

Use of the ATC/DDD methodology for drug utilisation surveillance and research

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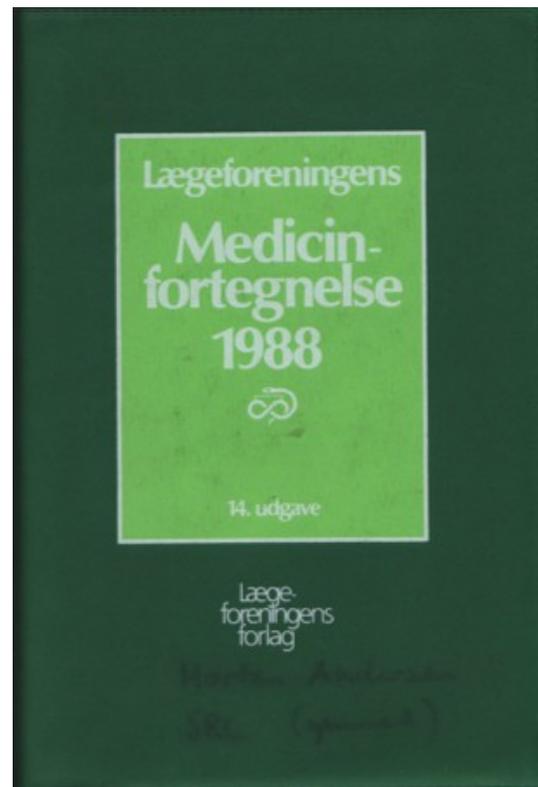
Conflicts of interest and disclaimer

- None directly related to the subject of this presentation
- Previously participated in research projects funded by AstraZeneca, H. Lundbeck & Mertz, Janssen, Novartis, Nycomed, Merck Sharp & Dohme and Pfizer, with grants paid to the institutions where I have been employed
- Personally receive(d) fees from Medicademy and Atrium, the Danish Pharmaceutical Industry Association for teaching at pharmacoepidemiology courses
- Professorship in pharmacovigilance 2017-2022 supported by the Novo Nordisk Foundation
- Member of the WHO International Working Group for Drug Statistics Methodology
- Views and opinions expressed in this presentation are entirely my own and I am not speaking on behalf of any organisation or institution

Overview

- ATC codes as a convenient way to organise drug knowledge and information
- ATC codes in ADR surveillance
- ATC codes as a way to describe comorbidity in research (based on the indications)

The previous drug handbook of the Danish Medical Association



Terapeutisk indeks efter hovedgrupper
(ATC = Anatomical Therapeutic Chemical System)

A	FORDJÆLSESORGANER OG STØFSKIFTE	15
A01	Mundhule og tænder, midler mod sygdomme i	15
A02	Ulcer sygdomme m.m., midler mod	16
A03	Spasmolytika og antikolinergika	32
A04	Antiemetika	37
A06	Laksantia	41
A07	Diaré, midler mod	52
A08	Anoreksika (appetitnedsættende midler)	59
A09	Digestiva, inkl. enzymer	61
A10	Antidiabetika	64
A11	Vitaminer	74
A12	Mineralpræparater	85
A13	Tonika	90
A14	Anabolske midler til systemisk brug	91
B	BLOD OG BLODDANNEDE ORGANER	93
B01	Koagulationshæmmende midler	93
B02	Hæmostatika	100
B03	Anæmi, midler mod	106
B04	Bloodregulerende midler	112
B05	Plasmasubstitutter, infusionsvæsker m.m.	116
B06	Hæmatologiske midler, andre, inkl. fibrinolytika/hyaluronidase	132
C	HJERTE OG KREDSLØB	134
C01	Hjerterterapi	134
C01A	Digitallykosider	134
C01B	Antiarytmika	139
C01C	Hjerte- og respirationsstimulerende midler	153
C01D	Koronarterapeutika	162
C07	Beta-receptorblokerende midler	173
C02	Antihypertensiva	187

Organising medicinal products by ATC code (Tayebati et al 2017 Int Marit Health)



ORIGINAL PAPER

Int Marit Health
2017; 68, 1: 39–45
DOI: 10.5603/IMH.2017.0007
www.intmarhealth.pl
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ISSN 1641-9251

Identification of World Health Organisation ship's medicine chest contents by Anatomical Therapeutic Chemical (ATC) classification codes

Seyed Khorsow Tayebati¹, Giulio Nittari¹, Syed Sarosh Mahdi, Nicholas Ioannidis²,
Fabio Sibilio³, Francesco Amenta^{1, 3}

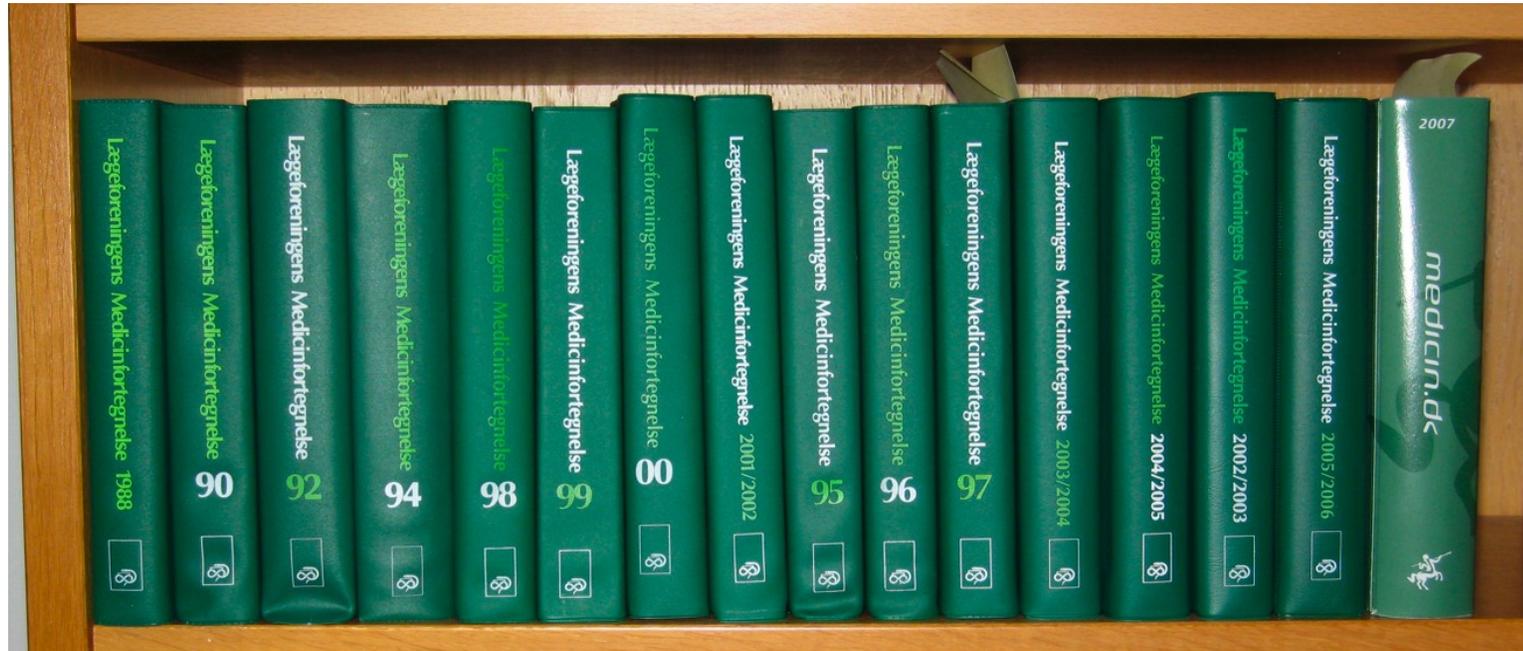
¹Telemedicine and Telepharmacy Centre University of Camerino, Camerino, Italy

