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Influenza Immunization for Adult and Pediatric Patients Undergoing Cancer Treatment

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Cancer Care Alberta

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Background

Seasonal influenza is an important cause of morbidity and mortality in Canada.[1] An estimated 12,200 hospitalizations and 3,500 deaths can be attributed to an epidemic of influenza; these include deaths related to pneumonia due to influenza virus or a secondary pathogen like *Streptococcus pneumoniae.*[2] People at greatest risk of influenza-related complications are children 0-5 years of age, pregnant women, older adults (>65 years), residents of nursing homes and other chronic care facilities, Indigenous people and people with underlying medical conditions.[3,4] Adult and pediatric patients with cancer are considered immunosuppressed, either as a result of their underlying disease or secondary to their treatment, and are therefore included in this high risk group. Influenza infection not only causes primary illness but also can lead to severe secondary medical complications, including viral pneumonia, secondary bacterial pneumonia, and worsening of underlying medical conditions.

Guideline Questions

1. What are the recommendations for influenza immunization for adult and pediatric patients with solid tumours or hematologic cancers in Alberta?
2. What is the current evidence for response to the influenza vaccine among adult and pediatric patients with cancer receiving chemotherapy or other systemic therapy?
3. What is the best timing for administering the influenza vaccine in relation to the therapy cycle for adult and pediatric patients with cancer?

Search Strategy

The MEDLINE database was searched according to the strategy outlined in Appendix B. The 2020 search yielded 84 citations, 9 of which met the criteria to be included in the evidence tables presented in a supporting document. A systematic search of grey literature included websites from the World Health Organization, Health Canada, the Public Health Agency of Canada, Alberta Health Services, Alberta Health, Centers for Disease Control and Prevention, and the American Academy of Pediatrics. A search for published clinical practice guidelines yielded results from the Infectious Diseases Society of America,[5] the National Comprehensive Cancer Network,[6] and the Italian Society of Medical Oncology.[7]

Target Population

The recommendations outlined in this guideline apply specifically to children and adults with solid tumours or hematologic malignancies.

Recommendations

The following recommendations have been adapted from existing practice guidelines, policy documents, and consensus statements, including those from the 2020 Alberta Health Services Immunization Program Standards Manual, 2020/21 Alberta Influenza Immunization Policy, Health

Canada, the Public Health Agency of Canada, the Centers for Disease Control and Prevention, and the American Academy of Pediatrics. Evidence from published clinical trials, retrospective reviews, and case study reports was also reviewed and considered.

This guideline outlines the recommendations for influenza immunization among adult and pediatric patients with cancer. For the most current Alberta Health Services information, clinical guidelines, and schedules on influenza immunization for the general population, please visit the Influenza Immunization webpage. For information specific to the delivery of influenza immunization services during COVID-19, please refer to Influenza Immunization During COVID-19 Guidance for the 2020-21 Season.

The 2020/2021 quadrivalent inactivated influenza vaccines being used in Alberta contain the following antigenic strains:[3,8-10]

- A/Guangdong-Maonan/SWL 1536/2019 (H1N1) pdm09-like virus
- A/Hong Kong/2671/2019 (H3N2)-like virus
- B/Washington/02/2019-like virus (B/Victoria lineage)
- B/Phuket/3073/2013-like virus (B/Yamagata lineage)

The 2020/2021 high dose trivalent inactivated vaccine being used in Alberta contain the following antigenic strains:

- A/Guangdong-Maonan/SWL 1536/2019 (H1N1) pdm09-like virus
- A/Hong Kong/2671/2019 (H3N2)-like virus
- B/Washington/02/2019-like virus (B/Victoria lineage)

Influenza Immunization: Adult Patients with Cancer

1. Annual administration of the **inactivated** influenza vaccine is recommended for most adult patients with cancer. Patients considered to be the highest priority are those on active treatment.[3,8,11] Individuals with malignant solid tumours (and on immunosuppressive therapy) who are three months post-chemotherapy and the cancer is in remission are no longer considered immunocompromised.[12] Individuals with malignant hematologic disorders who are more than three years post therapy and no longer on immunosuppressive medications are considered healthy and should be assessed for immunizations as per the general population.

Influenza vaccines that may be included in the 2020/21 Provincially Funded Program[10]

Product	Quadrivalent Inactivated Influenza Vaccine		High dose Trivalent Inactivated Vaccine
Influenza Vaccine Name	Fluzone® Quadrivalent FluLaval® Tetra	Afluria® Tetra Influvac® Tetra	Fluzone® High Dose
Presentation	Multidose Vial Pre-filled syringe	Pre-filled syringe	Pre-filled syringe
Age Group	≥ Six months of age	Afluria® Tetra, ≥ Five years of age Influvac® Tetra, ≥ Three years of age	≥ 65 years of age residing in a provincially funded Long-Term Care bed in auxiliary hospitals and nursing homes. If a facility with Long Term Care funded beds also has Designated Supportive Living beds, those residents can also be offered Fluzone® High Dose vaccine.

2. Age, duration, type of systemic therapy (with the exception of rituximab or other B-cell depleting antibodies, and CTLA-4, PD-1, or PD-L1 immune checkpoint inhibitor therapies), and curative versus palliative treatment intent do not appear to influence the response of adult patients with cancer to the influenza immunization. Adult patients with hematologic malignancies may have lower responses to immunization when compared to adult patients with solid tumours.

3. Timing of inactivated influenza immunization:
    a) The vaccine should ideally be given at least two weeks before the administration of any immune-suppressing cancer treatment or delayed until at least three months after immune-such treatment has stopped or is at the lowest possible level.[12] While administration of the vaccine at any time before, during or after immune-suppressing cancer treatment is safe, its efficacy may be reduced. Every effort should be made to time immunization so that optimal immunogenicity is achieved. Inactivated vaccine doses administered during cancer chemotherapy should not be considered valid doses unless there is documentation of a protective antibody response.
    b) Patients who are treated with rituximab or other B-cell depleting antibodies should have all inactivated vaccines postponed until at least six months after the last dose of rituximab.[5,13-15]
    c) Given the lack of safety information and the potential risk of a significant immune response, patients treated with CTLA-4 inhibitors (e.g., ipilimumab) alone or in combination with other anti-cancer agents and those who have discontinued treatment with CTLA-4 inhibitors in the past six months should not receive the influenza vaccine.
    d) Patients treated with PD-1 and PD-L1 inhibitors (e.g., nivolumab, pembrolizumab) and those who have discontinued treatment with PD-1 and PD-L1 inhibitors in the past six months may receive the inactivated influenza vaccine one week post-administration of

these agents so as not to mask any immune related effects related to administration of cancer therapies.

e) Patients on high-dose systemic steroids should wait four weeks after discontinuation of therapy before the vaccine is administered.[12]
f) Patients on clinical trial protocols should continue to follow instructions based on their specific protocol.

