Protocol for Human Subject Research

Protocol Title:
Healthy, Immunized Communities Study

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Version Date:
05/09/2019 (approved)

Clinicaltrials.gov Registration #:
NCT03854734

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1.0 Objectives

1.1 Study Objectives

Our project seeks to determine the efficacy of a multi-tiered school and community-based approach to improving rates of parental intent to vaccinate for middle school-aged vaccinations including Human Papillomavirus (HPV), meningitis (MCV) and Tetanus, Diphtheria, Pertussis (TDap). This project aims to increase awareness and education relating to vaccinations. This IRB submission is a continuation of the phase I work (IRB # 8659) where we conducted focus groups with the school and parents to help inform this (phase 2) intervention.

Through a randomized approach, two (of the four) middle schools will be selected to offer: community-based event to raise parental awareness of the importance of vaccination, and social marketing to target parents' attitudes and knowledge around vaccinations.

1.2 Primary Study Endpoints

The primary endpoint of this study is parental intention to vaccinate, influenced by awareness and education.

1.3 Secondary Study Endpoints

The secondary endpoint for this study is the timely uptake of required vaccinations among middle school-aged children, collected in aggregate and provided by the School District of Lancaster (study partner).

2.0 Background

2.1 Scientific Background and Gaps

Vaccines are considered one of the greatest public health successes. Unfortunately, an increasing rate of parental resistance in recent years has led to a reemergence of vaccine-preventable disease. Although overall rates of many recommended vaccinations remain high (≥95%) among Pennsylvania school-aged children, some are estimated to be much less utilized (<50%), including those protective for human papilloma virus (HPV).[1,2] Specifically, although national coverage for girls ages 13-17 who have received on or more doses of HPV vaccine is 63%, Pennsylvania rates are lower (< 59%).[2]

Every year, there are about 17,500 women and 9,300 men affected by HPV-related cancers in the U.S.[2] Many of these cancers could be prevented with vaccination. Research shows that a HPV vaccine education intervention for parents, healthcare staff and school staff can result in increased HPV vaccine knowledge and support among groups influential to the HPV vaccination behaviors of adolescent females.[3]

These programs work to overcome the leading barriers to vaccine, which include parental concern and distrust of the scientific evidence, lack of awareness, distrust of health care professionals and dissatisfaction with vaccine discussions.[4,5] Respectfully engaging in conversation with parents hesitant to vaccinate can convert nearly half of those initially opposed.[6] However, providing supportive tools to healthcare professionals to facilitate these difficult conversations is necessary.

However, healthcare professionals do not operate in a vacuum. SAGE Working Group proposed a model of vaccine hesitancy with three macro categories: contextual influences, vaccine or vaccination specific issues and individual or group influences.[7,8] Understanding how to support vaccination recommendations within a community requires thoughtful intervention across these categories. Therefore, we propose a school- and community-based intervention to address vaccine education in multiple tiers.

2.2 Previous Data

Data collected in phase I of this study (focus groups; IRB # 8659) was used to inform phase II development.

2.3 Study Rationale

By engaging in a community and school-based intervention of vaccination awareness and education and overcoming barriers to vaccination, we hypothesize that this study will increase parental intention to vaccinate. In addition, this study intends to improve rates of recommended vaccination among middle school-aged children, thereby improving the lives of the children involved and, by extension, others affected through the dissemination of this research.

3.0 Inclusion and Exclusion Criteria

3.1 Inclusion Criteria

1. 18 years or older
2. Parents and guardians of children who attend a School District of Lancaster middle school
3. Individuals who read and understand English
4. Individuals with an email address
5. Individuals who speak to a study team member in-person or over the phone

3.2 Exclusion Criteria

1. Individuals who are non-English speaking
2. Parents/Guardians <18 years or older who do not have children attending a middle school in the School District of Lancaster
3. Individuals who do not have an email address
4. Individuals who plan on moving out of the Lancaster City area in the next year.

