Why Drug Utilization Studies!? 

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Is there a need for DUR?
Do we address this need?

"'You think so?' 'Why, yes.'"

noun

1. a reason or explanation.
   "the whys and wherefores of these procedures need to be explained to students"
The briefing
Why do new medicines cost so much, and what can we do about it?

Tirsdag d. 31. jul. 2018 - kl. 15:15

Medicin smelter i varmen: Nu fjerner butikkerne den fra hylderne

Fredag d. 26. okt. 2018 - kl. 11:56

It-system kan have ført til tusindvis af medicinfejl

Patienter i Region Hovedstaden og Sjælland kan have taget forkerte doser medicin på grund af fejl i it-system

We slikken te veel, hoog tijd om te ontpillen

Your private medical data is for sale - and it's driving a business worth billions
Overdose Deaths Involving Opioids,

Inhaler errors

- Insufficient inspiratory effort
  - Turbohaler - Symbicort™
  - Diskus - Seretide™

- Did not breathe out to empty lungs before inhalation
  - Turbohaler - Symbicort™
  - Diskus - Seretide™

Inhaler device

- Ref: no error

Deaths per 100,000 population

Source: CDC/NCHS, National Vital Statistics System

https://wonder.cdc.gov/
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.
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Polypharmacy in older people
• Can we quantify, understand and evaluate the processes of prescribing, dispensing and consumption of medication in older people?
The rising tide of polypharmacy

Percentage patients receiving specified number of drugs by age group in Scotland

Guthrie 2015
Inter-practice variation in polypharmacy

% polypharmacy patients in General Practice across the Netherlands

Sinnige, 2016
Variation in polypharmacy by deprivation status

Percentage patients prescribed 10+ medications by age group and deprivation

Mair, 2017
Medication appropriateness late in life

Holmes 2006
American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

The American Geriatrics Society 2012 Beers Criteria Update Expert Panel

STOPP/START criteria for potentially inappropriate prescribing in older people: version 2
Denis O'Mahony, David O'Sullivan, Stephen Byrne, Marie Noelle O'Connor, Cristin Ryan, Paul Gallagher

Age and Ageing, Volume 44, Issue 2, 1 March 2015, Pages 213–218,

EDITOR'S CHOICE
STOPPFrail (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy): consensus validation
Amanda Hanora Lavan, Paul Gallagher, Carole Parsons, Denis O'Mahony

Age and Ageing, Volume 46, Issue 4, 1 July 2017, Pages 600–607,
https://doi.org/10.1093/ageing/afx005
Published: 24 January 2017  Article history
• Are we testing interventions to enhance the quality of polypharmacy in older people?
Interventions to improve the appropriate use of polypharmacy for older people (Review)

Rankin A, Cadogan CA, Patterson SM, Kerse N, Cardwell CR, Bradley MC, Ryan C, Hughes C

- 32 studies, variety of settings
- Majority complex multi-faceted pharmaceutical care-based approaches
- Delivered by general physicians, pharmacists and geriatricians
Author’s conclusion: It is unclear whether interventions to improve appropriate polypharmacy, such as reviews of patients’ prescriptions, resulted in clinically significant improvement; however, they may be slightly beneficial in terms of reducing potential prescribing omissions (PPOs); but this effect estimate is based on only two studies, which had serious limitations in terms of risk bias.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Result</th>
<th>Number of studies/patients</th>
<th>Evidence</th>
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<tbody>
<tr>
<td>proportion of patients with one or more PPOs</td>
<td>RR 0.40, 95% CI 0.18 to 0.85</td>
<td>5 studies; N = 1310</td>
<td>--</td>
</tr>
<tr>
<td>Hospital admissions</td>
<td>Data not pooled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality of life</td>
<td>Data not pooled</td>
<td></td>
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<tr>
<td>Medication-related problems</td>
<td>No consistent effect noted</td>
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Issues:
- Study design
- Interventions
- Outcomes

mean difference (MD); standardised mean difference (SMD); risk ratio (RR);
-- very low-certainty evidence; - low certainty of evidence
Features of complex health care interventions
Features of complex health care interventions

• Multiple, potentially interacting, components
• Social: depend on staff/patient behaviour
• Context sensitive: embedded in the system (health care/organisation)
• Dynamic: evolving over time with learning

Craig et al, 2008; Horton et al, 2018
Key elements of the development and evaluation of complex interventions

