

Emerging Infectious Disease HIV/AIDS

COM311 - Community Medicine Seminar

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Objectives

1. Describe the epidemiology and global burden of HIV/AIDS infection:

Introduction:

HIV, the virus that causes AIDS (acquired immunodeficiency syndrome), is one of the world's most serious health issues globally since the first cases were reported in 1981. Approximately 76 million people have become infected with HIV since the start of the epidemic, 38 million people are currently living with HIV, & tens of millions of people have died of AIDS-related causes.

HIV primarily affects those in their most productive years, it affects the individuals themselves, their households, their communities, as well as the development and economic growth of their countries.

Over the past two decades, in particular, major global efforts have been made to address the epidemic, and significant progress has been made. The number of newly infected individuals with HIV, especially children, and the number of AIDS-related deaths have declined over the years, and the number of people with HIV receiving treatment increased to 25.4 million in 2019.

Summary of the global HIV epidemic, 2019

	People living with HIV in 2019	People newly infected with HIV in 2019	HIV-related deaths 2019
Total	38.0 million [31.6 million – 44.5 million]	1.7 million [1.2 million – 2.2 million]	690 000 [500 000 – 970 000 million]
Adults	36.2 million [30.2 million – 42.5	1.5 million [1.1 million – 2.0 million]	600 000 [430 000 – 840 000]
Women	million] 19.2 million [16.4 million – 22.2 million]	790 000 590 000 – 1.1 million]	300 000 [220 000 – 420 000]
Men	17.0 million [13.8 million – 20.4 million]	870 000 630 000 – 1.2 million]	390 000 [280 000 – 560 000]
Children (<15 years)	1.8 million [1.3 million – 2.2 million]	150 000 [94 000 – 240 000]	95 000 [61 000 – 150 000]

Source: UNAIDS/WHO estimates



Number of new HIV infections in 2018 and change since 2010:

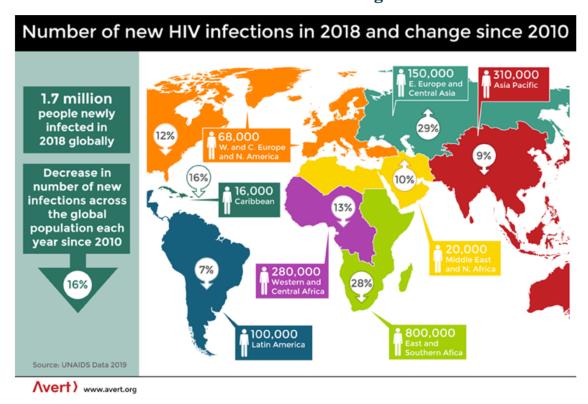
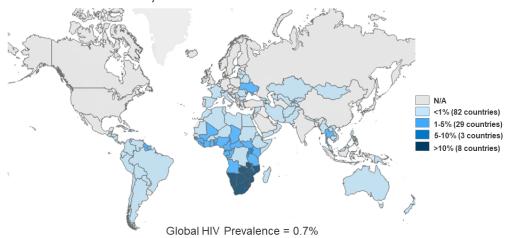


Figure 1

Adult HIV Prevalence, 2019



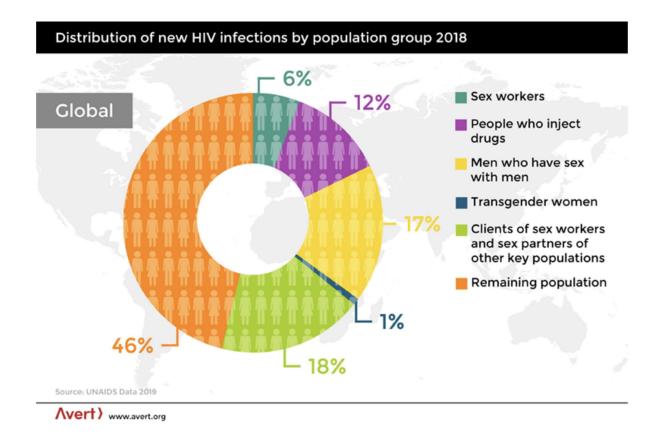
NOTES: Data are estimates. Prevalence includes adults ages 15-49. SOURCE: KFF, based on UNAIDS, AIDSinfo, Accessed July 2020.



