

Government of Manitoba

Influenza High Dose Vaccine Evaluation

2017/18 Influenza Season

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Background

Manitoba's (MB's) Seasonal Influenza Immunization Program (herein referred to as the Program) offers influenza vaccine at no charge to all Manitobans every year and encourages all those at higher risk of influenza and its complications to be immunized each year, including all seniors 65 years of age and older as well as those living in long term care facilities (LTCFs).

Although the circulating influenza strains vary each influenza season, the Influenza A(H3N2) strain causes severe illness and complications in seniors and young populations. Seniors are at significant risk of illness and complications associated with influenza. For the 2017/18 influenza season, Manitoba Health, Seniors and Active Living (MHSAL) introduced a new high-dose influenza vaccine (Fluzone® High-Dose) to the Program. Given the burden of Influenza A (H3N2) disease and the evidence of better efficacy of the high dose influenza vaccine (HD) for those 65 years of age and older, it is expected that HD vaccine should provide superior protection when compared with the standard dose vaccine (The National Advisory Committee on Immunization's Statement on Seasonal Influenza Vaccine, 2017-2018).

HD vaccine was offered to those 65 years of age and older who were residents of Long Term Care Facilities (LTCF). Each year, LTCFs are subject to influenza outbreaks in their residents that result in severe illness and complications. This population typically has the highest uptake rate of Influenza vaccine among Manitobans, but still experiences a disproportionate burden of Influenza illness. The following is an evaluation of the implementation of the HD Influenza vaccine in the 2017 – 2018 Influenza season. The document describes the program and its implementation, provides preliminary data analysis and results, as well as a high-level conclusion.

Program Description

Eligibility

For the 2017/18 influenza season, Fluzone® High-Dose vaccine (herein referred to as HD vaccine) was offered to residents of LTCFs who were 65 years and older.

For the purposes of HD vaccine eligibility in the 2017/18 season, LTCFs were defined as residential facilities for predominantly older persons with chronic illness or disability, also known as personal care homes or nursing homes.

Respite care clients at least 65 years of age admitted to LTCF on a temporary basis where care is provided on weekends or extended periods (e.g. vacation) were also eligible to receive HD vaccine while in the LTCF.

Clients in transitional beds, even though being assessed for LTCF eligibility, were NOT eligible for the publicly-funded HD vaccine. MHSAL recommended that standard dose seasonal influenza vaccine be offered to these clients.

Clients living in the following community-based housing “alternatives” were also not eligible for the publicly-funded HD vaccine. MHSAL recommended that standard dose seasonal influenza vaccine be offered to these clients. Not eligible were people living in:

- Supportive Housing which is a tenant/landlord situation with subsidized supports (non-medical/care) operated in conjunction with the RHAs (either directly or via service purchase agreement with private operators);
- Department of Families housing with support options (such as group homes); and,
- Privately operated assisted living sites.

Program Implementation

Once the Active Living, Population and Public Health Branch (ALPPHB) received approval to add HD vaccine into the Program, 9,000 doses were ordered from the manufacturer.

The Continuing Care Branch provided the ALPPHB with an estimate of the number of people in LTCFs in MB.

ALPPHB sent a communication outlining eligibility and availability of HD vaccine to the Continuing Care Council, which is comprised of regional representatives that oversee the LTCFs within their health regions. The communication was also sent to regional Medical Officers of Health, Public Health Managers and Immunization Coordinators to ensure regional coverage of the new HD vaccine in the Program. The communication included an order form specific for LTCFs as well as electronic informational resources (e.g. factsheets and a questions/answers document for HCPs) on the HD vaccine for health care providers, the staff, residents, family and supports.

Once the orders were placed by LTCFs, the ALPPHB reviewed them to ensure that the volume matched the number of beds to minimize potential vaccine wastage. Discussions between the LTCF staff and the ALPPHB’s Inventory Specialist occurred when there were discrepancies.

As it is unknown when influenza will begin circulating each year, MHSAL encourages all LTCFs to begin immunizing their residents and staff as soon as possible once the vaccine becomes available. It can take up to two weeks for the body to develop immunity against influenza once immunized. Therefore, getting immunized before influenza starts circulating is important, especially for vulnerable populations and those taking care of them.

Manitoba’s influenza vaccine shipments typically begin to arrive in mid-to-late September depending on the approvals from Health Canada and product availability. Once the Provincial Distribution Warehouse receives the vaccines, the orders are processed based on the publicly available distribution schedule.

LTCFs are priority locations for distribution of influenza vaccine. In 2017/18, HD vaccine arrived slightly later than the standard dose seasonal influenza vaccines, which delayed HD vaccine shipments to LTCFs compared to previous influenza seasons. When the product did arrive at the Provincial Distribution Warehouse, the orders were processed and shipped based on when orders were placed.

Based on higher than expected demand from HCPs and the identification of LTCFs that were not part of the Provincial Bed Map, there was insufficient product available. As a result, an additional 455 doses of HD vaccine was ordered for a total of 9,455 doses.

Once all product was shipped to HCPs, it was determined that any locations that required additional supply would need to review the supplies available throughout their health region. This allowed many doses to be used that may not have been used.

Implementation challenges identified:

- Not all LTCFs (based on the definition previously mentioned) are licensed or part of the Provincial Bed Map. The number of respite residents who reside in MB LTCFs is unknown, and the turnover that occurs in a LTCF as a result of death or transfers was not considered. This resulted in an undercount of the population within LTCFs and the number of vaccine doses required.
- Not all LTCFs order vaccines on their own. Many facilities have hospitals, pharmacies or public health offices ordering on their behalf. This added an extra challenge in the tracking and distribution of the HD vaccine.
- Since product was moved between facilities to enhance use of the limited supply, MHSAL did not have access to the final volumes distributed to each LTCF in order to match with usage.

