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Quality improvement initiative to improve revaccination rates after autologous stem cell transplantation

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BACKGROUND

Patients undergoing autologous haematopoietic stem cell transplants (ASCT) lose their acquired immunity against various pathogens due to reset and weakening of the immune system.[1] As such, Ontario Health guidelines recommend reimmunising these patients against vaccine-preventable diseases beginning 4–6 months post-transplant.[2] London Health Sciences Centre (LHSC) performs approximately 80–90 ASCT procedures annually for haematological malignancies such as multiple myeloma, non-Hodgkin's lymphoma and Hodgkin's lymphoma. The LHSC ASCT team routinely disseminates recommendations for revaccination, but prior to this project local data regarding adherence to these recommendations was not available. As such, this quality improvement project aimed to assess compliance with post-ASCT vaccinations at LHSC, and to explore ways to improve this compliance.

METHODS

In December 2020, 60 patients who received ASCT procedures at LHSC at least 6 months previously were identified by LHSC ASCT staff. Out of the transplanted patients, 53 were able to be contacted via telephone by a team of medical students (5 were not reachable by phone and 2 were deceased). Patients were asked to self-report their revaccination compliance, and those who were not fully compliant were asked to identify barriers to revaccination (see attachment online supplemental questionnaire script).

A root cause analysis was done to elucidate the major barriers to revaccination based on the December 2020 cohort (figure 1B). As the most commonly identified barriers were related to how to access and fund vaccines, a personalised information packet on these topics was designed (see attachment online supplemental information packet). Certain details were able to be individualised to each patient, including contact information for the nearest places they could access vaccination.

In March 2021, 20 new patients who received ASCT procedures at LHSC at least 6 months previously were identified, and information packets were personalised and mailed to them. In April 2021, these 20 patients were contacted via telephone and asked to self-report their revaccination compliance. They were also asked whether they found the information packet to be accessible and helpful.

No patients or members of the public were involved in the design, conduct, reporting or dissemination plans of the research.

RESULTS

At baseline, 72% of patients were compliant with post-ASCT revaccination (N=53 patients contacted in December 2020, who had received ASCT at least 6 months previously). Incompletely compliant patients identified vaccine cost and access to healthcare providers as major barriers (figure 1).

Among patients who received personalised information packets on how to access and fund vaccinations, 95% were compliant with revaccination (N=20 patients contacted in March 2021, who had received ASCT at least 6 months previously). The majority of patients described the intervention as accessible and helpful via descriptive patient surveys. There were negligible costs involved, primarily related to LHSC staff time and postage.

DISCUSSION

This study estimated the baseline rate of post-ASCT revaccination compliance at LHSC to be 72%. It is likely that revaccination rates are suboptimal across many institutions that perform ASCT. Indeed, revaccination