Table 1: Snapshot of Global Epidemic Today, by Region						
Region	% of Adults Living with HIV (Adult Prevalence)	# of People Living with HIV (% of Global Total)	# of People Newly Infected with HIV	# of AIDS-Related Deaths		
Global, Total	0.7%	38.0 million (100%)	1.7 million	690,000		
Eastern and Southern Africa	6.7%	20.7 million (54%)	730,000	300,000		
Western and Central Africa	1.4%	4.9 million (13%)	240,000	140,000		
Asia and the Pacific	0.2%	5.8 million (15%)	300,000	160,000		
Western and Central Europe and North America	0.2%	2.2 million (6%)	65,000	12,000		
Latin America	0.4%	2.1 million (6%)	120,000	37,000		
Eastern Europe and Central Asia	0.9%	1.7 million (4%)	170,000	35,000		
The Caribbean	1.1%	330,000 (<1%)	13,000	6,900		
Middle East and North Africa	<0.1%	240,000 (<1%)	20,000	8,000		

NOTES: Reflects 2019 data.

SOURCES: UNAIDS. AIDSinfo website; accessed July 2020. UNAIDS. Core Epidemiology Slides; July 2020.

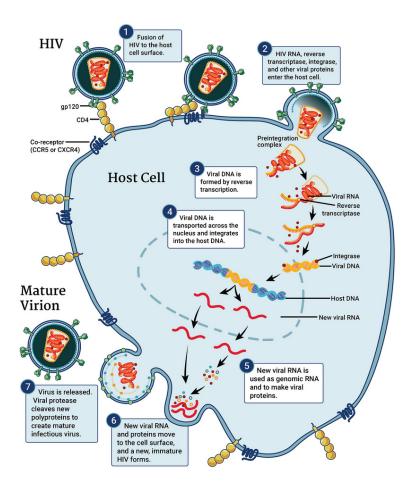


2. Describe how people get infected with HIV:

Pathophysiology:

HIV-1 gains access to cells without causing immediate lethal damages but the entry process can stimulate intracellular signal cascades, which in turn might facilitate viral replication. During the entry process, gp120 attaches to the cell membrane by first binding to the CD4+ receptor. Subsequent interactions between virus and chemokine co-receptors (eg, CCR5, CXCR4) trigger irreversible conformational changes.

The HIV viral burden directly and indirectly mediates CD4+ T-cell destruction. There is destruction of mature CD4+ cells; CD4+ progenitor cells in bone marrow, the thymus, and peripheral lymphoid organs; as well as CD4+ cells within the nervous system, such as microglia. The result of this destruction is failure of T-cell production and eventual immune suppression. ⁽¹⁾



Transmission of HIV:

HIV can be transmitted by many ways, for example the exchange of a variety of body fluids from infected people, such as blood, breast milk, semen and vaginal secretions. HIV can also be transmitted from a mother to her child during pregnancy and delivery. Also, knowledge about non-transmittable routes of HIV Infections is as important as knowledge about the most common way of HIV transmission. Individuals cannot become infected through ordinary day-to-day casual contact such as kissing, hugging, shaking hands, or sharing personal objects, food or water. **There are four common ways of HIV transmission:**

- Sexual Contact: HIV is commonly transmitted having anal or vaginal sex with an infected partner without using condoms or taking medications to treat or prevent HIV.⁽²⁾
- 2. Sharing needles: means using a needle or syringe after someone else used it to inject drugs or medicine or for tattoos or piercings, The risk for getting or transmitting HIV is very high if a Healthy person uses needles, syringes or other drug injection equipment after someone with HIV has used them, This is because the needle,

- syringe or injection equipment may have blood in them, and blood can carry HIV, And This also include needle stick injuries among health workers.
- 3. Blood contamination: HIV may also be spread through contact with infected blood. However, due to the screening of blood for evidence of HIV infection, the risk of acquiring HIV from blood transfusions is extremely low.
- **4. Mother-infant:** it is the most common way that children get HIV. Infected mothers can pass the virus on to their babies through several ways:
- During pregnancy: HIV can pass through the placenta and infect the fetus, mothers who receive treatment for the infection during pregnancy can significantly lower the risk of passing the virus to their babies.
- During delivery: A baby is exposed to any HIV in the mother's blood and other fluids while passing through the birth canal. During childbirth, scheduled C-section can reduce the risk of mother-to-child transmission
- Through breast feeding: Despite ongoing use of HIV medicines after childbirth, a
 woman with HIV can still pass it to her baby while breastfeeding. In the United
 States, infant's formula is a safe and widely available alternative to breast milk. For
 these reasons, women with HIV living in the United States should not breastfeed their
 babies.