3.3 Early Withdrawal of Subjects

3.3.1 Criteria for removal from study

Once enrolled, if participants indicate that they are no longer interested in participating in the study, the study team will remove them from the communication and indicate the date and reason for withdraw in a REDCap database. Additionally, if participants who did not enroll in-person or over the phone are not able to verify their enrollment over the phone, they will be removed from the study.

3.3.2 Lost to Follow-up

If participants screen to be enrolled in the study and consent, we will attempt to contact them no more than three times to encourage them to complete Survey 1 (pre-survey). If they do not complete Survey 1, they will be considered lost to follow up. Similarly, for Survey 2 (post-survey), we will contact participants up to 3 times to remind them to complete the survey by the end of November 2019.

4.0 Recruitment Methods

4.1 Identification of subjects

Potential parent subjects for the study will be identified through partnership with the School District of Lancaster. Researchers may recruit through electronic, in-person and mailed communication methods:

- Recruitment flyer (see attached) District may provide parent names and addresses to mail recruitment flyer/support letter to parents. (Letter attached)

- Online/electronic recruitment (i.e. Website, Facebook, email with linked recruitment flyer - see attached)
- Telephone script for pre-recorded district phone calls with phone number and email for study team (see attached)
- Parent meetings – when recruiting in-person will use same telephone screen script language as indicated above

4.2 Recruitment process

The research team's extensive history of collaboration and outreach with the school community will facilitate recruitment for the study. Parents will be recruited from January to June through various methods including mailed communication, online communication and in-person recruitment. Researchers aim to recruit up to 450 parents from four School District of Lancaster middle schools. Our recruitment goal is ~113 parents from each middle school, resulting in 225 parents in the intervention group and 225 parents in the control group. Recruitment numbers will be monitored to adhere to the recruitment plan, with some leeway given among individual buildings to reach 225 parents in each intervention group.

4.3 Recruitment materials

Recruitment flyer
Website and Facebook recruitment text
Pre-recorded telephone recruitment script
In-person recruitment script (for Parent meetings) same as phone screen script

4.4 Eligibility/screening of subjects

Once provided the recruitment flyer, interested participants can call our research study team to learn more, where they will be read the phone screening document which will ensure eligibility, inform them of study procedures and provide consent information. Study team will add and complete the screener form in REDCap during the phone conversation with the potential subject. (See attached screener). Additionally, in-person recruitment will involve electronic or paper screening where they will be provided the same information as above. Electronic screening will be done through REDCap through a Penn State secured ipad. and paper screening responses will be uploaded to REDCap by a study team member.

5.0 Consent Process and Documentation

5.1 Consent Process

5.1.1 Obtaining Informed Consent

5.1.1.1 Timing and Location of Consent

The consent process will take place at the beginning of the online survey screener where potential participants will be prompted with the Summary Explanation of Research document content (or read over the phone if participant is phone screened). Participants screened over the phone will be provided the opportunity to be emailed the summary explanation of research for their records. After provided the consent information, the following language will be used:

"The following questions will help the research team determine if you are eligible to participate in this study. By answering these questions, you are consenting to allow us to use this information to pre-screen you for the study and participate in the study if deemed eligible by the screener. With your

permission we will retain this information in the locked research office. This information will not be shared with anyone outside of the research team. If you do not want us to keep your information, we will destroy it following the study."

5.1.1.2 Coercion or Undue Influence during Consent

Participants will be reminded (verbally or in writing) that their participation is voluntary and they can decline to answer any questions they do not want to answer.

5.1.2 Waiver or alteration of the informed consent requirement

N/A

5.2 Consent Documentation

5.2.1 Written Documentation of Consent

N/A

5.2.2 Waiver of Documentation of Consent (Implied consent, Verbal consent, etc.)

This research presents no more than minimal risk of harm to subjects. Therefore, we will use implied consent. All participants will receive the Summary Explanation of Research text to read prior to completing the online screener, or have it read to them if they are screened via telephone.