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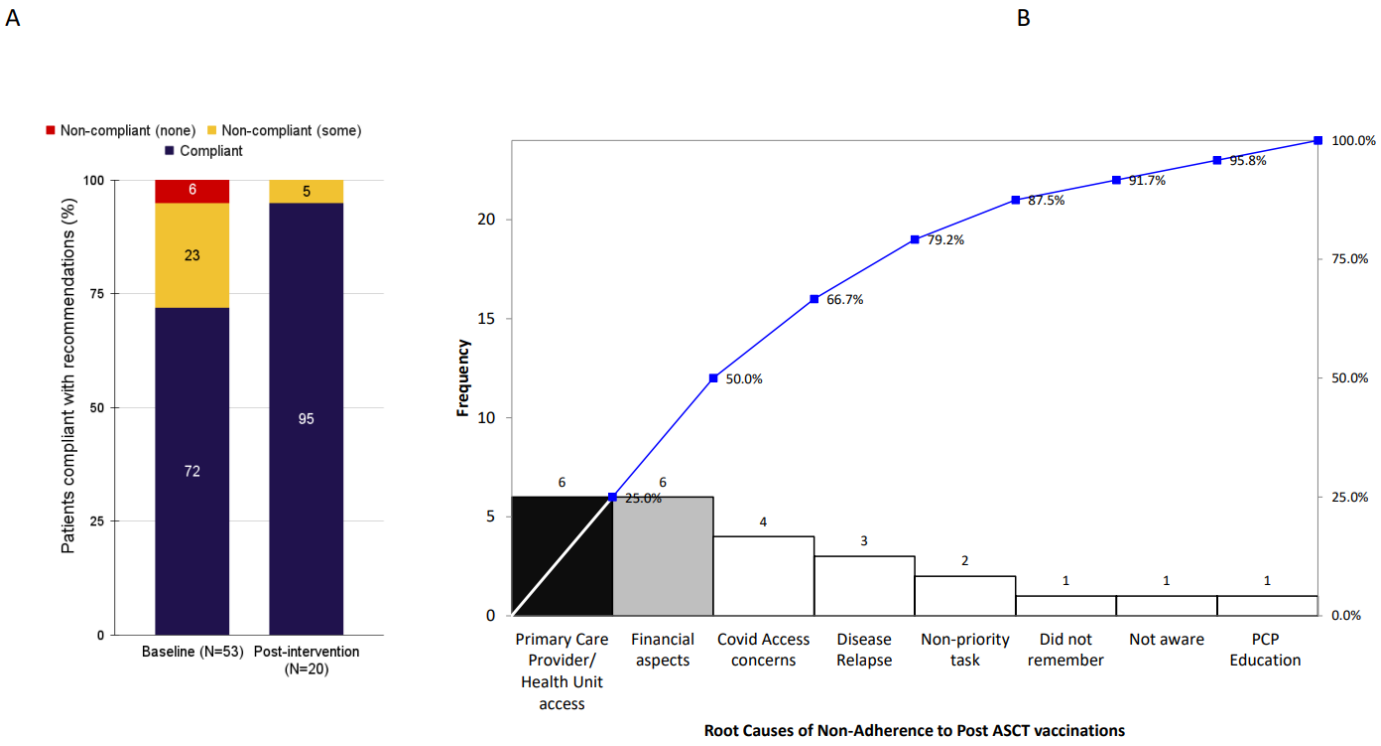

Figure 1 A. Re-vaccination compliance post ASCT at Baseline and after planned intervention. B. Pareto chart showing major root causes. ASCT, autologous haematopoietic stem cell transplant; PCP, Primary Care Provider.

compliance post stem cell transplant has been estimated at 76% at Yale New Haven Hospital in Connecticut, and 67% at the Karmanos Cancer Center Bone Marrow Transplant Center in Michigan.[3 4] It is not known how the ongoing COVID-19 pandemic might influence compliance rates. However, with increasing access to COVID-19 vaccines and decreasing provincial restrictions, it is likely these barriers will not persist long term.

This study identified vaccine cost and access to healthcare providers as major barriers to vaccine compliance among post-ASCT patients. This study suggests that mailing personalised information packets on how to access and fund vaccinations may be an effective low-cost strategy to improve post-ASCT revaccination compliance. In other institutions, increased efforts to educate patients and tailored follow ups have been identified as solutions to improve revaccination programmes.[5] In another study examining reasons for declined revaccinations, some cited reasons included time out from transplant, immunosuppressive therapy and prior adverse reactions.[6]

A key limitation of this study is its reliance on patient self-report of vaccination status, which may have led to an over-estimation of vaccine compliance (eg, if patients were unwilling to admit to non-compliance, or unsure of their compliance and unwilling to check their records). Further studies could consider using alternate methods to assess patient vaccination status (eg, accessing electronic medical records or asking for proof of vaccination). Further limitations include the lack of a control group that was not sent the information packets but was contacted simultaneously with the March 2021 group, and the lack of statistical analysis. This project also did not formally assess the long-term sustainability of mailing information packets, though the low costs incurred suggest this may be feasible. A questionnaire is planned in coming months to assess the sustainability of this intervention. To further lower financial, environmental and time costs, other institutions could consider options such as not personalising the information packets, emailing the information to patients rather than traditional mailing, or offering the information as a pamphlet during in-person appointments rather than mailing it.

In conclusion, a timely, patient centric, efficient and effective intervention described above is able to make a desired impact on improving revaccination rates in post-ASCT population at our centre. This low cost intervention can be replicated in other transplant centres to achieved the goal of high immunisation rates.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Because this study was identified as having low risk for participants by the ARECCI screening tool (A pRoject Ethics Community Consensus Initiative), no formal ethics review was completed.

Provenance and peer review Not commissioned; externally peer reviewed.