²Ship Medical Ltd., Athens, Greece

³Research Department, International Radiomedical Centre (CIRM), Rome, Italy

Conclusions: *The availability of an objective system to identify medicinal products is required for ships, which will contribute in making the identification of items purchased simpler, making it easier to understand which drug seafarers need to be administer, and consequently reduce possible therapeutic mistakes.*

The drug utilisation researcher's library



Use of ATC codes in surveillance of ADRs

Experiences of a data archeologist

- 24 years of adverse reaction reporting in Denmark 1968-1991 stored in a mainframe database system
- 33,813 reports retrieved
- 2,129 different drug names
- Reclassified to 1,239 different ATC codes
- 14,500 different drug-ADR combinations

International ADR surveillance: Data-mining and signal generation in spontaneous reports (Vigibase at the UMC)

Eur J Clin Pharmacol (2002) 58: 483–490
DOI 10.1007/s00228-002-0484-z

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

A. Bate · M. Lindquist · R. Orre · I.R. Edwards
R.H.B. Meyboom

Data-mining analyses of pharmacovigilance signals in relation to relevant comparison drugs

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Abstract Objective: The aim of this paper is to demonstrate the usefulness of the Bayesian Confidence Propagation Neural Network (BCPNN) in the detection of drug-specific and drug-group effects in the database of adverse drug reactions of the World Health Organization Programme for International Drug Monitoring. **Methods:** Examples of drug–adverse reaction combinations highlighted by the BCPNN as quantitative associations were selected. The anatomical therapeutic chemical (ATC) group to which the drug belonged was then identified, and the information component (IC) was calculated for this ATC group and the adverse drug reaction (ADR). The IC of the ATC group with the ADR was then compared with the IC of the drug–ADR by plotting the change in IC and its 95% confidence limit over time for both.

Conclusion: The BCPNN can be used to improve the ability of a signal detection system to highlight group and drug-specific effects.

Keywords BCPNN · Automated signal detection · Pharmacovigilance

Introduction

When deciding whether a drug side effect is unacceptably frequent, the alternatives to a drug treatment need to be considered, as well as the incidence of other adverse drug reactions (ADRs) and the benefits of the drug [1, 2]. The alternatives may be non-treatment, the prescribing of other drugs or other treatments. Spontaneous

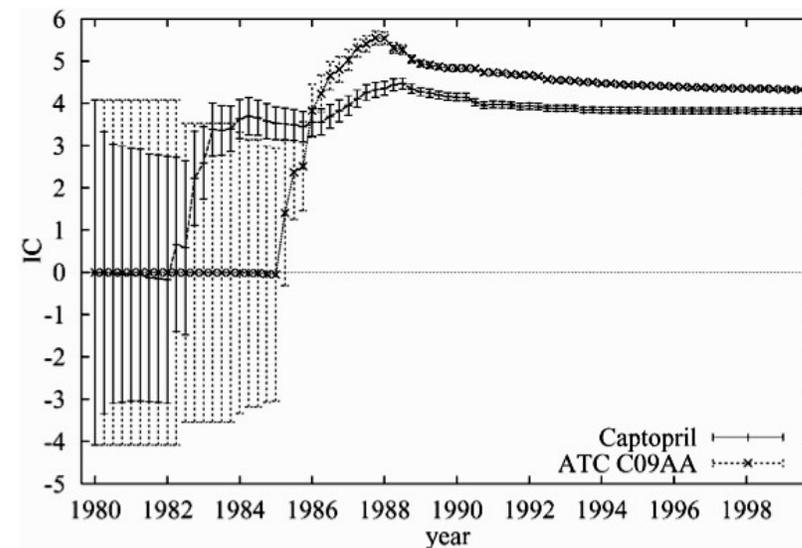


Fig. 2. Captopril, anatomic therapeutic chemical (ATC) group C09AA – coughing. This graph shows the change in information component (IC) over time of captopril with coughing until the end of the third quarter of 1999. The IC is plotted on the y axis and time (in quarters) on the x axis. On the same graph the ATC group C09AA angiotensin-converting enzyme (ACE) inhibitors (excluding captopril) with coughing is plotted. All data plotted are cumulative

ATC codes for defining drug-ADR combinations

Population-based drug utilisation surveillance: www.medstat.dk

Home Groups of medicines ATC code Product name [Data basis and description](#)

