Anatomical Therapeutic Chemical Classification (ATC)
&
And Defined Daily Dose (DDD)

Principles for classifying and quantifying drug use

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Course outline/objectives

- 1. Introduction: drug classification systems
- 2. ATC classification : definition, structure and principles
- 3. DDD: definition, concept, principles of assignment
- 4. DDD: measure of drug exposure
- 5. ATC/DDD: Applications
- 6. Resources
- 7 Group –work and discussions

INTRODUCTION

What are Drug classification systems

- **A common language** for describing drug assortment in a country or region.
- **A standard** for uniformity in collection and aggregation of drug use data
- **An international standard** for comparison of data between countries

Types of drug classification systems

- **The Anatomical Therapeutic Classification (AT)** developed by the European Pharmaceutical Market Research Association (EPhMRA)

- **The Anatomical Therapeutic Chemical (ATC)** classification developed by Norwegian researchers.

- **Uniform System Classification (USC)** used inCanada and the USA

Types of drug classification systems

- **How else do we classify drugs in various settings??**

What is ATC?

- **ATC classification**

- **A**natomical: The organ or body system on which a drug acts
- **T**herapeutic: Indication for typical use(s) of a drug
- **C**hemical: Structure and chemical properties of the active principle

ATC CLASSIFICATION SYSTEM

ATC = Anatomical Therapeutic Chemical

DDD = Defined Daily Dose

Download from:

http://www.whocc.no/filearchive/publications/2016_guidelines_web.pdf

"International language for drug utilisation research

MAIN PURPOSE OF ATC/DDD

- ***"An International language for drug utilization research"***

- A standadized tool for presenting drug utilization research for improving quality of drug use

- Comparison of data within a country and between countries

ATC/DDD administration

- The WHO Collaborating Centre for Drug Statistics Methodology (WHOCC)
- **www.whocc.no**

1982: A European WHO Centre in Oslo Norway

- 1996: **Globalization** of ATC/DDD system and **linked** to WHO Headquarters in Geneva

ATC/DDD: administration

- **WHO International Working Group for Drug Statistics Methodology**
- **Advisory** WHOcc
- **Comprises** of Experts
- **Represent** users of ATC/DDD in WHO global regions.

ATC/DDD: administration

- **The terms of reference of the Working Group are:**

- **Scientific development** of the ATC/DDD system.

- **Approval of** new ATC / DDD assignments and alterations

- **Promote use** of the ATC/DDD system in drug utilization studies.

- **Revise guidelines** for assignment and change of ATC/ DDDs.

ATC /DDD: administration

- **The mandate of the WHOCC and EXPERT Group is to:**

- **Maintain stable** ATC/DDDs over time

ATC: CLASSIFICATION STRUCTURE

ATC structure

- **Drugs are classified at 5 levels according to:**

- **Anatomical** site of therapeutic effect
- Main **therapeutic indication**
- **Pharmacological** effect
- **Chemical** class
- **Chemical** substance

Classification structure

- **5 different levels.**
- **1st level: 14** main groups according to the **organ system**
- **2nd level: The main therapeutic** indication.
- **3rd level:** The **pharmacological / therapeutic** sub-group
- **4th level**: The **chemical class**
- **5th level:** The **chemical substance.**

