

**Anatomical Therapeutic
Chemical (ATC) classification
and the Defined Daily Dose
(DDD): principles for classifying
and quantifying drug use**

DRAFT

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Disclosure

- Author is an employee of Merck
- A lot of slides are adopted from a prior ICPE English short course on drug utilization by Hege Salvesen Blix

Outline

- The ATC/DDD methodology
 - definitions, purpose, structure and principles
- Real world applications of ATC/DDD

What is ATC/DDD?

- ATC (Anatomical Therapeutic Chemical) classification
 - Don't confuse it with Anatomical Therapeutic (AT) classification developed by European Pharmaceutical Market Research Association (EPHRA)
- DDD (Defined Daily Dose) *The assumed average maintenance dose per day for a drug used for its main indication in adults*

Introduction to Drug Utilization Research, WHO 2003

Main Purpose

- “*International language for drug utilization research*”
 - to serve as a tool for presenting drug utilization research in order to improve quality of drug use
 - to compare data within a country and between countries

The WHO Collaborating Centre for Drug Statistics Methodology

- Established in 1982 as a European WHO Centre
- Since 1996 a global WHO Centre
- Located in the Department of Pharmacoepidemiology at the Norwegian Institute of Public Health
- The staff of the Centre is responsible for drug consumption statistics in Norway

The WHO Centre

- To classify drugs according to the ATC system and assign DDDs
- To review and revise as necessary the ATC classification system and DDDs
- To stimulate and influence the practical use of the ATC system
- To organize training courses in the ATC/DDD methodology

ATC Main Group

- A Alimentary tract and metabolism
- B Blood and blood forming organs
- C Cardiovascular system
- D Dermatologicals
- G Genito urinary system and sex hormones
- H Systemic hormonal preparations, excl. sex hormones and insulins
- J Antiinfectives for systemic use
- L Antineoplastic and immunomodulating agents
- M Musculo-skeletal system
- N Nervous system
- P Antiparasitic products, insecticides and repellents
- R Respiratory system
- S Sensory organs
- V Various

Structure of ATC Code

- **A** ALIMENTARY TRACT AND METABOLISM
(1st level, anatomical main group)
- **A10** DRUGS USED IN DIABETES
(2nd level, therapeutic subgroup)
- **A10B** BLOOD GLUCOSE LOWERING DRUGS, EXCL.
INSULINS
(3rd level, pharmacological subgroup)
- **A10BA** BIGUANIDES
(4th level, chemical subgroup)
- **A10BA02** METFORMIN
(5th level, chemical substance)

General Principles for ATC Classification

- Drugs are classified according to their main therapeutic use
- Only one ATC code for each administration form
- Several ATC codes:
 - Clearly different therapeutic uses reflected in different
 - Routes of administration (e.g. topical, systemic)
 - Strengths

“Simple” Codes

- Linagliptin (e.g. Trajenta): Antidiabetic → DPP-4 inhibitor → A10BH05
- Lamivudine (e.g. Epivir): HIV → Antiviral → J05AF05
- Sumatriptan (e.g. Imigran): Antimigraine → 5HT1 agonist → N02CC01
- Formoterol (e.g. Oxis): Antiasthmatic → β 2 agonist → R03AC13

Different Indication – One ATC Code

- Example duloxetine:
 - –Major Depressive Disorder (Cymbalta: 30mg, 60mg)
 - –Stress Urinary Incontinence (Yentreve: 20mg, 40mg)
 - –Diabetic neuropathic pain (Cymbalta)
 - Overlapping dosages used for the various indications
- ATC code as *antidepressant* (N06AX21)

Several ATC codes – “one indication”

Bone diseases/osteoporosis	ATC group
Vitamin D and analogues	A11CC
Calcium supplement	A12A
Estrogens/Tibolon/SERM	G03C/G03F/G03X
Parathyroid hormones	H05AA
Calcitonin	H05BA
Bisphosphonates	M05BA/M05BB

Several ATC Codes – Different Administration Forms and Therapeutic Use

- **Prednisolone**
 - A07EA01 (Enemas and rectal foams)
 - C05AA04 (Rectal suppositories)
 - D07AA03 (Creams, ointments and lotions)
 - H02AB06 (Tablets, injections)
 - R01AD02 (Nasal sprays/drops)
 - S01BA04 (Eye drops)
 - S02BA03 (Ear drops)