ATC code
Enter specific ATC code press ENTER

- ⊕ L (Antineoplastic and immunomodulating agents)
- ⊕ M (Musculo-skeletal system)
- ⊕ N (Nervous system)
 - ⊕ N01 (Anesthetics)
 - ⊕ N02 (Analgesics)
 - ⊕ N03 (Antiepileptics)
 - ⊕ N04 (Anti-parkinson drugs)
 - ⊕ N05 (Psycholeptics)
 - ⊕ N05A (Antipsychotics)
 - ⊕ N05B (Anxiolytics)
 - ⊕ N05C (Hypnotics and sedatives)
 - ⊕ N05CA (Barbiturates, plain)
 - ⊕ N05CC (Aldehydes and derivatives)
 - ⊕ N05CD (Benzodiazepine derivatives)
 - ⊕ N05CF (Benzodiazepine related drugs)
 - ⊕ N05CH (Melatonin receptor agonists)
 - ⊕ N05CM (Other hypnotics and sedatives)
 - ⊕ N06 (Psychoanaleptics)
 - ⊕ N07 (Other nervous system drugs)
- ⊕ P (Antiparasitic products, insecticides and repellants)
- ⊕ R (Respiratory system)
- ⊕ S (Sensory organs)
- ⊕ V (Various)

Year
2022
2021
2020
2019
2018
2017

Region
Entire Denmark
Hovedstaden
Nordjylland
Midtjylland
Sjælland
Syddanmark

Gender
Gender, combined
Male
Female

Age group (change)
All
0 - 17 y.o.
18 - 24 y.o.
25 - 44 y.o.
45 - 64 y.o.
65 - 79 y.o.

Sector
Primary sector
Hospital sector
Total

Search variable
Turnover
Paid reimbursement
Volume sold
Volume sold per 1,000 inhabitants per day
Number of users
Number of users per 1,000 inhabitants

Show result Show result in Excel

Last modified 13.03.2023

Using the output of medstat – examples

- Total DDDs
- Therapeutic intensity DDDs per TID (point prevalence surrogate)
- Number of users
- Users per 1000 inhabitants
- Average annual use DDD/user year

(insert graph examples)

Use in pharmacoepidemiology: Drug use (ATC codes) in the previous year as proxies for (co)morbidity

- Hypertension
 - Antihypertensives (C02)
 - Beta–blocking agents (C07)
 - Calcium channel blockers (C08)
 - Agents acting on the renin–angiotensin system (C09)
 - Low ceiling diuretics, thiazides (C03A)
 - Low ceiling diuretics excl. thiazides (C03B)
- Diabetes
 - Insulins and analogues (A10A)
 - Blood glucose lowering drugs, excl. insulins (A10B)

NOTE: Validity? Specificity and PPV?

Meaningful use of ATC levels: A, B, C, D...?

Table 2

Identified risk factors for reporting prescribed drugs upon admission†

	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Number of reimbursements†**		
One reimbursement		0.22 (0.13, 0.35)**
Two to four reimbursements		0.62 (0.4, 0.98)*
≥5 reimbursements		1
ATC group**		
Dermatologicals (ATC D)	0.04 (0.02, 0.12)**	0.05 (0.01, 0.16)**
Anti-infectives (ATC J)	0.11 (0.06, 0.17)**	0.15 (0.08, 0.26)**
Musculoskeletal (ATC M)	0.17 (0.09, 0.36)**	0.18 (0.09, 0.35)**
Sensory (ATC S)	0.23 (0.08, 0.66)*	0.23 (0.08, 0.64)**
Respiratory (ATC R)	0.35 (0.19, 0.62)**	0.30 (0.17, 0.53)**
Alimentary tract (ATC A)	0.38 (0.20, 0.72)**	0.35 (0.18, 0.66)**
Genitourinary (ATC G)	0.49 (0.18, 1.29)	0.37 (0.14, 0.96)*
Nervous (ATC N)	0.47 (0.27, 0.82)*	0.40 (0.32, 0.69)**
Hormones (ATC H)	0.46 (0.08, 2.60)	0.48 (0.08, 2.70)
Blood (ATC B)	0.51 (0.21, 1.24)	0.48 (0.20, 1.14)
Cardiovascular (ATC C)	1	1
Sex	NS	NS
Age	NS	NS

How should we put the drugs in our logistic regression: A, B, C, D...

Level one includes heterogeneous sublevels

Lack of meaningful interpretation!

Codes are not just letters and numbers – they should make clinical sense

Think about the clinical meaning , the context and make your choice!

Table 1 Incident prescribing of 20 drug groups [Anatomical Therapeutic Classification (ATC) code] by Danish GPs in the period 2000–2003

Main and therapeutic drug subgroups (ATC code)	Maximum no. of analogues available	Median no. of different analogues prescribed (range)	Median no. of drugs in the DU 90% segment (range)	Median FSI (range)
A: alimentary tract & metabolism				
A02BA: H2-receptor antagonists	5	3 (1–4)	2 (1–3)	0.66 (0.43–0.79)
A02BC: proton pump inhibitors	5	4 (3–5)	3 (1–4)	0.49 (0.19–0.76)
A10BB: oral antidiabetics	5	2 (1–5)	2 (1–4)	0.70 (0.28–0.80)
C: cardiovascular system				
C07A: beta-blocking agents	13	5 (1–8)	3 (1–5)	0.83 (0.71–0.91)
C08C: calcium channel blockers	8	3 (1–6)	2 (1–4)	0.84 (0.60–0.88)
C09A: ACE inhibitors	10	4 (1–9)	3 (1–6)	0.77 (0.54–0.90)
C09C: angiotensin II antagonists	6	4 (1–6)	3 (1–5)	0.64 (0.14–0.83)
C10A: serum lipid-reducing agents	12	4 (1–8)	3 (1–5)	0.82 (0.66–0.91)
D: dermatologicals				
D07A: corticosteroids (group I–IV)	12	8 (5–12)	4 (2–6)	0.78 (0.64–0.86)
G: genito-urinary system & sex hormones				
G03C: estrogens	5	3 (1–4)	2 (1–3)	0.69 (0.43–0.80)
J: anti-infectives for systemic use				
J01CA: penicillins, extended spectrum	5	4 (2–5)	3 (1–4)	0.64 (0.41–0.80)
J01FA: macrolides	5	4 (3–5)	3 (1–4)	0.55 (0.22–0.74)
M: musculo-skeletal system				
M01A: NSAIDs	22	13 (6–19)	5 (2–9)	0.86 (0.74–0.92)
N: nervous system				
N02A: opioids	13	7 (2–11)	2 (1–5)	0.88 (0.74–0.92)
N02CC: triptans	6	4 (1–6)	3 (1–5)	0.60 (0.28–0.81)
N05A: antipsychotics	30	8 (1–13)	6 (1–10)	0.84 (0.68–0.95)
N06AA: tricyclic antidepressants	9	3 (1–7)	3 (1–5)	0.80 (0.62–0.91)
N06AB: SSRIs	6	4 (1–6)	3 (1–5)	0.62 (0.38–0.80)
R: respiratory system				
R03A: adrenergics, inhalants	10	7 (3–9)	3 (1–6)	0.75 (0.52–0.86)
R03BA: glucocorticoids	4	3 (1–3)	2 (1–3)	0.67 (0.41–0.75)