Is it safe for a mother infected with HIV to breastfeed her baby?

- No, according to the CDC, HIV-infected mothers must avoid breastfeeding.
- The World Health Organization (WHO) recommends that HIV-infected mothers in resource-limited settings, such as some parts of Africa can breastfeed exclusively for the first 6 months of life and continue breastfeeding for at least 12 months, with the addition of complementary foods. These mothers should be given ART to reduce the risk of transmission through breastfeeding.

3. Understand the global initiatives to combat the rising burden of the disease:

Those working in the field of HIV, including policy makers, programmers, governments and community-based organisations all operate within the Sustainable Development Goals (SDG) framework. Under this framework there are 17 goals, one of them is (SDG3) which ensure healthy lives and promote wellbeing for all at all ages, and it includes two important targets related to HIV/AIDS:

- target 3.3: end AIDS as a public health threat by 2030.
- target 3.8: achieve universal health coverage, access to quality health care services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all. (1)

To reach these targets, many organizations engaged in the global response to HIV/AIDS such as UNAIDS, WHO and the Global Fund.

UNAIDS Fast-Track strategy (1):

It's a strategy that was launched in 2014 by the UNAIDS organization which plans to step up the HIV response in low- and middle-income countries to meet the SDG 3 target to end AIDS by 2030. To achieve this, the Fast Track strategy sets out targets for prevention and treatment, known as the **90-90-90 targets**, which aims as:

- By 2020, 90% of all people living with HIV will know their HIV status.
- By 2020, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy.
- By 2020, 90% of all people receiving antiretroviral therapy will have viral suppression.

1) Children, adolescents and adults living with HIV access testing, know their status and are immediately offered and sustained on affordable quality treatment (2):

- Voluntary HIV testing services accessible for people at risk of HIV infection
- Early infant diagnostic services accessible to all children exposed to HIV, and all children under 5 years living with HIV on treatment.
- All adults, adolescents and children offered antiretroviral therapy and linked to treatment services upon HIV diagnosis.
- People on treatment supported and monitored regularly, including scaled-up viral load monitoring, and treatment literacy and nutritional support.
- Immediate treatment accessible to all pregnant women living with HIV.

2) Young people, especially young women and adolescent girls, access combination prevention services and are empowered to protect themselves from HIV (2):

- Youth-friendly HIV, sexual and reproductive health and harm reduction information and services accessed independently and equally by young women and men.
- Twenty billion condoms available annually in low- and middle income countries for people of all ages.
- Additional 27 million men in high-prevalence settings voluntarily medically circumcised as part of access to integrated sexual and reproductive health services for men.
- Quality comprehensive sexuality education accessed by all adolescent and young people > Information accessed, awareness raised and demand created through traditional and new forms of communication and outreach.
- Three million people on pre-exposure prophylaxis annually, focused particularly on key populations and people at high risk in high prevalence settings.

3) AIDS response is fully funded and efficiently implemented based on reliable strategic information:

- Investment of at least US\$ 31.1 billion available for the global AIDS response annually in 2020 in low- and middle-income countries, with one quarter invested in prevention globally.(2)
- Adequate investments made in research and development for better diagnostics, antiretroviral medicines, prevention commodities, monitoring tools, vaccines and a cure.(2)

- The HIV investment by the Global Fund reached \$22.2 billion (2002-2020) which played a big role in reducing AIDS-related deaths & HIV incidence. (3)

4. Learn the features which characterize the pandemic in the EMR:

HIV estimates:

- HIV prevalence in the Region is 0.1% (low epidemic).
- The estimated number of people living with HIV (PLHIV) in the Region in 2016 is 360000.⁽¹⁾
- 70% (252 000) PLHIV live in 3 countries Pakistan, Islamic Republic of Iran and Sudan.⁽¹⁾
- The estimated number of new infections increased by 28% from 2010 to reach 360000 in 2017.⁽²⁾
- Mortality among people living with HIV (PLHIV) in EMR has also increased by 31% in 2017 compared to 2010. (2)

