Introduction to Drug Utilization Research
Methodological Framework and Research Skills

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(University of Technology Sydney, Australia)

This session was developed
on behalf of the **ISPE Drug Utilization Special Interest Group** by
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Professor Katja Taxis (University of Groningen, Netherlands)
Associate Professor Bjorn Wettermark (Karolinska Institute, Sweden)

This session

- What is Drug Utilization Research (DUR)?

- How does DUR relate to pharmacoepidemiology?

- DUR Conceptual Framework

- Types of DUR research

Drug Utilization Research

- "The marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" (WHO 1977)
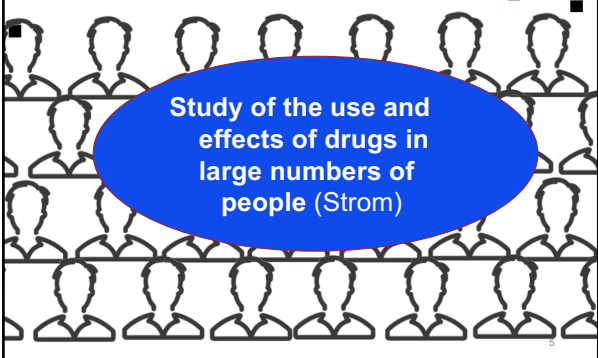

Current definition

"An eclectic collection of 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." (Wettermark and Vander Stichle, 2008)

Pharmacoepidemiology

Study of the use and effects of drugs in large numbers of people (Strom)

Pharmacoepidemiology

Outcomes

Safety

Population

Drug utilization research

- Health system characteristics
- Disease characteristics
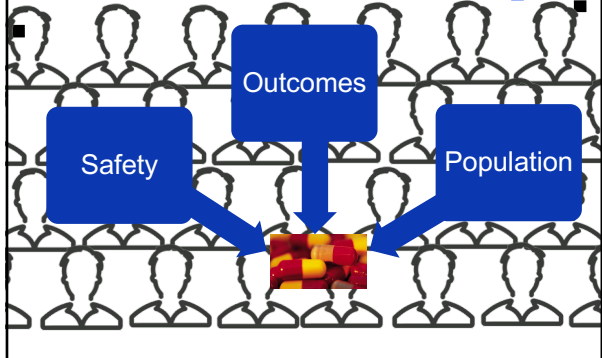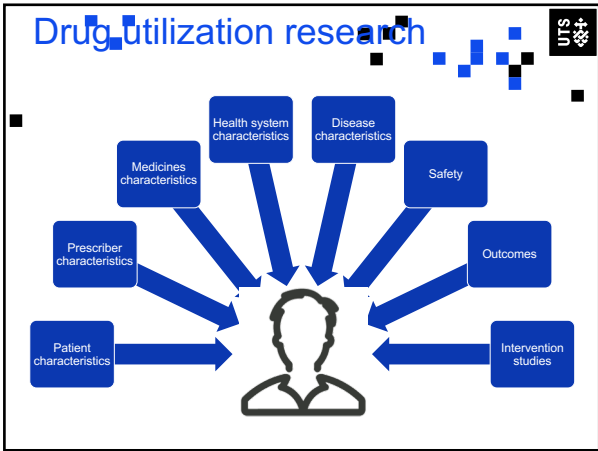- Safety
- Medicines characteristics
- Prescriber characteristics
- Outcomes
- Patient characteristics
- Intervention studies

Data sources

Primary data

- Patients
- Health care providers
- Prescriptions, dispensing records
- Medical records

Data sources

Secondary data

- Aggregate data: e.g. sales data
- Individual-level data:
  - electronic health records
  - pharmacy dispensing data
  - reimbursement data
  - patient registries
  - population health survey data
- Linking records from different sources

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Taxonomy and terminology

- Classification systems
  - Drug eg World Health Organisation ATC classification
  - Disease eg ICD, SNOWMED
- Measurement units
  - Defined daily dose (DDD)
  - Users
- Usage pattern definitions
  - eg Persistence, switching, commencement, cessation