Level 1: Anatomical groups (14) –one letter

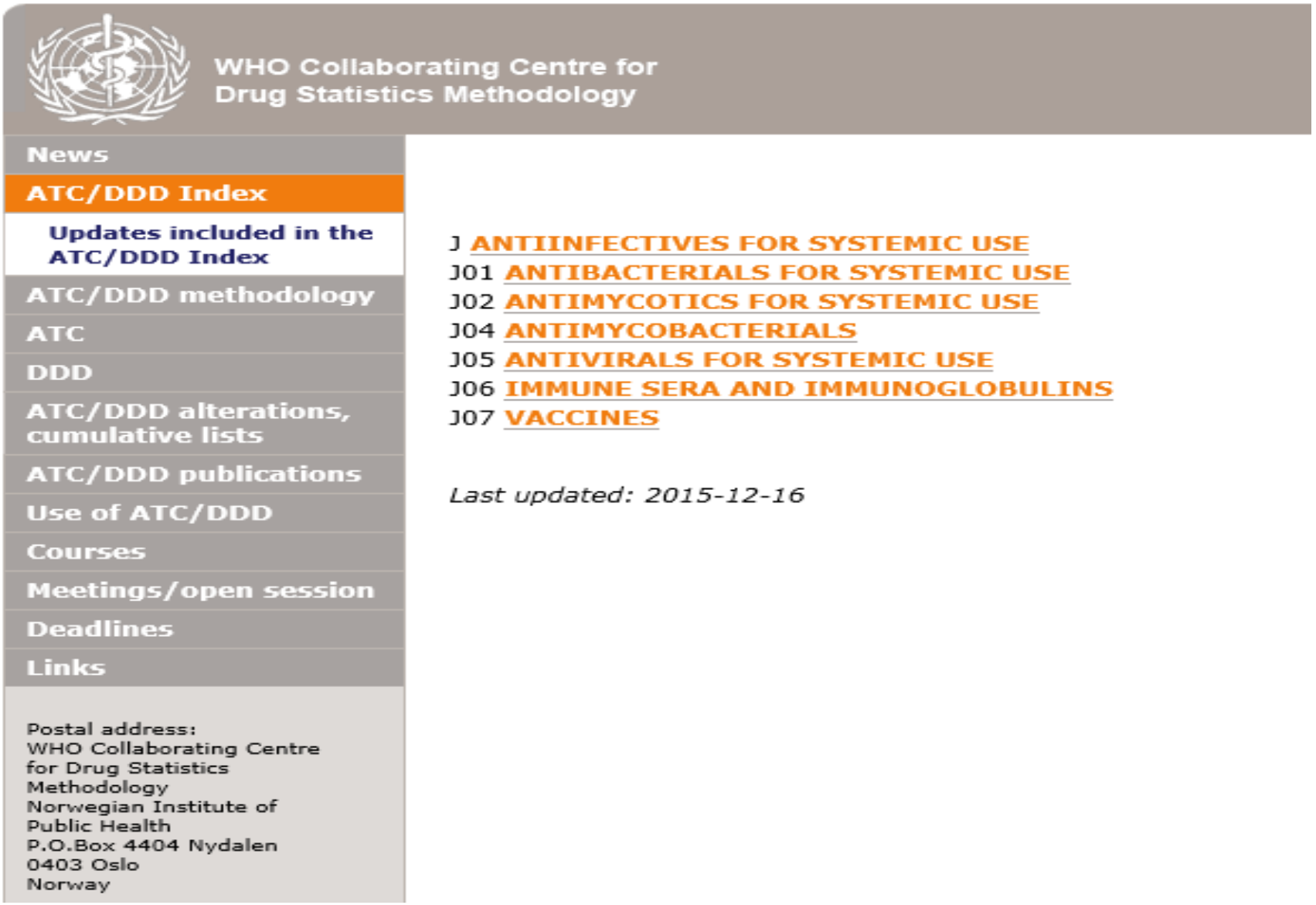
A	ALIMENTARY TRACT AND METABOLISM
B	BLOOD AND BLOOD FORMING ORGANS
C	CARDIOVASCULAR SYSTEM
D	DERMATOLOGICALS
G	GENITO -URINARY SYSTEM AND SEX HORMONES
H	SYSTEMIC HORMONAL PREPARATIONS, excl.sex hormones and insulin
J	ANTI-INFECTIVES FOR SYSTEMIC USE
L	ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS
M	MUSCULO-SKELETAL SYSTEM
N	NERVOUS SYSTEM
P	ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS
R	RESPIRATORY SYSTEM
S	SENSORY ORGANS
V	VARIOUS

Level 2: Therapeutic Indications- two digits

ATC2	*Selected Examples*
A10	DRUGS USED IN DIABETES
B05	BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS
C02	ANTIHYPERTENSIVES
C07	BETA BLOCKING AGENTS
H03	THYROID THERAPY
L04	IMMUNOSUPPRESSIVE AGENTS
M03	MUSCLE RELAXANTS
N01	ANESTHETICS
S01	OPHTHALMOLOGICALS
S02	OTOLOGICALS

EXAMPLES

ATC structure/website



Level 2: Therapeutic class- two digits

- R: Respiratory system- ATC level 1
- ATC: level 2
- R01 Nasal preparations
- R02 Throat preparations
- R03 Anti-asthmatics
- R05 Cough and cold preparations
- R06 Antihistamines for systemic use
- R07 Other respiratory products

Level 3: Pharmacologic category- one letter

- R03 Anti-asthmatics –ATC level 2
- R03A: Adrenergics, inhalants
- R03B : Other anti-asthmatics, inhalants
- R03C Adrenergics for systemic use
- R03D Other anti-asthmatics for systemic use.