4. For adult patients undergoing hematopoietic stem cell transplant (HSCT, autologous and allogeneic):[14,16]
    a) The inactivated influenza vaccine should be administered at least two weeks prior to harvest (allogeneic donor), in the first half of the interval between mobilization chemotherapy and harvest (autologous recipient), or at least two weeks prior to transplant conditioning (allogeneic recipient). **Live vaccines are contraindicated.**
    b) Immune system recovery post-HSCT is variable and requires assessment by the transplant physician. Some HSCT recipients will have a detectable antibody response to the influenza vaccine at 6 to 24 months post-transplant, while over 60% will have a detectable response at 24 months or more post-transplant.
    c) For HSCT recipients, influenza vaccine should ideally be administered six months post-transplant. Inactivated influenza vaccine can be given as early as four months post-transplant in outbreak situations; if given less than six months post-transplant, a second dose can be given four weeks later if there is ongoing circulation of influenza virus in the community.
    d) For patients on post-transplant maintenance therapy please refer to the Vaccination chapter of the Alberta Health Service BMT Standard Practice Manual.
    e) Inactivated immunization should not be delayed due to GVHD/immunosuppressive therapy. Live vaccines are contraindicated in patients with active GVHD.
    f) Household contacts and healthcare workers should be up to date for routine immunizations as per the Alberta Health Immunization Schedule, including annual influenza, to reduce the risk of disease transmission to transplant recipients.
    g) Individuals who have received the live nasal spray influenza vaccine (FluMist® Quadrivalent) should avoid close association with individuals with severe immunocompromising conditions (e.g., transplant recipients requiring protective isolation) for at least two weeks following immunization.[14] The live nasal spray influenza vaccine (FluMist®) is available for purchase in Alberta through community pharmacies.

5. Annual influenza immunization of family members and hospital or clinic staff and volunteers who are in contact with adult patients with cancer is strongly recommended. In many cases, this may be more important than immunizing the patients themselves, as some patients may be less likely to respond to the vaccine. Transmission of influenza between infected healthcare workers and their vulnerable patients results in significant morbidity and mortality; therefore, healthcare workers

should consider it their responsibility to provide the highest standard of care, which includes receiving the annual **inactivated** influenza vaccine.[2,3,17]

6. Contraindications and precautions for influenza immunization in adult patients with cancer are:[3,18,19]
    - a previous anaphylactic reaction to an influenza vaccine.
    - a known hypersensitivity to any component of the vaccine, with the exception of egg.
        - Egg-allergic adults with cancer may be safely immunized using inactivated influenza vaccine without a prior influenza vaccine skin test and with the full dose of vaccine, irrespective of a past severe reaction to egg. They can be immunized in any setting and should be kept under observation for 30 minutes following the administration the vaccine.
    - a history of severe oculo-respiratory syndrome that included lower respiratory symptoms within 24 hours of receiving the influenza vaccine, pending consultation with the Medical Officer of Health to review the risks and benefits of further immunization.
    - a history of developing Guillain-Barré Syndrome within six weeks of a previous dose of influenza vaccine.

Individuals with severe acute febrile illness should not be immunized until the symptoms have resolved; individuals with mild-to-moderate febrile illness may be immunized.

As with all vaccine administration, immunizers should have the necessary anaphylaxis equipment and protocols, and be prepared to respond to a vaccine emergency at all times. Vaccine recipients who have had an anaphylactic reaction to *any* agent should be kept under observation for at least 30 minutes post-immunization.

Influenza Immunization: Pediatric Patients with Cancer

1. Annual administration of the **inactivated** influenza vaccine is indicated for most pediatric patients with cancer who are six months of age and older. Given the burden of influenza B in children and the potential for lineage mismatch between the predominant circulating strain of influenza B and the strain in a trivalent vaccine, the quadrivalent influenza vaccine (Fluzone ® Quadrivalent, Flulaval® Tetra, Alfuria® Tetra or Influvac® Tetra) should be used for children.[3,20] The live attenuated influenza vaccine is not recommended for children with immune-compromising conditions.[3,8] Immunization with currently available influenza vaccines is **not** recommended for infants younger than six months of age. The recommended doses by age are as follows:

    - children nine years or older should receive one dose of influenza vaccine.
    - children previously unimmunized with influenza vaccine who are older than six months and less than nine years of age require **two** doses of influenza vaccine in the first year they are immunized, with a minimum interval of four weeks between doses.
    - children less than nine years of age who have been previously immunized with influenza vaccine in another season require only one dose of influenza vaccine.

- a full dose (0.5mL) of influenza vaccine should be used for all people who are receiving influenza immunization.

2. Although the data is limited, age, duration, and type of systemic therapy (with the exception of rituximab or other B-cell depleting antibodies) do not appear to influence the response of pediatric patients to influenza vaccine. Pediatric patients with hematologic malignancies may have lower responses to immunization when compared to pediatric patients with solid tumours. Patients who are treated with rituximab or other B-cell depleting antibodies should have all immunizations postponed until at least six months after the last dose of rituximab.[5,13-15]

3. Influenza vaccine should ideally be given at least two weeks before the administration of any immune-suppressing cancer treatment, to allow the patient to develop a sufficient antibody response. If early immunization is not possible or feasible, administration of the inactivated vaccine less than two weeks before the start of immune-suppressing cancer treatment, or between treatment cycles has been reported to be safe and is recommended over not receiving the vaccine at all, although the efficacy of the vaccine may be reduced in this situation.