Study designs in drug utilization

- Drug utilization
  - Descriptive
    - Survey (cross sectional)
    - Qualitative
  - Analytic
    - Experimental
      - Randomised controlled trial
      - Quasi experimental
    - Observational
      - Cohort Study
      - Cross sectional (Analytic)
      - Case Control

Adapted from Oxford University Centre for Evidence Based Medicine

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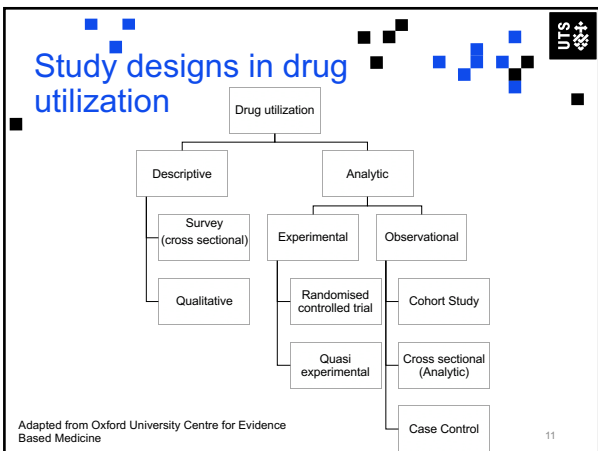
Conceptual Framework Drug Utilization Research

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Conceptual Framework

- **To quantify, understand and improve drug use and health outcomes**

Micro level
- Prescribing
- Supplying/dispensing
- Consumption

Macro level
- Health System (eg Clinic, hospital, region, country)

DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing				
Dispensing				
Consumption				

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The European Journal of Heart Failure 5 (2003) 187–193

The relevance of heart failure severity for treatment with evidence-based pharmacotherapy in general practice

Lisa G. Pont[a,*], Wiek H. van Gilst[b], Dirk J.A. Lok[b], Hans J.A. Kragten[c], Flora M. Haaijer-Ruskamp[a], on behalf of the Dutch Working Group on Heart Failure

[a]Department of Clinical Pharmacology, University of Groningen, Ant. Deusinglaan 1, 9713 AV Groningen, The Netherlands
[b]Department of Cardiology, Deventer Hospital, Deventer, The Netherlands
[c]Department of Cardiology, Atrium Medical Centre, Heerlen, The Netherlands

Received 18 March 2002; received in revised form 23 July 2002; accepted 3 October 2002

Table 3
Minimum evidence-based treatment: percentage of heart failure patients treated with the minimum evidence-based regime per NYHA class[a]

Severity	Minimum evidence-based treatment regime	Crude odds ratio (95% confidence interval)	Adjusted odds ratio (age/sex) (95% confidence interval)	Percentage of patients (95% confidence interval)
NYHA 1 (n=134)	ACEI	3.8 (2.2–6.7)	3.8 (2.1–6.7)	41.0 (32.7–49.4)
NYHA 2 (n=253)	ACEI	7.7 (4.6–12.7)	7.8 (4.6–13.0)	57.7 (52.0–64.2)
NYHA 3 (n=232)	ACEI + β-blocker	1.6 (0.9–2.7)	1.6 (0.9–2.8)	22.4 (17.0–27.8)
NYHA 4 (n=150)	ACEI + β-blocker	1	1	15.3 (9.6–21.1)
Total (n=769)				36.0 (32.6–39.4)

[a] Other cardiovascular drug treatments in addition to the minimum evidence-based regime may have been used.

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RESEARCH

Prevalence of Potentially Harmful Drug Interactions in Older People in Australian Aged-Care Facilities

Michael J Dolton, Lisa Pont, Gerard Stevens, Andrew J McLachlan

Journal of Pharmacy Practice and Research Volume 42, No. 1, 2012.