The total number of analogues available on the market, the median number and range of prescribed analogues per practice and two formulary measures [DU 90% and Formulary Selectivity Index (FSI)] calculated among 177 practices. *ACE* angiotensin-converting enzyme, *NSAIDs* non-steroidal anti-inflammatory drugs, *SSRIs* selective serotonin reuptake inhibitors

Think about the clinical meaning , the context and make your choice!

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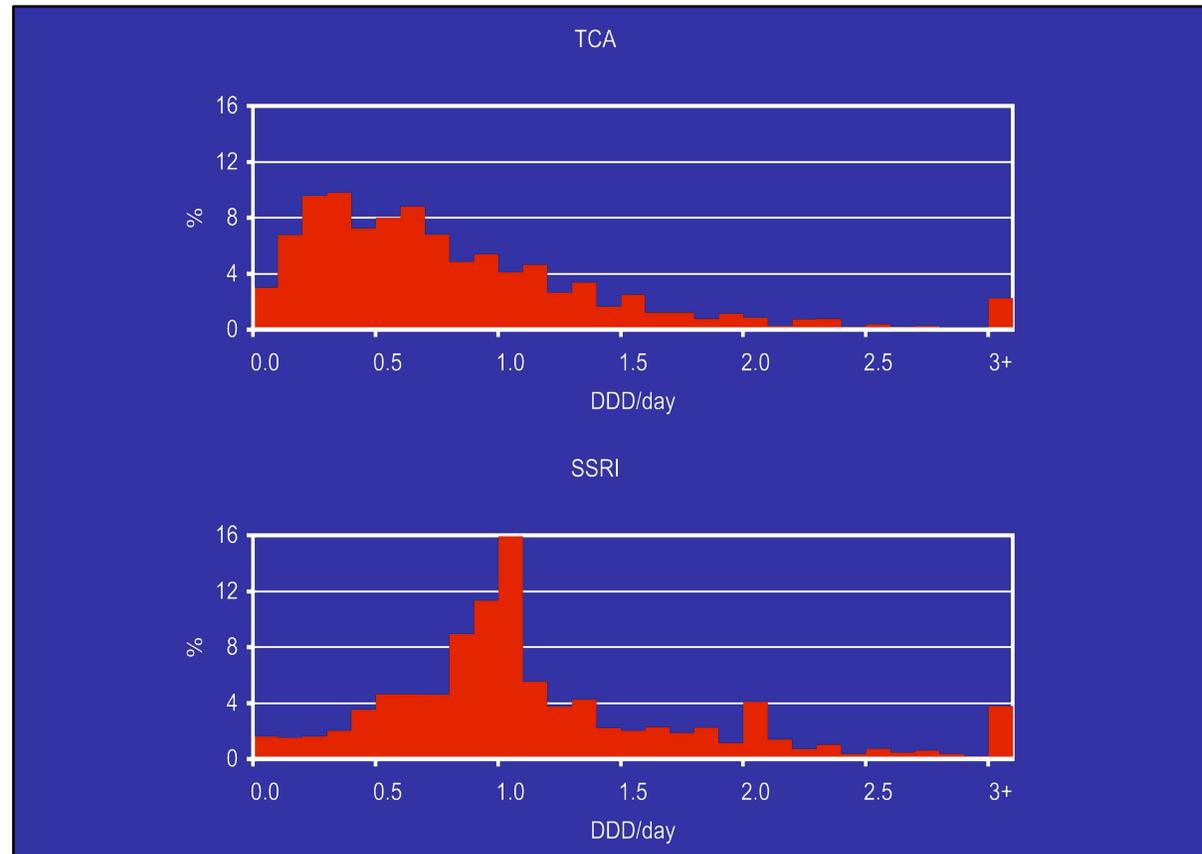
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A02BA: H ₂ -receptor antagonists	4 (3–5)	2 (1–5)		
A02BC: proton pump inhibitors	5 (1–8)	3 (1–6)		
A10BB: oral antidiabetics	4 (1–9)	4 (1–6)		
C: cardiovascular system	4 (1–6)	4 (1–8)		
C07A: beta-blocking agents	8 (5–12)			
C08C: calcium channel blockers	3 (1–4)			
C09A: ACE inhibitors	4 (2–5)			
C09C: angiotensin II antagonists	4 (3–5)			
C10A: serum lipid-reducing agents	3 (6–19)			
D: dermatologicals	7 (2–11)			
D07A: corticosteroids (group I–IV)	4 (1–6)			
G: genito-urinary system & sex hormones	8 (1–13)			
G03C: estrogens	3 (1–7)			
N06AB: SSRIs	6	4 (1–6)	3 (1–5)	0.62 (0.38–0.80)
R: respiratory system				
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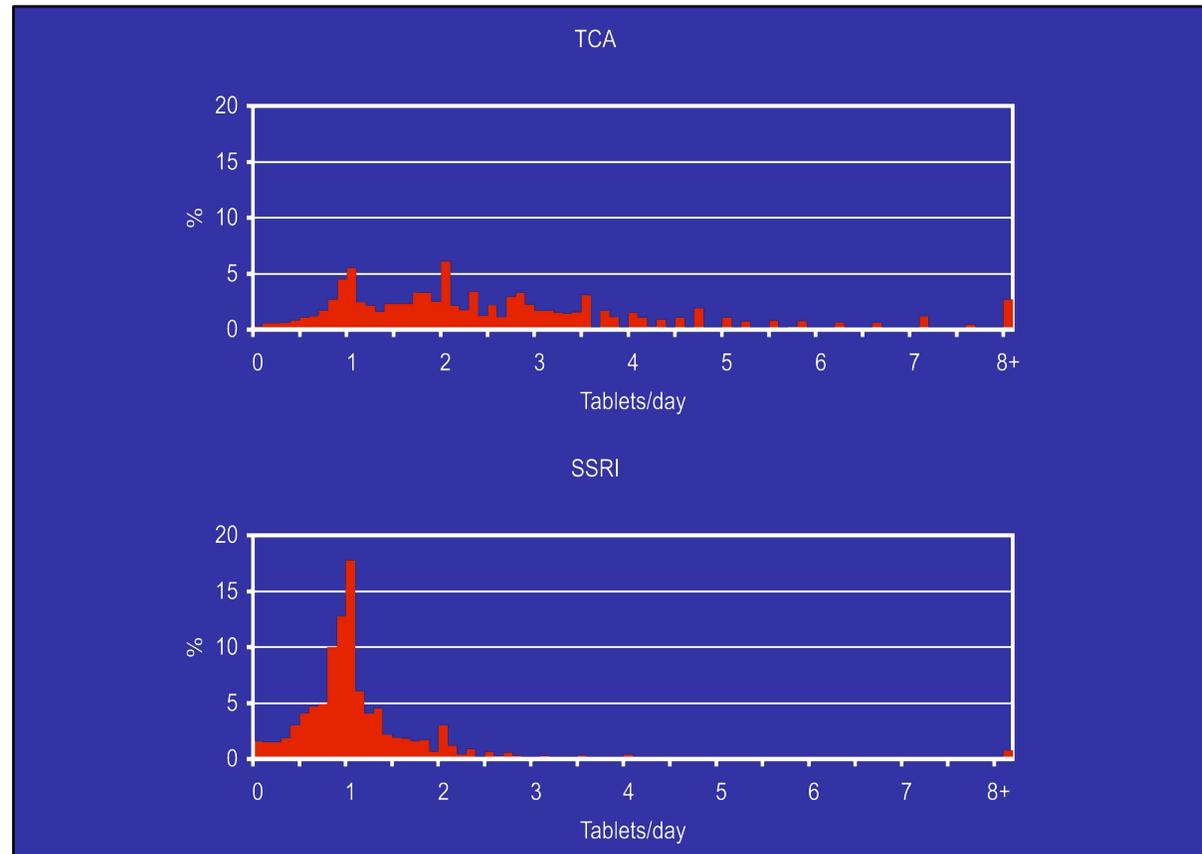
Use of DDDs in individual level dispensing data (RWD)

