

Substance misuse and Toxicity

-Substance Use Disorders (SUDs) are treatable, chronic diseases characterized by a problematic pattern of use of a substance or substances leading to **impairments in health, social function, and control over substance use**. It is a cluster of cognitive, behavioural, and physiological symptoms indicating that the **individual continues using the substance despite harmful consequences**

-A substance use disorder (SUD) is a mental disorder that affects a person's brain and behaviour, leading to a **person's inability to control their use of substances such as legal or illegal drugs, alcohol, or medications**

-Substance **misuse**: Using any substance at **high doses** or in **inappropriate situations** resulting in a **health or social problem**, immediately or overtime is known as substance misuse

-Substance **dependence**: Adaptation that results in **withdrawal symptoms** when substances are discontinued. It is an ordinary biological consequence of taking a substance for weeks or years. (cold turkey behaviour of sudden drop from taking substance)

-Substance addiction: The **loss of control** over the intense urges to take the substance **even at the expense of adverse consequences**. It is the continued substance use that persists in face of negative experience.

-Substance **tolerance**: A condition that occurs when the body gets used to medicine so that either **more medicine is needed or different medicine is needed**. **Diminished response** to a substance over the course of repeated or prolonged exposure

Why is SUD a public health issue?

35.6 million suffered from a drug-use disorder in 2020. Substance-use was directly and indirectly responsible for 11.8 million deaths globally. Globally, the number of disability-adjusted life-years (DALYs) caused by DUDs approximately increased by 2.6% yearly from 1990 to 2019

-Substance misuse **examples**: alcohol, prescription drugs(opioids/steroids), tobacco, psychoactive substances (methamphetamines, cannabis)

- WHO strives to **address the following challenges**:
 - Ensure access to needed controlled medicines for medical use.
 - Prevent and manage harms associated with drug use.
 - Providing universal access to effective treatment and care for people with drug use disorder.

Methamphetamine(ice)
2015 – 2019: surge in meth use despite increased enforcement (increased meth deaths -> adulterated with fentanyl -> consumer don't know what is inside the meth they buy)

History: >Amphetamine first synthesized (1887) then methamphetamine synthesized (1893), widely used by german and japanese soldiers in ww 2 for its stimulant effect and extended wakefulness, but found adverse effects of addiction and depression afterwards so regulated >1950s, indicated for treatment of obesity (increase metabolism, burn calories, lowers appetite) >1970s, became controlled drug in US >1980s, US tightened regulations around sale and use of ephedrine and illegal drug production turned to using pseudoephedrine as a precursor >1990s, widespread use of methamphetamines

Effects: >Euphoria, increase energy and alertness

>Chronic mood and cognitive changes: irritability, aggression, panic, hallucinations, memory impairment >Increased risk of early mortality and suicide attempts >Cardiovascular complications: arrhythmia, myocardial infarction, heart failure >Stroke

Prevention/Treatment in SG
>Legal Enforcement: Illegal to possess or consume within or outside of Singapore (Misuse of Drugs Act, listed as Class A controlled drug)
>Screening and assessment: prompted by signs and symptoms from patient's presentation, history and/or physical examination

>Drug testing: urine(7days), saliva(2days), blood and hair(90days)
>Diagnosis: DSM-5 diagnostic criteria: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)
>Management: psychosocial interventions largely: Motivational Interviewing, Drug counseling, Cognitive-behavioural therapy
>Preventive drug education by cnb in sg, continual pde engagement

Challenges for preventing drug misuse in SG
1. Surge in young drug abusers -> difficult to kick it off when they start young (2023, 51% of new drug abusers <30yo)

2. New Psychoactive Substances (NPS) -> (low cost, easy to produce || malleability of chem structure || falsely marketed as safe and legal)
long- and short-term consequences unknown (cannot be convicted because different chemical structures, names etc, which are loopholes)

Alcohol (alcohol use disorder most prevalent mental disorder globally)
Risk Factors: drinking at an early age, family history of alcohol problems, mental health condition and history of trauma
Effects: causal link and risk factor found in more than 200 diseases and injury, 5.1% of the global burden of disease and injury is attributable to alcohol, as measured in disability-adjusted life years (DALYs). (picture included)