3876 Australian nursing home residents in 26 nursing homes

6.1% had a potentially harmful drug interaction

The potential drug interaction with the highest prevalence was co-administration of methotrexate and aspirin (38%)

Use of antibacterial fixed-dose combinations in the private sector in eight Latin American Countries between 1999 and 2009

Private-sector sales data, based on information from manufacturers, retail wholesalers and, for some countries, pharmacies,

Tropical Medicine & International Health
Volume 18, Issue 4, pages 416-425, 5 FEB 2013 DOI: 10.1111/tmi.12068
http://onlinelibrary.wiley.com/doi/10.1111/tmi.12068/full#tmi12068-fig-0002

Outpatient antibiotic use in Europe and association with resistance: a cross-national database study

Herman Goossens, Matus Ferech, Robert Vander Stichele, Monique Elseviers, for the ESAC Project Group*

Goosens et al. Lancet 2005

Slide 1

A longitudinal study of constipation and laxative use in a community-dwelling elderly population

Barry L. Werth [a,*], Kylie A. Williams [b], Lisa G. Pont [a]

[a] Sydney Nursing School, University of Sydney, Sydney, NSW, Australia
[b] Discipline of Pharmacy, Graduate School of Health, University of Technology Sydney, Sydney, NSW, Australia

Laxatives used
(chart: % of laxatives by type — Psyllium, Senna, Bisacodyl, Lactulose, Sterculia & frangula, Docusate, Other oral, Enemas/suppositories; 1992-93, 2003-04)

Slide 2

DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing		■		
Dispensing		■		
Consumption		■		

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Slide 3

British Journal of Clinical Pharmacology

Measuring anticholinergic drug exposure in older community-dwelling Australian men: a comparison of four different measures

Lisa G. Pont, [1,2*] Johannes T. H. Nielen, [3,4,5*] Andrew J. McLachlan, [6,7] Danijela Gnjidic, [6,7] Lewis Chan, [8] Robert G. Cumming [7,9] & Katja Taxis [3]

Br J Clin Pharmacol / 80:5 / 1169–1175 / 1169

Agreement between anticholinergic drug exposure scales (Cohen's κ, 95% confidence interval) in the classification of anticholinergic exposure

	Anticholinergic Risk Scale (ARS)	Anticholinergic Drug Scale (ADS)	AnticholinergicCognitive Burden Scale (ACB)
Anticholinergic Risk Scale (ARS)			
Anticholinergic Drug Scale (ADS)	0.263 (0.226, 0.300)		
Anticholinergic Cognitive Burden Scale (ACB)	0.247 (0.208, 0.286)	0.628 (0.593, 0.664)	
Drug Burden Index -Anticholinergic (DBI-ACH)	0.237 (0.192, 0.282)	0.119 (0.084, 0.154)	0.091 (0.054, 0.128)

Slide 4

Figure 1
Overlap between medicines included in the different anticholinergic scales. The larger the generic name, the more scales that the medication appears on. (Figure created with wordle http://www.wordle.net/)

Slide 5

Attitudes of pharmacists to provision of Home Medicines Review for Indigenous Australians

Lindy Swain · Claire Griffits · Lisa Pont · Lesley Barclay

Impacts of findings on practice

- The access of Aboriginal Australians to home medication review needs to be improved.
- Pharmacists and their staff need assistance and training on dealing with the Aboriginal health service and workers.
- Government policies should support and encourage pharmacists to conduct medication reviews for Aboriginal and Torres Strait Islander patients.

Slide 6

Pharmacy customers' knowledge of side effects of purchased medicines in Mexico

Veronika J. Wirtz[1], Katja Taxis[2] and Anahi Dreser[1]