- Duration of exposure and aspects of adherence
 - Percentage of days covered by the dispensed amount
 - Persistence: Period from first prescription to discontinuation
- Limitation: DDD is meant to express a population average and may not reflect the average use in the individual

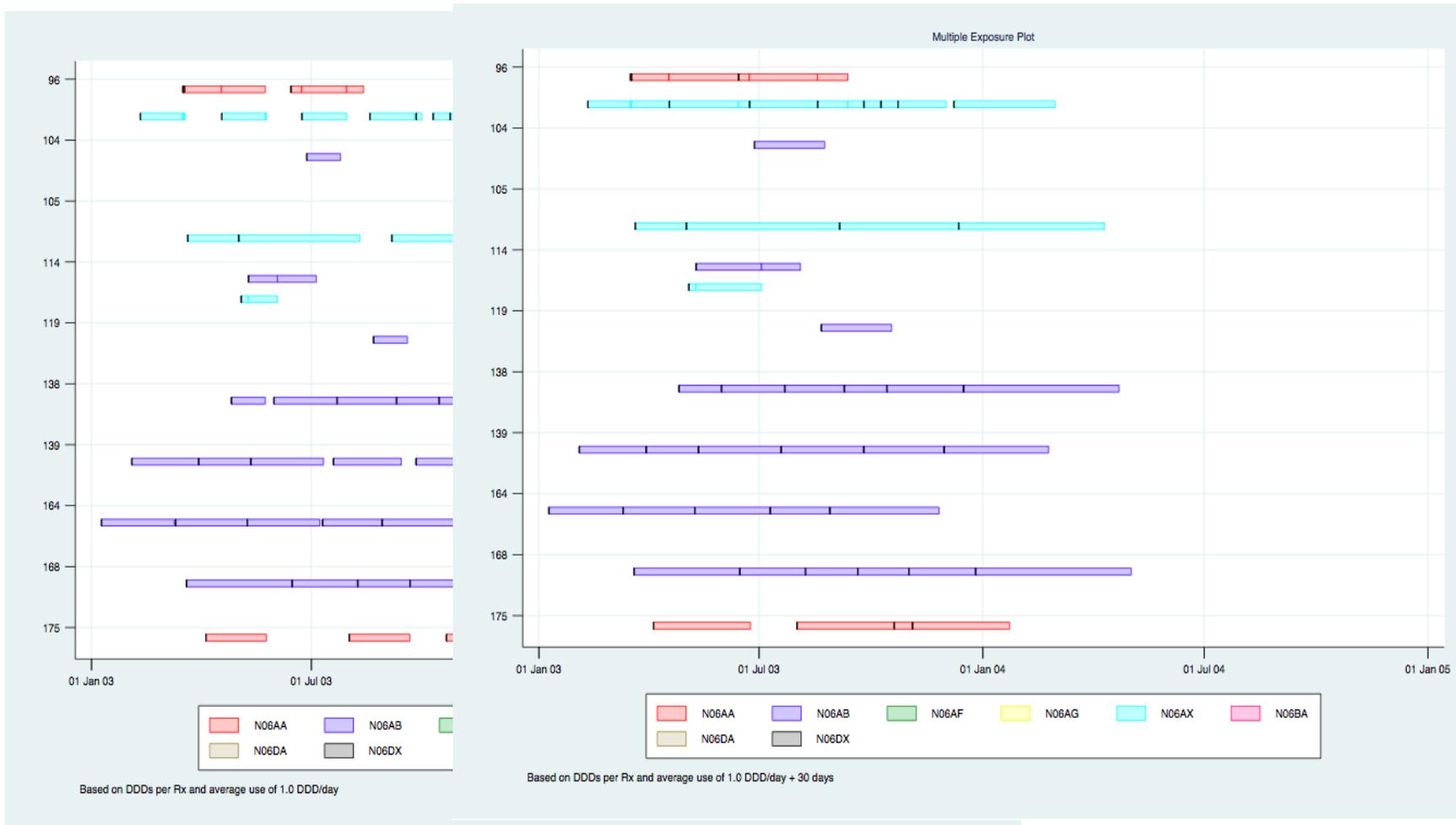
Average used daily dose of antidepressants in DDD/day (Rosholm et al, Eur J Clin Pharmacol 2001)



