

AWARD NUMBER: W81XWH-21-1-0347

TITLE: Increasing HPV Vaccination Coverage Among Adolescent and Young Adult (AYA) Cancer Survivors: A Multilevel Intervention

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CONTRACTING ORGANIZATION: University of Minnesota, Minneapolis, MN

REPORT DATE: September 2023

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution is unlimited.

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE September 2023	2. REPORT TYPE Annual	3. DATES COVERED 15Aug2022-14Aug2023
4. TITLE Increasing HPV Vaccination Coverage Among Adolescent and Young Adult (AYA) Cancer Survivors: A Multilevel Intervention		5a. CONTRACT NUMBER
		5b. GRANT NUMBER W81XWH-21-1-0347
		5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) Deanna Teoh, MD, MS E-Mail: dkteoh@umn.edu		5d. PROJECT NUMBER
		5e. TASK NUMBER
		5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Minnesota Office of Sponsored Projects Administration 200 Oak Street SE #24 Minneapolis, MN 55455-2009		8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012		10. SPONSOR/MONITOR'S ACRONYM(S)
		11. SPONSOR/MONITOR'S REPORT NUMBER(S)
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited		

13. SUPPLEMENTARY NOTES**14. ABSTRACT**

Background: Adolescent and young adult (AYA) cancer survivors are 2.8 times more likely to develop a human papillomavirus (HPV)-associated cancer than the general population. Thus, 3 doses of HPV vaccine are recommended for AYA cancer survivors 9-26 years of age. Unfortunately, HPV vaccination coverage among AYA cancer survivors is lower than that in the general population.

Objective: This project seeks to increase HPV vaccination initiation and completion among AYA cancer survivors by implementing a single multilevel intervention focused on the clinic, oncologist, and survivor.

Specific Aims:

Aim1: Test the efficacy of a multilevel intervention to increase HPV vaccination initiation among AYA cancer survivors.

Aim2: Compare efficacy of the GLAm app versus clinic-generated reminders to increase completion of the HPV vaccination series among AYA cancer survivors independent of scheduled survivorship visits.

Study Design: The multilevel intervention comprising a quality improvement (QI) study combined with a randomized controlled trial (RCT) was developed using the *Fogg Behavior Model*. The QI study comprises training and encouragement for oncologist and survivorship clinic staff to recommend HPV vaccination to all unvaccinated/incompletely vaccinated patients. The RCT will randomize survivors of childhood cancer 18+ years of age or caregivers for survivors of childhood cancer 9-17 years of age to usual care (QI intervention alone) versus use of a game-based learning avatar-navigated mobile (GLAm) app to increase knowledge about HPV and HPV vaccination and to motivate initiation and completion of the 3-dose HPV vaccine series.

Progress to date:

-Year 1: The QI study was implemented, and initial data abstraction and survey of healthcare provider satisfaction with the intervention was completed. Patient surveys to evaluate their impression of the QI intervention were distributed on a rolling basis. The GLAm app revised content was created, and the app development team worked on updating the app prototype

-Year 2: The QI study continues with the survivor clinic providers providing a strong recommendation for HPV vaccination to all eligible patients, and the recommendation for HPV vaccination has been added to the survivorship care plans. The 1-year provider/staff surveys have been completed, and patient/caretaker surveys continue to be distributed on a rolling basis. The first participants in the QI study are now being sent the 1-year follow-up surveys, and medical record abstraction for assessment of HPV vaccination uptake is ongoing. In July 2023 the RCT testing the patient-level GLAm app opened to accrual and participants have been enrolling consistently.