1 Center for Health Systems Research, National Institute of Public Health, Cuernavaca, Morelos, Mexico
2 Department of Pharmacy, Section of Pharmacotherapy and Pharmaceutical Care, University of Groningen, Groningen, The Netherlands
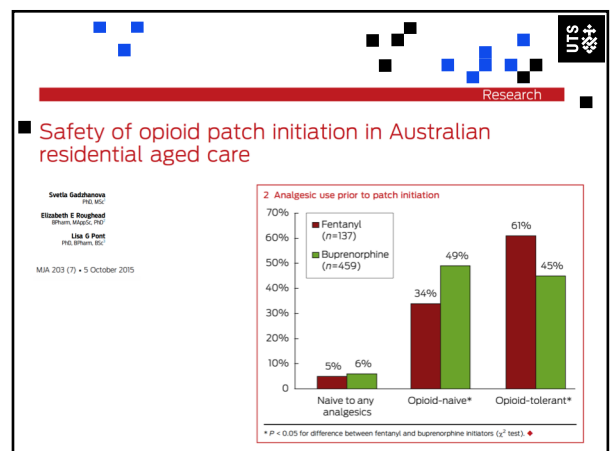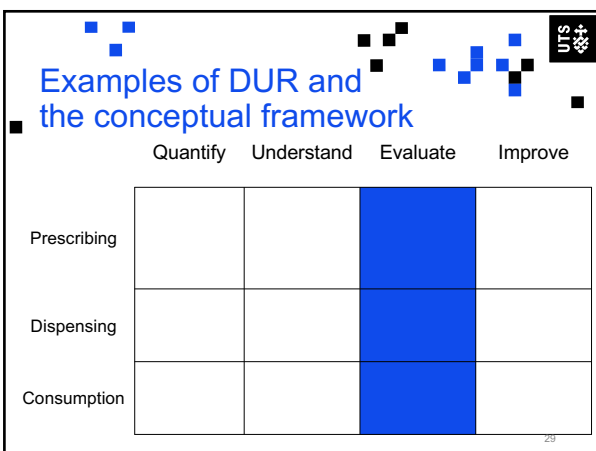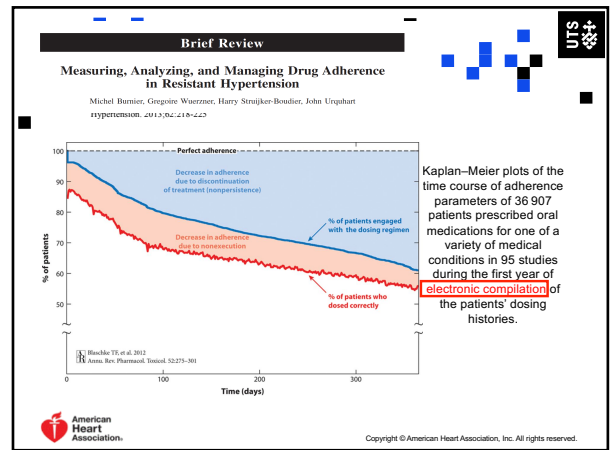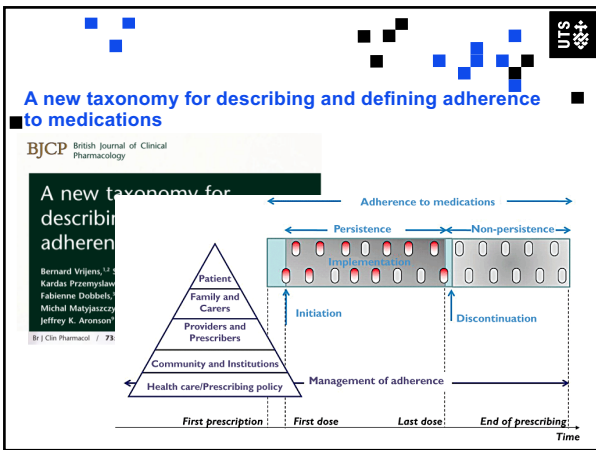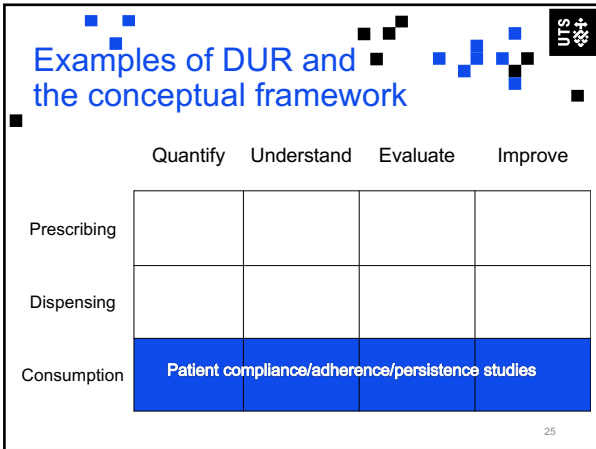
ORIGINAL ARTICLE