Level 3: Pharmacological groups –one letter

ATC3	Selected examples
A02A	Antacids
A06A	Laxatives
A10A	Insulin and analogues
N05A	Antipsychotics
N06A	Antidepressants
S01A	Anti-infectives
S01C	Anti-inflammatory and anti-infectives in comb
S02A	Anti-infectives

Example : ATC for metformin

	ATC Level	ATC Text	ATC Code
1	Anatomical Main Group (one letter)	*Alimentary tract and metabolism*	*A*
2	**Therapeutic Subgroup** (two digits	*Drugs used in Diabetes*	*A10*
3	Pharmacological subgroup (one letter)	*Oral glucose lowering drugs*	*A10 B*
4	Chemical Subgroup (one letter)	*Biguanides*	*A10 B A*
5	Chemical Substance (two digits)	*Metformin*	*A10BA 02*

Example : ATC for AMOXICILIN

J **General anti-infectives** for systemic use
(1st level, anatomical main group)

J01 **Antibacterials** for systemic use
(2nd level, therapeutic subgroup)

J01C **Beta-lactam antibacterials**, penicillins
(3rd level, pharmacological subgroup)

J01CA **Beta-lactamase sensitive penicillin**s with extended spectrum
(4th level, chemical subgroup)

J01CA04 Amoxicillin
(5th level, chemical substance)

ATC:
Principles for classification

ATC: General Principles

- **Main Principle:**
- Medicinal products are classified according to the main therapeutic use of the main active ingredient.
- **One ATC code**:
- Each route of administration
- Similar ingredients and strength
- Immediate and slow release tablets

More than one ATC code

- **When a drug has:**
- Two or more strengths
- Two or more routes of administration
- Clearly different therapeutic uses.

Different ATC codes: " different strengths"

- **Sex hormones**: Dosage forms and strengths for cancer - under L02 - *Endocrine therapy*
- Other dosage forms/strengths – under G03 - *Sex hormones and modulators of the genital system*

- **Finasteride:**
- A low strength tablet for male pattern baldness - under D11AX – *Other dermatologicals*.
- A high strength tablet for benign prostatic hypertrophy (BPH) - under G04C - *Drugs used in BPH.*

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)

Different indications – one ATC code

Example duloxetine:

- Major Depressive Disorder (Cymbalta®: 30 mg, 60mg)
- Stress Urinary Incontinence (20 mg, 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**
- Oestrogens/SERM: **G03C/G03F/G03X**
- Parathyroid hormones: **H05AA**
- Calcitonin: **H05BA**
- Bisphosphonates: M05BA/M05BB

ATC codes: Combination products

- Combination products with two or more active ingredients in the same 4th level are normally classified using the 5th level codes 20 or 30.
- Example:
- N01BB02 *lidocaine*
- N01BB04 *prilocaine*
- N01BB20 *combinations of lidocaine and prilocaine*

Principles for changes to ATC classification

- *Changes should be kept to a minimum.*

- **Alterations in ATC classification due to:**
- The main use of a drug has changed
- Create new groups for new substances
- Achieve better specificity in the groupings.

Other ATCs

- **ATCvet** is based on the same main principles as the ATC system for medicines for human use.

- **ATC herbal** is structurally similar to the official ATC system, but the herbal classification is not adopted by WHO.

- Classification can be found at website : www.whocc.no.