Program Evaluation

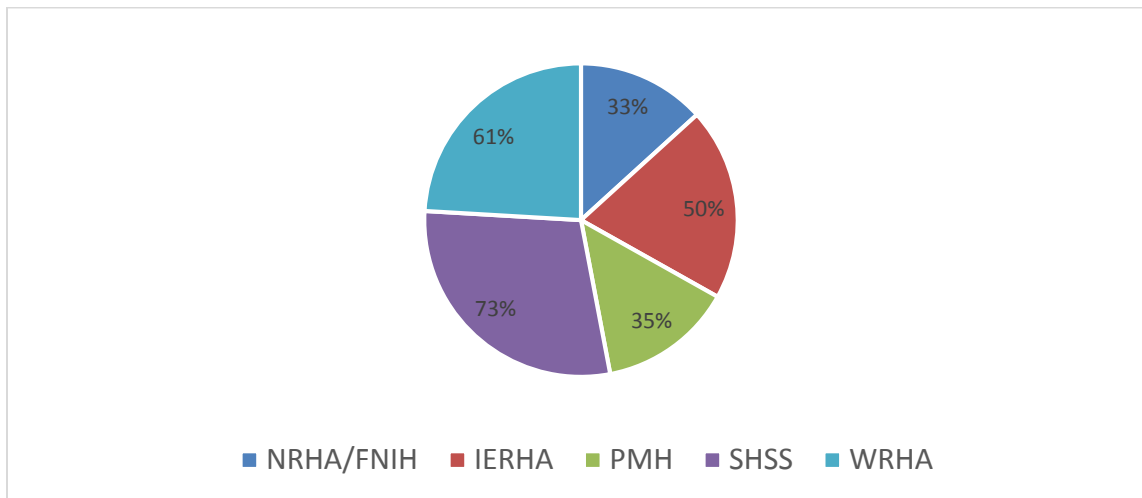
Long Term Care Facility Survey

One component of this program evaluation was a survey to gain feedback from the LTCFs in MB on the HD vaccine implementation, the perceived acceptability of HD vaccine from the residents and staff, and any specific suggestions to improve HD vaccine uptake for subsequent influenza seasons.

The survey was developed by staff of the ALPPHB, administered through Survey Monkey, and was communicated to LTCFs via two separate channels: the Continuing Care Council and regional Public Health Managers, to reach as many LTCFs in MB as possible. The results are available on request.

A total of 66 surveys were completed on Survey Monkey. Based on the Provincial Bed Map from the Continuing Care Branch, as of March 31, 2017 there were 125 LTCFs in MB, yielding a response rate of 52.8% and all regional health authorities (RHAs) were represented. Figure 1 below identifies the percentage of LTCFs within each RHA that responded to the survey.

Figure 1: Overall LTCF Response Rate within RHAs



From the responses and feedback provided in the survey, the addition of HD vaccine was well received by staff and residents in LTCFs in MB for the 2017/18 influenza season. The majority of residents accepted the vaccine. Materials developed by MHSAL were useful for the staff as well as the residents and their families. Uptake of HD vaccine appeared to be consistent with previous years' uptake of standard dose seasonal influenza vaccine in LTCFs and concerns with the potential of additional adverse events were reportedly minimized through education. The majority of LTCFs indicated that HD vaccine program for LTCFs should continue in order to protect this vulnerable population.

Additional feedback provided through the survey will assist MHSAL to improve its HD vaccine program in LTCFs for future influenza seasons. Based on survey respondent feedback, the following will be considered for upcoming influenza seasons:

- Earlier communication of the program plan: The roll out of the HD vaccine was late in the planning process for the 2017/18 influenza season as the decision to add the product to the Program was finalized in August. ALPPHB routinely communicates details of the Program throughout spring and summer of each year. Going forward, ALPPHB will include HD vaccine in the annual influenza immunization program plan and it will be communicated as early as possible.
- Development of a brochure comparing the available influenza vaccine products: MHSAL is updating its Seasonal Influenza Vaccine for Residents of Long-Term Care Facilities Public Health Factsheet to include information that would have been included in the brochure (e.g. comparing the high-dose to standard-dose inactivated seasonal influenza vaccine). A brochure will be considered in the future.
- Communication with long-term care facilities: MHSAL will target its communications to LTCFs using mechanisms such as the Continuing Care Council.
- Health Care Provider-specific factsheet: Influenza vaccine uptake among HCPs is reportedly low relative to national targets. Based on some of the responses to the survey, it appears that some HCPs continue to be misinformed about the use of

influenza vaccine. MHSAL will consider developing a factsheet directed to HCPs on the importance of being immunized against influenza; how influenza vaccines work at protecting providers and those around them; and, addressing some of the “myths” reflected in the survey responses.

- **HCPs ordering HD vaccine:** The process by which LTCFs order Fluzone® High-Dose vaccine will be reviewed and may be modified based on the feedback provided in order to increase accuracy, reduce wastage, and improve efficiency in this process. ALPPHB will consider adding “hybrid” locations, such as transitional/interim care beds, to Fluzone® High-Dose vaccine eligibility.

Preliminary Data Analysis

This evaluation is based on data available to MHSAL at the end of May, 2018. This evaluation is preliminary and further information such as hospitalization and intensive care unit (ICU) admission data for LTCF residents will be added as available.

Data Extracts

MHSAL extracted data from several databases and registries to complete the evaluation.

- Seasonal influenza cases were extracted from the Communicable Disease Control (CDC) surveillance system on May 31, 2018.
- PCH (also known as LTCF) residents were extracted from the provincial PCH registry on May 4, 2018.
- Respiratory outbreaks were extracted from the provincial Outbreak Tracking database on May 24, 2018.
- Influenza immunizations were extracted from the Manitoba Immunization Registry (Panorama) on May 31, 2018.
- Adverse events following immunization (AEFI) were extracted from the AEFI Module of Panorama and analyzed on June 14, 2018.