5.3 Consent – Other Considerations

5.3.1 Non-English Speaking Subjects

Non-English speaking is an exclusion criterion.

5.3.2 Cognitively Impaired Adults

N/A

5.3.2.1 Capability of Providing Consent

N/A

5.3.2.2 Adults Unable To Consent

N/A

5.3.2.3 Assent of Adults Unable to Consent

N/A

5.3.3 Subjects who are not yet adults (infants, children, teenagers)

5.3.3.1 Parental Permission

N/A

5.3.3.2 Assent of subjects who are not yet adults

N/A

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☒ **Not applicable, no identifiable protected health information (PHI) is accessed, used or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

☐ **Authorization will be obtained and documented as part of the consent process.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

☐ **Partial waiver is requested for recruitment purposes only (Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver is requested for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Alteration is requested to waive requirement for written documentation of authorization (verbal authorization will be obtained).** *[Complete all parts of sections 6.2 and 6.3]*

6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

6.2.1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2.1.1 Plan to protect PHI from improper use or disclosure
N/A

6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers
N/A

6.2.2 Explanation for why the research could not practicably be conducted without access to and use of PHI
N/A

6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization
N/A

6.3 Waiver or alteration of authorization statements of agreement
N/A

7.0 Study Design and Procedures

7.1 Study Design

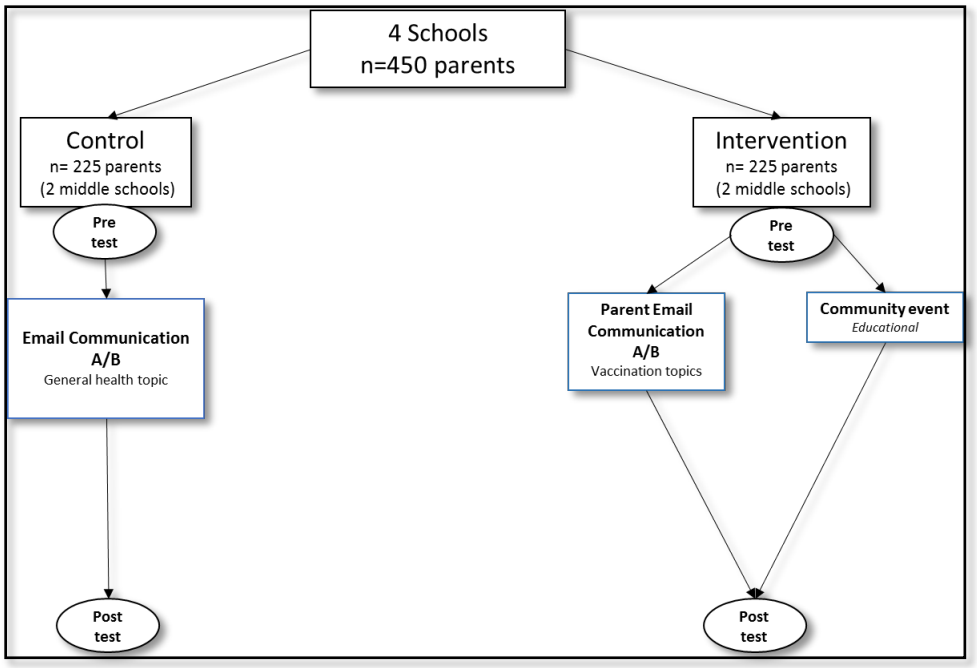
This study uses a randomized controlled trial design. We will randomize participating middle schools (n=4) to the multi-component intervention (n = 2) vs. usual care (n = 2). Randomization will take place through the use of a random number generator –each school will be assigned a number and then be assigned into control or intervention group based on random number selection. We will recruit parents form the 4 middle schools to participate in this study. Using the knowledge gained in the focus group study (IRB Study 8659), the intervention was adapted from existing evidence-based materials (CDC) and further developed to meet the specific barriers identified. The intervention components include:

community-based educational event to raise parental awareness of the importance of vaccination and emails to parents that include information designed to increase awareness and overcomes identified barriers to vaccinating their children.