DEFINED DAILY DOSE (DDD)

DDD: Definition

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

- A technical unit of measurement, represents an ”average” daily dose for the main indication

Defined Daily Dose (DDD)

- Drug exposure – expressed in DDDs
  - DDDs/1000 inhabitants/day (most common)
  - DDDs per100 bed-days
  - DDDs per inhabitants per year

  - E.g. 10 DDDs/1000 inhabitants/day = indicates that 1% of the population receive a certain treatment continuously (i.e. daily) – only true if the DDD is equal to the actual dose used

  - Used as a surrogate for point prevalence (therapeutic intensity)

The concept of DDD

DDD is a unit of measurement and does not necessarily reflect the recommended or **Prescribed Daily Dose (PDD)**

- Reflect global dosage irrespective of the wide inter- individual and inter-ethnic variations in PK of drugs

- DDDs is a fixed unit of measurement independent of **price, currencies, package size and strength.**

Principles for DDD assignment

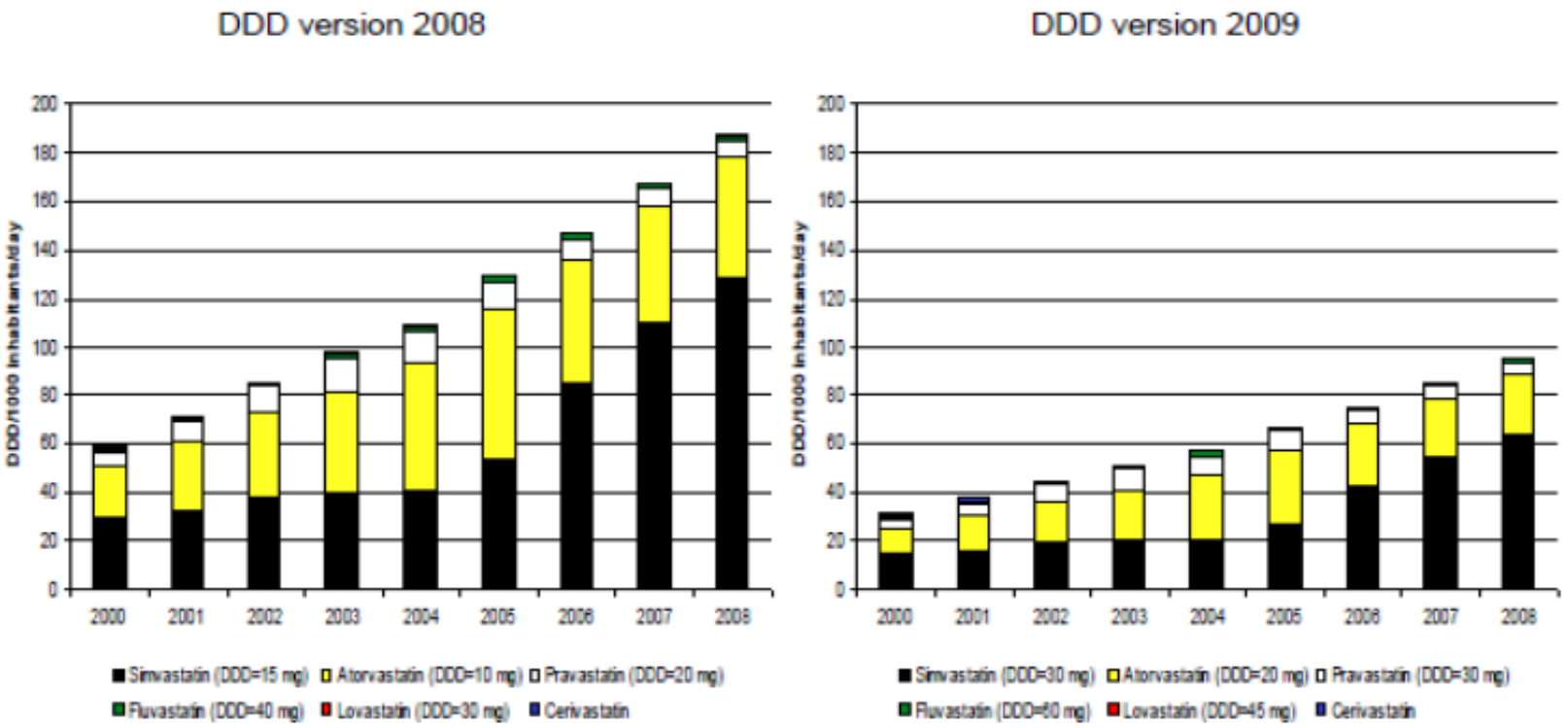
- A DDD is only assigned for drugs with **market authorization and have an ATC code**
- Assign **only one DDD per route** of administration within an ATC code.
- DDDs for single substances are based on **monotherapy**
- DDD may even be a dose that is seldom prescribed, because it is an **average of two or more commonly used doses**