Definitions

- **Influenza season for 2014/15 to 2017/18;** the influenza season is defined as September 1 to March 31.
- **Aged 65+:** at least 65 years of age as of October 1 each season
- **Long-term care facility (LTCF):** licensed Personal Care Homes (PCH). Based on the file named “2017 Licensed PCH Bed Map” provided by Continuing Care Branch.
- **Long-term care facility (LTCF) residents:** Non-respite residents, who resided in a licensed PCH at anytime between September 1 and March 31 each season.
 - The total population used for the evaluation was 10,808 residents in 2017/18. This is comparable to the other seasons during the evaluation period.
- **Influenza outbreaks:** respiratory outbreaks within LTCFs that reported at least one lab-confirmed influenza case.

Influenza Strains

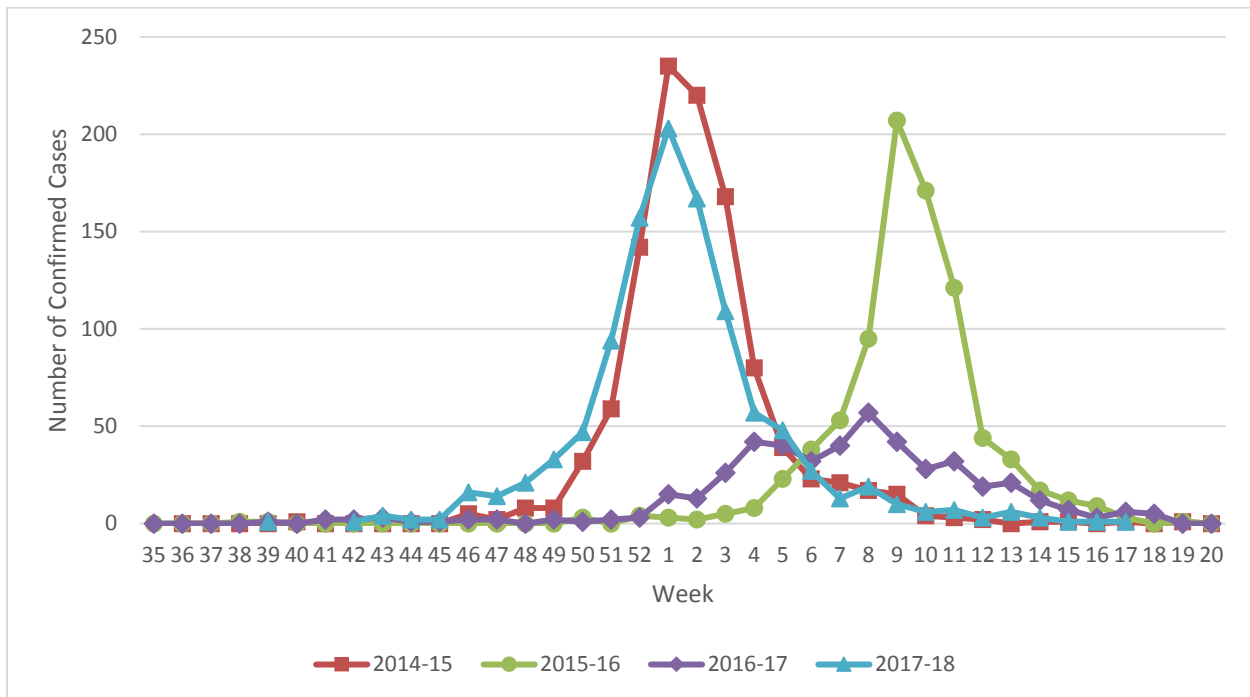
There are predominant influenza strains circulating during each influenza season. Until influenza arrives in MB and Canada, it is uncertain which strain will predominate. The following is a listing of the predominant influenza strain seen in the past four Influenza seasons:

Predominant type per season

- 2014/15: influenza A(H3N2)
- 2015/16: influenza A(H1N1)
- 2016/17: influenza A(H3N2)
- 2017/18: influenza A(H3N2)

For the purposes of evaluating HD vaccine in LTCFs for the 2017/18 influenza season, the primary comparator season used was the 2014/15 influenza season. In 2014/15, like 2017/18, the predominant Influenza A (H3N2) strain resulted in severe illness and complications throughout MB and in particular, the elderly population. The two influenza seasons also had similar timing (beginning and peak) compared to other seasons (see Figure 2).

Figure 2: Weekly Number of Laboratory-Confirmed Cases of Influenza by Season



Being that the predominant strain in the 2015/16 influenza season was Influenza A(H1N1) this season was not used as a comparator to the 2017/18 season.

Influenza A (H3N2) was the predominant strain during the 2016/17 influenza season, but its impact on the population in MB was much less than in the rest of the country. For this reason, the 2016/17 influenza season was not used as a primary comparator.

Each influenza season, Influenza B strains also circulate. This typically occurs after the peak of Influenza A activity starting late winter and into early spring. The number of Influenza B cases is typically smaller than the number of Influenza A cases. During the 2017/18 influenza season, Influenza B incidence was higher than in previous years. Because Influenza A, and in particular the H3N2 strain, has the greatest impact and burden on the elderly population, and served as rationale to introduce the HD vaccine program, this evaluation focuses on Influenza A when

reviewing strain particular data. In 2017/18, the predominant circulating B strain was a mismatch to the B strain included in the trivalent influenza vaccines, including the Fluzone® High-Dose vaccine.

Long Term Care Facilities and the Residents

As of March 31, 2017, there were 125 licensed LTCFs in Manitoba with a total of 9,697 beds (based on the Provincial Bed Map). The LTCFs are located throughout MB within all five RHAs.

The number of PCH residents who resided in a LTCF at anytime during each influenza season (September to March) varied. The length of stay varied between a few weeks, or less, to the whole season. Approximately 600 respite admissions in all four seasons were excluded from this evaluation (though they may have received HD vaccine).

Table 1. Total Residents in LTCFs aged 65+, 2014/15-2017/18

Influenza season	Number of Total Residents	Number of Residents 65+
2014/2015	11,447	10,923
2015/2016	11,210	10,692
2016/2017	11,394	10,873
2017/2018	11,319	10,808

Assumptions and Limitations of the Evaluation

Assumptions

- MB has a Seasonal Influenza Protocol (<http://www.gov.mb.ca/health/publichealth/cdc/protocol/influenza1.pdf>) that outlines the definitions of an outbreak in LTCFs and provides direction on reporting and testing. This evaluation assumes that all LTCFs follow this protocol throughout the influenza season.
- This evaluation assumes that there were no changes in testing procedures within LTCFs or at the provincial laboratory during the evaluation period.

