Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH (http://www.nih.gov))

Components of Participating Organizations

National Institute of Dental and Craniofacial Research (NIDCR (https://www.nidcr.nih.gov/))

Funding Opportunity Title

NIDCR Behavioral and Social Intervention Clinical Trial Planning and Implementation Cooperative Agreement (UG3/UH3 Clinical Trial Required)

Activity Code

UG3 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=ug3&Search.x=0&Search.y=0&Search_Type=Activity)/UH3 (//grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=uh3&Search.x=0&Search.y=0&Search_Type=Activity) Exploratory/Developmental Phased Award Cooperative Agreement

Announcement Type

Reissue of PAR-21-197 (https://grants.nih.gov/grants/guide/pa-files/PAR-21-197.html)

Related Notices

See Notices of Special Interest (https://grants.nih.gov/grants/guide/NOSIs_targetingList.cfm?GuideDocID=35846) associated with this funding opportunity

- NOT-OD-23-012 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-23-012.html) Reminder: FORMS-H Grant Application Forms and Instructions Must be Used for Due Dates On or After January 25, 2023 - New Grant Application Instructions Now Available
- NOT-OD-22-190 (/grants/guide/notice-files/NOT-OD-22-190.html) - Adjustments to NIH and AHRQ Grant Application Due Dates Between September 22 and September 30, 2022
  PAR-22-068 (https://grants.nih.gov/grants/guide/pa-files/PAR-22-068.html)- Continuation or Revision of NIDCR Clinical Trial Implementation Cooperative Agreement (UH3 Clinical Trial Required)
- **October 28, 2021** - Reminder: FORMS-G Grant Application Forms & Instructions Must be Used for Due Dates On or After January 25, 2022 - New Grant Application Instructions Now Available. See Notice NOT-OD-22-018 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-018.html).
- **September 13, 2021** - Updates to the Non-Discrimination Legal Requirements for NIH Recipients. See Notice NOT-OD-21-181 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-181.html).
- **August 5, 2021** - New NIH "FORMS-G" Grant Application Forms and Instructions Coming for Due Dates on or after January 25, 2022. See Notice NOT-OD-21-169 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-169.html)
- **August 5, 2021** - Update: Notification of Upcoming Change in Federal-wide Unique Entity Identifier Requirements. See Notice NOT-OD-21-170 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-170.html)
- **April 20, 2021** - Expanding Requirement for eRA Commons IDs to All Senior/Key Personnel. See Notice NOT-OD-21-109 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-109.html)
- **September 23, 2021** - NIDCR Guidance on Applications for Investigator-Initiated Clinical Trials. See Notice NOT-DE-21-014 (//grants.nih.gov/grants/guide/notice-files/NOT-DE-21-014.html)

Funding Opportunity Announcement (FOA) Number

PAR-21-317

Companion Funding Opportunity

None

Number of Applications

See Section III. 3. Additional Information on Eligibility.

Assistance Listing Number(s)

93.121

Funding Opportunity Purpose

The purpose of this Funding Opportunity Announcement (FOA) is to encourage UG3/UH3 phased cooperative agreement research applications to plan and implement behavioral and social intervention clinical trials. Studies appropriate for this announcement include clinical trials to develop and test behavior change interventions related to dental, oral, or craniofacial conditions. Awards made under this FOA will initially support a milestone-driven planning phase (UG3) for up to 2 years, with possible transition to a clinical trial implementation phase (UH3) of up to five years. Only UG3 projects that have met the scientific milestones and feasibility requirements may transition to the UH3 phase. The UG3/UH3 application must be submitted as a single application, following the instructions described in this FOA. The UG3 phase will permit both scientific and operational planning activities. Scientific planning activities include small-scale data collection to assess the feasibility and/or acceptability of a planned behavioral or social intervention and associated study procedures (e.g., acceptability of study content or mode of delivery; feasibility of proposed data collection procedures; preliminary testing of intervention training and fidelity monitoring procedures). Operational planning activities include, at a minimum, development of: the final clinical protocol; the intervention manual or equivalent; the data management system and other tools for data and quality management, safety and operational oversight plans; recruitment and retention strategies; and other essential documents. The UH3 phase will support the conduct of investigator-initiated intervention research at all stages, from early mechanistic research and intervention development (e.g., Stages 0/ I) through implementation and cost-effectiveness research (Stages IV/V).

Key Dates

Posted Date

September 01, 2021

Open Date (Earliest Submission Date)

August 09, 2021

Letter of Intent Due Date(s)

30 days prior to the application date

The following table includes NIH standard due dates (https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/due-dates.htm) marked with an asterisk.

Application Due Dates			Review and Award Cycles		
New	Renewal / Resubmission / Revision (as allowed)	AIDS	Scientific Merit Review	Advisory Council Review	Earliest Start Date
Not Applicable	Not Applicable	September 07, 2021 *	November 2021	January 2022	April 2022
October 06, 2021	November 08, 2021	January 07, 2022 *	March 2022	May 2022	July 2022

Application Due Dates			Review and Award Cycles		
New	Renewal / Resubmission / Revision (as allowed)	AIDS	Scientific Merit Review	Advisory Council Review	Earliest Start Date
February 08, 2022	March 08, 2022	May 07, 2022 *	July 2022	October 2022	December 2022
June 07, 2022	July 07, 2022	September 07, 2022 *	November 2022	January 2023	April 2023
October 04, 2022	November 04, 2022	January 07, 2023 *	March 2023	May 2023	July 2023
February 07, 2023	March 07, 2023	May 07, 2023 *	July 2023	October 2023	December 2023
June 06, 2023	July 06, 2023	September 07, 2023 *	November 2023	January 2024	April 2024
October 03, 2023	November 03, 2023	January 07, 2024 *	March 2024	May 2024	July 2024
February 06, 2024	March 06, 2024	May 07, 2024 *	July 2024	October 2024	December 2024

All applications are due by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on the listed date(s).

Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

Expiration Date

May 08, 2024

Due Dates for E.O. 12372

Not Applicable

Required Application Instructions

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000), except where instructed to do otherwise (in this FOA or in a Notice from NIH Guide for Grants and Contracts (//grants.nih.gov/grants/guide/)).

Conformance to all requirements (both in the Application Guide and the FOA) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions.

Applications that do not comply with these instructions may be delayed or not accepted for review.

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the NIH ASSIST system to prepare, submit and track your application online.

   Apply Online Using ASSIST

2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and eRA Commons (https://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.

3. Use Grants.gov (https://www.grants.gov/web/grants/applicants/download-application-package.html#search=true&oppNum=PAR-21-317) Workspace to prepare and submit your application and eRA Commons

(http://public.era.nih.gov/commons/) to track your application.

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Part 2. Full Text of Announcement

Section I. Funding Opportunity Description

Purpose

The purpose of this FOA is to provide support for planning and implementing well-designed, rigorously conducted behavioral or social intervention studies relevant to dental, oral, and craniofacial health. This FOA will support a broad range of intervention research projects, for participants of any age or developmental stage; for any dental, oral, or craniofacial condition with public health significance (e.g., dental caries, periodontal disease, craniofacial anomalies, oral cancers, salivary gland dysfunctions, oral mucosal diseases, orofacial pain); for a range of outcomes (e.g., direct intervention with patients to improve outcomes, intervention with practitioners to improve care, intervention on health systems to improve continuity of care); for stakeholders from different sectors (e.g., patients, families, social networks and communities, practitioners, care-delivery systems, professional organizations, policy-makers); and for behavioral or social intervention research at all stages, from early mechanistic research and intervention development (e.g., Stages 0/I) through implementation and health services research (Stages IV/V).

This FOA may also support basic behavioral experimental studies with humans that are considered clinical trials based on the NIH's revised clinical trial definition (please see Clinical Trial Requirements for Grants and Contracts (https://grants.nih.gov/policy/clinical-trials.htm) for guidance). Such studies are sometimes referred to as Basic Experimental Studies involving Humans (BESH), Stage 0 studies, Type 1 translation studies, or basic mechanistic studies. These studies now meet the NIH definition of a clinical trial, and so are appropriate for this FOA. Examples of such studies include experimental manipulation or laboratory-based studies in which behavioral or social probes are used to evoke participants' responses (e.g., emotional regulation, dental fear, social norms, pain intensity) under varied conditions, and for which proximal health-related behavioral or social outcomes—but not necessarily disease outcomes--are assessed.

This FOA does not support the testing of drugs, devices or biologics regulated by the FDA. Applicants interested in conducting such trials are encouraged to contact an NIDCR Program Official and to visit the NIDCR Clinical Trials Program website (http://www.nidcr.nih.gov/Research/DER/ClinicalResearch/ClinTrials.htm).

Background

The NIDCR behavioral and social sciences research program supports research consistent with two trans-NIH frameworks for approaching behavior change: the NIH Stage Model of intervention development, and the NIH Common Fund's Science of Behavior Change experimental medicine approach. Both frameworks emphasize the importance of understanding mechanisms of behavior change, as the building blocks of a cumulative science of behavior change, and as the essential elements of developing interventions and programs that can be adapted for sustainable delivery in their target settings.

The NIH Stage Model of Intervention Development

The Stage Model provides a framework for describing where an intervention is in the developmental pipeline, and specifies research activities appropriate for different stages of intervention development. For instance, the Stage Model describes different research activities that are typical in early intervention-development studies than are typical in effectiveness or implementation studies. The Stage Model also describes activities expected in all stages of intervention development, including the specification of hypothesized

mechanisms of action of the intervention, and the inclusion of fidelity monitoring activities, although use of fidelity data may change with the stage of intervention development. The NIH Stage Model provides a common language that facilitates discussion of intervention development research by applicants, reviewers, and funders. Applications for NIDCR support of clinical trials research are expected to identify research proposals using the NIH Stage Model framework, described in detail here (https://www.nia.nih.gov/research/dbsr/stage-model-behavioral-intervention-development).

The NIH Common Fund's Science of Behavior Change Program

The NIDCR behavioral and social sciences clinical research and clinical trials program also draws on the mechanisms-focused, experimental medicine approach encouraged by the NIH Common Fund's Science of Behavior Change (SOBC) program. The experimental medicine approach to behavior change research encourages clear a priori specification of the intended behavioral and social target(s) of an intervention, and methods that test the degree to which an experimental manipulation or intervention engaged those targets. The SOBC program describes 4 steps involved in the experimental medicine approach: 1) identifying one or more hypothesized intervention targets; 2) attempting to engage the target(s) through experimentation or intervention; 3) measuring the degree to which the experimental manipulation or intervention actually engaged the hypothesized target(s); and 4) testing the degree to which target engagement produces the desired change in health behaviors or clinical outcomes. For more information about the SOBC program, please visit the Science of Behavior Change website (https://scienceofbehaviorchange.org/). The purposes of this approach are to increase the contributions of each intervention study to a cumulative science of behavior change, to allow for mechanisms-based design of DOC behavior change interventions, and to facilitate testing of whether mechanisms-based interventions improve DOC health. Applications for NIDCR support of clinical trials research are expected to incorporate an experimental medicine approach. Applications that do not include an experimental medicine approach to behavior change must provide a strong justification for not doing so.

Scope of this UG3/UH3 FOA

Clinical Trial Planning Phase (UG3)

The UG3 award will provide up to 2 years of support for scientific and operational planning activities necessary to conduct the clinical trial. The UG3 planning phase should incorporate all activities required—and not yet completed--to prepare for conduct of a subsequent clinical trial (i.e., intervention or basic experimental study with humans).

When not yet already completed, at a minimum, UG3 planning activities should include the following activities, included as UG3 milestones:

Measurement of target engagement: Applications should include plans to measure the hypothesized intervention target(s) and the degree to which the intervention engaged (e.g., changed) the target(s). For instance, if a study intends to test an intervention meant to increase self-efficacy for oral hygiene, the UG3 phase should demonstrate that the study changes in self-efficacy in response to the intervention can be accurately measured.

Acceptability and feasibility of the study intervention(s) or procedures: If acceptability and/or feasibility of the intervention has not yet been established in the study population, the UG3 phase should propose activities necessary to ensure acceptability and feasibility. Relevant Stage I activities may include consultation with stakeholders, delivery of the intervention to gather feedback from participants and providers, and/or other activities. In addition to the acceptability and feasibility of the study intervention(s), planning activities should establish the acceptability and feasibility of proposed study procedures. If not already established, the UG3 planning phase should include pilot-testing of study procedures, such as participant recruitment, methods of data collection, interventionist training procedures, and other key aspects of study conduct.

Finalization of agreements for use of resources available within CTSAs, practice-based research networks, patient, registries, etc., as applicable.

Finalization of the clinical protocol and other required study documentation: To ensure adherence to the principles of Good Clinical Practice (International Conference on Harmonisation (ICH) E6 (https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf)), required documentation will include a clinical protocol, clinical quality management plan, data quality management plan, and participant consent/assent forms and procedures. For some studies, additional documentation may be required; for instance, a Manual of Operations is typically required for multi-site studies where site-level procedures may vary. Applications should describe plans for developing relevant study documentation that will require NIDCR review and approval before progressing to the UH3 phase.

Development of fidelity monitoring procedures: Monitoring the degree to which a study intervention is delivered as it was intended to be delivered (i.e., with fidelity) is expected at every stage of intervention development; although the way fidelity data is used differs depending on the stage of intervention development and the associated research question(s). For instance, in stages of intervention development where efficacy is being established, fidelity monitoring is used to ensure intervention fidelity, and to identify interventionists who may need re-training. For studies in later stages of intervention development where efficacy has already been established, and research questions concern effectiveness or implementation, fidelity data may be used to identify challenges to intervention delivery. If methods for monitoring the fidelity of intervention delivery are not already established, UG3 planning activities should include the development of these methods.

Completion of the data management system

Finalization of all materials required for regulatory approvals (IRB and applicable oversight committees)

Finalization of any other documents necessary to implement the trial

Clinical Trial Implementation Phase (UH3)

The UH3 award will provide up to 5 years of support to conduct the clinical trial in accordance with activities planned in the UG3 phase, and is contingent upon successful completion of the UG3 milestones. The NIDCR expects clinical trials supported during the UH3 phase to be hypothesis driven, milestone-defined, and to contribute meaningfully to a cumulative science of behavior change within the research mission of the NIDCR. The clinical trial must meet all applicable NIH, and Office of Human Research Protections (OHRP) policy requirements.

At a minimum, UH3 activities should include the following operational activities, expressed as UH3 milestones:

- Completion of regulatory approvals and site activation
- Registration of clinical trial in ClinicalTrials.gov
- Enrollment of the first subject
- If applicable, enrollment and randomization of 25%, 50%, 75%, and 100% of the projected study sample
- Completion of data collection
- Completion of primary study analyses
- Completion of the final study report

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Cooperative Agreement: A support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this FOA.

Application Types Allowed

New
Renewal
Resubmission
Revision

The OER Glossary (//grants.nih.gov/grants/guide/url_redirect.htm?id=11116) and the SF424 (R&R) Application Guide provide details on these application types. Only those application types listed here are allowed for this FOA.

Clinical Trial?

Required: Only accepting applications that propose clinical trial(s).

Need help determining whether you are doing a clinical trial? (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370)

Funds Available and Anticipated Number of Awards

The number of awards is contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications.

Award Budget

Application budgets are limited to less that $200,000 in direct costs per year for the two-year UG3 phase, or less than $300,000 in direct costs for a one-year UG3. Application budgets are not limited in the UH3 phase but need to reflect the actual needs of the proposed project.

Award Project Period

The total project period may not exceed two years for the UG3 phase and five years for the UH3 phase.

NIH grants policies as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made from this FOA.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations

Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

The following types of Higher Education Institutions are always encouraged to apply for NIH support as Public or Private Institutions of Higher Education:

- Hispanic-serving Institutions
- Historically Black Colleges and Universities (HBCUs)
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions
- Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Local Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized)

Federal Governments

- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

Other

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations

Foreign Institutions

Non-domestic (non-U.S.) Entities (Foreign Institutions) **are not** eligible to apply.

Non-domestic (non-U.S.) components of U.S. Organizations **are not** eligible to apply.

Foreign components, as defined in the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11118), **are** allowed.

Required Registrations

Applicant organizations

Applicant organizations must complete and maintain the following registrations as described in the SF 424 (R&R) Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of

Grant Applications (//grants.nih.gov/grants/guide/notice-files/NOT-OD-15-039.html) states that failure to complete registrations in advance of a due date is not a valid reason for a late submission.

- Dun and Bradstreet Universal Numbering System (DUNS) (http://fedgov.dnb.com/webform) - All registrations require that applicants be issued a DUNS number. After obtaining a DUNS number, applicants can begin both SAM and eRA Commons registrations. The same DUNS number must be used for all registrations, as well as on the grant application.
- System for Award Management (SAM) (https://www.sam.gov/portal/public/SAM/) – Applicants must complete and maintain an active registration, which requires renewal at least annually. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.
    - NATO Commercial and Government Entity (NCAGE) Code (//grants.nih.gov/grants/guide/url_redirect.htm?id=11176) – Foreign organizations must obtain an NCAGE code (in lieu of a CAGE code) in order to register in SAM.
- eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Applicants must have an active DUNS number to register in eRA Commons. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration, but all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- Grants.gov – Applicants must have an active DUNS number and SAM registration in order to complete the Grants.gov registration.

Program Directors/Principal Investigators (PD(s)/PI(s))

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with his/her organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the SF424 (R&R) Application Guide.

2. Cost Sharing

This FOA does not require cost sharing as defined in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11126)

3. Additional Information on Eligibility

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time. This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see NOT-OD-11-101 (//grants.nih.gov/grants/guide/notice-files/NOT-OD-11-101.html)).

Section IV. Application and Submission Information

1. Requesting an Application Package

The application forms package specific to this opportunity must be accessed through ASSIST, Grants.gov Workspace or an institutional system-to-system solution. Links to apply using ASSIST or Grants.gov Workspace are available in Part 1 of this FOA. See your administrative office for instructions if you plan to use an institutional system-to-system solution.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide (//grants.nih.gov/grants/guide/url_redirect.htm?id=12000) except where instructed in this funding opportunity announcement to do otherwise. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

Letter of Intent

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

By the date listed in Part 1. Overview Information, prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity

The letter of intent should be sent to:

Yasaman Shirazi, PhD
Telephone: 301-594-5593
Email: yasaman.shirazi@nih.gov (mailto:yasaman.shirazi@nih.gov?)

Page Limitations

All page limitations described in the SF424 Application Guide and the Table of Page Limits (//grants.nih.gov/grants/guide/url_redirect.htm?id=11133) must be followed.

Instructions for Application Submission

Note: Effective for due dates on or after January 25, 2023, the Data Management and Sharing (DMS) Plan will be attached in the Other Plan(s) attachment in FORMS-H and subsequent application forms packages. For due dates on or before January 24, 2023, the Data Sharing Plan and Genomic Data Sharing Plan GDS) will continue to be attached in the Resource Sharing Plan attachment in FORMS-G application forms packages.

The following section supplements the instructions found in the SF424 (R&R) Application Guide and should be used for preparing an application to this FOA.

SF424(R&R) Cover

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Project/Performance Site Locations

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Other Project Information

All instructions in the SF424 (R&R) Application Guide must be followed.

SF424(R&R) Senior/Key Person Profile

All instructions in the SF424 (R&R) Application Guide must be followed.

R&R Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

R&R Subaward Budget

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS 398 Cover Page Supplement

All instructions in the SF424 (R&R) Application Guide must be followed.

PHS 398 Research Plan

Other Plan(s):

Note: Effective for due dates on or after January 25, 2023, the Data Management and Sharing Plan will be attached in the Other Plan(s) attachment in FORMS-H and subsequent application forms packages. For due dates on or before January 24, 2023, the Data

Sharing Plan and Genomic Data Sharing Plan GDS) will continue to be attached in the Resource Sharing Plan attachment in FORMS-G application forms packages.

All applicants planning research (funded or conducted in whole or in part by NIH) that results in the generation of scientific data are required to comply with the instructions for the Data Management and Sharing Plan. All applications, regardless of the amount of direct costs requested for any one year, must address a Data Management and Sharing Plan.

All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

Significance: The significance of the proposed trial must be stated clearly. It should be supported by the following:

- A compelling argument should be presented of how the proposed study will contribute to a cumulative science of behavior change, and/or advance clinical practice. The application should describe any novel theoretical concepts, approaches or methodologies, instrumentation or interventions that will be used in the proposed clinical trial.
- For Stage III-V trials (e.g., effectiveness and implementation studies), the application should describe a strong rationale for the generalizability of potential findings to US populations.
- The application should present a compelling rationale for the need to conduct the study, as well as the timeliness of the study. This may include preliminary data, clinical and/or preclinical studies, information in the literature, or knowledge of behavioral, social or biological mechanisms.

Research Strategy: The Research Strategy should provide justification for the trial, and should include:

- A summary of the clinical trial's objectives describing the scientific rationale and clinical need for the trial, and an assessment of the previous preclinical and clinical studies and their quality.
- The translation of the clinical question(s) into a statistical hypothesis or hypotheses.
- A compelling rationale for the selected study population, including justification for exclusions of children or other age groups such as those 65 years and older. Applications should describe the degree to which the target population is available. Applications should propose plans for recruitment, outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up that are appropriate to ensure robust data collection.
- A discussion of potential ethical issues, including processes for obtaining informed consent or assent, and plans for assessing differences in the intervention effect due to sex/gender, race/ethnicity, and age.
- Plans for data management and quality control of data; planned analyses and statistical methods; and other relevant aspects of data management and analyses to ensure rigorous and successful completion of the study aims.
- An overview of the proposed study design that should justify the following:
    - Primary Purpose (e.g., Treatment, Prevention, Implementation, etc.)
    - Stage of Intervention Research (e.g., Stage I Early intervention development or adaptation to Stage V Implementation science).
    - The justification for the selected Stage. For example, there should be adequate evidence from previous studies to support specific Stage-I adaptations to an existing intervention for a new population or setting. Or there should be sufficient evidence from previous trials that an intervention is efficacious before conducting a Stage V Implementation study.
    - The scientific rationale and justification for the selection of an intervention's "dose" or number of sessions, frequency, and modality of administration.
    - Rationale for the intervention and the behavioral or social targets it is hypothesized to engage, at a level of specificity that makes the rationale falsifiable.
    - Plans for testing whether the intervention engaged the hypothesized target(s), as well as efficacy or effectiveness.
    - Where applicable, plans for testing and/or ensuring that the study procedures and intervention(s) are feasible and acceptable to the target population and interventionists.
    - Plans for monitoring and/or ensuring fidelity of intervention delivery.
    - Rationale for the intervention study design (e.g., cluster randomized controlled trial, multiple baseline, adaptive/SMART design, factorial) and allocation method.
    - Where applicable, methods to ensure masking or to minimize bias if complete masking is not possible or feasible.
    - Justification for selecting the study variables, including a specific explanation of the hypothesized relevance of each to the clinical and statistical hypothesis being tested (i.e., the hypothesized role each variable plays in the causal chain; specification of variables as hypothesized moderators, mediators, or outcomes).
    - A discussion of potential biases or challenges in the trial and how they will be addressed and minimized.

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide.

The following modifications also apply:

- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan. Applicants are encouraged to consider following the principles of open science, including making study materials freely accessible, pre-registering the study design and analysis plan, and posting study data in a public repository as appropriate.

Appendix:

Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide.

The NIH announced a policy limiting allowable appendix materials (NOT-OD-17-098 (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-098.html)); however this FOA allows specific materials to be included as appendices that are otherwise disallowed by the general policy. Applications may include as appendices the following materials: focus group guides, structured interview schedules, questionnaires or surveys with instructions, observational coding systems, fidelity monitoring checklists and rating tools, and draft or sample intervention manuals. These appendices should not include results or data from previous uses of the materials.

PHS Human Subjects and Clinical Trials Information

When involving human subjects research, clinical research, and/or NIH-defined clinical trials (and when applicable, clinical trials research experience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:

If you answered “Yes” to the question “Are Human Subjects Involved?” on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the SF424 (R&R) Application Guide must be followed.

For projects that involve more than one clinical trial during the UH3 phase, add a separate study record for each proposed clinical trial. The research strategy section of the application should justify the specifics of each proposed trial, such as the proposed intervention and its target(s), stage of intervention research, and characteristics of the study population.

Section 2 - Study Population Characteristics

2.7 Study Timeline and Milestone Plan

The filename "Study Timeline and Milestone Plan" should be used to name this attachment, which should include both the Study Timeline and Milestone Plan. The Study Timeline should describe the proposed trial's schedule of events, capturing time points and planned activities at study visits or data collection events. Applicants are encouraged to use the Schematic of Study Design (Section 4) in the NIDCR Interventional Protocol Template. (https://www.nidcr.nih.gov/research/human-subjects-research/toolkit-and-education-materials/interventional-studies/planning-and-start-up)

The study Study Timeline should include acceptable time windows for each activity.

Applications that lack the Study Timeline are considered incomplete and will be withdrawn without peer review.

Milestone Plan. The Milestone Plan must describe separate milestones for the UG3 and UH3 phases.

Milestones to be completed during the UG3 phase should include, as applicable:

- Measurement of intervention target engagement;
- Collection and analysis of any data to assess the acceptability of the study intervention(s) or other procedures to the target population and feasibility of operations in the target setting;
- Finalization of agreements for use of resources available within CTSAs, practice-based research networks, patient registries, etc.;
- Finalization of the clinical protocol and other required study documentation;
- Development of fidelity monitoring procedures;
- Completion of the data management system;
- Finalization of all materials required for regulatory approvals (IRB and applicable oversight committees);
- Finalization of any other documents necessary to implement the trial.

Milestones to be completed during the UH3 phase should include:

- Completion of regulatory approvals and site activation;
- Registration of clinical trial in ClinicalTrials.gov.
- Enrollment of the first subject;
- If applicable, enrollment and randomization, of 25%, 50%, 75% and 100% of the projected study population;
- Completion of data collection;
- Completion of primary study analyses;
- Completion of final study report.

Applications that lack the Milestone Plan are considered incomplete and will be withdrawn without peer review.

Section 3 - Protection and Monitoring Plans

3.3 Data and Safety Monitoring Plan

The Data and Safety Monitoring Plan should include a description of data monitoring activities, such as:

- Plans to ensure that validated systems and controls are in place to assure the integrity of the clinical trial data being collected;
- Proposed methods and systems for data collection (e.g., Case Report Forms/CRFs), data entry, data verification and data validation. Describe the data query process and frequencies and any planned mitigation strategies in the event of noncompliance;
- The process for locking the final trial datasets for analysis.

Do not name members of any oversight board in the application. The NIDCR will appoint members of any oversight committees after consultation with the clinical trial investigator team.

Delayed Onset Study

Note: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).All instructions in the SF424 (R&R) Application Guide must be followed.

The delayed onset designation does not apply to this FOA. While human subjects recruitment may not start immediately after successful transition from the UG3 to the UH3, this is considered a delayed start study, and not a delayed onset study.

PHS Assignment Request Form

All instructions in the SF424 (R&R) Application Guide must be followed.

3. Unique Entity Identifier and System for Award Management (SAM)

See Part 1. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov.

4. Submission Dates and Times

Part I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or Federal holiday (https://grants.nih.gov/grants/guide/url_redirect.html?id=82380), the application deadline is automatically extended to the next business day.

Organizations must submit applications to Grants.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11128) (the online portal to find and apply for grants across all Federal agencies). Applicants must then complete the submission process by tracking the status of the application in the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123), NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the NIH Policy on Late Application Submission.

Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

Information on the submission process and a definition of on-time submission are provided in the SF424 (R&R) Application Guide.

5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to intergovernmental review. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11142)

6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Pre-award costs are allowable only as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11143).

7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the SF424 (R&R) Application Guide. Paper applications will not be accepted.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit How to Apply – Application Guide (https://grants.nih.gov/grants/how-to-apply-application-guide.html). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Dealing with System Issues

(https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm) guidance. For assistance with application submission, contact the Application Submission Contacts in Section VII.

Important reminders:

All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF424(R&R) Application Package. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH. See Section III of this FOA for information on registration requirements.

The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management. Additional information may be found in the SF424 (R&R) Application Guide.

See more tips (//grants.nih.gov/grants/guide/url_redirect.htm?id=11146) for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review, NIH. Applications that are incomplete or non-compliant will not be reviewed.

Requests of $500,000 or more for direct costs in any year

Applicants requesting $500,000 or more in direct costs in any year (excluding consortium F&A) must contact a Scientific/ Research Contact at least 6 weeks before submitting the application and follow the Policy on the Acceptance for Review of Unsolicited Applications that Request $500,000 or More in Direct Costs as described in the SF424 (R&R) Application Guide.

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in the policy (//grants.nih.gov/grants/guide/url_redirect.htm?id=82299). Any instructions provided here are in addition to the instructions in the policy.

Section V. Application Review Information

1. Criteria

Note: Effective for due dates on or after January 25, 2023, the Data Sharing Plan and Genomic Data Sharing Plan (GDS) as part of the Resource Sharing Plan will not be evaluated at time of review.

Only the review criteria described below will be considered in the review process. Applications submitted to the NIH in support of the NIH mission (//grants.nih.gov/grants/guide/url_redirect.htm?id=11149) are evaluated for scientific and technical merit through the NIH peer review system.

A proposed Clinical Trial application may include study design, methods, and intervention that are not by themselves innovative but address important questions or unmet needs. Additionally, the results of the clinical trial may indicate that further clinical development of the intervention is unwarranted or lead to new avenues of scientific investigation.

Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria and additional review criteria (as applicable for the project proposed).

Scored Review Criteria

Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Significance

Does the project address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

For this particular announcement:

Will the results of this study contribute to a cumulative science of behavior, social, or organizational change, above and beyond demonstrating that an intervention produced an effect for a specific community or population?

Are the scientific rationale and need for a clinical trial to test the proposed hypothesis or intervention well supported by preliminary data, clinical and/or preclinical studies, or information in the literature or knowledge of biological mechanisms? For trials focusing on

clinical or public health endpoints, is this clinical trial necessary for testing the safety, efficacy or effectiveness of an intervention that could lead to a change in clinical practice, community behaviors or health care policy? For trials focusing on mechanistic, behavioral, physiological, biochemical, or other biomedical endpoints, is this trial needed to advance scientific understanding?

Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

With regard to the proposed leadership for the project, do the PD/PI(s) and key personnel have the expertise, experience, and ability to organize, manage and implement the proposed clinical trial and meet milestones and timelines? Do they have appropriate expertise in study coordination, data management and statistics? For a multicenter trial, is the organizational structure appropriate and does the application identify a core of potential center investigators and staffing for a coordinating center?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Does the design/research plan include innovative elements, as appropriate, that enhance its sensitivity, potential for information or potential to advance scientific knowledge or clinical practice?

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?

For this particular announcement:

Are the proposed research activities described in terms of Stage of intervention research, and are the activities appropriate and justified given the Stage of intervention research?

Are the scientific rationale and justification compelling for the selection of an intervention's "dose" or number of sessions, frequency and modality of administration?

Is there a strong rationale for the intervention and the behavioral or social target(s) it is hypothesized to engage? Is the rationale described at a level of specificity that makes it potentially falsifiable? Are there sufficient plans for testing and/or ensuring intervention target engagement?

Where applicable, are there rigorous plans for testing and/or ensuring that the study procedures and study intervention(s) are feasible and acceptable to the target population and interventionists?

Does the application propose acceptable plans for monitoring and/or ensuring fidelity of intervention delivery?

Does the application adequately justify the selection of study variables, including a specific explanation of the hypothesized relevance of each to the clinical and statistical hypothesis being tested (i.e., the hypothesized role each variable plays in the causal chain; specification of variables as hypothesized moderators, mediators, or outcomes)?

Does the application adequately address the following, if applicable

Study Design

Is the study design justified and appropriate to address primary and secondary outcome variable(s)/endpoints that will be clear, informative and relevant to the hypothesis being tested? Is the scientific rationale/premise of the study based on previously well-

designed preclinical and/or clinical research? Given the methods used to assign participants and deliver interventions, is the study design adequately powered to answer the research question(s), test the proposed hypothesis/hypotheses, and provide interpretable results? Is the trial appropriately designed to conduct the research efficiently? Are the study populations (size, gender, age, demographic group), proposed intervention arms/dose, and duration of the trial, appropriate and well justified?

Are potential ethical issues adequately addressed? Is the process for obtaining informed consent or assent appropriate? Is the eligible population available? Are the plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection? Are the planned recruitment timelines feasible and is the plan to monitor accrual adequate? Has the need for randomization (or not), masking (if appropriate), controls, and inclusion/exclusion criteria been addressed? Are differences addressed, if applicable, in the intervention effect due to sex/gender and race/ethnicity?

Are the plans to standardize, assure quality of, and monitor adherence to, the trial protocol and data collection or distribution guidelines appropriate? Is there a plan to obtain required study agent(s)? Does the application propose to use existing available resources, as applicable?

Data Management and Statistical Analysis

Are planned analyses and statistical approach appropriate for the proposed study design and methods used to assign participants and deliver interventions? Are the procedures for data management and quality control of data adequate at clinical site(s) or at center laboratories, as applicable? Have the methods for standardization of procedures for data management to assess the effect of the intervention and quality control been addressed? Is there a plan to complete data analysis within the proposed period of the award?

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

If proposed, are the administrative, data coordinating, enrollment and laboratory/testing centers, appropriate for the trial proposed?

Does the application adequately address the capability and ability to conduct the trial at the proposed site(s) or centers? Are the plans to add or drop enrollment centers, as needed, appropriate?

If international site(s) is/are proposed, does the application adequately address the complexity of executing the clinical trial?

If multi-sites/centers, is there evidence of the ability of the individual site or center to: (1) enroll the proposed numbers; (2) adhere to the protocol; (3) collect and transmit data in an accurate and timely fashion; and, (4) operate within the proposed organizational structure?

Additional Review Criteria

As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items.

For this particular announcement:

Are appropriate, evaluative milestones clearly defined for the UG3 and UH3 phases? Does the application provide a compelling proposal that the study is likely to meet these milestones within the proposed project period?

Study Timeline

Is the study timeline described in detail, taking into account start-up activities, the anticipated rate of enrollment, and planned follow-up assessment? Is the projected timeline feasible and well justified? Does the project incorporate efficiencies and utilize existing resources (e.g., CTSAs, practice-based research networks, electronic medical records, administrative database, or patient registries) to increase the efficiency of participant enrollment and data collection, as appropriate?

Are potential challenges and corresponding solutions discussed (e.g., strategies that can be implemented in the event of enrollment shortfalls)?

Protections for Human Subjects

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the Guidelines for the Review of Human Subjects (//grants.nih.gov/grants/guide/url_redirect.htm?id=11175).

Inclusion of Women, Minorities, and Individuals Across the Lifespan

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of individuals of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research (//grants.nih.gov/grants/guide/url_redirect.htm?id=11174).

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals. Reviewers will assess the use of chimpanzees as they would any other application proposing the use of vertebrate animals. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section (//grants.nih.gov/grants/guide/url_redirect.htm?id=11150).

Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Resubmissions

For Resubmissions, the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Renewals

For Renewals, the committee will consider the progress made in the last funding period.

Revisions

For Revisions, the committee will consider the appropriateness of the proposed expansion of the scope of the project. If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the committee, then the committee will consider whether the responses to comments from the previous scientific review group are adequate and whether substantial changes are clearly evident.

Additional Review Considerations

Note: Effective for due dates on or after January 25, 2023, the Data Sharing Plan and Genomic Data Sharing Plan (GDS) as part of the Resource Sharing Plan will not be evaluated at time of review.

As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact score.

Applications from Foreign Organizations

Not Applicable

Select Agent Research

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans

Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: (1) Data Sharing Plan (//grants.nih.gov/grants/guide/url_redirect.htm?id=11151); (2) Sharing Model

Organisms (//grants.nih.gov/grants/guide/url_redirect.htm?id=11152); and (3) Genomic Data Sharing Plan (GDS) (//grants.nih.gov/grants/guide/url_redirect.htm?id=11153).

Authentication of Key Biological and/or Chemical Resources:

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support

Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by the National Institute of Dental and Craniofacial Research, in accordance with NIH peer review policy and procedures (//grants.nih.gov/grants/guide/url_redirect.htm?id=11154), using the stated review criteria (file:///C:/Users/mckenziene/AppData/Local/Microsoft/Windows/INetCache/Content.Outlook/13V4QPZR/Research%20Draft.doc#_1._Criteria). Assignment to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications will receive a written critique.

Applications may undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.

Applications will be assigned on the basis of established PHS referral guidelines to the appropriate NIH Institute or Center. Applications will compete for available funds with all other recommended applications submitted in response to this FOA. Following initial peer review, recommended applications will receive a second level of review by the appropriate national Advisory Council or Board. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

3. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the eRA Commons (//grants.nih.gov/grants/guide/url_redirect.htm?id=11123). Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.
Information regarding the disposition of applications is available in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11156).

Section VI. Award Administration Information

1. Award Notices

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157).

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA signed by the grants management officer is the authorizing document and will be sent via email to the recipient's business official.

Recipients must comply with any funding restrictions described in Section IV.5. Funding Restrictions. Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

Any application awarded in response to this FOA will be subject to terms and conditions found on the Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158) website. This includes any recent legislation and policy applicable to awards that is highlighted on this website.

Individual awards are based on the application submitted to, and as approved by, the NIH and are subject to the IC-specific terms and conditions identified in the NoA.