Results: Interim analysis was performed after 1 year of the QI intervention. Provider/staff surveys showed that adding a recommendation for HPV vaccination does not interrupt clinic workflow, does not add significant time to the clinic visit, and that documentation of the recommendation does not add significant time to charting/workflow. During the first year, 322 age-eligible patients were seen in the survivor clinics, and 222 were eligible for the study based on receipt of <3 doses of the HPV vaccine. Chart review showed 66% received a provider recommendation for vaccination. 5.4% had a documented intention to receive the vaccine, and an additional 6.7% received a dose of the vaccine in the clinic; of note, this may be an underrepresentation since documentation of patient intention is not required in the study protocol, and administration of the vaccine in the clinic is not a part of the protocol since it is not stocked in either clinic, and is even only available from the pharmacy for administration in clinic at the University clinic. Among patient/caretaker respondents to the 1-month survey, 67% agreed/strongly agreed their provider strongly recommended HPV vaccination, and 83% agreed/strongly agreed the provider adequately responded to their questions/concerns about the vaccine. At the time of data abstraction 14% had received at least 1 dose of HPV vaccine following the QI intervention, and 2 participants had received 2 doses on study. Overall, 52% of survey respondents intend to vaccinate, irrespective of whether it had been initiated at the time of survey completion. 3 respondents reported they did not intend to vaccinate, and reasons were the patient does not like shots (n=1); do not have enough information (n=1); not enough data available on efficacy (n=1).

The RCT testing efficacy of the GLAm app to increase HPV vaccination initiation and completion is ongoing, and no interim analyses have been performed to date. At the time of this report 38 participants have enrolled in the RCT.

Significance: Routine recommendation for HPV vaccination does not interrupt or add significant time to the clinic workflow. The QI intervention has been moderately successful, and has resulted in increased intention and uptake of HPV vaccination. Significant barriers to uptake include inability to administer the vaccine in one clinic, and added time in an already long survivorship visit in another clinic due to inability to stock the vaccine in the clinic. Inability to provide reminders for subsequent doses, and lack of feasibility to auto-schedule subsequent doses when the first dose is administered in clinic is another barrier, especially since many patients live a great distance from the oncology clinic. An RCT is ongoing to test efficacy and ability to further increase HPV vaccination coverage among survivors of childhood cancer through provision of additional information about the vaccine in a fun and interactive manner, and through provision of text message reminders and links to vaccine locators proximal to the patient's home community.

15. SUBJECT TERMS

HPV vaccination; Cancer prevention; Cancer survivorship; childhood cancer

16. SECURITY CLASSIFICATION OF:

a. REPORT

Unclassified

b. ABSTRACT

Unclassified

c. THIS PAGE

Unclassified

17. LIMITATION OF ABSTRACT

Unclassified

18. NUMBER OF PAGES

14

19a. NAME OF RESPONSIBLE PERSON
USAMRDC**19b. TELEPHONE NUMBER** (include area code)

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1. INTRODUCTION:

Survivors of childhood cancer are 2.8 times more likely to develop a secondary human papillomavirus (HPV)-associated cancer than the general population. Unfortunately, HPV vaccination coverage among survivors of childhood cancer is even lower than that in the general population. Further, due to concerns about reduced immunogenicity in the setting of previous immunosuppressive cancer therapy, 3 doses of the HPV vaccine are recommended for all survivors of childhood cancer regardless of age at initiation of vaccination. The purpose of this study is to increase HPV vaccination initiation and 3-dose completion among survivors of childhood cancer, defined as age 25 years of age or younger at cancer diagnosis. This study employs a multilevel approach, including a quality improvement intervention targeting the oncologists and clinic staff to routinely provide a strong recommendation for HPV vaccination. The study will also test the efficacy of a game-based learning avatar-navigated mobile (GLAm) app versus usual care at the patient/caregiver level to increase vaccination initiation and completion independent of the clinic visit in a randomized controlled clinical trial.

2. KEYWORDS:

HPV vaccination; survivorship; childhood cancer; cancer prevention; mobile health technology.

3. ACCOMPLISHMENTS:

What were the major goals of the project?