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Telephone Script

Legend:
Blue italics: read aloud
Bold black: instructions, not to be read aloud

Hi, my name is _____, I am a medical student at Western University, working with Dr. Deotare and Dr. Xenocostas' stem cell transplant team at the London Regional Cancer Program at Victoria Hospital. We're interested in how many of their patients have been able to get their recommended vaccinations. Would it be okay if I asked you a couple questions about this?
(If not now, set a time to call back)

You had a stem cell transplant ___ months ago, is that right?
(If wrong, make a note)

Do you remember that there were some vaccinations they recommended that you get starting 6 months after your transplant?

- **If no → provide information, and confirm that not remembering is why they didn't get the vaccines**
- **If yes** → *Have you been able to get any of those vaccinations yet?*
    - **If no** → *Could you tell me about why not?*
        - **Go through the checklist (below)**
        - *Is there anything that the transplant team could do, or could have done, to help you get the vaccinations?*
    - **If yes** → *Have you been able to get all of the recommended ones so far, or only some of them?*
        - **All recommended:** *Great!*
        - **Some of recommended:** *Could you tell me why you haven't been able to get all of them?*
            - **Go through the checklist (below)**
            - *Is there anything that the transplant team could do, or could have done, to help you get the vaccinations?*

ONLY ask if during April 2021: *Did you also receive a letter outlining how to access the recommended vaccines from the LHSC? If so, did you find it helpful?*

Before we end this call, can I ask you if this conversation caused you any stress or anxiety?

- **If yes** → *I'm sorry to hear that. I just want to reassure you that the purpose of this call was to only find out whether people are able to get the vaccines, and if not then why not, to see if we can help. This call will not affect your care in any way!*
- **If no** → *That's good to hear! I just want to reassure you that the purpose of this call was to only find out whether people are able to get the vaccines, and if not then why not, to see if we can help. This call will not affect your care in any way!*

If participant is not fully vaccinated, go through this checklist to identify potential contributing barriers):

Human error

- *Did not remember (e.g., was informed about vaccine recommendations, but forgot to get vaccinated)*
- *Lost sheet given by transplant clinic containing information about vaccines*
- *Not aware (e.g., was never informed that vaccines were recommended)*

Vaccine hesitancy

- *Concerns about vaccine side effects*
- *Values surrounding vaccination (e.g., does not believe in vaccination)*
- *Non-priority task (e.g., busy with other things)*

COVID-related

- *COVID access concerns (e.g., could not access care during pandemic)*
- *COVID safety concerns (e.g., does not wish to leave home during pandemic)*

Institutional (non-COVID specific)

- *Primary care provider or health care unit access*
- *Health care professional education/communication (e.g., primary care provider or health unit unsure of why patient requires vaccines)*

Socioeconomic status/environmental

- *Financial aspects (e.g., cost of vaccines)*
- *Transport*
- *Caregiver access*

Other

- *Disease relapse*
- *Other; please describe*

London Health Sciences Centre

Blood and Marrow Transplant Program
800 Commissioners Rd. E., PO Box 5010
London, Ontario, Canada N6A 5W9

Date:

Dear (name),

There are a number of vaccines that are recommended after a stem cell transplant (see attached schedule). Most vaccines start 6 months after stem cell transplant. This document will lay out where you can access these vaccines, and how to pay for them.

- When to start getting your vaccines:

Where to get vaccines

1. **Primary Care Provider: Family doctor/Nurse Practitioner:** if you have a family doctor or primary health care nurse practitioner, contact them first. If you are not able to get the recommended vaccines from your primary care provider within 1 month of the time the vaccine is recommended, contact your local health unit.
    - Your primary care provider:

2. **Health unit:** if you do not have a primary care provider, or are unable to access a vaccine through them within 1 month of the time it is recommended, contact your local health unit.
    - Middlesex-London Health Unit: 519-663-5317 (Mon-Fri 8:30am to 4:30pm)
    - Options of Other Health units

3. **Pharmacy:** if you are unable to obtain a vaccine within 1 month of the time it is recommended, contact your local pharmacy.
    - Your local pharmacy:

4. **Blood and Marrow Transplant Program at Victoria Hospital:** if you are unable to obtain a vaccine after trying the steps above at all of the above locations, please contact the London Regional Cancer Program (LRCP) Blood and Marrow Transplant Team.