ClinicalTrials.gov: If an award provides for one or more clinical trials. By law (Title VIII, Section 801 of Public Law 110-85), the "responsible party" must register and submit results information for certain “applicable clinical trials” on the ClinicalTrials.gov Protocol Registration and Results System Information Website (https://register.clinicaltrials.gov (https://register.clinicaltrials.gov/)). NIH expects registration and results reporting of all trials whether required under the law or not. For more information, see https://grants.nih.gov/policy/clinical-trials/reporting/index.htm (https://grants.nih.gov/policy/clinical-trials/reporting/index.htm)

Institutional Review Board or Independent Ethics Committee Approval: Recipient institutions must ensure that all protocols are reviewed by their IRB or IEC. To help ensure the safety of participants enrolled in NIH-funded studies, the recipient must provide NIH copies of documents related to all major changes in the status of ongoing protocols.

Data and Safety Monitoring Requirements: The NIH policy for data and safety monitoring requires oversight and monitoring of all NIH-conducted or -supported human biomedical and behavioral intervention studies (clinical trials) to ensure the safety of participants and the validity and integrity of the data. Further information concerning these requirements is found at http://grants.nih.gov/grants/policy/hs/data_safety.htm and in the application instructions (SF424 (R&R) and PHS 398).

Investigational New Drug or Investigational Device Exemption Requirements: Consistent with federal regulations, clinical research projects involving the use of investigational therapeutics, vaccines, or other medical interventions (including licensed products and devices for a purpose other than that for which they were licensed) in humans under a research protocol must be performed under a Food and Drug Administration (FDA) investigational new drug (IND) or investigational device exemption (IDE).

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the *NIH Grants Policy Statement* (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120) as part of the NoA. For these terms of award, see the *NIH Grants Policy Statement* Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General (//grants.nih.gov/grants/guide/url_redirect.htm?id=11157) and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Recipients, and Activities (//grants.nih.gov/grants/guide/url_redirect.htm?id=11159). More information is provided at Award Conditions and Information for NIH Grants (//grants.nih.gov/grants/guide/url_redirect.htm?id=11158).

Recipients of federal financial assistance (FFA) from HHS must administer their programs in compliance with federal civil rights laws that prohibit discrimination on the basis of race, color, national origin, disability, age and, in some circumstances, religion, conscience, and sex. This includes ensuring programs are accessible to persons with limited English proficiency. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. Please see https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html (https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html) and http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html (http://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html).

HHS recognizes that research projects are often limited in scope for many reasons that are nondiscriminatory, such as the principal investigator's scientific interest, funding limitations, recruitment requirements, and other considerations. Thus, criteria in research protocols that target or exclude certain populations are warranted where nondiscriminatory justifications establish that such criteria are appropriate with respect to the health or safety of the subjects, the scientific study design, or the purpose of the research. For additional guidance regarding how the provisions apply to NIH grant programs, please contact the Scientific/Research Contact that is identified in Section VII under Agency Contacts of this FOA.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. HHS provides guidance to recipients of FFA on meeting their legal obligation to take reasonable steps to provide meaningful access to their programs by persons with limited English proficiency. Please see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html (https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html) and https://www.lep.gov (https://www.lep.gov). For further guidance on providing culturally and linguistically appropriate services, recipients should review the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care at https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53 (https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53).
- Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html (http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html).
- HHS funded health and education programs must be administered in an environment free of sexual harassment. Please see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html (https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html); https://www2.ed.gov/about/offices/list/ocr/docs/shguide.html; and https://www.eeoc.gov/eeoc/publications/upload/fs-sex.pdf (https://www.eeoc.gov/eeoc/publications/upload/fs-sex.pdf). For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see https://grants.nih.gov/grants/policy/harassment.htm (https://grants.nih.gov/grants/policy/harassment.htm).
- Recipients of FFA must also administer their programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-discrimination laws. Collectively, these laws prohibit exclusion, adverse treatment, coercion, or other discrimination against persons or entities on the basis of their consciences, religious beliefs, or moral convictions. Please see https://www.hhs.gov/conscience/conscience-protections/index.html

(https://www.hhs.gov/conscience/conscience-protections/index.html) and https://www.hhs.gov/conscience/religious-freedom/index.html (https://www.hhs.gov/conscience/religious-freedom/index.html).

Please contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at https://www.hhs.gov/ocr/about-us/contact-us/index.html (https://www.hhs.gov/ocr/about-us/contact-us/index.html) or call 1-800-368-1019 or TDD 1-800-537-7697.

In accordance with the statutory provisions contained in Section 872 of the Duncan Hunter National Defense Authorization Act of Fiscal Year 2009 (Public Law 110-417), NIH awards will be subject to the Federal Awardee Performance and Integrity Information System (FAPIIS) requirements. FAPIIS requires Federal award making officials to review and consider information about an applicant in the designated integrity and performance system (currently FAPIIS) prior to making an award. An applicant, at its option, may review information in the designated integrity and performance systems accessible through FAPIIS and comment on any information about itself that a Federal agency previously entered and is currently in FAPIIS. The Federal awarding agency will consider any comments by the applicant, in addition to other information in FAPIIS, in making a judgement about the applicant's integrity, business ethics, and record of performance under Federal awards when completing the review of risk posed by applicants as described in 45 CFR Part 75.205 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Part 75, 2 CFR Part 200, and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the recipients is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

The PD(s)/PI(s) will have the following primary responsibilities:

* All aspects of the study, including any modification of study design, conduct of the study, quality control, data analysis and interpretation, preparation of publications, dissemination of data, tools, and technologies, and collaboration with other investigators are the PD(s)/PI(s) responsibilities. The recipient agrees to accept close coordination, cooperation, and participation of NIDCR staff in those aspects of scientific and technical management of the study as stated in these terms and conditions.

- The PD(s)/PI(s) will meet NIDCR policy requiring that studies be monitored commensurate with the degree of potential risk to study subjects and the complexity of the study (NOT-DE-08-011, March 27, 2008).
- Upon implementation of the protocol, each study, whether a single entity or a consortium of entities, will follow the procedures required by the protocol regarding study conduct and monitoring, participant management, data collection, and quality control.

The PD(s)/PI(s) will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

- The PD(s)/PI(s) will manage involvement of industry or any other third party in the study. Except for licensing of patents or copyrights, support or involvement of any third party will occur only following notification of and concurrence by the NIDCR.
- The PD(s)/PI(s) will make all study materials and procedure manuals available in the public domain. Recipients are expected to publish and publicly disseminate results, data, and other products of the study, concordant with governance policies and protocols. Publications and oral presentations of work performed under this agreement will require appropriate acknowledgment of support by the NIDCR/NIH.
- The PD(s)/PI(s) will obtain prior written approval of the NIDCR Grants Management Specialist, in consultation with the NIDCR Program Officer, for changes in any of the key personnel identified in the Notice of Grant Award.

NIH staff will have the following primary responsibilities:

An NIDCR Program staff member(s) acting as a Project Scientist(s) will be assigned to have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below. Additional NIDCR staff members may be designated to have substantial involvement. The NIDCR Project Scientist(s) and any other substantially involved staff members will not attend peer review meetings of renewal (competing continuation) and/or supplemental applications. If such participation is deemed essential, these individuals will seek NIDCR waiver according to the NIDCR procedures for management of conflict of interest. Some Program Officials will also have substantial programmatic involvement. In that case, the individual involved will not attend peer review meetings of renewal (competing continuation) and/or supplemental applications or will seek an NIDCR waiver as stated above.

The main activities of the NIDCR substantially involved staff members include but are not limited to the following aspects:

- Providing input on experimental and clinical approaches, assisting in designing protocols, and consulting on updates to project milestones;
- Assisting and advising recipients with regard to various regulatory and compliance issues;
- Participating in monthly teleconferences with PDs/PIs to monitor progress and facilitate cooperation;
- Monitoring progress of the trial towards meeting its primary outcome;
- Tracking monthly accrual of participants; and
- Reviewing the progress of the study, and of each participating component, through consideration of the annual reports, site visits, logs, etc. This review may include, but not be limited to, compliance with the study protocol, meeting subject enrollment targets, adherence to uniform data collection procedures, and the timeliness and quality of data reporting.

An NIDCR Program Official will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice. An NIDCR Medical or Dental Officer will monitor the studies and serve as the Medical Monitor.

The NIDCR reserves the right to terminate, temporarily suspend, or modify a study or any portion of a study in the event of (a) failure to implement the study protocol, (b) a substantial shortfall in participant recruitment, follow-up, data reporting and dissemination, quality control or other major breach of the protocol, (c) substantive changes in the agreed-upon protocol with which the NIDCR does not concur, (d) reaching a major study objective substantially before schedule with persuasive statistical evidence, or human subject ethical issues that may dictate a premature termination.

Data Management and Sharing

Note: The NIH Policy for Data Management and Sharing is effective for due dates on or after January 25, 2023.

Consistent with the NIH Policy for Data Management and Sharing, when data management and sharing is applicable to the award, recipients will be required to adhere to the Data Management and Sharing requirements as outlined in the NIH Grants Policy Statement (/grants/policy/nihgps/HTML5/section_8/8.2.3_sharing_research_resources.htm#Data). Upon the approval of a Data Management and Sharing Plan, it is required for recipients to implement the plan as described.

3. Reporting

When multiple years are involved, recipients will be required to submit the Research Performance Progress Report (RPPR) (//grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the NIH Grants Policy Statement. (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161)

A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11161).

The Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for recipients of Federal grants to report information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All recipients of applicable NIH grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) available at www.fsrs.gov (//grants.nih.gov/grants/guide/url_redirect.htm?id=11170) on all subawards over $25,000. See the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11171) for additional information on this reporting requirement.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts from all Federal awarding agencies with a cumulative total value greater than $10,000,000 for any period of time during the period of performance of a Federal award, must report and maintain the currency of information reported in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently FAPIIS). This is a statutory requirement under section 872 of Public Law 110-417, as amended (41 U.S.C. 2313). As required by section 3010 of Public Law 111-212, all information posted in the designated integrity and performance system on or after April 15, 2011, except past performance reviews required for Federal procurement contracts, will be publicly available. Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75 – Award Term and Conditions for Recipient Integrity and Performance Matters.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

Application Submission Contacts

eRA Service Desk (Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that threaten submission by the due date, and post-submission issues)

Finding Help Online: http://grants.nih.gov/support/ (//grants.nih.gov/support/) (preferred method of contact)
Telephone: 301-402-7469 or 866-504-9552 (Toll Free)

General Grants Information (Questions regarding application instructions, application processes, and NIH grant resources)
Email: GrantsInfo@nih.gov (mailto:GrantsInfo@nih.gov) (preferred method of contact)
Telephone: 301-637-3015

Grants.gov Customer Support (Questions regarding Grants.gov registration and Workspace)
Contact Center Telephone: 800-518-4726
Email: support@grants.gov (mailto:support@grants.gov)

Scientific/Research Contact(s)

Melissa W. Riddle, PhD
National Institute of Dental and Craniofacial Research (NIDCR)
Telephone: 301-451-3888
Email: riddleme@mail.nih.gov (mailto:riddleme@mail.nih.gov)

Leila Khaki, DrPH
National Institute Of Dental & Craniofacial Research (NIDCR)
Phone: 301-594-2608
E-mail: leila.khaki@nih.gov (mailto:leila.khaki@nih.gov)

Peer Review Contact(s)

Yasaman Shirazi, PhD
National Institute of Dental and Craniofacial Research (NIDCR)
Telephone: 594-5593
Email: yasaman.shirazi@nih.gov (mailto:yasaman.shirazi@nih.gov)

Financial/Grants Management Contact(s)

Diana Rutberg, MBA
National Institute of Dental and Craniofacial Research (NIDCR)
Telephone: 301-594-4798
Email: rutbergd@mail.nih.gov (mailto:rutbergd@mail.nih.gov)

Section VIII. Other Information

Recently issued trans-NIH policy notices (//grants.nih.gov/grants/guide/url_redirect.htm?id=11163) may affect your application submission. A full list of policy notices published by NIH is provided in the NIH Guide for Grants and Contracts (//grants.nih.gov/grants/guide/url_redirect.htm?id=11164). All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement (//grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 2 CFR Part 200, 42 CFR Part 52 and 45 CFR Part 75.

Weekly TOC for this Announcement (/grants/guide/WeeklyIndex.cfm?09-03-21)
NIH Funding Opportunities and Notices (/grants/guide/index.html)

Note: For help accessing PDF, RTF, MS Word, Excel, PowerPoint, Audio or Video files, see Help Downloading Files (/grants/edocs.htm).

Recipient Information

1. Recipient Name
HEALTHPARTNERS INSTITUTE
8170 33RD AVE S
MINNEAPOLIS, MN 55425

2. Congressional District of Recipient
03

3. Payment System Identifier (ID)
1411670163A1

4. Employer Identification Number (EIN)
411670163

5. Data Universal Numbering System (DUNS)
029191355

6. Recipient's Unique Entity Identifier
H65GNDPBTRY7

7. Project Director or Principal Investigator
D. Brad Rindal, DDS (Contact)
Senior Research Investigator
donald.b.rindal@healthpartners.com
952-967-5026

8. Authorized Official
Ms. Sarah E. Toov

Federal Agency Information

9. Awarding Agency Contact Information
Susan Medve
Grants Management Specialist
NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH
Medves@mail.nih.gov
301-827-4634

10. Program Official Contact Information
LILLIAN SHUM
Director
NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH
shuml@nidcr.nih.gov
301-594-0618

Federal Award Information

11. Award Number
3UG3DE030063-01A1S1

12. Unique Federal Award Identification Number (FAIN)
UG3DE030063

13. Statutory Authority
42 USC 241 42 CFR PART 52

14. Federal Award Project Title
Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings

15. Assistance Listing Number
93.121

16. Assistance Listing Program Title
Oral Diseases and Disorders Research

17. Award Action Type
Supplement

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information

19. Budget Period Start Date 08/01/2023 **– End Date** 01/31/2024	
20. Total Amount of Federal Funds Obligated by this Action	$53,708
20 a. Direct Cost Amount	$33,993
20 b. Indirect Cost Amount	$19,715
21. Authorized Carryover	
22. Offset	
23. Total Amount of Federal Funds Obligated this budget period	$53,708
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$53,708
26. Project Period Start Date 08/01/2023 **– End Date** 07/31/2024	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$369,454

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
Debbie Pettitt

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Ph 1 Explor./Developmental Coop. Agreement
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH

SECTION I – AWARD DATA – 3UG3DE030063-01A1S1

Principal Investigator(s):
Patricia Lombard Mabry, PHD
D. Brad Rindal (contact), DDS

Award e-mailed to: hprfra@healthpartners.com

Dear Authorized Official:

The National Institutes of Health hereby awards a grant in the amount of $53,708 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to HEALTHPARTNERS INSTITUTE in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR PART 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Dental & Craniofacial Research of the National Institutes of Health under Award Number UG3DE030063. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

Debbie Pettitt
Grants Management Officer
NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Federal Direct Costs	$33,993
Federal F&A Costs	$19,715
Approved Budget	$53,708
Total Amount of Federal Funds Authorized (Federal Share)	$53,708
TOTAL FEDERAL AWARD AMOUNT	$53,708
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$53,708

SUMMARY TOTAL FEDERAL AWARD AMOUNT YEAR (1) (for this Document Number)	
AWARD NUMBER	**TOTAL FEDERAL AWARD AMOUNT**
3UG3DE030063-01A1S1	$53,708
1UG3DE030063-01A1	$315,746
TOTAL	**$369,454**

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
1	$53,708	$369,454
2	$53,707	$363,322

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier:	1411670163A1
Document Number:	UDE030063A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2023

IC	CAN	2023	2024
DE	8472268	$53,708	$53,707

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: Q2A / **OC**: 41028 / **Released**: Pettitt, Debbie 07/24/2023
Award Processed: 07/25/2023 12:24:19 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 3UG3DE030063-01A1S1

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – STANDARD TERMS AND CONDITIONS – 3UG3DE030063-01A1S1

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to obtain a unique entity identifier (UEI) and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a UEI requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) UG3DE030063. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

This award provides support for one or more clinical trials. By law (Title VIII, Section 801 of Public Law 110-85), the "responsible party" must register "applicable clinical trials" on the ClinicalTrials.gov Protocol Registration System Information Website. NIH encourages registration of all trials whether required under the law or not. For more information, see http://grants.nih.gov/ClinicalTrials_fdaaa/
This award provides support for one or more NIH defined Phase III Clinical Trials. The NIH Policy for research supported as an NIH Phase III Clinical Trial has been amended in Section II.B. of the NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research – Amended October 2001 (see http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm).

A description of plans to conduct analyses, as appropriate, by sex/gender and racial/ethnic groups must be included in clinical trial protocols. Cumulative subject accrual and progress in conducting subset analyses must be reported to NIH in the annual Progress Reports. Final analyses of sex/gender and racial/ethnic differences must be reported in the required Final Progress Report or Competitive Renewal Applications (or Contract Renewals/Extensions) as stated in Section II.B. of the Guidelines.

Recipients must administer the project in compliance with federal civil rights laws that prohibit discrimination on the basis of race, color, national origin, disability, age, and comply with applicable conscience protections. The recipient will comply with applicable laws that prohibit discrimination on the basis of sex, which includes discrimination on the basis of gender identity, sexual orientation, and pregnancy. Compliance with these laws requires taking reasonable steps to provide meaningful access to persons with limited English proficiency and providing programs that are accessible to and usable by persons with disabilities. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. See https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html and https://www.hhs.gov/.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. For guidance on meeting the legal obligation to take reasonable steps to ensure meaningful access to programs or activities by limited English proficient individuals, see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html and https://www.lep.gov.
- For information on an institution's specific legal obligations for serving qualified individuals with disabilities, including providing program access, reasonable modifications, and to provide effective communication, see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html.
- HHS funded health and education programs must be administered in an environment free of sexual harassment; see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html. For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see https://grants.nih.gov/grants/policy/harassment.htm.
- For guidance on administering programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-discrimination laws, see https://www.hhs.gov/conscience/conscience-protections/index.html and https://www.hhs.gov/conscience/religious-freedom/index.html.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:

Additional Costs

SECTION IV – DE SPECIFIC AWARD CONDITIONS – 3UG3DE030063-01A1S1

Clinical Trial Indicator: Yes

This award supports one or more NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

This award provides support under *(FOA PA20-272* Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp Clinical Trial Optional)*)* beginning (08/01/2023). These funds $53,708 Total Cost ($33,993 Direct Costs, and $19,715

Facilities and Administrative Costs) are to be used as requested in the grantee's proposal submitted *(06/01/2023)*. Funds awarded are available for carryover for awards given carryover authority as reflected in section III of this award notice. These funds remain restricted for the purpose in which the supplement was awarded, and may not be used for any other purpose without the written prior approval from the NIDCR.

In future years (if applicable) a separate progress report for the supplement is required as part of the progress report of the parent grant. In addition, unless this award is included under the Streamlined Noncompeting Award Process, a detailed budget page must be submitted.

SPREADSHEET SUMMARY
AWARD NUMBER: 3UG3DE030063-01A1S1

INSTITUTION: HEALTHPARTNERS INSTITUTE

Facilities and Administrative Costs	Year 1	Year 2
F&A Cost Rate 1	58%	58%
F&A Cost Base 1	$33,992	$33,992
F&A Costs 1	$19,715	$19,715

Recipient Information

1. Recipient Name
HEALTHPARTNERS INSTITUTE
8170 33RD AVE S

MINNEAPOLIS, 55425

2. Congressional District of Recipient
03

3. Payment System Identifier (ID)
1411670163A1

4. Employer Identification Number (EIN)
411670163

5. Data Universal Numbering System (DUNS)
029191355

6. Recipient's Unique Entity Identifier
H65GNDPBTRY7

7. Project Director or Principal Investigator
D. Brad Rindal, DDS (Contact)
Senior Research Investigator
donald.b.rindal@healthpartners.com
952-967-5026

8. Authorized Official
Ms. Sarah E. Toov

Federal Agency Information

9. Awarding Agency Contact Information
Susan Medve
Grants Management Specialist
NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH
Medves@mail.nih.gov
301-827-4634

10. Program Official Contact Information
LILLIAN SHUM
Director
NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH
shuml@nidcr.nih.gov
301-594-0618

Federal Award Information

11. Award Number
1UG3DE030063-01A1

12. Unique Federal Award Identification Number (FAIN)
UG3DE030063

13. Statutory Authority
42 USC 241 42 CFR PART 52

14. Federal Award Project Title
Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings

15. Assistance Listing Number
93.121

16. Assistance Listing Program Title
Oral Diseases and Disorders Research

17. Award Action Type
New Competing

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information

19. Budget Period Start Date 02/01/2023 **– End Date** 01/31/2024	
20. Total Amount of Federal Funds Obligated by this Action	$315,746
20 a. Direct Cost Amount	$199,839
20 b. Indirect Cost Amount	$115,907
21. Authorized Carryover	
22. Offset	
23. Total Amount of Federal Funds Obligated this budget period	$315,746
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$315,746
26. Project Period Start Date 02/01/2023 **– End Date** 01/31/2025	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$315,746

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
April Harrison

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Ph 1 Explor./Developmental Coop. Agreement
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH

SECTION I – AWARD DATA – 1UG3DE030063-01A1

Principal Investigator(s):
Patricia Lombard Mabry, PHD
D. Brad Rindal (contact), DDS

Award e-mailed to: hprfra@healthpartners.com

Dear Authorized Official:

The National Institutes of Health hereby awards a grant in the amount of $315,746 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to HEALTHPARTNERS INSTITUTE in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR PART 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Dental & Craniofacial Research of the National Institutes of Health under Award Number UG3DE030063. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

April Harrison
Grants Management Officer
NATIONAL INSTITUTE OF DENTAL & CRANIOFACIAL RESEARCH

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Salaries and Wages	$141,184
Fringe Benefits	$41,056
Personnel Costs (Subtotal)	$182,240
Travel	$100
Other	$17,499
Federal Direct Costs	$199,839
Federal F&A Costs	$115,907
Approved Budget	$315,746
Total Amount of Federal Funds Authorized (Federal Share)	$315,746
TOTAL FEDERAL AWARD AMOUNT	$315,746
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$315,746

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
1	$315,746	$315,746
2	$309,615	$309,615

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier:	1411670163A1
Document Number:	UDE030063A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2023

IC	CAN	2023	2024
DE	8472268	$315,746	$309,615

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: Q2A / **OC**: 41026 / **Released**: Harrison, April 01/17/2023
Award Processed: 01/26/2023 12:13:24 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 1UG3DE030063-01A1

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – STANDARD TERMS AND CONDITIONS – 1UG3DE030063-01A1

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as

those included in appropriations acts.

c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to obtain a unique entity identifier (UEI) and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a UEI requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) UG3DE030063. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

This award provides support for one or more clinical trials. By law (Title VIII, Section 801 of Public Law 110-85), the "responsible party" must register "applicable clinical trials" on the ClinicalTrials.gov Protocol Registration System Information Website. NIH encourages registration of all trials whether required under the law or not. For more information, see http://grants.nih.gov/ClinicalTrials_fdaaa/
This award provides support for one or more NIH defined Phase III Clinical Trials. The NIH Policy for research supported as an NIH Phase III Clinical Trial has been amended in Section II.B. of the NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research – Amended October 2001 (see http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm).

A description of plans to conduct analyses, as appropriate, by sex/gender and racial/ethnic groups must be included in clinical trial protocols. Cumulative subject accrual and progress in conducting subset analyses must be reported to NIH in the annual Progress Reports. Final analyses of sex/gender and racial/ethnic differences must be reported in the required Final Progress Report or Competitive Renewal Applications (or Contract Renewals/Extensions) as stated in Section II.B. of the Guidelines.

Recipients must administer the project in compliance with federal civil rights laws that prohibit

discrimination on the basis of race, color, national origin, disability, age, and comply with applicable conscience protections. The recipient will comply with applicable laws that prohibit discrimination on the basis of sex, which includes discrimination on the basis of gender identity, sexual orientation, and pregnancy. Compliance with these laws requires taking reasonable steps to provide meaningful access to persons with limited English proficiency and providing programs that are accessible to and usable by persons with disabilities. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. See https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html and https://www.hhs.gov/.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. For guidance on meeting the legal obligation to take reasonable steps to ensure meaningful access to programs or activities by limited English proficient individuals, see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html and https://www.lep.gov.
- For information on an institution's specific legal obligations for serving qualified individuals with disabilities, including providing program access, reasonable modifications, and to provide effective communication, see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html.
- HHS funded health and education programs must be administered in an environment free of sexual harassment; see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html. For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see https://grants.nih.gov/grants/policy/harassment.htm.
- For guidance on administering programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-discrimination laws, see https://www.hhs.gov/conscience/conscience-protections/index.html and https://www.hhs.gov/conscience/religious-freedom/index.html.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:

Additional Costs

SECTION IV – DE SPECIFIC AWARD CONDITIONS – 1UG3DE030063-01A1

Clinical Trial Indicator: Yes

This award supports one or more NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

Inflationary increases for future year commitments will be discontinued for all competing and non-competing research grant awards issued in FY 23, however adjustments for special needs (such as equipment and added personnel) will continue to be accommodated.

This award is issued in accordance with, and is subject to, the conditions set forth in (RFA/PA 21-317 NIDCR Behavioral and Social Intervention Clinical Trial Planning and Implementation Cooperative Agreement (UG3/UH3 Clinical Trial Required), which are hereby incorporated by

reference as special terms and conditions of this award. This RFA/PA may be accessed at: (https://grants.nih.gov/grants/guide/pa-files/PAR-21-317.html).

In keeping with NOT-OD-06-054, as this grant has multiple Principal Investigators (PIs), although the signatures of the PIs are not required on prior approval requests submitted to the agency, the grantee institution must secure and retain the signatures of all of the PIs within their own internal processes.

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) 2 CFR Part 200 Administrative Regulations, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Part 75, NIH Grants Policy Statement (which implements the aforementioned HHS Regulations (45 CFR Part 75), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement [reference mechanism], an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined above.

Milestones

1. Develop intervention materials:
    a. Complete qualitative interviews with dentists and hygienists to inform development of provider training materials
    b. Draft provider training and patient informational materials (e.g., scripted messages to be delivered by providers)
    c. Gather feedback from a sufficient number of patients to ensure that scripted messages meet patients' expectations for communications within a dental setting
2. Develop and test survey instruments.
3. Integrate intervention content (e.g., scripts, required data fields in the electronic health record) into the existing Clinical Decision Support (CDS) platform.
4. Finalize the fidelity monitoring plan to track provider participation in trainings and the use of intervention materials once implemented in the UH3 phase.
5. Finalize the data management system.
6. Ensure feasibility and acceptability of study materials and procedures via a small-scale study of providers randomized to the intervention condition.
7. Draft near-final clinical protocol and other required regulatory and study documents.
8. Draft IRB application materials, ready for submission upon successful transition to the UH3 phase.

Principal Investigator Roles and Responsibilities

The Principal Investigator will have the primary responsibility to define objectives and approaches, and to plan, conduct, analyze, and publish results, interpretations, and conclusions of their studies.

Recipient Roles and Responsibilities

Recipients are responsible for identifying specific milestones toward countermeasure development that will be achieved during the project period. Recipients will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

Collaborative Responsibilities

Where study management entities are established. NIH staff and the recipient will serve on the Steering/Executive Committee and other central coordinating components in which there is substantial scientific-programmatic involvement.

NIH Responsibilities

An NIH Project Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

- Each project will have the support of one or more Project Scientists from NIH program staff who have expertise in the implementation of the project.
- The NIH Project Scientists will have substantial scientific-programmatic involvement during the conduct of this activity, through technical assistance, advice, and coordination above and beyond normal program stewardship for grants.
- NIH Project Scientists will be responsible for assessing the progress of the projects toward the accomplishment of their goals and for recommending if further funds should be released to the project.
- The NIH Project Scientists will facilitate the establishment of contacts and collaborations between awardees and other persons or organizations whose participation will assist with the accomplishment of project goals. These persons or organizations may include the FDA, disease voluntary organizations, pharmaceutical companies, or research organizations that can provide essential services on contract.

The NIDCR Program Official is responsible for normal stewardship of the award. If the NIDCR Program Official is also serving as a Project Scientist on the award, their usual program stewardship responsibilities will be overseen by senior NIDCR leadership to mitigate conflict of interest and to ensure appropriate oversight of public funds.

Arbitration Process

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to arbitration. An Arbitration Panel composed of three members will be convened. It will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special arbitration procedure in no way affects the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations 42 CFR Part 50, Subpart D and HHS regulations 45 CFR Part 16.

The maximum amount NIH will award for compensation of a graduate student receiving support from a research grant is zero-level Kirschstein-NRSA Stipend in effect when NIH issues the grant award. Current levels are posted at: http://grants.nih.gov/training/nrsa.htm. Support recommended for future years has been adjusted accordingly, if applicable.

None of the funds in this award shall be used to pay the salary of an individual at a rate in excess of the applicable salary cap. Therefore, this award and/or future years are adjusted accordingly, if applicable. Current salary cap levels can be found in the following Notice:NOT-OD-23-056

SPREADSHEET SUMMARY
AWARD NUMBER: 1UG3DE030063-01A1

INSTITUTION: HEALTHPARTNERS INSTITUTE

Budget	Year 1	Year 2
Salaries and Wages	$141,184	$133,005
Fringe Benefits	$41,056	$38,703
Personnel Costs (Subtotal)	$182,240	$171,708
Travel	$100	$100

Other	$17,499	$24,151
TOTAL FEDERAL DC	$199,839	$195,959
TOTAL FEDERAL F&A	$115,907	$113,656
TOTAL COST	$315,746	$309,615

Facilities and Administrative Costs	Year 1	Year 2
F&A Cost Rate 1	58%	58%
F&A Cost Base 1	$199,839	$195,959
F&A Costs 1	$115,907	$113,656

PI: **Rindal, D. Brad**	Title: Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings	
Received: 03/07/2022	Opportunity: PAR-21-317	Council: 10/2022
Competition ID: FORMS-G	FOA Title: NIDCR Behavioral and Social Intervention Clinical Trial Planning and Implementation Cooperative Agreement (UG3/UH3 Clinical Trial Required)	
1UG3DE030063-01A1	Dual:	Accession Number: 4690896
IPF: 3566002	Organization: HEALTHPARTNERS INSTITUTE	
Former Number: 1UG3DE030063-01A1	Department: HealthPartners Institute	
IRG/SRG: ZDE1 YM (02)	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 199,839 Year 2: 199,953 Year 3: 482,533 Year 4: 489,520 Year 5: 476,631 Year 6: 438,384	Animals: N Humans: Y Clinical Trial: Y Current HS Code: Evaluative HESC: N HFT: N	New Investigator: Early Stage Investigator:
Senior/Key Personnel:	*Organization:*	*Role Category:*
D. Brad Rindal DDS	HealthPartners Institute	PD/PI
Patricia Mabry PhD	HealthPartners Institute	MPI
Stephen Asche MA	HealthPartners Institute	Other (Specify)-Co-Investigator/Statistician
Meghan JaKa MS, P	HealthPartners Institute	Co-Investigator
Elyse Kharbanda MD, M	HealthPartners Institute	Co-Investigator
Bryan Michalowicz DDS,	HealthPartners Institute	Co-Investigator

OMB Number: 4040-0001
Expiration Date: 12/31/2022

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION*

❍ Pre-application ❍ Application ● Changed/Corrected Application

4.a. Federal Identifier
UG3DE030063

b. Agency Routing Number

2. DATE SUBMITTED	Application Identifier	c. Previous Grants.gov Tracking Number
2022-03-04	A22-016	GRANT13565598

5. APPLICANT INFORMATION **UEI*:** H65GNDPBTRY7

Legal Name*: HealthPartners Institute
Department: HealthPartners Institute
Division:
Street1*: 8170 33rd Avenue South MS 21112R
Street2:
City*: Bloomington
County: Hennepin
State*: MN: Minnesota
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 55440-1524

Person to be contacted on matters involving this application
Prefix: Ms. First Name*: Sarah Middle Name: E. Last Name*: Toov Suffix:
Position/Title: Manager of Grant Development
Street1*: 8170 33rd Avenue South
Street2: P.O. Box 1524
City*: Minneapolis
County: Hennepin
State*: MN: Minnesota
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 55440-1524
Phone Number*: 952-967-5176 Fax Number: Email: hprfra@healthpartners.com

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1411670163A1

7. TYPE OF APPLICANT* M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*
❍ New ● Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institute of Dental and Craniofacial Research/NIH/D

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings

12. PROPOSED PROJECT
Start Date* Ending Date*
12/01/2022 11/30/2028

13. CONGRESSIONAL DISTRICTS OF APPLICANT
MN-003

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Dr. First Name*: D. Brad Middle Name: Last Name*: Rindal Suffix: DDS

Position/Title: Senior Research Investigator
Organization Name*: HealthPartners Institute
Department: HealthPartners Institute
Division:
Street1*: 8170 33rd Avenue South, MS 23301A
Street2: P.O. Box 1524
City*: Minneapolis
County: Hennepin
State*: MN: Minnesota
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 55440-1524
Phone Number*: 952-967-5026 Fax Number: 952-967-5022 Email*: donald.b.rindal@healthpartners.com

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$3,590,370.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$3,590,370.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Ms. First Name*: Sarah Middle Name: E. Last Name*: Toov Suffix:

Position/Title*: Manager of Grant Development
Organization Name*: HealthPartners Institute
Department: HealthPartners Institute
Division:
Street1*: 8170 33rd Avenue South
Street2: P.O. Box 1524
City*: Minneapolis
County: Hennepin
State*: MN: Minnesota
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 55440-1524
Phone Number*: 952-967-5176 Fax Number: Email*: hprfra@healthpartners.com

Signature of Authorized Representative*
Ms. Sarah E. Toov

Date Signed*
03/07/2022

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:

424 R&R and PHS-398 Specific
Table Of Contents

OMB Number: 4040-0010
Expiration Date: 12/31/2022

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	HealthPartners Institute
UEI:	H65GNDPBTRY7
Street1*:	8170 33rd Avenue South MS 21112R
Street2:	
City*:	Bloomington
County:	Hennepin
State*:	MN: Minnesota
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	55440-1524
Project/Performance Site Congressional District*:	MN-003

Additional Location(s) File Name:

Funding Opportunity Number: PAR-21-317. Received Date: 2022-03-07T11:53:21.000-05:00

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ● No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8

If NO, is the IRB review Pending? ● **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number 00000106

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	Project Summary.pdf
8. Project Narrative*	Project Narrative.pdf
9. Bibliography & References Cited	References.pdf
10.Facilities & Other Resources	Resources.pdf
11.Equipment	

Funding Opportunity Number: PAR-21-317. Received Date: 2022-03-07T11:53:21.000-05:00

Project Summary

Human papillomavirus (HPV) is the leading cause of oropharyngeal cancers in the US. Despite the safety and effectiveness of the HPV vaccine (HPV-V), coverage is far below that for other routine adolescent vaccines and the Healthy People 2030 goal of 80%. HPV-V promotion at dental visits is seen as a prime opportunity to prevent oropharyngeal and other cancers, yet many dental providers are not comfortable doing so due to lack of knowledge and self-efficacy, and fear of harming the patient-provider relationship. Using the NIH Stage Model of Behavioral Intervention Development as our guide, we propose to develop a theory-based intervention to address dental provider barriers to HPV-V promotion, elucidate the intervention's behavioral mechanisms, and test the real-world efficacy of the intervention in catalyzing provider HPV-V promotion. The intervention will consist of 1) *provider training* about HPV/HPV-V; 2) *tailored scripts* to aid providers in responding to patient/parent/guardian concerns about HPV-V. During the UG3 phase, we will randomize 21 HealthPartners Dental Group clinics to intervention vs. usual care (UC; n=~131 providers). UG3 aims are to: develop survey measures and pilot-test provider HPV-V promotion training (Aim 1) and tailored scripts (Aim 2); develop measures and methods for monitoring provider fidelity to the training and intervention activities (Aim 3); and draft compliance/study documents and obtain IRB/NIDCR approvals (Aim 4). During the UH3 phase, we will conduct a cluster (clinic)-randomized clinical trial (intervention vs. UC) to test the real-world efficacy of the intervention to increase HPV-V promotion activity (Aim 5). We will assess whether the intervention impacted the three intended behavioral mechanism targets: increased knowledge of HPV/HPV-V; increased self-efficacy for HPV-V promotion; and reduced fear of HPV-V promotion negatively affecting the patient-provider relationship (Aim 6). For each target, we will also assess whether the intervention's effects followed the full mechanistic pathway to the endpoint behavior, HPV-V promotion (Aim 7). Beyond our aims, we will conduct exploratory work examining two additional candidate behavioral mechanisms: adequacy of material resources to support dental providers in promoting HPV-V, and providers' perception that HPV-V promotion comports with their professional identity. We will also conduct an exploratory analysis of the intervention's efficacy in increasing HPV-V uptake (30-day post-visit patient vaccination rates). Our long-term goal is to reduce HPV and oropharyngeal cancer prevalence through HPV-V promotion by dental providers. Significant impact of the project includes: 1) developing the first theory-based behavioral intervention for HPV-V promotion aimed at dental providers; 2) delivering the first evidence of real-world efficacy of such an intervention; 3) illuminating behavioral mechanisms purported to underlie provider behavior change; 4) producing fundamental knowledge to guide future HPV-V promotion intervention development; and 5) advancing the science of behavior change by revealing behavioral principles underlying provider behavior change.

Project Narrative

Training dental providers to effectively promote the human papillomavirus vaccine (HPV-V) with their patients could prevent future HPV-related cancer of the mouth and throat in those who become vaccinated. This study will develop HPV-V promotion training and tailored scripts to support dental providers in promoting HPV-V. By testing this intervention in a real-world dental setting, this project has the potential to help increase HPV vaccination rates, reduce HPV-related cancers, and serve as a model for other organizations providing dental care.