Alcohol consumption centered approaches:
-Reduce population-level consumption by: Raise alcohol taxes, Raise the minimum price of alcohol sold at retail, raising legal minimum drinking age, Reduce permitted hours for sale of alcohol late at night, Advertising restrictions

Injury centered approaches:
-Reduce alcohol-related road injuries by: Publicity campaigns, Police enforcement of drink-driving laws – fines, driving license suspension etc., Random breath testing, Ignition or alcohol interlock devices
-Reduce alcohol-related interpersonal violence by: Reduce trading hours for licensed venues, Improve venue security, **Ignition interlock devices** (not in sg yet, introduced in several EU countries): do breathe test before start engine
Prevention of alcohol misuse in sg

-Legality: legal drinking age of 18 years old, anyone caught drinking with a breath alcohol content > 30 mcg alcohol in 100ml of breath; or > 80mg of alcohol in 100ml of blood can be charged with drink-driving. If found guilty, persons can be liable for a maximum fine of SGD 10000 and/or up to a year's jail

-Recommendation: 2 standard drinks per day for men and 1 standard drink per day for women, standard drink (one can 330ml of 5% beer, half glass 100ml of 5% wine, one nip 30ml of 40% spirit), men have lower percentage body fat than women, men produce more alcohol dehydrogenase enzyme
-Screening and assessment: Patient's alcohol history, physical examination on potential comorbidities and complications, laboratory investigation.
-Diagnosis: DSM-5 criteria

-Management: Patient education on drinking limits and law, Psychosocial interventions, Consider referral to community resources or psychiatric services where appropriate

Opioids Effects
-A class of prescription drug used to reduce pain.

-Act on the opioid receptors in the brain and/or spinal cord for: Analgesia, Cough suppression, Sedation, Respiratory depression, Euphoria
History of opioids: started with Morphine **Overdose**
-Symptoms: Constricted pupils, breathing difficulty, Unconsciousness, May have seizures
-Management: Antidote: Naloxone (opioid antagonist), Supportive care (to improve breathing and ventilation) **Withdrawal**

-Symptoms: Sweating, Bone or joint aches, Runny nose or tearing, Tremor, Restlessness, Anxiety or irritability
-Management: Pharmacological (Buprenorphine/Naloxone), Symptomatic management
Prevention of opioid misuse

Increase the availability of opioid dependence treatment, Reduce and prevent irrational or inappropriate opioid prescribing, Monitoring opioid prescribing and dispensing, Limit inappropriate over-the-counter sales of opioids.

-Legal regulations > Opioids are controlled drugs in Singapore
License requirement to import, store, wholesale, export or manufacture controlled drugs, Regulations for bringing personal medication to Singapore, Requires approval from Health Science Authority (HSA), Restriction on supply by retail sale of

codeine cough preparations
-National guidelines on safe prescribing of opioids
Opioids should not be prescribed as first line treatment for acute and chronic pain, Identify risk factors and patient factors before initiating opioid therapy, Monitoring of patients under opioid therapy, Patient education
Drug Courts: An alternative to incarceration for drug dependent offenders.

Treatment courts could involve: Participation in community-based substance abuse treatment, Indiv case management, Regular urine drug screening, Sanctions and rewards to motivate continued drug treatment and compliance, Regularly scheduled contact with the Drug Court Judge for assessment of progress, Regular assessment of eligibility for graduation
Benefits:

1. Better treatment & social outcomes (Factors to consider: Recidivism, Mental Health, Somatic Health, Crime Rates)
2. Better compliance to substance abuse treatment (Early sanctioning is associated with treatment failure due to non-adherence, while a jail sanction initiated later may better foster treatment compliance in less refractory individuals.)
3. Achieve greater cost effectiveness (Every \$1 spent on drug courts yields more than \$2 in savings in the criminal justice system: Reduced cost from additional re-arrest and incarceration. Improved public safety from sustained recovery of person with substance use disorder)

Challenges:
1. Eligibility criteria for drug courts (People who have been arrested or incarcerated have higher rates of substance use disorder than the nation at large, 80% of prison population suffers from substance abuse, 60% of people who are arrested test positive for illicit drugs in their system, 50% of all inmates suffer from drug or alcohol addiction, <10% of inmates receive proper addiction treatment while incarcerated)

Individual Factors: Employment & Education (Unemployed status and lower educational attainment are associated with treatment failure hazard during drug treatment court.)

