UNIT-II

# 1.International Classification of Diseases (ICD)

## Overview:

The **International Classification of Diseases (ICD)** is a globally recognized system developed to standardize the classification of diseases, health conditions, and related health problems. It provides a common language for reporting and monitoring diseases, allowing for consistent data collection, analysis, and comparison worldwide.

The ICD is maintained by the **World Health Organization (WHO)** and is used by healthcare providers, researchers, policymakers, and public health officials to classify diagnoses, symptoms, and procedures in clinical and administrative settings.

## History and Development:

- The ICD has its origins in the late 19th century, initially developed from the **International List of Causes of Death** in 1893.
- The first ICD version was published in 1900.
- Since then, it has undergone multiple revisions to reflect advances in medicine and changing health needs.
- The current version, **ICD-11**, was adopted by the World Health Assembly in May 2019 and came into effect on January 1, 2022.
- ICD-11 incorporates digital technologies and modern medical knowledge, making it more comprehensive and easier to use.

## Structure of ICD:

ICD classifies diseases and related health problems into **categories and codes** that reflect clinical diagnosis and epidemiological information.

- Diseases and conditions are organized into **chapters** based on body systems or types of diseases (e.g., infectious diseases, neoplasms, mental disorders).
- Each disease or condition is assigned a **unique alphanumeric code** (e.g., A00 for cholera in ICD-10).
- The coding system allows for detailed subcategories to capture specifics such as severity, location, or cause.

## Objectives of ICD:

1. **Standardization:** To provide a universal system for coding diseases and health conditions to ensure consistency in data reporting across countries and healthcare settings.
2. **Epidemiology:** To facilitate the collection, analysis, and comparison of health data worldwide, aiding in the monitoring of disease patterns, outbreaks, and health trends.
3. **Clinical Use:** To assist healthcare professionals in diagnosis, treatment planning, and communication.
4. **Health Management:** To support healthcare planning, resource allocation, and policy development.
5. **Research:** To enable statistical analysis and research on morbidity and mortality.
6. **Billing and Reimbursement:** To provide a standardized method for coding diagnoses and procedures for health insurance claims and reimbursements.

## Importance of ICD:

- **Global Comparability:** Enables comparison of health data internationally to understand disease burden, risk factors, and health system performance.
- **Public Health Surveillance:** Essential for tracking disease outbreaks, pandemics, and chronic disease prevalence.
- **Healthcare Quality Improvement:** Helps identify patterns in disease outcomes and guide improvements in care.
- **Resource Allocation:** Governments and health organizations use ICD data to allocate resources efficiently.

- **Research:** Facilitates clinical and epidemiological research by providing consistent disease definitions.

### Key Features of ICD-11:

- **Digital Friendly:** Designed for use in electronic health records and digital health applications.
- **More Detailed:** Expanded codes for new diseases, conditions, and health-related factors.
- **Multilingual:** Available in multiple languages for global use.
- **Modular Design:** Easier to update and adapt to new medical knowledge.
- **Integration:** Can be linked with other classifications like SNOMED CT for detailed clinical terminology.

### ICD and Pharmacovigilance:

- ICD codes are often used in pharmacovigilance to classify and code adverse drug reactions (ADRs), medical events, and diagnoses.
- Consistent coding helps in signal detection, data analysis, and sharing of drug safety information globally.

## Daily Defined Dose (DDD)

### Definition:

The **Defined Daily Dose (DDD)** is a statistical measure of drug consumption, defined by the **World Health Organization (WHO)** as the assumed average maintenance dose per day for a drug used for its main indication in adults.

## Purpose:

DDD is used primarily to standardize the comparison of drug usage between different drugs or health care environments (e.g., hospitals, countries) regardless of dosage form or strength.

It helps in:

- Monitoring and analyzing drug consumption patterns.
- Facilitating drug utilization research.
- Comparing usage between different settings or countries.
- Identifying trends in prescribing and potential misuse or overuse.