HealthPartners and HealthPartners Institute

Facilities and Other Resources

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HealthPartners, Inc.

HealthPartners is the largest consumer-governed nonprofit health care organization in the country, providing care, coverage, research, and education to improve health and well-being in partnership with its members, patients and community. Included under HealthPartners' umbrella are Regions Hospital, HealthPartners Care Group, HealthPartners Center for Memory & Aging, Park Nicollet Methodist Hospital and HealthPartners Institute. HealthPartners has formal relationships with hospitals and clinics throughout Minnesota and western Wisconsin, including Westfields Hospital (New Richmond, WI), Lakeview Hospital (Stillwater, MN), Hudson Hospitals and Clinics (Hudson, WI), Amery Hospital and Clinic (Amery, WI), St Francis Regional Medical Center (Shakopee, MN), Hutchinson Health (Hutchinson, MN), TRIA Orthopaedic Center, and Physicians Neck and Back Clinic.

Founded in 1957, the HealthPartners family of care serves more than 1.8 million medical and dental health plan members and more than 1.2 million patients. HealthPartners is one of the top-ranked commercial health plans in Minnesota and is also one of the highest rated plans in the nation, according to the National Committee for Quality Assurance's Health Insurance Plan Rankings 2018-2019.

HealthPartners Institute

HealthPartners Institute (the Institute) is a 501c(3) nonprofit organization dedicated to conducting high-quality, public-domain health research, often in collaboration with other academic and research organizations throughout the world. On January 1, 2016, HealthPartners Institute for Education and Research and Park Nicollet Institute combined to form one of the largest medical research and education centers in the region. The combined HealthPartners Institute employs 33 career research investigators and more than 400 clinician researchers and encompasses vast and varied areas of research including neurosciences, critical care, dental and oral health, maternal and child health, chronic disease, cancer, clinical research, health economics, mental health, Struthers Parkinson's Center, and Park Nicollet International Diabetes Center. In addition, the Institute participates in 10 national research networks including the Health Care Systems Research Network, the Vaccine Safety Datalink, the Cancer Research Network, and the Mental Health Research Network.

Institute Administrative Infrastructure

A large **in-house professional support team** helps investigators with proposal development, research study coordination, accessing and processing data, and a range of other needs. The professional staff includes full-time study coordinators, phone coaches, research technicians, and administrative staff. The onsite Center for Evaluation and Survey Research conducts surveys and chart review. A research librarian conducts literature searches. Office resources include more than 300 workstation computers networked with the HealthPartners- and Institute-owned computer systems that reside with HealthPartners-owned systems at a secure offsite computing facility.

The Institute has an **accounting and finance** unit that tracks all grants and contracts. In 2022, the Institute has a budget of $34.7 million from grants and contracts from various government agencies (NIH, CDC, AHRQ), foundations and corporations.

The Institute has implemented a comprehensive internal **Regulatory Process** to ensure scientific merit and research subject safety. The Institute is one component of a larger organization defined as an affiliated covered entity (ACE) under HIPAA regulations. The Institute's link with the HealthPartners Care Group and affiliated hospitals enables researchers to explore the feasibility of protocol design and identify participants for study proposals from member and patient databases. In compliance with HIPAA regulations, the Institute established a firewall between the overall data warehouse, which includes medical records and administrative data, and all research staff. As a result, only Institute programmers have direct access to protected health information as defined by HIPAA. They also have permission to release certain information to researchers in preparation for research, and once projects have received the required approvals (scientific and Institutional Review Board [IRB]), direct access to use of medical records data and other administrative data will be granted.

The Institute's **IRB** meets twice monthly to review pending proposals and has the capacity to serve as the central IRB for multi-site studies. The IRB is accredited by the Association for the Accreditation of Human Research Protection Programs. The Institute also has a **Research Review Committee.** This committee evaluates the scientific importance, feasibility, and likelihood of the proposed project to 1) contribute new, generalizable knowledge to the field, and 2) improve the health and well-being, experience, or affordability of care for our patients, members, or the community. All applications to conduct research that involve HealthPartners patients or members, including internal grant applications, must be reviewed and approved by the research review committee.

The Institute supports new and **early-stage investigators (ESIs)** by providing a mentorship team approach and extensive administrative support. ESIs are supported through the proposal development, implementation and completion processes by a professional staff of pre-award and post-award grants managers, project managers and coordinators, statisticians and programmers. The Institute's Center for Evaluation and Survey Research works with ESIs to develop and implement sophisticated recruitment and data-collection strategies, both of which include state-of-the-art software for process management, tracking and reporting. The Institute services staff support the production of documents for both grant and publication submission (eg, reference documentation, editing, biographical sketch and curriculum vitae maintenance). To encourage career development, each ESI is matched with a veteran investigator who helps with professional research development. This mentor aids the ESI in the development of a network of relationships that support a progression of research opportunities. Typically, ESIs initially serve as project managers, co-investigators or statisticians on projects of established researchers. They then begin helping senior researchers develop new proposals aligned with the ESI's career direction and explore funding opportunities that support the development of small or pilot projects, including Institute internal grants, which can lead to the development of larger studies. During this development period, they also can work in the greater HealthPartners system to form relationships to support them as they develop their research path and work with the implementation of research findings in clinical practice.

Institute Technology Infrastructure

The HealthPartners 8170 campus features multiple **seminar and conference rooms** that allow for video and audio conferencing. Conference rooms have an overhead projection system to display computer images, an installed PC, a DVD player and VCR combo to view a DVD or video through the projection system, a Cisco TelePresence System, 70' high definition flat screen television, maneuverable mounted camera, and microphones that have muting capability with indicator lights. These rooms also include: easel/flipchart, e-net (LAN) computer connection for internet/server access, a digital phone to reach meeting attendees, and an analog phone line with dial out capabilities for conference calls. There are multiple training rooms with equipment including: computers, a portable projector, a manual pull down screen, easel/flipchart, TV/VCR, E-net (LAN) connection for internet/server access, and a whiteboard.

The Institute's **Research Informatics and Information Systems (RIIS)** team, led by Teri DeFor, MS, includes 12 programmer analysts with expertise in tracking database development and SAS query. The RIIS team works with researchers to identify and analyze information to answer research questions. Members help with proposal development and use tools and technologies to extract and combine data from different data sources to create a comprehensive record for research. Managers of this team ensure adequate staffing so that a team is convened at the start of a project.

RIIS also supports the **Virtual Data Warehouse** (**VDW) Architecture and Operations.** The VDW is a long-term effort to facilitate collaboration with other research organizations by allowing the pooling and manipulation of common data elements. Currently, 2.25 programmer analysts are dedicated to supporting the VDW.

The Institute's **Software Engineering Team (SET)** provides support for informational technology (IT) needs for research and evaluation projects. Managed by Deepika Appana, who has over 25 years of software engineering experience, SET is comprised of a team of full stack Java engineers, data architects, UI/UX developers, ETL developers, infrastructure engineers and EMR analysts. The members of the team have specialized roles with respect to building and deploying software per industry and security standards. The roles have the following expertise and functions:

- Software Engineering: Full stack Java engineers develop, test, and deploy applications, including web and mobile applications. They work closely with investigators to design and develop software solutions in Java or other languages as appropriate. These solutions can be standalone applications, websites, or clinical decision support systems integrated into the EMR. The team develops applications based on the latest standards such as Fast Healthcare Interoperability Resources (FHIR) and OAuth using opensource frameworks like Spring, Hibernate and various Apache frameworks. In addition, software engineers provide routine maintenance and support sharing of project documents, uploading and downloading data files, overseeing data security, and managing users and permissions.
- Epic programming: Epic certified developers with expertise in EpicCare programming design and develop systems that interface with the Epic EHR. They create the build documents, which outline rules and specifications for Epic-interfacing tools and work closely with HealthPartners IS&T to deploy tools while ensuring no disruptions to care systems.
- User interface/user experience (UI/UX): Engineers with UI/UX expertise help develop applications with functionality that is intuitive to the targeted users. They are involved from the beginning of the design process to develop journey maps, conduct usability testing, configure layout specifications using wireframes, and fine tune applications to ensure optimal user experience.
- Data Architects: Data architects design and develop the entity relationships and table structures and configure how the data are distributed among different schemas. They partner with HealthPartners IS&T to design the physical structures that hold the data, devise backup and recovery strategies, and oversee process of authentication and authorization for data access.
- Extract, transform, and load (ETL): Developers with ETL expertise are responsible for the movement of data between operational databases and the reporting environment and for generation and distribution of use reports.
- Infrastructure engineers: Infrastructure engineers lead the development of highly available and fault tolerant architecture to support continuity of applications and systems in the event of software or hardware failure. Infrastructure engineers set up load balanced clusters of servers and establish secure infrastructure for the exchange of data. They are responsible for monitoring the infrastructure and upkeep of security patches and preventing vulnerabilities.

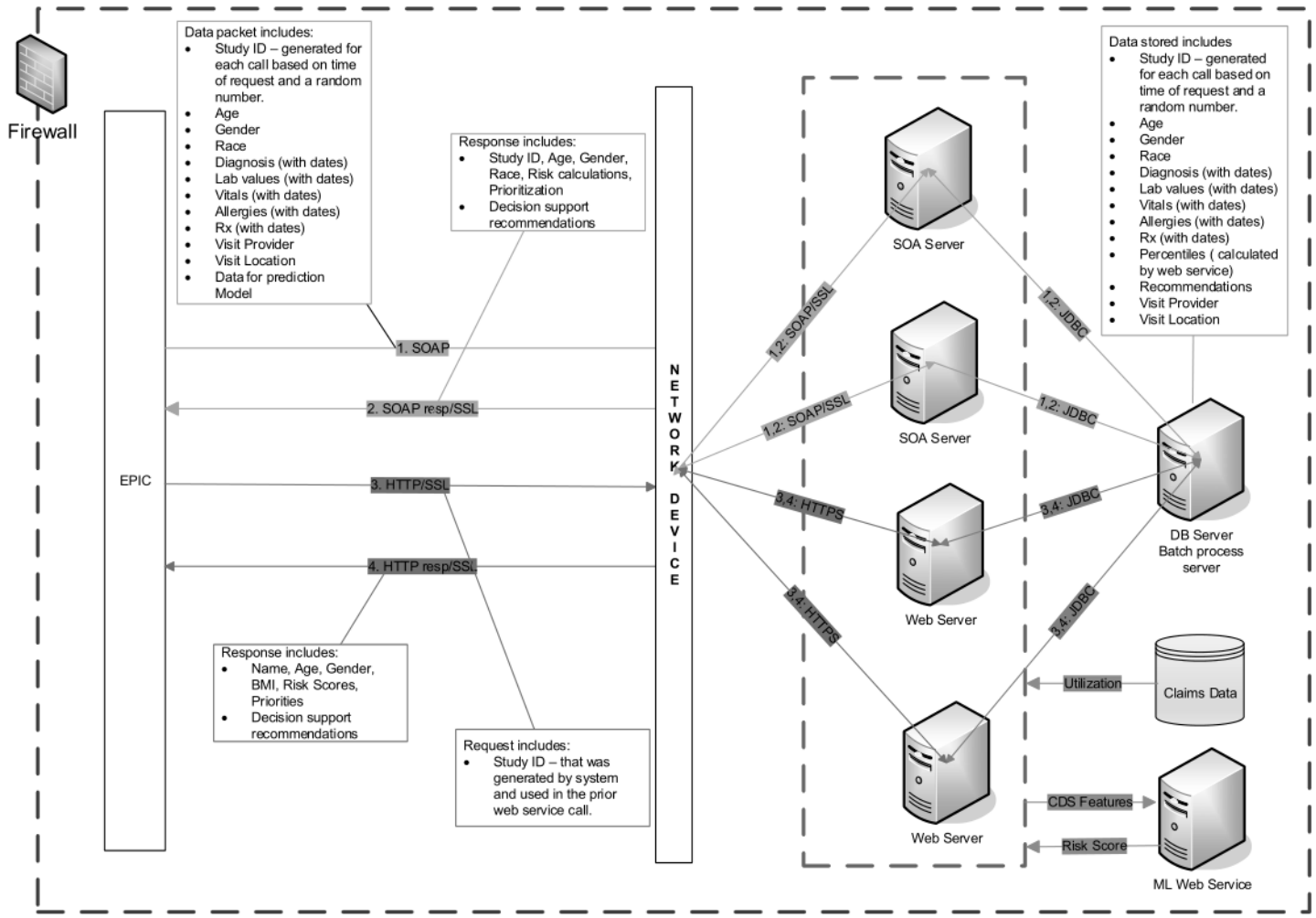
Experience with Clinical Decision Support & EHR Integration

HealthPartners Institute has developed a point-of-care clinical decision support (CDS) platform which synthesizes electronic health information and uses algorithms based on clinical guidelines to drive best practices in care. Embedded in the electronic health record (EHR), it helps physicians easily prioritize care and drug decisions based on individual patient risk factors. The CDS platform can be used by all care team members and, because it is maintained and delivered through a web-based system, there are no geographic limits or boundaries to its use. The design of the system is HIPAA compliant and allows implementation with any EHR vendor.

HealthPartners Institute software engineers have developed both the platform and front-end user display. The CDS interfaces have been developed by the Institute with input from user experience and user interface design experts in addition to thorough testing with providers and patients. An example of the provider interface is included in the figure to the right.

The CDS system includes a web service that identifies eligible patients, computes risks, prioritizes clinical conditions, and provides treatment recommendations based on a complex set of evidence-based algorithms. Although the printout is displayed and printed from the EMR, the printout is controlled from the CDS website and, therefore, the website must have the patient's name and other PHI. A web-based display of the results is then provided to the clinician. Several measures are in place to ensure security of PHI: (1) Data transfer to and from the EMR, the web service, and the web display uses a Simple Object Access Protocol (SOAP) with Secure Sockets Layer (SSL) encryption over Hypertext Transfer Protocol Secure (HTTPS); The connection uses a public private certificate to ensure there is no data exposure along the way; (2) The servers reside on an internal network protected by multiple firewalls; and (3) The web server sits in the demilitarized zone (DMZ) so it can communicate with external systems. The calls to the web use OAuth protocol for security. The remaining processing and data storage occur on servers located inside the second firewall. No external system can access these servers directly, providing maximum security to the data that reside on these servers. A figure that describes the systems complex data security confirmation is included below.

The original CDS platform was implemented and tested using randomized controlled research trials targeting patients with diabetes or high cardiovascular risk and completed research has shown that the CDS platform does improve outcomes among these patients. The HealthPartners CDS research has been published in eight peer-reviewed publications since 2010. Researchers at HealthPartners Institute continue to develop and customize the CDS platform for new conditions including serious mental illness, prediabetes, hypertension, opioid use disorder, cancer prevention screening, adolescents with hypertension, and tobacco users within dental practices. They also envision expanded applications for the tool, including: artificial intelligence, quality improvement opportunities, medication reconciliation, and support registries for population outreach.



Data Sources & Systems

Data System Capabilities: The Institute's networked workstation computers communicate with the larger HealthPartners corporate network. Our systems for storing and backing up data reside both at the HealthPartners corporate headquarters and in a secure offsite facility. Data are backed up daily, weekly and monthly. Backups are saved for 7 years. The Institute's computer and data needs are supported by the larger organization's Information Systems & Technology Department (IS&T). IS&T maintains all HealthPartners computer hardware, software and data, including EMR and administrative data.

Membership System: The membership system is a corporate database of people covered by HealthPartners health insurance from 1990 to today. The membership system provides comprehensive member data collected by the health plan for administrative and financial purposes. Membership data is collected through enrollment forms, individually, by government programs or from an employer group. Sales/Marketing gathers employer group information with input from Actuarial/Underwriting. Membership Accounting enters the information into the system for use by all enterprise applications. In addition, if a patient arrives at a clinic and they are not yet enrolled, a mini-registration process allows clinic staff to register the patient, issue a chart number and proceed with treatment. The major business functions of the membership application are: 1) maintaining employer group information, 2) maintaining member information, 3) regulatory processing, and 4) membership reporting. For research, this database identifies people with HP insurance and includes address and demographic information and information allowing linkage with the EMR and other health data.

Electronic Medical Record (EPIC/Clarity): All medical care provided by HealthPartners-owned facilities (including clinics and hospitals) is captured and maintained in an EMR. Epic supports clinical care and tracks billable treatments. For research and other reporting purposes, a subset of this data is extracted nightly into an Epic database called Clarity. Clarity includes demographic, encounter, admission/discharge/transfer, order, medication, chemotherapy/infusion, laboratory, radiology, pathology, vital sign, diagnosis, procedure,

immunization, patient-reported outcomes (eg, PHQ-9), physician notes, dates of service, provider, facility, billing, scheduling, flowsheet, online access and social history data. Epic data elements that do not flow to Clarity can be obtained from a production server, Chronicles, which supports the EMR. Lab results go back to 1990 and encounter data goes as far back as 1997. Computerized physician order entry started in 2005. Data originating from Park Nicollet after July, 2011 are available in Epic. Prior to that time, data are available in the legacy Park Nicollet electronic medical record.

Clinical Data Warehouse (CDW): The CDW is a unified warehouse of clinical information sourced from both the HealthPartners and Park Nicollet EMR. Standardized field names and classification schemes are used to perform advanced analytics that maximize operational efficiency.

Administrative Data Warehouse (ADW): The ADW is a database of claims processed by the HealthPartners health plan. These data include demographic, enrollment, medical claims, pharmacy claims, dental claims, diagnosis, procedure, dates of service, provider, facility, laboratory tests performed, referrals to other specialists and financial and other billing codes. Medical and pharmacy claims data is available back to 1990.

Research Data Mart (RDM): RDM is a subset of the ADW that allows efficient retrieval for standard types of research questions. The database is optimized for questions related to identification of patients with particular conditions based on codes (eg, ICD codes, pharmacy). This dataset is a readily accessed archive of research data from the ADW back to the 1990s.

Virtual Data Warehouse (VDW): The VDW facilitates collaboration with other research organizations by allowing pooling and manipulation of common data elements. The VDW is “virtual” in the sense that the research data remain at each Health Care Systems Research Network (HCSRN) site; the VDW is a local database designed in collaboration with other HCSRN sites and built to a common set of standardized file definitions. Content areas and data elements represent commonly required elements for research studies. Primary content areas include enrollment, demographics, pharmacy, utilization and cancer (tumor registry). Other content areas are census, vital signs, laboratory values and death. For each content area, data specifications define the common format for each element, such as variable name, variable label, extended definition, code values and value labels. Local site programmers have mapped and transformed data elements from their local data systems into the standardized set of variable definitions, names and codes. The VDW facilitates multisite research in the HCSRN because much of the preparatory work for pooling existing data at multiple sites has been done.

Research Electronic Data Capture (REDCap): In 2011, the Institute became a REDCap consortium partner. REDCap is a secure Web application for building and managing online surveys and databases using: 1) the online method from a Web browser using the Online Designer; and/or 2) the offline method by constructing a data dictionary template file in Microsoft Excel that can be uploaded into REDCap. Both surveys and databases (or a combination) can be built using these methods. REDCap provides audit trails for tracking data manipulation and user activity and automated export procedures for data downloads to Excel, PDF, and common statistical packages (SPSS, SAS, Stata, R). Also included are a built-in project calendar, scheduling module, reporting tools and advanced features such as branching logic, file uploading and calculated fields.

MyVoice Online Patient/Member Feedback Portal: MyVoice is an online forum run by HealthPartners Market Research Division and used to solicit patient feedback, opinions and suggestions of interest for HealthPartners Insurance Plan. HealthPartners recently used feedback from myVoice to update its outreach message explaining the importance of adolescent immunizations. Dr. Rindal, co-Principal Investigator of the application, also utilized myVoice to garner feedback for an opioid de-implementation project to understand what information patients wanted when discussing analgesic options with their dentists.

Institute Methodology & Data Coordinating Center

The **HealthPartners Institute Research Methodology Group (RMG)** leads the methodological and statistical activities associated with internally and externally funded projects. RMG consists of three PhD-level and four master-level methodologists. The group expertise includes study design, epidemiologic methods, randomized trials, comparative effectiveness research, causal inference, biostatistics, psychometrics, and demography. RMG facilitates all steps of research, from grant writing, planning and execution, to analysis and writing for publications.

The **HealthPartners Institute's Health Economics** team includes two PhD-level health economists (Drs. Michael Maciosek and Steven Dehmer) with specialized support from the Institute's statisticians, project managers and software engineering team. They have been recognized for their cost-effectiveness modeling experience, analysis of evidence-based preventive care policies, and economic analysis of clinical and community-based interventions. The work, which has been under way since 1999, has been used in multiple ways to inform policy and medical decision-making locally and nationally. Most recently, the modeling work has featured two of the HealthPartners Institutes microsimulation models – ModelHealth™: CVD and ModelHealth™: Tobacco. The Health Economics team has evolved these models to conduct analyses of state and national tobacco policy, targeted hypertension control interventions, and low-dose aspirin to prevent CVD and colorectal cancer for the US Preventative Services Task Force. The team assists other HealthPartners investigators and external collaborators in analysis of economic aims as part of broader intervention effectiveness and priority-setting projects.

The **HealthPartners Institute Center for Evaluation and Survey Research (CESR)** provides insight into patient, member, community and healthcare provider experience by collecting high-quality survey, interview and focus group data for HealthPartners and the broader research community. CESR is led by experienced survey methodologist and health services researcher Jeanette Ziegenfuss, PhD, who has more than 15 years of experience in survey research in the health field, with support from Meghan JaKa, PhD, an experienced behavioral scientist with qualitative and mixed methods expertise. and a team of other scientists, project managers and interviewers. The CESR team carries out data collection and recruitment for a wide range of project types, from small-scale program evaluations to multi-site clinical trials and FDA studies.

Traditionally involved from proposal development through dissemination and also available for consultation, CESR conducts surveys, interviews and focus groups, and recruits participants into studies using multiple modes, including web, mail and phone. CESR's phone center conducts phone calls from 9 am to 8:30 pm weekdays and during the day on Saturdays. For multi-site data collection, times are altered to align with local time zones. CESR has a number of professional telephone interviewers who conduct interviews in English, Spanish, Hmong and Somali as well as staff trained in qualitative interview and focus group facilitation. Across modes, all data is tracked in project-specific REDCap databases. Call management is orchestrated across all projects through a proprietary call management system that wraps around REDCap. These standardized tools and processes help minimize costs by leveraging economies of scale. In addition, CESR can create and capture paper survey data using scannable forms through Teleform Elite software. Project sizes vary from small studies with 1-2 subjects per month to large, complex, multi-state projects with thousands of participants. Also housed within CESR are behavioral science-grounded evaluation services and nurse chart abstractors who work with our patient electronic health records (EHRs). Comprehensively, CESR offers the following services:

- Survey, interview and focus group methods and recruitment consultation
- Survey, interview and focus group design and formatting
- Survey, interview and focus group data collection:
    - Multilingual data capture via mail, telephone, web, in-person and mixed mode
    - Subject recruitment via web, mail and phone
    - Outreach with trained, multilingual telephone interviewers using computer-assisted telephone interviewing (CATI) software
    - Chart abstraction
    - REDCap (data collection software) consultation, training, and development
- Qualitative and quantitative data management:
    - Data entry
    - Survey, interview and focus group data management
    - Survey, interview and focus group data cleaning and analytic data set preparation
    - Qualitative data recording and transcript production
    - Secure data storage and transmission
- Qualitative and quantitative data analysis

  - Qualitative data coding and analysis using NVivo qualitative software
  - Disposition reporting using AAPOR standard dispositions
  - Data visualization
- Behavioral science evaluation services
  - Theory-driven logic model development, conceptual model and program design
  - Evaluation plan design and intervention mapping; measurement identification
  - Measurement of program implementation and outcomes
  - Comprehensive summary of program findings
- Nurse chart abstraction
- Project administration:
  - Tracking of progress and administrative tasks
  - Reporting of recruitment/survey/interview/focus group progress
  - Incentive handling and administration
  - Project closure services

HealthPartners Care Group

In 2013, HealthPartners and Park Nicollet Health Services combined under the name HealthPartners and a single consumer-governed board of directors. The new organization includes a multispecialty group practice of more than 1,800 physicians; eight hospitals; 55 primary care clinics; 22 urgent care locations; 24 dental clinics; and numerous specialty practices in Minnesota and western Wisconsin.

HealthPartners Care Group has physicians practicing in 55 medical and surgical specialties. Access to data from the primary care clinics, hospitals, the International Health Center, and specialty centers allows HealthPartners Institute to conduct research on large patient populations and subpopulations.

HealthPartners Dental Group (HPDG) is a staff model group practice of more than 66 dentists, including specialists in oral surgery, periodontics, endodontics, prosthodontics, orthodontics, and pediatric dentistry. The practice also has a staff of 5 dental therapists, more than 79 hygienists, and 129 dental assistants. HPDG provides both pre-paid and fee-for-service dental and oral-care services in 25 HealthPartners dental clinics. HPDG provides care for approximately 115,000 patients. Collectively, HealthPartners provides dental coverage for about 540,000 members when including contracted providers outside of the staff model clinics. Data for the contracted groups are limited to claims data so their utility for research is limited. HPDG uses Wisdom, Epic's electronic dental record module, allowing for capture of all medical and dental health information in one integrated EHR. HPDG has been very committed to improving care for its members. As part of accomplishing that goal they have developed care guidelines that address risk assessment and risk reduction efforts for caries and periodontal disease. Data are kept on the patients' risk level and risk factors, risk reduction interventions and diagnosis codes related to all dental procedures. This type of data collection is not readily available in most dental databases, providing a unique and rich source of data for research and care improvement efforts.

HealthPartners Hospitals

Regions Hospital is a 454-bed hospital and a recognized leader in critical care and trauma care. It is designated as a Level I Trauma Center by the American College of Surgeons for both adults and for children with the expertise and technology to treat the most serious injuries. The emergency center is comprised of 50,000 square feet of clinical space with 55 treatment rooms, and includes onsite radiology and lab services. A trauma operating room is staffed around the clock, helicopter service is available for transporting emergency patients, and a complete program of care is available for burn victims. The Regions organizations serve as a referral center for primary care physicians in the east metropolitan and surrounding communities in Minnesota and Wisconsin. Regions also features the Center for Undergraduate and Graduate Clinical Education, a full medical library, a psychiatric unit associated with the emergency department, an HIV/AIDS program, digestive care center, birth center and same-day surgery. As an inner city hospital, Regions serves a culturally and

economically diverse population. For more than 100 years, the Regions organizations have provided excellent health services to those who are unable to pay for care. The hospital is the state's second largest provider of charity care, contributing about $18.2 million in uncompensated care annually.

Methodist Hospital is a 426-bed facility with more than 960 physicians on the medical staff. Methodist Hospital is renowned for high-quality patient care, medical expertise and disease management. The hospital is recognized as an area leader in cardiovascular, neurologic, orthopedic, cancer and maternity care. Park Nicollet Methodist Hospital's Emergency Center treats any medical problem ranging from life-threatening or traumatic injuries to minor illnesses. An expert care team provides a comprehensive range of emergency services, including rapid evaluation and treatment for heart attack and stroke.

Hudson Hospital and Clinic is a 25-bed critical access hospital with 1,500 annual inpatient admissions and more than 10,000 emergency center and 10,000 specialty clinics patients annually. It is one of Western Wisconsin's only hospitalist services and the region's only 24/7 Emergency Medicine Physicians. Its Birth Center is known for providing the area's premier birthing experiences along with nursing staff ranking in the top 90 percent nationwide according to Press Ganey patient survey data, which is why patient volumes have more than doubled in the last 5 years. They serve as regional partner of The Cancer Center of Western Wisconsin and in 2011 expanded specialty services to include the Pediatric Chemotherapy and Infusion Center. In 2019, the Centers for Medicare and Medicaid (CMS) awarded Hudson Hospital and Clinic a four-star rating for its quality of patient care, placing it in the top 30.5 percent of hospitals nationally.

Lakeview Hospital and Stillwater Medical Group are an integrated, non-profit clinic, and hospital system serving the eastern Twin Cities' metro area and western Wisconsin. Lakeview is an acute care hospital that offers medical and surgical services as well as a broad range of specialties. More than 60 physicians and 500 employees deliver medical services in a 90-bed hospital. Seeing more than 7,000 patients annually, the emergency room includes an orthopedic room, acute-care room, and six other patient exam areas. In 2019 Stillwater Gazette Reader's Choice Awards named Stillwater Medical Group as the best clinic and best urgent care and Lakeview as the best hospital and Emergency Room. Lakeview was named a Five-Star Hospital by the Centers for Medicare and Medicaid Services (CMS) for the quality of patient care in 2019, which places them in the top 6.4 percent of hospitals in the U.S.

Westfields Hospital and Clinic consists of eight family practice physicians, two general surgeons, one gastroenterologist, one pediatrician, and three physician assistants. Hospital Medicine providers, support in part by physicians from Regions Hospital, focus their practice on the care of hospitalized patients and provide better continuity of care for patients. They are specially trained in internal medicine and coordinate communication between all physicians involved in a patient's inpatient care. The Transitional Care Unit (TCU) for patients who are stable yet not ready to go home is committed to providing rehabilitation that meets all of the patient's needs to help them onto their next transition. TCU provides skilled therapies from Registered Nurses, Physical Therapists, Occupational Therapists, Speech Therapists as well as other therapies. Named a Top 20 Critical Access Hospital in the U.S., scoring best among critical access hospitals as determined by the Chartis Center for Rural health for overall performance.

Hutchinson Health, in partnership with HealthPartners, includes primary and specialty care clinics, emergency services, and specialty programs. Hutchinson Health includes an Intensive Care Unit, featuring eICU technology, as well as a facility-wide clinical monitoring system. We have over 30 full time physicians, over 30 visiting physician specialists, 20 additional clinicians and practitioners along with our support staff of 650 employees that are ready to make a difference in your life. After five decades of providing exceptional medical care, Hutchinson Health has partnered with HealthPartners to expand capabilities to better serve patients and the community. Hutchinson Health continues to offer a licensed 66-bed, Level 4 Trauma Center, including 12 inpatient mental health unit. The Hutchinson Health Clinic and Urgent Care, Hutchinson Health Hospital, BirthCare and new Cancer Center, along with our multiple locations and services, enhance patient convenience and options, and is an example of how truly committed we are to promoting health and wellness.

HealthPartners Olivia Hospital & Clinic has a long tradition of providing excellent, trusted care through its Olivia, Minnesota-based hospital and clinic, and its outpatient clinics in nearby Hector and Renville. As an organization, we are committed to building a strong rural health system that keeps care local, expands access to specialties, addresses affordability, and promotes health and well-being. Together we can better serve the people of Olivia, Hector, Renville and surrounding communities. With a 16-bed critical access hospital and

three outpatient clinics in Olivia, Hector and Renville, HealthPartners Olivia Hospital & Clinic has a long tradition of providing excellent care in its local communities. Through the HealthPartners affiliation, area residents will have access to expanded services and specialties.

Centers for Care, Research, and Medical Education

Center for Oral Health Integration

The Institute's Center for Oral Health Integration (COHI) is focused on promoting oral health in the context of overall health through research and education efforts that bridge the gap between the dental and medical domains. COHI's mission is to improve health through integration of dentistry, medicine, research and education utilizing a sustainable learning health system approach. COHI key stakeholders include HealthPartners Dental Group, HealthPartners Care Group, the dental plan, the health plan, and HealthPartners Institute. Located within an integrated health system, the COHI team has the unique ability to conduct studies and initiatives that leverage the integrated medical and dental EHR system as well as claims data. COHI supports the use of technology, including clinical decision support (CDS) tools embedded in the EHR, to improve the delivery of evidence-based care. Through COHI, CDS tools have been developed and integrated into the dental module of the EHR. The CDS platform, Dental Wizard, has been developed to fit into the clinical workflow and adapted to increase the delivery of tobacco cessation interventions and quitline referrals by dental providers as well as to support dentists in safe and appropriate prescribing analgesics in order to reduce opioid use in dentistry. These interventions were developed and tested through federally funded studies led by Brad Rindal, DDS (U01DE026135, U01DE027441). Interventions shown to efficacious are implemented into routine patient care in HealthPartners dental clinics utilizing COHI resources. COHI leverages both internal and external funding to accomplish its goals.

Center for Chronic Care Innovation

Over the past 15 years, the HealthPartners Institute Center for Chronic Care Innovation (CCCI) has been awarded over $26M of federal research funding to develop and implement state of the art technology interventions to improve population health including provider simulation training and EHR-based clinical decision support (CDS) under the leadership of Co-Directors, Dr. Patrick O'Connor and Dr. JoAnn Sperl-Hillen.

The CCCI's overall mission is to improve the quality of chronic disease care and prevention through promoting research and the translation of research into innovative practice changes for patients, providers, and health systems. Specific objectives of the CCCI are to:

(a) Promote development, implementation, dissemination, and marketing of various interventions or inventions that have the potential to improve the quality of outpatient care or population health. These may include, but are not limited to: CDS Support systems such as Wizard, simulated learning interventions for providers or patients, Learning Healthcare System interventions.
(b) Develop or refine big data analytic methods such as machine learning, artificial intelligence, data mining, marginal structural modeling, or other methods that can improve the accuracy of risk prediction or quantify the potential benefits or risks of various care options, and discover optimal methods to communicate information about benefits, risks, and prioritization of various treatment options.
(c) Collaborate with internal, regional, national, and international experts who are interested in similar objectives or methods to improve care.
(d) Network broadly with various stakeholders who have an interest in improving chronic disease care or population health, or are working on innovations or technologies that could complement or advance the CCCI objectives.
(e) Mentor new investigators and sponsor a limited amount of investigator time that can be devoted to development of the data systems and analytic methods needed to advance CCCI objectives.

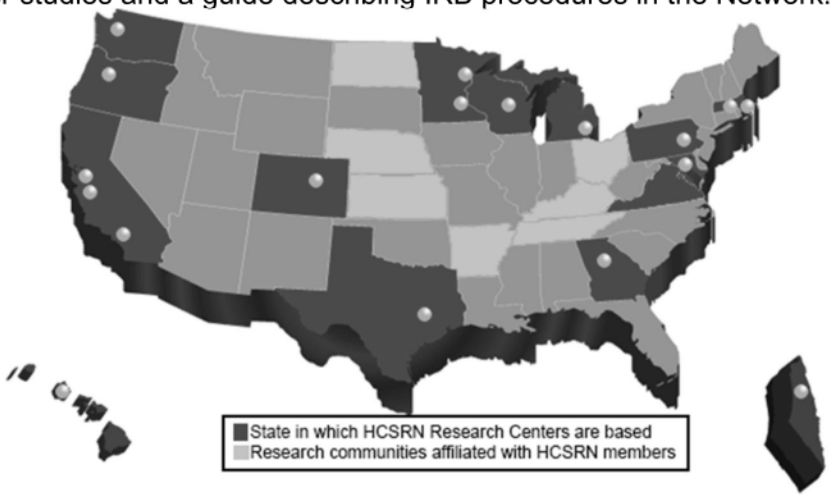
External Partnerships

The National Dental Practice-Based Research Network

The National Dental-Practice Based Research Network (National Dental PBRN) is a consortium of participating practices and dental organizations from across the country which is committed to advancing knowledge of dental practice and improving oral healthcare through research conducted in the real-world setting. The Institute has served as the administrative site for the Midwest Node of the National Dental-Practice Based Research Network (National Dental PBRN) since 2012 (U19DE022516/U19DE028717). Brad Rindal, DDS, Regional Node Director, leads the local team which includes Regional Node Coordinators who provide training and support for research studies implemented in participating dental practices in the Midwest Region (comprised of 10 states including Illinois, Indiana, Iowa, Michigan, Minnesota, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin). Dr. Rindal and the Midwest Node team work closely with Dr. Gregg Gilbert, National Network Director, and leaders from the network's National Administrative and Resource Center at University of Alabama, the five other regional nodes, a specialty node, and the network data coordinating center based at Kaiser Permanente Center for Health Research to develop and carry out research studies with investigators. The team prioritizes the dissemination of findings to benefit real-world daily clinical practice

Health Care Systems Research Network

The Health Care Systems Research Network (HCSRN), is a voluntary consortium of 19 health care delivery organizations with both defined patient populations and formal, recognized research capabilities. The network gives HealthPartners Institute access to a large and diverse population and many capable collaborators. HCSRN has been described as "a model for its capacity to implement studies and capture data within the context of usual care." The network has achieved milestones, including consolidating multiple large network projects in the use of a single distributed data resource, setting up data counters, developing cross-network governance to facilitate use of distributed data resources and reviewing potential new clinical studies. A number of utilities are exclusively available to members of the HCSRN, including a project-management portal, a guide to optimizing recruitment in multicenter studies and a guide describing IRB procedures in the Network.



HCSRN members include Harvard Pilgrim Health Care Institute (Boston), Henry Ford Health System Research (Southeastern Michigan), HealthPartners Institute (Minneapolis/St. Paul), Essentia Institute of Rural Health (Rural Wisconsin/Minnesota/North Dakota/Idaho), Palo Alto Medical Foundation Research Institute (Northern California), Meyers Primary Care Institute (Central Massachusetts), Marshfield Clinic Research Institute (Wisconsin), Baylor Scott & White Health Research (Texas), Geisinger Center for Health Research (Pennsylvania), Kaiser Permanente Washington Health Research Institute (formerly Group Health Research Institute, Washington/Idaho), St. Louis University AHEAD Institute , Maccabi Institute for Research & Innovation (Tel Aviv, Israel), and Kaiser Permanente Centers for Health Research in Hawaii, Northwest (Oregon and Washington), Northern California, Colorado, Southern California, Mid-Atlantic and Georgia.