4. For pediatric patients undergoing hematopoietic stem cell transplant (HSCT, autologous and allogeneic):[14,20]
    a) Administer the inactivated influenza vaccine at least two weeks prior to harvest (allogeneic donor), in the first half of the interval between mobilization chemotherapy and harvest (autologous recipient), or at least two weeks prior to transplant conditioning (allogeneic recipient). **Live vaccines are contraindicated.**
    b) Immune system recovery post-HSCT is variable and requires assessment by the transplant physician. Some HSCT recipients will have a detectable antibody response to the influenza vaccine at 6 to 24 months post-transplant, while over 60% will have a detectable response at 24 months or more post-transplant.
    c) For HSCT recipients, influenza vaccine should ideally be administered six months post-HSCT. Inactivated influenza vaccine can be given as early as four months post-transplant in outbreak situations, with the approval of the transplant physician; if given less than six months post-transplant, a second dose can be given four weeks later if there is ongoing circulation of influenza virus in the community.
    d) For patients on post-transplant maintenance therapy please refer to the Vaccination chapter of the Alberta Health Service BMT Standard Practice Manual.
    e) Inactivated immunization should not be delayed due to GVHD/immunosuppressive therapy. Live vaccines are contraindicated in patients with active GVHD.
    f) Household contacts and healthcare workers should be up to date for routine immunizations as per the Alberta Health Immunization Schedule, including annual influenza, to reduce the risk of disease transmission to pediatric transplant recipients.
    g) Individuals who have received the live nasal spray influenza vaccine (FluMist® Quadrivalent) should avoid close association with individuals with severe

immunocompromising conditions (e.g., transplant recipients requiring protective isolation) for at least two weeks following immunization.[14] The live nasal spray influenza vaccine (FluMist®) is available for purchase in Alberta through community pharmacies.

5. Annual influenza immunization of family members, out-of-home caregivers, and hospital or clinic staff and volunteers in contact with pediatric patients with cancer is strongly recommended. In many cases, this may be more important than immunizing the patient themselves, as some patients may be less likely to respond to the vaccine. Transmission of influenza between infected healthcare workers and their vulnerable patients results in significant morbidity and mortality; therefore, healthcare workers should consider it their responsibility to provide the highest standard of care, which includes receiving the annual **inactivated** influenza vaccine.[2,3,17]

6. Contraindications and precautions for influenza immunizations in pediatric patients with cancer include:[3,18,19]
    - Age less than six months.
    - A previous anaphylactic reaction to an influenza vaccine.
    - A known hypersensitivity to any component of the vaccine, with the exception of egg.
        - Egg-allergic children with cancer may be safely immunized using inactivated influenza vaccine without a prior influenza vaccine skin test and with the full dose of vaccine, irrespective of a past severe reaction to egg. They can be immunized in any setting and should be kept under observation for 30 minutes following the administration the vaccine.
    - A history of severe oculo-respiratory syndrome that included lower respiratory symptoms within 24 hours of receiving the influenza vaccine, pending consultation with the Medical Officer of Health to review the risks and benefits of further immunization.
    - A history of developing Guillain-Barré Syndrome within six weeks of a previous dose of influenza vaccine.

Children with severe acute febrile illness should not be immunized until the symptoms have resolved; children with mild-to-moderate febrile illness may be immunized.

As with all vaccine administration, immunizers should have the necessary anaphylaxis equipment and protocols, and be prepared to respond to a vaccine emergency at all times. Vaccine recipients who have had an anaphylactic reaction to *any* agent should be kept under observation for at least 30 minutes post-immunization.

Discussion

In general, there is a paucity of evidence from well-controlled studies on influenza immunization in adult and pediatric patients with cancer. Articles included in this review repeatedly cite the need for universally accepted guidelines on the types of vaccines that produce best immunologic response,

the number of administrations, the timing of administration in relation to severity of immunosuppression, and the timing of administration in relation to chemotherapy schedules. The recommendations included in the current guideline are based, in part, on data extrapolated from healthy populations and combined with the best practices and opinions of experts in Alberta.

Influenza Immunization: Adult Patients with Cancer

Cancer treatments can produce acute and profound immunosuppression in this patient population, although published literature suggests that the degree may differ according to the specific regimen, doses, and duration of treatment. Annual administration of the inactivated influenza vaccine is therefore recommended for most adult patients with cancer, with the exception of patients treated with B-cell depleting antibodies (e.g., rituximab) and CTLA-4 immune checkpoint inhibitor therapies (e.g., ipilimumab).

Interpreting the results of influenza vaccine efficacy in adult patients with cancer is difficult, as patient characteristics, cancer types, vaccine strains, and assessment of responses vary between published studies. In a review of 1225 patients from the Surveillance, Epidemiology, and End Results (SEER) and Medicare databases, Earle *et al.* reported that among patients undergoing chemotherapy for stage IV colorectal cancer, those who had been immunized had lower rates of influenza and pneumonia than those who were not immunized (1.1% vs. 3.8%, p=.004).[21] In addition, the immunized patients had significantly fewer interruptions in the chemotherapy cycles, showed a trend towards using fewer health care resources, and were more likely to survive to the next influenza season (HR for death=0.88, 95% CI 0.77-0.99). Similarly, a 2013 Cochrane review of four studies involving 2124 adult patients with cancer receiving chemotherapy concluded that influenza immunization was associated with lower mortality and that infection rates were lower or similar in patients who were vaccinated versus those who were not.[22]

Patients with cancer who develop influenza are at a high risk for serious complications and death. In a review of 11 published studies involving adult patients undergoing chemotherapy treatment or hematopoietic stem cell transplantation (HSCT), Kunisaki *et al.* reported case fatality rates ranging from 11% to 33% for the studies involving chemotherapy.[23] Similarly, in a report of 168 critically ill patients admitted to Canadian intensive care units at the peak of the 2009-2010 H1N1 influenza outbreak, Kumar *et al.* reported that 98.2% of these patients had one or more major co-morbidities, including immunosuppression due to cancer or cancer therapies.[24]