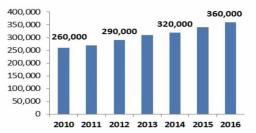


Fig. 1 Estimated number of PLHIV in the Region 2010–2016

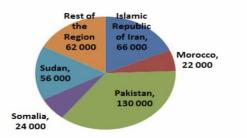
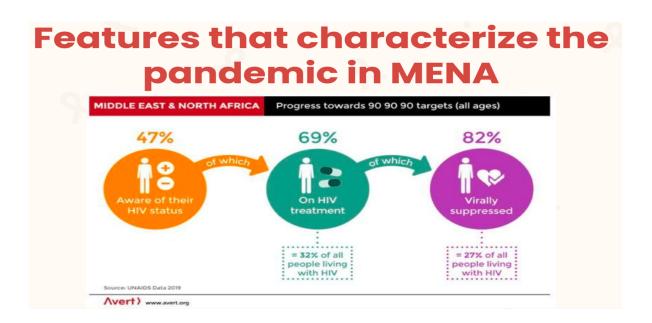


Fig 2. Distribution of PLHIV in the Region



Populations at higher risk of HIV:(3)

The mid-1980s saw the first reported cases of HIV and AIDS in this region. By 1990, every country had detected HIV in their populations. This was linked primarily to exposure abroad as well as contaminated blood transfusions and organ transplants. However, by the early 1990s, a new pattern of transmission had emerged among certain groups:

- People who inject drugs (PWID).
- Female sex workers.
- Men who have sex with men (MSM).
- Migrants and mobile populations.
- Women.

Testing:⁽¹⁾

- Only 30% of estimated PLHIV in the Region knew their status by 2016.
- Testing and treatment acceleration action plans to close these gaps were developed and are now being implemented in these countries.
- The Regional Office is supporting selected countries in revising their HIV testing policies and strategies and adapting the WHO HIV testing services guidelines at national level

ART coverage:(1)

- The number of PLHIV receiving antiretroviral therapy doubled from 2013 reaching 54300 in 2016. Nonetheless, the Region continues to demonstrate the lowest coverage.
- ART coverage varies across countries in the region as a result of the high cost of ART; where high ART coverage is reported in high-income countries such as Qatar, Kuwait, Saudi Arabia, Jordan, on the other hand countries which are classified as low-income countries such as Afghanistan, Pakistan and Sudan still have a very low coverage.

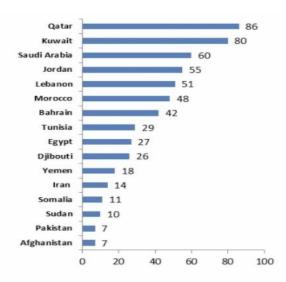


Fig. 7 ART coverage in selected countries 2016

Issues and challenges:

- 1) National AIDS programmes in most countries continue to face major challenges in terms of:⁽³⁾
- political commitment of national leaders,
- financial resources,
- health and community system weaknesses
- cultural acceptability of public health approaches to HIV prevention and control
- stigmatization and discrimination against PLHIV
- 2) There is concern that HIV estimates **are not very accurate** in most countries of the Region because the data is scarce and not always of good quality.⁽¹⁾
- 3) The majority of PLHIV in the Region do **not access HIV testing** and therefore do not know their HIV status.⁽¹⁾

Features that characterize the pandemic in MENA

Awareness	Social stigma	Government
Many people in the MENA region are unaware of how HIV is transmitted, they think that it can only be transmitted by sex or sexual acts but it can also be transmitted by sharing of needles or through pregnancy.	Most of the population in the region are religious people so talking about sex or drugs or STDs in general is frowned upon due to social stigma.	Many governments of the MENA region believe that due to low infections rates AIDS and HIV aren't a big problem

The Arab Strategic Framework for the Response to HIV and AIDS (2014–2020) endorsed by the Council of Arab Ministers of Health, aims to support Arab States to achieve the goals and targets of the 2011 United Nations General Assembly High Level Meeting on HIV and AIDS. The Arab AIDS Strategy includes 10 goals. It promotes

engagement and emerging leadership from countries, and mentions addressing issues including:

- Cultural and socio-economic barriers.
- Stigma and discrimination.
- Structural and resource barriers.
- Data barriers.
- Legal barriers and punitive laws.
- Restrictions on entry, stay and residence.