Limitations

- LTCFs do not have access to the Manitoba Immunization Registry (herein referred to as the Registry) and therefore are unable to record the immunizations that they give to their residents. In order for doses to be recorded in the Registry, the LTCF must record the information on a form and send it to their local public health office (PHO). The PHO then records the administration of the vaccine in the Registry through data entry clerks. This process may result in:
 - LTCFs not recording or reporting their doses to be entered to the PHO, resulting in missing data;

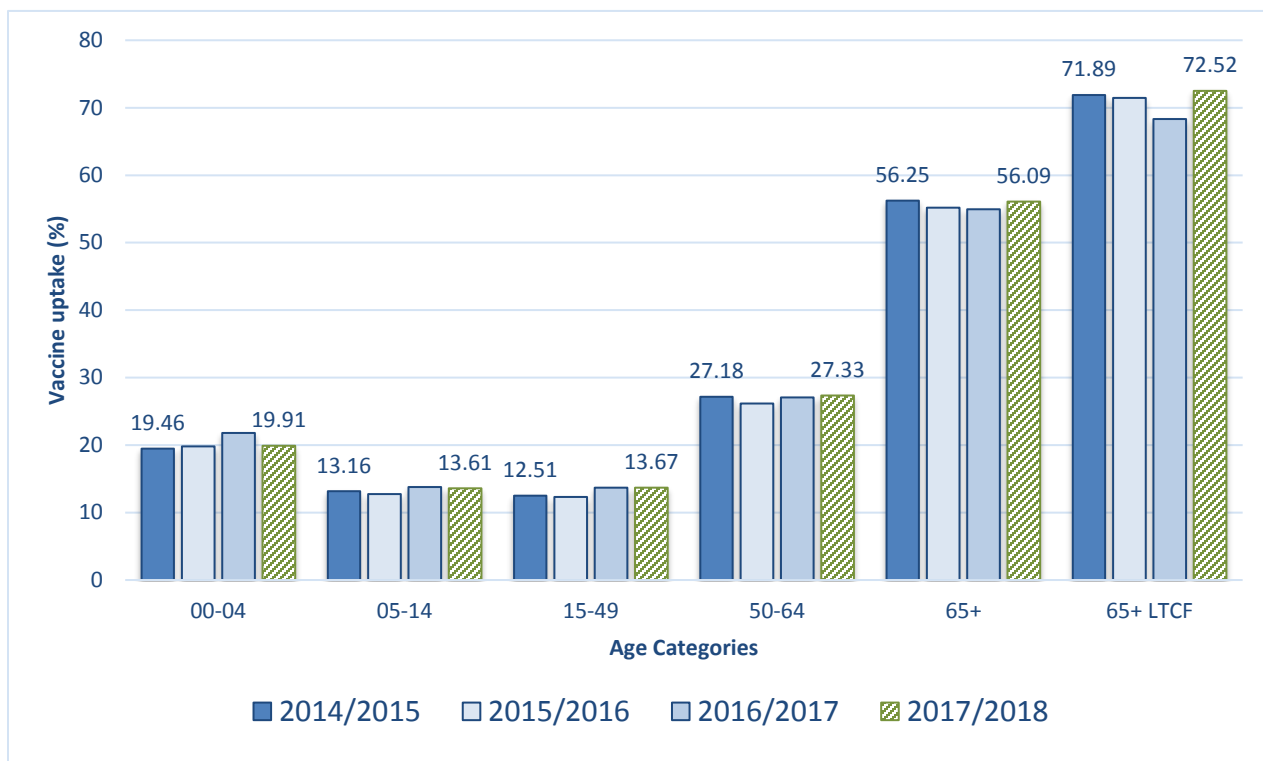
- Data entry clerks are not always familiar with the immunization products or program changes, which results in incorrect data entry of the administered immunizations in the Registry. NOTE: MHSAL worked closely with RHA staff to have the doses administered in LTCFs accurately entered in the Registry.
 - It is expected that not all doses administered were recorded into the Registry (historically there is a 10% undercount in the Registry) and that not all incorrect entries were corrected when the data was pulled.
- As Fluzone[®] High-Dose is approved for use in Canada for those 65 years of age and older, the evaluation focused on that age cohort.
 - Through the review of the data, ALPPHB noted that the Registry showed 99 LTCF residents *under* the age of 65 who received HD vaccine. It is unknown whether vaccines were incorrectly administered, or whether there were data reporting/recording errors. There are no safety concerns if the HD vaccine is given to adults under 65 years of age.
- Although respite residents were included in the eligibility criteria for HD vaccine, they were excluded from this program evaluation for data quality purposes and the transient nature of that population.
- There were inconsistencies in outbreak notification and completion of investigation reports by LTCFs. This may have resulted in incomplete or missing outbreak data.
- As of May 31, 2018 additional data sources were not available to MHSAL, preventing their inclusion in the program evaluation.

Results

Influenza Immunization Coverage in Manitoba

Flu vaccine uptake in MB has been consistent over the past several influenza seasons. Figure 3 (below) identifies the influenza vaccine uptake in MB among age categories covering the entire life span, including uptake in LTCFs.