Institutional Factors: Working Industry / Trades (Highest use for: Mining 17.5% + Construction 16.5% - Alcohol, Accommodations and food service industry - Illicit Drug 19.1% + SUD 16.9%)

Workplace Safety and Health
- **Work can affect health**: Accidents and injuries (injuries and accidents with machinery etc). Obvious diseases (diseases from working with chemicals in work etc), Hidden diseases (eg sick building syndrome - poor maintenance or cleaning leading to mold, mental stress - from quicker deadline due to fast work pace etc), Incurable diseases (contact with asbestos can cause cancer etc)

- **Health can affect work**: Decrease productivity (illness reduce output and work performance), Danger to self (illness/medication may cause danger when working with machinery/dangerous areas, can result in safety lapses and affect health), Danger to others / community (eg bus driver getting heart attack and cause accident will affect passengers' life)
- Occupational Health (Work - Health) -> health of the working population

- identify potential dangers and hazards at the workplace
 - prevent diseases and injuries
 - promote healthy and productivity workforce
- Challenges / Changes**

-Industrial Revolutions of work (evolution of work overtime):
IR1: Introduction of steam power, mechanised production, Child labour common, Hazardous work environment, Little WSH legislation
IR2: Electric power, internal combustion engine, Age of mass production, New WSH laws, Use of epidemiological and experimental methods to examine causality between work exposures and disease

IR3: Use of electronics, IT to automate production, Increased sedentary work, Rising NCDs, Move to integrate workplace health promotion with WSH (e.g. Total Worker Health, Total Workplace Safety and Health)
IR4: New technologies, e.g. nanotechnology, additive manufacturing, synthetic biology, Changing work conditions e.g. 24/7 digital platforms; work from home, New employment relationships e.g. gig economy

Demographic of SG population: 70% in workforce, sizeable amount in diseases group, need to keep working population healthy and allow them to work as long as they want to
Shrinking workforce due to declining fertility rate (TFR > 2.1 for replacement of population, sg on constant decrease below TFR)

Rapidly aging population and workforce (more percentage of population is elderly and aging population)
The health of our working population is worse off than the general population (obesity/health problems due to people emphasis on work, more sedentary lifestyle that comes with working)

Cutting back on foreign manpower (need to use sg own population)
Opportunities and Developments

- WSH Legislations (Workplace safety and health act 2006, work injury compensation act 2019)
- Total workplace safety and health (total WSH): work, safety and health are inter-related
>work (poor work processes, aggravate health / cut oneself when not careful)
- >health (infection, uncontrolled diabetes, frequent MCs affecting productivity / fainting spell causing accidents & injuries)
- >safety (cuts, injuries, economic and reputation losses to company / wound affected by diabetes)
- >Looking at work, safety and health together so as to achieve workers' well-being

Public Health Genomics
What is a **Genome** – All living organisms – plants, bacteria, & animals have distinct genomes, which contain "instructions" to create an organism, encoded in chemicals known as "DNA" of letters Adenine(A), Guanine (G), Cytosine(C) & thymine(T)/Uracil(U), RNA)

Genome size	170,000 bp	4.6 million bp	130 million bp	3.2 billion bp	150 billion bp
Common name	Virus	Bacteria	Fruit fly	Human	Canopy plant

Amount of **base-pairs (bp)** does not represent more advanced/sophisticated organism Pathogens such as viruses & bacteria tend to have smaller genomes > SARS-CoV-2 ~30kbp / TB Bacteria ~ 4.5 Mbp
Different strains will have different molecular fingerprint patterns (genotypes) -> similar genotype likely 'linked' by recent transmission & vice-versa