HCSRN has the vision of being the research partner of choice for those seeking to shape health and health care delivery. A number of aims accompany this purpose:

- To be recognized as the nation's premier resource for population-based health and health care research by leveraging the Network's unparalleled member and geographic diversity, research and research translation strengths, and organizational, human capital and data resources

- Contribute to national and global dialogs on health research and policy by being a credible source of evidence-based information and representing integrated delivery system-based research perspectives
- Promote and establish HCSRN as a preferred research partner of funding agencies and others by capitalizing on its research and research translation strengths and communicating to increase its visibility, collective capabilities and accomplishments
- Foster HCSRN-led collaborative studies by enhancing awareness of research interests, resources and capabilities of the member centers and their investigators and endorsing them and publicizing their successes
- Share methodologies, best practices and consultative expertise derived from HCSRN's successful research enterprise by holding an annual conference; strengthening investigator development through shared recruitment strategies, fellowships and mentoring programs; joining forces with public and private agency initiatives; and enlisting both traditional and new dissemination technologies

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

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E-Mail*: donald.b.rindal@healthpartners.com

Credential, e.g., agency login: eRA Commons User Name

Project Role*: PD/PI Other Project Role Category:

Degree Type: DDS Degree Year: 1975

Attach Biographical Sketch*: File Name: DBRindal Biosketch.pdf

Attach Current & Pending Support: File Name:

Tracking Number: GRANT13567964 Funding Opportunity Number: PAR-21-317 . Received Date: 2022-03-07T11:53:21.000-05:00

PROFILE - Senior/Key Person

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Degree Type: PhD Degree Year: 1996

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Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

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Project Role*: Other (Specify) Other Project Role Category: Co-Investigator/Statistician

Degree Type: MA Degree Year: 1992

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Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

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Project Role*: Co-Investigator Other Project Role Category:

Degree Type: PhD Degree Year: 2016

Attach Biographical Sketch*: File Name: JaKa Biosketch.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

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Project Role*: Co-Investigator Other Project Role Category:

Degree Type: MD, MPH Degree Year: 2004

Attach Biographical Sketch*: File Name: Kharbanda Biosketch.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Bryan Middle Name S Last Name*: Michalowicz Suffix: DDS, MS

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E-Mail*: bryan.s.michalowicz@healthpartners.com

Credential, e.g., agency login: eRA Commons User Name

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: DDS, MS Degree Year: 1998

Attach Biographical Sketch*: File Name: Michalowicz Biosketch.pdf

Attach Current & Pending Support: File Name:

OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: D. Brad Rindal, DDS

eRA COMMONS USER NAME (credential, e.g., agency login): eRA Commons User Name

POSITION TITLE: Senior Investigator

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date YYYY	FIELD OF STUDY
University of Minnesota, Minneapolis, MN	BS	1973	General Sciences
University of Minnesota, Minneapolis, MN	DDS	1975	Dentistry

A. Personal Statement

I am a Senior Investigator, Associate Dental Director for Research, and a practicing dentist who specializes in the management of Temporomandibular Disorders (TMD) and orofacial pain. My dual career endeavors in research and clinical practice have provided me a unique perspective on evidence-based care, and as the Director of the Midwest Node of the NIDCR-funded National Dental Practice-Based Research Network (National Dental PBRN; U19DE028717), I have become particularly interested in conducting research within real-world clinical settings. I have considerable experience using clinical decision support (CDS) tools within the electronic health record (EHR) to support providers in making clinically useful, evidence-based care decisions. Currently, I serve as Co-PI of a study examining approaches to de-implement unnecessary opioid prescribing following dental extractions using CDS embedded into the electronic dental record (U01DE027441). I also have expertise in applying Screening, Brief Intervention, and Referral to Treatment (SBIRT) approaches in the dental setting. I have used this approach in a series of studies which have developed and tested a CDS-driven brief tobacco cessation intervention (CDC/200-2009-28537, RC1DE020295, R34DE023895, U01DE026135). Currently, I serve as the Co-PI for a multi-site clinical trial testing the tobacco cessation CDS tool in a number of community dental clinics as well as in two dental schools (U01DE026135). With the support of the HealthPartners Center for Oral Health Integration, I am currently overseeing the development and implementation of a comprehensive EHR-embedded CDS platform (Dental Wizard) for HealthPartners dental providers. This CDS platform will incorporate elements from our previous CDS grants focused on promoting tobacco cessation and reducing opioid prescribing and will also include HPV vaccination status information and targeted alerts, allowing us to leverage and build from this platform for the proposed study.

As Co-PI of the proposed study, I will work closely with Dr. Mabry to develop and implement the intervention in HealthPartners dental practices, evaluate the results, and disseminate study findings. Given my prior experience implementing provider-focused interventions in the dental clinics and my close relationship with the HealthPartners Dental Group, I am well positioned to oversee study implementation and work with stakeholders to gather feedback and troubleshoot any issues throughout the study.

1. **Rindal DB**, Mabry PL. Leveraging clinical decision support and integrated medical-dental electronic health records to implementing precision in oral cancer risk assessment and preventive intervention. J Pers Med. 2021 Aug 25;11(9). PMCID: PMC8470765.
2. **Rindal DB**, Gilbert GH, Carcelén C, Funkhouser E, Durand E, Uppgaard DA, Fellows J, Ikeda J, Kerr AR, Brar B, Gordan VV, Agarwal S, Barnett P, Pickard RK, Gillison M. Feasibility and acceptance of oral human papillomavirus detection in the dental office: Results from The National Dental Practice-Based Research Network. J Am Dent Assoc. 2019 Feb;150(2):130-139.e4. doi: 10.1016/j.adaj.2018.10.022. PubMed PMID: 30691571; PubMed Central PMCID: PMC6800070.

3. Sperl-Hillen JM, Rossom RC, Kharbanda EO, Gold R, Geissal ED, Elliott TE, Desai JR, **Rindal DB**, Saman DM, Waring SC, Margolis KL, O'Connor PJ. Priorities Wizard: Multisite Web-Based Primary Care Clinical Decision Support Improved Chronic Care Outcomes with High Use Rates and High Clinician Satisfaction Rates. EGEMS (Wash DC). 2019 Apr 3;7(1):9. PMCID: PMC6450247.
4. **Rindal DB**, Asche SE, Gryczynski J, Kane SM, Truitt AR, Shea TL, Ziegenfuss JY, Schwartz RP, Worley DC, Mitchell SG. De-Implementing Opioid Use and Implementing Optimal Pain Management Following Dental Extractions (DIODE): Protocol for a Cluster Randomized Trial. JMIR Res Protoc 2021Apr 12;10(4):e24342. PMCID: PMC8076983.

Ongoing projects that I would like to highlight include:

Implementing Dental Quality Measures in Practice (Walji)
Source: NIDCR/R01DE024166
Role: Site PI 07/01/2021-06/30/2026
We are currently faced with an uneven oral healthcare delivery system where a few lucky patients receive evidence-based and person-centered care, while others receive too much care or no care at all. Our current quality measurement work has shown that we can use data captured in electronic health records (EHRs) to accurately measure the quality of dental care. We expect that the outcomes of our research will arm dental institutions with both the knowledge and know-how to measure and improve the quality of patient care resulting in better oral health for our patients.

De-Implementing Opioid Use and Implementing Optimal Pain Management Following Dental Extractions (Rindal/Mitchell)
Source: NIDCR/U01DE027441
Role: PI 09/01/2017-08/31/2021
The overarching goal of this project is to de-implement the reliance of opioid analgesics and to implement reliance on non-opioid analgesics to manage postoperative pain following dental extractions. We will compare different strategies to reduce the reliance on opioids and increase the use of alternative pan management approaches utilizing information support tools aimed at both providers and their dental extraction patients.

De-Implementing Opioid Use and Implementing Optimal Pain Management Following Dental Extractions: Supplement (Rindal/Mitchell)
Source: NIDCR/U01DE027441
Role: PI 09/01/2018-08/31/2021
The supplement will allow for additional exploration of: 1. how minor patients and their parents/guardians make decisions about opioid use after dental extractions through interviews; 2. diffusion of intervention effects on opioid prescribing related to other procedures (such as root canal treatment) and general management of pain complaints following dental procedures; and 3. disparities in opioid prescribing.

A Clinic-Randomized Trial of a Clinical Decision Support System to Improve Dental Provider Delivery of Brief Tobacco Interventions and Quitline Referrals (Rindal)
Source: NIDCR/U01DE026135
Role: PI 08/01/2016-06/30/2022
This project is the next step in this program and aims to evaluate the effectiveness of clinical decision support (CDS) to improve dental provider delivery of brief tobacco interventions and referrals to tobacco quitlines for further tobacco counseling.

The National Dental PBRN Administrative and Resource Center (Gilbert)
Source: NIDCR/R44DE026663
Role: Site PI 06/07/2019-05/31/2022
The network's overall goal is to do science that is immediately applicable to everyday clinical practice, to foster movement of its findings into everyday clinical practice, and thereby improve the health of the nation. The network will continue to be a highly collaborative environment wherein clinicians in everyday clinical practice, academic researchers, patient representatives, and their communities become engaged in “win-win” activities that each group sees as mutually beneficial and which improves health.

B. Positions, Scientific Appointments, and Honors
Positions
2013-pres. Associate Dental Director for Research, HealthPartners Dental Group, Minneapolis, MN
2012-pres. Regional Director, Midwest Node of the National Dental PBRN

1998-pres. Senior Investigator, Dental Health Services Research, HealthPartners Institute
1984-2012 Clinic Chief, TMD/Orofacial Pain/Dental Sleep Medicine Clinic at HealthPartners
1978-1984 Chief of Dental Services at the Spring Lake Park Clinic of the HealthPartners Dental Group
1977-pres. Staff dentist at HealthPartners Dental Group (HPDG), general dentistry for 20 years and TMD/Orofacial for 25 years
1975-1977 Captain in the Dental Corp of the United States Air Force

Scientific Appointments

2013-pres. American Association for Dental Research MN Section Treasurer
2010-pres. HPDG Quality Measures Committee
2008-pres Minnesota Dental Association Evidence-Based Dentistry Taskforce
2008-pres. Oral Examiner, American Board of Orofacial Pain
2004-2005 President, St. Paul District Dental Society
1997 Board Certification, Diplomate of the American Board of Orofacial Pain
1995-pres. HPDG Guideline Development Steering Committee

Awards and Honors

2012 Recipient of the Excellence in Research Award. Annually, HealthPartners honor Medical and Dental Group physicians, dentists and researchers who, by virtue of their outstanding skills and commitment to excellence, have been selected by their colleagues as exceptional within the divisions of Primary Care (including Hospital Services), Specialty Care (including Behavioral Health), Dental Care, Research and Medical Education
1991 Dr. Maurice Visscher Award. Selected by fellow dentists and physicians in recognition of outstanding clinical skills, dedicated service to patients, exemplary support of colleagues and ancillary staff, and significant contributions to Group Health, Inc.
1990 President's Award. This award was presented for outstanding performance in serving the members and staff of Group Health, Inc.

C. Contributions to Science

1. **Translational Research and Evidence-Based Practice**. My research activity is focused on ways to improve the translation of evidence into daily practice and practice-based research. As a research investigator in HealthPartners Institute, a leader with the HealthPartners Dental Group, and a practitioner at the HealthPartners TMD/Orofacial Pain Clinic, I have a unique perspective within each arena that affords opportunities to support translation of evidence-based findings into practice. My research has focused on the utilization of Health Information Technology to both improve patient care and speed the translation of new evidence into daily practice so patients benefit (R01DE022332). I also serve as the Director of the Midwest Region of the National Dental Practice-Based Network (DPBRN) which engages providers across the nation (U19DE028717).
   a. **Rindal DB**, Flottemesch TJ, Durand EU, Godlevsky OV, Schmidt AM, Gilbert GH; National Dental PBRN Collaborative Group. Practice change toward better adherence to evidence-based treatment of early dental decay in the National Dental PBRN. Implement Sci. 2014 Dec 2;9:177. PMCID: PMC4260248.
   b. McBride R, Leroux B, Lindblad A, Williams OD, Lehmann M, **Rindal DB**, Botello-Harbaum M, Gilbert GH, Gillette J, Demko C; CONDOR Collaborative Group. Measuring the impact of practice-based research networks on member dentists in the Collaboration on Networked Dental and Oral Health Research, CONDOR. J Dent. 2013 May;41(5):393-403. PMCID: PMC3825028.
   c. **Rindal DB**, Gordan VV, Fellows JL, Spurlock NL, Bauer MR, Litaker MS, Gilbert GH; DPBRN Collaborative Group. Differences between reported and actual restored caries lesion depths: results from The Dental PBRN. J Dent. 2012 Mar;40(3):248-54. PMCID: PMC3279178.
   d. Thyvalikakath P, Durand E, Spallek H, Enstad CJ, Asche SE, **Rindal DB**, Rush WA. Dental Hygienists' usage of tobacco-cessation decision support tools in practice: A qualitative study. Intern J Evidence-Based Prac Dental Hygienist. Summer 2015. Vol 1 Issue 1 Pages 57-65.

2. **Clinical Decision Support.** One area of particular interest for me is the use of clinical decision support tools embedded in electronic health records to assist providers in delivering optimal care. I have led and contributed to a series of studies that have developed and tested a CDS-driven brief tobacco cessation intervention (CDC/200-2009-28537, RC1DE020295, R34DE023895, U01DE026135). The CDS, which guided providers in addressing tobacco cessation with patients and providing referrals to treatment

programs, was so well received that it has now been adopted by all of the HealthPartners dental clinics. I am currently leading a multi-site clinical trial testing the tobacco cessation CDS tool in a number of community dental clinics as well as in two dental schools (U01DE026135). In addition, I am Co-PI of a study which is testing the use of a CDS system to promote appropriate prescribing of analgesics and reduce unnecessary opioid prescribing following dental extractions (U01DE027441).

a. **Rindal DB**, Rush WA, Schleyer TK, Kirshner M, Boyle RG, Thoele MJ, Asche SE, Thyvalikakath T, Spallek H, Durand EC, Enstad CJ, Huntley CL. Computer-assisted guidance for dental office tobacco-cessation counseling: a randomized controlled trial. Am J Prev Med. 2013 Mar;44(3):260-4. PMCID: PMC3579569.
b. Rush WA, Schleyer TK, Kirshner M, Boyle R, Thoele MJ, Lenton PA, Asche S, Thyvalikakath T, Spallek H, Durand EC, Enstad CJ, Huntley CL, **Rindal DB**. Integrating tobacco dependence counseling into electronic dental records: a multi-method approach. J Dent Educ. 2014 Jan;78(1):31-9. PMCID: PMC6697074.
c. **Rindal DB**, Asche SE, Gryczynski J, et al. De-implementing opioid use and implementing optimal pain management following dental extractions (DIODE): protocol for a cluster randomized trial. JMIR Res Protoc. 2021;10(4):e24342. PMCID: PMC8076983.

3. **Medical-Dental Integration**. While medicine and dentistry practices developed separately and often remain siloed, our understanding of the interconnectedness between oral health and overall health has grown significantly in recent years. As a provider in an integrated health system that leverages one combined electronic health record system, I have had the unique opportunity to conduct research that leverages both medical and dental electronic health data as well as claims data to investigate the myriad of relationships between oral health and other health conditions. I have also contributed to studies that aim to improve care by leveraging the integrated EHR to provide dental providers with enhanced information on patient health. I was a co-investigator on a study to use eMedical Record (EMR), eDental Record (EDR), and a Personal Health Record (PHR) to improve the quality and safety of dental care for patients with chronic illnesses (R18HS017270). Since then, the capabilities to integrate data have greatly evolved, and have allowed me to work with partners from across the organization to address shared priorities including tobacco cessation and human papillomavirus (HPV) vaccination. The HealthPartners Center for Oral Health Integration (COHI) was established to formalize our ongoing commitment to improving health through the integration of dentistry, medicine, research and education utilizing a sustainable learning health system approach. In close collaboration with stakeholders from HealthPartners Dental Group, HealthPartners Care Group, the dental plan, and the health plan, I lead COHI efforts including the development of a comprehensive CDS platform for use in dental clinics.

   a. **Rindal DB**, Mabry PL. Leveraging clinical decision support and integrated medical-dental electronic health records to implementing precision in oral cancer risk assessment and preventive intervention. J Pers Med. 2021 Aug 25;11(9). PMCID: PMC8470765.
   b. Sperl-Hillen JM, Rossom RC, Kharbanda EO, Gold R, Geissal ED, Elliott TE, Desai JR, **Rindal DB**, Saman DM, Waring SC, Margolis KL, O'Connor PJ. Priorities Wizard: Multisite Web-Based Primary Care Clinical Decision Support Improved Chronic Care Outcomes with High Use Rates and High Clinician Satisfaction Rates. EGEMS (Wash DC). 2019 Apr 3;7(1):9. Review. PMCID: PMC6450247.
   c. Larsen AJ, **Rindal DB**, Hatch JP, Kane S, Asche SE, Carvalho C, Rugh J. Evidence Supports No Relationship between Obstructive Sleep Apnea and Premolar Extraction: An Electronic Health Records Review. J Clin Sleep Med. 2015 Dec 15;11(12):1443-8. doi: 10.5664/jcsm.5284. PubMed PMID: 26235151; PubMed Central PMCID: PMC4661337.
   d. Fricton J, **Rindal DB**, Rush W, Flottemesch T, Vazquez G, Thoele MJ, Durand E, Enstad C, Rhodus N. The effect of electronic health records on the use of clinical care guidelines for patients with medically complex conditions. J Am Dent Assoc. 2011 Oct;142(10):1133-42.

4. **Dental Practice-Based Research Network.** I have extensive experience with development of the infrastructure of the National Dental PBRN as well as development of research protocol. I am currently the Director of the Midwest Region of the National Dental Practice-Based Research Network (U19DE028717). The National Dental Practice-Based Research Network is a national expansion of our previous Dental Practice-Based Research grant on which I served as Minnesota PI (U01DE16747). The network is now in the third year of its second seven year funding cycle. I was the Principal Investigator on a study to assess whether participation in Dental PBRN impacts clinical treatment (R03DE022089). The National Dental

PBRN is focused on improving daily clinical practice and I have a significant role in developing studies that achieve and measure that goal.

a. **Rindal DB**, Gilbert GH, Carcelen C, Funkhouser E, Durand E, Uppgaard DA, Fellows JL, Ikeda J, Kerr AR, Brar B, Gordan VV, Agarwal S, Barnett P, Pickard RK, Gillison M, National Dental PBRN Collaborative Group. Feasibility and acceptance of oral HPV detection in the dental office: results from the National Dental PBRN. Journal of the American Dental Association.
b. Gilbert GH, Williams OD, Korelitz JJ, Fellows JL, Gordan VV, Makhija SK, Meyerowitz C, Oates TW, **Rindal DB**, Benjamin PL, Foy PJ, for the National Dental PBRN Collaborative Group. Purpose, structure and function of the United States National Dental PBRN. Journal of Dentistry 2013 Nov; 41(11): 1051-1059. EPub 2013 Apr 15. PMCID: PMC3812393.
c. **Rindal DB**, Gordan VV, Fellows JL, Spurlock NL, Bauer MR, Litaker MS, Gilbert GH for The DPBRN Collaborative Group. Differences between reported and actual restored caries lesion depths: results from dentists in The Dental PBRN. J Dent. 2012 Mar;40(3):248-254. PMCID: PMC3279178.
d. **Rindal DB**, Gordan VV, Litaker MS, Bader JD, Fellows JL, Qvist V, Wallace-Dawson MC, Anderson ML, Gilbert GH; DPBRN Collaborative Group. Methods dentists use to diagnose primary caries lesions prior to restorative treatment: findings from the Dental PBRN. J Dent. 2010 Dec;38(12):1027-32. PMCID: PMC3267573.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/d.%20brad.rindal.1/bibliography/public/

OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

NAME: Patricia Lombard Mabry (Formerly, Patricia Lombard Fiero), PhD

eRA COMMONS USER NAME (credential, e.g., agency login) eRA Commons User Name

POSITION TITLE: Research Investigator, HealthPartners Institute; Adjunct Faculty, Department of Informatics, School of Informatics, Computing, and Engineering, Indiana University

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Virginia Tech, Blacksburg, VA	BS	03/1985	Accounting
George Mason University, Fairfax, VA	MA	05/1991	Psychology
University of Virginia (UVA), Charlottesville, VA	PhD	08/1996	Clinical Psychology
Medical University of South Carolina (MUSC), Charleston, SC	Postdoctoral Fellow	08/1998	Clinical Psychology

A. Personal Statement

I am an interdisciplinary scientist and Research Investigator at HealthPartners Institute. My doctoral training is in clinical psychology and I have spent a significant portion of my career working as a behavioral scientist to advance the nation's research agenda in health. As a doctoral student, I delivered individual psychological services (direct patient care) at the University of Virginia Hospital's Behavioral Medicine Clinic, where patients presenting with medical complaints were referred by other specialties in the hospital for treatment with cognitive-behavioral interventions. As part of my dissertation work, I delivered a behavioral intervention (thermal biofeedback) to diabetic patients at the Behavioral Medicine Clinic. During my internship and early post-doctoral career, I worked as a clinician-researcher in an academic medical center at the Medical University of South Carolina. I spent more than five years delivering cognitive and behavioral interventions at the individual- and couples-level to adults with a variety of presenting conditions including anxiety, depression, headache, stress, grief, eating disorders, learning disabilities, and tobacco, alcohol and drug addiction. In the early part of my career – while at MUSC, Personal Improvement Computer Systems (a small business), and at the National Cancer Institute's Tobacco Control Research Branch, I focused my research on developing behavioral interventions aimed at helping individual smokers achieve tobacco cessation.

In the past 10-15 years I have been promoting and applying cutting edge methodologies, such as systems science and data science to research questions in a range of applied health areas at the population level. While I continue my work in this vein, my move to HealthPartners in 2019 has presented me with the opportunity to again conduct research on developing behavioral interventions for delivery in clinical settings. I have also spent over a decade working at the National Institutes of Health: in intramural research (as a fellow in the Clinical Psychobiology Branch at NIMH), as Director of the Tobacco Intervention Research Clinic, and as a Senior Advisor in both the Office of Behavioral and Social Sciences Research (OBSSR) and the Office of Disease Prevention. Working at the NIH gave me exposure to numerous behavioral intervention studies and the opportunity to hone my research skills at executing and evaluating scientific rigor across a variety of research designs and study topics. I have received national recognition for my contributions to behavioral science: I was elected by my peers to be a Fellow of the Society of Behavioral Medicine in 2012 and my work has been recognized through various positions and awards. Related to the proposed study, I have a pending award to develop a tool to support patient-provider shared decision in the context of diabetes.

These experiences have prepared me well for my role as a co-Principal Investigator on the proposed study. I will work closely with Dr. Brad Rindal to co-lead the study, and in particular, I will contribute my expertise in clinical psychology and health behavior research to oversee the development, implementation, and evaluation of the provider-focused behavioral intervention. Specifically, I look forward to advancing our understanding of the behavioral mechanisms among dental providers that influence providers' decisions to promote HPV

vaccination and how these mechanisms can be targeted to increase vaccine promotion, referrals to vaccine scheduler, and ultimately vaccination receipt.

1. Rindal DB, **Mabry PL**. Leveraging clinical decision support and integrated medical-dental electronic health records to implementing precision in oral cancer risk assessment and preventive intervention. J Pers Med. 2021 Aug 25;11(9). PMCID: PMC8470765.
2. Jerome A, **Fiero PL**, Behar A. Computerized scheduled gradual reduction for smokeless tobacco cessation: development and preliminary evaluation of a self-help program. Computers in Human Behavior. 2000 Sept;16(5):493-505.
3. Stoddard JL, Augustson EM, **Mabry PL.** The importance of usability testing in the development of an internet-based smoking cessation treatment resource. Nicotine Tob Res. 2006 Dec;8 Suppl 1:S87-93.
4. **Fiero PL**. Behavioral aspects of nicotine replacement for tobacco dependence treatment: Limitations of treatment and opportunities for research. Invited speaker to graduate students and faculty in the Department of Psychology at the University of Virginia (Clinical Area Colloquia). Charlottesville, VA, March 2008.

Ongoing and recently completed projects I would like to highlight include:

SCISIPBIO: Constructing Heterogeneous Scholarly Graphs to Examine Social Capital Accumulation During Mentored K Awardees Transition to Research Independence: Explicating a Matthew Mechanism
Source: National Science Foundation, Award # 2122232
Role: PI 09/01/2021-08/31/2025

The long-term goal of the broader program of research into which this project fits is to strengthen the biomedical research workforce by making it more fair, equitable, diverse, open, transparent, and scientifically rigorous. The goal of this project is to understand the etiology of NIH funding gaps between the successful and unsuccessful NIH applicants. To do this, we examine the complex career trajectories of Mentored K award recipients during their multi-year quest for an NIH R01 (or equivalent) grant. We first integrate NIH award data with publication data for a set of over 11K MK awardees and convert the data to heterogeneous scholarly graphs. Doing so enables us to represent complex multidimensional, time-varying relationships between MK recipients, their scholarly achievement and social capital, and R01 success as they unfold and evolve over their careers. It also allows us to use deep learning and other artificial intelligence tools to find complex patterns in the data that can expand our understanding of the hypothesized mechanisms of social capital accrual among this group of scholars, or even help us generate new hypotheses, that would otherwise escape detection by more simplistic methods. One implication of this work is a better understanding of the complex dynamic forces that create and maintain a divide between majority and underrepresented groups in the biomedical research workforce. The results of this work also has the potential to improve NIH's return on investment in the Mentored K program by identifying areas for increasing efficiencies (e.g., by converting a greater percentage of MK awardees into R01-equivalent awardees).

National Leadership Grant-Project: Shared BigData Gateway for Research Libraries (SBD-Gateway): A Cloud-based Cyberinfrastructure for Sharing Research Assets and Advancing Library and Information Science (Wittenberg/Mabry)
Source: Institute of Museum and Library Services/LG-70-18-0202-18
Role: Co-Project Director 07/01/2019-09/30/2020
The Shared BigData Gateway for Research Libraries is a two-year IMLS-funded project to develop, seed, and maintain a cloud-based, extendable cyberinfrastructure for sharing large academic library data resources with a growing community of scholars. The gateway will initially be seeded with a combination of open and licensed bibliometric datasets, including Microsoft Academic and Web of Science data.

Simulation Model on Colorectal Cancer Screening to Inform HealthPartners Practice (Mabry)
Source: HealthPartners Institute and HealthPartners - Health Promotion Department
Role: PI 05/01/2019-12/31/2021
We built a dynamic simulation model to aid health care decision makers in gaining insight on the future impact of their decisions pertaining to colorectal cancer screening strategies over a thirty-year time horizon.

B. Positions and Honors
Positions and Employment

2019-Pres. Research Investigator, HealthPartners Institute, Minneapolis, MN

2019 Adjunct faculty, Department of Informatics, School of Informatics, Computing, and Engineering, Indiana University, Bloomington, IN. Terminated per policy upon acceptance of subaward.
2015-2018 Senior Research Scientist, Indiana University Network Science Institute (IUNI) and School of Public Health, Indiana University, Bloomington, IN.
2015-2018 Executive Director, Indiana University Network Science Institute (IUNI) and Senior Research Scientist, School of Public Health, Indiana University, Bloomington, IN.
2014-2015 Senior Advisor for Disease Prevention, Office of Disease Prevention (ODP), National Institutes of Health (NIH), Rockville, MD
2013-2014 Acting Deputy Director, Office of Behavioral and Social Sciences Research (OBSSR), National Institutes of Health (NIH), Bethesda, MD
2008-2014 Senior Advisor, Office of Behavioral and Social Sciences Research (OBSSR), National Institutes of Health (NIH), Bethesda, MD
2005-2008 Health Scientist Administrator, Office of Behavioral and Social Sciences Research (OBSSR), National Institutes of Health (NIH), Rockville, MD
2004-2005 Proposal Developer, Centurion Technology, Inc., Ithaca, NY
2002-2005 Behavioral Scientist, Science Applications International Corporation (SAIC-Frederick), Contracted to the Tobacco Control Research Branch, National Cancer Institute (NCI), National Institutes of Health (NIH), Rockville, MD
2001-2002 Scientific Advisor (IPA), Tobacco Control Research Branch (TCRB), National Cancer Institute (NCI), National Institutes of Health (NIH), Rockville, MD
2000-2002 Assistant Professor of Psychology, Department of Psychiatry & Behavioral Sciences, Medical University of South Carolina (MUSC), Charleston, SC
1998-2002 Staff Psychologist, Counseling and Psychological Services (CAPS), Department of Student Life, Medical University of South Carolina , Charleston, SC
1998-2000 Instructor, Department of Psychiatry & Behavioral Sciences, Medical University of South Carolina (MUSC), Charleston, SC
1996-1997 Research Scientist, Personal Improvement Computer Systems, Inc. (PICS), Reston, VA
1995-1996 Clinical Psychology Intern, Medical University of South Carolina (MUSC), Charleston, SC

*The NIH uses an official job title of Health Scientist Administrator (HSA) for the GS-601 series.

Honors and Awards (Selected)

2020 Senior author (1 of 4) on a paper nominated for the 2021 for the PNAS Cozzarelli Prize: Murphy, M. C., Mejia, A. F., …**Mabry PL,** Ressel S, Diekman A, & Pestilli F. (2020). Open science, communal culture, and women's participation in the movement to improve science. Proceedings of the National Academy of Sciences (PNAS), 117(39), 24154-24164.

2015 NIH Office of the Director Honor Award (OD Honor Award). For leading the ODP Portfolio Analysis Development Team, "for your outstanding efforts to develop new processes and tools to analyze the NIH prevention research portfolio".

2013 Best Paper Award for Edward Ip, Qiang Zhang, Ji Lu, Laurette Dube and **Patricia Mabry**.Feedback dynamic between emotional reinforcement and healthy eating: An application of the reciprocal Markov model. Presented at the *International Conference on Social Computing, Behavioral-Cultural Modeling and Prediction* (SBP13).

2011 NIH Director's Award (group award). *"For leadership and collaboration to advance and accelerate progress in addressing the nation's childhood obesity epidemic through the National Collaborative on Childhood Obesity Research (NCCOR)."*

2008 Inaugural Applied Systems Thinking Prize (group award). Member of nine-member CDC-NIH System Dynamics Collaborative; prize awarded by the Applied Systems Thinking Institute

2008 NIH Office of the Director Merit Award, "*For extraordinary contributions to advancing the NIH mission by implementing the major goal for systems science, methods and modeling, as specified in OD-OBSSR's strategic prospectus*."

2004 & 2005 NIH Plain Language Awards for work on Smokefree.gov, a tobacco cessation website.

2001 & 2002 Golden Apple Teaching Awards, Medical University of South Carolina, Department of Psychiatry & Behavioral Sciences, by vote of 4th year medical students for teaching unit on treating tobacco dependence

C. Contributions to Science

1. Strengthening the Biomedical Research Enterprise and Workforce:

I am a champion for strengthening the biomedical research enterprise and its workforce. I have worked to promote scientific rigor and methodological innovation (e.g, by founding a program of systems science and health), established guidelines (Nosek et al 2015) and platforms (i.e., CADRE, Mabry et al., 2020; Bridge 2AI projects – see pending support) for reproducibility, openness, fairness, inclusivity and, transparency in science. I have conducted original research to understand funding disparities in the biomedical research workforce (NSF Award # 2122232) and worked to promote a communal culture in science (Murphy et al 2020). I am a recognized leader in facilitating interdisciplinary team science (e.g., in Mabry et al 2008; as Executive Director of IU Network Science Institute; as a member of Bridge 2AI teams).

a. Nosek, B. A., Alter, G., Banks, G. C., Borsboom, D., Bowman, S. D., Breckler, S. J, … **Mabry, P,** ... & Contestabile, M. (2015). Promoting an open research culture. *Science, 348*(6242), 1422-1425. Impact Factor: 41.063 (2018); Citation count: 1088. Note: authors in alphabetical order after first author.
b. Murphy MC, Mejia AF, … ***Mabry PL,** *Ressl S, *Diekman AB, *Pestilli F. "Open science, communal culture, and women's participation in the movement to improve science." *Proceedings of the National Academy of Sciences* 117, no. 39 (2020): 24154-24164.***Senior authors**. Article nominated for Cozzarelli Prize.
c. **Mabry, PL**, Yan X, Pentchev V, Van Rennes R, McGavin SH, & Wittenberg JV. "CADRE: A Collaborative, Cloud-Based Solution for Big Bibliographic Data Research in Academic Libraries." *Frontiers in Big Data* 3 (2020): 42.

2. Creating a Research Community for System Science and Health

Through a broad range of programmatic, outreach and educational activities (documented in Mabry and Kaplan, 2013), I was instrumental in integrating system science approaches with behavioral and social science research (BSSR) at NIH. I did this by raising awareness of what systems science approaches were (i.e., system dynamics modeling, agent-based modeling, network science, and other forms of modeling and simulation) and how they could be applied to BSSR (e.g., Mabry et al., 2008). I founded and co-directed the *Institute on Systems Science and Health* (ISSH) an annual week-long course (2009-2012) for extramural researchers of all levels, designed to help them learn the basics of a particular systems science methodology through small group hands-on learning, plenary sessions, and professional networking opportunities. When new bureaucratic requirements threatened the viability of ISSH, I wrote a funding opportunity to enable the investigator community to develop its own courses: RFA-OD-13-009, Short Courses on Innovative Methodologies in the Behavioral and Social Sciences (R25). I authored funding opportunities for methodological innovation in systems science (detailed in Mabry and Kaplan, 2013). Importantly, I created a listserv to communicate systems science with a unified voice across disciplinary silos, culminating with1200 subscribers spanning the globe. I Co-founded and Co-Chaired Envision, a network of 11 research teams focused on modeling obesity policy (described in Mabry and Bures, 2014).

a. **Mabry PL**, Olster DH, Morgan GD, Abrams DB. Interdisciplinarity and systems science to improve population health: a view from the NIH Office of Behavioral and Social Sciences Research. Am J Prev Med. 2008 Aug;35(2 Suppl):S211-24. PMCID: PMC2587290.
b. Gortmaker SL, Swinburn BA, Levy DT, Carter R, **Mabry PL**, Finegood DT, Huang TT, Marsh T, Moodie ML. Changing the future of obesity: science, policy, and action. Lancet. 2011 Aug 27;378(9793):838-847. PMCID: PMC3417037.
c. **Mabry PL,** Bures RM. Systems science for obesity-related research questions: an introduction to the theme issue. Am J Public Health. 2014 July;104(7):1157-1159. PMCID: PMC4056202.
d. **Mabry PL** & Kaplan RM. Systems science: a good investment for the public's health. Health Educ Behav. 2013 Oct;40(1 suppl), 9S-12.

3. Tobacco Cessation Research – NRT Dosing.

Nicotine Replacement Therapy (NRT), a first-line treatment for tobacco dependence. It works by replacing the nicotine the smoker would otherwise extract from cigarettes with a non-tobacco, therapeutic (clean) source, NRT, which is then gradually withdrawn. My work drew attention to a critical but neglected issue: the need for more specificity in the dosing guidelines for nicotine replacement therapy (NRT) which are extremely vague (e.g., a five-fold difference between the upper and lower bounds of the dosing range for nicotine nasal spray). Instruction for tapering off NRT once smoking abstinence is achieved is also lacking. Wide dosing windows does accommodate customizing dosing according to individual need and nicotine metabolism varies dramatically between smokers. However, lack of specificity in dosing arguably leaves too much discretion to

the patient, who is often unable to determine the minimum dosing necessary to help him or herself stay abstinent. My basic research study provided the first (and to date the only) data on the relationships between levels of nicotine intake (from cigarettes during smoking and from nicotine replacement therapy during an ad libitum course of nicotine nasal spray), nicotine and cotinine blood levels, withdrawal symptoms, and cravings across time before and during the first three days of a quit attempt under controlled conditions. In the course of this study, I also developed and piloted a new method to addresses a significant confound faced by researchers studying physiological correlates of smoking. Smoking behavior is notoriously sensitive to environmental cues, so smoking patterns change when research participants are brought into the laboratory. This prevents researchers from taking invasive physiological measures under ecologically valid conditions. My method derives a smoker's typical smoking schedule based on smoking behavior captured with a computerized cigarette dispenser in the smoker's natural environment. This innovation allows researchers to replicate each smoker's own unique typical smoking pattern under controlled laboratory conditions where invasive measures can be taken, without sacrificing the ecological validity of the smoker's usual schedule. Results of the study provided new and novel information about self-dosing of nicotine nasal spray under tightly controlled, ad libitum conditions, revealed the alarming degree to which self-dosing failed to match prescribing instructions, and demonstrated the failure of ad libitum nicotine nasal spray use to recover nicotine blood levels achieved with baseline smoking.

a. **Mabry PL**, Tooze JA, Moser RP, Augustson EM, Malcolm RJ, Benowitz NL. Nicotine, cotinine, withdrawal, and craving patterns during smoking and nicotine nasal spray use: results from a pilot study with African American men. Nicotine Tob Res. 2007 Jan;9(1):65-82.