Figure 3: Manitoba's Influenza Vaccine Uptake by Age Category

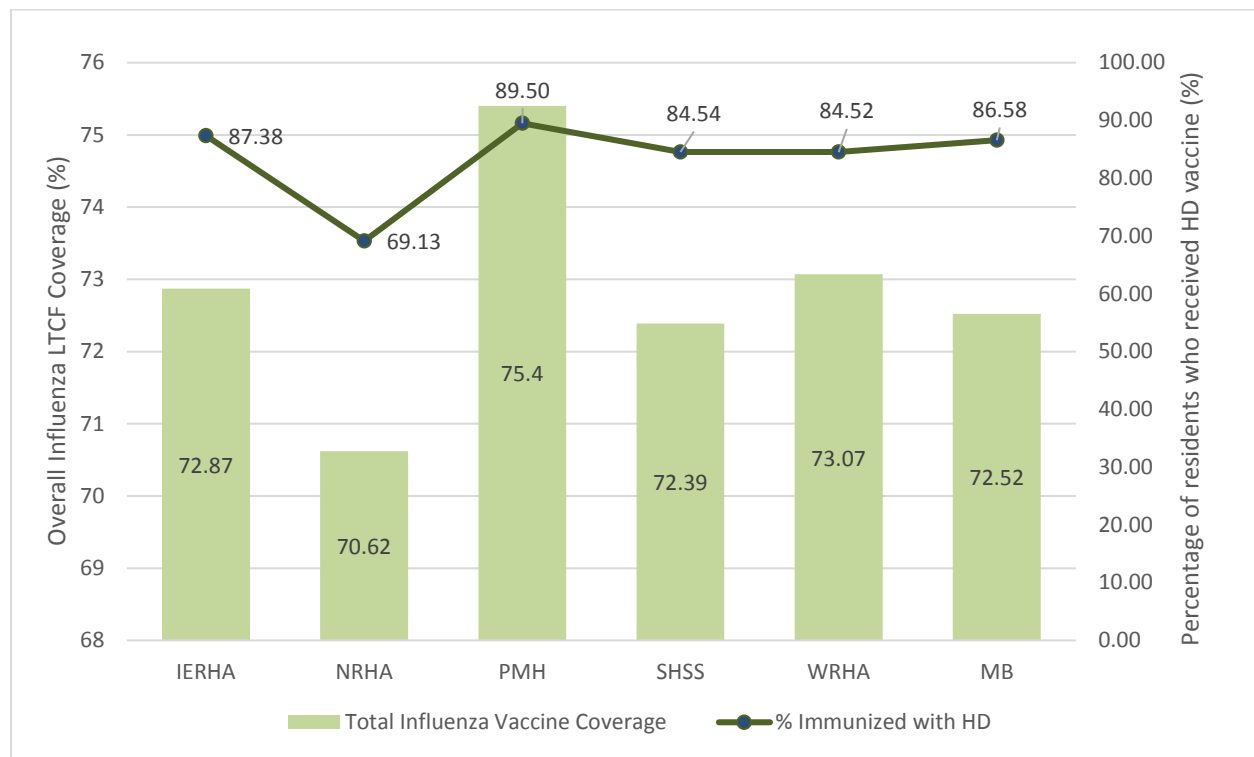


Influenza vaccine uptake in LTCFs among seniors aged 65 and older is the highest of all age categories; this is consistent over the past four influenza seasons.

The population living in LTCFs has access to continuous care from health care professionals who discuss the importance of influenza vaccination with the residents and/or their families, and provide them with resources to assist in making informed decisions.

When looking more specifically at influenza vaccine coverage within LTCFs and acceptance of the use of the HD vaccine, Figure 4 (below) identifies that of the immunized LTCF residents 65 years of age and older (n=7,838), 86.58% (n=6,786) were immunized with HD vaccine. The use of HD vaccine in LTCFs was high in all RHAs.

Figure 4: Percentage of HD Vaccine Administered in LTCFs in 2017/18



The influenza vaccine uptake in LTCFs is very likely higher than reported. As identified in the limitations section (above), not all LTCFs report the immunizations administered (although reporting is a MHSAL public health policy), and of those that are reported, there are likely data entry errors in the Registry due to reporting and data entry processes.

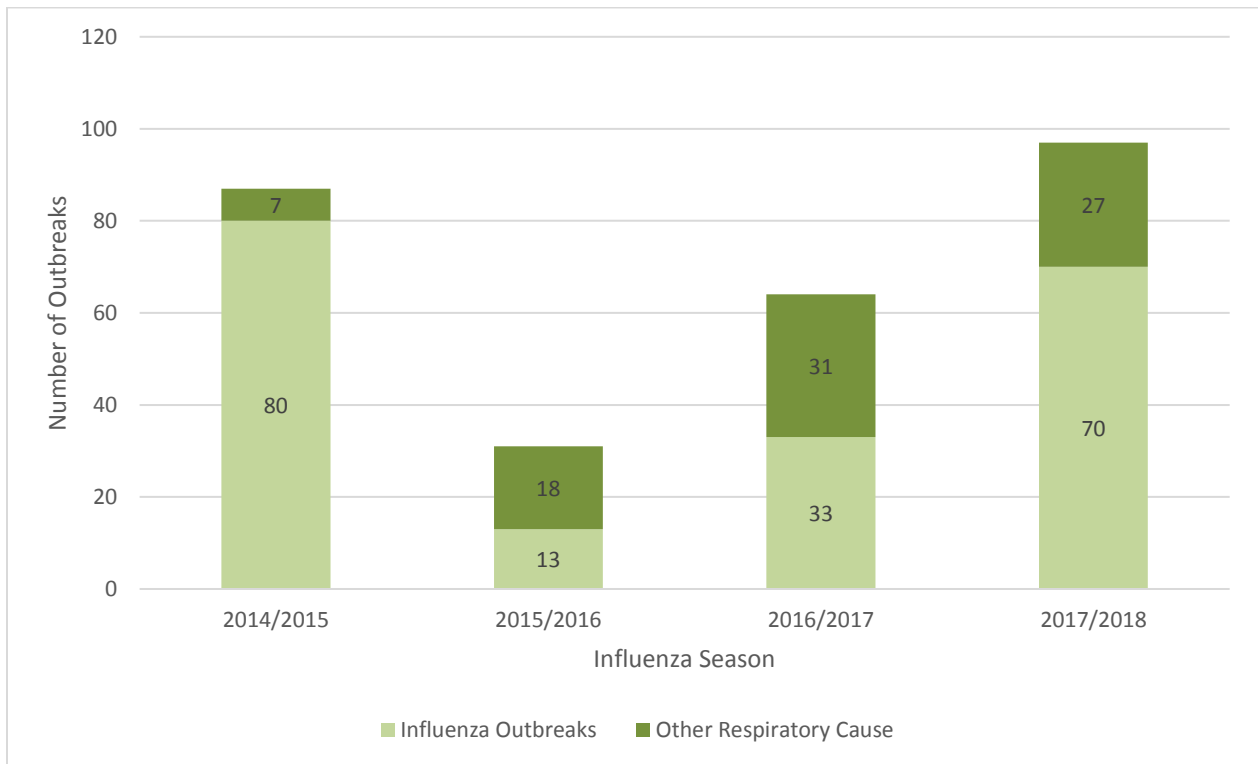
ALPPHB followed up with the Northern Regional Health Authority (NRHA) regarding lower HD vaccine coverage compared to the other RHAs and the MB average. NRHA identified that it is most likely due to data entry errors in the Registry or errors in the reporting of the vaccine used by LTCFs.