Defined Daily Dose (DDD)

- DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults

The Concept of the DDD

- A technical unit of measurement, represents an "average" daily dose for the main indication
- Useful for measuring and comparing volume of drug use
- Should not be interpreted as the recommended or prescribed dose but as an international compromise based on review of available documentation
- DDD may even be a dose that is seldom prescribed, because it is an average of two or more commonly used doses

Sources Used When Assigning DDDs

- Approved dose recommendations for the main indication
- Submitted documentation from the applicant, textbooks, and data from clinical trials

Commonly Used Measures

- DDDs per 1000 inhabitants per day
- DDDs per 100 bed-days
- DDDs per inhabitants per year

ATC/DDD Alterations

- Alterations of ATC and DDDs may occur in order to reflect changes in drug therapy.
- It is important to describe the version of the ATC/DDD system used in research.

Drug Exposure – Expressed in DDDs

- Is normally given as:
- **DDDs/1000 inhabitants/day** *Example: 10 DDDs/1000 inhabitants/day*
- **Indicates that 1% of the population can receive a certain treatment continuously (i.e. daily)**
- Note: Only true if the DDD is equal to the actual dose used
- **Used as surrogate for point prevalence (therapeutic intensity)**

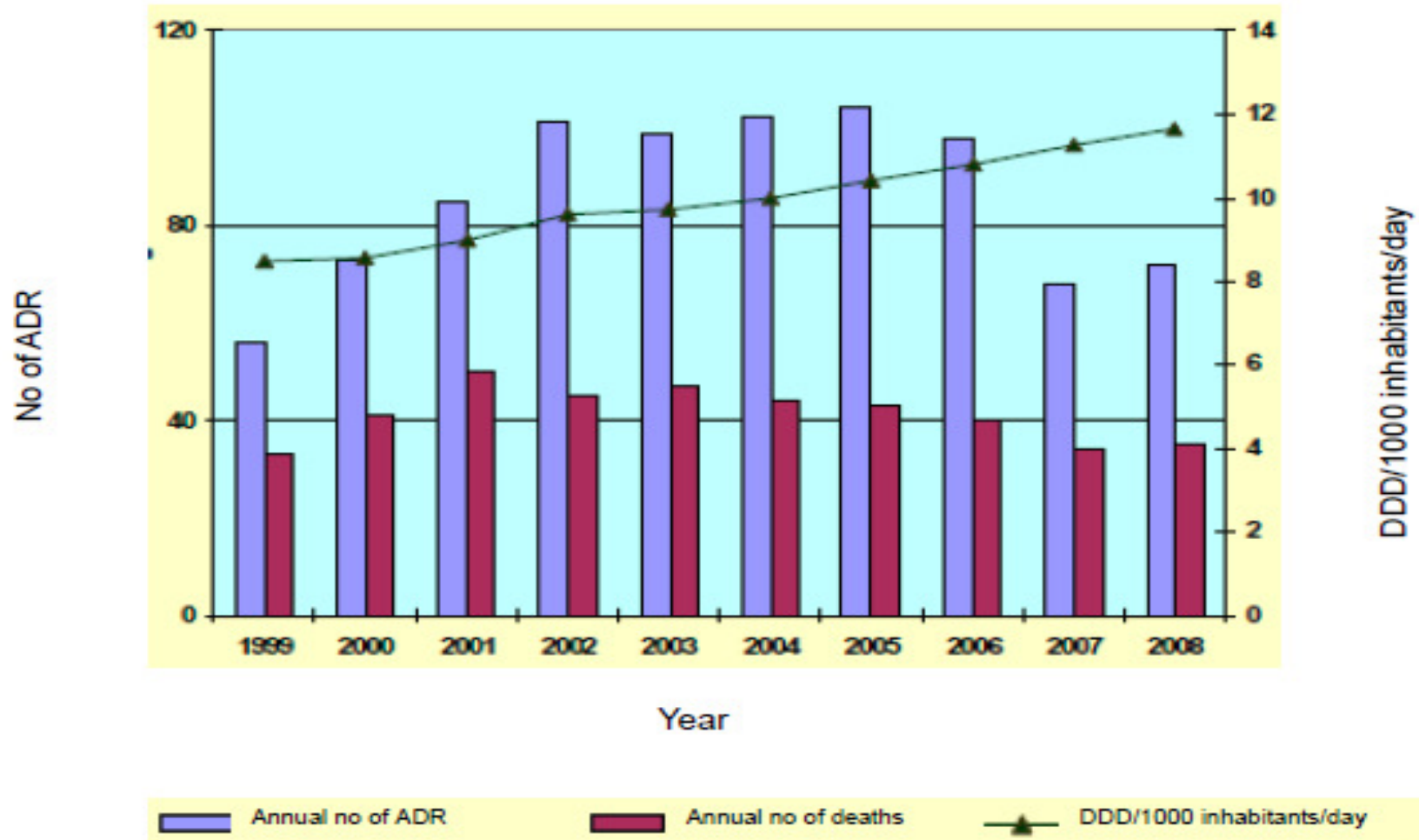
Applications of the ATC/DDD

- Drug utilization and pharmacoepidemiology
 - Pharmacovigilance
 - Regulatory intervention and impact of drug use

Pharmacovigilance

- Trends in frequency of ADR reports examined against drug exposure
- Ratio: ADR/DDDs (or DDD/1000 inhab/day)