Complete List of Published Work: https://www.ncbi.nlm.nih.gov/myncbi/patricia.mabry.2/bibliography/public/

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BIOGRAPHICAL SKETCH

NAME: Stephen E. Asche, MA

eRA COMMONS USER NAME (credential, e.g., agency login) eRA Commons User Name

POSITION TITLE: Research Investigator, HealthPartners Institute

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Minnesota, Minneapolis, MN	BA	1986	Psychology
University of Minnesota, Minneapolis, MN	MA	1992	Educational Psychology

A. Personal Statement

As a statistician at HealthPartners Institute, I have extensive experience in the conceptualization, design and analysis of pragmatic cluster-randomized trials, particularly those involving clinical decision support (CDS) tools. One of these trials (2R01HL090965) included the assessment of mechanisms underlying treatment effects as examined by mediation analysis. I currently serve as lead statistician on two NIDCR-funded studies led by Dr. Brad Rindal which are leveraging CDS tools with the respective goals of de-implementing opioid use following dental extractions (U01DE027441) and promoting smoking cessation in dental clinics (U01DE026135). I also am the lead statistician on several other clinic-randomized studies implementing and testing CDS for promoting 1.) cancer screening and HPV vaccination (R01CA193396); 2.) obesity management in patients with diabetes (R01DK128281); 3.) detection and treatment of hypertension in children and adolescents (R18HS027402). Previously I served as the lead statistician on five other cluster-randomized trials that involved other types of interventions: a clinic-randomized trial assessing interventions designed to reduce clinical inertia in the care of adults with type 2 diabetes (R01DK068314), a clinic-randomized trial using simulated patients to improve dental treatment plans (R01DE022332), a clinic-randomized trial testing the effects of a blood pressure telemonitoring device and pharmacist case management on blood pressure outcomes (2R01HL090965), a provider-randomized trial of learning programs using simulated patients to improve physician prescribing and diabetes care (R18DK079861), a provider-randomized trial using a simulated learning environment to improve blood pressure outcomes (R01HL0894), and improving the detection and management of elevated blood pressure in adolescents (R01HL115082). My project work has provided me with extensive experience in using data from study databases generated from case report forms, the electronic health record used in the medical and dental clinics, claims and administrative data from the health plan, and surveys of patients and providers. Most of my projects involve the use of multi-level modeling to take into account factors at the patient, provider, clinic, and medical group levels.
On this project, I will be responsible for all quantitative analytic activities, including refining denominator definitions, study randomization, directing the development of analytic databases, developing and providing input on all variable definition and measurement decisions, developing data dictionaries, assuring the quality of the data during data clean up and recoding, preparing materials for safety monitoring, monitoring fidelity to the intervention, and conducting the analysis to assess the effect of the intervention. I will work with Institute programmers to consolidate data from all sources, and will co-author manuscripts.

1. Kharbanda EO, Nordin JD, Sinaiko AR, Ekstrom HL, Stultz JM, Sherwood NE, Fontaine PL, **Asche SE**, Dehmer SP, Amundson JH, Appana DX, Bergdall AR, Hayes MG, O'Connor PJ. TeenBP: Development sand piloting of an EHR-linked clinical decision support System to improve recognition of hypertension in adolescents. EGEMS (Wash DC). 2015 Jul 9;3(2):1142. PMCID: PMC4537153.
2. Margolis KL, **Asche SE**, Bergdall AR, Dehmer SP, Groen SE, Kadrmas HM, Kerby TJ, Klotzle KJ, Maciosek MV, Michels RD, O'Connor PJ, Pritchard RA, Sekenski JL, Sperl-Hillen JM, Trower NK. Effect of

home blood pressure telemonitoring and pharmacist management on blood pressure control: a cluster randomized clinical trial. JAMA. 2013 Jul 3;310(1):46-56. PMCID: PMC4311883.
3. Rindal DB, Rush WA, Schleyer TK, Kirshner M, Boyle RG, Thoele MJ, **Asche SE**, Thyvalikakath T, Spallek H, Durand EC, Enstad CJ, Huntley CL. Computer-assisted guidance for dental office tobacco-cessation counseling: a randomized controlled trial. Am J Prev Med. 2013 Mar;44(3):260-4. PMCID: PMC3579569.
4. Margolis KL, **Asche SE**, Bergdall AR, Dehmer SP, Maciosek MV, Nyboer RA, O'Connor, PJ, Pawloski PA, Sperl-Hillen JM, Trower NK, Tucker AD, Green BB. A successful multifaceted trial to improve hypertension control in primary care: Why did it work? J Gen Intern Med. 2015 Nov;30(11):1665-72. PMCID: PMC4617923.

Ongoing projects that I would like to highlight include:

Ongoing Research Support

De-Implementing Opioid Use and Implementing Optimal Pain Management Following Dental Extractions (Rindal/Mitchell)
Source: NIDCR/U01DE027441 09/01/2017-08/31/2021
Role: Co-Investigator/Statistician
Opioid medications make a significant contribution to our nation's epidemic of fatal and non-fatal overdoses. Inappropriate prescribing (ie, prescribing opioids when not clinically necessary, or in higher doses or for longer than needed) is a key factor driving the opioid epidemic and requires fundamental changes at the practice level. Millions of dental extractions are performed each year on a wide range of patients. The overarching goal of this project is to de-implement the reliance of opioid analgesics and to implement reliance on non-opioid analgesics to manage postoperative pain following dental extractions. We will compare different strategies to reduce the reliance on opioids and increase the use of alternative pan management approaches utilizing information support tools aimed at both providers and their dental extraction patients.

De-Implementing Opioid Use and Implementing Optimal Pain Management Following Dental Extractions: Supplement (Rindal/Mitchell)
Source: NIH/U01DE027441 09/01/2018-08/31/2021
Role: Co-Investigator/Statistician
This administrative supplement builds off of the parent grant (U01DE027441). The supplement will allow for additional exploration of: 1. how minor patients and their parents/guardians make decisions about opioid use after dental extractions through interviews; 2. diffusion of intervention effects on opioid prescribing related to other procedures (such as root canal treatment) and general management of pain complaints following dental procedures; and 3. disparities in opioid prescribing.

A Clinic-Randomized Trial of a Clinical Decision Support System to Improve Dental Provider Delivery of Brief Tobacco Interventions and Quitline Referrals (Rindal)
Source: NIDCR/U01DE026135 08/02/2016-06/30/22
Role: Co-Investigator/Statistician
This clinic-randomized trial will examine the rate at which dental providers deliver a smoking intervention and refer to a quitline when their EDR system includes health information technology-driven CDS compared with providers in control clinics without assistance from the CDS. The primary outcome is a binary variable indicating whether the provider delivered a brief intervention or referral for treatment, as reported by the patient. By leveraging the dental encounter as an opportunity to deliver smoking cessation, we can further decrease smoking rates, leading to improved population health.

Improving Recognition and Management of Hypertension in Youth: Comparing Approaches for Extending Effective CDS for use in a Large Rural Health System (Kharbanda/Benziger)
Source: AHRQ/ R18HS027402 08/1/2020-07/31/2025
Role: Co-Investigator/Statistician
Our team has developed, implemented, and evaluated a clinical decision support (CDS) tool to appropriately identify high blood pressure in children. In a previous study, we showed that in a large urban and suburban health system, our CDS tool successfully promoted care consistent with national guidelines, improved recognition of high blood pressure, and was well accepted by providers. This study will adapt the existing CDS for use in a primarily rural health system and compare approaches to CDS implementation in 45 primary care clinics treating children in Minnesota, Wisconsin and North Dakota, thus advancing implementation science and addressing a critical need for youth at-risk for cardiovascular disease and with limited access to pediatric subspecialty care.

Optimizing the Value of PROMs in Improving Care Delivery through Health Information Technology (Solberg)
Source: AHRQ/R18HS025618 08/31/2017-07/31/2022
Role: Co-Investigator/Statistician
Evaluation of the feasibility, effectiveness, efficiency, and patient/physician reactions to the systematic incorporation and use of patient-reported outcomes measures and patient contextual information in both care and improvement activities for orthopedics operations in a large integrated care system.

Implementing Cancer Prevention Using Patient - Provider Clinical Decision Support (Elliott)
Source: NCI/R01CA193396 03/24/2016-02/28/2022
Role: Statistician
If primary and secondary prevention practices for breast, colorectal, and cervical cancer were improved, more than 100,000 cancer deaths a year could be delayed or averted in the United States and the burden of these diseases on quality of life reduced. In this project, we will adapt, implement, and evaluate a proven electronic health record-linked, Web-based, personalized clinical decision support system to identify patients needing primary and/or secondary cancer prevention care. The objectives of this project are to improve the quality and consistency of primary and secondary prevention of common cancers in rural areas by providing patient-centered and evidence-based treatment recommendations to both primary care provider teams and patients at the point of care and provide an efficient and effective model for implementation and dissemination of cancer prevention in rural settings.

Pragmatic Trial Comparing Telehealth Care and Clinic-based Care for Uncontrolled High Blood Pressure (Hyperlink-3) (Margolis)
Source: PCORI/IHS-1507-31146 07/01/2016-06/30/2022
Role: Statistician
This randomized trial provides dentists with simulated patients posing evidence-based challenges of effective treatment and build in treatment-specific decision support. We will assign HealthPartners dentists into a usual-care and simulation group and measure their treatment-planning patterns after the simulation group is exposed to evidence-based simulations and feedback support. We expect to find that the dentists exposed to the simulation encounters will exhibit practice patterns more congruent with successful patterns practiced in the simulation. While conducting this project, we will also plan the distribution of the simulation tool to the broader dental community.

A Team-Based and Technology Driven Adherence Intervention to Improve Chronic Disease Outcomes (Sperl-Hillen)
Source: NHLBI/ R01HL136937 02/15/2018-01/31/2023
Role: Co-Investigator
Poor adherence to medications for chronic diseases is common, but providers often fail to identify patients with adherence issues and/or lack adequate time to address them. New strategies are needed to provide nonadherent patients the support they need to make fully informed choices about their medications and understand the impact of adherence on clinical outcomes. In this project, we implement and evaluate a team-based, informatics-driven intervention that integrates primary care clinical decision support with active outreach from pharmacists.

Completed Research Support (within the last 3 years)

EHR-Based Clinical Decision Support to Improve BP Management in Adolescents (Kharbanda)
Source: NHLBI/R01HL115082
Role: PI 08/01/2012-07/31/2019
The innovative intervention provides a useful template for extending EHR-based clinical decision support to other domains of adolescent care, in order to translate massive public and private investments in EHR technology into improved adolescent health outcomes.

B. Positions and Honors

Positions and Employment

2003-Pres.	Research Investigator and Manager of Statistical Services, HealthPartners Institute, Minneapolis, MN
1997-2003	Research Scientist, Health Program Research and Evaluation, Performance Measurement and Quality Improvement Division, Minnesota Department of Human Services, St. Paul, MN

1988-1997 Research Fellow, Department of Psychology, University of Minnesota, Minneapolis, MN
1988 Project Manager, Survey Research Group, Personnel Decisions Research Institute, Minneapolis, MN

C. Contributions to Science

1. **Clinical decision support**. I have designed and/or lead the analysis of cluster-randomized trials testing the effects of clinical decision support on patient outcomes. These trials include an NHLBI-funded study on improving detection and management of elevated blood pressure in adolescents (R01HL115082), and NIDCR-funded study using the electronic dental record to assist providers in offering smoking cessation intervention (R34DE023895), and a trial examining the impact of clinical decision support on diabetes outcomes (R01DK068314).
   a. Kharbanda EO, **Asche SE**, Sinaiko A, Ekstrom HL, Nordin JD, Sherwood NE, Fontaine P, Dehmer SP, Appana D, O'Connor PJ. Clinical decision support for recognition and management of hypertension: a randomized trial. Pediatrics. 2018 Feb;141(2):e20172954. PMCID: PMC5810603.
   b. Kharbanda EO, **Asche SE**, Sinaiko AR, Nordin JD, Ekstrom HL, Fontaine PL, Dehmer SP, Sherwood NE, O'Connor PJ. Evaluation of an electronic clinical decision support tool for incident elevated BP in adolescents. Acad Pediatr. 2018 Jan-Feb;18(1):43-50. PMCID: PMC5756693.
   c. Margolis KL, **Asche SE**, Bergdall AR, Dehmer SP, Groen SE, Kadrmas HM, Kerby TJ, Klotzle KJ, Maciosek MV, Michels RD, O'Connor PJ, Pritchard RA, Sekenski JL, Sperl-Hillen JM, Trower NK. Effect of home blood pressure telemonitoring and pharmacist management on blood pressure control: a cluster randomized clinical trial. JAMA. 2013 Jul 3;310(1):46-56. PMCID: PMC4311883.
   d. O'Connor PJ, Sperl-Hillen JM, Rush WA, Johnson PE, Amundson GH, **Asche SE**, Ekstrom HL, Gilmer TP. Impact of electronic health record clinical decision support on diabetes care: a randomized trial. Ann Fam Med. 2011 Jan-Feb;9(1):12-21 PMCID: PMC3022040.
2. **Cluster randomized trials design and analysis**. I have designed and/or lead the analysis of several cluster-randomized trials on other subjects including several examining the effect of simulated patient learning environments on provider actions. An NHLBI-funded study assessed the long-term effectiveness of home blood pressure monitoring (R01HL090965). Simulated patient studies have included a trial examining the impact of personalized physician learning on diabetes outcomes (R01DK068314), a trial testing the effect of simulating patients on resident physician knowledge and actions for diabetes patients (R18DK079861), and a trial testing the effect of simulated learning on dental providers' development of treatment plans (R01DE022332).
   a. O'Connor PJ, Magid DJ, Sperl-Hillen JM, Price DW, **Asche SE**, Rush WA, Ekstrom HL, Brand DW, Tavel HM, Godlevsky OV, Johnson PE, Margolis KL. Personalised physician learning intervention to improve hypertension and lipid control: randomised trial comparing two methods of physician profiling. BMJ Qual Saf. 2014 Dec;23(12):1014-22. PMCID: PMC4557778.
   b. Sperl-Hillen J, O'Connor P, Ekstrom H, Rush W, **Asche S**, Fernandes O, Appana D, Amundson G, Johnson P. Using simulation technology to teach diabetes care management skills to resident physicians. J Diabetes Sci Technol. 2013 Sep 1;7(5):1243-54. PMCID: PMC3876368.
   c. Kerby TJ, **Asche SE**, Maciosek MV, O'Connor PJ, Sperl-Hillen JM, Margolis KL. Adherence to a telemonitoring intervention in a cluster-randomized clinical trial. J Clin Hypertens (Greenwich). 2012 Oct;14(10):668-74. PMCID: PMC3464948.
   d. O'Connor PJ, Desai J, Solberg LI, Reger L, Crain AL, **Asche SE**, Pearson T, Clark C, Rush WA, Cherney LM, Sperl-Hillen JM, Bishop DB. Randomized trial of quality improvement intervention to improve diabetes care in primary care settings. Diabetes Care.2005 Aug;28(8):1890-7.
3. **Chronic Disease**. I have extensive expertise in chronic disease epidemiology and statistical analysis. I have designed and lead the analysis for studies on diabetes, hypertension, and adolescent blood pressure management and others. These experiences have provided me with the opportunity to be a versatile statistician in terms of content area, as well as with the key methodological tools to manage sophisticated data health systems, and analyze data using multilevel models. As part of my research focus within HealthPartners Institute, I have collaborated on Diabetes Inertia, a clinic-randomized trial assessing interventions designed to reduce clinical inertia in the care of adults with type 2 diabetes (R01DK068314), Hyperlink, a study to assess the long-term effectiveness of a telehealth intervention (R01HL090965), and a NHLBI-funded study on improving detection and management of elevated blood pressure in adolescents (R01HL115082).

a. **Asche SE**, O'Connor PJ, Dehmer SP, Green BB, Bergdall AR, Maciosek MV, Nyboer RA, Pawloski PA, Sperl-Hillen JM, Trower NK, Margolis KL. Patient characteristics associated with greater blood pressure control in a randomized trial of home blood pressure telemonitoring and pharmacist management. J Am Soc Hypertens. 2016;10(11): 873-880. PMCID: PMC5107124.
b. Margolis KL, **Asche SE**, Bergdall AR, Dehmer SP, Maciosek MV, Nyboer RA, O'Connor, PJ, Pawloski PA, Sperl-Hillen JM, Trower NK, Tucker AD, Green BB. A successful multifaceted trial to improve hypertension control in primary care: Why did it work? J Gen Intern Med. 2015 Nov;30(11):1665-72. PMID: 25952653; PMCID: PMC4617923.
c. Sperl-Hillen J, O'Connor PJ, Ekstrom HL, Rush WA, **Asche SE**, Fernandes OD, Apana D, Amundson GH, Johnson PE, Curran DM. Educating Resident Physicians Using Virtual Case-Based Simulation Improves Diabetes Management: A Randomized Controlled Trial. Acad Med. 2014 Dec;89(12):1664-73. PubMed PMID: 25006707.
d. Solberg LI, **Asche SE**, Pawlson LG, Scholle SH, Shih SC. Practice systems are associated with high quality care for diabetes. Am J Man Care 2008 Feb;14(2):85-92.

4. **Patient-centered care.** My experience as co-investigator and lead statistician on the PCORI-funded "Measuring Patient Outcomes from High Tech Diagnostic Imaging Studies" provides a background in patient centered research, using a variety of data sources including patient surveys, electronic medical records used in the medical group, and claims and administrative data from the health plan. Several other studies on which I have served as statistician have focused on patient preferences, values, attitudes, and shared decision making.
   a. Solberg LI, **Asche SE**, Butler J, Carrell D, Norton CK, Jarvik JG, Smith-Bindman R, Tillema JO, Whitebird RR, Werner AM, Ziegenfuss JY. Patient Centered Outcomes Measurement: Does it Require Information from Patients? J Patient Cent Res Rev. 2017 Nov;4:221-229. PMCID: PMC6664353.
   b. Solberg LI, **Asche SE**, Butler J, Carrell D, Norton CK, Jarvik JG, Smith-Bindman R, Tillema JO, Whitebird RR, Ziegenfuss JY. The Effect of Achieving Patient-Reported Outcome Measures on Satisfaction. J Am Board Fam Med. 2015 Nov-Dec;28(6):785-92.
   c. Solberg LI, **Asche SE**, Butler J, Carrell D, Norton CK, Jarvik, JG, Smith-Bindman R, Tillema JO, Whitebird RR, Ziegenfuss JY. It is Time to Ask Patients What Outcomes are Important to Them. Am J Accountable Care 2015 Dec;3(4):48-54.
   d. Solberg LI, **Asche SE**, Sepucha K, Thygeson NM, Madden JE, Morrissey L, Kraemer KK, Anderson LH. Informed choice assistance for women making uterine fibroid treatment decisions: a practical clinical trial. Med Decis Making. 2010 Jul-Aug;30(4):444-52.

5. **Health systems transformation**. I have been a lead methodologist in the area of health systems transformation and specifically medical home transformation, as well as the measurement of practice systems in clinic settings. One project examined changes in care quality during the transformation of primary care clinics to primary care medical homes (R18HS19162).
   a. Scholle SH, **Asche SE**, Morton S, Solberg LI, Tirodkar MA, Jaén CR. Support and strategies for change among small patient-centered medical home practices. Ann Fam Med. 2013 May-Jun;11 Suppl 1:S6-13. PMCID: PMC3707241.
   b. Solberg LI, **Asche SE**, Fontaine P, Flottemesch TJ, Anderson LH. Trends in quality during medical home transformation. Ann Fam Med. 2011 Nov-Dec;9(6):515-21. PMCID: PMC3252197.
   c. Solberg LI, **Asche SE**, Fontaine P, Flottemesch TJ, Pawlson LG, Scholle SH. Relationship of clinic medical home scores to quality and patient experience. J Ambul Care Manage. Jan-Mar 2011;34(1):57-66.
   d. Scholle SH, Pawlson LG, Solberg LI, Shih SC, **Asche SE**, Chou AF, Thoele MJ. Measuring practice systems for chronic illness care: accuracy of self-reports from clinical personnel. Jt Comm J Qual Patient Saf. 2008 Jul;34(7):407-16.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/steve.asche.1/bibliography/47516400/public/?sort=date&direction=descending

OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

NAME: Meghan M. JaKa, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): eRA Commons User Name

POSITION TITLE: Research and Evaluation Associate and Supervisor, Center for Evaluation and Survey Research

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Rutgers University, New Brunswick, NJ	BS	05/2007	Exercise Physiology
Oregon State University, Corvallis, OR	MS	06/2009	Physical Activity and Health
University of Minnesota, Minneapolis, MN	PhD	08/2016	Social and Behavioral Epidemiology

A. Personal Statement

I have extensive experience in behavioral and implementation intervention design, behavior change theory, and intervention fidelity within and outside healthcare. I have received a depth of quantitative and qualitative methodological training and mentoring related to this work and have a breadth of applied experience with research project management and implementation of qualitative methods in the healthcare setting. My experience designing and evaluating implementation of interventions in various areas and managing a number of behavioral clinical trials have provided me with a solid foundation of knowledge about specifying intervention components, measuring changes in behavior as well as related mediators and moderators, and evaluating intervention fidelity. As a Senior Evaluation Scientist and Supervisor within the Institute's Center for Evaluation and Survey Research (CESR), I collaborate on a wide variety of health system research and evaluation projects, many of which aim to evaluate behavior change and related outcomes in providers, patients, and/or members. I oversee numerous on-going health system evaluations that use a mix of quantitative and qualitative methods related to health systems improvement, many of which focus on provider behavior change. My current research projects include a state-wide care coordination study aimed at understanding the impact of social and medical care coordination models, for which I am overseeing clinician, care coordinator, and patient interviews (PCORI/IHS-2019C1-15625), as well as serving as a co-investigator on a study which is implementing and testing a clinical decision support (CDS) tool to improve detection and management of cognitive impairment (R61AG069770). Recently, I collaborated with Dr. Patricia Mabry on a study aimed at developing a simulation model for colorectal cancer screenings, for which I developed and analyzed patient interviews to inform model inputs.

As a co-investigator on this proposal, I will lend my expertise in behavior change, intervention fidelity monitoring, and qualitative research methods to the study design, implementation and analysis. During the UG3 phase of the grant, I will lead and analyze provider interviews, work closely with Dr. Mabry to develop the provider training based on the interview feedback and behavior change theory, and help finalize plans for monitoring intervention fidelity. Subsequently, during the UH3 phase, I will contribute to ongoing fidelity monitoring efforts as well as the interpretation and dissemination of results. Given my role in CESR, I am also well positioned to help develop patient and provider survey tools and assist CESR staff in implementing the survey protocol.

1. **JaKa MM**, French SA, Wolfson J, Jeffery RW, Lorencatto F, Michie S, Levy RL, Langer SL, Sherwood NE. Understanding outcomes in behavior change interventions to prevent pediatric obesity: the role of dose and behavior change techniques. Health Educ Behav. 2019 Apr;46(2):312-21. PMCID: PMC6417983.
2. **JaKa MM,** Haapala JL, Trapl ES, Kunin-Batson A, Heerman B, Olson-Bullis BA, Berge JM, Moore S, Matheson D, & Sherwood NE. Reporting of treatment fidelity in behavioural paediatric obesity intervention trials: a systematic review. Obes Rev. 2016 Dec;17(12):1287-1300. PMCID: PMC5193220.

3. **JaKa MM,** Dinh JM, Ziegenfuss JY, Siy JC, Doshi AP, Platt Y, & Dressen JR. Clinical Outcomes and Patient and Care Team Perspectives of Telemedicine in Critical Access Hospitals. J Hosp Med. 2020 Jun;15(6):345-348.
4. Palmsten K, Bredesen D, **JaKa MM**, Kumar PC, Ziegenfuss JY, Kharbanda, EO. "I know my body better than you:" Patient focus groups to inform a decision aid on oral corticosteroid use during pregnancy. Pharmacoepidemiol Drug Saf. 2021 Apr;30(4):451-461.

Ongoing and recently completed research projects I would like to highlight include:

Pragmatic Trial Comparing Telehealth Care and Clinic-based Care for Uncontrolled High Blood Pressure (Hyperlink-3) (Margolis)
Source: PCORI/ IHS-1507-31146
Role: Co-Investigator 07/01/2016-06/30/2022
The study is designed to respond to PCORI's Improving Healthcare Systems Program by 1) comparing two alternative health care service-delivery designs for improving hypertension care outcomes and 2) including innovative technology.

A Technology-Driven Intervention to Improve Early Detection and Management of Cognitive Impairment (Hanson/Sperl-Hillen)
Source: NIH/R61AG069770
Role: Co-Investigator 09/21/2020-08/31/2022
In this project, we implement and evaluate a low-cost, highly scalable CI-CDS system integrated within the electronic health record that has high potential to improve early CI detection and care and translate massive public and private sector investments in health informatics into tangible health benefits for large numbers of people.

Comparing Two Approaches to Care Coordination for High-Cost/High-Need Patients in Primary Care (Dehmer)
Source: PCORI/IHS-2019C1-15625
Role: Co-Investigator 05/01/2020-03/31/2024
In Minnesota, many primary care clinics are using a method called care coordination to improve the health of patients who have a number of chronic diseases (some examples of chronic diseases include diabetes, heart disease, asthma and depression). With care coordination, a nurse in the clinic helps the various doctors, clinics, and specialists to work together, in the interest of the patient. This proposal compares the effectiveness of care coordination led entirely by a team of medical professionals versus care coordination with the additional support of a social worker.

Comparing Fingerstick Blood Glucose Monitoring versus Continuous Glucose Monitoring in Primary Care (Bergenstal)
Source: PCORI
Role: Co-Investigator 11/01/2021-10/31/2025
This research trial will randomize 20 clinics and 354 patients in accordance with their primary care clinic assignment to 2 different glucose monitoring and care support strategies (SMBG Clinic Care vs. CGM Clinic Care) and compare the effectiveness through a pragmatic clinic cluster randomized design. The 2 groups being compared are: a. SMBG Clinic Care: Patients instructed to use self-monitored fingerstick blood glucose testing (SMBG) based on current clinical practice guidelines with primary care support, and b. CGM Clinic Care: Patients instructed to use continuous glucose monitoring (CGM) for glucose monitoring with availability of on-demand glucose levels and Ambulatory Glucose Profile (AGP) data with primary care support.

Simulation Model on Colorectal Cancer Screening to Inform HealthPartners Practice (Mabry)
Source: HealthPartners Institute
Role: Co-I 05/01/2019-04/30/2020
The proposed project will establish a new partnership between the Computational Epidemiology and Public Health Informatics Laboratory (CEPHIL) at the University of Saskatchewan (UofS) and HealthPartners Institute (HPI). Initially, we propose to build a dynamic model to provide visual and quantitative estimates of the impact that insurance plan options and healthcare services have on screening rates and cost. These estimates will be calculated for groups of people with differing levels of risk for developing cancer. Model estimates will be useful to health systems in the U.S. and Canada and could be used to inform decisions by health plans about services offered, leading to cost savings and healthier populations in both countries.

B. Positions, Scientific Appointments, and Honors

Positions

2018-Present Senior Evaluation Scientist and Supervisor, HealthPartners Institute, Minneapolis, MN
2017-2018 Manager, DC Department of Behavioral Health, Applied Research & Evaluation
2016-2017 Senior Research Associate, Allina Health, Division of Applied Research, Minneapolis, MN
2016 Teaching Assistant, Obesity & Eating Disorders, University of Minnesota
2014-2016 Predoctoral Trainee, University of Minnesota, Minneapolis, MN
2012-2014 Research Assistant, University of Minnesota, Minneapolis, MN
2009-2016 Research Project Manager, HealthPartners Institute, Minneapolis, MN
2007-2009 Research Assistant, Oregon State University, Portland, OR
2007-2009 Teaching Assistant (Sole Instructor), Various Courses, Oregon State University, Portland, OR

Professional Memberships

2020-Present Academy Health
2018-Present American Evaluation Association
2015-2016 The Obesity Society
2014-2016 International Society of Behavioral Nutrition & Physical Activity
2010-2016 Society of Behavioral Medicine
2007-2012 American College of Sports Medicine
2005-2006 National Strength & Conditioning Association

Honors/Awards

2015-2016 Discovery Grant, HealthPartners Institute
2014-2015 JB Hawley Student Research Award, University of Minnesota
2004 National Society of Collegiate Scholars, Rutgers University
2003-2007 Academic Scholarship, Rutgers University

Speaking Engagements

2021 Health Care Systems Research Network Learning Health Systems Interest Group Ancillary Meeting. *Health Care Systems Research Network Conference.* May 15.
2020 Evaluation in a Continuously Learning Health System: Findings from a Critical Access Hospital Telemedicine Program. *Health Care Systems Research Network Conference.* (In-person meeting canceled due to COVID-19).
2020 Theory, Frameworks and Conceptual Models in Federal Grant Writing. Minnesota Learning Health Systems K12 Design Shop. July 7.
2019 Embedding Evaluation in the Healthcare System. American Evaluation Association's Annual Meeting. November 11-16.
2019 Clinical Outcomes and Patient and Care Team Perspectives of Telemedicine in Critical Access Hospitals. HCSRN Implementation Group Conference. October 9.
2018 Identifying behavioral health needs in school. District of Columbia's Task Force on School Mental Health Meeting. March 12.
2015 Creating a Culture of Health in Minnesota. Weight of the Fox Valley Community Health Connections. July 15.
2014 Process Evaluation in Pediatric Obesity. Division of Epidemiology & Community Health, University of Minnesota. February 25.

C. Contribution to Science

1. **Determine active ingredients in behavior change interventions.** Behavioral interventions to prevent and treat obesity are a public health priority, but have shown inconsistent success to date. By identifying which intervention components are most associated with weight outcomes, researchers can begin to design more focused and effective interventions. Researchers in psychotherapy have been studying the delivery of "active ingredients" since the 1970s. Recently, this work has expanded to behavior change research, mainly in smoking cessation interventions. Learning from this cross-disciplinary work, I have studied how the delivery of these active ingredients are measured and reported in the field of behavioral obesity. I have implemented methods to more rigorously measure intervention fidelity and presented novel ways of using this data to improve behavioral interventions. My work in this area has helped shape the way researchers design, measure, and report behavioral interventions.
   a. **JaKa MM**, French SA, Wolfson J, Jeffery RW, Lorencatto F, Michie S, Levy RL, Langer SL, Sherwood NE. Understanding outcomes in behavior change interventions to prevent pediatric obesity: the role of

dose and behavior change techniques. Health Educ Behav. 2019 Apr;46(2):312-21. PMCID: PMC6417983.

b. **JaKa MM**, Seburg EM, Roeder AM, Sherwood NE (2015). Objectively coding intervention fidelity during a phone-based obesity prevention study. J Obes Overweight. 2015;1(1). PMCID: PMC4662548.
c. **JaKa MM**, Sherwood NE, Flatt SW, Pacanowski CR, Pakiz B, Thomson CA, Rock CL (pending publication). Mediation of weight loss and weight loss maintenance through dietary disinhibition and restraint. J Obes Weight Loss Ther. 2015 Apr;5(2). pii: 253. PMCID: PMC4852882.
d. **Senso MM** (2014). Measuring active ingredients in behavioral pediatric obesity prevention interventions. Seminar presented at the University of Minnesota's Obesity Research Group, Minneapolis, MN.

2. **Solutions to behavioral research issues via objective measurement.** When trying to measure human behaviors, whether they are participant behaviors like physical activity or interventionist behaviors like protocol implementation, the field often relies on self-report. Though these measures have many benefits, including reduced time and cost, the strong potential for bias outweighs these benefits. Objective methods, such as accelerometry to measure physical activity, lessen these biases. I have shown this propensity for self-presentation bias in adult behavioral maintenance trials. And, more recently I have studied the correlates of accelerometer wear time in young children to determine how researchers may further alleviate bias in accelerometry methodology. Additionally, I have done work using objective measures to answer questions previously reliant on self-report, such as the association between occupational and leisure-time physical activity. I have also applied this more rigorous methodology to measuring components of intervention delivery and have shown that interventionists can reliably report some intervention components, while consistently over-reporting others when compared to an independent coder. My work will continue to improve the validity and accuracy of measurement in behavioral research through the creative use of objective measures.
   a. **JaKa MM,** French SA, Wolfson J, Jeffery RW, Lorencatto F, Michie S, Langer SL, Levy RL, Sherwood NE. Feasibility of standardized methods to specify behavioral pediatric obesity prevention interventions. J Behav Med. 2017 Oct;40(5):730-739. PMCID: PMC5755711.
   b. **JaKa MM,** Haapala JL, Wolfson J, French SA. Describing the relationship between occupational and non-occupational physical activity using objective measurement. Prev Med Rep. 2015;2:213-217. PMCID: PMC4435612.
   c. **Senso MM**, Anderson CP, Crain AL, Sherwood NE, Martinson BC. Self-reported activity and accelerometry in 2 behavior-maintenance trials. Am J Health Behav. 2014 Mar;38(2):254-64. PMCID: PMC4104794.

3. **Intervention Fidelity.** Fundamental to valid research outcomes is the assurance that proposed interventions are delivered as intended. This is particularly important in factorial clinical trial designs as there is a higher likelihood of contamination across conditions. My research has focused on issues of treatment and intervention fidelity aligning pediatric obesity behavior change interventions with best practices in design, implementation and reporting, including application of the NIH Treatment Fidelity Framework. I have also worked to identify methods for reducing contamination across treatment arms, and improving elements of treatment fidelity such as participant receipt and enactment of intervention content.
   a. **JaKa MM**, Haapala JL, Trapl ES, Kunin-Batson A, Heerman B, Olson-Bullis BA, Berge JM, Moore S, Matheson D, & Sherwood NE. Reporting of treatment fidelity in behavioural paediatric obesity intervention trials: a systematic review. Obes Rev. 2016 Dec;17(12):1287-1300. PMCID: PMC5193220.
   b. Heerman B, **JaKa MM**, Berge JM, Trapl E, Sommer E, Jackson N, Haapala JL, Kunin-Batson A, Olson-Bullis BA, Hardin H, Sherwood NE, Barkin S. The dose of behavioral interventions to prevent and treat childhood obesity: a systematic review and meta-regression. Int J Behav Nutr Phys Act. 2017 Nov 15;14(1):157. PMCID: PMC5688650.

4. **Patterns of and parental influence on child weight and weight-related behaviors.** Broadly, researchers know that physical (in)activity and dietary behaviors lead to the energy imbalance that eventually causes obesity. But, the etiology of pediatric obesity is complex. Important work is being done in behavioral obesity research to understand the nuance in patterns of these behaviors and how parent behaviors may influence child behaviors, ultimately leading to obesity. I have expanded this work in a number of ways. First, I have worked on identifying specific patterns and types of activity accumulated throughout a day to better understand how to target behavioral interventions. My colleagues and I have also examined how combined adherence to different diet and physical activity guidelines may impact

obesity risk. Finally, I have examined how parents' behaviors and parenting practices and styles work together to predict these obesogenic behaviors. My future work in uncovering patterns of and familial influences on weight and weight-related behaviors will help guide her in developing more effective behavioral obesity prevention interventions.

a. **Senso MM**, Trost SG, Crain AL, Seburg EM, Anderson JD Sherwood NE (2014). Activity patterns of preschool-aged children at risk for obesity. J Phys Act Health. 2015 Jun;12(6):861-8. PMCID: PMC4329288.
b. **Senso MM**, Trost SG, Fleming CK, Rein DM, Levy RL, Langer SL, Jeffery RW, Hayes MG, Sherwood NE (2012). Promoting Parenting Skills to Increase Physical Activity & Decrease Television Viewing in Children. *Oral poster presentation at the American College of Sports Medicine National Conference*. San Francisco, CA.
c. Sherwood NE, **Senso MM**, Fleming CK, Roeder AM (2014). Behavioral risk factors for overweight and obesity: diet and physical activity. In A Coulston, C Boushey, M Ferruzzi (Eds.), Nutrition in the prevention and treatment of disease (3rd Ed.) Burlington, MA: Elsevier Academic Press.
d. Kunin-Batson A, Seburg EM, Crain AL, **JaKa MM**, Langer SL, Levy RL, Sherwood NE. Household factors, family behavior patterns, and children's adherence to dietary and activity guidelines. J Nutr Educ Behav. 2015 May-Jun;47(3):206-15. PMCID: PMC4428928.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1XSKY-a2k9n5T/bibliography/public/

OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

NAME: Elyse Olshen Kharbanda, MD, MPH

eRA COMMONS USER NAME (credential, e.g., agency login): eRA Commons User Name

POSITION TITLE: Senior Investigator and Executive Director of Research, HealthPartners Institute

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date	FIELD OF STUDY
University of California, Berkeley	BA	1994	Biochemistry
Albert Einstein College of Medicine	MD	1998	
Children's Hospital of New York Presbyterian		2001	Residency in Pediatrics
Columbia University, Mailman School of Public Health	MPH	2004	General Public Health
Children's Hospital Boston and Boston Medical Center		2005	Fellowship in Adolescent Medicine

A. Personal Statement

I am a Senior Research Investigator and Executive Director of Research at HealthPartners Institute as well as a pediatrician and adolescent medicine specialist with expertise specific to HPV vaccination and clinical decision support. Currently, I serve as Project Director of the HealthPartners Vaccine Safety Datalink (VSD) infrastructure team (CDC/200-2012-53526), and through the VSD, I have led and contributed to studies specifically examining HPV vaccine safety. Recently, I led a VSD study examining the risk of spontaneous abortion, adverse pregnancy and birth outcomes following inadvertent HPV vaccination during pregnancy, and I also served as Co-PI on VSD studies evaluating the safety of influenza and Tdap vaccination during pregnancy. Currently, I am the PI of two VSD studies which are examining the risk of adverse maternal and infant outcomes following receipt of COVID-19 vaccinations during pregnancy. Furthermore, I have been the PI of three clinical trials aimed at improving patient care through clinical decision support (CDS), including the NHLBI-funded Peds&TeenBP CDS study (R01HL115082), a current study testing implementation and scalability of the Peds&TeenBP CDS in a rural health system (R18HS027402), and a NICHD-funded study aimed at supporting more appropriate use of diagnostic imaging for pediatric and young adult patients with abdominal pain (R01HD079463). HPV vaccine has long been an area of research interest. As a fellow in Adolescent Medicine, I led one of the first studies qualitatively evaluating parental views on the the HPV vaccine. With funding from HRSA, I later led a text messaging intervention to increase timeliness of receipt of the next HPV vaccine dose (R40MC08961). More recently, I served as Chair of the NIH Special Emphasis Panel, Linking Provider Recommendation to Adolescent HPV Vaccine Uptake.