## Key Features:

- **Standardized Unit:** DDD provides a fixed unit of measurement for drug consumption, independent of price, dosage form, or strength.
- **Average Dose:** It represents an average dose for the main indication, not necessarily the recommended or prescribed dose for every patient.
- **Adult Dose:** Based on adult maintenance dose; pediatric doses are not considered.
- **Not a Therapeutic Recommendation:** It is a technical unit used for drug utilization studies, not intended to guide individual treatment.

## How is DDD Used?

- Drug consumption is often expressed as the number of DDDs per 1,000 inhabitants per day to estimate the proportion of the population treated daily with a particular drug.
- It allows researchers to compare drug use over time or between populations.

**Example:**
If a country uses 50 DDDs of a drug per 1,000 inhabitants per day, it means that on average, 5% of the population is treated with that drug daily (50/1,000 = 0.05 or 5%).

### Importance in Pharmacovigilance and Healthcare:

- **Assessment of Drug Use:** Helps in identifying patterns that might indicate underuse, overuse, or misuse.
- **Resource Allocation:** Enables healthcare planners to understand drug consumption for budgeting and supply management.
- **Research and Policy Making:** Provides data for policy decisions, drug regulation, and stewardship programs.
- **Benchmarking:** Healthcare facilities and countries can benchmark their drug use against international standards or peers.

### Limitations:

- DDD is an **average dose** and may not reflect actual doses used in clinical practice.
- Does not consider patient-specific factors like age, severity of disease, or comorbidities.
- Not suitable for pediatric populations or drugs with multiple indications at different doses.

## How to Calculate DDD

### Basic formula:

**Basic formula:**

$$\text{Number of DDDs} = \frac{\text{Total amount of drug consumed (mg or units)}}{\text{WHO-assigned DDD (mg or units)}}$$

### Steps to calculate:

1. **Find the total amount of drug consumed**
   This is usually the total quantity of the drug dispensed or prescribed over a specific period (e.g., in milligrams, grams, tablets, capsules).

2. **Identify the WHO-assigned DDD**
   The WHO assigns a standard DDD value for each drug, representing the average maintenance dose per day for its main indication in adults (e.g., 500 mg).
3. **Divide the total amount consumed by the DDD**
   This gives the total number of DDDs used.

# 3.International Nonproprietary Names (INN) for Drugs

## Overview:

The **International Nonproprietary Name (INN)** system is a globally accepted method of assigning unique, universally recognized names to pharmaceutical substances (drugs). The INN provides a standardized, generic name for each drug, which is independent of brand names or trademarks.

This system is coordinated and maintained by the **World Health Organization (WHO)** and plays a critical role in ensuring clear communication and safety in the use of medicines worldwide.

## Purpose of INN:

1. **Universal Identification:**
   To provide a unique, universally accepted name for each pharmaceutical substance that healthcare professionals and regulatory authorities can use globally without confusion.
2. **Avoid Confusion:**
   To minimize medication errors and confusion that may arise due to multiple brand names or local names for the same drug.
3. **Facilitate Communication:**
   To enhance clear communication among healthcare providers, researchers, regulators, and patients across countries and languages.
4. **Support Regulation and Trade:**
   To aid regulatory bodies in approving and monitoring drugs, as well as facilitating international trade and distribution of pharmaceuticals.

5. **Promote Rational Use:**
   To help prescribers and pharmacists recognize drugs by their generic names, supporting rational prescribing and dispensing.

## Characteristics of INN:

- **Unique and Standardized:** Each drug substance receives one INN globally, which cannot be patented or owned by any company.
- **Simple and Pronounceable:** Names are designed to be easy to pronounce and remember by healthcare professionals.
- **Meaningful:** INNs often contain **stems** or suffixes that indicate the pharmacological or chemical class of the drug (e.g., "-pril" for ACE inhibitors, "-olol" for beta-blockers).
- **Non-proprietary:** INNs are generic names and not related to any brand or trademark.