We will determine program effectiveness through a pre and post intervention survey of participating parents (n=450), and will also explore parent awareness and knowledge about vaccines. We will additionally evaluate pre- and post-vaccination rates for the intervention vs. control schools as provided in aggregate level by the school district (secondary outcome).

Timeline Overview:
January-June 2019 – parent recruitment and Survey 1 (pre-test survey)
April – November2019 – intervention monthly emails/community event
November 2019– Survey 2 (post-test survey)

Consort Diagram: [*needs to be edited*]



7.2 Study Procedures

Note – Researchers are currently working with the School District of Lancaster to finalize a Memorandum of Understanding (MOU) which outlines the responsibilities of Penn State PRO Wellness and the School District of Lancaster. The MOU will be uploaded to the IRB prior to the start of study recruitment and procedures.

7.2.1 Survey 1 (Pre-test Survey)

Participants that screen "eligible" by completing the online or paper screener will be emailed Survey 1 via REDcap. The survey includes approximately 60 questions on attitudes, knowledge, and communication methods around vaccinations. Participants will be compensated with a $20 electronic gift card for completing the survey. (see attached Survey 1)

7.2.2 Parent Emails – Intervention Schools

Participants in the intervention schools will receive a total of six emails between April 2019 and November 2019 that will provide evidence-based information on vaccinations. Within the intervention group, participants will be placed into one of two groups. Group A will receive emails on vaccinations using an approach that seeks to influence parents who may be more hesitant towards vaccinations. Group B will receive emails on vaccinations using an approach that seeks to provide information to parents who are less hesitant towards vaccinations. The topic areas between the sets of emails will remain the same, however the language used to discuss vaccinations will be slightly altered. (See attached emails for Groups A and B) The purpose of this is to determine whether there is a difference in outcomes among the email groups.

The first three emails for each intervention group are included for review. Email text for the last 3 emails will be submitted for IRB review and approval prior to distribution (see table below) if study is not exempt.

	Intervention Email - Group A	Intervention Email - Group B	Control Group Emails
Email 1	Welcome to study	Welcome to study	Welcome to study
Email 2	Adolescent vaccines	Adolescent vaccines	Staying healthy in winter
Email 3	HPV vaccine	HPV vaccine	Bullying
Email 4	TBD	TBD	Healthy study habits
Email 5	TBD	TBD	Depression
Email 6	TBD	TBD	Breakfast

7.2.3 Parent Emails – Control Schools

Participants in the control schools will receive a total of six emails between April 2019 and November 2019 that will provide evidence-based information on health and wellness. (See attached email text and table above).

7.2.4 Community Event – Intervention Schools

Participants in the intervention schools will be invited to a community event located in the school's immediate community that will include information on vaccinations and wellness education. Plans for this community event, along with materials for distribution to study participants will be reviewed and approved by the IRB prior to promoting for or conducting the event.

7.2.5 Survey 2 (Post-test Survey)

All participants will be emailed Survey 2 in November 2019 which will mirror questions asked in Survey 1. Participants will be compensated with a $25 electronic gift card for completing the survey. Survey 2 will be submitted for IRB review and approval prior to distribution.

7.2.6 Analysis of Data

Dr. Kraschnewski will oversee analysis of the data. The plan for statistical analysis is included in section 8.3.

7.3 Duration of Participation

Participants will be enrolled in the study from approximately February-November 2019. They will be asked to complete a 20 minute survey in February-June and again in November 2019. During the study,

participants will receive emails to improve engagement. Emails will take 1-2 minutes to read. Participants will be invited to a community event lasting 1 – 3 hours, however the duration of their participation could be much less than that.