DDD assignment & changes

- WHO uses approved dose recommendations for the main indication
- Submitted documentation from the applicant, textbooks and data from clinical trials
- Important to be aware of ATC/DDD alterations (e.g. C10SAA – Statins: changed twice, latest in 2009)
- Alterations of ATC and DDDs may occur in order to reflect changes in drug therapy
- Important to describe the version of the ATC/DDD system used in research

Importance of correct reporting

Sales of Statin (C10AA) in Norway 2000-2008



New

WHO Collaborating Centre for Drug Statistics Methodology

Norwegian Institute of Public Health

News
ATC/DDD Index
ATC/DDD methodology
ATC
DDD
ATC/DDD alterations, cumulative lists
ATC/DDD publications
Use of ATC/DDD
Courses
Meetings/open session
Deadlines
Links

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ATC classification of combinations of opioids and other analgesics

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The ATC classification of opioids in combination with other analgesics was on the agenda for the International Working Group for Drug Statistics Methodology meeting in October 2015. A proposal to classify all combination of opioids and other analgesics in a new ATC 4th level *N02AJ Opioids in combination with non-opioid analgesics* was decided. All combinations of opioids and other analgesics will be classified in *N02A Opioids*, independent of the amount of opioid.

Since the alterations will have implications for many users of the ATC/DDD methodology, **the deadline for objections and comments to the temporary alterations in N02A Opioids is extended from 1 February to 15 February 2016.**

You will find an overview of the temporary classification below.

Please note that the proposal was published on our website in December 2015 and is available here.

The existing DDDs of the combination products moved to N02AJ, expressed in unit dose (UD), will be kept.

The following new ATC 4th level and 5th levels will be assigned for opioids in combination with non-opioid analgesics:

Archive

22.01.16 ATC classification of combinations of opioids and other analgesics
18.12.15 ATC/DDD course 9-10 June 2016 in Oslo
09.12.15 New ATC/DDD included in the index of 2016
09.12.15 List of DDDs for three years revision
08.12.15 Updates of the list of DDDs for combined products
02.12.15 New ATC/DDDs and alterations from the October 2015 meeting
28.10.15 ATC/DDD course in Oslo 9-10 June 2016
05.05.15 Updates of the list of DDDs for combined products
30.04.15 New ATC/DDDs and alterations from the March 2015 meeting
16.12.14 List of DDDs for three years revision

Paediatric DDDs

- DDDs are assigned based on **use in adults**
- For **paediatric medications**, dose recommendations are based on **age and body weight**
- Most pediatric medications are **used off-label** and documentation regarding dose regimens not available
- WHO has concluded that it is not possible to assign pediatric DDDs
- Prevalence of drug use in children to be based on **PDD or indications in paediatric** populations

Prescribed Daily Dose (PDD)

- **PDD** = Average daily amount of a drug that is actually prescribed
- Determined from prescription studies, medical- or pharmacy records and patient interviews
- Relate the PDD to the diagnosis on which dosage is based
- If substantial discrepancy between the PDD and DDD - important to take into account when evaluating and interpreting drug consumption figures
- **Consumed daily dose:** Specially designed studies including patient interviews are required to measure actual drug intake at the patient level

Prescribed Daily Dose (PDD)