On the proposed study, I will lend my knowledge of HPV vaccination and clinical decision support to assist with the development of the protocol and provider training, as well as the implementation and evaluation of the intervention. I am very familiar with the vaccine data available through the electronic health record, insurance claims, and the state vaccine registries and I am available to advise on key variables and nuances of the data. Further, I will contribute my expertise in HPV vaccination guidelines and barriers to vaccine uptake to the interpretation and dissemination of study results.

1. **Kharbanda EO**, Vazquez-Benitez G, DeSilva MB, Naleway AL, Klein NP, Hechter RC, Glanz JM, Donahue JG, Jackson LA, Sheth SS, Greenberg V, Panagiotakopoulos L, Mba-Jonas A, Lipkind HS. Association of Inadvertent 9-Valent Human Papillomavirus Vaccine in Pregnancy With Spontaneous Abortion and Adverse Birth Outcomes. JAMA Netw Open. 2021 Apr 1;4(4):e214340. PMCID: PMC8022219.
2. **Kharbanda EO**, Parker E, Nordin JD, Hedblom B, Rolnick SJ. Receipt of human papillomavirus vaccine among privately insured adult women in a U.S. Midwestern Health Maintenance Organization. Prev Med. 2013 Nov;57(5):712-4. PMID: 23859927.
3. DeSilva M, Vazquez-Benitez G, Nordin JD, Lipkind HS, Romitti PA, DeStefano F, **Kharbanda EO**. Tdap Vaccination During Pregnancy and Microcephaly and Other Structural Birth Defects in Offspring. JAMA.

2016 Nov 1;316(17):1823-1825.
4. **Kharbanda EO**, Vazquez-Benitez G, Lipkind H, Klein NP, Cheetham TC, Naleway AL, Omer SB, Hambidge SJ, Lee GM, Jackson ML, McCarthy NL, DeStafano F, Nordin JD. Evaluation of the association of maternal pertussis vaccination with obstetric events and birth outcomes. JAMA. 2014 Nov 12; 312(18): 1897-904.

Ongoing and recently completely research projects I would like to highlight include:

Ongoing Research Support

Improving Recognition and Management of Hypertension in Youth: Comparing Approaches for Extending Effective CDS for use in a Large Rural Health System (Kharbanda/Bezinger)
Source: AHRQ/R18HS027402
Role: Co-PI 09/30/2020-08/31/2025
Our team has developed, implemented, and evaluated a clinical decision support (CDS) tool to appropriately identify high blood pressure in children. In a previous study, we showed that in a large urban and suburban health system, our CDS tool successfully promoted care consistent with national guidelines, improved recognition of high blood pressure, and was well accepted by providers. This study will adapt the existing CDS for use in a primarily rural health system and compare approaches to CDS implementation in primary care clinics, thus advancing implementation science and addressing a critical need for youth at-risk for cardiovascular disease and with limited access to pediatric subspecialty care.

Vaccine Safety Datalink Infrastructure (Kharbanda)
Source: CDC/ 200-2012-53526
Role: PI 09/28/2017-09/27/2022
The Vaccine Safety Datalink (VSD) is a collaboration between the Centers for Disease Control and Prevention (CDC) and several large health care organizations, which conducts surveillance of the safety of vaccines currently licensed in the United States. The purpose of this task order is to add a site to the VSD infrastructure which will fulfill administrative, data management, and vaccine safety assessment activities.

Evaluation of COVID-19 Vaccine Safety in Pregnancy and Fetal Death in the Vaccine Safety Datalink (Kharbanda/Lipkind)
Source: CDC/200-2012-53526
Role: Co-PI 09/20/2020-09/21/2023
Pregnant women are not part of ongoing COVID-19 vaccine trials, however, implementation of a widespread vaccination program would include women of reproductive age, and pregnant women may be intentionally or inadvertently exposed to the vaccine(s). The purpose of this task order is to develop a protocol, coordinate, and lead a study within the Vaccine Safety Datalink (VSD) to evaluate and monitor the risk of pregnancy loss following COVID-19 vaccine in pregnant women.

COVID-19 Vaccine Safety Evaluation in Pregnant Women and their Infants (Kharbanda)
Source: CDC/200-2012-53526
Role: PI 09/20/2020-09/19/2025
Pregnant women are not part of ongoing COVID-19 vaccine trials, however, implementation of a widespread vaccination program would include women of reproductive age, and pregnant women may be intentionally or inadvertently exposed to the vaccine(s). The purpose of this task order is to develop protocols, coordinate, and lead studies within the Vaccine Safety Datalink (VSD) in order to evaluate the risk of pregnancy, birth and infant outcomes following COVID-19 vaccine in pregnant women.

Selected Completed Research Support (within last three years)

EHR-based Decision Support for Pediatric Acute Abdominal Pain in Emergency Care (Kharbanda)
Source: NICHD/R01HD079463
Role: Co-PI 03/01/2015-02/28/2021
This project (a) uses EHR technology to deliver patient-specific CDS to Emergency Department (ED) providers at the point of care, (b) assesses the impact of this intervention on the use of diagnostic imaging and clinical outcomes, and (c) assesses the impact of the intervention on the costs of care delivered. This innovative project will be a template for extending EHR-based CDS to other domains of emergency care to ultimately improve a broad range of pediatric acute care outcomes.

Evaluating the Risk of Spontaneous Abortion Following 4vHPV and 9vHPV (Kharbanda)
Source: CDC/200-2012-53526
Role: PI 09/30/2015-09/29/2020
In this task order we propose methods for developing a protocol, coordinating, and leading surveillance activities in order to evaluate the risk of both pregnancy and birth outcomes following influenza, Tdap, and HPV vaccination during pregnancy.

EHR-Based Clinical Decision Support to Improve BP Management in Adolescents (Kharbanda)
Source: NHLBI/R01HL115082
Role: PI 08/01/2012-07/31/2019
Over the past few decades, rates of hypertension have increased substantially among adolescents, yet diagnosis and care of hypertension in this age group continues to be suboptimal. This project (a) uses electronic health record (EHR) technology to deliver patient-specific clinical decision support (CDS) to adolescent providers at the point of care, (b) assesses the impact of this intervention on identification and clinical care of hypertension in adolescents, and (c) assesses the impact of the intervention on costs of care.

B. Positions and Honors

Positions and Employment

2021-present	Executive Director of Research, HealthPartners Institute, Minneapolis, MN
2015-present	Senior Investigator, HealthPartners Institute, Minneapolis, MN
2010-2015	Research Investigator, HealthPartners Institute, Minneapolis, MN
2006-2010	Assistant Clinical Professor of Population and Family Health, Columbia University, Mailman School of Public Health, New York, NY
2005-2010	Assistant Clinical Professor Pediatrics, Columbia University School of Medicine, New York, NY
2002-2005	Clinical Instructor, Department of Pediatrics, Harvard University School of Medicine, Boston, MA
2002-2005	Clinical Instructor, Department of Pediatrics, Boston University School of Medicine, Boston, MA
2001-2002	Clinical Instructor, Division of Emergency Medicine, Department of Pediatrics, Columbia University, New York, NY

Professional Committee Assignments and Awards

2018-2019	Member, Advisory Committee on Immunization Practices, Maternal Flu Immunization Sub-WG
2018	Paper of the Year, Health Care Systems Research Network Annual Meeting
2017-2018	Chair, Special Emphasis Panel, Linking Provider Recommendation to Adolescent HPV Uptake
2015-2021	Chair, HealthPartners Research Review Committee
2015-2020	Member, Health Services Organization and Delivery Study Section
2014-2017	Deputy Director of Publications, Society for Adolescent Health and Medicine
2013-2017	Vice Chair, Regions Hospital Clinical Research Sub-Committee
2012-2018	Consultant for Committee on Immunization, Society for Adolescent Health and Medicine,
2011-2013	Member, Regions Hospital Clinical Research Sub-Committee for the Institutional Review Board
2007-2011	Member, Advisory Committee on Immunization Practices, Influenza Vaccine Working Group

C. Contribution to Science

1. **Maternal vaccine safety.** Over the past ten years I have served as the primary investigator or Co-Investigator on multiple observational studies of vaccine safety funded by the Centers for Disease Control and Prevention (200-2012-53526; 200-2002-00732). In collaboration with my colleagues, I have developed methods for specifically evaluating vaccine safety during pregnancy and for validating safety outcomes within large healthcare databases. Findings from this work on maternal vaccine safety have been presented to the Advisory Committee on Immunization Practices and the National Vaccine Program Office, influencing vaccine policy on a national level.
   a. **Kharbanda EO**, Haapala J, DeSilva M, Vazquez-Benitez G, Vesco KK, Naleway AL, Lipkind HS. Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy. JAMA. 2021 Oct 26;326(16):1629-1631. PMCID: PMC8427483. Erratum in: JAMA. 2021 Oct 5;326(13):1331. PMID:34505868.
   b. **Kharbanda EO**, Vazquez-Benitez G, Romitti P, Naleway A, Cheetham TC, et al. First trimester influenza vaccination and risks for major structural birth defects in offspring. J Pediatr. 2017 Aug;187: 234-9. PMCID: PMC6506840.
   c. Lipkind HS, Vazquez-Benitez G, DeSilva M, Vesco KK, Ackerman-Banks C, Zhu J, Boyce TG, Daley MF, Fuller CC, Getahun D, Irving SA, Jackson LA, Williams JTB, Zerbo O, McNeil MM, Olson CK,

Weintraub E, **Kharbanda EO**. Receipt of COVID-19 Vaccine During Pregnancy and Preterm or Small-for-Gestational-Age at Birth - Eight Integrated Health Care Organizations, United States, December 15, 2020-July 22, 2021. MMWR Morb Mortal Wkly Rep. 2022 Jan 7;71(1):26-30. PMCID: PMC8735559.

d. Nordin JD, **Kharbanda EO**, Vazquez Benitez G, Lipkind H, Vellozzi C, Destefano F; Vaccine Safety Datalink. Maternal influenza vaccine and risks for preterm or small for gestational age birth. J Pediatr. 2014;164(5): 1051-1057.

2. **EHR-linked clinical decision support.** I have served as the PI on two NIH-funded R01 studies aimed at improving patient care through clinical decision support – one of these projects was focused on improving blood pressure control in adolescents (R01HL115082) and the other aims to support more appropriate and effective use of diagnostic imaging for pediatric patients with abdominal pain (R01HD079463). With funding from AHRQ, I am now co-leading study in which we are examining implementation approaches and scalability of implementing the Peds&Teen CDS in a large, rural health system (R18HS027402).
   a. Kharbanda AB, Vazquez-Benitez G, Ballard DW, Vinson DR, Chettipally UK, Dehmer SP, Ekstrom H, Rauchwerger AS, McMichael B, Cotton DM, Kene MV, Simon LE, Zhu J, Warton EM, O'Connor PJ, **Kharbanda EO**. Clinical Research on Emergency Services and Treatments Network (CREST) and the Critical Care Research Center, HealthPartners Institute. Effect of Clinical Decision Support on Diagnostic Imaging for Pediatric Appendicitis: A Cluster Randomized Trial. JAMA Netw Open. 2021 Feb 1;4(2):e2036344. PMCID: PMC7873779.
   b. Kharbanda AB, Madhok M, Krause E, Vazquez-Benitez G, **Kharbanda EO**, Mize W, Schmeling D. Implementation of electronic decision support for pediatric appendicitis. Pediatrics. 2016 May;137(5).
   c. **Kharbanda EO**, Nordin JD, Sinaiko AR, Ekstrom HL, Stultz JM, Sherwood NE, et al. TeenBP: Development and piloting of an EHR-linked clinical decision support system to improve recognition of hypertension in adolescents. EGEMS (Wash DC). 2015 Jul 9;3(2):1142. PMCID: PMC4537153.
   d. Kharbanda A, Vazquez Benitez G, Ballard DW, Vinson DR, Chettipally UK, Kene MV, Dehmer SP, Bachur R, Dayan P, Kuppermann N, O'Connor PJ, **Kharbanda EO**. Development and validation of a novel pediatric Appendicitis Risk Calculator (pARC). Pediatrics. 2018 Apr;141(4). pii: e20172699. PMCID: PMC5869337.

3. **Vaccine coverage.** In other vaccine-related work conducted at HealthPartners and at Columbia University over the past fifteen years, I have reported on vaccine coverage for adolescents and adults, how data source used (EHR versus claims) impacts the assessment of vaccine coverage, and how policies and personal beliefs can impact vaccine coverage.
   a. Groom HC, Henninger ML, Smith N, Koppolu P, Cheetham TC, Glanz JM, Hambidge SJ, Jackson LA, **Kharbanda EO**, Klein NP, McCarthy NL, Nordin JD, Weintraub ES, Naleway AL. Influenza Vaccination During Pregnancy: Influenza Seasons 2002-2012, Vaccine Safety Datalink. Am J Prev Med. 2016 Apr;50(4):480-488. PMID: 26526159.
   b. **Kharbanda EO**, Parker ED, Nordin JD, Hedblom B, Rolnick SJ. Receipt of human papillomavirus vaccine among privately insured adult women in a U.S. Midwestern Health Maintenance Organization. Prev Med. 2013 Nov;57(5):712-4.
   c. **Kharbanda EO**, Parker ED, Nordin JD, Hedblom BD, Rolnick SJ. Influenza and pertussis vaccination coverage among privately insured women of reproductive age. Matern Child Health J. 2013 Nov;17(9)1631-7.
   d. DeSilva MB, Haapala J, Vazquez-Benitez G, Daley MF, Nordin JD, Klein NP, Henninger ML, Williams JTB, Hambidge SJ, Jackson ML, Donahue JG, Qian L, Lindley MC, Gee J, Weintraub ES, **Kharbanda EO.** Association of the COVID-19 Pandemic With Routine Childhood Vaccination Rates and Proportion Up to Date With Vaccinations Across 8 US Health Systems in the Vaccine Safety Datalink. JAMA Pediatr. 2022 Jan 1;176(1):68-77. PMCID: PMC8498937.

4. **Pediatric hypertension and obesity.** As a Board Certified Pediatrician and Subspecialty Boarded Adolescent Medicine specialist who provided direct clinical care to children and adolescents in a variety of settings over a 12-year period, I have diverse experience in child and adolescent health. I joined HealthPartners Institute in 2010, and soon after served as a co-investigator on the Childhood Hypertension and Obesity: Diagnosis, Care, and Costs study (R01HL093345). As a result of my work on that study, in 2012, I was awarded a new investigator R01 from NHLBI to implement and evaluate a clinical decision support (CDS) tool embedded within the Electronic Health Record (EHR) to improve recognition of elevated blood pressures among adolescents presenting for outpatient care (R01HL115082), resulting in the Peds&Teen CDS tool which we are now testing and disseminating more broadly with funding from

AHRQ.

a. Parker ED, Sinaiko AR, **Kharbanda EO**, Margolis KL, Daley MF, Trower NK, Sherwood NE, Greenspan LC, Lo JC, Magid DJ, O'Connor PJ. Change in weight status and development of hypertension. Pediatrics. 2016 Mar;137(3):e20151662. PMCID: PMC4771125.
b. **Kharbanda EO,** Asche SE, Sinaiko AR, Ekstrom HL, Nordin JD, Sherwood NE, Fontaine PL, Dehmer SP, Appana D, O'Connor P. Clinical decision support for recognition and management of hypertension: a randomized trial. Pediatrics. 2018; Feb;141(2). pii: e20172954. PMCID: PMC5810603.
c. **Kharbanda EO**, Asche SE, Sinaiko A, Nordin JD, Ekstrom HL, Fontaine P, Dehmer SP, Sherwood NE, O'Connor PJ. Evaluation of an electronic clinical decision support tool for incident elevated BP in adolescents. Acad Pediatr. 2018 Jan - Feb;18(1):43-50. PMCID: PMC5756693.
d. **Kharbanda EO**, Parker ED, Sinaiko AR, Daley MF, Margolis KL, Becker M, Sherwood NE, Magid DJ, O'Connor PJ. Initiation of oral contraceptives and changes in blood pressure and body mass index in healthy adolescents. J Pediatr. 2014 Nov;165(5):1029-33. PMCID: PMC4252822.

Complete List of Published Work in My Bibliography: https://www.ncbi.nlm.nih.gov/myncbi/elyse.olshen-kharbanda.1/bibliography/public/

OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

NAME: Bryan S. Michalowicz, DDS, MS

eRA COMMONS USER NAME (credential, e.g., agency login) eRA Commons User Name

POSITION TITLE: Clinical Research Investigator, HealthPartners Institute

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Case Western Reserve University, Cleveland, OH	BS	05/1981	Pre-Dentistry
Case Western Reserve University School of Dentistry, Cleveland, OH	DDS	05/1983	Dentistry
University of Minnesota, Minneapolis, MN	MS	04/1988	Dentistry/Periodontics

A. Personal Statement

I have been involved in clinical dental research for over 30 years, and currently serve as a part-time research investigator with HealthPartners Institute. Personal Info from clinical practice after 30+ years as a board-certified periodontist. In addition, I am a former professor and current adjunct professor at the University of Minnesota School of Dentistry. From 2002 to 2013, I directed the University of Minnesota School of Dentistry's Clinical Research Center where I assembled and led investigative teams for projects ranging from single-site studies to large, multi-centered clinical trials. I have served as PI or co-investigator for numerous NIH and industry-sponsored clinical research projects including a NIDCR-funded study which examined the effect of non-surgical periodontal therapy on HbA1c levels in patients with type 2 diabetes and periodontitis (U01DE018902). Recently, in my role at HealthPartners Institute, I served as PI of a study examining the relationship between periodontal disease and coronary heart disease, cerebrovascular disease and diabetes (R03DE026797). On this R03 and other studies, I have worked closely with Dr. Rindal and his dental research partners from the Institute and HealthPartners Dental Group. In addition, I recently was a co-investigator on a study aimed at identifying risk factors for periodontal disease and eventual tooth loss in order to better monitor changes in the periodontal disease status of individual patients and develop care recommendations (R01DE024984). I also previously served on the American Dental Association's Council on Scientific Affairs and on numerous ad hoc NIH/NIDCR scientific review panels.

As a co-investigator on the proposed study, I will contribute my expertise in clinical research to assist Drs. Rindal and Mabry in planning and implementing the trial, interpretating the data, and disseminating results to medical and dental professionals through publications and presentations. Given the role that dental providers have in the preventing and identifying oropharyngeal cancers, the majority of which are attributable to HPV, this study represents a great opportunity to better understand how to engage dental providers in HPV vaccine promotion.

1. Engebretson SP, Hyman LG, **Michalowicz BS**, Schoenfeld ER, Gelato MC, Hou W, Seaquist ER, Reddy MS, Lewis CE, Oates TW, Tripathy D, Katancik JA, Orlander PR, Paquette DW, Hanson NQ, Tsai MY. The effect of nonsurgical periodontal therapy on hemoglobin A1c levels in persons with type 2 diabetes and chronic periodontitis: a randomized clinical trial. JAMA. 2013 Dec 18;310(23):2523-32. PMCID: PMC4089989.
2. **Michalowicz BS**, Hodges JS, DiAngelis AJ, Lupo VR, Novak MJ, Ferguson JE, Buchanan W, Bofill J, Papapanou PN, Mitchell DA, Matseoane S, Tschida PA; OPT Study. Treatment of periodontal disease and the risk of preterm birth. N Engl J Med. 2006 Nov 2;355(18):1885-94.
3. **Michalowicz BS**, Hodges JS, Lussky RC, Bada H, Rawson T, Buttross LS, Chiriboga C, Diangelis AJ, Novak MJ, Buchanan W, Mitchell DA, Papapanou PN. Maternal periodontitis treatment and child neurodevelopment at 24 to 28 months of age. Pediatrics. 2011 May;127(5):e1212-20.
4. Preshaw PM, Hefti AF, Novak MJ, **Michalowicz BS**, Pihlstrom BL, Schoor R, Trummel CL, Dean J, Van Dyke TE, Walker CB, Bradshaw MH. Subantimicrobial dose doxycycline enhances the efficacy of

scaling and root planing in chronic periodontitis: a multicenter trial. J Periodontol. 2004 Aug;75(8):1068-76.

Ongoing and recently completed projects I would like to highlight include:

Randomized Trial of Non-Surgical Therapy and Oral Hygiene Instruction to Reduce Risk of Infective Endocarditis (Lockhart)
Source: NIDCR/UG3DE031250
Role: Co-I 02/01/2022-01/31/2027
This study uses pre-existing healthcare claims and electronic medical record (EMR) data. Preliminary data includes 4,086 HealthPartners patient-members (including commercial, Medicare and Medicaid products) who also have a dementia diagnosis to examine the factors related to increased healthcare utilization among patients with dementia with Lewy bodies (DLB) in comparison to patients with Alzheimer's disease (AD), vascular dementia (VD), unspecified dementia, and age/gender-matched healthy controls.

Examining the Relationship of Periodontal Treatment and Improved Health Outcomes for Coronary Heart Disease, Cerebrovascular Disease and Diabetes (Michalowicz)
Source: NIDCR/R03DE026797
Role: PI 09/01/2018-08/31/2020
The high medical costs in the United States for treating diabetes, coronary heart disease, and cerebrovascular disease are concerning for healthcare providers, businesses in healthcare, and government insurance programs. Estimates on the total cost to treat diabetes was $245 billion in year 2012 and $315 billion to treat heart disease and stroke in 2010. It is of great interest to control these costs. The proposed study attempts to do so by analyzing 10+ years of medical, pharmacy, laboratory, dental, and insurance claims data to explore whether treatment of periodontal disease (an infection that damages the gums and jawbone) is associated with less hospital visits to treat diabetes, heart disease, and stroke and therefore a reduction in medical costs. The study will attempt to control for unforeseen factors that may have an impact on the relationship between periodontal disease treatment and the targeted diseases by applying powerful statistical analyses not included in previous studies that have assessed this relationship.

Spatiotemporal Models for Periodontal Disease Monitoring and Recall Frequencies (Bandyopadhyay)
Source: NIDCR/R01DE024984
Role: Site PI 09/25/2015-07/31/2019
Periodontal disease (PD), which contributes to eventual tooth loss, remains a major global oral health burden, particularly in the US. One possible means of addressing this concern is more efficient checkup/treatment allocation. The 6-month time intervals for administering dental therapies (or, perio-recall intervals) has, so far, been mostly driven by a one-size-fits-all paradigm. We propose novel methods to make full use of these data to achieve the following objectives: identify risk factors for PD and eventual tooth loss, monitor changes in the PD status of individual patients, and develop a policy for periodontal recall recommendations.

B. Positions and Honors

Positions and Employment

2016-present	Research Investigator, HealthPartners Institute
2015-2021	Staff periodontist, HealthPartners
2015-present	Adjunct Professor, Department of Developmental and Surgical Sciences, University of Minnesota, Minneapolis, MN
2008-2015	Professor, Department of Developmental and Surgical Sciences, University of Minnesota Minneapolis, MN,
2002-2014	Director, UMN Oral Health Clinical Research Center, Minneapolis, MN
1997-2007	Associate Professor (tenured), University of Minnesota, Minneapolis, MN,
1991-1997	Assistant Professor, University of Minnesota, Minneapolis, MN

Other Experience and Professional Memberships

2010-2014	Member, American Dental Association's Council on Scientific Affairs
2003-pres	Member, Task Force on Design and Analysis
1999	Research Sabbatical, Molecular Genetic Epidemiology Section, NIDCR, NIH
1991-2021	Diplomate, American Board of Periodontology

Honors

2006	Century Club (UMN School of Dentistry) Professor of the Year

2002-2014 Erwin Schaffer Chair in Periodontal Research
2001,2007 Clinical Research Award, American Academy of Periodontology
1993 Omicron Kappa Upsilon Honorary Dental Fraternity (President, Beta Beta Chapter, 2003-4)
1988 Balint Orban Award for Outstanding Graduate Research, American Academy of Periodontology

C. Contribution to Science

1. **Evidence-based periodontal patient care.** As a board-certified periodontist and researcher, I believe that the adoption of evidence-based approaches to disease prevention and treatments is the most powerful factor in reducing the burden of oral diseases. Therefore, much of my research has centered on evidence-based periodontal care. For example, I was the co-investigator on an Private Source systematic review and meta-analysis on nonsurgical treatment of patients with chronic periodontitis, which led to the development of associated clinical practice guidelines. I was also a co-investigator on a NIH-funded project to determine the association between periodontitis and osteonecrosis of the jaw (R21DE018717). With colleagues, I studied the role of poor oral hygiene as a risk factor for infective endocarditits, and more recently, I worked with others to systematically explore role of various oral hygiene adjuncts in controlling periodontal inflammation.

   a. Smiley CJ, Tracy SL, Abt E, **Michalowicz BS**, John MT, Gunsolley J, Cobb CM, Rossmann J, Harrel SK, Forrest JL, Hujoel PP, Noraian KW, Greenwell H, Frantsve-Hawley J, Estrich C, Hanson N. Evidence-based clinical practice guideline on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts. J Am Dent Assoc. 2015 Jul;146(7):525-35.
   b. Smiley CJ, Tracy SL, Abt E, **Michalowicz BS**, John MT, Gunsolley J, Cobb CM, Rossmann J, Harrel SK, Forrest JL, Hujoel PP, Noraian KW, Greenwell H, Frantsve-Hawley J, Estrich C, Hanson N. Systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts. J Am Dent Assoc. 2015 Jul;146(7):508-524.e5.
   c. Kotsakis GA, Lian Q, Ioannou AL, **Michalowicz BS**, John MT, Chu H. A network meta-analysis of interproximal oral hygiene methods in the reduction of clinical indices of inflammation. J Periodontol. 2018 May;89(5):558-570. PMCID: PMC5984142.
   d. Lockhart PB, Brennan MT, Thornhill M, **Michalowicz BS**, Noll J, Bahrani-Mougeot FK, Sasser HC. Poor oral hygiene as a risk factor for infective endocarditis-related bacteremia. J Am Dent Assoc. 2009 Oct;140(10):1238-44. PMCID: PMC2770162.

2. **Periodontal disease and maternal and child health.** Periodontal disease is one of the most common chronic conditions. We know that periodontal disease is responsible for a chronic inflammatory challenge in the body and therefore can complicate or exacerbate other medical conditions. It may also have an effect on birth outcomes and infant development if a woman is not appropriately treated during pregnancy. It has been an interest of mine to study how maternal periodontal disease impacts the health of their child. I served as Principal Investigator for two NIH-funded projects related to this topic. One examined the treatment of periodontal disease in pregnant women and whether it improves mental and motor development in their infants. The other study titled “The Effects of Periodontal Therapy on Preterm Birth” examined whether maternal periodontal disease is associated with an increased risk of preterm birth and whether treatment of periodontal disease improved mental and motor development in infants (U01DE014338). A focus of my research has also been in periodontal disease and genetic outcomes. I was the Principal Investigator for a NIH-funded study about the heritability of temporomandibular joint (TMJ)-related symptoms (R01DE008158).

   a. **Michalowicz BS**, Hodges JS, DiAngelis AJ, Lupo VR, Novak MJ, Ferguson JE, Buchanan W, Bofill J, Papapanou PN, Mitchell DA, Matseoane S, Tschida PA; OPT Study. Treatment of periodontal disease and the risk of preterm birth. N Engl J Med. 2006 Nov 2;355(18):1885-94.
   b. **Michalowicz BS**, Pihlstrom BL, Hodges JS, Bouchard TJ Jr. No heritability of temporomandibular joint signs and symptoms. J Dent Res. 2000 Aug;79(8):1573-8.
   c. **Michalowicz BS**, Hodges JS, Lussky RC, Bada H, Rawson T, Buttross LS, Chiriboga C, Diangelis AJ, Novak MJ, Buchanan W, Mitchell DA, Papapanou PN. Maternal periodontitis treatment and child neurodevelopment at 24 to 28 months of age. Pediatrics. 2011 May;127(5):e1212-20. PMCID: PMC3081189.
   d. Diehl SR, Wu T, **Michalowicz BS**, Brooks CN, Califano JV, Burmeister JA, Schenkein HA. Quantitative measures of aggressive periodontitis show substantial heritability and consistency with traditional diagnoses. J Periodontol. 2005 Feb;76(2):279-88.

3. **Relationship between periodontal disease and medical chronic diseases.** Chronic disease and chronic disease complications are a major public health concern and are often associated with increased risk for oral health complications. My research has been particularly focused on the association between periodontal disease and diabetes. I was a co-investigator on The Diabetes and Periodontal Therapy Trial (DPTT), a NIH-funded study that evaluated whether non-surgical treatment of periodontal disease influenced diabetes management among persons with Type 2 diabetes and periodontitis (U01DE018902). The aim of this study was to evaluate DPTT's many recruitment strategies in terms of enrollment success. I have also researched the connection between disorders of the jaw, specifically osteonecrosis and TMD, and periodontal disease. I also helped clarify the relationship between invasive dental procedures and prosthetic joint infections.

    a. Skaar DD, O'Connor H, Hodges JS, **Michalowicz BS**. Dental procedures and subsequent prosthetic joint infections: findings from the Medicare Current Beneficiary Survey. J Am Dent Assoc. 2011 Dec;142(12):1343-51.
    b. Engebretson SP, Hyman LG, **Michalowicz BS**, Schoenfeld ER, Gelato MC, Hou W, Seaquist ER, Reddy MS, Lewis CE, Oates TW, Tripathy D, Katancik JA, Orlander PR, Paquette DW, Hanson NQ, Tsai MY. The effect of nonsurgical periodontal therapy on hemoglobin A1c levels in persons with type 2 diabetes and chronic periodontitis: a randomized clinical trial. JAMA. 2013 Dec 18;310(23):2523-32. PMCID: PMC4089989.
    c. Thumbigere-Math V, **Michalowicz BS**, Hodges JS, Tsai ML, Swenson KK, Rockwell L, Gopalakrishnan R. Periodontal disease as a risk factor for bisphosphonate-related osteonecrosis of the jaw. J Periodontol. 2014 Feb;85(2):226-33. PMCID: PMC3972496.
    d. **Michalowicz BS**, Hyman L, Hou W, Oates TW Jr, Reddy M, Paquette DW, Katancik JA, Engebretson SP; Diabetes and Periodontal Therapy Trial Study Team. Factors associated with the clinical response to nonsurgical periodontal therapy in people with type 2 diabetes mellitus. J Am Dent Assoc. 2014 Dec;145(12):1227-39.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/bryan.michalowicz.1/bibliography/41151922/public/?sort=date&direction=ascending

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: HealthPartners Institute

Start Date*: 12-01-2022 **End Date*:** 11-30-2023 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	D. Brad		Rindal	DDS	PD/PI	Institutional Base Salary	EFFORT			20,370.00	3,870.00	24,240.00
2 .	Dr.	Patricia	L	Mabry	PhD	PD/PI					17,420.00	5,749.00	23,169.00
3 .	Mr.	Stephen	E.	Asche	MA	Co-Investigator/ Statistician					13,670.00	4,511.00	18,181.00
4 .	Dr.	Meghan	M	JaKa	MS, PhD	Co-Investigator					18,425.00	6,080.00	24,505.00
5 .	Dr.	Elyse	O.	Kharbanda	MD, MPH	Co-Investigator					10,185.00	1,630.00	11,815.00
6 .	Dr.	Bryan	S	Michalowicz	DDS, MS	Co-Investigator					4,074.00	725.00	4,799.00

Total Funds Requested for all Senior Key Persons in the attached file **0.00**

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **106,709.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Programmer	1.2			11,500.00	3,795.00	15,295.00
1	Dental Advisor	EFFORT			3,500.00	823.00	4,323.00
1	Project Manager	4.8			42,040.00	13,873.00	55,913.00
1	Sr. Project Coordinator				0.00	0.00	0.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**75,531.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**182,240.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-21-317 . Received Date: 2022-03-07T11:53:21.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: HealthPartners Institute

Start Date*: 12-01-2022 **End Date*:** 11-30-2023 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	100.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**100.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

UEI*: H65GNDPBTRY7
Budget Type*: ● Project ○ Subaward/Consortium
Organization: HealthPartners Institute

Start Date*: 12-01-2022 **End Date*:** 11-30-2023 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Costs	17,499.00
Total Other Direct Costs	**17,499.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**199,839.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	57	199,839.00	113,908.00
		Total Indirect Costs	**113,908.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Arif M. Karim-A, 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**313,747.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	313,747.00

L. Budget Justification* File Name: Budget Justification.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: HealthPartners Institute

Start Date*: 12-01-2023 **End Date*:** 11-30-2024 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	D. Brad		Rindal	DDS	PD/PI	Institutional Base Salary	EFFORT			20,370.00	3,870.00	24,240.00
2 .	Dr.	Patricia	L	Mabry	PhD	PD/PI					17,942.00	5,921.00	23,863.00
3 .	Mr.	Stephen	E.	Asche	MA	Co-Investigator/ Statistician					14,080.00	4,646.00	18,726.00
4 .	Dr.	Meghan	M	JaKa	MS, PhD	Co-Investigator					12,651.00	4,175.00	16,826.00
5 .	Dr.	Elyse	O.	Kharbanda	MD, MPH	Co-Investigator					8,148.00	1,304.00	9,452.00
6 .	Dr.	Bryan	S	Michalowicz	DDS, MS	Co-Investigator					4,074.00	725.00	4,799.00

Total Funds Requested for all Senior Key Persons in the attached file **0.00**

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **97,906.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Programmer	1.2			11,845.00	3,909.00	15,754.00
1	Dental Advisor	EFFORT			3,605.00	847.00	4,452.00
1	Project Manager	4.8			43,301.00	14,289.00	57,590.00
1	Sr. Project Coordinator				0.00	0.00	0.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**77,796.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**175,702.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-21-317 . Received Date: 2022-03-07T11:53:21.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: HealthPartners Institute

Start Date*: 12-01-2023 **End Date*:** 11-30-2024 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	100.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**100.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

UEI*: H65GNDPBTRY7
Budget Type*: ● Project ○ Subaward/Consortium
Organization: HealthPartners Institute

Start Date*: 12-01-2023 **End Date*:** 11-30-2024 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Costs	24,151.00
Total Other Direct Costs	**24,151.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**199,953.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	57	199,953.00	113,973.00
		Total Indirect Costs	**113,973.00**

Cognizant Federal Agency DHHS, Arif M. Karim-A, 214-767-3261
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**313,926.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	313,926.00

L. Budget Justification* File Name: Budget Justification.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: HealthPartners Institute

Start Date*: 12-01-2024 **End Date*:** 11-30-2025 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	D. Brad		Rindal	DDS	PD/PI	Institutional Base Salary	EFFORT			50,925.00	9,676.00	60,601.00
2 .	Dr.	Patricia	L	Mabry	PhD	PD/PI					46,202.00	15,247.00	61,449.00
3 .	Mr.	Stephen	E.	Asche	MA	Co-Investigator/ Statistician					29,004.00	9,571.00	38,575.00
4 .	Dr.	Meghan	M	JaKa	MS, PhD	Co-Investigator					19,547.00	6,450.00	25,997.00
5 .	Dr.	Elyse	O.	Kharbanda	MD, MPH	Co-Investigator					20,370.00	3,259.00	23,629.00
6 .	Dr.	Bryan	S	Michalowicz	DDS, MS	Co-Investigator					20,370.00	3,626.00	23,996.00

Total Funds Requested for all Senior Key Persons in the attached file **0.00**

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **234,247.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Programmer	3			30,501.00	10,065.00	40,566.00
1	Dental Advisor	EFFORT			18,566.00	4,363.00	22,929.00
1	Project Manager	4.8			44,600.00	14,718.00	59,318.00
1	Sr. Project Coordinator	2.4			15,914.00	5,251.00	21,165.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**143,978.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**378,225.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-21-317 . Received Date: 2022-03-07T11:53:21.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: HealthPartners Institute

Start Date*: 12-01-2024 **End Date*:** 11-30-2025 **Budget Period: 3**

C. Equipment Description		
List items and dollar amount for each item exceeding $5,000		
Equipment Item		**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file		**0.00**
	Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	5,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**5,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

UEI*: H65GNDPBTRY7
Budget Type*: ● Project ○ Subaward/Consortium
Organization: HealthPartners Institute

Start Date*: 12-01-2024 **End Date*:** 11-30-2025 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Costs	99,308.00
Total Other Direct Costs	**99,308.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**482,533.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	57	482,533.00	275,044.00
		Total Indirect Costs	**275,044.00**

Cognizant Federal Agency DHHS, Arif M. Karim-A, 214-767-3261
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**757,577.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	757,577.00

L. Budget Justification* File Name: Budget Justification.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: HealthPartners Institute

