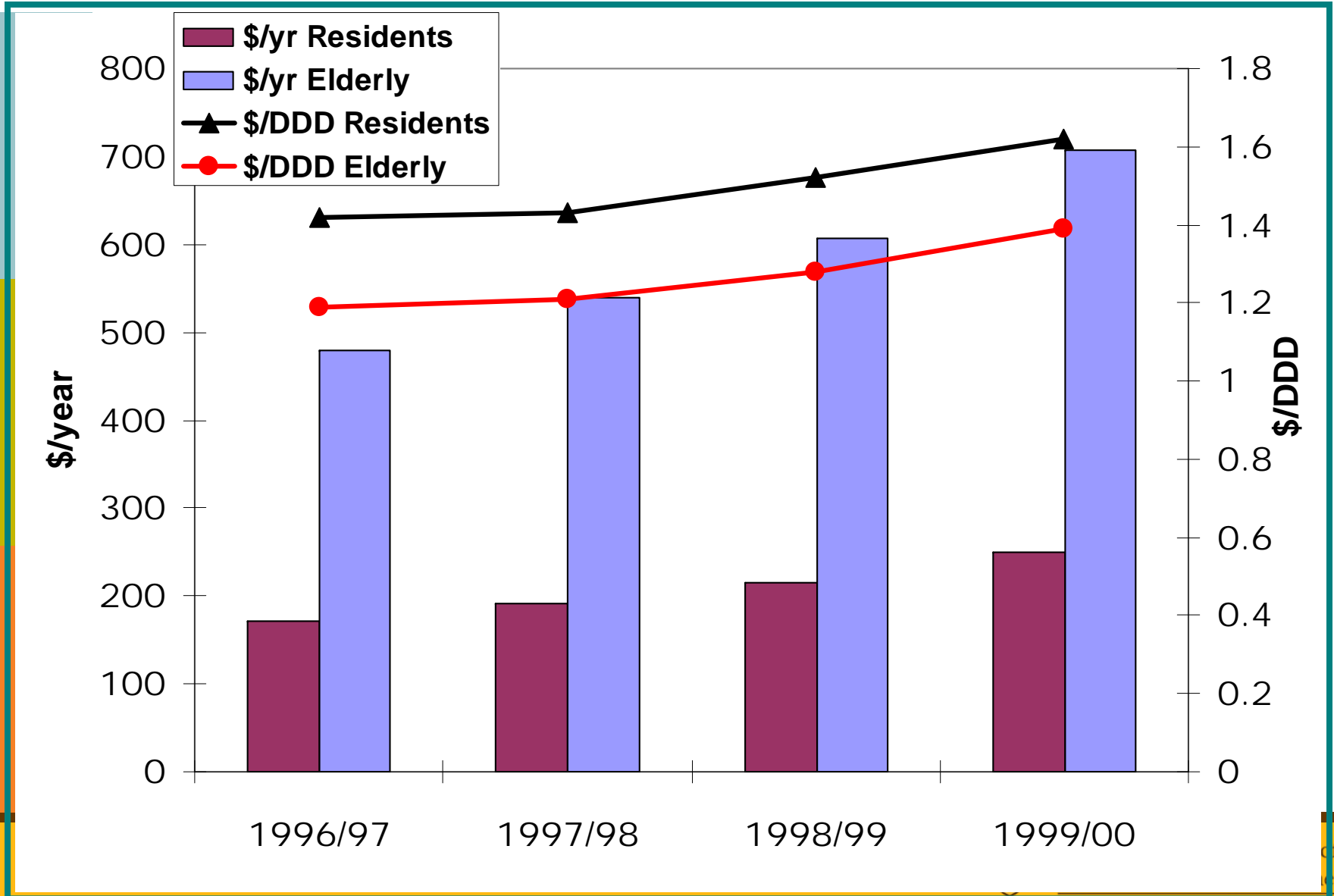


# Selected Population Use per Manitoba resident, 1996-2000 (fiscal)



% users 1996 (calendar): 66.3 (86.1)  
 # DDDs 1996 (calendar): 131.0  
 Expenditures 1996 (calendar): \$164.82