Spontaneous ADR Reports of Warfarin (B01AA03) in Norway 1999-2008

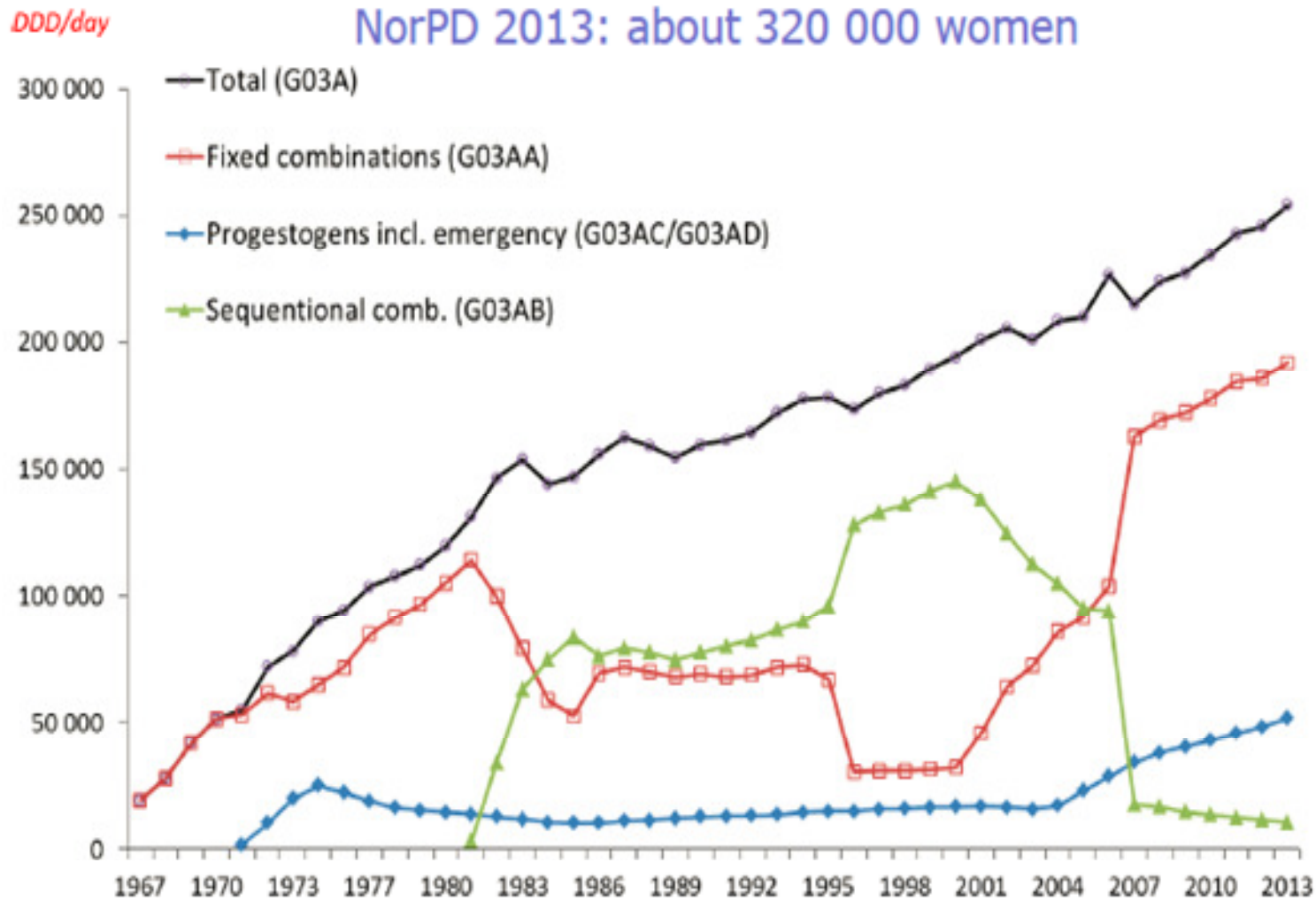


Source: Norwegian Medicines Agency, Annual report 2008

Following and Comparing Trends in Drug Expenditure

- ATC: to determine to what extent increased costs can be attributed to increased use of a drug group
- DDD: to compare costs of two formulations of the same active ingredient
- DDD: to follow the expenditure of a certain treatment

Sales of Contraceptives in Norway (ATC gr.G03A) 1967-2013 (excl. IUDs, vaginal rings, implants and inj.)



ATC 2014

Practical Use in Drug Utilization...

- Challenge:
 - It provides a tool where ATC and DDD are established for generic substances. The users have to make the correct link between the ATC/DDD value and the medicinal product.

National Drug Register – Link to ATC/DDD

- ATC codes should be linked correctly to the product on the package level
