

# Validity of data sources in pharmacoepidemiology

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# Disposition

- 1. Defining validity
- 2. Internal vs external validity
- 3. Describing the process from prescribing to ingestion
- 4. Areas of major and minor uncertainty in the prescribing process
  - Prescribed vs purchased medication
  - Purchased vs ingested medication
  - Ingested medication vs verbal account of medication
- 5. Some examples of validity studies of data sources.
- 6. How to read a paper on validity
- 7. Does the choice of data source make a difference in QI?
- 8. Some conclusions
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# Validity definition

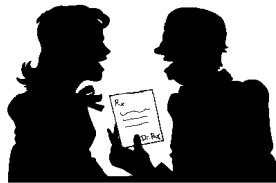
- Of latin verb *valere*: being strong
- The validity of a measurement can be defined as the degree with which the measured value reflects the characteristic it is intended to measure.
- Roger J. Lewis,
- - implies the comparison of a measurement against a superior representation (or measurement) of its object.

# Internal and external validity

- Internal: pertains to the study sample itself
  - Are the data correct?
    - Technical problems in data transfer?
    - Which data source is most accurate? (for what purpose?!)
- External: pertains to the reality outside the study sample
  - Is the studied population representative?

# Describing the process from prescribing to ingestion

Event



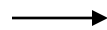
# Describing the process from prescribing to ingestion

**Event**

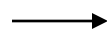
**Proxy**



Physician administrative system, e.g. GPRD in UK



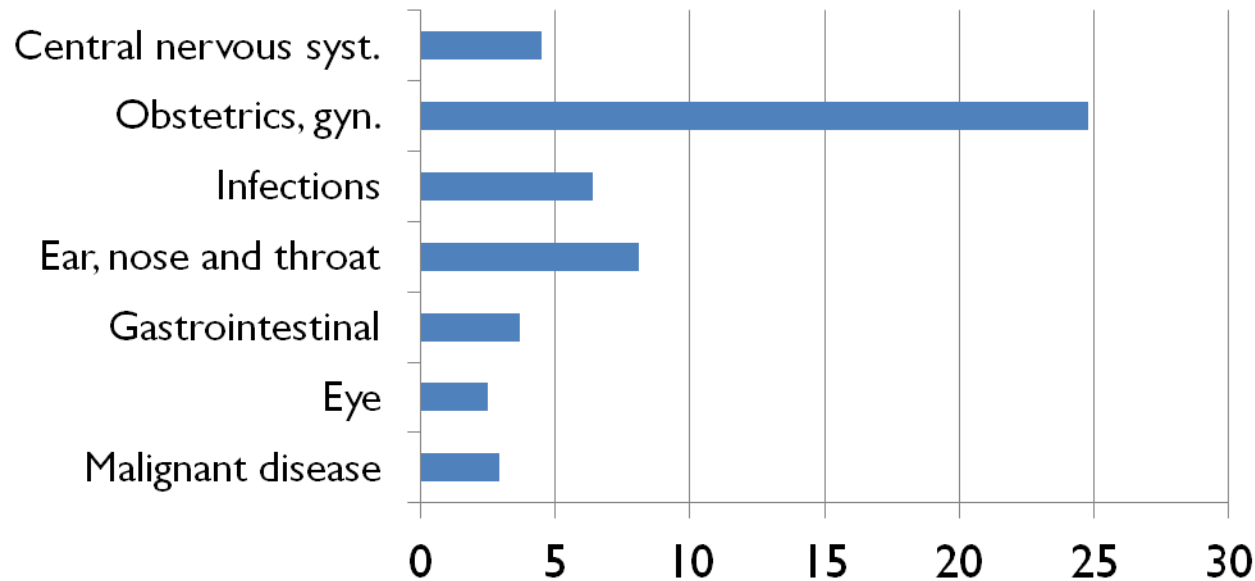
Pharmacy-based prescription database, e.g. MEDICAID, MEMO, OPED



Interview

# Primary non-compliance; what prescriptions are not redeemed?

20.921 prescriptions issued in a large rural practice  
retrieved in a pharmacy-based research database  
(MEMO, Scotland).

