



VACCINATION AGAINST SEASONAL INFLUENZA IN ADULT HIGH RISK GROUPS: GLOBAL AND SOUTH ASIAN RECOMMENDATIONS

Raja Dhar

MD, MRCP (UK), MSc (EBM, UK), CCT (UK), FCCP (US)

Consultant Respiratory Physician, Fortis

Director, Education and Research

NAABI Kolkata

docaardee@yahoo.com

Points for discussion today

- **Defining the high risk population**
- **Specific risk factors for Influenza A: H1N1 (if any)**
- **Influenza is special risk population: Focus on South Asian Guidelines**
- **Recommendations in other high risk populations**
- **Poor Influenza vaccine uptake in certain countries**



**World Health
Organization**

Organisation mondiale de la Santé

Weekly epidemiological record Relevé épidémiologique hebdomadaire

23 NOVEMBER 2012, 87th YEAR / 23 NOVEMBRE 2012, 87^e ANNÉE

No. 47, 2012, 87, 461–476

<http://www.who.int/wer>

Contents

461 Vaccines against influenza
WHO position paper –
November 2012

**Vaccines against influenza
WHO position paper –
November 2012**

**Note de synthèse de l'OMS
concernant les vaccins
antigrippaux – novembre 2012**

- **Pregnant women – highest priority group – vaccination in any trimester**
- **Healthcare workers (HCW)**
- **Children 6 to 59 months of age**
- **The elderly**
- **Those with high-risk conditions**

Table 2. List of high-risk underlying health conditions

1. Respiratory disease a. Asthma b. Chronic bronchitis and emphysema c. Other pulmonary diseases
2. Cardiac disease a. Atherosclerotic heart disease b. Cardiomyopathy/chronic congestive heart failure c. Congenital heart disease
3. Neurodevelopmental disorders a. cerebral palsy b. musculodystrophy c. cognitive disorders
4. Metabolic disorders a. Diabetes
5. Immunocompetency disorders a. HIV/AIDS b. Chemotherapy c. Transplant patients on immunosuppressive agents d. Chronic corticosteroid therapy
6. Chronic renal insufficiency on dialysis
7. Chronic liver disease especially with cirrhosis.
8. Morbid obesity
9. Hematological diseases a. Sickle cell anemia b. Thalassemia major
10. Chronic aspirin therapy in children (risk of Reye's syndrome)
Other groups to consider (not necessarily with a chronic illness): 1. Members of socially disadvantaged minority groups. 2. Residents of long term care facilities.

WHO POSITION PAPER 2012

Recommendation: Individuals with Underlying Health Conditions

- Persons with specific chronic diseases are at high risk for severe influenza illness. These groups have often been targeted for influenza vaccination, and continue to be an appropriate target group for vaccination. However, identification of these individuals in many settings is often challenging and requires considerable ongoing effort and investment.

CDC recommendations

Figure 2. Vaccines that might be indicated for adults aged 19 years or older based on medical and other indications¹

VACCINE ▼	INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding HIV infection) ^{4,5,7,8,13}	HIV infection CD4+ count (cells/ μ L) ^{4,5,7,8,13}		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, on hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia and persistent complement deficiencies ^{8,11,12}	Chronic liver disease	Diabetes	Healthcare personnel	
				< 200	\geq 200								
Influenza ^{2,3}													1 dose annually
Tetanus, diphtheria, pertussis (Td/Tdap) ^{2,3}		1 dose Tdap each pregnancy											Substitute Tdap for Td once, then Td booster every 10 yrs
Varicella ⁴			Contraindicated										2 doses
Human papillomavirus (HPV) Female ⁵													3 doses through age 26 yrs
Human papillomavirus (HPV) Male ⁵													3 doses through age 21 yrs
Zoster ⁶			Contraindicated										1 dose
Measles, mumps, rubella (MMR) ⁷			Contraindicated										1 or 2 doses depending on indication
Pneumococcal 13-valent conjugate (PCV13) ⁸													1 dose
Pneumococcal polysaccharide (PPSV23) ⁸													1, 2, or 3 doses depending on indication
Hepatitis A ⁹													2 or 3 doses depending on vaccine
Hepatitis B ¹⁰													3 doses
Meningococcal 4-valent conjugate (MenACWY) or polysaccharide (MPSV4) ¹¹													1 or more doses depending on indication
Meningococcal B (MenB) ¹¹													2 or 3 doses depending on vaccine
<i>Haemophilus influenzae</i> type b (Hib) ¹²													3 doses post-HSCT recipients only
													1 dose