## Process of Assigning INN:

1. **Submission:** A manufacturer or applicant submits a proposed name for a new pharmaceutical substance to the WHO INN Expert Group.
2. **Expert Review:** The expert group reviews the proposed name for suitability, checking for:
   a. Clarity and distinctiveness
   b. Avoidance of confusion with existing drug names
   c. Compliance with naming conventions and stems
3. **Public Consultation:** The proposed INN is published for public comment to allow stakeholders to raise concerns.
4. **Finalization:** After considering feedback, WHO assigns the final INN, which becomes internationally recognized.

## Importance of INN in Healthcare:

- **Patient Safety:** Helps prevent medication errors caused by confusing drug names.

- **Prescribing and Dispensing:** Facilitates clear prescribing, ensuring pharmacists dispense the correct medication.
- **Pharmacovigilance:** Enables accurate identification and reporting of adverse drug reactions (ADRs).
- **Education:** Assists in training healthcare workers worldwide on drug identification.
- **International Trade:** Simplifies regulatory approvals and drug imports/exports by standardizing names.

## Examples of INN:

| INN | Drug Class | Common Brand Names |
|---|---|---|
| Paracetamol | Analgesic, Antipyretic | Tylenol, Panadol |
| Atorvastatin | Statin (Lipid-lowering) | Lipitor |
| Amoxicillin | Antibiotic (Penicillin) | Amoxil |
| Omeprazole | Proton Pump Inhibitor | Prilosec |

## INN vs Brand Names:

| Aspect | INN | Brand Name |
|---|---|---|
| Ownership | Non-proprietary, WHO-assigned | Proprietary, owned by companies |
| Universality | Used worldwide | Varies by country and company |
| Purpose | Standardized generic identification | Marketing and differentiation |
| Examples | Ibuprofen, Metformin | Advil, Glucophage |

# 4.MedDRA (Medical Dictionary for Regulatory Activities)

## Overview:

**MedDRA** is a highly standardized, multilingual medical terminology dictionary developed to facilitate the sharing of regulatory information internationally related to medical products such as pharmaceuticals, vaccines, and biologics. It is used worldwide by regulatory authorities, pharmaceutical companies, and researchers for coding adverse events, clinical information, and other medical data.

MedDRA is maintained by the **MedDRA Maintenance and Support Services Organization (MSSO)** under the auspices of the International Council for Harmonisation (ICH).

## Purpose of MedDRA:

- To provide a consistent and standardized terminology for describing medical conditions, signs, symptoms, diagnoses, and adverse events.
- To enable efficient coding, retrieval, and analysis of safety data during clinical trials, pharmacovigilance, post-marketing surveillance, and regulatory reporting.
- To support harmonization and transparency in the regulatory review and monitoring of medicines globally.

## Structure of MedDRA:

MedDRA has a hierarchical structure with **five levels** of terms:

1. **System Organ Class (SOC):** Broadest category grouping related medical concepts by body system or etiology (e.g., Cardiovascular disorders).
2. **High Level Group Terms (HLGT):** Grouping of related High Level Terms.
3. **High Level Terms (HLT):** Grouping of related Preferred Terms.
4. **Preferred Terms (PT):** Single medical concepts representing a symptom, diagnosis, or condition (e.g., "Myocardial infarction").
5. **Lowest Level Terms (LLT):** More specific synonyms or descriptions linked to a PT (e.g., "Heart attack").

### Uses of MedDRA:

- Coding adverse drug reactions (ADRs) in clinical trials and post-marketing safety databases.
- Facilitating signal detection and risk management in pharmacovigilance.
- Standardizing safety data submissions to regulatory authorities.
- Enabling effective communication between healthcare professionals and regulators.

## WHO Drug Dictionary

### Overview:

The **WHO Drug Dictionary** is a comprehensive, standardized database of medicinal products and substances maintained by the **Uppsala Monitoring Centre (UMC)** on behalf of the **World Health Organization (WHO)**. It is widely used in pharmacovigilance and drug safety for coding medication names reported in adverse event reports, clinical trials, and other healthcare data.

### Purpose:

- To provide a **standardized and internationally recognized dictionary** of drug names for use in safety data management.
- To facilitate **coding and classification** of medications in adverse event reports.
- To enable **efficient retrieval, analysis, and sharing** of drug-related information across different organizations and countries.
- To support **signal detection and risk management** in pharmacovigilance activities.