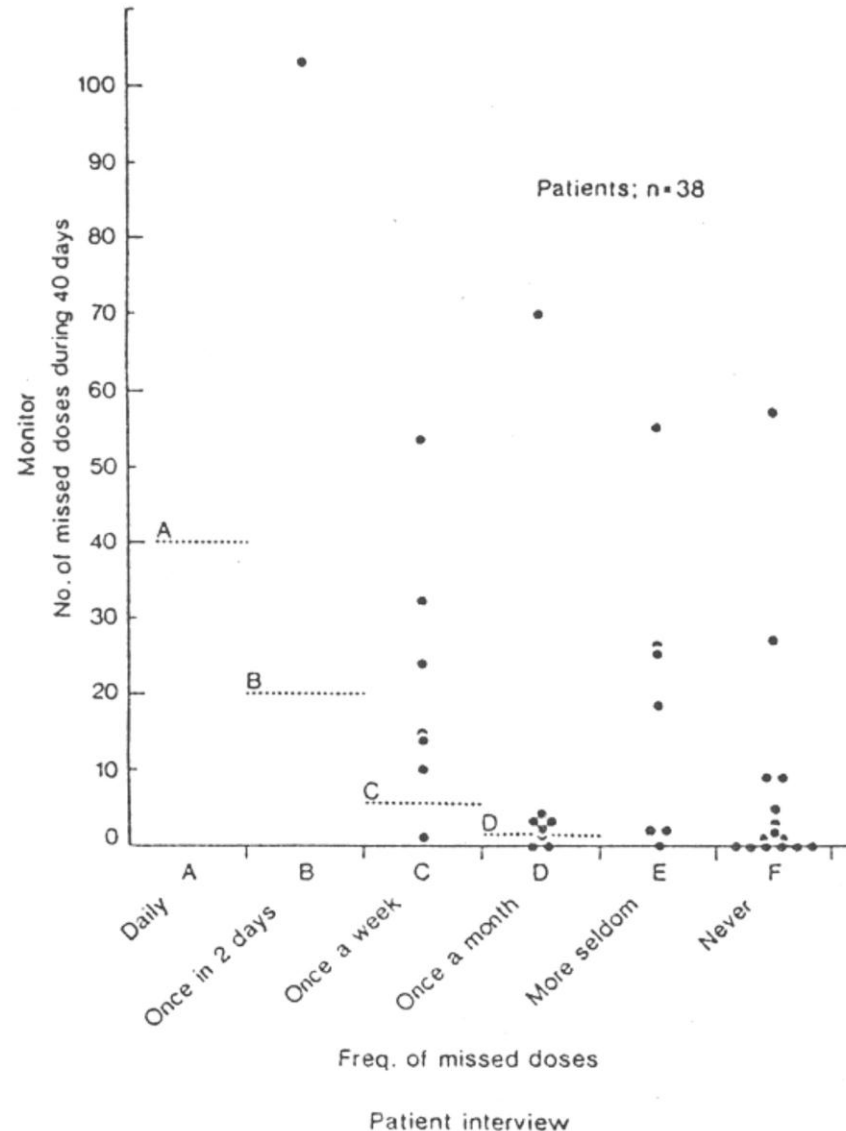


**"Observational studies of drug exposure can be more accurately estimated from dispensing rather than prescriber data"**

# Validity problems; can patients' account be trusted?

- 38 patients
- Pilocarpin eyedrop t.i.d. for 40 days
- Compliance estimate by structured interview
- Compliance measured by electronic device

Norell SE. Soc Sci Med 1981;  
15E: 57-61.





# Comparison of interview and electronic monitoring device: findings

- No statistical correlation between estimated and actual compliance
- Gross non-compliance occurred among subjects with an estimated perfect compliance
- Patient were never more compliant than claimed

Norell SE. Soc Sci Med 1981;  
15E: 57-61.

# Data on drug exposure

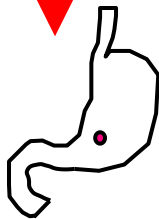
## Which is best?