- 1) Obtain IRB/HRPO approval (months 1-6): HRPO approval obtained 1/31/22. Children's Minnesota approved all study documents 4/28/22. SMART IRB (UMN single site IRB) approval obtained 5/26/22. OHRO approval obtained 9/5/22.
- 2) Convert GLAm app to focus on HPV vaccination for survivors of childhood cancer (months 1-8): 90% complete. Educational modules, app update mock-ups, app videos and infographics submitted to the app developers. Per communication with the app development team 9/1/22, the app revisions have been coded and are undergoing final review by the development team before review by the study team.
- 3) Conduct a RCT to determine the effect of the GLAm app to increase HPV vaccination among survivors of childhood cancer (months 8-35): Delayed due to delay in app revisions. The IRB is also requiring that we store the app on a server approved by the IRB due to concerns about HIPAA compliance (note: the app development group creates HIPAA-compliant apps for non-research clinical use, but the IRB has required that we move the app to a different server).
- 4) Conduct QI study to determine the effect of a strong oncologist recommendation for HPV vaccination & EHR reminders to increase HPV vaccination (months 1-42): EHR alert programming in progress (10%). The EHR alert programming has been stalled due to loss of staff and de-prioritization of HPV vaccination alerts at the health system level. Oncologist and staff training completed (UMN 3/3/22, Children's Minnesota 3/9/22). QI study initiated at UMN CCSP clinic 5/2/22. QI study initiated at Children's Minnesota 6/15/22. Data abstraction from the medical record is ongoing. The first quarter oncologist/staff surveys to assess satisfaction with the QI intervention and impact on workflow was sent 7/22/22 and have been completed. The first set of patient surveys to assess impression of HPV vaccination recommendation, intention to vaccinate, and barriers to vaccination were sent 8/22/22, with surveys sent to patients on a rolling basis based on the date of their clinic visit.
- 5) Conduct QI study to measure the effect of sending EHR-generated reminders to patients for dose 2,3 of the HPV vaccine: EHR-generated reminders being programmed (10%). Delays in the EHR reminders has been delayed due to IT staff shortages and de-prioritization of HPV vaccination reminders at the health system level.
- 6) Conduct a RCT to determine the effect of GLAm app-generated reminders to complet the HPV vaccination series: GLAm app re-design in progress (90%). Initiation of the RCT delayed due to the delay in completion of the GLAm app revisions.

What was accomplished under these goals?

- 1) Obtain regulatory approval: HRPO approval obtained. Children's Minnesota (study site) IRB approved the protocol and study documents. SMART IRB (University of Minnesota single-site IRB) approval obtained. OHRO approval obtained. Annual regulatory reviews have been approved, and annual DSMC review 9/2023 revealed no concerns.
- 2) Conversion of GLAm app to focus on HPV vaccination among survivors of childhood cancer: App content revisions reviewed, revised and approved by the study Advisory Panel. Revisions spreadsheet submitted to and reviewed by app developers. All app videos created and edited, and videos have been reviewed and approved by the Advisory Panel. The app has been updated and moved to the HIPAA-secure Health Sciences server for secure collection of data. The app is currently in use in the RCT.
- 3) QI study initiated: Training for oncology providers and staff completed. QI clinic procedures implemented 5/2/22 at UMN CCSP clinic. QI intervention implemented at Children's Minnesota LTFU clinic 6/15/22. 1-year of staff/provider survey data show that routine recommendation for HPV vaccination does not significantly impact clinic workflow or add significant time to the clinic visit or documentation time. One-month post-visit patient/caretaker surveys are ongoing, and the first participants have been sent a 1-year follow-up survey. Data collection (medical record abstraction and surveys) are ongoing, but preliminary analysis shows that 66% of patients have received a strong recommendation for HPV vaccination (per electronic medical record documentation by the provider and patient/caregiver survey responses). 14% of QI participants had received at least 1 dose of the HPV vaccine on study, and 52% of survey respondents reported an intention to vaccinate, irrespective of whether they had initiated it. Only 3 survey respondents reported they did not intend to vaccinate due to not liking shots, lack of enough information, and lack of data on efficacy (n=1 for each reason).
- 4) EHR reminders stalled: Proposal previously reviewed and discussed with the Health Informatics team. Plan for integration of proposal with the current best practice EHR changes in development for the primary care clinics tailored for implementation in the Childhood Cancer Survivorship Program Clinic. The IT staff leading this project left the University, and this project has been de-prioritized at the health system level. EHR reminders have been omitted from the study at this time due to lack of IT support.
- 5) Conduct RCT to determine the effect of the GLAm app to increase HPV vaccination initiation among survivors of childhood cancer: The RCT was opened to enrollment 7/26/23. To date 38 participants have been enrolled.