5. A- Recognize the epidemiology, and Burden of disease:

In the Kingdom of Saudi Arabia (KSA), HIV is increasingly recognized as a major health problem. In 1984 the first HIV case was identified in Saudi Arabia.(2),(3),(4)

A cross sectional hospital-based survey study was conducted among attendees of the Ministry of Health (MOH) hospitals, Kingdom of Saudi Arabia (KSA) between 2013 and 2014 that was carried out in five geographical areas; Central, Eastern, Western, Northern and Southern parts of KSA found that among 3,994 participants The number of people infected with STIs was 248 (6.2%) and the rate of HIV infection was (0.05%).

The study concluded that The prevalence of STIs including HIV in Saudi Arabia is low as compared with other countries. (1)

STIs was more common among non-Saudi (10.9%), compared to Saudi (5.7%), and more common among illiterates (8%) and less educated people (9.3%), compared to secondary and highly educated individuals, respectively (5.9% and 4.0%). (1)

STIs were more common in Arar (16.4%), Riyadh (8%), and Asir (5.3%), compared to those living in Dammam and Jeddah respectively (2% and 1.9%). There was no statistically significant difference between infected and non infected individuals with STIs regarding gender, occupation and marital status. (1)

According to Saudi MOH, the most prominent HIV/AIDS transmission methods include the forbidden sexual intercourse by 96% (414 cases out of 431), the injection drug abuse by 2.5 % (11 cases), and then Mother-to-fetus infection by 1.5% (6 cases). Jeddah Province still compromises the highest number of new cases with AIDS recording 39% of Saudis, and 45% of non-Saudis.(5)

Clinical, demographic and epidemiologic characteristics of 602 HIV-1 infected patients followed in the adult Infectious Diseases Clinic of King Faisal Specialist Hospital and Research Centre, in Riyadh, Kingdom of Saudi Arabia a tertiary referral center were longitudinally collected from 1989 to 2010, found that at diagnosis, opportunistic infections were found in 49% of patients, Pneumocystis jirovecii pneumonia (PCP) was the most frequently diagnosed opportunistic disease (27%, n=50), followed by Candida esophagitis (25%, n=45). Mycobacterium tuberculosis (MTB) and cytomegalovirus (CMV) infections was recorded in 29 patients each and represented 16% of all opportunistic infections. (6)

5. B- National measures to prevent spread of HIV/AIDS in KSA:

1-Saudi National AIDS program (NAP): was established in the year 1994. The HIV screening program for blood and blood products was introduced in 1984, when the first case was detected. Since then, the response was to develop a central unit at the national capital Riyadh and regional centers in the twenty health provinces. The program supports HIV prevention, care, treatment and other support services for the marginalized and the vulnerable groups, while provides awareness and education for general public.(1)



- For free
- Total confidentiality

- Highly Availability
- Providing Free Counselling with professional family physicians.(1)



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- **2- Pre-marital counselling program:** it was implanted by Saudi Ministry of health in 2004, and was only concerning to Genetic disorders (thalassemia and sickle cell anemia), In 2008 it was updated to involve some of serious infectious diseases as (HIV, HCV and HBV) .(1)
- 3-Expatriate medical tests.(2)
- 4- Imposed regular Medical test (include HIV screening) among special workers:
- -Medical students and Health care providers.
- -Military sector
- -Barbershop's workers (3)
- **5- Standards and safe blood transfusion system** is applying throughout the Kingdom by blood screening for HIV virus and others.(1)
- 5. C- Differentiate what could work best, as far as prevention and control efforts are concerned, in our region:

HIV is a major global public-health crisis of our time. However, it is a manageable chronic condition and its prevention is crucial as there is no effective cure that exists. Studies have proven that the most cost-effective way to help prevent the spread of this epidemic is school-based HIV/AIDS education programs. (1) It can remove the stigma surrounding the disease, reduce youth risky behaviors, and increase the use of condoms and contraception. (1) However, this method may not be applicable in our country due to the sensitive social topic in Saudi Arabia. There are other various methods of prevention that can be utilized locally to lower the risk of transmitting HIV:

1-Pre-Exposure Prophylaxis (PrEP):

It's a pill taken once a day for people who don't have HIV but at a very high risk of getting infected - for example, those whose partner is HIV positive; it can reduce the risk of infection by over 90%. (2)

2-Antiretroviral therapy (ART):