Outbreaks

Not all respiratory outbreaks in LTCFs are due to influenza. Many other pathogens can cause respiratory outbreaks within these facilities.

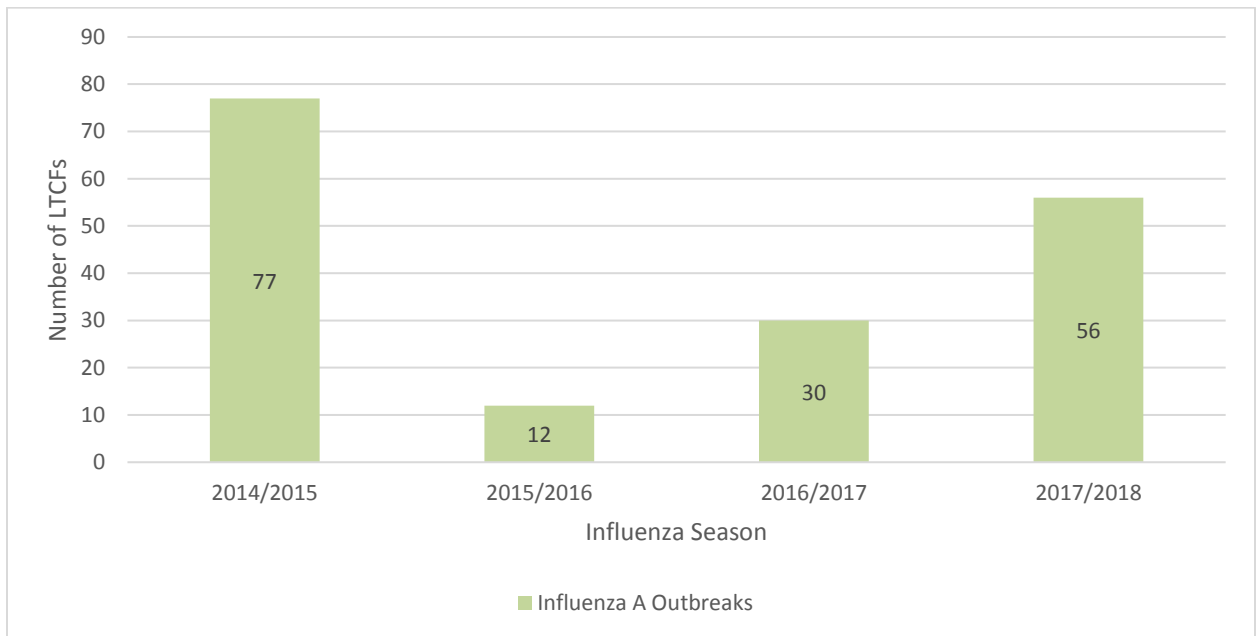
In 2014/15, 91.95% of the laboratory-confirmed respiratory outbreaks were due to influenza. In 2017/18, there were more laboratory-confirmed respiratory outbreaks than in 2014/15 but only 72.16% of them were due to influenza (see Figure 5 below). Figure 5 includes all influenza outbreaks regardless of influenza strain subtype.

Figure 5: Causes of Respiratory Outbreaks in LTCFs



Looking at influenza outbreaks by influenza strain (either influenza A or influenza B), there was a reduction (n=21) in the number of Influenza A outbreaks in 2017/18 compared to 2014/15 (see Figure 6 below).

Figure 6: Influenza A Outbreaks in LTCFs



Influenza Infection

MHSAL evaluated the incidence of laboratory-confirmed influenza during all four influenza seasons and calculated the attack rate. The Centers for Disease Control and Prevention defines attack rate (or incidence proportion) as the *proportion of an initially disease-free population that develops disease, becomes injured, or dies during a specified (usually limited) period of time* (<https://www.cdc.gov/opphss/csels/dsepd/ss1978/lesson3/section2.html>).

The provincial attack rate overall for laboratory-confirmed influenza A in all those 65 years of age and older was 0.29% (data not shown) in 2017/18, which was comparable to the attack rate of 0.33% in 2014/15.

When looking at the number of laboratory-confirmed influenza A cases in 2014/15 and 2017/18 (see Figure 7 below), there were 126 fewer confirmed cases of influenza A in 2017/18 compared to 2014/15 in LTCFs. The attack rate was a statistically significant decrease from 2.98% in 2014/15 to 1.85% in 2017/18.