Epidemiology -> study of the distribution & determinants of health-related outcomes in a specified population & the application of this study to control health problems
Genomic Epidemiology -> use of genomic data (highly similar genome, 1 base change) to determine the distribution & determinants of health-related outcomes in a specified population & the application of this information to control health problems

Pathogen Genomic Epidemiology: Combining pathogen genomic and epidemiological data to control and limit spread of infectious diseases.
Genes determine what traits are passed down from parents to children. Each human cell contains 23 pairs of chromosomes (long strings of DNA bases A, G, T & C) each from dad & mom. 0.1% (of 3.2 billion bp) difference in genes of 2 individuals

Genetics -> the study of genes, genetic variation & heredity (traits passed) -> Cystic fibrosis (CFTR gene) sticky mucus build up;
Genomics -> the study of the genome, consisting of the entire set of genes & its interaction with the environment of their structure, function & evolution
Varying degrees of genetic effects -> 100% due to environment (car accident) vs 100% due to genetics (monogenic disorder, down syndrome, CF) -> complex traits & diseases (height, cholesterol levels, cancer...)

Mutations: Inherited (Germline) -> Any variant that occurs in a gamete (egg or sperm) or cells that produce gametes
Acquired (Somatic) -> Cells that are not part of the germline are called somatic cells, Somatic mutations are not present in every cell in the body, and are not passed from parent to child, Happens at some point later in your life (due to errors in DNA replication, or exposure to environmental factors such as UV light, smoking etc)

Precision medicine considers individual variations in genetics/genomes, environmental & lifestyle factors -> to more accurately predict which treatment & prevention strategies will work in different groups of people -> accurate prediction of health conditions; faster diagnosis; optimised treatment; novel treatments

Pharmacogenomics -> Use of genetic & genomic information to tailor pharmaceutical treatment -> curated specialised pharmac treatment catered to indivs -> Carbamazepine to control Epilepsy (seizures), Stevens-Johnson -> HLA-B*1502 Ethnicity, legal & social implications How should counselling be offered? Who else needs to be tested? When should they be informed of late-onset diseases? Should the data be kept, how long, by whom? Necessary to reanalyse?

Cancer Genomics -> Breast Cancer is classified according to whether certain genes expressed in the tumour, like the human epidermal growth factor receptor 2 (HER2), Drugs such as Herceptin (trastuzumab) can be used for treatment of HER2 breast cancer

Translation and Implementation in Public Health and Healthcare
Clinical Genetic Tests: Used to predict, diagnose or guide treatment of medical conditions (e.g. predictive or diagnostic testing for cancers), In SG only doctors are allowed to offer clinical genetic testing, subject to regulatory standards
Non-clinical genetic Tests: Used for personal well-being and recreational purposes (e.g. ancestry, personality, behavioural or nutrigenomic testing), though more commonly sold online, such tests can be accessed through local and overseas stores
Newborn Genomic Screening

- The incorporation of genomic sequencing in newborn sequencing, i.e. determine the genomes of these babies, are able to
- Increase the chances for early detection of treatable rare diseases
- The genomic data can be used to predict the risks of developing health conditions later

Communicable Diseases / Infectious Diseases: HIV/AIDS, tuberculosis, malaria, dengue • disease that you can catch from another person/organism due to transmission of a biological agent • biological agents/pathogens/bugs: virus, bacteria, fungi, protists

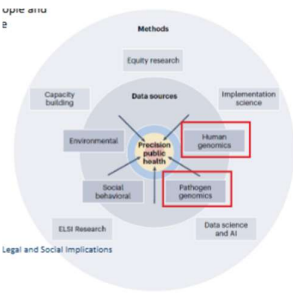
Noncommunicable Diseases (NCDs): Cardiovascular diseases, diabetes, cancers, mixture of environment and genetic factors

Infectious Disease Transmission: Identifying individuals/samples related to disease transmission, Different strains will have different molecular fingerprint patterns (genotypes). Patients with similar genotypes are likely to be 'linked' by recent transmission. Patients with different genotype patterns are highly unlikely to be part of the same transmission