There is conflicting evidence regarding the timing of influenza immunization with respect to chemotherapy administration. The majority of research studies, reviews, and published guidelines suggest that since immunosuppressive chemotherapy regimens may depress the patients' immune response to vaccines, it is most beneficial to immunize patients approximately 10 to 14 days prior to beginning chemotherapy, to allow for sufficient antibody production by the patient.[4,18,25,26] In a study involving patients with breast cancer, geometric mean titers were significantly lower among individuals immunized at day 16 of chemotherapy versus those immunized at day 4.[27] However, a recent pilot study of 18 patients with solid tumours immunized either one week before or on the first

day of chemotherapy reported that all patients did mount an immune response to the vaccine, and there were no significant differences in seroconversion or seroprotection rates against the three influenza strains between the two groups of patients.[28] If early immunization is not possible, administration of the inactivated vaccine *between* chemotherapy cycles has been reported to be safe and is recommended over not receiving the vaccine at all, although the efficacy of the vaccine may be reduced in this situation.[4,6,21,29] In such situations, administration of the vaccine is preferable when therapy is at the lowest level possible.[18]

There is a growing body of published data on safety of the influenza vaccine (live or inactivated) in patients with cancer treated with immune checkpoint inhibitor therapies including CTLA-4 inhibitors (e.g., ipilimumab) or PD-1 and PD-L1 inhibitors (e.g., nivolumab, pembrolizumab).[30-36] Many of the clinical trial protocols evaluating ipilimumab did not routinely allow for influenza immunization. Therefore, until more evidence is available, it is the consensus of the Alberta Provincial Tumour Teams that patients currently receiving ipilimumab alone or in combination with other anti-cancer agents, as well as those who have discontinued ipilimumab in the past six months should not receive the influenza vaccine. A recent study of 23 lung cancer patients treated with a PD-1 or PD-L1 inhibitor who received the seasonal influenza vaccine reported an adequate humoral immune response to the vaccine and a high rate of seroconversion rate compared to healthy controls. However, the frequencies of severe immune-related adverse events in the long-term clinical course following vaccination were significantly higher than those reported in the safety data of PD-1 immune checkpoint inhibitor trials.[37-39] It is the consensus of the Alberta Provincial Tumour Teams that patients receiving nivolumab or pembrolizumab alone or in combination with other anti-cancer agents may be immunized with the inactive influenza vaccine; the timing of the immunization is not clearly studied in this population, but can be considered one week post-administration of these agents. Patients should be advised to monitor themselves closely, and to report any adverse events to their oncologist.

Adult patients with hematologic malignancies undergoing hematopoietic stem cell transplantation (HSCT) are at a significant risk for infections prior to immune regeneration. Preparation for both autologous and allogeneic HSCT involves intensive high-dose regimens of chemotherapy and/or radiotherapy, which leave the patient acutely and profoundly immunocompromised for several months following transplantation. The impact of seasonal influenza on HSCT recipients can be devastating. Llungman *et al.* reported a case fatality rate of 23% among over 1900 patients in Europe over three influenza seasons.[16] Kumar and colleagues recently reported the results of a multicentre prospective observational study of pediatric and adult solid organ transplant (SOT) and HSCT patients carried out across 20 sites from the United States, Canada, and Spain. They documented 616 patients with confirmed influenza (477 SOT; 139 HSCT) over a 5-year study period; the annual incidence of pneumonia ranged between 11.3-35.0% and ICU admission rates ranged between 8.1-14.3%. The receipt of vaccine in the same influenza season was associated with a decrease in disease severity as determined by the presence of pneumonia, and antiviral treatment within 48 hours was associated with improved outcomes.[40] No significant differences were noted between SOT and HSCT patients

with regard to pneumonia and ICU care. However, HSCT patients had a higher 6-month mortality (13.8% vs 4.8%, p<0.001) and viral load at disease onset (median viral load 1.04 × 105 copies/mL vs 8.04 × 103 copies/mL, p=0.001) compared to SOT patients.

There is variability in the efficacy of influenza immunization in HSCT patients reported in the literature. One study documented serologic responses ranging from 0% in allogeneic transplant patients to 32% in autologous transplant patients. Another study reported immune responses of 29% to 34% in patients who underwent HSCT, and 46% to 62% in a group of healthy matched controls.[41,42] In a study of 82 allogeneic HSCT recipients who received the 2009-2010 H1N1 vaccine, Issa *et al.* reported that seroprotective antibody titers were detected in 51% of patients, and this rate was not affected by the presence of chronic graft-versus-host disease or type of conditioning regimen.[43] Patients were more likely to have higher seroprotective titers the further away they were from the transplant (OR=1.79 per year, 95% CI 1.12-2.85), and rituximab administration prior to immunization was associated with lower seroprotective titers (OR=0.11, 95% CI 0.01-0.97). Bedognetti *et al.* reported the results of a study comparing response to the seasonal influenza vaccine in 31 patients with non-Hodgkin lymphoma in complete remission after treatment with rituximab-containing regimens to 34 age-matched healthy subjects.[44] They reported that CD27+ memory B-cells were significantly reduced in patients treated with rituximab-based chemotherapies, and this reduction correlated with lower responses to influenza immunization. Similarly, in a study of 67 patients with lymphoma who were treated with rituximab alone or in combination with chemotherapy, Yri *et al.* reported that only five patients had a measurable but non-protective antibody titer after immunization, and the remaining 62 patients had no detectable titers at all, giving a seroprotection rate of 0%. This is in comparison to the 82% seroprotection rate for the healthy control patients. The investigators suggest that the non-responsiveness was due to the B-cell depletion caused by rituximab therapy.[45] Similarly, Berglund and colleagues reported the results of a subgroup analysis of rituximab-treated patients among 96 adult outpatients with cancer who were undergoing treatment. Of the 13 patients treated with rituximab, only one responded to immunization against influenza A (H1N1) and none responded to immunization against seasonal influenza.[15] Patients who are treated with rituximab or other B-cell depleting antibodies should therefore have all immunizations postponed until at least 6 months after the last dose of rituximab or other B-cell depleting therapies.[5,13-15,45]

Lower-respiratory tract infection (LRTI) is a complication of influenza infection that frequently leads to lung injury and death, and profound lymphopenia is one of the most significant risk factors for progression from upper- to lower-respiratory tract involvement.[46] Risk factors for progression of H1N1 influenza to LRTI in patients with hematologic malignancies are unknown at the present time.