Figure 7: Influenza A Attack Rate in those aged 65+ in LTCFs

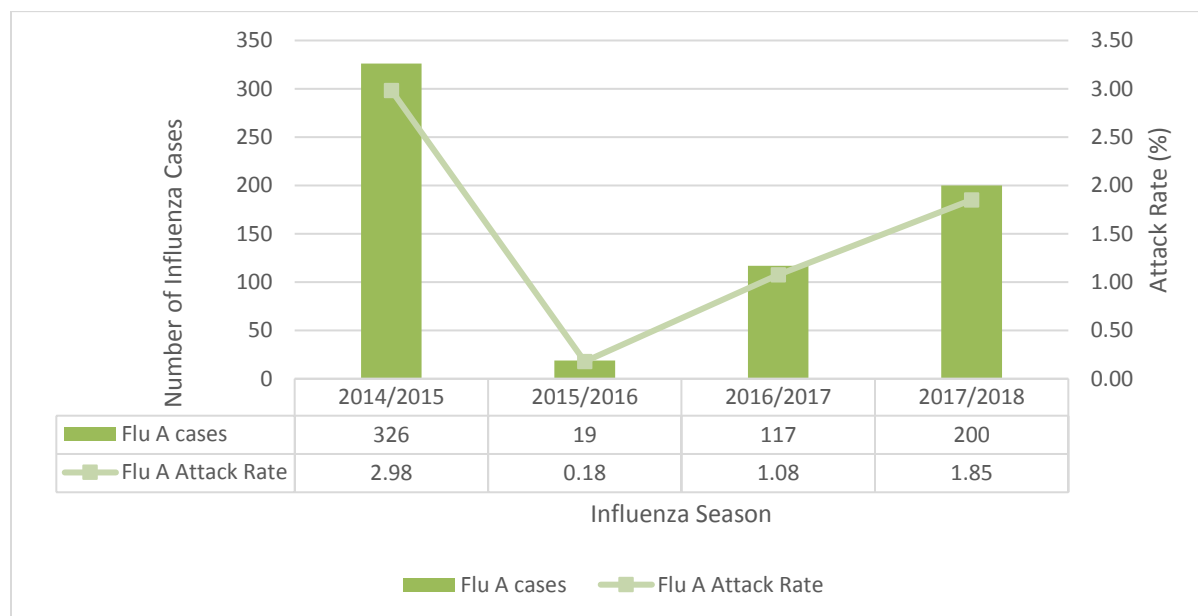
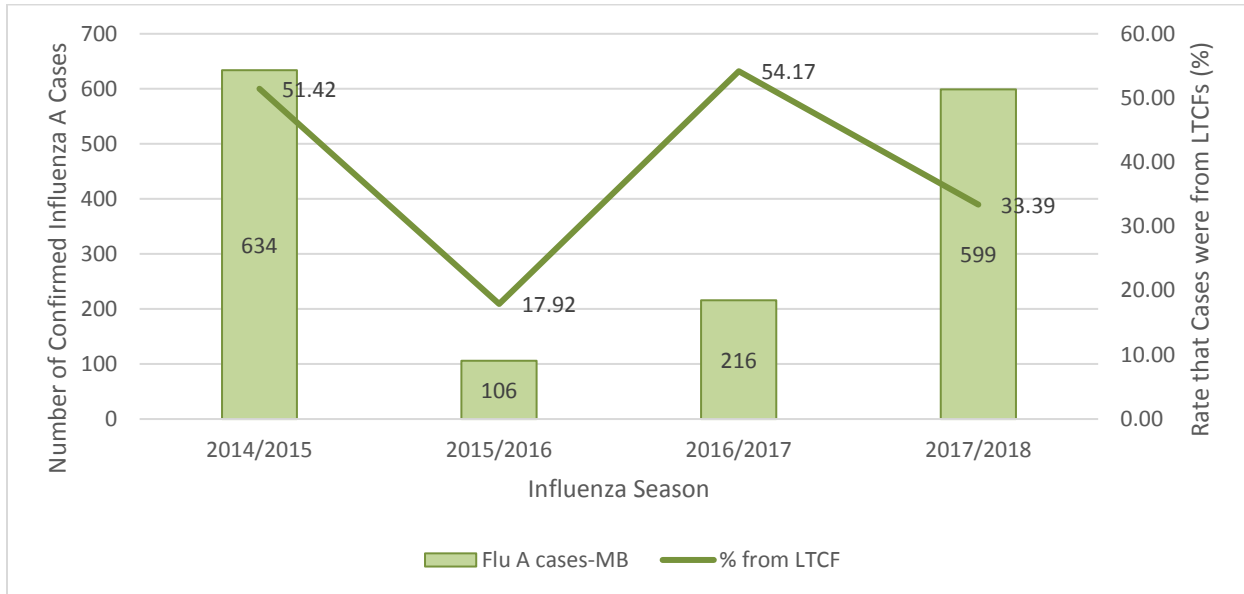


Figure 8 (below) looks at all laboratory-confirmed influenza A cases in MB in those 65 years of age and older and identifies how many were from LTCFs. In 2014/15, over 50% of confirmed cases of Influenza A came from LTCFs whereas in 2017/18, only 33.39% of laboratory-confirmed cases were reported from LTCFs.

In LTCF's, laboratory testing is only performed on suspect cases until the cause of the outbreak is determined. Thus, the attack rate is an underestimate. However, this process was consistent throughout the evaluation period.