### Structure and Features:

The WHO Drug Dictionary includes:

1. **Medicinal Product Names:** Brand names, generic names, and synonyms for medicinal products from multiple countries.
2. **Active Substances:** Information about active pharmaceutical ingredients (APIs) in each medicinal product.
3. **Therapeutic Classification:** Drugs are classified by therapeutic group, pharmacological class, and chemical group.
4. **Route of Administration:** Information on how the drug is administered (oral, injectable, topical, etc.).
5. **Dosage Forms and Strengths:** Details of formulation and strength.
6. **Country-Specific Information:** Reflects variations in drug availability and naming across countries.

## Use in Pharmacovigilance:

- When adverse drug reactions (ADRs) are reported, the WHO Drug Dictionary helps **code the drug names** into standardized terms, enabling clear identification of the suspect and concomitant medications.
- Facilitates **linking drug names with their active substances** and classes to detect class effects or product-specific issues.
- Supports **signal detection systems** by enabling aggregated analysis of ADRs by drug or drug class.
- Used extensively in databases such as **VigiBase**, the WHO global database of individual case safety reports (ICSRs).

## Versions of WHO Drug Dictionary:

- **WHO Drug Dictionary (WHO-DD):** The standard version containing medicinal products and active substances.
- **WHO Drug Dictionary Enhanced (WHO-DDE):** An enhanced version that includes additional coding features and more detailed drug classification, supporting more complex queries and reporting requirements.

### Advantages:

- **International Standard:** Used worldwide by national pharmacovigilance centers, pharmaceutical companies, and regulatory authorities.
- **Regularly Updated:** Reflects current drug market with continuous updates.
- **Multilingual:** Supports drug names from many countries and languages.
- **Facilitates Data Quality:** Improves consistency and accuracy in coding medication names.

## 5.EudraVigilance Medicinal Product Dictionary (EVMPD)

### Overview:

The **EudraVigilance Medicinal Product Dictionary (EVMPD)** is a comprehensive, standardized database maintained by the **European Medicines Agency (EMA)**. It contains detailed information about medicinal products authorized in the European Union (EU). The EVMPD is specifically designed to support the management and monitoring of adverse drug reactions (ADRs) and safety data within the **EudraVigilance system**, which is the EU's centralized pharmacovigilance database.

### Purpose:

- To provide a **standardized reference** of all medicinal products authorized or under evaluation in the EU.
- To facilitate accurate **coding and identification of medicinal products** in adverse event reports submitted to EudraVigilance.
- To support the **pharmacovigilance processes** including signal detection, risk assessment, and regulatory decision-making.
- To ensure consistent and unambiguous communication regarding medicinal products between pharmaceutical companies, regulatory authorities, and healthcare professionals.

## Content and Structure:

The EVMPD contains detailed information about each medicinal product, including:

- **Product Name:** Brand name and generic name.
- **Active Substance(s):** The pharmacologically active ingredients.
- **Pharmaceutical Form:** Such as tablet, injection, cream, etc.
- **Strength:** The amount of active substance per dosage unit.
- **Route of Administration:** Oral, intravenous, topical, etc.
- **Authorization Status:** Whether the product is authorized, withdrawn, or under evaluation.
- **Marketing Authorization Holder:** The company responsible for the product.
- **Packaging Information:** Details of pack sizes and types.
- **ATC Code:** Anatomical Therapeutic Chemical classification code to classify drugs by therapeutic use.

## Role in EudraVigilance System:

- The EVMPD serves as the **master list of medicinal products** used when reporting suspected adverse drug reactions to EudraVigilance.
- It ensures that all safety reports include **standardized and validated product identifiers**, reducing errors caused by inconsistent drug naming.
- Enables **efficient data retrieval, signal detection, and analysis** across diverse safety reports involving the same or related medicinal products.
- Supports **regulatory reporting requirements** mandated by the EU pharmacovigilance legislation.