It is recommended that both the recipient and donor (for allogeneic transplants) receive influenza immunization at least two weeks prior to the transplant.[16,18,47,48] While only 10-30% of HSCT recipients will have a detectable antibody response to the influenza vaccine at 6-24 months post-transplant, over 60% will have a detectable response at 24 months or more post-transplant.[49] Immune system recovery post-transplant is variable and requires individual assessment by the transplant

physician. For example, patients treated with rituximab post-transplant will have a delay in their B-cell recovery by at least six months following the final dose.[16,44] In addition, adult transplant patients with chronic graft-versus-host disease may require up to 24 months or more post-transplant to recover CD4+ counts. It is recommended that HSCT patients receive annual seasonal influenza immunization beginning *at least* four months post-transplant.[16,18,47,48]

In an effort to reduce the risk of disease transmission, immunization of family members and hospital staff in contact with patients who are at high risk for severe or complicated seasonal influenza is strongly recommended. Influenza immunization rates of health care workers is associated with a reduction in influenza infections in cancer patients.[50] The Public Health Agency of Canada (PHAC) states that people who are potentially capable of spreading influenza to those who are at high risk should be immunized, regardless of whether the high-risk person has been immunized.[18] Immunization of family members and hospital staff who are in contact with HSCT recipients is also of particular importance, as these patients are severely immunocompromised and cannot be immunized themselves for at least four months post-transplant. In this situation, family members and health care providers should receive the inactivated influenza vaccine beginning the season before the transplant and annually for 24 months or more post-transplant.[47,48] If the family member or healthcare worker will only accept the live nasal spray influenza vaccine, they should wait two weeks following immunization before continuing to provide care to severely immunocompromised individuals.[3,17]

Influenza Immunization: Pediatric Patients with Cancer

Pediatric patients with cancer are highly susceptible to influenza infections and have an increased rate of influenza infection compared to healthy children.[51] In addition, hospitalization rates due to influenza infection for children under the age of five years with chronic health conditions have been reported to be significantly higher than for healthy children in the same age group.[52] Annual administration of the inactivated influenza vaccine is indicated for all pediatric patients with cancer over the age of six months. Immunization with currently available influenza vaccines is **not** recommended for infants younger than six months of age.

Given the burden of influenza B in children, and the potential for lineage mismatch between the predominant circulating strain of influenza B and the strain in a trivalent vaccine, NACI continues to recommend that a quadrivalent influenza vaccine be used.[3,11] Current recommendations regarding influenza vaccine doses in healthy children state that those nine years of age and older should receive one dose of the vaccine annually. Children younger than nine years of age who have not previously received the trivalent or quadrivalent influenza vaccine require two doses of the vaccine **in the first year** they are immunized, with the second dose being administered four weeks or more after the first dose. The live vaccine is contraindicated in children with immune compromising conditions.[3]

Similar to the literature regarding adult patients with cancer, interpreting the limited published results of influenza vaccine efficacy in pediatric patients with cancer is difficult, as patient characteristics, cancer types, vaccine strains, and assessment of responses vary between published studies. In a meta-analysis of nine controlled clinical trials and one randomized controlled trial involving 770

children, Goossen *et al.* reported that immune responses to the seasonal influenza vaccine in children receiving chemotherapy were consistently weaker than in those children who had completed their chemotherapy regimen and in healthy controls.[53] Several studies have reported that pediatric patients with cancer who have completed their chemotherapy regimens have increased rates of seroconversion, suggesting that the timing of influenza immunization with regards to the chemotherapy cycle is an important factor in this population.[51,54] Seroconversion rates are also influenced by the type of cancer (solid tumour vs. hematologic malignancy)[55] and the type of chemotherapy.[56] Similar to the recommendations made for adults with cancer, it is likely most beneficial to immunize pediatric patients with cancer two weeks prior to beginning chemotherapy, to allow for sufficient antibody production by the patient. Shahgholi *et al.* assessed the immune response of 32 pediatric patients with ALL and compared them to a control group of 30 healthy siblings. The trivalent influenza vaccine was well tolerated in the patients with ALL, and the immune responses were acceptable but limited. The percentage of ALL patients versus healthy controls with a fourfold increase in antibody titers were 56.2% versus 80% for H1N1 (p=0.04), 40.6% versus 53.3% for H3N2 (p=0.31), and 59.4% versus 83.3% for influenza B (p=0.038).[57]

The recommendations for pediatric patients undergoing HSCT are similar to those for adult patients, with appropriate adjustments made for vaccine doses.[14,16,20,47] It is recommended that both the recipient and donor (for allogeneic transplants) receive the inactivated influenza vaccine two weeks prior to the transplant. Immune system recovery following transplant is variable and depends on factors such as the types of therapies administered and the presence of graft-versus-host disease; therefore, individual assessment is required by the transplant physician. Influenza vaccine should ideally be administered six months post-HSCT in pediatric patients. Inactivated influenza vaccine can be given as early as four months post-transplant in outbreak situations, with the approval of the transplant physician; if given less than six months post-transplant, a second dose can be given four weeks later if there is ongoing circulation of influenza virus in the community.[20,47,58]

Similar to the recommendations made for adult patients with cancer, immunization of family members, caregivers, and hospital staff in contact with pediatric patients who are at high risk for severe or complicated influenza is **strongly recommended**.[18] Immunization of family members and hospital staff who are in contact with pediatric HSCT recipients is also of particular importance, as these patients are severely immunocompromised and cannot be immunized themselves for at least four months post-transplant. In this situation, family members and health care providers should receive the inactivated influenza vaccine beginning the season before the transplant and annually for 24 months or more post-transplant.[20,47] If the family member or healthcare worker will only accept the live nasal spray influenza vaccine, they should wait two weeks following immunization before continuing to provide care to severely immunocompromised individuals.[3,14]