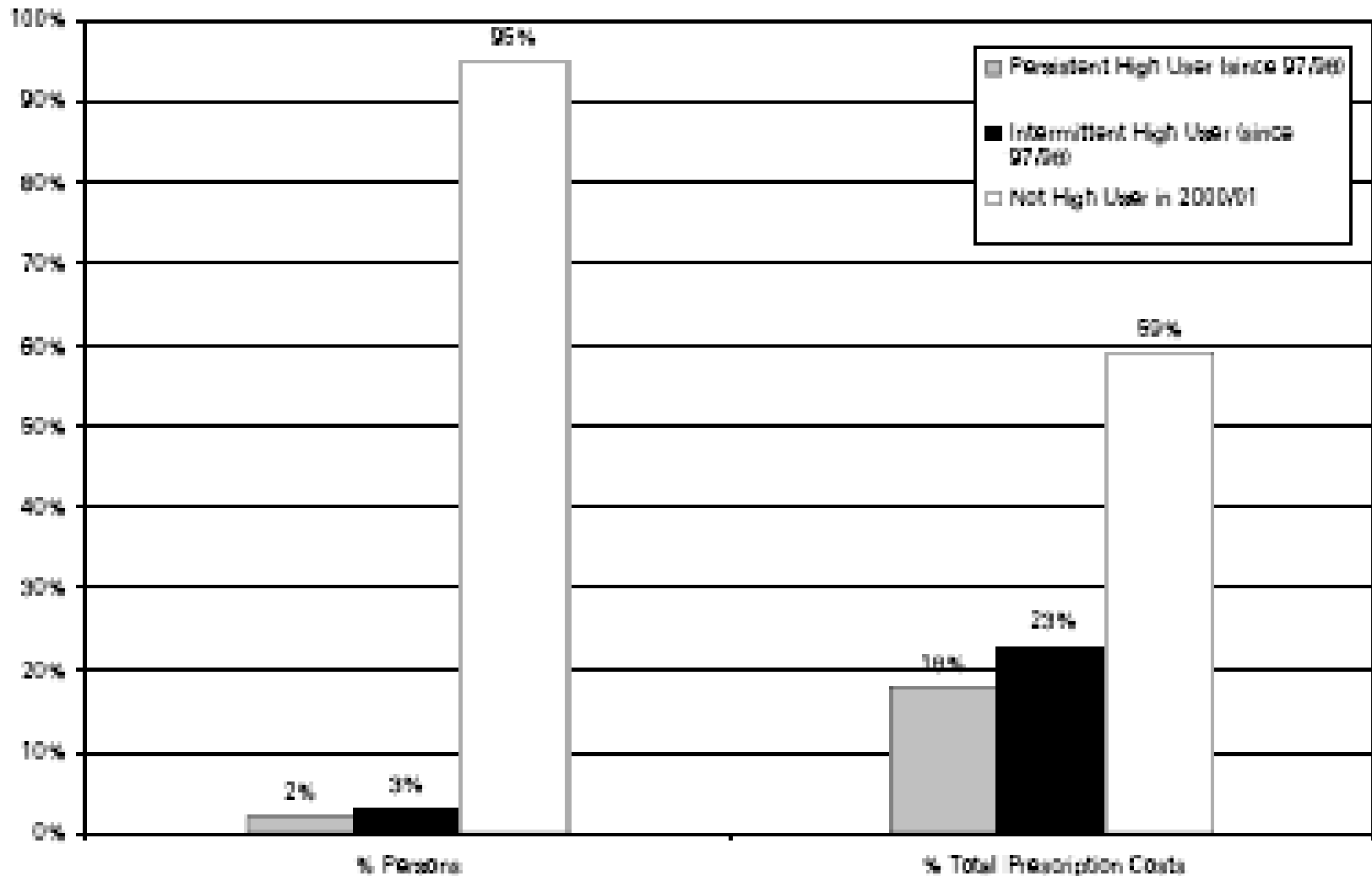
# \$s /DDD: Older Manitobans vs. Under-65s, 1996/2000



# High-Cost Users of Pharmaceuticals: Who Are They?

Kozyrskyj A, Lix L, Dahl M, Soodeen RA. MCHP 2005

Figure 1: High-Cost Pharmaceutical Users in 2000/01 - Percentage of Prescription Costs vs Percentage of Population Across User Groups