8.0 Subject Numbers and Statistical Plan

8.1 Number of Subjects

We intend to recruit 450 parents from four School District of Lancaster middle schools. Our recruitment goal is ~112 parents from each middle school, resulting in 225 parents in the intervention group and 225 parents in the control group.

8.2 Sample size determination

See notes described in section 8.3

8.3 Statistical methods

Primary Outcome: The intention by parents to vaccinate will be measured pre and post-intervention in the intervention and control group. The change between the pre- and post-intervention proportions will be compared within the study groups as well as between the two groups using a generalized estimating equations (GEE) model that includes factors for time, study group, and the interaction between the time and study group. Given that there is no specific power calculation for a GEE model, we will focus on a subcomponent of this analysis for the comparison of the change within the intervention group between pre and post and double the sample size to account for the control group. The comparison of the change between the pre- and post-intervention proportions could be accomplished with a McNemar's test. From previous study, we estimate that the combined proportion of discordant pairs (those parents who switch their intention from Yes to No or No to Yes between pre and post) will be 11%. If we assume a significance level of 0.05 for a two-sided McNemar's test with 80% power given a proportion of discordant pairs of 11%, the sample size needed to find a difference in pre and post proportions of 10% is 67. Accounting for a 10% drop-out rate, the total group size will be 74. If we double that to include the control group, that would be a total sample size of 148. We will recruit 450 parents to allow for additional exploratory, secondary analyses.

9.0 Confidentiality, Privacy and Data Management

See Research Data Plan Review Form

10.0 Data and Safety Monitoring Plan

Not applicable: This study does not involve more than minimal risk to subjects, and the magnitude of harm/discomfort is not greater than that ordinarily encountered in daily life.

11.0 Risks

Risks involved in participating in this study are low. The questions asked in the survey are not sensitive in nature but will be addressing personal opinions on the barriers to vaccination, community connectedness and school district involvement in the vaccination process. Loss of confidentiality is a potential risk.

12.0 Potential Benefits to Subjects and Others

12.1 Potential Benefits to Subjects

If benefits to participants exist, they may include an increase in knowledge around vaccinations or wellness. Long term benefits may include changes in health behavior to vaccinate.

12.2 Potential Benefits to Others

Potential benefits to others are long term. The results of this study may direct future resources available to influence beneficial vaccination rates.

13.0 Sharing Results with Subjects

Results will be shared with participants upon request.

14.0 Subject Stipend (Compensation) and/or Travel Reimbursements

Participants will receive compensation for survey completion. Upon completion of Survey 1, all participants will receive a $20 gift card. Upon completion of Survey 2, all participants will receive a $25 gift card.

15.0 Economic Burden to Subjects

15.1 Costs

There are no financial costs associated with participating in this research.

15.2 Compensation for research-related injury

N/A

16.0 Resources Available

16.1 Facilities and locations

The school community event with parents will take place at a community location, such as the School District of Lancaster at a time convenient to most (i.e., after normal working hours).

16.2 Feasibility of recruiting the required number of subjects

Current relationships, work and connection with the school district will allow for feasibility of recruitment through electronic and mail methods.

16.3 PI Time devoted to conducting the research

Dr. Kraschnewski will monitor the progress of participant recruitment and hold weekly meetings with research staff.

16.4 Availability of medical or psychological resources

It is not anticipated that medical or psychological resources will be needed, given that study procedures are minimal risk.

16.5 Process for informing Study Team

The investigators and project coordinator/study staff have completed their required Collaborative IRB Training Initiative (CITI) in the protection of human research subjects. The study team will be educated on the importance of confidentiality, and proper data handling and storage.

17.0 Other Approvals

17.1 Other Approvals from External Entities

Researchers are currently working with the School District of Lancaster to finalize a Memorandum of Understanding (MOU) which outlines the responsibilities of Penn State PRO Wellness and the School District of Lancaster. The MOU will be uploaded to the IRB prior to the start of study recruitment and procedures.