- Number of DDDs per package should be calculated
- Procedures for updating the medicinal product register according to the latest ATC/DDD version should be introduced
- It is recommended that this task is administered by persons with detailed knowledge of the methodology
- Note:
 - Unofficial ATC codes and DDDs
 - Lack of update according to annual ATC/DDD alterations

Drug Register – Example

Unique identifier	Brand name and formulation	Strength	Package size	ATC code	Generic name	DDD value	DDD/package
454173	Zocor tablets	20mg	100	C10AA01	simvastatin	30mg	66.67
438454	Efexor depot capsules	150mg	98	N06AX16	venlafaxine	100mg	147

http://ec.europa.eu/health/ph_projects/2001/monitoring/fp_monitoring_2001_frep_12_1_en.pdf/

Are Published Data Comparable?

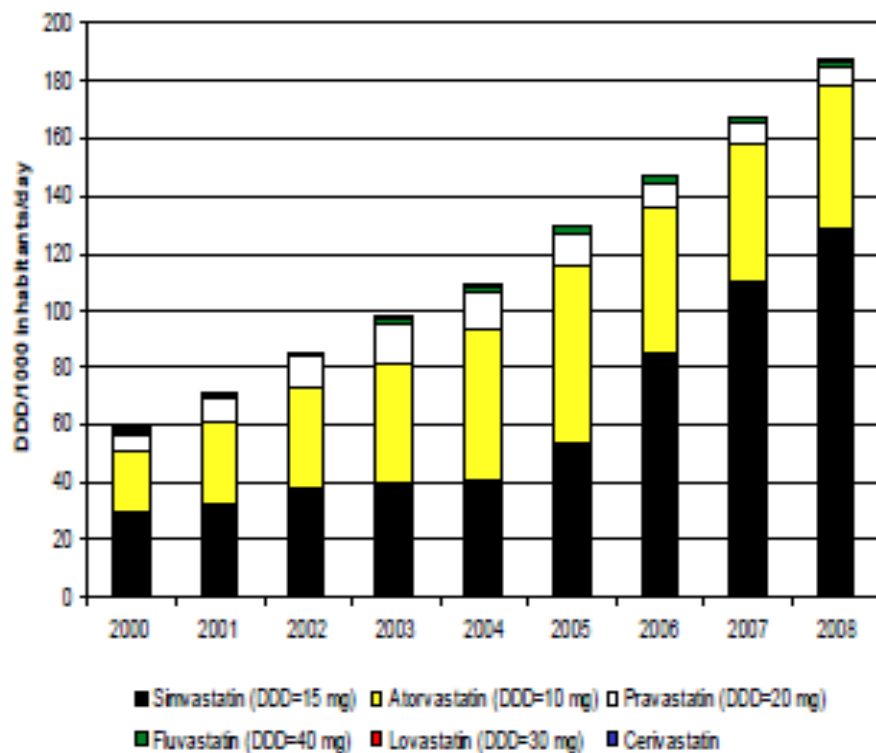
- ESSENTIAL INFORMATION:
 - Which ATC codes and DDDs are used