Average used daily dose of antidepressants in tablets/day (Rosholm et al, Eur J Clin Pharmacol 2001)



Exposure episodes in pharmacoepi studies: Amount in DDDs (1 DDD/day)

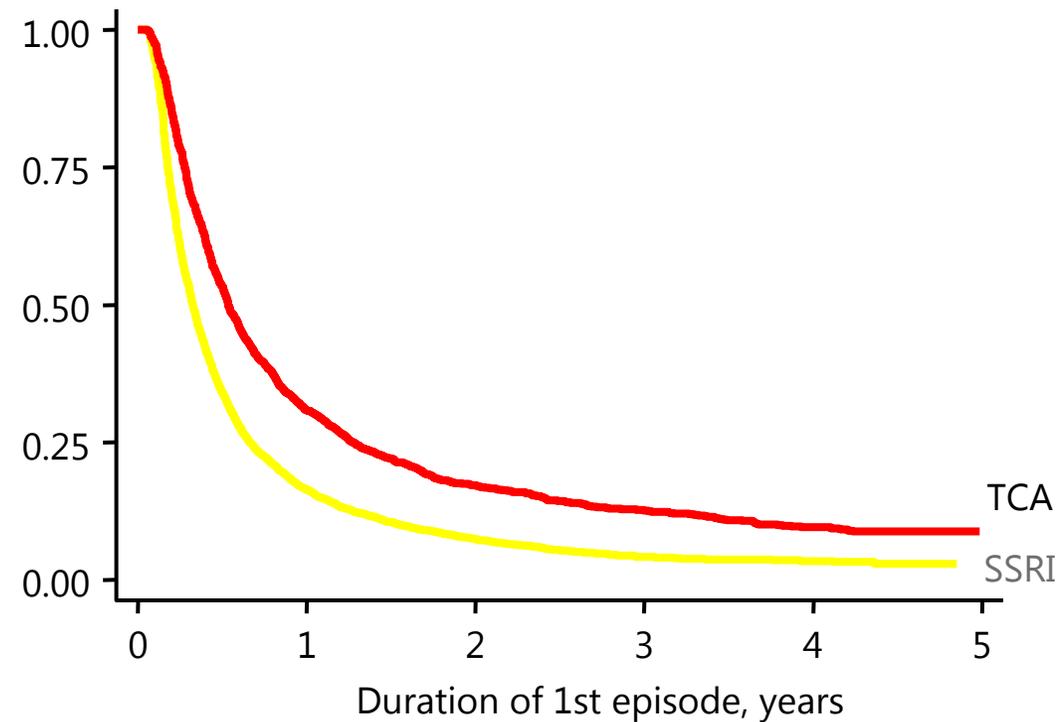


When you have built treatment episodes using tablets, not DDDs

Duration of treatment with TCA and SSRI

(Rosholm et al, Eur J Clin Pharmacol 2001)

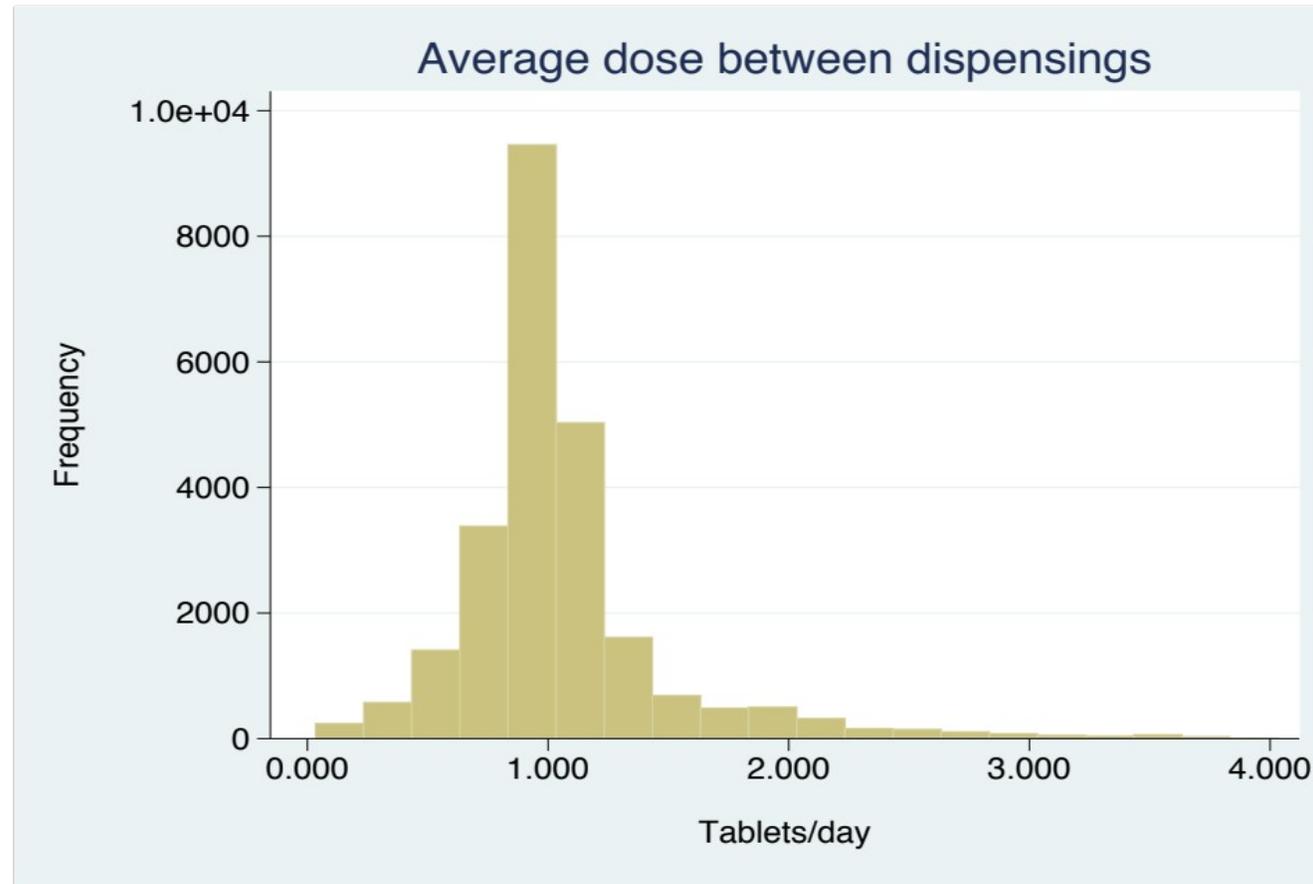
Kaplan-Meier estimates of persisting treatment