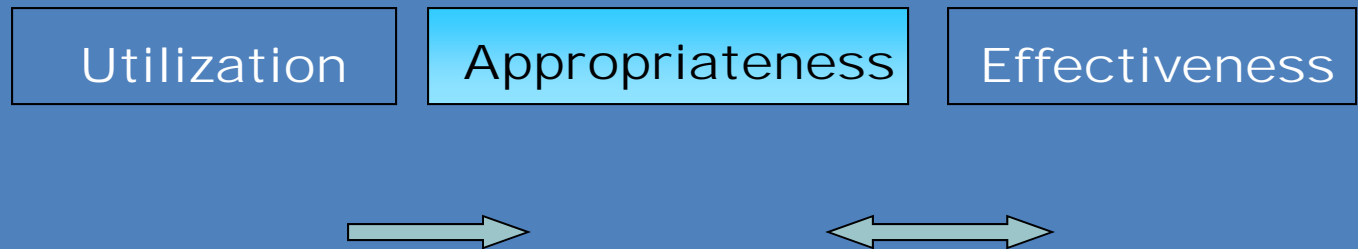


# Why appropriateness? and Where does it fit in assessing the Quality of Pharmaceutical Use?

*Romanow, 2002*



*MCHP, 2002*



*Donabedian, 1980*



# Agents acting on the renin- angiotensin system

## APPROPRIATENESS CRITERIA

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### *STEP UP\* APPROACH (to prescribing)*

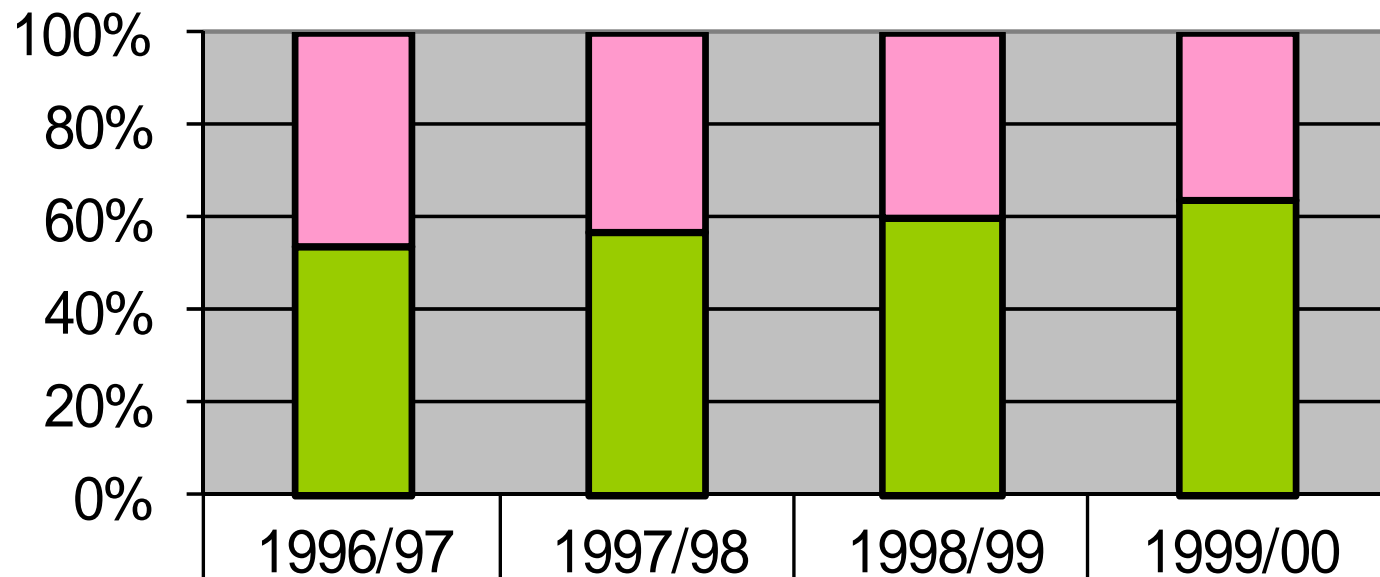
- in persons with a presumed diagnosis of uncomplicated hypertension (HTN) or hypertension with at least one existing comorbidity like diabetes, CHF, PVD, stroke

\*The act of applying (or prescribing) the minimum pharmacological force necessary to achieve a stated therapeutic objective when initiating therapy.