- LRCP Blood and Marrow Transplant Team: 519-685-8600 press 1 then 3

How to pay for vaccines

1. **Publicly funded:** Most of the recommended vaccines are available for free in Ontario. The recommended vaccines available without cost are:
    - DTaP-IPV-Hib (Pediacel), or Quadracel and Hib (Act-hib)
    - Pneumococcal C-13
    - Pneumococcal P-23
    - Influenza (seasonal – inactivated formulations only)
    - Varicella
    - MMR
    - Shingles (Shingrix) for seniors aged 65-70 years
    - For men who have sex with men, some of the other recommended vaccines may also be publicly funded (see below)

2. **Unfunded vaccines:** Some of the recommended vaccines are not publicly funded in Ontario. If you are able to, you can consider paying for these vaccines out of your own pocket. The recommended vaccines that are NOT publicly funded, and their estimated costs, are:

Recommended vaccine	Estimated cost to patient
Hepatitis A (Havrix)	$65.00 per dose (estimate) Note: cost is covered for men who have sex with men
Hepatitis B (Engerix/Recombivax)	$200 per dose (estimate)
HPV (Gardasil-9)	$175.00 per dose, with 3 doses required (estimate) Note: cost is covered for men aged 26 years or younger who have sex with men.
Meningococcal conjugate (Menactra)	$120.00 (estimate for MLHU)

Shingles (Shingrix) For those outside of age 65-70	$200.00 (estimate)

3. **Private insurance:** if you have private insurance, the cost of some vaccines may be covered. If the cost of a specific vaccine is not covered, it may be covered if you provide them with a note from your transplant physician stating that it is recommended. If you require a note, please contact the LRCP Blood and Marrow Transplant Team.
    - LRCP Blood and Marrow Transplant Team: 519-685-8600 press 1 then 3

4. **London Regional Cancer Program:** if you are unable to pay for a recommended vaccine via one of the above methods, you may be eligible for funding from the LRCP Patient Assistance Fund. Please contact a social worker at the Patient Assistance Fund at LRCP to ask about your eligibility for funds.
    - LRCP Patient Assistance Fund: 519-685-8600 ext. 53627

COVID 19 vaccinations

We are getting many questions about the COVID vaccine. There are currently four Health Canada authorized vaccines for COVID-19. There are great resources available now to answer questions about the vaccines including a list of questions and answers here:
https://files.ontario.ca/moh-covid-19-vaccines-fact-sheet-en-2021-02-05.pdf

Eligibility for the vaccine is determined by Ontario government and then timing is determined the availability of the vaccine in your community. Stem cell transplant patients will be eligible in **Phase 2** of the Ontario vaccination plan.
https://covid-19.ontario.ca/ontarios-covid-19-vaccination-plan

Each public health unit is developing a vaccine plan tailored to their own community's needs. To know when you are eligible in your area we recommend you check with your local public health unit website. Each health unit has special vaccination clinics dedicated to the COVID vaccine.
Middlesex London: https://www.healthunit.com/novel-coronavirus

Despite the lack of data, there is no immunologic rationale to suggest that these COVID vaccines might be harmful, and there is no risk of developing COVID from these vaccine products. In general, other vaccine products have not shown a risk of post-transplant complications. Thus, despite the lack of data, it would be reasonable to conclude that these vaccines are likely safe in recipients of stem cell transplant.

Patients that are immunocompromised might not develop the same immunologic response to the vaccine and might not benefit to the same degree as a member of the general public. That said, in most patients, given the very significant risk associated with COVID infection, the potential benefit associated with the vaccine is likely greater than any risks.

The LHSC BMT Program recommend that stem cell transplant patients receive COVID vaccination starting no earlier than 3 months after transplant when you are eligible.

We also recommend a gap of at least 2 weeks in between any 2 vaccinations or prior to any chemotherapy or immunosuppressive therapy to facilitate development of immunity to the previous vaccine.

If you are eligible for the vaccine but are not sure if it is appropriate for you, please contact us at the number below so we can answer your questions:

- LRCP Blood and Marrow Transplant Team: 519-685-8600 press 1 then 3

London Health Sciences Centre
Blood and Marrow Transplant Program

Immunization Guidelines Post Stem Cell Transplant

Vaccination Documentation for: Click here to enter text. **Date of Transplant:** Click here to enter a date.