¹Covered by the Vaccine Injury Compensation Program

 Recommended for all persons who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection; zoster vaccine is recommended regardless of past episode of zoster
 Recommended for persons with a risk factor (medical, occupational, lifestyle, or other indication)
 No recommendation
 Contraindicated

Risk Factors for Severe Outcomes following 2009 Influenza A (H1N1) Infection: A Global Pooled Analysis

Maria D. Van Kerkhove^{1,2}, Katelijn A. H. Vandemaele¹, Vivek Shinde¹, Giovanna Jaramillo-Gutierrez¹, Artemis Koukounari², Christl A. Donnelly², Luis O. Carlino³, Rhonda Owen⁴, Beverly Paterson⁴, Louise Pelletier⁵, Julie Vachon⁵, Claudia Gonzalez⁶, Yu Hongjie⁷, Feng Zijian⁷, Shuk Kwan Chuang⁸, Albert Au⁸, Silke Buda⁹, Gerard Krause⁹, Walter Haas⁹, Isabelle Bonmarin¹⁰, Kiyosu Taniguichi¹¹, Kensuke Nakajima¹², Tokuaki Shobayashi¹², Yoshihiro Takayama¹², Tomi Sunagawa¹¹, Jean Michel Heraud¹³, Arnaud Orelle¹³, Ethel Palacios¹⁴, Marianne A. B. van der Sande¹⁵, C. C. H. Lieke Wielders¹⁵, Darren Hunt¹⁶, Jeffrey Cutter¹⁷, Vernon J. Lee^{18,19}, Juno Thomas²⁰, Patricia Santa-Olalla²¹, Maria J. Sierra-Moros²¹, Wanna Hanshaoworakul²², Kumnuan Ungchusak²², Richard Pebody²³, Seema Jain²⁴, Anthony W. Mounts^{1*}, on behalf of the WHO Working Group for Risk Factors for Severe H1N1pdm Infection

Background : Since the start of the 2009 influenza A pandemic (H1N1pdm), the World Health Organization and its member states have gathered information to characterize the clinical severity of H1N1pdm infection and to assist policy makers to determine risk groups for targeted control measures.

Methods : Data were collected on approximately 70,000 laboratory-confirmed hospitalized H1N1pdm patients, 9,700 patients admitted to intensive care units (ICUs), and 2,500 deaths reported between 1 April 2009 and 1 January 2010 .

Data was collected from **19 countries** —Argentina, Australia, Canada, Chile, China, France, Germany, Hong Kong SAR, Japan, Madagascar, Mexico, the Netherlands, New Zealand, Singapore, South Africa, Spain, Thailand, the United States, and the United Kingdom

Kerhove et al continued

The patients were categorized into 3 levels of severity: hospitalizations, ICU admissions, and deaths.

The proportion of H1N1pdm patients with at least one chronic medical condition generally increased with severity . The median among all countries that provided data was 31.1% , 52.3% , and 61.8% of hospitalized, ICU-admitted and fatal H1N1pdm cases, respectively.

This pattern was observed for most countries individually as well.

Chronic respiratory conditions excluding asthma (median =10.3%, 17.2%, and 20.4%, respectively) and asthma (median =17.6%, 9.8%, and 5.3%, respectively) were the risk factors most often reported among severe cases.