# Agents acting on the renin-angiotensin system

Treatment with an ACEI should be initiated prior  
to the use of an ARB

## Percent of New ARBs Users by Previous ACEI Prescriptions, 1996-1999



■ Previous ACEI	549	663	1196	1308
■ No Previous ACEI	646	874	1812	2302

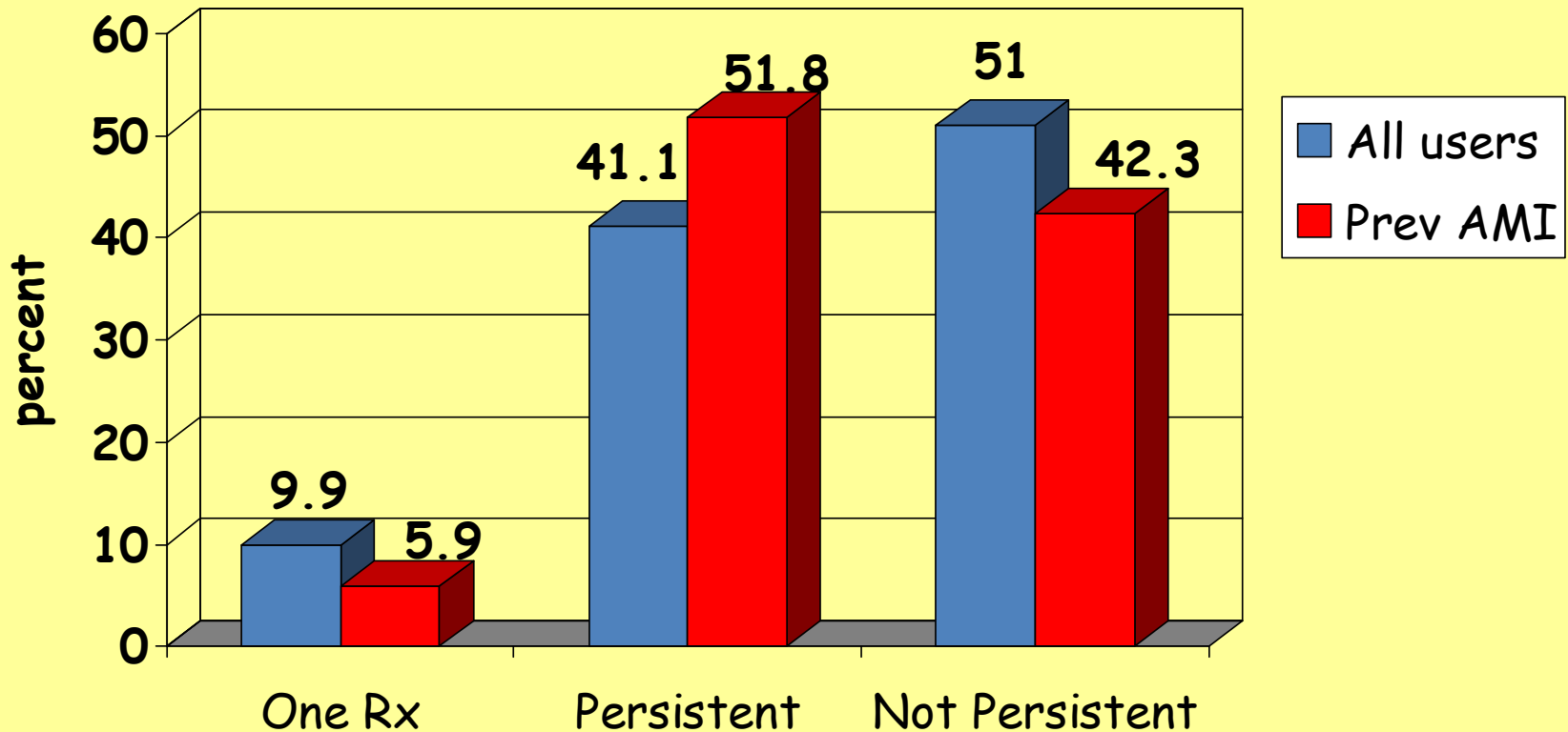
# Serum lipid reducing agents (statins) **THERAPY INITIATION**

## ***NEW Statin User?***

<b><i>Myocardial Infarction in previous 6 months?</i></b>		<b>Yes (n)</b>	<b>%</b>
	Yes	172	<b>2.4</b>
	No	7101	97.6
		7273	100

# Serum lipid reducing agents (statins) **PERSISTENCE TO TREATMENT**

Persistence to statin therapy given  
previous myocardial infarction, 1996/97



# Model for examining the population's use of pharmaceuticals

## Donabedian's Model on Measures of Health Care Quality

<i>STRUCTURE</i>	<i>PROCESS</i>	<i>OUTCOME</i>
Professional & organizational resources associated with the provision of care	Things done to and for the patient in the course of treatment	Desired states resulting from care, including a decrease in morbidity/mortality and an increase in QOL