Physician administrative system, e.g. GPRD



Pharmacy-based prescription database

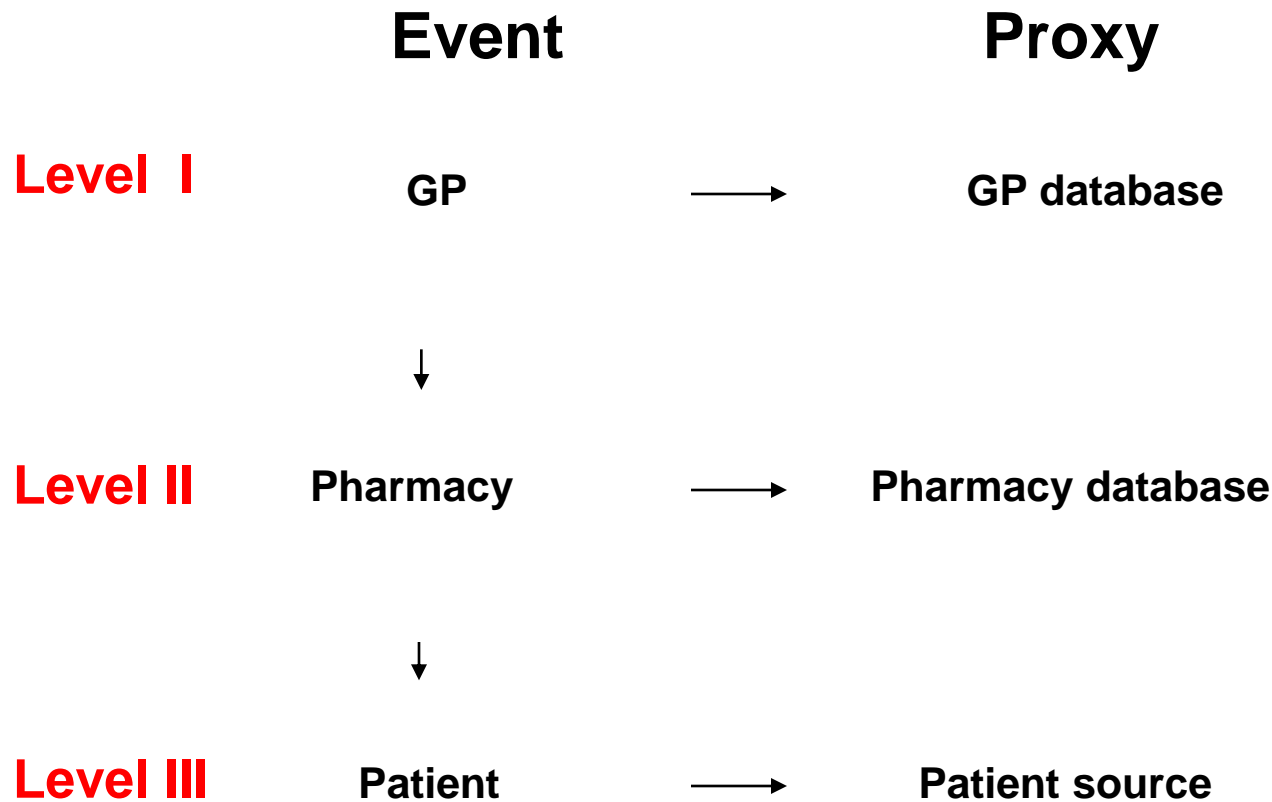


Interview



Area of major uncertainty

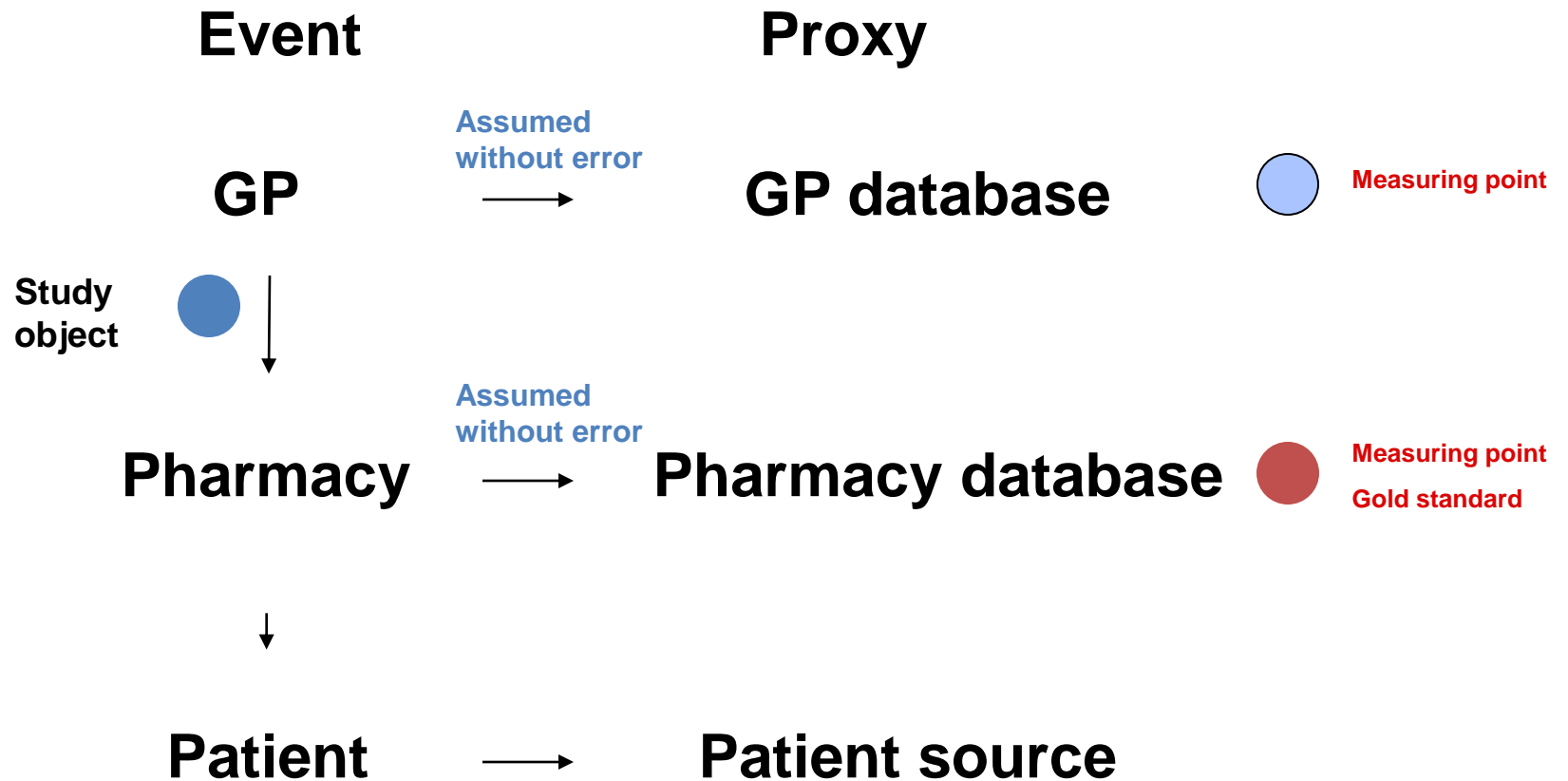
# Validity studies: grid of data flow



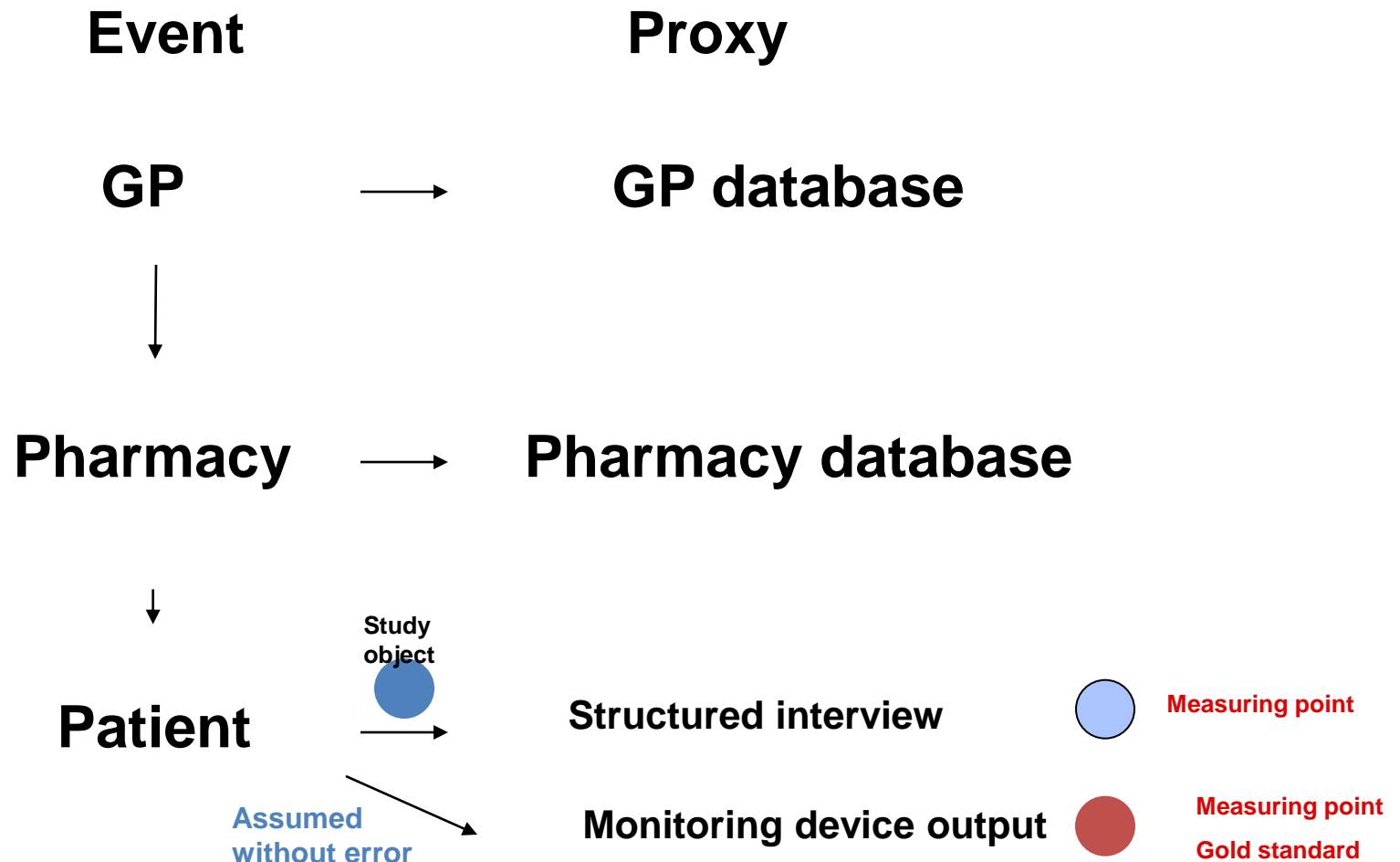
# Measuring internal validity: taxonomy

- Indicate levels of comparison (level I-III)
- Indicate patient group
- Indicate gold standard for comparison
- Indicate tools for data acquisition (level I-III)
- Indicate possible limitations/exemptions of data transfer (level I-III)