Causes of intravenous medication errors: an ethnographic study

K Taxis, N Barber

See editorial commentary, pp 326–7   Qual Saf Health Care 2003;12:343–348

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Slide 25

Examples of DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing				
Dispensing				
Consumption	Patient compliance/adherence/persistence studies			

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Slide (A new taxonomy)

A new taxonomy for describing and defining adherence to medications

BJCP British Journal of Clinical Pharmacology

A new taxonomy for describing and defining adherence to medications

Bernard Vrijens,[1,2] Sabina De Geest,[3,4] Dyfrig A. Hughes,[5] Kardas Przemyslaw,[6] Jenny Demonceau,[1] Todd Ruppar,[3,7] Fabienne Dobbels,[3] Emily Fargher,[5] Valerie Morrison,[5] Pawel Lewek,[6] Michal Matyjaszczyk,[6] Comfort Mshelia,[8] Wendy Clyne,[8] Jeffrey K. Aronson[9] & J. Urquhart,[1,10] for the ABC Project Team

Br J Clin Pharmacol / 73:5 / 691–705 / 691

Slide (taxonomy with figure)

A new taxonomy for describing and defining adherence to medications

Slide (Brief Review)

Brief Review

Measuring, Analyzing, and Managing Drug Adherence in Resistant Hypertension

Michel Burnier, Gregoire Wuerzner, Harry Struijker-Boudier, John Urquhart

Hypertension. 2013;62:218-225

Kaplan–Meier plots of the time course of adherence parameters of 36 907 patients prescribed oral medications for one of a variety of medical conditions in 95 studies during the first year of electronic compilation of the patients' dosing histories.

Blaschke TF, et al. 2012 Annu. Rev. Pharmacol. Toxicol. 52:275–301

Slide 29

Examples of DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing				
Dispensing				
Consumption				

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Slide (opioid patch)

Research

Safety of opioid patch initiation in Australian residential aged care

Svetla Gadzhanova PhD, MSc
Elizabeth E Roughead BPharm, MAppSc, PhD[1]
Lisa G Pont PhD, BPharm, BSc[1]

MJA 203 (7) • 5 October 2015

2 Analgesic use prior to patch initiation

* P < 0.05 for difference between fentanyl and buprenorphine initiators (χ^2 test). ♦

Slide 1

RESEARCH ARTICLE

Antihypertensive-related adverse drug reactions among older hospitalized adults

Tariq M. Alhawassi[1,2] · Ines Krass[2] · Lisa G. Pont[3]

This study shows that antihypertensive medications are associated with an increased risk of an ADR leading to hospital admission for older adults.
In our cohort of 500 older adults, one in ten experienced an ADR that was potentially related to their antihypertensive medication either leading to or during their hospital admission.

Slide 2

frontiers in Pharmacology

Changes in Prescribing Symptomatic and Preventive Medications in the Last Year of Life in Older Nursing Home Residents

Helene G. van der Meer[*], Katja Taxis[†] and Lisa G. Pont[‡]

FIGURE 2 | Number of symptomatic, preventive, and other medication in the last year of life. Estimated marginal means (EMMs), adjusted for number of bed days in facility[*] age[†], and number of medication at 365 days before death[‡].

Slide 3

Examples of DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing			**Prescribing quality indicators**	
Dispensing				
Consumption				

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Slide 4

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Lisa G. Pont · Petra Denig · Thys van der Molen
Willem Jan van der Veen · Flora M. Haaijer-Ruskamp

Validity of performance indicators for assessing prescribing quality: the case of asthma

Validation process

We validated indicators that targeted sub-optimal treatment patterns related to four steps included in the 1997 National Institutes of Health (NIH guidelines) [12].