The DDD is an average – maybe the “1 DDD” tablet does not exist: DDDs of statins as an example

ATC	Substance	DDD (mg)
C10AA01	simvastatin	30
C10AA02	lovastatin	45
C10AA03	pravastatin	30
C10AA04	fluvastatin	60
C10AA05	atorvastatin	20
C10AA06	cerivastatin	0.2
C10AA07	rosuvastatin	10
C10AA08	pitavastatin	2

Exploratory analysis: average tablets/day



DDDs or tablets for studying adherence and persistence?

- Antidepressants and statins are marketed in different strengths and are individually dosed, most often as one tablet per day
- Difficulties in using DDDs for determining individual treatment patterns for substances where tablet strengths are not a multiple of 1 DDD
- Defining continuous use based on tablets gave more reasonable results
- Treatment discontinuation: Interval between prescriptions
> number of tablets + 90 days (allowed gap)
- Considerations like this may be similar for other drug groups

Benzodiazepines, benzodiazepine related drugs and cancer

- Case-control study
- Incident cancer cases identified in the Danish Cancer Register
- Controls matched on birth year and sex based on incidence density sampling from the entire population
- Benzodiazepines dispensed before the index date from the Danish National Prescription Register
- Cumulative dose in DDDs
- Length of exposure
- Average dose DDDs/day

(Pottegård et al, Br J Clin Pharmacol 2013)

Risk related to cumulative and average dose, calculated using DDDs

Table 3

Association between exposure to benzodiazepine or benzodiazepine related drugs and cancer risk, specified by exposure pattern within the entire follow-up-period, excluding the last year prior to the index date

Subgroup	Cases	Controls	Crude OR (95% CI)	Adjusted OR* (95% CI)
	Exposed/unexposed	Exposed/unexposed		
Cumulative amount of all BZRD				
1–99 DDD	21 756/118 067	167 226/957 778	1.06 (1.04, 1.07)	1.03 (1.01, 1.05)
100–199 DDD	3 206/118 067	24 378/957 778	1.08 (1.04, 1.12)	1.04 (1.00, 1.08)
200–499 DDD	3 107/118 067	22 159/957 778	1.13 (1.08, 1.17)	1.08 (1.04, 1.13)
500–999 DDD	1 628/118 067	11 722/957 778	1.13 (1.08, 1.20)	1.09 (1.03, 1.15)
>1000 DDD	1 596/118 067	11 466/957 778	1.13 (1.07, 1.19)	1.07 (1.01, 1.13)
Length of exposure				
<1 year	21 839/118 067	167 443/957 778	1.06 (1.04, 1.08)	1.03 (1.02, 1.05)
1.0–2.9 years	6 170/118 067	46 052/957 778	1.09 (1.06, 1.12)	1.05 (1.02, 1.08)
3.0–6.9 years	2 826/118 067	20 276/957 778	1.13 (1.08, 1.17)	1.07 (1.03, 1.12)
>7 years	458/118 067	3 180/957 778	1.19 (1.07, 1.31)	1.11 (1.01, 1.23)
Average amount per day within periods classified as exposed				
0.00–0.09 DDD/day	8 976/118 067	69 627/957 778	1.05 (1.02, 1.07)	1.02 (1.00, 1.05)
0.10–0.19 DDD/day	8 118/118 067	62 203/957 778	1.06 (1.04, 1.09)	1.03 (1.01, 1.06)
0.20–0.49 DDD/day	9 216/118 067	68 986/957 778	1.08 (1.06, 1.11)	1.04 (1.02, 1.07)
0.50–0.99 DDD/day	3 687/118 067	26 612/957 778	1.12 (1.09, 1.17)	1.08 (1.04, 1.12)
>1.00 DDD/day	1 296/118 067	9 523/957 778	1.11 (1.04, 1.17)	1.04 (0.98, 1.11)

BZRD, benzodiazepine and benzodiazepine related drugs. Note: All cancer sites are included. *Adjusted for use of aspirin, non-aspirin-NSAIDs, 5- α -reductase inhibitors, statins, angiotensin-II antagonists, oral contraceptives and hormone supplements, antidepressants, antipsychotics, diagnoses of inflammatory bowel disease, COPD, diabetes, alcohol abuse and Charlson Comorbidity Index score.

Risk related to cumulative and average dose, calculated using DDDs

(Pottegård et al, Br J Clin Pharmacol 2013)

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one or benzodiazepine related drugs and cancer risk, specified by exposure pattern within the entire the index date