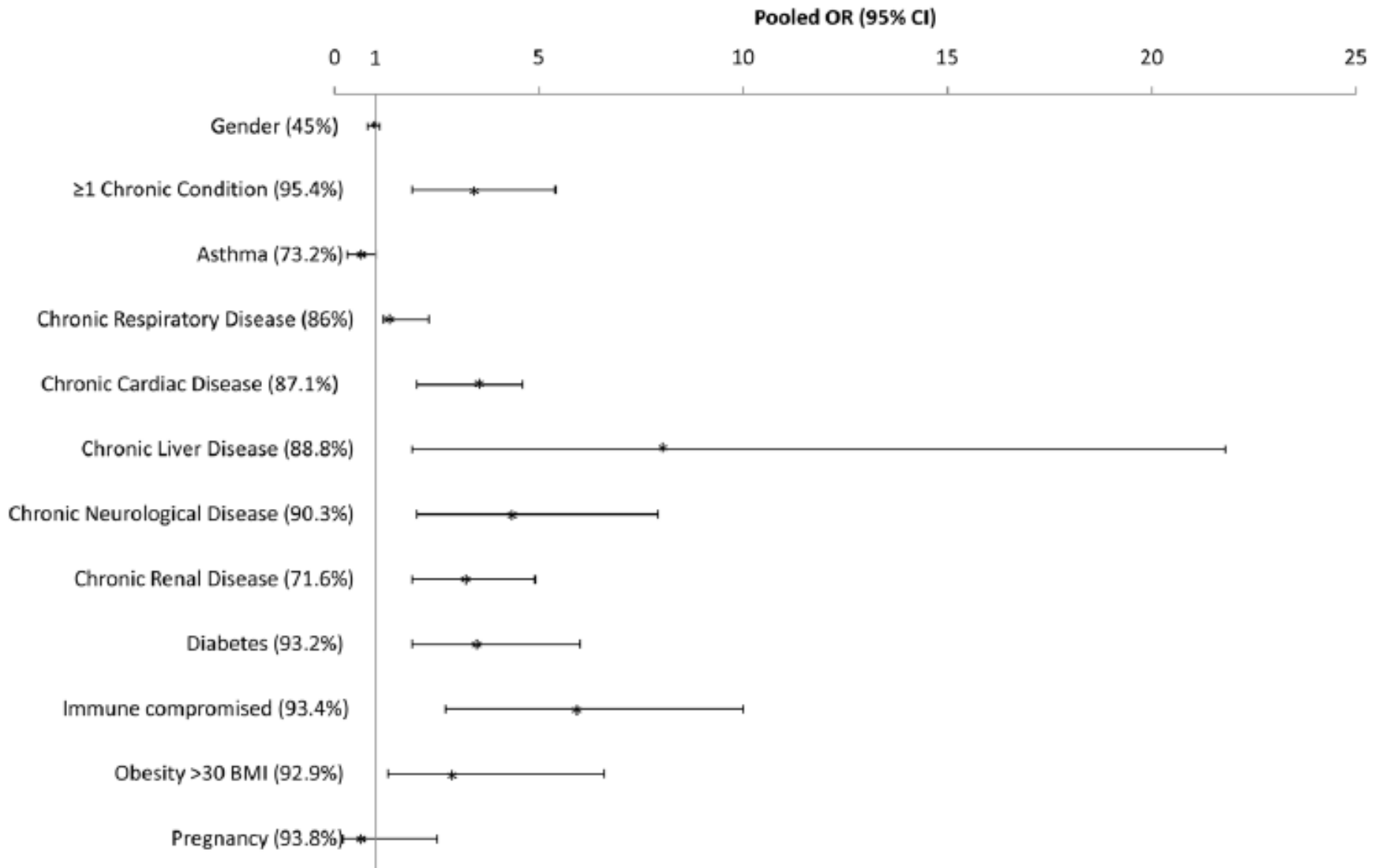
These were followed closely by diabetes (median = 9.0%, 13.6%, and 14.4%, respectively) and chronic cardiac conditions (median = 7.1%, 10.9%, and 12.1%, respectively)

Comparing the severity of Influenza in Chronic diseases

Risk Factor ^a	Severity Level ^b						RR of Severe Disease (IQR) ^c			
	<i>n</i> ^d	Hospitalized Cases	<i>n</i> ^d	ICU-Admitted Cases	<i>n</i> ^d	Fatal Cases	<i>n</i> ^d	RR _{hosp}	<i>n</i> ^d	RR _{death}
Chronic medical illness										
Respiratory disease	12	10.3 (5.0–21.7)	11	17.2 (10.5–29.9)	16	20.4 (9.3–29.5)	5	3.3 (2.0–5.8)	8	7.8 (4.9–26.6)
Asthma	11	17.6 (10.0–20.4)	9	9.8 (5.6–14.3)	15	5.3 (4.0–10.6)	3	1.8 (1.2–2.6)	6	1.7 (1.5–2.1)
Diabetes	14	9.0 (3.5–12.6)	12	13.6 (9.3–17.3)	17	14.4 (13.0–18.0)	7	0.9 (0.5–1.7)	10	4.0 (3.1–6.9)
Cardiac disease	12	7.1 (3.7–10.9)	11	10.9 (8.8–15.0)	15	12.1 (10.0–16.4)	6	2.0 (1.5–2.2)	8	9.2 (5.4–10.7)
Renal disease	13	4.0 (2.0–5.1)	11	6.3 (3.5–8.4)	16	7.1 (5.0–8.1)	2	4.4 (4.2–4.5)	3	22.7 (21.0–25.4)
Liver disease	9	1.1 (0.3–2.0)	9	2.4 (0.9–5.0)	12	4.9 (2.7–6.0)	3	5.7 (3.2–15.7)	4	17.4 (11.6–28.0)
Neurological disease	11	4.0 (2.5–7.5)	11	7.0 (3.5–9.5)	14	13.9 (5.5–18.4)	2	1.1 (0.9–1.3)	3	13.1 (8.4–32.4)
Immune compromised	13	5.0 (2.0–7.2)	11	6.7 (3.2–18.4)	15	12.5 (7.9–18.4)	2	24.3 (16.1–32.6)	4	27.7 (14.0–66.5)
Cases with ≥1 chronic medical illnesses	14	31.1 (19.0–47.1)	10	52.3 (41.1–58.7)	16	61.8 (48.5–67.9)		NA		NA

