Methodological Framework and Tools for Cross-National comparisons of Drug Utilization Data

Vander Stichele RH, MD, PhD

Heymans Institute of Pharmacology, Ghent University, Belgium

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OVERVIEW

1. Definition of drug utilization research and deliniation from other scientific fields

2. Methodological framework for drug utilization research

3. The micro level of drug utilization
   Understanding prescribing behavior and patient drug taking behavior

4. The macro level of drug utilization
   Tools for cross-national comparisons of drug utilization data
Definitions

Epidemiology
Clinical pharmacology
Pharmaco-epidemiology

Drug utilization research
DISEASE

Epidemiology

POPsULATION

Pharmacoepidemiology

DRUG

Clinical pharmacology
Pharmacoepidemiology

Epidemiology

Clinical pharmacology

Public Health

Pharmacoepidemiology

POPULATION

DISEASE

DRUG
DEFINITIONS

Epidemiology

“the study of the distribution and determinants of health-related states and events in the population, and the application of this study to control health problems”

Clinical Pharmacology

“the study of effect of drugs in humans.”

Pharmacoe-epidemiology

“the study of the utilization and effects of drugs in large numbers of people.”
Pharmaco-epidemiology (delineation of its core)

- To determine the (balance between benefit and) risk of the use of medicines using population-based databases

Related to:
- Pharmacovigilance
- Pharmaceutical Outcomes Research
- Pharmacoconomics
- Health Technology Assessment
DEFINITION OF DRUG UTILIZATION RESEARCH

Drug utilization research

is an eclectic discipline, integrating
descriptive and analytical methods for
the quantification,
the understanding and
the evaluation of
the processes of
prescribing,
dispensing and
consumption of medicines
and for
the testing of interventions
to enhance the quality of these processes.
Methodological framework
## Conceptual framework for drug utilization research

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[Diagram showing the framework with the focus on Patient compliance studies]
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Historical roots of the field:

In Europe

Development of the drug classification system (WHO ATC/DDD) system in the Nordic countries for wholesaler drug sales statistics from 1969 (Euro-DURG).

In the US and Canada

Drug Utilization Review (Evaluation) in hospitals with the start of Clinical pharmacy (Brodie, 1972).

In the world

Movement to promote rational drug prescribing (INRUD – 1972)
FOUR FACES OF DRUG UTILIZATION RESEARCH

- Drug utilization monitoring systems
- Prescribing quality indicators
- Qualitative research
- Intervention research
THE MICRO LEVEL OF DRUG UTILIZATION RESEARCH

Understanding prescribing and drug taking behavior
The drug choice process of the physician

- 4000 products on the national market
- 200 products prescribed by 1 GP
- Clinical problem
- Evoked set
- 4
- 1 prescribed product

(De Muijnck, 2002)
The drug choice process of the patient

To be aware of a problem

To go and see the doctor

To go and see the pharmacist

To accept and start the prescribed medicine

To continue the treatment
Dynamical changes in risk/benefit ratio

Benefit

Risk

Dosing events

time
Dynamical changes in risk/benefit ratio

Benefit
Risk

Dosing events

time
THE MACRO LEVEL OF
DRUG UTILIZATION RESEARCH

Tools for cross-national comparison of
drug utilization
Examples of methods used for international (cross-national) drug utilization research

Health surveys
Cross sectional descriptive studies
Rapid assessment of health services
Qualitative studies
Disease register studies
Clinical Cohort studies
Database Cohort studies
Claims and prescription database studies
FOCUS ON:

Cross-national studies,
aiming to compare overall drug utilization patterns
(of all medicines or of big classes of medicines)
of the entire population of the country
by collecting census data,
consistent over time
Basic requirements of a minimal national data set on Drug Utilization Data for cross-national comparisons

Comprehensive collection of drug consumption data
- from all citizens of the country
- from all medicines (legal definition ?)

Splitable into
- ambulatory care / hospital care
- Prescription / Over The Counter
- Reimbursed / not reimbursed

Validly linked to ATC / DDD

In terms of quantity consumed and money spent

Consistent over time (decades)

In months, quarters and years
Two illustrations:

1. European Surveillance of Antibiotic Consumption (ESAC project)
2. Long term longitudinal national data from Belgium
Illustration 1:

The ESAC project
Total outpatient antibiotic use in 26 European countries in 2002

(Lancet, ESAC, Goossens et al., 2005)
Seasonal variation in antibiotic use (1997-2002)

(Goossens et al., Lancet, 2005)
Need for methodological rigor
in cross-national drug utilization research
with administrative databases

European Surveillance of Antimicrobial Consumption
(ESAC): Data Collection Performance and
Methodological Approach

R. H. Vander Stichele, M. M. Elseviers, M. Ferech, S. Blot, H. Goossens & the ESAC Project Group

ESAC Management Team, Department of Microbiology, University of Antwerp, Antwerp, Belgium

Checklist for evaluating the validity of the data

1. Problems with population coverage
2. Problems with drug coverage
3. Problems with ambulatory/hospital care mix
Initial consumption data of Greece and Spain

Total AC Consumption 2001

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<th>GR</th>
<th>ES</th>
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<td>Spain</td>
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Suspected bias

Up to 10% overestimated due to parallel exports

Up to 30% underestimated due to exclusion of OTC sales
Corrected data after validity check

Total AC Consumption 2001

Greece
Spain
Corrected data after validity check

Total AC Consumption 2001

Greece

Spain
Problems with the link of the national drug code to international Anatomical Therapeutic Chemical Classification (ATC)
ATC/DDD Classification Problems in ESAC project:

Switch from G04 to J01MB, J01XE and J01XX:
consumption not recorded before 2000 in Luxemburg
Suspicion of misclassification bias

TOTAL ANTIBIOTIC USE IN AC

- Others: J01B+J01G+J01R+J01X
- Sulfonamides: J01E
- Quinolones: J01M
- Macrolides: J01F
- Tetracyclines: J01A
- Cephalosporins: J01D
- Penicillins: J01C
Rectification of misclassification bias
Relationship between consumption and resistance in 19 European countries (2000)

Figure 6: Correlation between penicillin use and prevalence of penicillin non-susceptible S. pneumoniae
AT, Austria; BE, Belgium; HR, Croatia; CZ, Czech Republic; DK, Denmark; FI, Finland; FR, France; DE, Germany; HU, Hungary; IE, Ireland; IT, Italy; LU, Luxembourg; NL, The Netherlands; PL, Poland; PT, Portugal; SI, Slovenia; ES, Spain; UK, England only.
Illustration 2:

Long term longitudinal national data from Belgium

Expenditures on drugs (1990 to 2005) in Belgium

Drug utilization (2000-2005) in Belgium
Longitudinal trends in pharmaceutical expenditures in Belgium (1990 – 2005)

Fig.2: 15 years of pharmaceutical annual per capita expenditures in Belgium (in constant EUR 2005)

(Acta Clinica Belgica, Vander Stichele et al., 2003)
Longitudinal trends in drug consumption in Belgium (2000-2005) (10.4 Million inhabitants)
Kymograph print?
Evolution of consumption of drugs for peptic ulcer disease in Belgium between 2003 and 2006
Impact of restrictions of reimbursement and of the publication of an evidence report

Van Driel et al., 2007
Application of time series analysis
IN CONCLUSION:

• Drug utilization research is part of pharmaco-epidemiology and clinical pharmacology

• Consumption of drugs must be studied both at the micro level and at the macro level.

• It is an eclectic discipline both in content and in methodology.