What opportunities for training and professional development has the project provided?

Dr. Teoh has been invited to be a member of the Society of Gynecologic Oncology task force which aims to reduce the incidence of cervical cancer through improved prevention, as well as improve treatment of cervical cancer.

How were the results disseminated to communities of interest?

1. Study presented as a work-in-progress at the University of Minnesota Women's Health Research Conference 2/23/23 (cancelled due to inclement weather; abstract sent electronically to people who reserved a ticket for the event).
2. Oral plenary of preliminary results from the QI intervention at the Heartland Association of Gynecologic Oncology conference 9/26/23.
3. Poster presentation at the University of Minnesota Masonic Cancer Center Symposium 10/30/23.

What do you plan to do during the next reporting period to accomplish the goals?

1) QI study assessment: Medical record data abstraction will continue to determine the proportion of eligible patients who have received a recommendation for HPV vaccination, and vaccination uptake. We anticipate a 3-month delay for state immunization registry data to be uploaded to the electronic health record, and will review immunization records on an ongoing basis. Surveys will be sent on a rolling basis at 1-month and 1-year post-visit to patients meeting criteria for inclusion in the QI intervention to assess impression of HPV vaccination recommendation, vaccination intention and uptake, as well as to collect additional data on barriers to vaccination. Participants who report receiving vaccination outside of Minnesota, consent for Release of Information will be signed to request vaccination information.

2) Continue the RCT to determine the effect of the GLAm app to increase HPV vaccination initiation among survivors of childhood cancer: Enrollment is ongoing, and data collection is in progress. The PI meets with the study coordinator at each site weekly to discuss any challenges to enrollment or study progress, and all co-investigators meet monthly to discuss study progress and any barriers. If enrollment slows, we will continue to explore alternative recruitment methods, including recruitment via email or patient portal outside of the clinic visit.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Implementation of a routine recommendation for HPV vaccination during the survivor visit has resulted in increased uptake of HPV vaccination, and >50% of patients intended to vaccinate even if they have not yet initiated vaccination.

Impact of the patient/caretaker-level app to further increase uptake/completion of HPV vaccination has not yet been determined, although RCT to answer this question is ongoing.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

The QI intervention was initiated without EHR vaccination reminders due to staff shortages and de-prioritization of EHR HPV vaccination reminders at the health system level. The EHR reminders were never intended for the Children’s Minnesota clinic, and thus only impact the study design at the University of Minnesota. At this time, the plan for EHR reminders has been abandoned due to lack of support from the health system’s IT team. While this may decrease the efficacy of HPV vaccination completion among patients at University of Minnesota, it does simplify data analysis as the QI intervention is now the same at both study sites.

Actual or anticipated problems or delays and actions or plans to resolve them

Delay in the GLAM app revisions: The GLAM app revisions were delayed by 1 year due to lack of staffing at ETI (the app development team). Testing of the app in the RCT was further delayed for an additional 6 months due to need to move the app to the Health Sciences server and a delay in response to multiple contacts (email; telephone calls) to the IT team. Prioritization of this study in the Cancer Prevention group at the Masonic Cancer Center ultimately resulted in expedited moving of the app to the Health Sciences server, and the RCT has been opened to enrollment.