Craig et al 2008
More details on development

Bleijenberg et al 2018

Chandler et al, 2016
Example: Pharmacist-led intervention

• Development of a pharmacist-led intervention for frail diabetes patients with multimorbidity/polypharmacy

• Study part 1: literature review: Van Eikenhorst et al 2018
Meta-analysis shows an overall significant effect on HbA1c favouring the intervention. Subgroup analyses showed no significant differences between groups.
Example: Pharmacist-led intervention

- Study part 2: Qualitative interviews with 35 health professionals (physicians, nurses, pharmacists, pharmacy-assistants) and patients/carers
- Study part 3: Qualitative analysis of communication skills of pharmacists using videos
- Study part 4: Quantitative analysis of the number of vulnerable patients
Example: Medication reviews in nursing homes

RCT of medication reviews to discontinue inappropriate medication in nursing homes
Primary outcome: % residents ≥1 inappropriate medication(s) successfully discontinued

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<tr>
<th>Control</th>
<th>Intervention</th>
<th>OR [95% CI]</th>
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</thead>
<tbody>
<tr>
<td>29.5%</td>
<td>39.1%</td>
<td>1.57 [1.03-2.39]</td>
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Adjusted for sex, age, marital status, length of stay in nursing home, Charlson's comorbidity index, and dementia diagnosis

Wouters et al, Annals of Int Medicine, 2017
Are results of practice trials generalisable beyond the study setting?

Editorial by Holly and Riester, 2017: “…unclear how the patient's perspective influenced deprescribing …the results do not reveal details about the pharmacists' thinking processes.”

Sawan et al 2017: “Interventions that consider contextual factors, such as the organizational culture of the nursing home, are critical to improve inappropriate prescribing.”
Qualitative study alongside the RCT: 35 interviews

Embedding of the medication reviews in other cooperations between physicians and pharmacists is essential.

All staff want to involve patients/relatives into decision-making, but practical implementation is difficult.

Sharing clinical information with the pharmacist can be an issue.

Patients: Assessing patient perspective is a check of willingness of the patient to explain the illness.

Physicians: Physicians value the pharmacotherapeutic knowledge of the pharmacist and the perspective of an “outsider.”

Nursing Staff: Know resident/family perspective on stopping medication, observe whether medication is effective, patients experience side effects, can communicate changes to the resident/family.
Fig 1 Key functions of process evaluation and relations among them (blue boxes are the key components of a process evaluation.

Context
- Contextual factors that shape theories of how the intervention works
- Contextual factors that affect (and may be affected by) implementation, intervention mechanisms and outcomes
- Causal mechanisms present within the context which act to sustain the status quo, or potentiate effects

Description of intervention and its causal assumptions
- Implementation process (How delivery is achieved; training, resources etc)
- What is delivered
- Fidelity
- Dose
- Adaptations
- Reach

Mechanisms of impact
- Participant responses to and interactions with the intervention
- Mediators
- Unexpected pathways and consequences

Outcomes

Graham F Moore et al. BMJ 2015;350:bmj.h1258
Reporting on complex interventions

- Hoffmann et al 2014: Template for Intervention Description and Replication (TIDieR) checklist (12 items)
Outcome measures

- Hospitalizations; Drug-related Hospitalizations; Mortality
- Beer’s criteria (AGS 2012)
- STOPP/START criteria (O'Mahony 2015)
- Drug Burden Index (Hilmer 2007)
- Quality of Life
- Living with Medicines Questionnaire (Krska 2017)
- Patients’ attitudes towards deprescribing Questionnaire (Reeve 2016)
- Adverse events
- Pharmacological properties
- Number of medication
- Medication complexity regimen index (George 2004)
- Patient experiences
<table>
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<tr>
<th><strong>Adverse events</strong></th>
<th>Drug-related hospital admissions</th>
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<tr>
<td><strong>Medication use</strong></td>
<td>Overuse, underuse, potentially inappropriate medications, clinically significant drug-drug interactions</td>
</tr>
<tr>
<td><strong>Patient reported outcomes</strong></td>
<td>Quality of life, pain relief</td>
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• Can we quantify, understand and evaluate the processes of prescribing, dispensing and consumption of medication in older people?

• Are we testing interventions to enhance the quality of polypharmacy in older people?

Yes, to some extent
Final remarks

• DUR is multidisciplinary
  • Include the patient perspective
  • Work with all stakeholders including policy makers
• Use theoretical frameworks such as for complex interventions
• Consider wider context for implementation/up-scaling of interventions
• Develop good outcome measures
Thank you!
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What should be the focus of DUR?