## Benefits:

- **Consistency:** Provides a uniform language for medicinal products in safety databases, improving data quality.
- **Accuracy:** Helps avoid duplication or ambiguity in identifying products in adverse event reports.

- **Regulatory Compliance:** Supports pharmaceutical companies and regulators in meeting EU pharmacovigilance obligations.
- **Improved Safety Monitoring:** Facilitates better detection of product-specific or class-wide safety signals.

# 6.Basic Drug Information Resources

## Overview:

Basic drug information resources are authoritative references that provide comprehensive, reliable, and up-to-date information about drugs, including their properties, uses, dosages, side effects, interactions, and regulatory status. These resources are essential for healthcare providers, pharmacists, researchers, and regulators to ensure safe and effective medication use.

## Types of Basic Drug Information Resources:

1. **Drug Compendia and Reference Books:**
    a. **United States Pharmacopeia (USP):**
    Official compendium containing drug standards, quality, purity, strength, and formulation guidelines.
    b. **British National Formulary (BNF):**
    A comprehensive UK resource covering drug indications, dosages, contraindications, and interactions.
    c. **Martindale: The Complete Drug Reference:**
    International drug reference detailing drugs, chemicals, and herbal medicines.
    d. **Physicians' Desk Reference (PDR):**
    A widely used resource in the USA containing FDA-approved drug labeling and prescribing information.
2. **Online Drug Databases:**

a. **Micromedex:**
   Provides evidence-based drug information including dosing, side effects, interactions, and toxicology.
b. **Lexicomp:**
   Offers comprehensive drug monographs, interaction checkers, and patient education materials.
c. **Drugs.com:**
   Publicly accessible resource with detailed drug information and tools for interaction checking.
d. **Medscape Drug Reference:**
   Online resource with drug summaries, dosing guidelines, and clinical information.

3. **Regulatory Agency Databases:**
   a. **FDA (Food and Drug Administration):**
      Provides drug approval status, labeling, safety alerts, and adverse event reporting systems.
   b. **EMA (European Medicines Agency):**
      Offers information on medicines authorized in the EU, safety updates, and pharmacovigilance data.
   c. **WHO (World Health Organization):**
      Publishes the Model List of Essential Medicines and international drug safety data.
4. **Pharmacovigilance Databases:**
   a. **VigiBase:**
      WHO's global database of individual case safety reports (ICSRs).
   b. **EudraVigilance:**
      EU's system for monitoring adverse drug reactions, linked with the EVMPD.
5. **Textbooks and Clinical Guidelines:**
   a. Clinical pharmacology textbooks (e.g., **Goodman & Gilman's The Pharmacological Basis of Therapeutics**).
   b. Treatment guidelines by professional societies (e.g., American Diabetes Association, American Heart Association).

### Importance of Drug Information Resources:

- **Ensures Safe Medication Use:** By providing accurate dosing, contraindications, and interaction information.
- **Supports Rational Prescribing:** Helps clinicians select appropriate drugs based on evidence.
- **Facilitates Pharmacovigilance:** Enables identification and management of adverse drug reactions.
- **Promotes Patient Education:** Offers information that can be shared with patients for better compliance.
- **Assists in Research and Development:** Supports drug development and clinical research with detailed pharmacological data.

### How to Choose a Drug Information Resource:

- **Reliability:** Prefer peer-reviewed, official, or regulatory sources.
- **Scope:** Choose resources covering the required therapeutic area or drug class.
- **Accessibility:** Consider whether the resource is freely available or subscription-based.
- **Update Frequency:** Use sources regularly updated to reflect new drug approvals and safety information.
- **Usability:** Resources should be user-friendly with clear organization and search functions.

## Q-8.Establishing a Pharmacovigilance Programme

Pharmacovigilance (PV) is the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. Establishing an effective pharmacovigilance programme is essential to ensure patient safety and compliance with regulatory requirements.