Step 1. Under-treatment of short-acting inhaled β-agonists for all asthma patients
Step 2. Under-treatment of inhaled corticosteroids for mild, moderate or severe persistent asthma
Step 3. Inadequate dose of inhaled corticosteroids for moderate or severe persistent asthma
Step 4. Under-treatment of inhaled long-acting β-agonists for severe persistent asthma

Indicator	Relevant asthma severity classes targeted by each indicator (number of patients)	Sensitivity	Positive predictive value
Step-1 indicator	All severity classes ($n = 146$)	0.86 (0.71–0.95)	0.52 (0.38–0.65)
Step-2A indicator	Severity classes 2, 3 & 4 ($n = 95$)	0.74 (0.57–0.88)	0.46 (0.33–0.60)
Step-2B indicator	Severity classes 2, 3 & 4 ($n = 95$)	0.37 (0.19–0.58)	0.71 (0.42–0.92)
Step-3 indicator	Severity classes 3 & 4 ($n = 86$)	0.07 (0.00–0.32)	0.20 (0.00–0.72)
Step-4 indicator	Severity class 4 ($n = 16$)	Not validated due to inadequate sample size	

Slide 5

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Lisa G. Pont · G.Th. van der Werf
P. Denig · F.M. Haaijer-Ruskamp

Identifying general practice patients diagnosed with asthma and their exacerbation episodes from prescribing data

Table 3 Sensitivity, specificity and predictive values for criteria to identify asthma exacerbation from prescribing data (95% confidence intervals in parentheses)

Asthma exacerbation identification criteria	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Short-course oral corticosteroid	0.23 (0.20–0.28)	0.99 (0.99–0.99)	0.67 (0.59–0.75)	0.93 (0.92–0.94)
Short-course oral corticosteroid or short-course antibiotic	0.55 (0.50–0.60)	0.96 (0.96–0.97)	0.58 (0.53–0.63)	0.95 (0.95–0.96)

Slide 6

IJPP INTERNATIONAL JOURNAL OF Pharmacy Practice

IJPP
International Journal of Pharmacy Practice

Research Paper

Validity of prescribing indicators for assessing quality of antibiotic use in Australian general practice

Lisa G. Pont[a], Tessa K. Morgan[b], Margaret Williamson[b], Flora M. Haaijer[c] and Mieke L. van Driel[d]

[a]Centre for Health Systems and Safety Research, Australian Institute of Health Innovation, Macquarie University, North Ryde, [b]NPS MedicineWise, Sydney, NSW, Australia, [c]University of Groningen, Groningen, The Netherlands and [d]University of Queensland, Brisbane, QLD, Australia

Drug-specific indicators	Validity for monitoring antibiotic resistance	Validity for monitoring benefit to individual patients	Validity for monitoring value for money	Validity for policy makers
1 Consumption of all antibiotics for systemic use	7 (1.5)	6 (1.9)	7 (26.8)	8 (5.5)
2 Consumption of penicillins	7 (5.5)	7 (3.8)	8 (67.8)	8 (5.6)
3 Consumption of cephalosporins	7 (2.4)	7 (3.8)	8 (1.5)	8 (3.2)
4 Consumption of macrolides	7 (2.7)	7 (4.3)		
5 Consumption of quinolones	8 (2.6)	6.5 (2.5)		
6 Consumption of combination penicillins	7 (4.1)	6 (1.9)		
7 Consumption of third- and fourth-generation cephalosporins	8 (6.1)	7 (2.6)		
8 Consumption of quinolones	8 (4.1)	6 (1.7)		
9 Ratio broad-spectrum to narrow-spectrum antibiotics	7 (3.4)	7 (3.5)		
10 Consumption of antibiotics commonly used for upper respiratory tract infections (URTIs)	7 (1.5)	7 (1.5)		