17.2 Internal PSU Committee Approvals

N/A

Check all that apply:

☐ Anatomic Pathology – Hershey only – Research involves the collection of tissues or use of pathologic specimens. Upload a copy of HRP-902 - Human Tissue For Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Animal Care and Use – All campuses – Human research involves animals and humans or the use of human tissues in animals

☐ Biosafety – All campuses – Research involves biohazardous materials (human biological specimens in a PSU research lab, biological toxins, carcinogens, infectious agents, recombinant viruses or DNA or gene therapy).

☐ Clinical Laboratories – Hershey only – Collection, processing and/or storage of extra tubes of body fluid specimens for research purposes by the Clinical Laboratories; and/or use of body fluids that had been collected for clinical purposes, but are no longer needed for clinical use. Upload a copy of HRP-901 - Human Body Fluids for Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Clinical Research Center (CRC) Advisory Committee – All campuses – Research involves the use of CRC services in any way.

☐ Conflict of Interest Review – All campuses – Research has one or more of study team members indicated as having a financial interest.

☐ Radiation Safety – Hershey only – Research involves research-related radiation procedures. All research involving radiation procedures (standard of care and/or research-related) must upload a copy of HRP-903 - Radiation Review Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ IND/IDE Audit – All campuses – Research in which the PSU researcher holds the IND or IDE or intends to hold the IND or IDE.

☐ Scientific Review – Hershey only – All investigator-written research studies requiring review by the convened IRB must provide documentation of scientific review with the IRB submission. The scientific review requirement may be fulfilled by one of the following: (1) external peer-review process; (2) department/institute scientific review committee; or (3) scientific review by the Clinical Research Center Advisory committee. NOTE: Review by the Penn State Hershey Cancer Institute Scientific Review Committee is required if the study involves cancer prevention studies or cancer patients, records and/or tissues. For more information about this requirement see the IRB website at: http://www.pennstatehershey.org/web/irb/home/resources/investigator

18.0 Multi-Site Research

N/A

19.0 Adverse Event Reporting

19.1 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

20.0 Study Monitoring, Auditing and Inspecting

20.1 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the Penn State quality assurance program office(s), IRB, the sponsor, and government regulatory bodies, of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

21.0 Future Undetermined Research: Data and Specimen Banking

21.1 Data and/or specimens being stored

All survey data will be administered and stored electronically through REDCap.

21.2 Location of storage

Secured folder on Penn State Hershey network, and locked filing cabinets.

21.3 Duration of storage

Data will be stored indefinitely.

21.4 Access to data and/or specimens

Access to data will be limited to project staff.

21.5 Procedures to release data or specimens

N/A

21.6 Process for returning results

N/A

22.0 References

1. Pennsylvania Department of Health. *School Immunization Summary by County.* 2016.
2. Centers for Disease Control and Prevention. *Diseases and Vaccines that Prevent them.* 2015.
3. Reiter PL, Stubbs B, Panozzo CA, Whitesell D, Brewer NT. HPV and HPV vaccine education intervention: effects on parents, healthcare staff, and school staff. *Cancer Epidemiol Biomarkers Prev.* 2011;20(11):2354-2361.
4. Berenson AB. An update on barriers to adolescent human papillomavirus vaccination in the USA. *Expert Rev Vaccines.* 2015;14(10):1377-1384.
5. Benin AL, Wisler-Scher DJ, Colson E, Shapiro ED, Holmboe ES. Qualitative analysis of mothers' decision-making about vaccines for infants: the importance of trust. *Pediatrics.* 2006;117(5):1532-1541.
6. Edwards KM, Hackell JM, Committee On Infectious Diseases TCOP, Ambulatory M. Countering Vaccine Hesitancy. *Pediatrics.* 2016;138(3).
7. SAGE Working Group dealing with vaccine hesitancy. *Strategies for addressing vaccine hesitancy - a systematic review.* October 2014.

8. SAGE Working Group dealing with vaccine hesitancy. Summary WHO SAGE conclusion and recommendation on vaccine hesitancy. January 2015.