## Model on Measures of the Quality of Pharmaceutical Use

<i>UTILIZATION</i>	<i>APPROPRIATENESS</i>	<i>EFFECTIVENESS</i>
Quantitative data on the access, extent, variability & cost of the use of medications	Determination of whether the right drug was prescribed to the right person at the right time and dose	Outcomes or the net of benefit and harm* when a pharmaceutical is prescribed, dispensed, and taken under real-life circumstances

\*Measures of outcome typically used to describe either outcome or effectiveness are the five *D*'s: death, disease including a co-morbid condition like side effects, disability or loss of optimal functioning, discomfort, and dissatisfaction (Lohr & Donaldson, 1990).

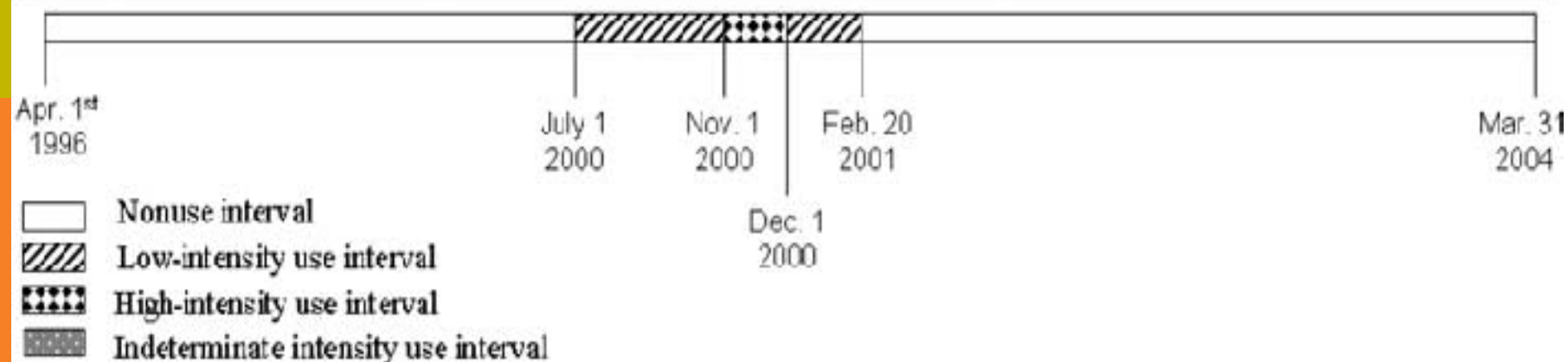
*Metge C, Grymonpre R, Dahl M, Yogendran M. Pharmaceutical Use among Older Adults: Using administrative data to examine medication-related issues. Can J Aging 2005; 24 (Suppl 1): 81-95.*

# Putting the Model Together

- Utilization
  - Targownik LE, Metge C, Leung S. (2007)
- Appropriateness
  - Targownik LE, Metge CJ, Leung S. (2008)
- Effectiveness
  - Targownik LE, Metge CJ, Leung S, Chateau D. (2008)
- Safety
  - Targownik LE, Lix LM, Metge CJ, Prior HJ, Leung S, Leslie WD. (2008)

## Example 1

Drug Filled	Dose/ pill	Date Filled	Qty Suppl.	Days Between Dispensations (DBD)	Final Date	Standard Dose	Calculated Dose Intensity (CDI)	Actual Dose Intensity (ADI)
Omeprazole	20	July 1 <sup>st</sup> , 2000	60	62	Aug. 31 <sup>st</sup> , 2000	20	1.03	1.03
Omeprazole	20	Sept. 1, 2000	60	61	Oct. 31, 2000	20	1.02	1.02
Omeprazole	20	Nov. 1, 2000	60	30	Nov. 30 <sup>th</sup> , 2000	20	2.00	2.00
Omeprazole	20	Dec 1 <sup>st</sup> , 2000	30	40	Jan. 9 <sup>th</sup> , 2001	20	0.75	0.75
Omeprazole	20	Jan 10 <sup>th</sup> , 2001	30	Terminal	Feb. 20 <sup>th</sup> , 2001	20	undefined	0.75