- **Subject to variability**

- **What factors may influence PDD??**

PDD: interpretation

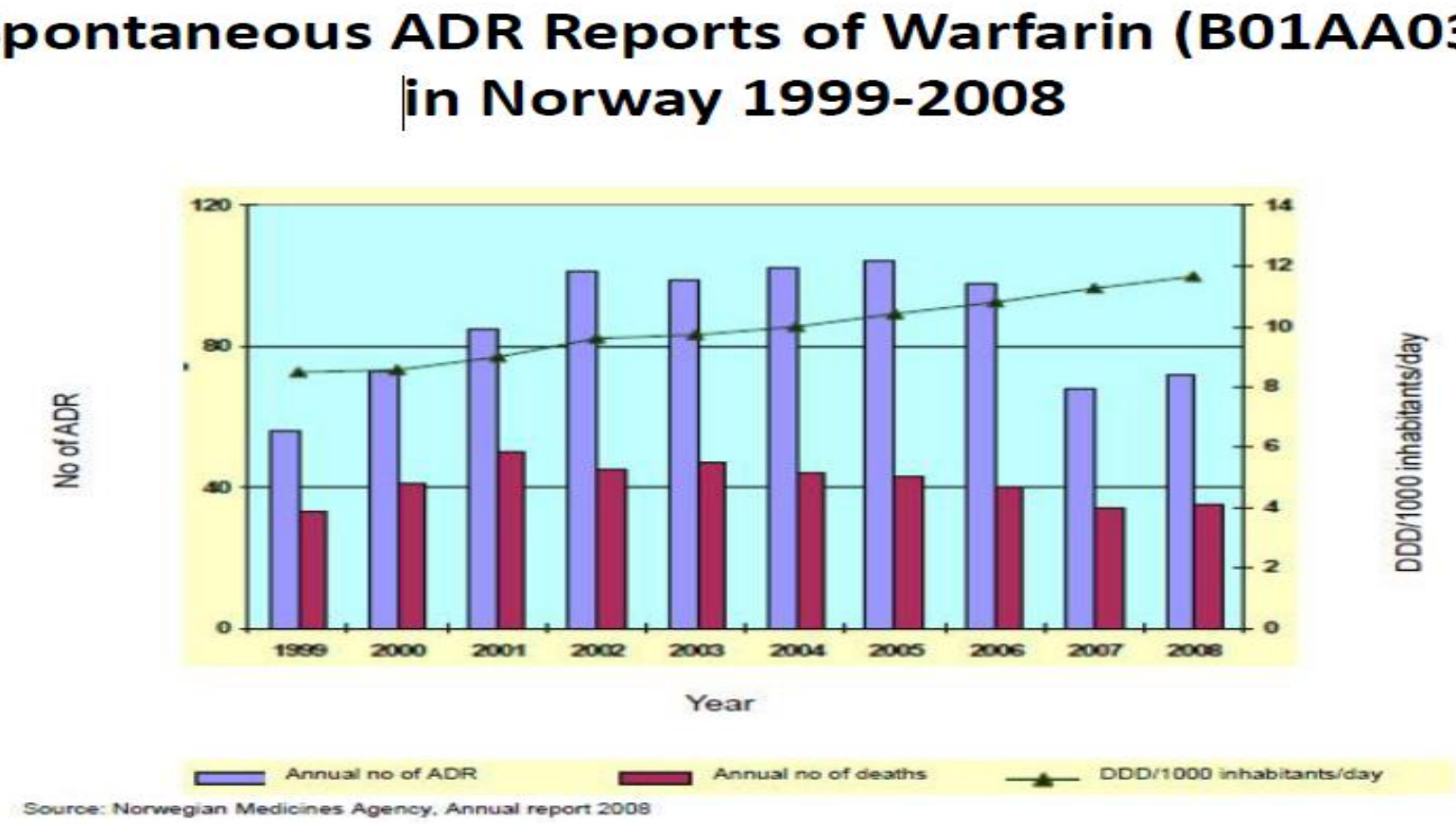
- **PDD vs DDD**
- **PDD may be affected by various factors:**
- Morbidity/diagnosis
- Demographic characteristics
- Severity of illness
- Ethnic variability
- Prescribing habits
- Dispensing habits
- Patient compliance

ATC/DDD in drug utilisation research

- Study patterns of drug use and changes over time
- Evaluate the impact of e.g. information efforts and regulatory changes
- Study drug exposure in relation to adverse drug reactions
- Indicate over-use, under-use and misuse/abuse of drugs
- Define need for further drug utilisation studies

Pharmacovigilance

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



CONCLUSION

- ATC/DDD system is the **“gold standard”** for international drug utilisation research

- ATC/DDD is a tool for exchanging and comparing data on medicine use at local, national and international levels

- **Use ATC/DDD website for updates: www.whocc.no**

- Annual courses in Oslo, Norway