References

1. Statistics Canada. Table 13-10-0394-01 Leading causes of death, total population, by age group. Accessed September 2, 2020: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310039401
2. Young K, Gemmill I, Harrison R. Summary of the NACI Seasonal Influenza Vaccine Statement for 2020-2021. *Can Commun Dis Rep*. May 7 2020;46(5):132-137.
3. National Avdisory Committee on Immunization. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2020-2021 (2020). Accessed September 2, 2020: https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/healthy-living/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2020-2021/naci-2020-2021-seasonal-influenza-stmt-eng.pdf.
4. Melcher L. Recommendations for influenza and pneumococcal vaccinations in people receiving chemotherapy. *Clinical oncology (Royal College of Radiologists (Great Britain))*. 2005;17(1):12-15.
5. Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2014;58(3):309-318.
6. National Comprehensive Cancer Network. Prevention and treatment of cancer-related infections. Version 2.2020. Accessed September 2, 2020: https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf
7. Pedrazzoli P, Piralla A, Valentino F, Cinieri S, Baldanti F. Update of the recommendations of the Italian Society of Medical Oncology on vaccination for seasonal influenza and pneumococcal infection in patients with cancer: Focus on prevention of pneumonia. *European Journal of Cancer Care*. 2018;27(2):e12817.
8. Grohskopf L, Alyanak E, Broder K, Blanton L, Fry A, Jernigan D, Atmar R. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices - United States, 2020-21 influenza season (MMWR Recomm Rep) 1-24 (2020).
9. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2020-2021 northern hemisphere influenza season. Accessed September 2, 2020: https://www.who.int/influenza/vaccines/virus/recommendations/202002_recommendation.pdf?ua=1
10. Alberta Health. Alberta Influenza Immunization Policy (2020). Accessed September 2, 2020: https://open.alberta.ca/dataset/dda65fc8-6d06-4650-840b-663702375e83/resource/3042f9a0-bb39-4770-8f99-681dc436c1e8/download/health-aip-influenza-immunization-policy-2020.pdf
11. Alberta Health Services. Immunization Program Standards Manual (2020). Accessed September 2, 2020: https://www.albertahealthservices.ca/info/page10802.aspx
12. Alberta Health Services. Standard on the Immunization of Individuals with Chronic Health Conditions and/or Immunosuppression. Standard#08.305 (2020). Accessed September 2, 2020: https://www.albertahealthservices.ca/assets/info/hp/cdc/if-hp-cdc-ipsm-chronic-conditions-immunosuppression.pdf
13. Alberta Health. Immunization for Adult Hematopoietic Stem Cell Transplant (HSCT) Recipients. 2020. Accessed September 2, 2020: https://open.alberta.ca/dataset/aip/resource/c74197ab-4f13-4052-9dce-73ab84c3314f/download/AIP-Adult-HSCT.pdf
14. Alberta Health. Principles of Immunization in Hematopoietic Stem Cell Transplant (HSCT) Recipients and Solid Organ Transplant (SOT) Recipients (2020). Accessed September 2, 2020: https://open.alberta.ca/dataset/aip/resource/c48b05ab-a495-4efd-b1fb-4a51343a4b92/download/AIP-Principles-Immunization-HSCT-SOT.pdf
15. Berglund A, Willen L, Grodeberg L, Skattum L, Hagberg H, Pauksens K. The response to vaccination against influenza A(H1N1) 2009, seasonal influenza and Streptococcus pneumoniae in adult outpatients with ongoing treatment for cancer with and without rituximab. *Acta Oncologica (Stockholm, Sweden)*. 2014;53(9):1212-1220.
16. Ljungman P, Cordonnier C, Einsele H, et al. Vaccination of hematopoietic cell transplant recipients. *Bone marrow transplantation*. 2009;44(8):521-526.
17. Alberta Health Services. *Standard for Influenza Immunization. Standard#15.100*. 2020. Accessed September 3, 2020: https://www.albertahealthservices.ca/assets/info/hp/cdc/if-hp-cdc-standard-influenza-immunization-15-100.pdf

18. Public Health Agency of Canada. Canadian Immunization Guide (2020). Accessed September 3, 2020: https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html
19. Alberta Health Services. *Section 5.0: Standard on the Contraindications and Precautions Related to Immunization*. Vol. Standard #05.100. 2016. Accessed September 12: https://www.albertahealthservices.ca/assets/info/hp/cdc/if-hp-cdc-ipsm-standard-contraindications-precautions.pdf
20. Alberta Health. Immunization for Child Hematopoietic Stem Cell (HSCT) Recipients (2020). Accessed September 2, 2020: https://open.alberta.ca/dataset/aip/resource/0c6e889c-5fff-464a-906e-87eb9e7d2d11/download/AIP-Child-HSCT.pdf
21. Earle CC. Influenza vaccination in elderly patients with advanced colorectal cancer. *Journal of Clinical Oncology*. 2003;21(6):1161-1166.
22. Eliakim-Raz N, Vinograd I, Zalmanovici Trestioreanu A, Leibovici L, Paul M. Influenza vaccines in immunosuppressed adults with cancer. *The Cochrane database of systematic reviews*. 2013;10:CD008983.
23. Kunisaki KM, Janoff EN. Influenza in immunosuppressed populations: a review of infection frequency, morbidity, mortality, and vaccine responses. *The Lancet infectious diseases*. 2009;9(8):493-504.
24. Kumar A, Zarychanski R, Pinto R, et al. Critically ill patients with 2009 influenza A(H1N1) infection in Canada. *Jama*. 2009;302(17):1872-1879.
25. Arrowood JR, Hayney MS, Mena R, Longtin J. Immunization recommendations for adults with cancer. *Annals of Pharmacotherapy*. 2002;36(7-8):1219-1229.
26. Robertson JD, Nagesh K, Jowitt SN, et al. Immunogenicity of vaccination against influenza, Streptococcus pneumoniae and Haemophilus influenzae type B in patients with multiple myeloma. *British journal of cancer*. 2000;82(7):1261-1265.
27. Meerveld-Eggink A, de Weerdt O, van der Velden AM, et al. Response to influenza virus vaccination during chemotherapy in patients with breast cancer. *Annals of Oncology: Official Journal of the European Society for Medical Oncology / ESMO*. 2011;22(9):2031-2035.
28. Waqar SN, Boehmer L, Morgensztern D, et al. Immunogenicity of Influenza Vaccination in Patients With Cancer. *American Journal of Clinical Oncology*. 2018;41(3):248-253.
29. Sommer AL, Wachel BK, Smith JA. Evaluation of vaccine dosing in patients with solid tumors receiving myelosuppressive chemotherapy. *Journal of Oncology Pharmacy Practice*. 2006;12(3):143-154.
30. Chong CR, Park VJ, Cohen B, Postow MA, Wolchok JD, Kamboj M. Safety of Inactivated Influenza Vaccine in Cancer Patients Receiving Immune Checkpoint Inhibitors (ICI). *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*. 2020;70(2):193-199.
31. Gwynn ME, DeRemer DL, Saunders KM, Parikh J, Bollag RJ, Clemmons AB. Immune-mediated adverse events following influenza vaccine in cancer patients receiving immune checkpoint inhibitors. *Journal of Oncology Pharmacy Practice: Official Publication of the International Society of Oncology Pharmacy Practitioners*. 2020;26(3):647-654.
32. Awadalla M, Golden DLA, Mahmood SS, et al. Influenza vaccination and myocarditis among patients receiving immune checkpoint inhibitors. *Journal for Immunotherapy of Cancer*. 2019;7(1):53.
33. Bersanelli M, Giannarelli D, Castrignanò P, et al. INfluenza Vaccine Indication During therapy with Immune checkpoint inhibitors: a transversal challenge. The INVIDIa study. *Immunotherapy*. 2018;10(14):1229-1239.
34. Strowd RE, Russell G, Hsu F-C, et al. Immunogenicity of high-dose influenza vaccination in patients with primary central nervous system malignancy. *Neuro-Oncology Practice*. 2018;5(3):176-183.
35. Wijn DH, Groeneveld GH, Vollaard AM, et al. Influenza vaccination in patients with lung cancer receiving anti-programmed death receptor 1 immunotherapy does not induce immune-related adverse events. *European Journal of Cancer (Oxford, England: 1990)*. 2018;104:182-187.
36. Branagan ARMD, Duffy E, Albrecht RAP, et al. Clinical and serologic responses following a two dose series of high-dose influenza vaccine in plasma cell disorders: a prospective, single-arm trial. *Clinical Lymphoma, Myeloma & Leukemia*. 2017;17(5):296-304.e2.
37. Läubli H, Balmelli C, Kaufmann L, et al. Influenza vaccination of cancer patients during PD-1 blockade induces serological protection but may raise the risk for immune-related adverse events. *Journal for Immunotherapy of Cancer*. 2018;6(1):40.