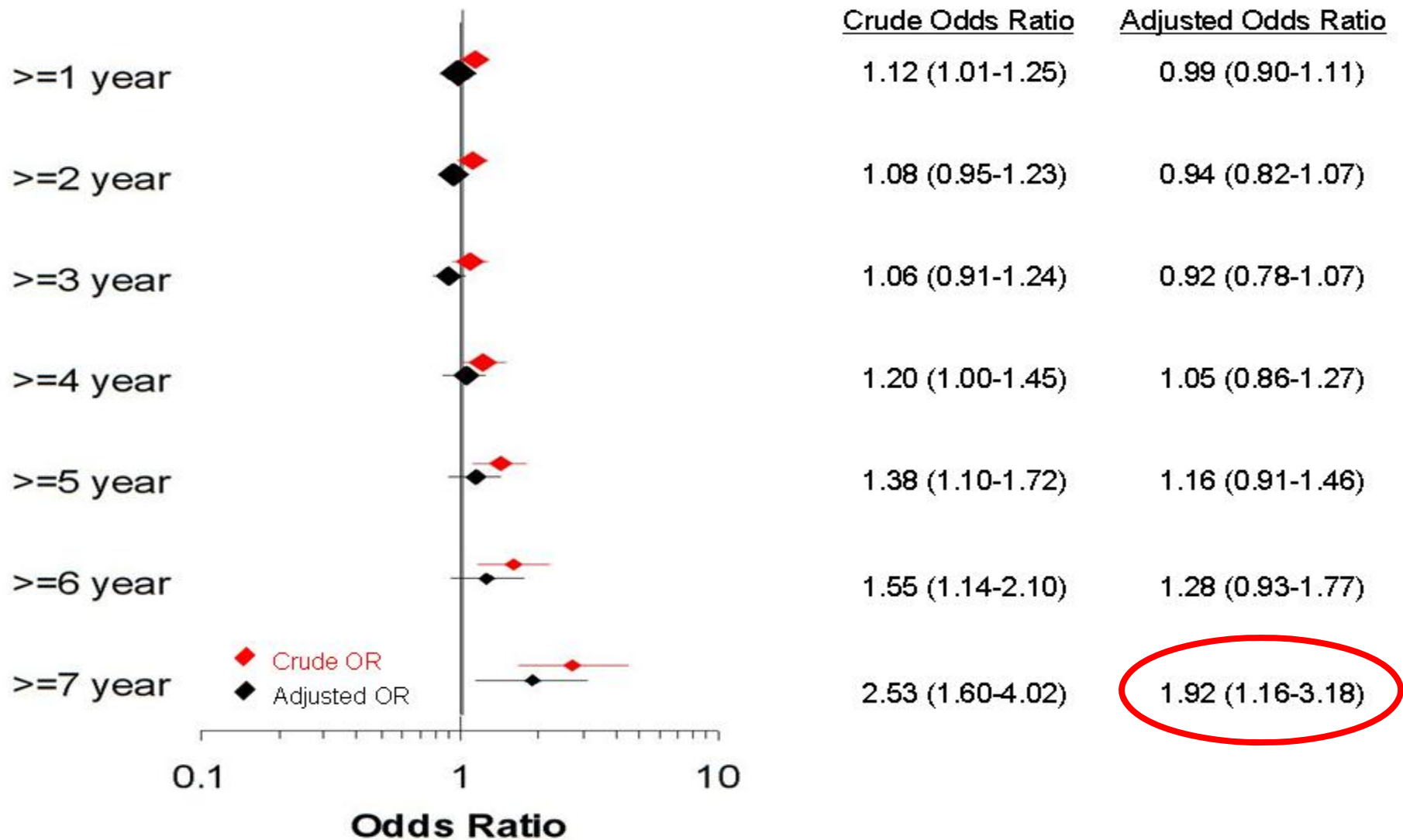


# Results

## odds of osteoporotic fracture for intervals of PPI exposure

- Conditional logistic regression analyses (odds ratios [OR] and 95% confidence intervals) are adjusted for:
  - income, region of residence, diagnoses (short/long term diabetes, epilepsy, ischemic heart disease, myocardial infarction, hypertension, arthritis, solid organ transplant, chronic obstructive pulmonary disease, substance use, depression, schizophrenia, dementia), home care use and multiple medications.
  - reference group is subjects with no PPI or H2RA use.

(a) Combined hip, vertebral, and wrist fractures



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