# Validity grid: Beardon study



# Validity grid: Norell study

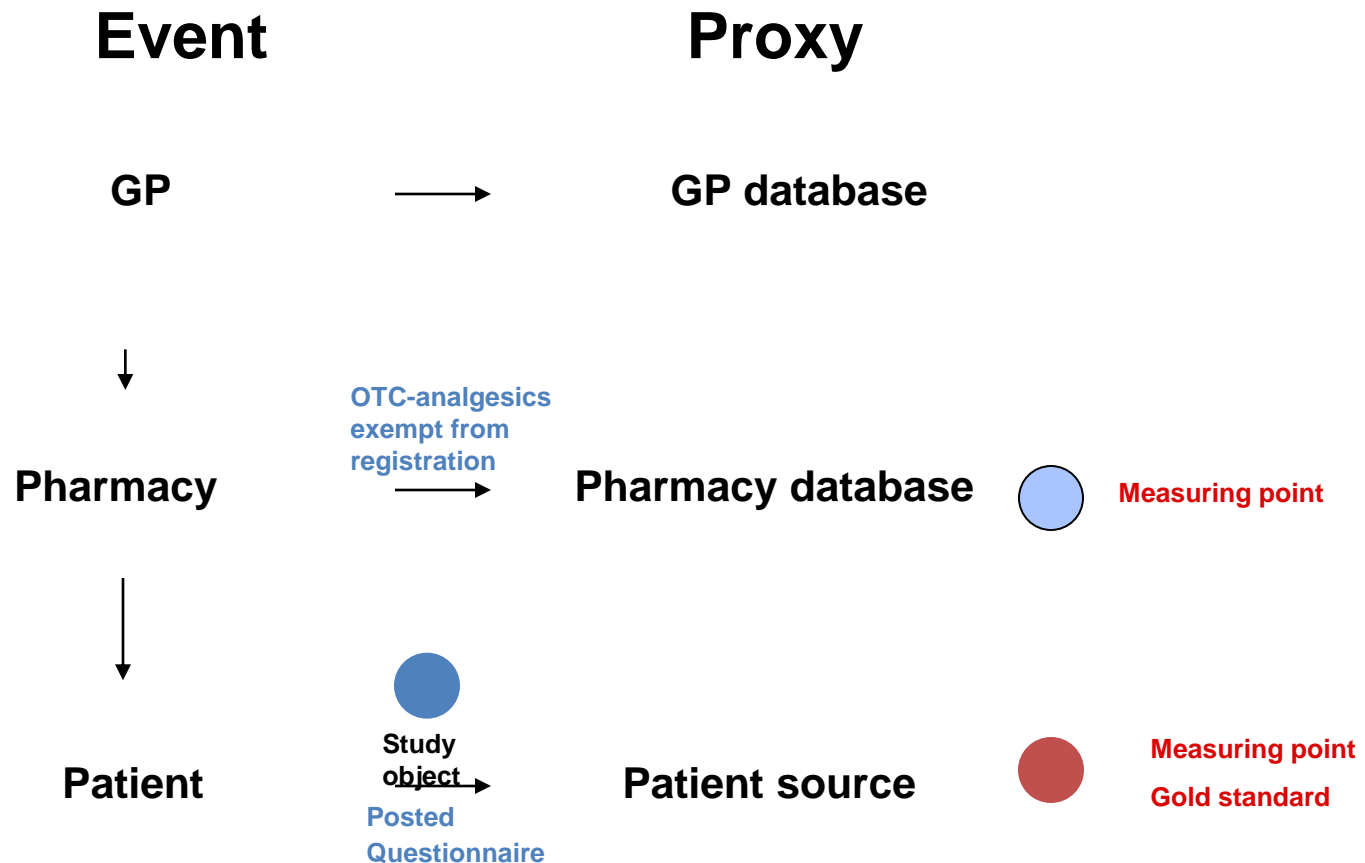


## Comparison between interview and register data

- Participants in a questionnaire-based national survey of pregnant women (N=2041) were retrieved in a prescription database (PDNJ) by use of a 120 day window

Drug	Reported by interview	Retrieved in database
Beta-blockers	6	5
Insulin	11	11
Thyroid drugs	12	9
Diuretics	4	3
Antidepressants	11	10
Analgesics	828	17
Topic corticosteroid	25	55
Antibiotics	204	310