38. Hofmann L, Forschner A, Loquai C, et al. Cutaneous, gastrointestinal, hepatic, endocrine, and renal side-effects of anti-PD-1 therapy. *European Journal of Cancer (Oxford, England: 1990)*. 2016;60:190-209.
39. Postow MA, Sidlow R, Hellmann MD. Immune-Related Adverse Events Associated with Immune Checkpoint Blockade. *The New England Journal of Medicine*. 2018;378(2):158-168.
40. Kumar D, Ferreira VH, Blumberg E, et al. A Five-year Prospective Multi-center Evaluation of Influenza Infection in Transplant Recipients. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*. 2018;67(9):1322-1329.
41. Gandhi MK, Egner W, Sizer L, et al. Antibody responses to vaccinations given within the first two years after transplant are similar between autologous peripheral blood stem cell and bone marrow transplant recipients. *Bone marrow transplantation*. 2001;28(8):775-781.
42. Pauksen K, Linde A, Hammarstrom V, et al. Granulocyte-macrophage colony-stimulating factor as immunomodulating factor together with influenza vaccination in stem cell transplant patients. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America*. 2000;30(2):342-348.
43. Issa NC, Marty FM, Gagne LS, et al. Seroprotective titers against 2009 H1N1 influenza A virus after vaccination in allogeneic hematopoietic stem cell transplantation recipients. *Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation*. 2011;17(3):434-438.
44. Bedognetti D, Zoppoli G, Massucco C, et al. Impaired response to influenza vaccine associated with persistent memory B cell depletion in non-Hodgkin's lymphoma patients treated with rituximab-containing regimens. *Journal of immunology (Baltimore, Md: 1950)*. 2011;186(10):6044-6055.
45. Yri OE, Torfoss D, Hungnes O, et al. Rituximab blocks protective serologic response to influenza A (H1N1) 2009 vaccination in lymphoma patients during or within 6 months after treatment. *Blood*. 2011;118(26):6769-6771.
46. Casper C, Englund J, Boeckh M. How I treat influenza in patients with hematologic malignancies. *Blood*. 2010;115(7):1331-1342.
47. Centers for Disease Control, Prevention, Infectious Disease Society of America, American Society of Blood and Marrow Transplantation. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. *MMWRRecommendations and reports : Morbidity and mortality weekly reportRecommendations and reports/ Centers for Disease Control*. 2000;49(RR-10):1-7.
48. Alberta Health Services. Clinical Practice Guideline: Lymphoma. Version 12. Accessed September 3, 2020: https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-lyhe002-lymphoma.pdf
49. Engelhard D, Nagler A, Hardan I, et al. Antibody response to a two-dose regimen of influenza vaccine in allogeneic T cell-depleted and autologous BMT recipients. *Bone marrow transplantation*. 1993;11(1):1-5.
50. Frenzel E, Chemaly RF, Ariza-Heredia E, et al. Association of increased influenza vaccination in health care workers with a reduction in nosocomial influenza infections in cancer patients. *American Journal of Infection Control*. 2016;44(9):1016-1021.
51. Chisholm J, Howe K, Taj M, Zambon M. Influenza immunisation in children with solid tumours. *European journal of cancer (Oxford, England : 1990)*. 2005;41(15):2280-2287.
52. Whitley RJ, Monto AS. Prevention and treatment of influenza in high-risk groups: children, pregnant women, immunocompromised hosts, and nursing home residents. *Journal of Infectious Diseases*. 2006;194(Suppl 2):133.
53. Goossen GM, Kremer LCM, van de Wetering MD. Influenza vaccination in children being treated with chemotherapy for cancer. *The Cochrane Database of Systematic Reviews*. 2013;(8):CD006484.
54. Matsuzaki A, Suminoe A, Koga Y, Kinukawa N, Kusuhara K, Hara T. Immune response after influenza vaccination in children with cancer. *Pediatric Blood & Cancer*. 2005;45(6):831-837.
55. Bate J, Yung CF, Hoschler K, et al. Immunogenicity of pandemic (H1N1) 2009 vaccine in children with cancer in the United Kingdom. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America*. 2010;51(12):95.
56. Reilly A, Kersun LS, McDonald K, Weinberg A, Jawad AF, Sullivan KE. The efficacy of influenza vaccination in a pediatric oncology population. *Journal of pediatric hematology/oncology*. 2010;32(5):177.