Start Date*: 12-01-2025 **End Date*:** 11-30-2026 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	D. Brad		Rindal	DDS	PD/PI	Institutional Base Salary	EFFORT			50,925.00	9,676.00	60,601.00
2 .	Dr.	Patricia	L	Mabry	PhD	PD/PI					47,588.00	15,704.00	63,292.00
3 .	Mr.	Stephen	E.	Asche	MA	Co-Investigator/ Statistician					29,874.00	9,859.00	39,733.00
4 .	Dr.	Meghan	M	JaKa	MS, PhD	Co-Investigator					20,133.00	6,644.00	26,777.00
5 .	Dr.	Elyse	O.	Kharbanda	MD, MPH	Co-Investigator					20,370.00	3,259.00	23,629.00
6 .	Dr.	Bryan	S	Michalowicz	DDS, MS	Co-Investigator					20,370.00	3,626.00	23,996.00

Total Funds Requested for all Senior Key Persons in the attached file **0.00**

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **238,028.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Programmer	2.4			25,133.00	8,294.00	33,427.00
1	Dental Advisor	EFFORT			19,123.00	4,494.00	23,617.00
1	Project Manager	4.8			45,938.00	15,160.00	61,098.00
1	Sr. Project Coordinator	2.4			16,391.00	5,409.00	21,800.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**139,942.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**377,970.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-21-317 . Received Date: 2022-03-07T11:53:21.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: HealthPartners Institute

Start Date*: 12-01-2025 **End Date*:** 11-30-2026 **Budget Period: 4**

C. Equipment Description		
List items and dollar amount for each item exceeding $5,000		
Equipment Item		**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file		**0.00**
	Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	5,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**5,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

UEI*: H65GNDPBTRY7
Budget Type*: ● Project ○ Subaward/Consortium
Organization: HealthPartners Institute

Start Date*: 12-01-2025 **End Date*:** 11-30-2026 **Budget Period:** 4

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Costs	106,550.00
Total Other Direct Costs	**106,550.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**489,520.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	57	489,520.00	279,026.00
		Total Indirect Costs	**279,026.00**

Cognizant Federal Agency DHHS, Arif M. Karim-A, 214-767-3261
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**768,546.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	768,546.00

L. Budget Justification* File Name: Budget Justification.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: HealthPartners Institute

Start Date*: 12-01-2026 **End Date*:** 11-30-2027 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	D. Brad		Rindal	DDS	PD/PI	Institutional Base Salary	EFFORT			50,925.00	9,676.00	60,601.00
2 .	Dr.	Patricia	L	Mabry	PhD	PD/PI					49,016.00	16,175.00	65,191.00
3 .	Mr.	Stephen	E.	Asche	MA	Co-Investigator/ Statistician					38,463.00	12,693.00	51,156.00
4 .	Dr.	Meghan	M	JaKa	MS, PhD	Co-Investigator					20,737.00	6,843.00	27,580.00
5 .	Dr.	Elyse	O.	Kharbanda	MD, MPH	Co-Investigator					20,370.00	3,259.00	23,629.00
6 .	Dr.	Bryan	S	Michalowicz	DDS, MS	Co-Investigator					30,555.00	5,439.00	35,994.00

Total Funds Requested for all Senior Key Persons in the attached file **0.00**

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **264,151.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Programmer	1.8			19,415.00	6,407.00	25,822.00
1	Dental Advisor	EFFORT			19,696.00	4,629.00	24,325.00
1	Project Manager	4.8			47,316.00	15,614.00	62,930.00
1	Sr. Project Coordinator	2.4			16,883.00	5,571.00	22,454.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**135,531.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**399,682.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-21-317 . Received Date: 2022-03-07T11:53:21.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: HealthPartners Institute

Start Date*: 12-01-2026 **End Date*:** 11-30-2027 **Budget Period: 5**

C. Equipment Description		
List items and dollar amount for each item exceeding $5,000		
Equipment Item		**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file		**0.00**
	Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	9,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**9,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

UEI*: H65GNDPBTRY7
Budget Type*: ● Project ○ Subaward/Consortium
Organization: HealthPartners Institute

Start Date*: 12-01-2026 **End Date*:** 11-30-2027 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Costs	67,949.00
Total Other Direct Costs	**67,949.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**476,631.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	57	476,631.00	271,680.00
		Total Indirect Costs	**271,680.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Arif M. Karim-A, 214-767-3261

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**748,311.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	748,311.00

L. Budget Justification* File Name: Budget Justification.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 6

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: HealthPartners Institute

Start Date*: 12-01-2027 **End Date*:** 11-30-2028 **Budget Period: 6**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	D. Brad		Rindal	DDS	PD/PI	Institutional Base Salary	EFFORT			50,925.00	9,676.00	60,601.00
2 .	Dr.	Patricia	L	Mabry	PhD	PD/PI					50,486.00	16,660.00	67,146.00
3 .	Mr.	Stephen	E.	Asche	MA	Co-Investigator/ Statistician					47,540.00	15,688.00	63,228.00
4 .	Dr.	Meghan	M	JaKa	MS, PhD	Co-Investigator					21,359.00	7,048.00	28,407.00
5 .	Dr.	Elyse	O.	Kharbanda	MD, MPH	Co-Investigator					20,370.00	3,259.00	23,629.00
6 .	Dr.	Bryan	S	Michalowicz	DDS, MS	Co-Investigator					30,555.00	5,439.00	35,994.00

Total Funds Requested for all Senior Key Persons in the attached file **0.00**

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **279,005.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Programmer	0.6			6,666.00	2,200.00	8,866.00
1	Dental Advisor	EFFORT			19,930.00	4,684.00	24,614.00
1	Project Manager	4.8			48,736.00	16,083.00	64,819.00
1	Sr. Project Coordinator	2.4			17,389.00	5,738.00	23,127.00
4	**Total Number Other Personnel**					**Total Other Personnel**	**121,426.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**400,431.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PAR-21-317 . Received Date: 2022-03-07T11:53:21.000-05:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 6

UEI*: H65GNDPBTRY7

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: HealthPartners Institute

Start Date*: 12-01-2027 **End Date*:** 11-30-2028 **Budget Period: 6**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	**0.00**
Total Equipment	**0.00**

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	8,000.00
2. Foreign Travel Costs	0.00
Total Travel Cost	**8,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		0.00
2. Stipends		0.00
3. Travel		0.00
4. Subsistence		0.00
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	**0.00**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 6

UEI*: H65GNDPBTRY7
Budget Type*: ● Project ○ Subaward/Consortium
Organization: HealthPartners Institute

Start Date*: 12-01-2027 **End Date*:** 11-30-2028 **Budget Period: 6**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	0.00
2. Publication Costs	0.00
3. Consultant Services	0.00
4. ADP/Computer Services	0.00
5. Subawards/Consortium/Contractual Costs	0.00
6. Equipment or Facility Rental/User Fees	0.00
7. Alterations and Renovations	0.00
8. Other Costs	29,953.00
Total Other Direct Costs	**29,953.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**438,384.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	57	438,384.00	249,879.00
		Total Indirect Costs	**249,879.00**

Cognizant Federal Agency DHHS, Arif M. Karim-A, 214-767-3261
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**688,263.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	688,263.00

L. Budget Justification* File Name: Budget Justification.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings

HealthPartners Institute

Budget Justification

Personnel Staffing Table

Name/*Role*	% Effort/Period					
	UG3 Phase		UH3 Phase			
	1	2	3	4	5	6
Brad Rindal, DDS *Co-Principal Investigator*	EFFORT					
Patricia Mabry, PhD *Co-Principal Investigator*						
Steve Asche, MA *Co-Investigator/Statistician*						
Meghan JaKa, PhD *Co-Investigator*						
Elyse Kharbanda, MD, MPH *Co-Investigator*						
Bryan Michalowicz, DDS *Co-Investigator*						
Donald Worley, DDS *Dental Advisor*						
TBN, Programmer/Analyst	10.00	10.00	25.00	20.00	15.00	5.00
TBN, Principal Project Manager	40.00	40.00	40.00	40.00	40.00	40.00
TBN, Sr. Project Coordinator			20.00	20.00	20.00	20.00

Fringe benefits are calculated at 33% of salary unless otherwise noted. Salaries at or above the NIH salary cap are calculated accordingly at $203,700. Salaries below the cap and other expenses are increased 3% yearly.

Key Personnel

D. Brad Rindal, DDS (Co-Principal Investigator) is a board certified dentist, Senior Research Investigator at HealthPartners Institute (the Institute), and Associate Dental Director for Research for HealthPartners Dental Group (HPDG). Dr. Rindal's clinical focus is temporomandibular disorder (TMD)/orofacial pain and his research focus is on practice-based research and testing new approaches to improve the translation of research into daily practice. He is the director of the Midwest Region of the National Dental Practice-Based Research Network (U19DE028717, PI: Gregg Gilbert) funded by the National Institute of Dental and Craniofacial Research (NIDCR) through the University of Alabama, Birmingham (National Dental PBRN). The network involves practicing dentists in the development of clinically important research questions and the collection of research data. He has acted as PI or co-investigator on several large, federally funded research projects, including studies leveraging clinical decision support (CDS) tools embedded in the electronic health record (EHR) to support providers in the delivery of evidence-based care. He currently serves as Co-PI of a study that uses CDS to promote the delivery of brief tobacco cessation interventions and quit line referrals in community dental practices and in two dental schools (U01DE026135). In addition, he serves as co-PI on a trial examining approaches to de-implement unnecessary opioid prescribing following dental extractions using CDS (U01DE027441). With the support of the HealthPartners Center for Oral Health Integration, Dr. Rindal is currently overseeing the development and implementation of a comprehensive EHR-embedded CDS platform (Dental Wizard) for HealthPartners dental providers, which will expand the use of the CDS tools to translate research findings into to regular clinical care. This CDS platform will also include human papillomavirus (HPV)

vaccination status information, patient education materials and vaccine order functionality, allowing it to be leveraged as part of the proposed study to deliver tailored scripts to providers in intervention clinics.

On the proposed study, Dr. Rindal will serve as Co-PI along with Dr. Patricia Mabry, and will provide his oversight on all study activities to ensure successful and timely completion according to the study milestones. As Contact PI, Dr. Rindal will have primary responsibility for communicating progress to NIH and will provide fiscal and administrative management. Given his leadership role with HPDG and his experience working with the dental group to implement similar studies, Dr. Rindal is also well positioned to serve as the primary liaison with HPDG stakeholders. He will engage with HPDG stakeholders, including leaders, providers, and clinic staff, during the UG3 phase to get input on the intervention development, and throughout the UH3 phase to ensure the successful implementation and maintenance of the intervention. Dr. Rindal will contribute his expertise in practice-based dental research and cluster-randomized clinical trials leveraging CDS and tailored scripts to all aspects of the study including protocol and intervention development, implementation, analysis and dissemination. Along with Dr. Mabry, Dr. Rindal will lead regular study team meetings, develop and finalize all documents necessary for NIDCR and IRB approval, ensure methodological design compliance, supervise personnel assigned to this project, and ensure completion of all data collection and analysis. In addition, he will lead dissemination efforts by presenting study results at conferences and to HealthPartners organizational leaders and he will prepare manuscripts for publication in peer-reviewed journals. Effort for Dr. Rindal is budgeted at EFFORT calendar months (CM) in Years 1-2, and EFFORT in Years 3-6. Fringe benefits are calculated at 19% of salary.

Patricia Mabry, PhD (Co-Principal Investigator) is a Research Investigator at HealthPartners Institute with a doctoral degree in clinical psychology. Relevant to the proposed project, she has experience as a clinician providing direct patient care in medical settings and as researcher conducting behavioral intervention development. Prior to joining the Institute in 2019, Dr. Mabry was a Senior Research Scientist and Executive Director of the interdisciplinary Indiana University Network Science Institute (IUNI). She served as Founding Director of the Systems Science program at the NIH Office of Behavioral & Social Sciences Research (OBSSR), and was founding Co-Director of the Envision Modeling Network of the National Collaborative on Childhood Obesity Research (NCCOR), among other roles across NIH, academia, private industry, and government. Dr. Mabry earned a PhD in clinical psychology from the University of Virginia, and spent more than five years delivering cognitive and behavioral interventions to individuals and couples for a variety of conditions including anxiety, depression, headache, stress, grief, eating disorders, learning disabilities, and tobacco, alcohol and drug addiction. Immediately following completion of her PhD, she worked for a small business, Personal Improvement Computer Systems, Inc. (PICS) developing behavior change interventions (i.e., tobacco cessation, dietary and exercise interventions) funded by NIH Small Business Innovative Research grants, using theory to conceptualize mechanisms of behavior change. This work continued in the form of subawards from PICS when she moved to the Medical University of South Carolina to complete her clinical post-doc (and as a tenure-track Assistant Professor at MUSC). She was recruited to the National Cancer Institute where she was the founding director of the Tobacco Intervention Research Clinic, with the intention of pursuing research on tobacco cessation intervention development, but after 2 years it was shuttered due to budget cuts that coincided with the ending of the doubling of the NIH budget. Subsequently, developed expertise in applying state of the science research methods, including systems science, network science and artificial intelligence to behavioral and social science research questions pertinent to health and health care; she has a keen interest in addressing health disparities and promoting open science and diversity. Dr. Mabry has experience in user-centered design (smokefree.gov), leading and contributing to several federally funded grants including co-leading the development of the IMLS-funded cloud science gateway, Collaborative Archive & Data Research Environment (CADRE). She currently serves as PI of a NSF-funded grant focused on to identifying and characterizing social capital accumulation pathways that may explain funding gaps in the biomedical research workforce (NSF/2122232).

As Co-PI, Dr. Mabry will work closely with Dr. Rindal to carry out all aspects of the study including intervention development, implementation, analysis, and dissemination. Dr. Mabry will contribute her expertise in behavior change throughout the study, and will assume leadership for incorporating behavior change theory and The NIH Stage Model of Intervention Development into the development of the intervention and study design as well as the analysis and interpretation of results. She will work closely with Dr. JaKa to develop an interview guide to capture the perspectives of dental providers and will guide the use of interview data to inform the development of the provider training and scripts in a way that most effectively engages the targeted behavioral mechanisms. She will also guide plans for measuring behavioral mechanisms via provider surveys as well as the plans for monitoring provider fidelity to the intervention. In close collaboration with the project manager, Dr.

Mabry will oversee the delivery of the provider training to all relevant staff in the intervention clinics. With Dr. Rindal, Dr. Mabry will lead study team meetings, develop and finalize the study protocol and other necessary study documents, and oversee the timely completion of activities according to the timeline and study milestones. She will also lead the development of manuscripts, particularly those focused on the use of behavior change theory and the proposed mediation analysis, and will also disseminate results through presentations in academic forums. Effort for Dr. Mabry is budgeted at EFFORT calendar months (CM) in Years 1-2, and EFFORT in Years 3-6.

Steve Asche, MA (Co-Investigator/Statistician) is a Senior Research Investigator and manager of the Research Methodology Group at the Institute. He has a strong background in biostatistics and has served as lead statistician on many federally funded projects. Mr. Asche not only has experience with cluster-randomized trials, but also has extensive experience analyzing data for observational studies, including multi-level modeling to take into account factors at the patient, provider, clinic, and medical group levels. Mr. Asche has worked on projects that address a wide range of clinical domains related to preventive care and chronic disease care. Currently, he works with Dr. Rindal on the two NIDCR-funded CDS studies on which this project builds: 1) De-Implementing Opioid Use and Implementing Optimal Pain Management (U01DE027441); and 2) A Clinic-Randomized Trial of a Clinical Decision Support System to Improve Dental Provider Delivery of Brief Tobacco Interventions and Quitline Referrals (U01DE026135). He also is the lead statistician on several other clinic-randomized studies implementing and testing CDS for promoting 1.) cancer screening and HPV vaccination (R01CA193396); 2.) obesity management in patients with diabetes (R01DK128281); and 3.) detection and treatment of hypertension in children and adolescents (R18HS027402). His work utilizes data from various sources including surveys, electronic medical and dental records, and health care administrative and claims data.

On this project, Mr. Asche will lead the quantitative analysis. During the UG3 phase, he will contribute to the development of the protocol and data quality management plan to ensure the strength of the methodology and plans for ensuring accurate data. Mr. Asche will participate in weekly research team meetings, develop and provide input for variable definition and measurement decisions, direct the development of the analytic database, assure the quality of the data during data cleaning and recoding, perform preliminary analyses, develop appropriate hierarchical analytic models, and apply any covariate adjustment methods that may be needed. He will work with the programmer to consolidate data from all sites and sources (EHR data and survey data) into a common format and combine data elements into uniform files. In addition, he will create the randomization scheme to ensure the stratified randomization of clinics as described in the proposal. He will also contribute to the dissemination of findings through publications and presentations. Due to the timing and nature of his work, Mr. Asche's effort is budgeted at EFFORT in Years 1-2, EFFORT in Years 3-4, EFFORT in Year 5, and EFFORT in Year 6.

Meghan JaKa, PhD (Co-Investigator) is an Evaluation Associate within the Center for Evaluation and Survey Research (CESR) at HealthPartners Institute with extensive experience designing, implementing and evaluating behavior change interventions in the healthcare setting and publishing and disseminating findings. She has particular expertise in intervention fidelity, health behavior change theory, and recruitment methods. Dr. JaKa brings expertise in mixed-methods research and has experience applying various mixed-methods and qualitative research frameworks as well as coding and analyzing qualitative data. In her role with CESR, Dr. JaKa oversees over 10 health system evaluations that use a mix of quantitative and qualitative methods related to health systems improvement, many of which focus on provider behavior change. She currently is a co-investigator on a state-wide care coordination study aimed at understanding the impact of social and medical care coordination models, for which she is overseeing clinician, care coordinator, and patient interviews (PCORI/IHS-2019C1-15625). She is also a co-investigator on a study which is implementing and testing a CDS tool to improve detection and management of cognitive impairment (R61AG069770). In addition, Dr. JaKa recently collaborated with Dr. Patricia Mabry on a study aimed at developing a simulation model for colorectal cancer screenings, for which she developed and analyzed patient interviews to inform model inputs.

As a co-investigator on this proposal, Dr. JaKa will lend her expertise in behavior change, intervention fidelity monitoring, and qualitative research methods to the design, implementation and analysis. During the UG3 phase of the grant, she will lead and analyze provider interviews, and will work closely with Dr. Mabry to develop the provider training based on the interview feedback and behavior change theory, and help finalize plans for monitoring intervention fidelity. Subsequently, during the UH3 phase, she will assist with provider trainings and contribute to the interpretation and dissemination of results. She will also help with development of survey tools and oversee the administration of patient and provider surveys by her team in CESR. Given her

role in CESR, Dr. JaKa is also well positioned to help develop patient and provider survey tools and assist CESR staff in implementing the survey protocol. Dr. JaKa's effort is budgeted at EFFORT in Year 1 as well as Years 3-6, and EFFORT in Year 2.

Elyse Kharbanda, MD, MPH (Co-Investigator) is a Senior Research Investigator and Executive Director of Research at HealthPartners Institute and a board-certified pediatrician with expertise in HPV vaccination and interventions using CDS. Dr. Kharbanda currently serves as co-PI on the Centers for Disease Control and Prevention (CDC) funded Vaccine Safety Datalink (VSD) Project, leading several multisite observational studies of vaccine safety during pregnancy (200-2002-00732). Recently she was PI of a VSD task order examining the risk of spontaneous abortion following inadvertent human papilloma virus (HPV) vaccination, and she also served as co-PI on another VSD study evaluating the safety of HPV, influenza and Tdap vaccinations for pregnant women and newborns. Currently, Dr. Kharbanda is PI of two VSD studies which are examining the risk of adverse maternal and infant outcomes following receipt of COVID-19 vaccinations during pregnancy. Furthermore, she has been the PI of three clinical trials aimed at improving patient care with the help of CDS tools, including the NHLBI-funded Peds&TeenBP CDS study (R01HL115082), a current study testing implementation and scalability of the Peds&TeenBP CDS in a rural health system (R18HS027402), and a NICHD-funded study aimed at supporting more appropriate use of diagnostic imaging for pediatric and young adult patients with abdominal pain (R01HD079463). As a fellow in Adolescent Medicine, Dr. Kharbanda led one of the first studies qualitatively evaluating parental views on the HPV vaccine. With funding from HRSA, she later led a text messaging intervention to increase timeliness of receipt of the next HPV vaccine dose (R40MC08961).

As a co-investigator on this study, Dr. Kharbanda will contribute her expertise in vaccine safety and uptake as well as current processes for vaccine administration and vaccine promotion efforts within the HealthPartners system. In addition, she will contribute her expertise in provider-focused inventions leveraging CDS and use of vaccine data for research. Further, she will contribute to provider trainings, lending credibility to messaging as an expert in vaccine safety and will respond to providers' questions and concerns about HPV vaccination. She will also play an important role in the dissemination of study results through presentations and publications. Dr. Kharbanda is budgeted at EFFORT in Year 1, EFFORT in Year 2, and EFFORT in Years 3-6. Fringe benefits are calculated at 16% of salary.

Bryan Michalowicz, DDS (Co-Investigator) is a periodontist, clinical investigator at the Institute, and an adjunct professor at the University of Minnesota School of Dentistry. He was a board-certified periodontist with HPDG for over 30 years and was formerly Professor within the Department of Developmental and Surgical Sciences at the University of Minnesota. He has over 20 years of clinical dental research experience and previously served as the Director of the University of Minnesota School of Dentistry's Clinical Research Center. Dr. Michalowicz has served as PI or site-PI for numerous NIH- and industry-sponsored multi-center clinical trials. He recently was PI of a study examining the relationship between periodontal disease and coronary heart disease, cerebrovascular disease and diabetes (R03DE026797). Currently, he is a co-investigator on a study using electronic health data to examine the factors related to increased healthcare utilization among patients with dementia with Lewy bodies in comparison to patients with Alzheimer's disease, vascular dementia, unspecified dementia, and age/gender-matched healthy controls. (UG3DE031250). Previously, Dr. Michalowicz has led studies examining the relationship between maternal periodontal disease and risk of preterm birth as well as mental and motor development in infants (U01DE014338) as well as the effect of non-surgical periodontal therapy on HbA1c levels in patients with type 2 diabetes and periodontitis (U01DE018902). He has served on the American Dental Association's Council on Scientific Affairs and on numerous ad hoc NIH/NIDCR scientific review panels.

As a co-investigator, Dr. Michalowicz will contribute his expertise in clinical research to assist Drs. Rindal and Mabry in planning and implementing the trial, and interpretating the data. He will also contribute to the dissemination of results to medical and dental professionals through publications and presentations. Dr. Michalowicz is budgeted at EFFORT in Years 1-2, and EFFORT in Years 3-4, and EFFORT in Years 5-6. Fringe benefits are calculated at 17.8% of salary.

Non-Key Personnel

Don Worley, DDS (Dental Advisor) is a dentist who has practiced clinical dentistry for over 30 years and has held leadership roles during that period. Until recently he served as Quality and Operations Consultant with HPDG, a role in which he assisted with initiatives to streamline dental processes and supported the dental group in leveraging the data and functions available to them through the EHR. Dr. Worley was involved in

customizing the HealthPartners electronic dental record, and more recently contributed to efforts to transition the practice to the integrated medical and dental record, Epic Wisdom. From this experience, Dr. Worley has a strong understanding of the EHR, and has worked directly with the Epic team on implementing and operationalizing approved changes within the EHR for the dental group. Dr. Worley also contributes to research and patient safety initiatives. Currently, he collaborates on Dr. Rindal's study "De-Implementing Opioid Use and Implementing Optimal Pain Management Following Dental Extractions" (U01DE027441). Dr. Worley chaired the HealthPartners regulatory compliance and patient safety committee for more than 25 years and has chaired several guideline development groups. He continues to be involved in HealthPartners' efforts to implement clinical guidelines and develop quality measures aligning with the guidelines.

Given his knowledge of dental clinic workflows and operations, and EHR processes, Dr. Worley is well suited to contribute to the proposed study. He will work with Dr. Rindal to engage stakeholders from the dental group and the dental clinics involved in the study. In collaboration with HPDG, HealthPartners Informatics, and the study team, including the Institute's Software Engineering & Technology team, Dr. Worley will help support the smooth implementation of the intervention, including the roll out of the enhanced CDS with tailored scripts to the intervention clinics. He will also work directly with the Epic team to add any additional structured data fields for providers to record if they discussed and recommended HPV vaccination with the patient. Throughout the study, Dr. Worley will assist with troubleshooting workflow issues and will advise the programmer on how to best implement changes within the EHR to fit provider needs and expectations. Effort for Dr. Worley is budgeted at EFFORT in Years 1-2, and EFFORT in Years 3-6. Fringe benefits are calculated at 23.5% of salary.

TBN, Senior Programmer/Analyst will be an Institute programmer with particular expertise in EpiCare and SAS programming and the creation of data tables within Clarity. The Institute has several programmers that have the necessary experience and knowledge to identify and extract all necessary electronic health data, including HPV vaccine data. The programmer/analyst will also lead the development of the analytic database and the data management plan working in close collaboration with Mr. Asche. The programmer will pull and clean the data that comprise the analytical data files, perform quality assurance checks, and assist Mr. Asche in the development of the data dictionary. Patient data will be protected as specified in the Protection of Human Research Subjects section of the project application and in compliance with HIPAA and other federal, state, and local patient privacy procedures. The senior programmer/analyst is budgeted at 1.20 CM in Years 1-2, 3.0 CM in Years 3, 2.40 CM in Year 4, 1.80 CM in Year 5, and 0.60 CM in Year 6.

TBN, Project Manager (Principal) will be responsible for managing the day-to-day and longer-term activities of the proposed study. The Institute has multiple experienced and highly qualified project managers assigned to projects based on necessary expertise and availability. Most have master's degrees in public health, public policy, nutrition, or social science and/or more than 10 years of experience managing federal grants and contracts situated within health systems. During the UG3 planning phase, the project manager will work with Drs. Rindal and Mabry to complete IRB applications and all necessary study documents including the study protocol, clinical quality management plan, and data quality management plan. They will also facilitate planning discussions with the care system stakeholders and will facilitate the piloting of the intervention. During the UH3 phase, the project manager will help coordinate study implementation across the 21 HealthPartners dental clinics. They will help schedule and present trainings to staff at intervention clinics, communicate study-specific information to clinic staff, and respond to any implementation issues throughout the study period. Throughout the study, the project manager will facilitate study team meetings and coordinate activities across the team including interview and survey activities by the Center for Evaluation and Survey Research and programming tasks to ensure smooth implementation and data collection. They will also be charged with managing internal and external communications for this study and will systematically report study progress information to NIDCR. The project manager will identify and report critical barriers to timely coordination of study tasks to Drs. Rindal and Mabry and will work collaboratively to create solutions to these barriers. Effort of a principal-level project manager is budgeted at 4.80 CM in each year.

TBN, Sr. Project Coordinator will assist the project manager in coordinating UH3 activities. In particular, the project coordinator will assist with scheduling and facilitating provider trainings, compiling progress reports, and coordinating study and stakeholder team meetings. The Sr. Project Coordinator is budgeted at 2.4 CM during the UH3 phase (Years 3-6).

Travel – Domestic

Conference Travel: Travel is budgeted at $2,000 per trip for Drs. Rindal and Mabry or other members of the research team to attend conferences to gain new knowledge related to the project or disseminate study results. Costs per trip are itemized in the table to the right. A total of 12 trips are budgeted during the UH3 phase (2 trips in Years 3 and 4, and 4 trips in Years 5 and 6) for a total cost of $24,000 in conference travel.

Travel Expenses	Unit Cost	Total Cost
Airfare	$650	$650
Hotel	$225 p/night, 2 nights	$450
Meals & incidentals	$100 p/day, 3 days	$300
Conference Fees	$500	$500
Ground Transportation	$100	$100
Total Cost Per Trip		**$2,000**

Mileage: Mileage costs are budgeted to cover travel to participating HealthPartners dental clinics, located in the greater Minneapolis/St. Paul metropolitan area, to conduct meetings and on-site trainings or gather feedback from clinic staff and leaders throughout the study. In Years 1 and 2, $100/year is budgeted for mileage to clinics for piloting and intervention development activities. In Years 3-5, $1000 is budgeted for mileage to clinics for training and intervention implementation and troubleshooting. Throughout the study a total of $3,200 is budgeted for mileage, which, based on the Internal Revenue Service's 2022 mileage reimbursement rate ($0.585/mile), will cover approximately 5,470 miles for local travel.

Other Costs

Software Engineering and Technology (SET) Team: Managed by Deepika Appana, Director of Technology, the HealthPartners Software Engineering Team (SET) provides internal support for informational technology (IT) needs for research and evaluation projects. With internal funding from the HealthPartners Center for Oral Health Integration, SET is currently leading the development of a comprehensive EHR-embedded CDS platform for use in dental clinics that will include HPV vaccine status information and provide alerts for patients who are overdue for a vaccine dose. This CDS platform will be implemented within HealthPartners Dental Group clinics by the time the study starts, allowing SET to leverage and expand on this platform by creating an enhanced CDS which will include tailored scripts for providers in intervention clinics. Specifically for the study, SET will:

- Incorporate tailored scripts into the enhanced CDS in Year 2
- Assist with rolling out enhanced CDS to intervention clinics in Years 3-4
- Assist with data management
- Provide new security using Fast Healthcare Interoperability Resources (FHIR) updates per the latest version of Epic and software protocols
- Monitor the CDS infrastructure and provide ongoing maintenance
- Provide reports on CDS data elements to the study team

SET is comprised of a team of full stack java engineers, data architects, user interface/user experience (UI/UX) developers, ETL (extract, transform, load) developers, infrastructure engineers and EHR analysts. The members of the team have specialized roles with respect to building and deploying software per industry and security standards. A cross section of this team is required to fulfill the requirements of this project. The primary roles that will be involved will be:

- **Senior Software Engineers** with training and experience in full stack Java development will be responsible for (a) designing the web application to process EHR-extracted data through clinical algorithms, (b) updating, developing and testing CDS algorithms in close collaboration with Drs. Rindal and Mabry, (c) coding these algorithms in JAVA, (d) assisting with the clinical deployment of the CDS tool, (e) implementing clinic specific trigger criteria per randomization, (f) implementing the latest open-standard authorization (OAuth) security using the FHIR standards. In addition, senior web application developers will be responsible for providing routine maintenance, sharing of project documents, uploading and downloading data files, data security, and managing users and permissions.
- **Infrastructure Engineers** will be responsible for establishing a fault tolerant architecture to allow the CDS to continue to function in the case of software or hardware malfunctions outside of the team's control. The infrastructure engineer will set up load balanced cluster of servers and work with the team to set up a secure infrastructure.

- **ETL Developers** are responsible for the movement of data between the operational databases and the reporting environment and for generation and distribution of use reports as per project requirements and for analysis.
- **Senior Epic Developers** with expertise in EpiCare programming will develop the design of the systems interfacing with the CDS tools. They will be responsible for creating the build documents and working closely with HealthPartners informatics to deploy the enhanced CDS. They will also ensure that the appropriate data is being used and captured by the CDS and will support testing the systems in all applicable environments.

A total of $257,989 is budgeted for the SET. Costs are divided across study years based on the study timeline and as shown by year in the table.

Year	1	2	3	4	5	6	Total
SET	$4,190	$21,576	$79,367	$81,750	$47,153	$23,953	**$257,989**

Food for trainings: To encourage attendance at trainings, we have budgeted for lunches to be provided for staff during training times. For up to 11 intervention clinics, $500 is budgeted per clinic for a total of $5500. Based on the study timeline, costs are split between years 3 ($4000) and 4 ($1500).

Center for Evaluation and Survey Research: The Institute's Center for Evaluation and Survey Research (CESR) serves as the Institute's onsite service center for recruitment, data collection, and evaluation. CESR will handle three main tasks related to this project:

1.) Assisting Dr. JaKa with provider interviews in Year 1. CESR staff will help with scheduling up to 10 provider interviews with dentists and hygienists which will inform the development of the intervention. They will also assist with recording, transcribing and coding the interviews.

2.) Administering the provider surveys, including creating the online REDCap survey and tracking all responses. During the rolling training and implementation period from end of Year 3 to beginning of Year 4, all providers from intervention clinics will be asked to complete surveys immediately before and after training, and all providers from usual care clinics will be asked to complete a baseline survey. During Year 4, all providers will receive a six-month post-implementation survey.

CESR Costs	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Postage			$54	$111	$86	$251
Materials	$2,250		$56	$115	$89	$2,510
Labor	$11,059	$2,575	$10,056	$16,344	$12,626	$52,660
Total	$13,309	$2,575	$10,166	$16,570	$12,801	**$55,421**

3.) Managing and conducting the patient/guardian surveys in Years 3-5 with a subset of approximately 400 eligible patients. Surveys will be administered by phone and CESR will also manage and track incentives.

CESR costs by year are detailed in the table above. In total, $55,421 is budgeted for CESR activities.

Patient Survey Reimbursement: Patients/guardians who complete a phone survey will receive a $15 gift card. Survey reimbursement is budgeted for 400 respondents for a total of $6,000 across Years 3-5. Based on the study time, survey reimbursement costs have been split between years as follows: $1,275 in Year 3, $2,730 in Year 4, and $1,995 in Year 5.

Continuing Medical Education Accreditation: The study team will work with HealthPartners Dental Group and HealthPartners Institute Office of Continuing Medical Education (CME) to allow for providers participating in the training sessions to receive CME credit. The HealthPartners CME program is accredited by the Accreditation Council for Continuing Medical Education to sponsor CME for clinicians. The CME team partners with quality improvement teams, medical and dental departments, administration and HealthPartners Institute divisions to translate and disseminate evidence-based clinical knowledge to clinicians locally, regionally and nationally. In Year 3, $4,500 is budgeted for CME expenses related to accreditation oversight, gap analysis and completion of CME planning guide, disclosure, development of materials and templates, communication and correspondence, analysis, evaluation and outcomes measurements, recording credit and distribution of certificates, and reporting requirements.

Publication Costs: A key part of the dissemination plan is the publication of study results in relevant academic journals. A total of $16,000 is budgeted to cover publication costs over the course of the study ($4,000 in Year 4, and $6,000 in Years 5 and 6).

Indirect Costs

The federally negotiated indirect rate for HealthPartners Institute is 57% of modified total direct costs.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		1,220,046.00
Section B, Other Personnel		694,204.00
Total Number Other Personnel	24	
Total Salary, Wages and Fringe Benefits (A+B)		1,914,250.00
Section C, Equipment		0.00
Section D, Travel		27,200.00
1. Domestic	27,200.00	
2. Foreign	0.00	
Section E, Participant/Trainee Support Costs		0.00
1. Tuition/Fees/Health Insurance	0.00	
2. Stipends	0.00	
3. Travel	0.00	
4. Subsistence	0.00	
5. Other	0.00	
6. Number of Participants/Trainees	0	
Section F, Other Direct Costs		345,410.00
1. Materials and Supplies	0.00	
2. Publication Costs	0.00	
3. Consultant Services	0.00	
4. ADP/Computer Services	0.00	
5. Subawards/Consortium/Contractual Costs	0.00	
6. Equipment or Facility Rental/User Fees	0.00	
7. Alterations and Renovations	0.00	
8. Other 1	345,410.00	
9. Other 2	0.00	
10. Other 3	0.00	
11. Other 4	0.00	
12. Other 5	0.00	
13. Other 6	0.00	
14. Other 7	0.00	
15. Other 8	0.00	
16. Other 9	0.00	
17. Other 10	0.00	
Section G, Direct Costs (A thru F)		2,286,860.00
Section H, Indirect Costs		1,303,510.00

Funding Opportunity Number: PAR-21-317 . Received Date: 2022-03-07T11:53:21.000-05:00

Section I, Total Direct and Indirect Costs (G + H)	3,590,370.00
Section J, Fee	0.00
Section K, Total Costs and Fee (I + J)	3,590,370.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 09/30/2024

1. Vertebrate Animals Section

Are vertebrate animals euthanized? ○ Yes ○ No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

○ Yes ○ No

If "No" to AVMA guidelines, describe method and provide scientific justification

2. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period	*Anticipated Amount ($)	*Source(s)

PHS 398 Cover Page Supplement

3. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ○ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, check the box indicating that one from the registry will be used:

❑ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

4. Human Fetal Tissue Section

*Does the proposed project involve human fetal tissue obtained from elective abortions? ○ Yes ● No

If "yes" then provide the HFT Compliance Assurance

If "yes" then provide the HFT Sample IRB Consent Form

5. Inventions and Patents Section (Renewal applications)

*Inventions and Patents: ○ Yes ○ No

If the answer is "Yes" then please answer the following:

*Previously Reported: ○ Yes ○ No

6. Change of Investigator/Change of Institution Section

☑ Change of Project Director/Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name: Bryan

Middle Name:

*Last Name: Michalowicz

Suffix:

❑ Change of Grantee Institution

*Name of former institution:

PHS 398 Research Plan

OMB Number: 0925-0001
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reviewers' comments

SPECIFIC AIMS

For the US population, oral or oropharyngeal cancer carry a lifetime risk of 1.2%, and each year, an estimated 53,000 adults are newly diagnosed with these cancers[5]. Up to 70% of oropharyngeal cancers are attributable to persistent human papillomavirus (HPV) infections.[1,2] Effective vaccinations exist to prevent persistent HPV infections and associated cancers;[3,4] yet, HPV vaccine uptake is far below national goals. [5,6]

Several authoritative bodies[7,8] have advanced the idea of HPV vaccine (HPV-V) promotion by dental providers to increase vaccine uptake, but it is a novel and underexplored approach,[2] and one that remains to be tested for efficacy. Currently, many providers lack the knowledge and self-efficacy to discuss HPV/HPV-V, and fear that doing so will damage the patient-provider relationship.[9-11] To realize dental providers full potential in preventing oropharyngeal cancers through HPV-V promotion, barriers must be addressed. Of paramount importance are those barriers that are both widely expressed and lie on the critical path of behavioral mechanisms that are ultimately responsible for whether the provider will promote HPV-V with their eligible patients. Three such barriers to HPV-V promotion - provider knowledge gaps, provider lack of self-efficacy, provider fear of damaging the patient-provider relationship[9,12,13] - will be the targets of our intervention. In developing interventions for HPV-V promotion, it will also be important to know if they are effective in convincing patients, parents, or guardians to follow through in becoming fully vaccinated

We propose to develop a theory-based behavioral intervention to support dental providers in promoting HPV-V and to test the intervention's efficacy and underlying behavioral mechanisms in a real-world dental setting. In the UG3 phase, guided by the NIH Stage Model of Behavioral Intervention Development,[14,15] we will develop and pilot-test provider training and tailored scripts to support dental providers in promoting HPV-V (NIH Stage 1). In the UH3 phase, we will conduct a clinic-randomized efficacy trial (NIH Stage 3) to test the intervention's real-world efficacy in increasing HPV-V promotion among dental providers at eligible visits in intervention vs. usual care (UC) clinics. We will also examine the three behavioral mechanisms hypothesized to underlie the two intervention components (provider training, tailored scripts). Therefore, the aims of this study are:

UG3 Phase:

Aim 1: Develop and pilot-test *provider training* designed to increase knowledge of HPV/HPV-V promotion, including preliminary assessment of the intervention's ability to act on the purported behavioral mechanisms and development of provider surveys to enable measurement of these behavioral mechanisms.