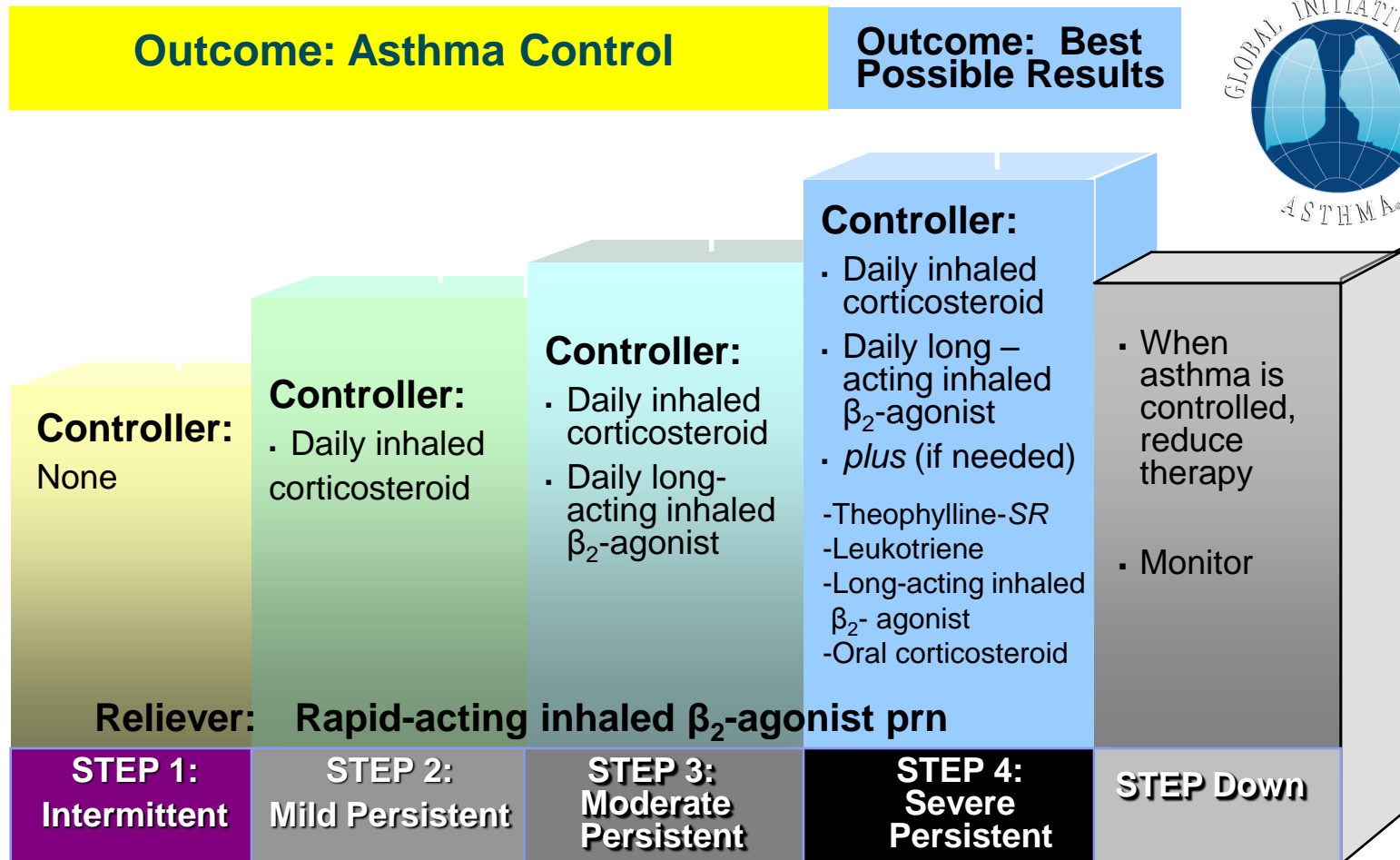
# Validity grid, Olesen study





**Does the choice of data  
source make a difference in QI?**

# Stepwise Approach to Asthma Therapy - Adults



Alternative controller and reliever medications may be considered (see text).

# Validity of quality indicators for assessing the quality of asthma prescribing


- Dutch GP based prescription database (N=30.486) in 1997
- 146 patients aged 18-49 with asthma
- Subjected to database analysis
- Subjected to interview and diagnostic work-up (gold standard)

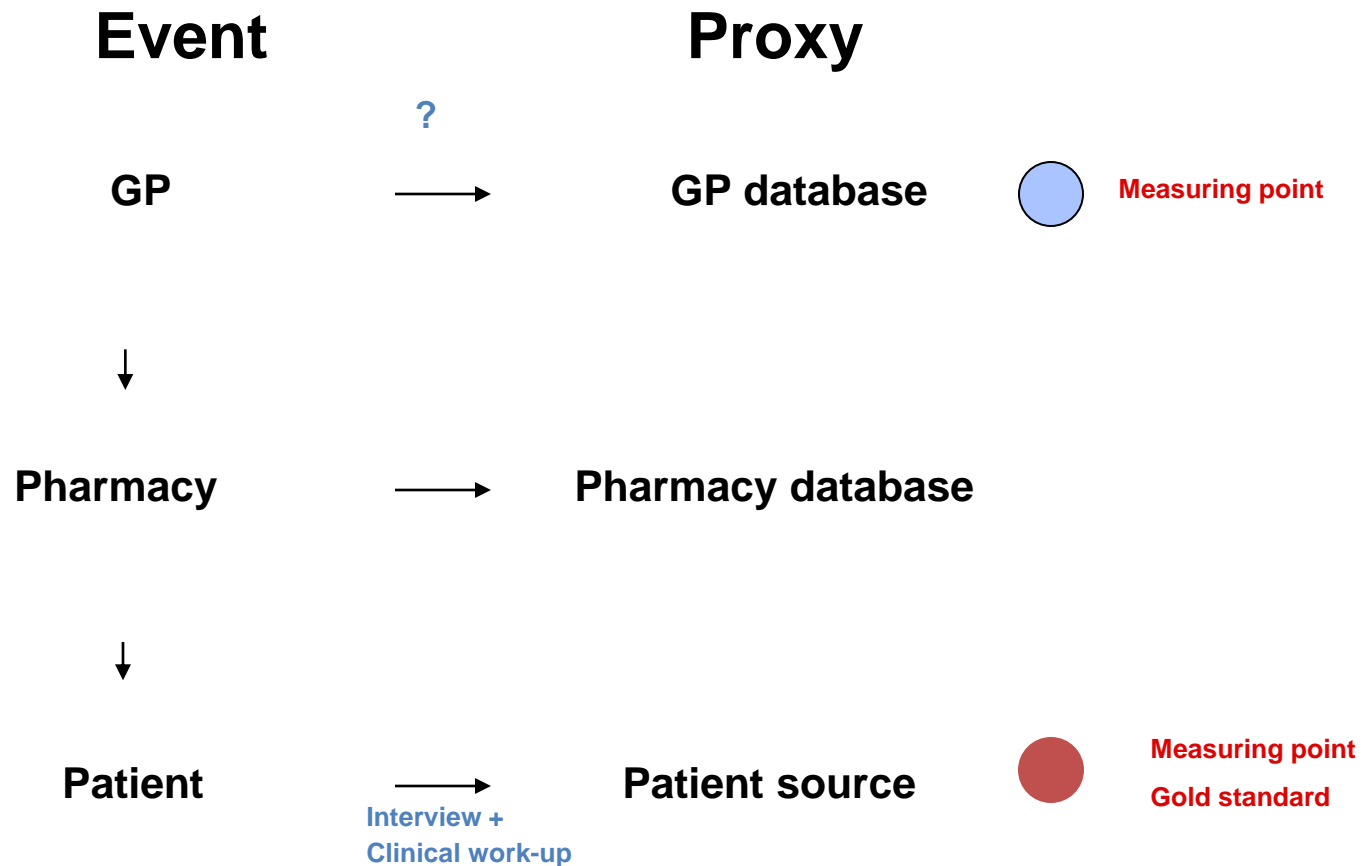
## Sensitivity and positive predictive values for database-derived quality indicators in asthma