Vaccine	Comments	Time Post-Transplant (months)								
		6	7	8	10	12	14	18	24	Other
DTaP Hib IPV* (Pediacel®)		X	X	X				X		
Hepatitis B (40 mcg)	High dose vaccine	X	X			X				
Hepatitis A (Havrix®)	If risks or travel present	X				X				
Pneumococcal C-13	(Prevnar®)	X	X	X						4th dose only if GVHD or on IST
Pneumococcal P-23	(Pneumovax®)						X *Avoid if GVHD or on IST*			Booster > 1 yr post initial
Meningococcal Conjugate	(quadrivalent - Menactra®)	X		X						
Influenza	Start at least 6 months post-transplant in flu season	Yearly								
Varicella**	Additional dose 3 months later if no seroconversion								X	See below
MMR**									X	See below
HPV	Females and males 9-26 years of age and older depending on risk	X		X		X				
Shingrix®	Two doses at least 1 month apart starting 6-12 months	X		X						
Contraindicated live vaccines: BCG, intranasal influenza, rotavirus, live oral typhoid, oral polio										

GVHD – graft versus host disease, IST – immunosuppressive therapy

Additional Comments

*DTaP-IPV vaccine

- Includes diphtheria, tetanus, acellular pertussis, hemophilus influenza B and inactivated polio virus.
- In Canada the combination options are to give Pedicacel® or Quadricel® with Act HIB vaccine

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London Health Sciences Centre
Blood and Marrow Transplant Program

Immunization Guidelines Post Stem Cell Transplant

Vaccination Documentation for: Click here to enter text. **Date of Transplant:** Click here to enter a date.

**Varicella & MMR:

- Can be given provided recipient does not have ongoing significant immunosuppression or chronic GVHD.
- 2-1-5 rule: At least 2 years post-transplant, at least 1 year off immunosuppressive therapy and at least 5 months since last infusion of IVIG, plasma or VZIG.
- Check serology at 24 months prior to vaccination to optimize which patients may not need re-vaccination, particularly in autologous transplant recipients.
- If unsure, please contact transplant centre.

Vaccination Dosing

Vaccine	When to start	Dosing Schedule
Diphtheria*	6-12 months	3 doses, each one month apart
Pertussis*	6-12 months	1 dose, if given alone. 3 doses if given as part of combined vaccine
Polio*	6-12 months	3 doses, each one month apart
Tetanus*	6-12 months	3 doses, each one month apart
Hemophilus influenza B*	6-12 months	3 doses, at least 4 weeks apart
Hepatitis B	6-12 months	3 doses at 0, 1 and 6 months. Use high dose vaccine (40 ug dose). Monitor HBsAb titres
Pneumococcal C-13 (Prevnar®)	6-9 months	3 doses, 1 month apart, 4th dose if GVHD or IST
Pneumococcal P-23 (Pneumovax®)	6-12 months after last C-13 dose	1 dose with booster after 12 months
Meningococcal Conjusgate (quadrivalent)	6 months	1 dose. A second dose is only required if the first dose is given within 6 months of transplant (if so, the second dose can be given 2 months after the first dose)
Shingrix®	6-12 months	2 doses, 2 months apart

Questions: Please contact the London Regional Cancer Program Blood and Marrow Transplant Team – 519 685 8600 extension 3

Reference: Cancer Care Ontario Immunization Following Stem Cell Transplant in Adults: Position Statement Stem Cell Transplant Steering Committee, Feb 2018 https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/43096

London Health Sciences Centre
Blood and Marrow Transplant Program

Immunization Guidelines Post Stem Cell Transplant

Vaccination Documentation for: Click here to enter text. **Date of Transplant:** Click here to enter a date.

Vaccine	Formulation	Time Post-Transplant (months)								
		6	7	8	10	12	14	18	24	Other
DTaP Hib IPV	Pediacel® or Quadricel® + Act HIB	Date given:	Date given:	Date given:				Date given:		
Hepatitis B	40 mcg	Date given:	Date given:			Date given:				
Hepatitis A		Date given:				Date given:				
Pneumococcal C-13	Prevnar®	Date given:	Date given:	Date given:			*If GVHD or IST* Date given:			**4th dose only if GVHD or on IST**
Pneumococcal P-23	Pneumovax®						*If no GVHD/IST* Date given:			Booster > 1 yr post initial Date given:
Meningococcal conjugate	Quadrivalent Menactra®	Date given:		Date given:						
Influenza		Date given 1st Year:			Date given 2nd Year:			Date given 3rd year:		
Varicella		Check serology prior to see if immunization required							Date given:	Check serology
MMR		Check serology prior to see if immunization required							Date given:	Check serology
HPV *Females and males 9-26 yrs or older if risk*		Date given:		Date given:		Date given:				
Herpes zoster	Shingrix® (**not** Zostavax®)	Date given:		Date given:						