ART is the treatment for HIV, it involves a combination of HIV medicines that slows down the effects of HIV in your body. It can't cure HIV but can help people stay healthy and live longer for many years. ART lowers the amount of HIV in your body (called your viral load). If a person's HIV viral load is so low that a test can't detect it, it's called "undetectable viral load". Having an undetectable viral load prevents the sexual transmission of HIV to another partner

3-Post-Exposure Prophylaxis (PEP):

It's the use of antiretroviral drugs very soon after a potential exposure to HIV that reduces your chances of getting it. PEP must be started within 72 hours (3 days), after an exposure to HIV for it to work. (3)

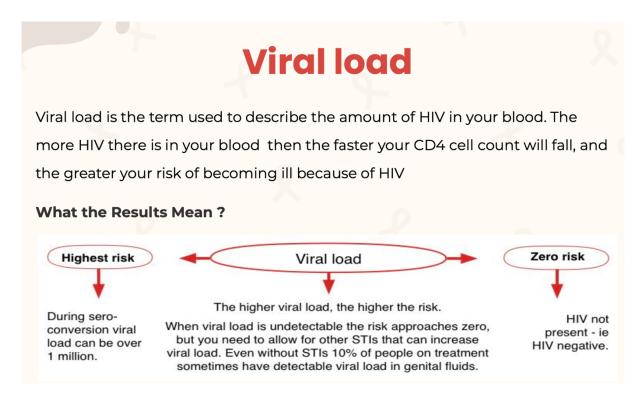
4-Prevention of mother-to-child transmission (PMTCT):

MTCT is the transmission of HIV from an HIV-positive mother to her child during pregnancy, childbirth, or breastfeeding. PMTCT offers a range of services for an infected woman to stop their infants from acquiring HIV. For instance, mothers are treated with ART during pregnancy and after birth babies born receive HIV medicine to reduce the risk of getting HIV.

5-Syringe service programs (SSPs):

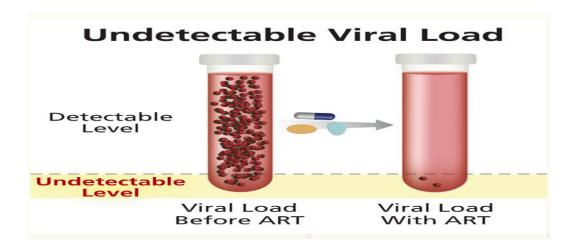
These are community-based programs that can prevent the spread of infectious disease through injection drug use. They offer testing, vaccination, and linkage to treatment for infectious diseases. Also, access to sterile syringes and education on overdose prevention and safer injection practices. SSPs are associated with an approximately 50% reduction in HIV and hepatitis C virus (HCV) incidence. (4)

The concept of Viral Load



Antiretroviral therapy (ART) reduces HIV-related morbidity and mortality at all stages of HIV infection

ART can suppress viral load, maintain high CD4 cell counts



References:

1st Objective:

- 1. Published: Jul 13, 2. (2020, July 13). The Global HIV/AIDS Epidemic. Retrieved November 20, 2020, from https://www.kff.org/global-health-policy/fact-sheet/the-global-hivaids-epidemic/
- 2. WHO | Data and statistics. WHO [Internet]. 2020 [cited 2020 Nov 5]; Available from: http://www.who.int/hiv/data/en/
- 3. Global HIV and AIDS statistics | Avert [Internet]. [cited 2020 Nov 7]. Available from: https://www.avert.org/global-hiv-and-aids-statistics

2nd Objective:

- 1. Simon, V., Ho, D.D. and Abdool Karim, Q. (2006). HIV/AIDS epidemiology, pathogenesis, prevention, and treatment. *The Lancet*, [online] 368(9534), pp.489–504. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2913538/.
- 2. "Ways HIV Can Be Transmitted | HIV Transmission | HIV Basics | HIV/AIDS | CDC." Www.Cdc.Gov, 3 Nov. 2020, www.cdc.gov/hiv/basics/hiv-transmission/ways-people-get-hiv.html.
- 3. What Can Increase HIV Risk? | HIV Risk Reduction Tool | CDC [Internet]. [cited 2020 Nov 5]. Available from: https://hivrisk.cdc.gov/can-increase-hiv-risk/
- 4. Transmission of HIV/AIDS | Stanford Health Care [Internet]. [cited 2020 Nov 5]. Available from: https://stanfordhealthcare.org/medical-conditions/sexual-and-reproductive-health/hiv-aids/causes.html