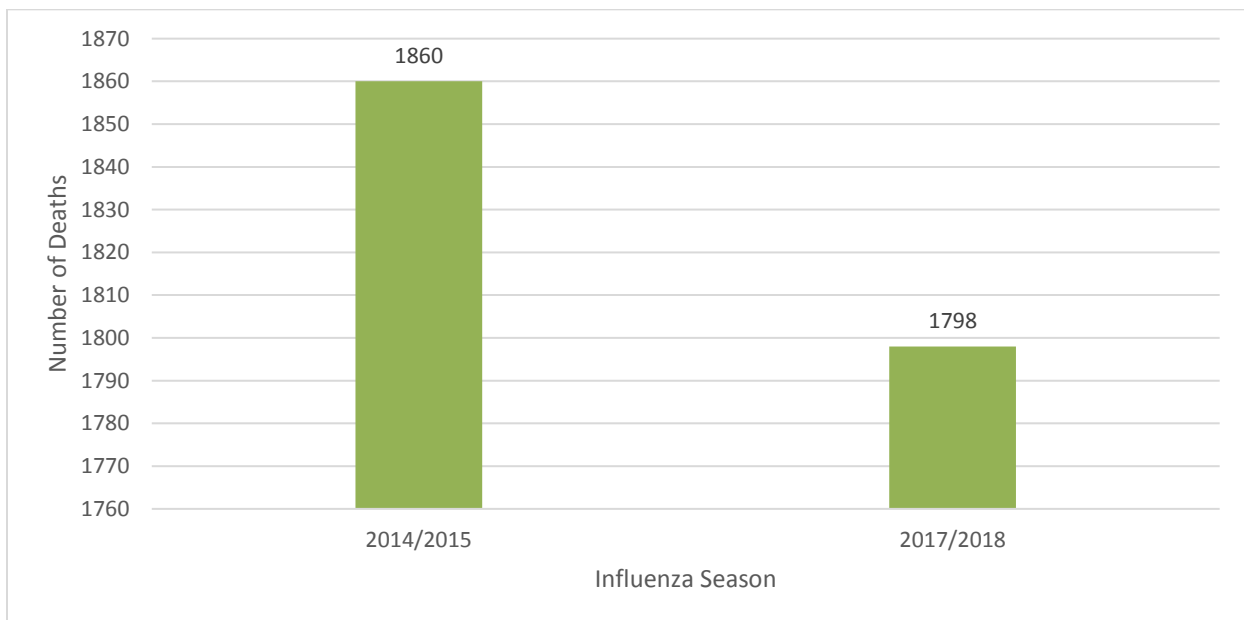
Figure 8: Proportion of MB's Total Influenza A Cases from LTCFs in those aged 65+



Deaths

MHSAL looked at the number of deaths in LTCFs **by all causes**. The cause of death may (or may not) be due to influenza. However, influenza may exacerbate existing comorbidities and contribute to the mortality. When analyzing all cause death in LTCFs between the comparable influenza seasons (Figure 9 below) where the timeframes are the same and the population numbers were similar, there were 62 fewer deaths in 2017/18 than in 2014/15.

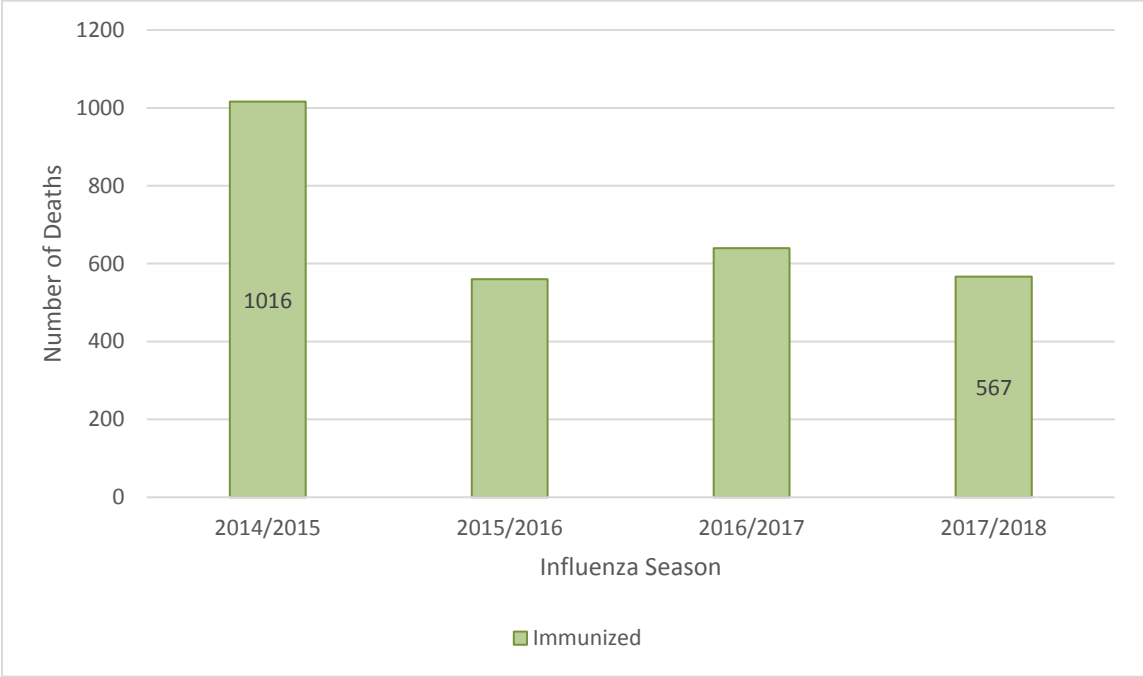
Figure 9: Number of All-Cause Deaths in those aged 65+ in LTCFs



After reviewing the immunization status of the deceased residents 65 years of age and older in LTCFs (Figure 10 below), the following was noted:

- There were 449 fewer deaths in immunized residents in 2017/18 compared to 2014/15.
- Immunized residents in 2017/18 had a 45% lower risk of dying compared to those immunized in 2014/15.

Figure 10: All-Cause Deaths in Immunized LTCF Residents aged 65+ years



Safety

No safety signal was detected through Manitoba’s passive surveillance system.

Conclusion

After one season, it is difficult to draw definitive conclusions on HD influenza vaccine effectiveness. However, based on the survey responses and feedback, the HD vaccine was well accepted by the residents and there were no safety issues identified. The feedback provided will be used by MHSAL to improve the HD vaccine program in future years.

Comparing the 2017/18 influenza season to the comparable influenza season of 2014/15 (i.e. similar strain, timing of season, and severity) there appears to have been:

- Fewer outbreaks of influenza A in LTCFs (21 fewer than 2014/15);
- Fewer confirmed cases of influenza among LTCF residents aged 65+ (126 fewer than 2014/15);
- Statistically significant decrease in the influenza A attack rate (from 2.98% in 2014/15 to 1.85% in 2017/18) among LTCF residents aged 65+;
- Fewer all-cause deaths among LTCF residents aged 65+ (62 fewer than 2014/15); and

- Fewer all-cause deaths in immunized residents aged 65+ (449 fewer than 2014/15).

Further analysis will be done as additional data becomes available. As the HD vaccine is administered in LTCFs in subsequent influenza seasons more data will be available to evaluate HD vaccine as part of the evaluation of each influenza season.