In cases of > 1 chronic illnesses the severity of Influenza rises exponentially .

Pooled odds ratios for deaths among chronic diseases



Conclusions

- The results demonstrated that risk factors for severe H1N1pdm infection are similar to those for seasonal influenza, except for - younger age groups and obesity.
- There is a need to identify and protect groups at highest risk of severe outcomes.



Influenza in Special Risk Population- South Asian Recommendations

Influenza in Special Risk Population –Diabetes

- Diabetes results in increased risk of infections and death associated with infectious disease.
 - During influenza epidemics, there is 5-15% increase in the mortality among diabetes patients.
- Benefits of influenza vaccination
 - Reduced complications
 - Less hospitalizations
 - Reduced mortality
 - Lower mortality for diabetes mellitus

Recommendations for Diabetes Patients

- Every one with diabetes over the age of six month - Maintain good glycemic control, take influenza vaccination yearly for minimizing infective episodes, except who are allergic to eggs.
- Influenza immunization is strongly recommended yearly in all people with diabetes with renal failure, immunocompromised state due to concomitant illness and co-morbidities, chronic respiratory diseases, poor hygienic conditions and those who frequently travel to high risk areas.
- Younger persons with diabetes (18-50 years)- Counseling to be done about influenza vaccination.
- People with diabetes with long duration of disease and poor control have greater susceptibility to infection by Influenza virus hence should be vaccinated.
- Elderly people with diabetes >50 years of age and with co-morbidities should be strongly motivated for mandatory vaccination against influenza.

Influenza in Special Risk Population –Renal Disease

- There is increased risk of frequency and severity of infections due to alterations in the immune functions and frequent exposure to medical interventions.
- Recommendations
 - All patients with chronic kidney disease (CKD) and all kidney transplant recipients should be advised to receive annual influenza vaccine.
 - Household contacts and health care workers should also be vaccinated annually to decrease the transmission to high risk CKD or post-transplant patients

Recommendations for Renal Disease Patients

- **In Dialysis:** Both peritoneal dialysis and hemodialysis patients should receive the standard annual dose of the vaccine.
- **Kidney Transplant:** Inactivated influenza vaccine may be given to transplant recipients despite intensive immunosuppression. It is best to wait until the first 3–6 months after kidney transplantation, the period of intense immunosuppression, before attempting vaccination.
 - Inactivated influenza vaccination can be administered as early as one month after kidney transplant to time it before onset of the flu season.
 - Influenza vaccine use in transplant recipients was associated with lower rates of allograft loss and death.

Influenza in Special Risk Population –Respiratory Disease

- Patients with chronic respiratory disease are at a higher risk of complications from influenza.
 - 27% of COPD exacerbations were associated with respiratory viruses.
- The effectiveness of influenza vaccination in respiratory diseases is proved in clinical trials
 - Reduced outpatient visits and hospitalizations in patients with COPD.
 - Lesser medical consultations, reduced hospitalization rate, and reduced mortality.

Recommendations for Respiratory Disease Patients

- All patients with chronic respiratory diseases including bronchial asthma, COPD, bronchiectasis, interstitial lung disease and chronic smoker should receive annual influenza vaccination.
- Smoking may increase the risk of hospitalization in smokers and ex-smokers when infected by the influenza virus.

Influenza in Special Risk Population –Recommendations in Heart Disease

- Influenza is associated with significant morbidity and mortality in patients with chronic disease such as congestive heart failure.
- The increased risk of heart related problems in patients with influenza may be related susceptibility to thrombosis due to several biochemical, cellular, and hemostatic changes
- Recommendations
 - Influenza vaccination is recommended for patients with atherosclerotic heart disease, cardiomyopathy/chronic congestive heart failure, and congenital heart disease.
 - Patients with valvular heart disease should also receive annual influenza vaccination.