3rd Objective:

- 1. Avert. 2020. Global HIV Targets. [online] Available at: https://www.avert.org/global-hiv-targets
- 2. Unaids.org. 2020. UNAIDS Strategy. [online] Available at: https://www.unaids.org/en/goals/unaidsstrategy
- 3. Theglobalfund.org. 2020. [online] Available at: https://www.theglobalfund.org/media/10103/corporate 2020resultsreport report en.pdf

4th Objective:

- 1. World Health Organization, HIV in the WHO Eastern Mediterranean Region. [cited 2020Nov14]. Available from: http://www.emro.who.int/asd/about/hiv-situation-region.html
- 2. World Health Organization, Editorial: The diverse and rapidly growing HIV epidemic in the WHO Eastern Mediterranean Region: will countries succeed in their control?. [cited 2020Nov14]. Available from: http://www.emro.who.int/emhj-vol-19-2013/12/editorial-the-diverse-and-rapidly-growing-hiv-epidemic-in-the-who-eastern-mediterranean-region-will-countries-succeed-in-their-control.html
- 3. World Health Organization, Partner notification in the Eastern Mediterranean Region: is there a way?. [cited 2020Nov14]. Available from: http://www.emro.who.int/emhj-volume-25-2019/volume-25-issue-9/partner-notification-in-the-eastern-mediterranean-region-is-there-a-way.html

5th Objective:

Α-

- 1- Filemban, S. M., Yasein, Y. A., Abdalla, M. H. H., Al-Hakeem, R., Al-Tawfiq, J. A., &. Memish, Z. A. (2015). Prevalence and behavioral risk factors for STIs/HIV among attendees of the Ministry of Health hospitals in Saudi Arabia. The Journal of Infection in Developing Countries, 9(04), 402-408. https://doi.org/10.3855/jidc.5964
- 2-Obermeyer CM. HIV in the Middle East. BMJ 2006; 333:

851-854.

3- Al-Mozaini M, Alrahbeni T, Al-Mograbi R, Alrajhi A. Antiretroviral resistance in HIV-1 patients at a tertiary medical institute in Saudi Arabia: a retrospective study and analysis. BMC Infect Dis 2018; 18: 425.

4- National Aids Program - KSA (NAPKSA). [cited 2020]. Available at: https://www.linkedin.com/in/napmoh/?originalSubdomain=sa

5- KINGDOM OF SAUDI ARABIA MINISTRY OF HEALTH

,https://www.moh.gov.sa/en/Ministry/MediaCenter/Publications/Pages/Publications-2013-11-30-001.aspx

6- Al-Mozaini, M. A., Mansour, M. K., Al-Hokail, A. A., Mohmed, M. A., Daham, M. A., Al-Abdely, H. M., Frayha, H. H., Al-Rabiah, F. A., Alhajjar, S. H., Keshavjee, S., Adra, C. N., & Alrajhi, A. A. (2014). HIV-Care Outcome in Saudi Arabia; a Longitudinal Cohort. Journal of AIDS & clinical research, 5(11), 370. https://doi.org/10.4172/2155-6113.1000370

B-

- 1-Ministry of health in Saudi Arabia- www.moh.gov.sa
- 2-Ministery Of Interior- www.moi.gov.sa
- 3- bureau of experts at the council of ministers- www.laws.boe.gov.sa

C-

1-Kirby D, Laris BA, Rolleri R., Impact of Sex and HIV Education Programs on Sexual Behaviors of Youth in Developing and Developed Countries, 2005Research Triangle Park, NCFamily Health International Available at:

http://www.ungei.org/resources/files/sex_ed_working_paper_final.pdf

- 2-Pre-Exposure Prophylaxis (PrEP) | HIV Risk and Prevention | HIV/AIDS | CDC [Internet]. [cited 2020 Nov 5]. Available from: https://www.cdc.gov/hiv/risk/prep/index.html
- 3-Post-Exposure Prophylaxis (PEP) | HIV Risk and Prevention | HIV/AIDS | CDC [Internet]. [cited 2020 Nov 5]. Available from: https://www.cdc.gov/hiv/basics/pep.html
- 4- Platt L, Minozzi S, Reed J, Vickerman P, Hagan H, French C, et al. Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs. Vol. 2017, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2017.