Delay in EHR reminder programming: We have been unable to resolve this issue due to lack of IT support. The EHR reminders, which were only planned for the University clinic, have been abandoned.

Changes that had a significant impact on expenditures

Year 1

The initial award was for a study which was to be conducted at a single site. However, due to changes in clinic volume due to the COVID pandemic, we added Children’s Minnesota as a second study site under a subaward. The budget was revised and has been approved by the DOD.

There was a delay in hiring a research coordinator, thus budgeted costs for the first 9 months were not spent. We had to revise our posting and hired a research coordinator with less experience than initially planned, thus the salary for the research coordinator is decreased compared to the original estimate.

Year 2

None

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS

- **Publications, conference papers, and presentations**

Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Wanberg LJ, Kim A, Vogel RI, Sadak KT, Teoh D. Usability and satisfaction testing of a Game-based Learning Avatar-navigated mobile (GLAm), an app for cervical cancer screening: Mixed Methods Study. JMIR Formative Research, 2023;7:e45541. Doi: 10.2196/45541.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

Other publications, conference papers and presentations.

1. Oral presentation: HPV vaccination in childhood cancer survivors: Multilevel Intervention—Works in Progress. 17th Annual UMN Women’s Health Research Conference. University of Minnesota, Minneapolis, MN. 2/23/23
**Cancelled due to inclement weather; abstract sent to ticketed attendees*
2. Oral plenary: Increasing HPV vaccination among survivors of childhood cancer: Analysis of a quality improvement initiative. Heartland Association of Gynecologic Oncology Annual Meeting. Minneapolis, MN. 9/26/23.
3. Poster presentation: Increasing HPV vaccination among survivors of childhood cancer: Analysis of a quality improvement initiative. Masonic Cancer Center Symposium. Minneapolis, MN. 10/30/23.

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Not applicable.

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Not applicable.

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Not applicable.

- **Other Products**

GLAm app: A game-based learning avatar-navigated mobile app which provides education about HPV and HPV vaccination in a fun learning environment. The app also has links to additional education resources, reminders for HPV vaccination, and links to help users identify locations where then can get vaccinated.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Deanna Teoh

Project Role: PI

Researcher Identifier: 0000-0002-1931-1445

Nearest person month worked: 2.4

Contribution to project: Regulatory approvals; Oversight of app development; Oversight of survey development/revisions; Oversight of QI project implementation

Name: Karim Sadak

Project Role: Co-I
Researcher Identifier: 0000-0002-4511-5456
Nearest person month worked: 1.2
Contribution to project: Contributed to app revisions; Implementation of QI project

Name: Rachel Vogel
Project Role: co-I
Researcher Identifier: 0000-0003-0149-8464
Nearest person month worked: 1
Contribution to project: Protocol revisions

Name: Helen Parsons
Project Role: co-I
Researcher Identifier: 0000-0003-3822-9858
Nearest person month worked: 1.2
Contribution to project: Protocol revisions; Design of QI implementation

Name: Julia Gourde
Project Role: Children's Minnesota site PI
Researcher Identifier: NA
Nearest person month worked: 1
Contribution to project: Implementation of QI project

Name: Andrea Iverson
Project Role: Children's Minnesota Research Coordinator
Researcher Identifier: NA
Nearest person month worked: 1.2
Contribution to project: Regulatory approval at Children's Minnesota; Implementation of QI project

*All other research personnel contributed <1 person-month

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Katharine Lange, site PI at Children's Minnesota LTFU left the institution. She has been replaced by Julia Gourde, CNP as co-investigator on the study, and site PI at Children's Minnesota LTFU.

What other organizations were involved as partners?

None.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Not applicable

QUAD CHARTS: Not applicable

9. APPENDICES:

Appendix 1: HAGO slides

Appendix 2: MCC poster (note: title “poster slide” not included, as it was provided by the MCC symposium personnel).