Challenges for Epidemiology investigation for TB: Airborne
Transmitted – Difficult to assess exposure, especially in congregate settings, long infectious periods – Patients recall might be incomplete or unreliable, common in poor and marginalized communities

Genome Similarity not equals Transmission: Strains that are similar in their genomes are more likely to share an epidemiological association, i.e. part of a transmission, Transmission pathways (and the direction of transmission) cannot be assumed to mirror phylogeny (without other data), Causal links (e.g., between cases and exposures) cannot be assumed from sequence data alone

Global Pathogen Genomic Surveillance: Key Objectives: Improve access to tools for better geographical representation, Strengthen the workforce to deliver at speed, scale and quality, Enhance data sharing and utility for streamlined local to global public health decision-making, Maximize connectivity for timely value-add in the broader surveillance architecture, Maintain a readiness posture



Introduction to Global Health
Black Death (1300-1600): estimated 100 million deaths (about 25% of world's population), started when habitats of wild rodents in central asia disrupted by human/farming expansion/iron trading patterns
Venice 1348, Believed that plague came by ships, Adopted 30-day detention period, Expanded to 40-days (ie "quarantine"), Island as quarantine station (lazaretto), Didn't work (spread by fleas on rats), Bar exit of people/goods from cities/regions
-Public health measures are local and unilateral

Imperialism/ Colonialism (late 1400s):
-Transmission of disease in multiple directions, Europeans carried influenza, typhus, smallpox, cholera, Falciparum malaria from Africa to Americas via European slave ships, Syphilis from Americas (early Spanish/ Portuguese explorers) back to Europe...

-High occupational mortality among displaced indigenous groups, bonded labourers, African slaves
-Decision to counter infectious diseases ("tropical diseases") based on external interests: Protect health of European and American colonial personnel and workers, Enhance productivity, safeguarding commerce, Top-down, local compliance was achieved through compulsion, Narrow focus (on single disease)

International Health (1850s):
-Fear of epidemic: Large-scale immigration from Europe and Asia to the Americas, Explosion of mineral extraction, manufacturing, trade, marketing of goods + revolution of transportation (steamships, railroads, Suez Canal), 6 cholera pandemics between 1816-1899

-On-the ground cooperation deemed as beneficial for: Control of outbreaks (of tropical diseases), Stabilise colonies and emerging nation states, Improve diplomatic relations, Expand consumer markets, Encourage transfer and internationalising scientific, bureaucratic and cultural values
-International Health Organisations (e.g. Rockefeller Foundation – "scientific philanthropy", Save the Children, League of Nations Health Organisation), De-colonisation, UN, World Bank, IMF, WHO

Global health today: Focused on "improvement of health worldwide, the reduction of disparities, and protection of societies against global threats that disregard national borders."

Key Elements of Global Health: Transcends national boundaries / Requires global cooperation / Prevention and clinical care / Health equity for all / Interdisciplinary, multidisciplinary within and beyond health sciences
Equity is the absence of avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically, or geographically. (WHO)

Health inequities are systematic differences in the health status or in the distribution of health resources between different population groups, arising from the social conditions in which people are born, grow, live, work and age. (WHO)

Why is Global Health relevant to us?
Health is interconnected globally (diseases know no borders, global health security), Shared health challenges (increased risk factors for NCD), Health inequities persist (health disparities even in developed countries), Climate change impacts everyone's health (global issue affecting health of all populations, regardless of country), Economic impacts of global health crisis (disruptions in trade, increased healthcare costs, reduced productivity)

	Public Health	International Health	Global Health
Geographical Reach	Focuses on issues that affect the health of the population of a particular community or country	Focuses on health issues of countries other than one's own, esp those of low-income and middle-income	Focuses on issues that directly or indirectly affect health but that can transcend
Level of Cooperation	Does not usually require global cooperation	Usually requires binational cooperation	Often requires global
Individuals or Populations	Mainly focused on prevention programmes for populations	Embraces both prevention in populations and clinical care of individuals	Embraces both prevention in populations and clinical care of individuals
Access to Health	Health equity within a national or community is a major objective	Seeks to help people of other nations	Health among nations and for all people is a major objective