Notice DDD alterations

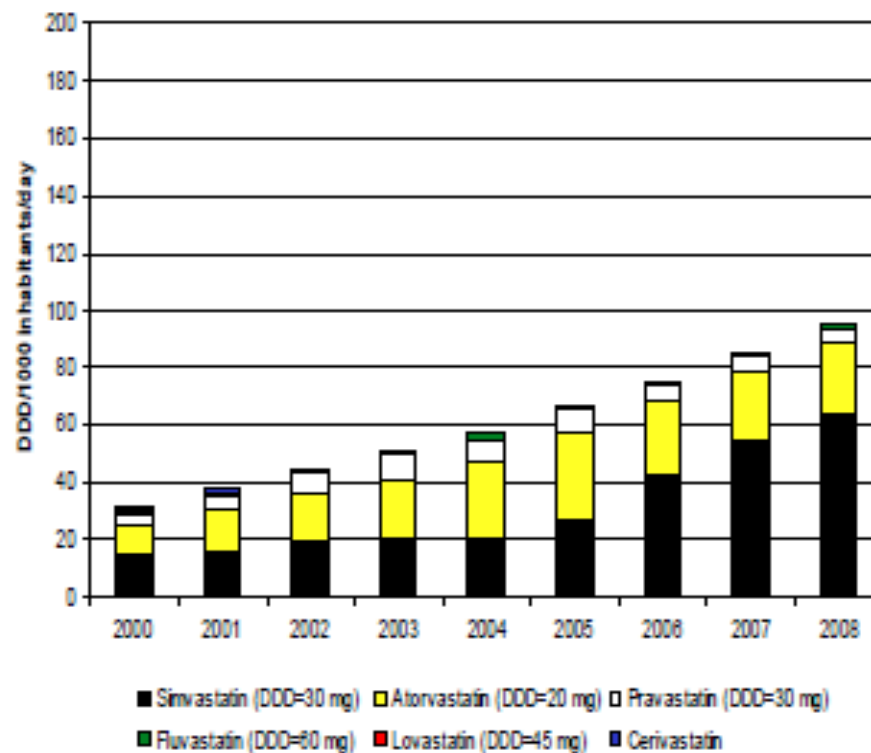
- Important to be aware of
- Cumulative list of ATC/DDD alterations
www.whooc.no
- DDD alteration example :
 - Statins - C10AA (changed twice, latest 2009)

Sales of Statin (C10AA) in Norway 2000-2008

DDD version 2008



DDD version 2009



ATC/DDD in Drug Utilization Research

- Study patterns of use and changes over time
- Evaluate the impact of information efforts, regulatory changes etc.
- Study drug exposure in relation to adverse drug reactions
- Indicate over-use, under-use and misuse/abuse of drugs
- Define need for further pharmacoepidemiology studies
- Proper knowledge about the ATC/DDD system

“Success Factors”

- Correct link of ATC code and DDD value (i.e. number of DDDs/package) at the medicinal product package level
- Request new ATC codes and DDDs if they are not available
- Describe the ATC/DDD version used, i.e. give proper references in all publications and statistics

Conclusion

- ATC/DDD system is “the gold standard” for international drug utilization research
- •ATC/DDD is a tool for exchanging and comparing data on drug use at local, national or international levels

More Information

www.whooc.no

.... or annual ATC/DDD courses in Oslo, Norway