## 1. Establishing Pharmacovigilance in a Hospital

Hospitals play a critical role in pharmacovigilance as they are primary sites where adverse drug reactions (ADRs) can be detected and reported. Establishing a PV programme in a hospital involves:

- **Creating a Pharmacovigilance Committee:**
  Comprising clinicians, pharmacists, nurses, and other healthcare professionals responsible for overseeing ADR monitoring and reporting.
- **Developing Reporting Systems:**
  Establish simple, accessible ADR reporting forms or electronic systems that healthcare providers can use to report suspected ADRs.
- **Training and Awareness:**
  Educate all hospital staff about the importance of pharmacovigilance, how to recognize ADRs, and the reporting process.
- **Monitoring and Data Collection:**
  Regularly collect and review ADR reports; encourage active surveillance methods like chart reviews and patient monitoring.
- **Communication:**
  Feedback to healthcare professionals about reported ADRs and safety alerts; promote a culture of safety.
- **Collaboration:**
  Coordinate with national pharmacovigilance centres and regulatory authorities to submit reports.

## 2. Establishment and Operation of Drug Safety Department in Industry

Pharmaceutical companies are legally required to monitor the safety of their marketed products. Setting up a drug safety department involves:

- **Organizational Structure:**
  Create a dedicated drug safety or pharmacovigilance unit staffed with trained professionals (pharmacists, physicians, data managers).
- **Standard Operating Procedures (SOPs):**
  Develop SOPs covering all pharmacovigilance activities, including adverse event collection, case processing, risk management, and regulatory reporting.

- **Safety Data Collection:**
  Implement systems to collect safety data from clinical trials, spontaneous reports, literature, and post-marketing sources.
- **Case Processing and Evaluation:**
  Evaluate and assess causality, seriousness, and expectedness of adverse events.
- **Regulatory Reporting:**
  Ensure timely submission of Individual Case Safety Reports (ICSRs) to regulatory authorities according to legal timelines (e.g., expedited reporting of serious ADRs).
- **Risk Management and Signal Detection:**
  Monitor safety data for new risks and develop risk minimization plans.
- **Training:**
  Continuous training of staff on pharmacovigilance regulations and procedures.
- **Compliance and Audits:**
  Conduct internal audits and ensure compliance with international guidelines such as ICH, GVP, and FDA regulations.

## 3. Role of Contract Research Organizations (CROs) in Pharmacovigilance

CROs provide outsourced clinical trial and pharmacovigilance services to pharmaceutical companies. Their role in pharmacovigilance includes:

- **Data Collection and Management:**
  Handling adverse event data from clinical trials and post-marketing studies.
- **Safety Monitoring:**
  Performing ongoing safety assessments and data analysis.
- **Regulatory Reporting:**
  Preparing and submitting safety reports to regulatory authorities on behalf of sponsors.
- **Risk Management Support:**
  Assisting in development of risk management plans and safety communication.
- **Expertise and Resources:**
  Providing specialized knowledge and infrastructure, especially for companies without in-house PV departments.
- **Compliance:**
  Ensuring all activities meet regulatory standards and Good Pharmacovigilance Practices (GVP).

## 4. Establishing a National Pharmacovigilance Programme

A national pharmacovigilance programme coordinates drug safety monitoring at the country level. Key steps include:

- **Policy and Regulatory Framework:**
  Establish legal requirements and guidelines mandating ADR reporting and pharmacovigilance activities.
- **National Coordinating Centre:**
  Set up a central pharmacovigilance centre responsible for collecting, analyzing, and disseminating safety data (e.g., Pharmacovigilance Programme of India - PvPI).
- **Network of Reporting Centres:**
  Develop a network of hospitals, clinics, and other health facilities that report ADRs.
- **Data Management Systems:**
  Implement electronic databases to store and analyze adverse event reports.
- **Capacity Building and Training:**
  Conduct training programs for healthcare professionals and stakeholders to raise awareness and improve reporting rates.
- **Public Awareness:**
  Inform the public about the importance of reporting adverse drug reactions.
- **Collaboration:**
  Coordinate with international bodies like WHO-UMC for global safety data sharing.
- **Monitoring and Evaluation:**
  Regularly assess the programme's performance and update policies accordingly.