<b>Indicator</b>	<b>Problem</b>	<b>Sensitivity</b>	<b>Positive predictive value</b>
<b>Step 1</b>	<b>No inhaled beta-agonist</b>	<b>0.86</b>	<b>0.52</b>
<b>Step 2A</b>	<b>No inhaled corticosteroid, +/- inhaled betaagonist</b>	<b>0.74</b>	<b>0.46</b>
<b>Step 2B</b>	<b>Daily use of an inhaled beta-agonist, no inhaled corticosteroid</b>	<b>0.37</b>	<b>0.71</b>
<b>Step 3</b>	<b>Inhaled beta-agonist &gt; once daily but low dose inhaled corticosteroid</b>	<b>0.07</b>	<b>0.20</b>
<b>Step 4</b>	<b>Inhaled beta-agonist &gt;once daily, adequate dose inhaled corticosteroid, no LABA</b>	<b>Too few patients to validate</b>	

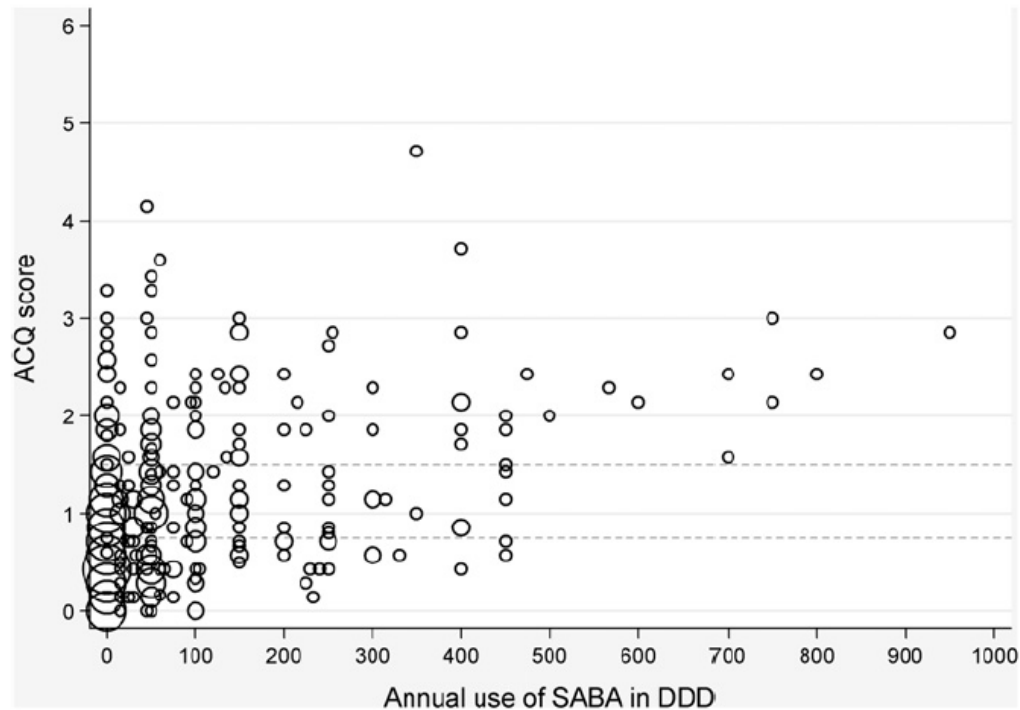
Pont Lisa G, Eur J Clin Pharmacol 2004

# Validity grid: Pont study

  
Study  
object



# Lack of validity for database derived asthma QI, why



**Fig. 2.** Distribution of ACQ scores according to individual annual use of SABA in DDD. Area of circles proportional to the number of subjects for each data point. ACQ = Asthma Control Questionnaire. SABA = short-acting beta-2-agonists. DDD = defined daily dose.