Influenza in Special Risk Population –Recommendations in Liver Disease

- Influenza A can be responsible for hepatic decompensation and hospitalization in patients with cirrhosis and patients waiting for liver transplantation.
- Swine influenza may be associated with sudden clinical deterioration and risk of death in cirrhotic patients making cirrhotic patients suitable candidates for yearly influenza vaccination.
- Cirrhotic patients including patients under treatment, and liver transplant recipients can receive benefit from influenza vaccination.
- Recommendations
 - Influenza vaccination is recommended for patients with chronic liver disease with cirrhosis (both compensated and decompensated cirrhosis).
 - Annual vaccination is also recommended for Chronic Hepatitis (especially Hepatitis B and C) and alcoholics.

Influenza in Special Risk Population –Recommendations in Elderly

- Influenza is associated with significant morbidity and mortality in elderly people.
- Trivalent seasonal influenza vaccination in elderly people results reduction in ;
 - All-cause mortality, pneumonia-related mortality, hospitalization rate, influenza-like illness, hospitalization for pneumonia and influenza and mortality.
- Recommendations
 - Influenza vaccine is recommended in patients >50 years of age. Currently in India the high dose vaccine is not available. Available trivalent inactivated vaccine may be given to elderly people

Influenza in Special Risk Population –Recommendations in Pregnancy

- Pregnant women are at high risk of complications for influenza related hospitalizations and complications. Therefore constitute a high priority for influenza vaccination.
- About 63% reduction in proven influenza illness with inactivated influenza vaccination in infants up to six months of age
- Reduction in febrile respiratory illnesses in mothers as well as infants.
- Recommendations
 - Influenza vaccination should be given to all pregnant women.
 - Influenza vaccine can be given in any trimester of pregnancy
 - LAIV is contraindicated in pregnancy

Influenza in Special Risk Population –Recommendations in Healthcare Workers

- Health care workers have significantly higher risk of influenza compared to nonhealthcare professionals
 - Vaccination can reduce days of work loss and febrile respiratory illness
- Recommendations
 - Influenza vaccine is recommended in all healthcare workers with direct or indirect interaction with patients or hospital staff as well as office staff.
- In case of inadequate vaccine supply, following prioritization is recommended
 - Those who are in close, prolonged contact and repeated contact with high risk patients should be vaccinated first.
 - Close but not in prolonged or repeated contact with high risk patients, those work with high risk patients, perform the essential patient care functions and HCP who are in contact with patients not at risk should be given second priority
 - Other healthcare personnel

Influenza in Special Risk Population –Recommendations in Neurological Disorders, Obesity and Autoimmune Diseases

- Patients with influenza may have higher risk of stroke due to susceptibility to thrombosis.
 - Influenza vaccination can decrease the risk of acute neurovascular event particularly stroke.
- Recommendations
 - Vaccination should be recommended in all patients with chronic vascular disease
 - Patients with history of stroke or transient ischemic attacks should receive an annual influenza vaccination
 - Patients with diabetes mellitus or with a combination of risk factors that further increases risk of stroke should receive vaccination
 - Obese patients should be considered priority group for influenza vaccination
 - Patients with rheumatoid arthritis, systemic lupus erythematosus and Sjogren's syndrome should be considered for annual influenza vaccination.

Influenza in Special Risk Population –Recommendations in Immunocompromised, Cancers and Blood Disorders

- Influenza can result in severe complications in HIV infections patients leading to increased risk of hospitalisation and death.
 - Influenza vaccination is well tolerated in these patients, but the response is lower compared to immunocompetent people.
- Recommendations
 - Annual vaccination for HIV-infected individuals with inactivated vaccine is recommended.
 - Severely impaired antibody responses are observed in HIV infected individuals with CD4+ T-lymphocyte counts $<100 \times 10^6/l$. Annual vaccination of HIVinfected individuals with CD4+ T-lymphocyte counts exceeding $100 \times 10^6/l$ seems to be worthwhile, although it may not be expected to render the same level of protection against influenza as in non-infected individuals.
 - Annual influenza vaccination is recommended in cancer and solid organ transplant (SOT) recipients.