57. Shahgholi E, Ehsani MA, Salamati P, Maysamie A, Sotoudeh K, Mokhtariazad T. Immunogenicity of trivalent influenza vaccine in children with acute lymphoblastic leukemia during maintenance therapy. *Pediatric blood & cancer*. 2010;54(5):716-720.
58. Ljungman P, Nahi H, Linde A. Vaccination of patients with haematological malignancies with one or two doses of influenza vaccine: a randomised study. *British journal of haematology*. 2005;130(1):96-98.

Appendix A: Additional Resources

Canadian Resources

Alberta Health Services. Immunization Program Standards Manual:
https://www.albertahealthservices.ca/info/page10802.aspx

Alberta Health Services, Influenza Immunization:
www.albertahealthservices.ca/influenza/influenza.aspx

Alberta Health Services. Influenza Information for Health Professionals:
www.albertahealthservices.ca/influenza/Page12438.aspx

Alberta Health. Influenza Immunization During Covid-19. Guidance for the 2020-21 Season:
https://open.alberta.ca/dataset/ad9f877f-3c71-4ee1-9635-f160e1d5b26f/resource/c0c8550b-52e0-488c-be20-98b8b82ccbfe/download/health-influenza-immunization-during-covid-19.pdf

Alberta Bone Marrow and Blood Cell Transplant Program. Standard Practice Manual:
www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-bmt-manual.pdf

Public Health Agency of Canada. National Advisory Committee on Immunization (NACI) Advisory Committee. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2020-2021:
https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/healthy-living/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2020-2021/naci-2020-2021-seasonal-influenza-stmt-eng.pdf

Public Health Agency of Canada. Canadian Immunization Guide:
www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php

International Resources

World Health Organization. Global Influenza Programme:
www.who.int/influenza/en/

Centers for Disease Control and Prevention. Advisory Committee on Immunization Practices (ACIP): Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2020–21 Influenza Season.
https://www.cdc.gov/mmwr/volumes/69/rr/rr6908a1.htm?s_cid=rr6908a1_w

Centers for Disease Control and Prevention. Cancer, the Flu, and You. What Cancer Patients, Survivors, and Caregivers Should Know About the Flu:
www.cdc.gov/cancer/flu/

National Comprehensive Cancer Network. Prevention and Treatment of Cancer-Related Infections, version 2.2020 (requires free registration and login):
https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf

American Academy of Pediatrics (AAP). Policy Statement: Recommendations for the Prevention and Control of Influenza in Children, 2019-2020 (no changes in AAP influenza vaccines for the 2020-2021 flu season):
https://pediatrics.aappublications.org/content/early/2019/08/29/peds.2019-2478#T1

Appendix B: Search Strategy

Database	Date	Search Strategy	Results
Medline	Aug 5. 2020	1. exp Neoplasms/	3347460
		2. exp Carcinoma/	643670
		3. “cancer”.ab.	1434014
		4. “cancer”.ti.	980631
		5. “tumor”.ab.	1069164
		6. “tumor”.ti.	269966
		7. “tumour”.ab.	193066
		8. “tumour”.ti.	47469
		9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	4102770
		10. exp Influenza A virus/	43712
		11. “influenza A virus”.ab.	8915
		12. “influenza A virus”.ti.	4994
		13. exp Influenza B virus/	4186
		14. “influenza B virus/”.ab.	1206
		15. “influenza B virus/”.ti.	521
		16. 10 or 11 or 12 or 13 or 14 or 15	47547
		17. exp Immunization	175364
		18. “immunization”.ab.	78391
		19. “immunization”.ti.	27396
		20. 17 or 18 or 19	225284
		21. 9 and 16 and 20	144
		22. limit 21 to (english language and yr=”2019-Current”)	5
		23. 16 or 20	267147
		24. 9 and 23	30361
		25. limit 24 to (english language and yr=”2019-Current”)	1601
		26. exp Influenza, Human/	49244
		27. 9 and 26	997
		28. influenza.ab.	75288
		29. influenza.ti.	70113
		30. 26 or 28 or 29	104266
		31. 9 and 20 and 30	564
		32. limit 31 to (english language and yr=”2019-Current”)	37
		33. exp Vaccination/	84871
		34. vaccination.ab.	106362
		35. vaccination.ti.	50621
		36. 20 or 33 or 34 or 35	287549
		37. 9 and 30 and 36	940
		38. limit 37 to (english language and yr=”2019-Current”)	84
		39. from 38 keep 1, 4, 7, 10-11, 19, 27-29…	21

Development and Revision History

This guideline was reviewed and endorsed by the Alberta Provincial Tumour Teams. Members include surgical oncologists, radiation oncologists, medical oncologists, dermatologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Tumour Teams, external participants identified by the Working Group Lead, and a methodologist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed and posted to the website in November 2009. The guideline was revised and reposted in September 2010, October 2011, October 2012, September 2013, September 2014, October 2015, October 2016, October 2017, October 2018, October 2019, and October 2020.

Maintenance

An annual review will next be conducted in September 2021. If critical new evidence is brought forward before that time, however, the guideline will be revised and updated accordingly.

Abbreviations

ACIP	Advisory Committee on Immunization Practices
ALL	acute lymphoblastic leukemia
CI	confidence interval
HR	hazard ratio
HSCT	hematopoietic stem cell transplant
LRTI	lower respiratory tract infection
NACI	National Advisory Committee on Immunization
OR	odds ratio
PHAC	Public Health Agency of Canada
QIV	quadrivalent inactivated influenza vaccine
SEER	Surveillance, Epidemiology, and End Results database
SOT	solid organ transplant
TIV	trivalent inactivated influenza vaccine

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Tumour Teams and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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