# Studies of agreement between prescription data sources

Reference	Drugs	Comparators Gold standard	Finding
Norell 1981	Eye drops	Interview vs EMD III vs III	Poor correlation between estimated and actual compliance
Pont LG 2004	Asthma medication	Interview + work-up vs GP. I vs III	Poor performance of GP derived quality indicators
Barat I 2001	All, elderly patients	Interview vs GP I vs. III	20-70% non-adherence, depending on dose regime, knowlegde about drug, toxicity etc
Olesen C 2002	All, pregnant women	Questionnaire vs pharmacy. II vs III	Good agreement for chronic treatments, poor for antibiotics and analgesics
Enlund H 1981	Users of antihypertensives	Interview vs pharmacy. II vs III	94% agreement. Patient interview gave an overestimation of compliance
de Jong-van den Berg LT 1993	All, pregnant women	Interview vs pharmacy. II vs III	The two modes are complementary. Performance dependent on study object. Pharmacy record preferable in long recall or complicated regimes
Van den Brandt PA 1991	All prescribed	Questionnaire vs pharmacy. II vs III	Sensitivity 61%, specificity 100%
Lau HS 1997	All prescribed	Medical inventory vs pharmacy II vs III	Sensitivity improved with increased observation window
West SL 1995	NSAID and estrogen up to 12 years in the past	Interview vs pharmacy. II vs III	Sensitivity 41-78& depending aot on number of prescriptions. Sprecificity 92-100%
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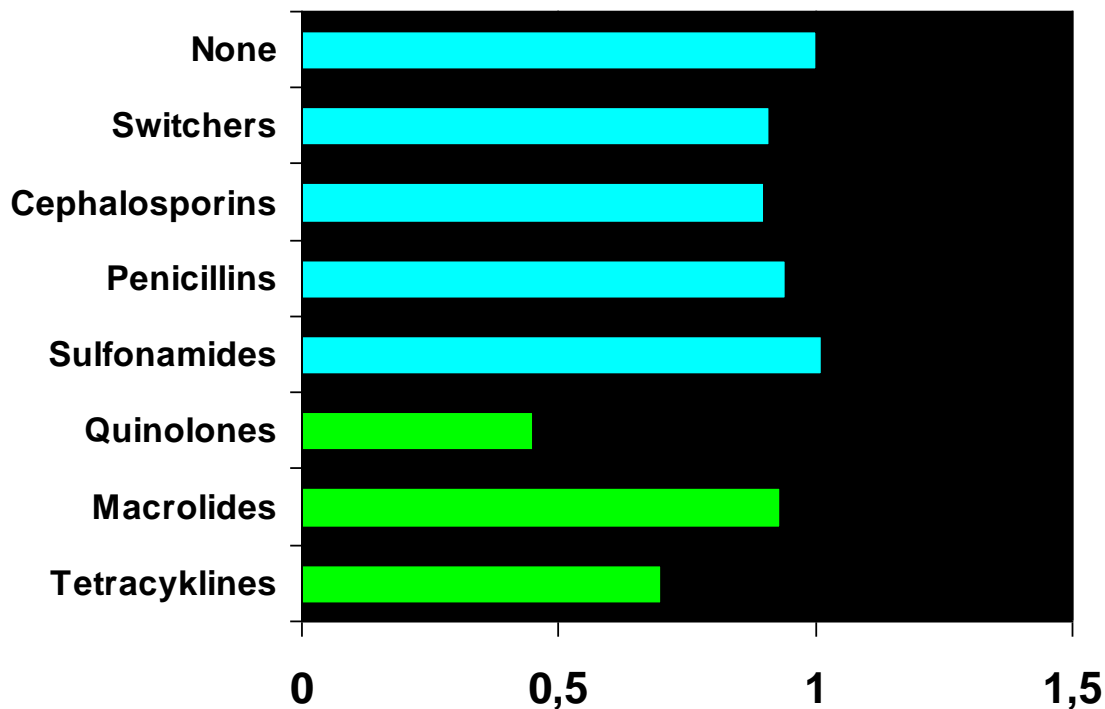
# Studies of internal data validity, statements

- True gold standards do not exist. They are all alloys.
- Technical data errors are rarely reported
- Non-compliance is substantial and is difficult to ascertain
- Failure to redeem prescription is a minor problem for most drug classes
- Databases may have important limitations, e.g. absence of non-subsidized prescription medication
- Recall errors of omission are much more common than errors of commission. Rather forget than make something up.
- Recall is dependent on chronicity



# Data on drug exposure

## An example; antibiotics and myocardial infarction



**Background: Antibiotics with effect against Chlamydia Pneumonia might protect against AMI**

**Exposure: any antibiotic 3 years before the index date.**

**Cases: 3315 persons with first-time MI**

**Controls :13,139 without MI.**

# Question

- Given that the source of data has a strong impact on QI, should we endeavour to use
  - GP source?
  - Patient level source?
  - Something else?

When assessing the quality of the prescribing?