Antibiotics are indicated for acute cystitis. There is no value in monitoring their use in terms of quality of prescribing. Monitoring which ones are used would be of value. GP 4

Not sure how relevant this is, as it is common practice to give antibiotics for urinary tract infection, the type and duration of treatment much more relevant. GP 1

Mixed methods analysis

Slide 1:

ORIGINAL RESEARCH

Treatment quality indicators predict short-term outcomes in patients with diabetes: a prospective cohort study using the GIANTT database

Grigory Sidorenkov,[1,2] Jaco Voorham,[1,2] Dick de Zeeuw,[1] Flora M Haaijer-Ruskamp,[1,2] Petra Denig[1,2]

Prescribing indicator: "a measurable element of prescribing performance for which there is evidence or consensus that it can be used to assess quality"

Slide 2:

Examples of DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing				Intervention studies
Dispensing				
Consumption				

Slide 3:

Research
Effect of humour therapy on psychotropic medication use in nursing homes

IMAGE: VALDA & JOANNA IN PLAY UP SESSION (LYNNE MALCOLM)
IMAGE: VALDA ENJOYING A SING ALONG (LYNNE MALCOLM)
IMAGE: AILEEN & HER FAMILY DURING A PLAY UP SESSION (LYNNE MALCOLM)
IMAGE: AILEEN WITH HER FAMILY (LYNNE MALCOLM)

Slide 4:

Research
Effect of humour therapy on psychotropic medication use in nursing homes

Jerome BY Leow
Faculty of Medicine, University of New South Wales, New South Wales, Australia

Lisa Pont
Sydney Nursing School, The University of Sydney, New South Wales, Australia

Lee-Fay Low
Faculty of Health Sciences, The University of Sydney, Sydney, New South Wales, Australia

Table 1: Prevalence (%) of psychotropic medication use in Australian nursing homes before Play Up program and after Play Up program

	Any psychotropic	Antipsychotics	Benzodiazepines	Antidepressants
Pre-Play Up	169	94	63	65
(n = 361)	(46.8%)	(26.0%)	(17.5%)	(18.0%)
Post-Play Up	151	82	52	61
(n = 361)	(41.8%)	(22.7%)	(14.4%)	(16.9%)
Change (%)	−5.00	−3.30	−3.1	−1.1
P value	0.002*	0.024*	0.001*	0.289

*Indicates significant decrease (P < 0.05) in prevalence from pre- to post-Play Up period.

Slide 5:

Discontinuation of inappropriate medication in nursing home residents (DimNHR study)

FOR HOW MANY RESIDENTS CAN WE DISCONTINUE 1 OR MORE INAPPROPIATE MEDICATION(S)?

39,1 %
INTERVENTION GROUP
1 or more inappropiate medication(s) could be successfully discontinued from 39,1% of the 233 residents in the intervention group

29,5 %
CONTROL GROUP
1 or more inappropiate medication(s) could be successfully discontinued from 29,5% of the 193 residents in the intervention group

Wouters et al, 2014; Wouters et al, Ann Int Med, in press

Slide 6:

Reducing the anticholinergic and sedative load in older patients on polypharmacy by pharmacist-led medication review: A randomized controlled trial

Helene G. van der Meer[*1], Hans Wouters[*1], Lisa G. Pont[*2], Katja Taxis[*1]

BMJ Open (in press)

Table 2 Primary outcome - Proportion of patients having a decrease in DBI ≥ 0.5			
	Proportion with decrease of DBI ≥ 0.5 (%, n)	Odds ratio (95% CI) *	p-value
	Intervention / Control		
Intention to treat (n=157)	17.3% (13) / 15.9% (13)	1.04 [0.47-2.64]	0.927
Per protocol analysis (n=145)	18.5% (12) / 16.3% (13)	1.09 [0.45-2.63]	0.857

* Binary logistic regression, adjusted for age, gender, number of medication at baseline, level of DBI at baseline.

Examples of DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing				Risk management
Dispensing				
Consumption				

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The risk management cycle, Guideline on Good Pharmacovigilance Practices (Module V) of EMA.