Influenza in Special Risk Population –Recommendations in Immunocompromised, Cancers and Blood Disorders

- Recommendations
 - Donors and recipients of solid organ transplant should be updated regarding
 - Post organ transplant, it is advisable to postpone influenza vaccination for the first two months, but in
 - the event of an outbreak in the community, injectable vaccine can be given after one month of transplant. Live vaccines are not advised in this group of patients.
 - Vaccine should be given prior to the immunosuppressive therapy if possible.
 - Live vaccines if needed should be given at least four weeks before immunosuppression and should be avoided two weeks prior to immunosuppression. Inactivated vaccines can be given two weeks or more prior to immunosuppression

Influenza in Special Risk Population –Recommendations in Immunocompromised, Cancers and Blood Disorders

- Recommendations
- Annual vaccine with inactivated influenza vaccine is recommended for all immunocompromised patients aged six months after the immune-suppressive therapy except those who are unlikely to respond (e.g. those receiving intensive chemotherapy or those who have received anti B cell antibody in last six months). Live influenza vaccine should not be given to these patients.
- Household members immunosuppressed members should preferably given the inactivated vaccine, especially for hematopoietic stem cell transplant recipients within two months after transplant, or for those with subacute combined immunodeficiency.
- Patients aged six months and more with hematological malignancy or solid tumor except those receiving anti B cell antibodies or intensive chemotherapy for induction or consolidation of leukemia should receive influenza vaccine every year.
- Acute leukemia patients on chemotherapy should not receive the vaccine. Before chemotherapy, they can receive the vaccine.

Influenza in Special Risk Population –Recommendations in Other High Risk Populations (Hajj, Kumbh Mela, Umrah, Military, Army, Air Force, Hostellers, Prisoners and Other High Risk Situations Conditions like Corporates, Manufacturing Units, Miners, Frequent Air Travelers, etc.)

- Recommendations
 - Vaccination of workers/employees for influenza substantially reduces influenza like illness and absenteeism in all types of industries. Thus annual influenza vaccination is beneficial in these settings.
 - Vaccination should be taken before traveling
 - Military, paramilitary and emergency personnel are prone to outbreaks of respiratory illnesses including influenza for variety of reasons. Therefore, influenza vaccination is recommended to the armed forces personnel from Army, Navy or Air-force.
 - Hostellers/boarding school and medical colleges: Mass immunization is very effective in increasing the uptake of vaccination and success rate.
 - It is important to immunize the prison staff rather than the residents. Staff with influenza like illness should stay home and remain home at least for seven days after symptoms subside

Influenza in Special Risk Population –Recommendations in Other High Risk Populations (Hajj, Kumbh Mela, Umrah, Military, Army, Air Force, Hostellers, Prisoners and Other High Risk Situations Conditions like Corporates, Manufacturing Units, Miners, Frequent Air Travelers, etc.)

- Recommendations
 - In airline personnel - In case ill, they should discontinue work as soon as possible without affecting flight safety and start working after 24 hours after the resolution of symptoms for Disinfection and cleaning of aircraft after the outbreak is important.
 - Hajj & Umrah- Severe crowding, shared accommodation, reduced personal hygiene, and environmental pollution and Hajj and Umrah may collectively lead to increased transmission of respiratory viruses, notably influenza. The Centre for Disease Control and Saudi Government recommend that international pilgrims be vaccinated against seasonal influenza before arriving in the country. The group endorses this recommendation.

Poor Influenza Vaccine Uptake in Many Countries

- Vaccine uptake in many countries including India is dismal among the high risk population including healthcare workers, COPD, diabetics, and pregnant women.
- Recommendations for Improving the Implementation of Influenza Vaccination
 - Efforts should be made to create and maintain disease specific registries for systemic tracking and reminders for vaccination
 - Periodic training of the staff accompanied by ongoing assessment of immunization rate and workflow with close follow up is essential
 - Quality assurance and standards of care should be maintained.
 - Clinics using vaccination should try to maintain the records to assess the efficacy of vaccines and occurrence of complications.

Poor Influenza Vaccine Uptake in many countries

- Recommendations for Improving the Implementation of Influenza Vaccination
 - Awareness among patients as well as physicians should be improved for improving vaccination uptake rate.
 - Along with the vaccine recommendation, the patients should also be educated about the risk of the illness and its complications which can be prevented by vaccination.
 - Access to vaccination is key minimize risk of pandemic influenza. Vaccine should be made available at any time especially in high risk areas.
 - Multiple vaccines given in single visit, reduction of financial barriers and use of all possible means to create awareness are some of the useful measures to improve the uptake rates of influenza.
 - Vaccination reminders through cellular companies as a part of corporate social responsibility can be considered



THANK YOU!