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200–499 DDD	118 067 / 22 159/957 778	1.13 (1.08, 1.18)	1.08 (1.04, 1.13)
500–999 DDD	118 067 / 11 722/957 778	1.13 (1.08, 1.18)	1.09 (1.03, 1.15)
>1000 DDD	118 067 / 11 466/957 778	1.13 (1.07, 1.19)	1.07 (1.01, 1.13)
Length of exposure			
<1 year	118 067 / 11 466/957 778	1.13 (1.07, 1.19)	1.03 (1.02, 1.05)
1.0–2.9 years	118 067 / 167 443/957 778	1.06 (1.04, 1.08)	1.05 (1.02, 1.08)
3.0–6.9 years	118 067 / 46 052/957 778	1.09 (1.06, 1.12)	1.07 (1.03, 1.12)
>7 years	118 067 / 20 276/957 778	1.13 (1.08, 1.18)	1.11 (1.01, 1.23)
118 067 / 3 180/957 778	1.19 (1.07, 1.32)		
Average amount per day within periods classified as exposed			
0.00–0.09 DDD/day	118 067 / 69 627/957 778	1.05 (1.02, 1.08)	1.02 (1.00, 1.05)
0.10–0.19 DDD/day	118 067 / 62 203/957 778	1.06 (1.04, 1.08)	1.03 (1.01, 1.06)
0.20–0.49 DDD/day	118 067 / 68 986/957 778	1.08 (1.06, 1.10)	1.04 (1.02, 1.07)
0.50–0.99 DDD/day	118 067 / 26 612/957 778	1.12 (1.09, 1.15)	1.08 (1.04, 1.12)
>1.00 DDD/day	118 067 / 9 523/957 778	1.11 (1.04, 1.18)	1.04 (0.98, 1.11)

one or benzodiazepine related drugs and cancer risk, specified the index date

gs. Note: All cancer sites are included. *Adjusted for use of aspirin, non-asp one supplements, antidepressants, antipsychotics, diagnoses of inflammatory

Short-acting beta-agonist use in DDD/year and association with clinically uncontrolled asthma (Davidsen JR et al, Pulm Pharmacol Ther, 2011)

Table 2

Associations between uncontrolled asthma, age, gender, and anti-asthmatic drug use.

		Uncontrolled asthma N (%) ^a	Crude OR (95% CI) ^b
Gender	Women	52 (25.7)	1.00
	Men	44 (28.4)	1.14 (0.71–1.83)
Age (Years)	18–24	14 (20.0)	1.00
	25–34	36 (26.1)	1.41 (0.70–2.84)
	35–44	46 (30.9)	1.79 (0.90–3.53)
SABA use (DDD/year)	0–99	48 (19.6)	1.00
	100–199	19 (36.5)	2.36 (1.24–4.51)
	200–399	10 (29.4)	1.71 (0.77–3.81)
	≥400	19 (73.1)	11.14 (4.43–28.02)
LABA	No	33 (32.7)	1.00
	Yes	63 (24.6)	0.67 (0.41–1.11)
ICS	No	19 (39.6)	1.00
	Yes	77 (24.9)	0.51 (0.27–0.95)
Leukotriene receptor antagonists	No	89 (27.6)	1.00
	Yes	7 (20.6)	0.68 (0.29–1.62)
Oral glucocorticosteroids	No	79 (25.3)	1.00
	Yes	17 (37.8)	1.79 (0.93–3.45)
Long-acting anticholinergs	No	92 (26.4)	1.00
	Yes	4 (50.0)	2.79 (0.68–11.40)
Oral beta-2-agonists	No	94 (26.6)	1.00
	Yes	2 (50.0)	2.76 (0.38–19.83)
Methylxanthines	No	95 (26.9)	
	Yes	1 (100.0)	– ^c

Abbreviations: ACQ = Asthma Control Questionnaire. IBA = inhaled beta-2-agonists. SABA = short-acting beta-2-agonists. LABA = long-acting beta-2-agonists. ICS = inhaled corticosteroids. DDD = defined daily dose. CI = confidence interval.

^a Number and percentages of uncontrolled subjects in each stratum.

^b Female gender, lowest age category, lowest SABA use category, and non-use of specific anti-asthmatic drug categories were considered as references.

^c Not applicable.

Short-acting beta-agonist use in DDD/year and association with clinically uncontrolled asthma (Davidsen JR et al, Pulm Pharmacol Ther, 2011)

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Understanding or misunderstanding the system?

Implications of a defined daily dose fixed database for drug utilization research studies: The case of statins in Portugal (Abrantes et al 2020 Br J Clin Pharmacol)

After noting the differences between using different DDDs over time, recalculating them and comparing to PDDs (estimated as one tablet/day), the authors conclude:

“The principle of maintaining a stable DDD system (i.e., “fixed database”) should be reconsidered by the WHO-CC-DSM. A more flexible and dynamic system, based on an **annually updated national DDD**, would be able to reduce discrepancies between DDDs and PDDs, as well the bias in DUR studies. Further studies are needed to address other limitations of this system, such as the influence of different age pyramid profiles in DUR studies due to the different proportions of paediatric patients.”

Comment: Annually updated national DDDs = no standard

Suggestion: Work WITH the system, not AGAINST it, for example presenting *specifically selected statistics* with a national “correction factor” (could be dynamic, could be age-specific)

The DEFINED Daily Dose

- Means the WHO-DDD, a standard DEFINED by the WHO (Collaborating Centre and the International Working Group for Drug Statistics Methodology)
- Based on this you can make derived units for a specific purpose
 - PDD – Prescribed Daily Dose
(assuming one tablet per day, based on evidence from guidelines, database dosing information, surveys...)
 - CDD – Corrected Daily Dose*
(based on a specific correction factor applied to the DDD)
 - UDD – Estimated average Used Daily Dose*
(based on dispensing data from healthcare databases, note: incorporates adherence)

* Note: non-standard abbreviations and definitions suggested by the presenter

Critique of the ATC and DDD system (and solutions *for the researcher*)

- Changes over time (necessary evolution: recode, regroup)
- Not assigned immediately for new drugs (do it yourself)
- Fixed combination drugs: Imprecise ATC and non-specific DDD (if necessary make your own *ad-hoc* solution)
- The same substance under different ATC codes (be aware of the exceptions)
- The DDD does not reflect the average dosage for all indications and patient groups (it is not meant to, recalculate if possible)
- 1 DDD between 2 tablet strengths (allowed according to the definition: be aware, use another approach if possible)

Recommendations for use of the ATC/DDD methodology in research

- Population-based studies
 - Meaningful cross-national comparisons and time series
 - Keep as close as possible to the standards
 - Re-calculate historical figures
 - **Refer to the used ATC/DDD version**
- Individual-based drug utilisation studies
 - More "creativity" allowed
 - Combination of different ATC-groups
 - Partitioning combination drug use into separate substances
 - Factors for converting DDDs to estimated Used Daily Doses
 - Explore your data, e.g. distribution of estimated average used daily dose
 - **Be transparent! Always make assumptions explicit and use the standard classification and metrics as a reference point**