Joinpoint Regression Program analysis for atypical antipsychotics use among elderly patients with dementia. The data points represent patients 65 years and older with dementia (smoothed 6-month averages); the solid line, fitted joinpoint time series. IMS data.

Dorsey et al. Impact of FDA Black Box Advisory on Antipsychotic Medication Use. Arch Intern Med. 2010 January 11; 170(1): 96–103

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Examples of DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing				
Dispensing				
Consumption				Patient education

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PATIENT VOICE

Amplifying the voice of ME/CFS and Fibromyalgia patients in a noisy world

Debate & Analysis
Solutions to problematic polypharmacy: learning from the expertise of patients

British Journal of General Practice, June 2015 **319**

Article

health:

Lay knowledge, social movements and the use of medicines: Personal reflections

Health 2016, Vol. 20(3) 77–93 © The Author(s) 2015 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav DOI: 10.1177/1363459315619021 hea.sagepub.com

Nicky Britten and Kath Maguire
University of Exeter, UK

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Examples of DUR and the conceptual framework

	Quantify	Understand	Evaluate	Improve
Prescribing				
Dispensing	Comparisons, benchmarking Health services and policy research			
Consumption				

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Challenges in Drug Utilization Research

"I think you should be more explicit here in step two."

Challenges in drug utilization research

Descriptive quantitative studies may have problems with poor data validity and limited generalizability

Analytical studies may suffer from the same problems as all pharmacoepidemiological studies, i.e., variation by chance, bias and confounding

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r=0.791
P<0.0001

Correlation between Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.

Messerli FH. N Engl J Med 2012;367:1562-1564.

Association between storks and newborn babies in Western Germany 1965-1980

Sies H. Nature 332;495

Final thoughts

- **Drug utilization research**
- explores practice based issues
- using varied methodologies and data sources
- putting the prescriber, supplier and consumer at the centre of the research
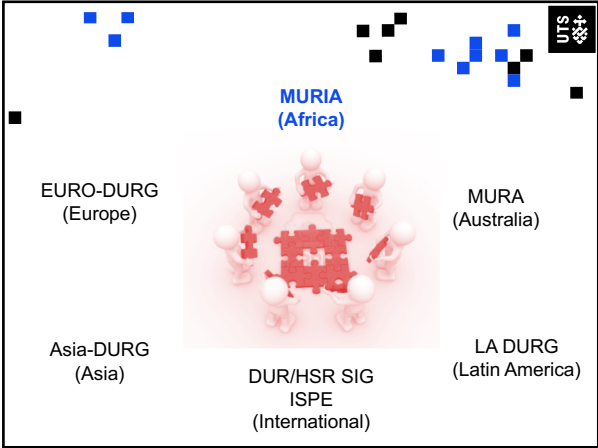- to inform and improve health practice, policy and patient outcomes.

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Drug Utilization Research Methods and Applications

Monique Elseviers, Björn Wettermark, Anna Birna Almarsdóttir, Morten Andersen, Ria Benko, Marion Bennie, Irene Eriksson, Brian Godman, Janet Krska, Elisabetta Poluzzi, Katja Taxis, Vera Vlahovic-Palcevski, Robert Vander Stichele

Drug Utilization Research (DUR) is an eclectic scientific discipline, integrating descriptive and analytical methods for the quantification, understanding and evaluation of the processes of prescribing, dispensing and consumption of medicines and for the testing of interventions to enhance the quality of these processes. The discipline is closely related and linked mainly to the broader field of pharmacoepidemiology, but also to health outcomes research, pharmacovigilance and health economics.

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Asia-DURG
(Asia)

LA DURG
(Latin America)

DUR/HSR SIG
ISPE
(International)

International Society for Pharmacoepidemiology

34TH ICPE
INTERNATIONAL CONFERENCE ON PHARMACOEPIDEMIOLOGY
& THERAPEUTIC RISK MANAGEMENT
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34th International Conference on Pharmacoepidemiology &
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