Aim 2: Develop and pilot-test *tailored scripts* designed to support providers in promoting the HPV-V.

Aim 3: Develop and finalize measures and methods to monitor fidelity to components of the intervention.

Aim 4: Draft compliance and study documents and obtain necessary approvals from the IRB and NIDCR.

UH3 Phase:

Aim 5: Test the real-world efficacy of a theory-based behavioral intervention designed to increase HPV-V promotion among dental providers.

H5: Compared to usual care clinics, intervention clinics will show a greater pre- to post-intervention increase in the percentage of eligible visits with HPV-V promotion by dental providers.

Aim 6: Assess whether the intervention impacts behavioral mechanism targets as intended. We hypothesize that, compared to UC clinics, providers at intervention clinics will show greater pre- to post-intervention…

H6a: … increases in their knowledge of HPV/HPV-V.

H6b: … increases in their self-efficacy for HPV-V promotion.

H6c: … decreases in their fear of negative consequences from promoting HPV-V.

Aim 7: Assess whether the intervention's effects follow the full behavioral mechanistic pathway to the target behavior (HPV-V promotion). We will utilize path analysis models with latent mediator variables to quantify the intervention's effects at each step along the various pathways from intervention exposure, through mediators in Aim 6, to HPV-V promotion activity.

IMPACT: This study addresses NIDCR's strategic priority to advance prevention of head and neck cancers,[16] and will be the first to develop an HPV vaccine promotion intervention directed at dental providers. The knowledge gained on behavioral mechanisms will pave the way for vaccine promotion in dental settings more broadly and will be applicable to the development of a wide range of provider-directed interventions.

A. SIGNIFICANCE

A.1. Human papillomavirus (HPV) epidemiology, sequelae and vaccine

HPV is the most prevalent sexually transmitted disease in the United States.[17-21] There are more than 200 subtypes of HPV, with 16 and 18 being the most prevalent oncogenic strains.[22] Chronic infection with oncogenic strains can cause a range of cancers, including cervical, vaginal, vulvar, penile, anal, rectal, and oropharyngeal. While up to 90% of individuals in the US have been exposed to HPV, an estimated 15% are infected with oncogenic strains.[23] In the United States, each year ~46,000 cases of cancer are attributed to HPV; cervical and oropharyngeal cancers are the most common.[24] About 90% of the 15,000 new cases of cervical cancer and 70% of the 19,000 annual cases of oropharyngeal cancer are attributed to HPV infection.[24] The number of HPV-positive oropharyngeal cancers has surpassed that of HPV-positive cervical cancers.[25-27] Many oropharyngeal cancer patients suffer disfigurement, fatigue, speech problems, difficulty swallowing, memory loss, hearing difficulty, and sinus damage. Management of HPV-related oropharyngeal cancer accounts for nearly 80% of all oropharyngeal cancer-related care costs.[28]

The 2016 US Cancer Moonshot Report included HPV vaccine (HPV-V) promotion as an important goal for cancer prevention. In the US, the 9-valent HPV-V in use protects against known oncogenic subtypes 16, 18, 31, 33, 45, 52, and 58, and subtypes 6 and 11 that cause genital warts.[21] For the vaccine to be most effective, it must be administered before exposure occurs. Unfortunately, HPV-V rates in the US are significantly lower than for other pediatric or adolescent vaccines.[5,29] Moreover, while vaccinations of all types were significantly disrupted across the country due to the pandemic, recent reports indicate that HPV-V administration lagged behind other adolescent vaccines during 2020-2021.[30,31] While direct evidence of oropharyngeal cancer prevention is lacking[32], the vaccine is effective against oral infection with HPV oncogenic strains.[33] In the US, oral HPV infections targeted by HPV-V are 88% lower among vaccinated (0.11%) than unvaccinated young adults (1.61%).[34] Oropharyngeal cancer burden is projected to rise. Efforts to achieve the HPV vaccination goal of 80% coverage should be a public health priority.[35]

A.2. Role of dental providers in HPV-V promotion

Dental providers are uniquely positioned to promote HPV vaccination because they manage a segment of the population that may not regularly visit a physician, they often enjoy long-term and trusting relationships with their patients, and parents and their children often receive care in the same office. With their focus on oral health and regular examinations that include a visual inspection for oropharyngeal cancers, promoting strategies to prevent these cancers is a natural extension of current dental practice. In 2016, about 85% of children visited a dentist.[36] In contrast, adolescents typically have fewer than 2 primary medical care visits per year, and a third of adolescents do not have a primary care visit between the ages of 13 and 17,[37] an important target age range for HPV vaccination. One of the objectives in NIDCR's Strategic Plan is to "*advance prevention, early detection, and treatments for benign and malignant head and neck cancers*".[16] One way to prevent these cancers is through HPV vaccination, and the CDC, the American Dental Association (ADA) and the American Academy of Pediatric Dentistry (AAPD) all recommend that dental providers promote HPV vaccination.[7,8] Despite these recommendations, many providers still perceive vaccine promotion as within the purview of medicine rather than dentistry.[12,38,39]

A.3. Provider barriers to HPV-V promotion in the dental setting

Several groups have studied HPV-related knowledge and opinions among dental providers.[9-11,40-44] Barriers to HPV-V promotion include a lack of knowledge and self-efficacy for discussing HPV and HPV-V with patients.[12,38,45] Dentists are generally reluctant to administer the vaccine in dental offices.[13,46,47] Providers, however, are interested in increasing their HPV-V knowledge and in distributing educational materials.[12,13,38,48] Despite having a legitimate role in HPV-V promotion, there is limited evidence for interventions to increase HPV-V promotion by dental providers. We found only one published *trial* testing the efficacy of dental provider training on knowledge and intention to promote HPV-V.[49] Providers were trained to verbally recommend all necessary vaccines (not only HPV) to patients 11-17 years of age, and to provide parents with follow-up appointment instructions. Providers were given basic scripts to address parent concerns about age indications and vaccine safety. Despite these efforts, only 25% of parents recalled having received a verbal vaccine recommendation from the provider. This is important because a provider's recommendation, and especially the perceived strength of that recommendation, correlates with vaccine uptake.[50] We found no published trials that evaluated dental provider training or Clinical Decision Support (CDS) tools on provider promotion of vaccine uptake.

Historically, many dental providers believe that vaccine promotion is outside their professional purview.[13,51] Relatively few dental providers receive formal training in vaccine promotion and report feeling ill-equipped to

discuss HPV and HPV-V with patients.[12,13,39,45] They also report having *inadequate information* or material resources about HPV-V, *fear* of negative consequences related to offending patients, inadequate chair time for discussions, and *discomfort* discussing sex-related topics with patients.[45] Dental providers also recognize their treatment rooms are less private than medical clinics, which can hinder patient discussions about HPV.[41,45] Relatively few express concerns about HPV-V safety and effectiveness.[12,13,39] Overall, dentists appear more comfortable than hygienists discussing and recommending HPV-V.[46] Among hygienists, those who are less knowledgeable about HPV are less likely to discuss HPV with their patients than those who are more knowledgeable.[9]

A.4. Intervention strategies for addressing provider barriers to HPV-V promotion

Structured and multi-dimensional training programs can help healthcare providers deliver effective HPV-V recommendations. Leung et al. identified interventions from the literature that improved HPV vaccination rates.[52] They screened over 1000 papers but found only 5 randomized trials that evaluated HPV-V uptake as an outcome;[53-57] none involved dentistry. Low provider knowledge was again associated with low vaccine recommendation rates. Although all training programs included didactic instruction, and most included communication training, a variety of complementary interventions were identified, including the use of practice-specific fact sheets, a parental education website, images depicting diseases associated with HPV, decision aids for HPV vaccination, repeated contact with providers, the provision of continuing medical education (CME) credits, and electronic health record (EHR) prompts. Consistent with the literature, the intervention in the current application will include: 1) ***provider training*** in the form of didactic instruction to increase knowledge and self-efficacy related to HPV-V and oropharyngeal risk, 2) ***tailored scripts*** to support providers in conversations with patients/parents/guardians to increase provider self-efficacy and reduce fear of negative consequences promoting HPV-V will have on the patient-provider relationship. The intervention will be delivered on the Epic EHR-based CDS platform used by providers in both intervention and UC conditions. The CDS includes HPV-V status for all patients, a prompt to recommend HPV-V to patients at eligible visits, and a quick scheduling feature to facilitate patient referral to the vaccine scheduler.

Few groups have evaluated the efficacy of HPV-V promotion training programs for dental providers. Pampena et al[58] found that lecture presentations increased provider knowledge regarding HPV and HPV-V, but changes in clinical practice behaviors and vaccine uptake were not measured. Waiwaiole et al[49] randomly assigned providers in 8 of 16 dental clinics to receive 45 minutes of training in verbally recommending vaccines, including HPV-V, using basic scripts to address parent concerns. They found that relatively few parents recalled having received a verbal vaccine recommendation, suggesting the providers did not communicate HPV-V messages adequately. Others have articulated the need to further develop and test “talking points and communication training” to aid dentists and hygienists in their HPV-V promotion efforts.[46]

A.5. NIH Stage Model of Behavioral Intervention Development

This proposal is in response to PAR-21-317,[59] in which applicants are advised to use the NIH Stage Model of Behavioral Intervention Development (aka NIH Stage Model)[14] as a framework for the proposed work. “*The Stage Model is designed to guide behavioral intervention development and is composed of six stages: basic science (Stage 0), intervention generation, refinement, modification, and adaptation and pilot testing (Stage I); traditional efficacy testing (Stage II); efficacy testing with real-world providers (Stage III); effectiveness research (Stage IV) and; dissemination and implementation research (Stage V). Examination of mechanisms of behavior change is encouraged in every stage of intervention development.*”[14] We begin the UG3 phase by ensuring we have selected viable intervention targets (Stage 1). To guard against the tendency for interventions developed in research settings to weaken when implemented in community settings,[15] we will conduct our study in a real-world setting – HealthPartners Dental Group (HPDG) clinics - where we can test treatment fidelity and efficacy with community practitioners (Stage III) before conducting an effectiveness trial (Stage IV) which we defer to a future study. Per the NIH Stage Model recommendations, in the proposed study, we will examine behavioral mechanisms during intervention delivery,[14] (i.e., during UH3 phase Aim 6, 7 and exploratory analyses).

B. Preliminary Data

B.1. Current vaccination rates among HealthPartners dental patients

Based on data from the HealthPartners Dental Group HPDG EHR, an estimated 15,646 patients, age 11-26, visited a general or pediatric dentist in 2021. Slightly over half (54%) of these patients are female, 46% are White, 20% are Black, 10% are Asian, 9% list more than one race, 14% are of unknown or “other” race, 12% are Hispanic, and 47% had Medicaid coverage at the time of the dental exam. Forty-eight percent (n = 7517) had completed the vaccination series. About 25% (n = 3870) had not initiated HPV vaccination and 27% (n =

4259) had initiated but not completed the vaccination series. Therefore, a large pool of HPDG patients are eligible to receive HPV-V promotion from their dental provider (i.e., denominator for Aim 5). Table 1 summarizes HPV-V status of dental clinic patients by sex and age group. As expected, HPV-V receipt rates are relatively low in the youngest age group. Only 17% of females and 18% of males completed the series by age 12. In young adults, 18-26 years, disparities are evident given the proportion who have completed the vaccine series among Whites (68%) and Blacks (57%).

Table 1. HPV-V status for patients with preventive dental visits in 2021 (n=15,646)

	N with dental visits	HPV-V not initiated	In progress	Series complete
Female 11-12	1436	46%	36%	17%
Female 13-17	3153	17%	30%	53%
Female 18-26	3972	17%	19%	64%
Male 11-12	1420	49%	33%	18%
Male 13-17	3050	19%	30%	51%
Male 18-26	2615	29%	25%	47%

B.2. Initial survey of dental providers

In July 2019, we surveyed general, pediatric and orthodontic dentists, dental therapists (mid-level care providers) and hygienists in HPDG to assess their current HPV-V promotion practices and willingness to provide brief educational interventions to increase a patients' HPV-related knowledge and to promote HPV-V. Forty-three dentists, 4 dental therapists and 57 hygienists completed the survey, with response rates of 77%, 100% and 64%, respectively. Few (6%) of our providers routinely discussed the importance of HPV vaccination for adolescents and young adults, similar to providers statewide [12]. Common reasons cited by providers for not promoting HPV-V included a lack of time (42% of dentists), forgetting to discuss HPV vaccination with patients (35%) and a perceived lack of qualifications to engage in this activity (37%). Many (71% of hygienists and 100% of dental therapists) felt unqualified to promote HPV-V. All respondents thought HPV-V was effective at preventing oropharyngeal cancer, and less than 5% had concerns with the vaccine's safety. Overall, the majority of our respondents (86% overall and 98% of dentists) were willing to provide patients with written materials and nearly 70% (83% of dentists) were willing to provide an educational intervention to patients if trained to do so. Few (<20%) thought dentists should *administer* the vaccine, mirroring provider attitudes in other states.[13] Thus, our providers are representative of the broader dental community and intervention effects should be detectable given their current perceptions and practices.

C. Innovation

The proposed work is innovative in several aspects: First, we will be the first to test an evidence-based provider-directed intervention to support HPV-V promotion *designed around the specific needs and barriers experienced by dental professionals in their practice settings*. This focus on providers in practice settings will help ensure the intervention is ready for uptake and widespread dissemination and implementation after the trial. Second, we will develop *tailored scripts* to guide providers in responding to the most common patient reactions to vaccine promotion which will both help streamline the discussion for dental professionals in a busy practice and give them the confidence and specific language for discussing HPV and HPV-V with all patients and guardians, even those with vaccine hesitancy. Third, in addition to measuring changes in the proximal outcome targeted by our intervention (i.e., provider HPV-V promotion), as an exploratory exercise, *we will examine changes in patient health behavior (receipt of initial and follow-up doses within 30-days of eligible visit)*. To our knowledge, this is the first-time patient vaccination behavior has been measured before and after an intervention aimed at dental providers. Fourth, our intervention will be highly generalizable across EHR systems and other platforms. We will leverage an existing CDS system within the dental module of the HPDG EHR that provides a user-friendly platform for integrating the intervention resources into clinical workflows. The automation afforded by the CDS is expected to enhance our intervention, but it is not a requirement - provider training and tailored scripts will be suitable for use with or without CDS, will be easy to integrate into other EHR systems, and suited to delivery on other electronic devices (e.g., tablets, computers).

D. APPROACH

D.1. Overview

The primary objectives of this project are to: 1) develop, refine and test the efficacy of a provider-directed, theory-based intervention for HPV-V promotion in real-world dental settings, and 2) examine three behavioral mechanisms thought to be primarily responsible for providers' promotion of HPV-V. During the project's two-year UG3/Stage 1 phase, we will use findings from our preliminary provider survey, the literature, and provider interviews to further understand provider barriers to vaccine promotion, and pilot-test intervention components (provider training, tailored scripts), which are informed by the Theory of Planned Behavior and Theoretical Domains Framework (Section D.2). During the UH3/Stage 3 phase, we will test the efficacy of the provider-

directed intervention using a clinic-randomized trial design in which clinics are assigned to receive either the intervention or usual care (UC). During the UH3 phase we will also conduct a mediation analysis to examine three behavioral mechanisms thought to underlie the intervention's efficacy: increased knowledge of HPV/HPV-V; increased self-efficacy for HPV-V promotion; and reduced fear of HPV-V promotion negatively affecting the patient-provider relationship. Two candidate behavioral mechanisms will be the subject of exploratory mediation analyses: adequacy of material resources for HPV-V promotion; and providers' perception that HPV-V promotion is within their scope of practice.

Our intervention will be directed at dentists and dental hygienists, hereafter referred to jointly as "dental providers." For each provider, we will designate their home clinic defined as where they see most of their HPV-V-eligible patients (i.e., those aged 11-26).

Usual care (UC) clinic providers receive:
1. HPV patient education brochures about HPV, its sequelae and HPV-V
2. CDS containing HPV-V status and alert, standard scripts (no tailoring), and vaccine order functionality

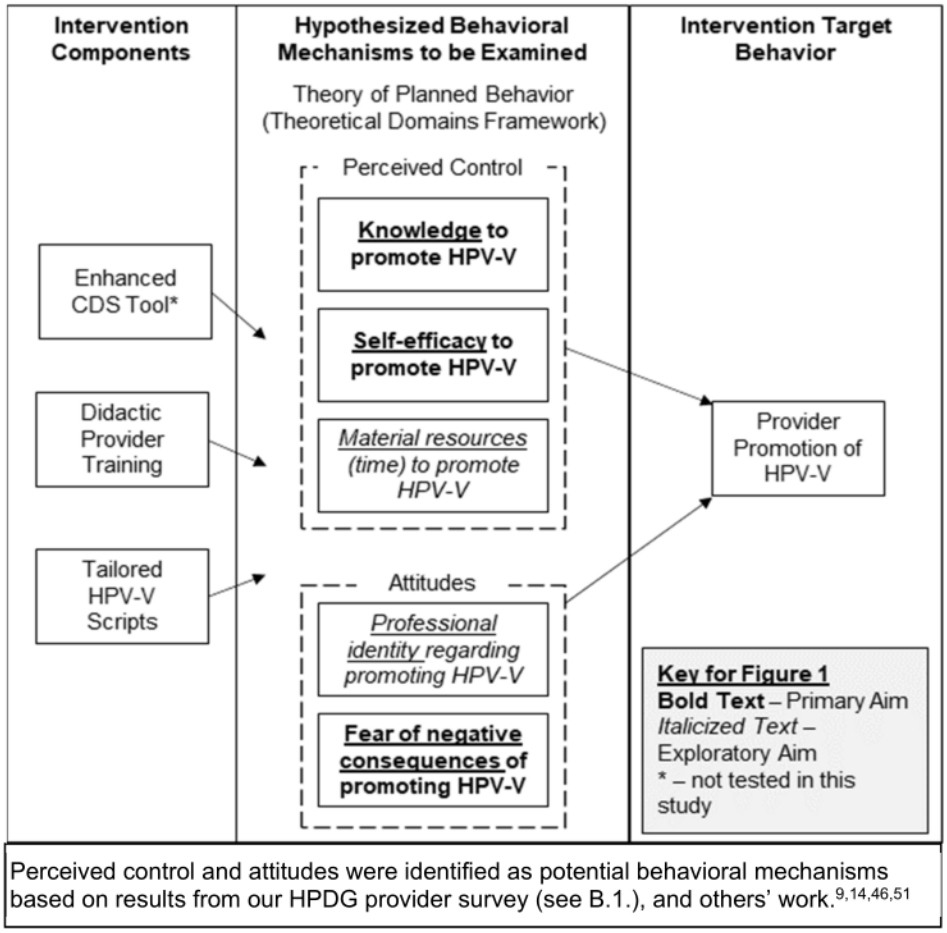
Intervention clinic providers receive:
All components of UC ***plus***:
1. Provider training (didactic instruction) to increase knowledge about HPV and HPV-V
2. Tailored scripts delivered via CDS, designed to give providers specific language for addressing issues likely to be raised by patients/parents/guardians in discussions of HPV-V.

In accordance with national guidance,[8,60] HPDG leaders believe that all dental providers should receive some support for HPV-V promotion, and therefore it was necessary to provide some basic, standardized training and support to UC clinic providers. Prior to the study, we will complete modifications to our existing EHR-based CDS to include patient HPV-V status, alerts indicating HPV-V dose past due, standard scripts with basic language provider can use to promote the HPV-V, and automated referral to vaccine scheduling for patients who agree to be referred. Patient education brochures about HPV and oropharyngeal cancer prevention will be distributed to all clinics prior to study start.

D.2. Conceptual Model of Provider Behavior

The Theory of Planned Behavior has commonly been used to understand barriers to delivery of various recommendations by healthcare professionals.[61] To ground our intervention in theory, we first mapped the provider-identified barriers to HPV-V promotion to the Theoretical Domains Framework,[62] which provides standard language and constructs for behavior change research, and then mapped these constructs to Theory of Planned Behavior categories (p*erceived control* and attitudes). Figure 1 reflects this mapping and shows how our intervention will be designed to intervene on provider behavior via these frameworks. Dental providers' *perceived control* over promoting HPV-V relates to knowledge of HPV and HPV-V dosing guidelines as well as self-efficacy for promoting HPV-V. These behavioral mechanisms are thought to be primarily responsible for the intervention's efficacy, along with fear of negative consequences such as alienating patients and parents and will be examined in Aim 6. *Perceived control* also includes adequacy of available material resources such as time for discussing HPV-V, which will be explored in an exploratory analysis. The primary mechanism among provider *attitudes* thought to impede HPV-V promotion is a fear of negative consequences,[12,13,39,45] which we will examine in Aim 6. Lastly the role of the identified barrier that HPV-V promotion is outside the scope of dental practice (i.e., labeled in Figure 1 as professional identity regarding HPV-V promotion) will be the subject of exploratory analysis. Our intervention will be carefully designed to address these known barriers through provider training and tailored scripting to support HPV-V promotion.

Figure 1. Conceptual model depicting impact of the intervention on psychosocial determinants of provider's intention to promote the HPV vaccine



D.3. UG3 Study Activities

In the UG3 phase, we will identify *provider* knowledge gaps and gain a deeper, more nuanced understanding of the personal and workplace barriers to HPV-V promotion and develop an intervention that closely addresses these barriers. Colquhoun et al[63] identified four components of interventions designed to change healthcare provider behaviors: identify barriers, select intervention components, use theory, and engage end-users. We will incorporate all these features into our intervention development process.

D.3.1. Random Assignment of Clinics to Study Conditions. To avoid contaminating providers working in UC clinics during the real-world efficacy trial (UH3 phase) we must take care not to expose these providers to the intervention during the UG3 phase. We do this by randomly assigning each of 21 clinics to condition (intervention vs. UC) at the beginning of UG3 phase so that we can restrict participation in UG3 intervention development activities (provider interviews and pilot testing) to providers whose home clinic is assigned to the intervention condition. At the outset of UG3, 131 participating providers will be assigned a "home clinic", defined as the clinic in which most of their patients ages 11-26 are seen.

Covariate-based constrained randomization[64] will be used to enhance study arm balance on key factors during randomization. This method permits the use of multiple balance factors and can yield improved study arm balance and increased statistical power beyond simple randomization when balance factors are included in both the design and analysis phase[65]. Clinic-level attributes of patient characteristics are derived from EHR data and will be used as balance factors to be ascertained for care occurring in study clinics during the 12 months prior to randomization (we have data pre-dating the study). A total of 2-3 clinic-level balance factors will be used in the randomization and may include baseline levels of HPV-V receipt, co-location of a medical clinic for HPV-V delivery, visit volume for patients aged 11-26, and proportion of patients with government-aid dental care. Randomization will be carried out with the CCR macro for use within SAS 9.4.

D.3.2 Development of Intervention Components (Aims 1 & 2)

Provider interviews to refine intervention components. As described above, providers participating in

interviews (n=10) will be restricted to those whose home clinic is an intervention clinic. Semi-structured interviews with dentists (n=5) and dental hygienists (n=5) will be used to obtain information about provider-perceived barriers to HPV-V promotion, including HPV/HPV-V knowledge gaps, self-efficacy, fears, and workflow issues. No more than two providers from any clinic will participate in UG3 activities. Semi-structured qualitative interviews will be designed following best practices by Dr. JaKa in the Center for Evaluation and Survey Research (CESR). CESR interviewers are experienced in interviewing healthcare providers. As a part of this phase, all interviewers will also be trained in study-specific content areas. An interview guide, developed by the Dr. JaKa and the study team, will include a set of root questions tied to anticipated provider barriers in alignment with the Theory of Planned Behavior Model. Questions will be accompanied by a list of generic and specific probes to ensure rich, qualitative responses. A combination deductive and inductive thematic content analysis will be conducted to identify key themes as they pertain to each of the proposed mechanisms. Interviews will be audio recorded, transcribed, and coded by a team of CESR coders. Major and minor themes will be identified and used to refine intervention components.

Provider training: content development – After identifying provider barriers through provider interviews (including knowledge gaps), we will utilize resources available through the HPV Roundtable[60] composed of multiple members including the American Dental Association and the American Cancer Society to create a training program. These groups have developed didactic training materials for providers and support staff,[8] including slide presentations and videos. The training will address identified HPV/HPV-V knowledge gaps, relay the importance of HPV-V in cancer prevention, and coach providers in how to effectively address questions about vaccine safety and effectiveness. These activities will be led by Dr. Elyse Kharbanda, pediatrician, vaccine researcher and Co-I. Provider training may be modified based on pilot-testing.

Tailored script development – All providers in both conditions will have access to two standard scripts (1. HPV and oropharyngeal risk; and 2. HPV-V and prevention) for HPV-V promotion via CDS as part of usual care. Based on our initial provider survey, provider interviews conducted during the UG3 phase, and materials available through professional organizations,[60] we will develop and pilot-test *tailored* scripts for providers in intervention clinics. Each scripted message will be tailored to address a specific concern raised by the patient/parent/guardian including hesitancy and distrust of the HPV-V. We will review the literature on patient views on HPV-V and vaccines more broadly, including reports of their interactions with providers to further inform the development of the tailored scripts. We will mine the literature for tested provider scripts to use and/or adapt for use in responding to these barriers, and create new ones as needed. According to Levinson et al.,[66] "*Patient-centered communication seeks to increase health care providers' understanding of patients' individual needs, perspectives, and values; to give patients the information they need to participate in their care; and to build trust and understanding between physicians and patients. This communication occurs through both verbal and nonverbal behavior."* Thus, in the development of scripts we will adhere to principles of patient-centered care[66] and take care to script our messages using Plain Language.[67]

Pilot testing for acceptability and feasibility of the study interventions and procedures- As specified in PAR-21-317, we will conduct a pilot-test to see whether the intervention appears to impact the intended behavioral mechanism targets and work through any logistical issues. A small number of providers (a subset of five who completed the interview) will pilot-test the intervention. As with any pilot test, the objective is not to measure intervention effects with statistical rigor. Rather, the goal is to examine whether the intervention is targeting appropriate mechanisms and is feasible for the providers and setting in which it will be implemented. During pilot testing, the intervention will be delivered to providers by study investigators and providers will be surveyed before and immediately after the intervention. We will note if and how the intervention affected the intended behavioral mechanism targets (i.e., knowledge, self-efficacy and fear of negative consequences) and strengthen training and tailored scripts if indicated.

We have implemented similar provider CDS-based interventions in clinics and had high uptake/provider satisfaction ratings;[68] the current work will leverage a similar approach. To gauge patient acceptability regarding the tailored scripted messages, we will use HealthPartners' patient feedback portal, myVoice (see details in Resources section). We will use myVoice to query patients and parents of minors and seek feedback regarding the content and wording of the proposed tailored scripts and modify them accordingly. As the final step, the pilot-tested tailored scripts and related information about HPV-V will be incorporated into the CDS platform. During the UG3 phase, the study team will work with an Epic programmer from the Institute's Software Engineering and Technology team to complete this final step in developing the intervention. We have experience successfully utilizing tailored scripting in the delivery of tobacco cessation interventions (U01DE026135, 5U01DE027441)[69] and incorporating them into the CDS.

Survey development. To measure the intervention effects on the behavioral mechanistic pathways hypothesized in our conceptual model, we will need provider surveys of perceived control and attitudes, which we will develop in UG3. Relatively few HPV-related knowledge assessment tools have been used in dentistry.[9,12,46] Most studies also simply report responses for individual questionnaire items. In contrast, Daley et al[9] used a 31-item questionnaire (true/false format) to gauge a provider's HPV-related knowledge. We will include items to assess knowledge regarding HPV epidemiology, biology and pathogenicity, its role in oropharyngeal cancer, HPV-V safety and effectiveness, and HPV-V age-specific dosing recommendations. We will develop our survey instruments in accordance with best practices[72] and adapt existing instruments used to evaluate determinants of behavior change (perceived control, attitudes).[70,71] Where possible, we will use items and instruments with known psychometric properties, modified only as needed. For new items, survey design practices that reduce measurement error will be used; instruments will be reviewed by clinical experts for face validity.[72] Survey items will be pilot tested and revised as needed. Survey development will be led by Dr. JaKa with support from the Institute's Center for Evaluation and Survey Research (CESR), both of which have experience conducting survey development for oral health research.

D.3.3 Fidelity monitoring procedures (Aim 3). Fidelity monitoring procedures will be developed and finalized during the UG3 phase following the Treatment Fidelity Framework developed by the NIH Behavior Change Consortium[73] and related guidelines.[74] For provider fidelity to training, we will track the number of training sessions held, the content delivered at each session, and provider attendance. For provider HPV-V promotion activity we will utilize fields in the CDS created for this purpose. We will track eligible visits conducted by providers who work in clinics other than their "home" clinic and remind providers to deliver their assigned intervention only when working in their "home" clinic. For providers (typically the dentist) whose home clinic is UC, and also work in an intervention clinic, a different trained provider (likely the dental hygienist) will deliver the HPV-V promotion for all eligible study visits at the intervention clinic. We will also measure design, delivery, receipt and enactment of content and dose of intervention component (provider training, tailored scripts) as well as possible contamination in the UC arm.

D.3.4. Development of NIDCR-required study documentation to ensure adherence to the principles of Good Clinical Practice (Aim 4). As specified in PAR-21-317, we will finalize a clinical protocol, clinical quality management plan, and data quality management plan during the UG3 phase. We will develop a Manual of Operations to document how study procedures can vary across clinics. These documents will be prepared primarily by Dr. Rindal (PI), and the project manager, although Dr. Mabry (Co-PI) and other study team members will assist in developing various components for these materials according to their respective expertise. Finally, we will seek and obtain IRB approval for all study activities as needed.

E. UH3 Study Activities (Aims 5, 6, & 7)

E.1. Study Design and Intervention Delivery

***Study design overview*.** We will utilize a 2-arm, parallel, cluster (clinic)-randomized controlled trial design with baseline measures of dental provider HPV-V promotion activities and will balance and randomly allocate 21 clinics in a 1:1 ratio to either intervention or usual care (UC). The real-world efficacy of the full intervention will be assessed by comparing intervention clinics to UC clinics on the primary outcome: pre-to post-intervention change in percentage of eligible visits with HPV-V promotion (Aim 5). The effect of the intervention on purported mechanisms of behavior change (aka mediators, i.e., provider HPV/HPV-V knowledge, provider self-efficacy for HPV-V promotion, and provider fear of negative consequences from HPV-V promotion) will be examined in Aims 6 and 7.

Provider Intervention Delivery. With support of HPDG Director David Gesko, DDS (see attached letter), we will work with clinic managers and leaders on a plan to deliver the interventions. Providers will receive continuing education credits for their participation. The intervention (training and tailored scripts) will be delivered in a manner that allows for scheduling flexibility so we can reach all intervention arm providers. Based on experience, we anticipate developing a training video that will standardize the training and can be delivered either in person or virtually utilizing study staff to answer questions and provide any additional training as needed.

Provider Eligibility. General and pediatric dentists (n=47), dental hygienists (n=79) and dental therapists (n=5) who work full- or part-time within HPDG intervention clinics will be trained to deliver the intervention. Other dental specialists will not participate because they either do not routinely see adolescents or young adults in their practice or do not examine patients during preventive care visits. Because many US states do not have dental therapists, we will analyze data two ways: including and excluding patient encounters with

therapists and will compare the results to determine if inclusion of dental therapists is having an outsized effect on our results.

Eligible Study Visits. An eligible visit is defined as the first dental visit during the study period at which preventive care is delivered for any patient aged 11 to 26 years of age who has neither initiated nor completed the HPV-V dosing series.

E.2. Study Outcomes

E.2.1. HPV-V promotion activity (Aims 5 &7). The primary outcome for the intervention is the percentage of eligible visits at which HPV-V was promoted over a 12-month period. The occurrence of HPV-V promotion at eligible visits will be operationalized using a binary composite measure: If the provider pushes a toggle switch in the CDS indicating that they promoted HPV-V at the visit and/or the provider invokes the CDS quick-scheduling capability to refer the patient to a vaccine scheduler, the visit will count as one at which HPV-V promotion did occur. Otherwise, HPV-V will be presumed to have not occurred at that visit. The main comparison for Aim 5 is the differential pre- to post-intervention change by study arm in the percentage of eligible visits at which HPV-V promotion occurred. HPV-V promotion is assessed in the 12 months pre-intervention and 12 months post-intervention, following a 6-month run-in period. In subsequent sections, we refer to this comparison between the two timepoints as "*pre- to post-intervention*".

E.2.2. Intervention Impact on Behavioral Mechanisms (Aim 6). Provider surveys developed in Aim 1 will be used to assess between-groups differences in pre- to post-intervention change in targeted behavioral mechanisms, i.e., provider HPV/HPV-V-related knowledge (H6a), self-efficacy for HPV-V promotion (H6b) and fear of negative consequences from promoting HPV-V (H6c). Behavioral mechanisms will be measured immediately prior to intervention delivery and at 6 months post-intervention, to allow for an intervention run-in period.

E.2.3. Parent/Patient/Guardian perceptions of HPV-V promotion delivery. To determine if provider HPV-V promotion is being effectively communicated to the intended recipients, we will measure patient/parent/guardian reports of HPV-V promotion activity at a random sample of eligible visits (n=~800 of 8,000 total eligible visits). Sampled patients/parents/guardians will be contacted by phone 1 to 3 days following the eligible visit and asked if their provider promoted HPV-V. Surveys will be developed and conducted by CESR. Consistent with CESR's past experience, we anticipate a 50% response rate (400 completed surveys).

E.2.4. Covariates

Provider characteristics. Provider characteristics are gathered to describe the study sample and for use as covariates. Provider characteristics come from the health plan administrative data and include provider type (general dentist, pediatric dentist, hygienist, and dental therapist), gender and years in practice.

Patient characteristics. Patient characteristics will be used to describe the study sample, describe clinic case-mix for randomization, to utilize as covariates in analyses, and to define subgroups for analysis of treatment effect heterogeneity. Patient characteristics come from the EHR and health plan administrative data and include patient age, sex, race, and insurance status.

E.3. Plan of Analysis and Analytic Methods

Analytic approach, Aim 5: H5 posits a larger increase in percentage of eligible visits at which HPV-V promotion occurred from pre-intervention to 6-months post-intervention implementation (i.e., "pre- to post-intervention" as described in E.2.1) in intervention vs. UC clinics. Because clinics are randomized and the endpoint varies at the patient level, we will use generalized linear mixed-model regression with a logit link and binomial error distribution to test the effect of the interventions using the model specified below.

$$\text{HPV\_Vaccination\_Promotion}_{ji} = \gamma_{00} + \gamma_{10}\text{StudyArm}_j + \gamma_{01}\text{Time}_i + \gamma_{11}\text{StudyArm}_j{*}\text{Time}_i + \gamma_{02}\text{PtCovariates}_i + \gamma_{20}\,\text{StratFactors}_j + [u_{j0} + e_{ji}] \qquad j=\text{clinic, i=patient}$$

HPV-V promotion rates (H5) will be predicted by a fixed effect study arm term (StudyArm_j), an indicator for an eligible visit in the pre- to post-intervention period (Time), their interaction ($\text{StudyArm}_j{*}\text{Time}_i$), covariates ($\text{PtCovariates}_i$) to potentially include patient age group (11-17, 18-26), sex, and prior vaccination status (not initiated, initiated), and stratification factors used in the clinic randomization (StratFactors_j). A random intercept for clinics (u_{j0}) will account for the clinic-level randomization. A statistically significant interaction (alpha=.05) between study arm and time, and a pattern of pre- to post-intervention differences by study arm in the expected direction will support the H5 predictions for Aim 5.

Analytic approach, Aim 6: *H6a, H6b, H6c* posit that dental providers in the intervention arm compared to usual care arm will have larger increases when comparing their pre- to post-intervention implementation scores on HPV/HPV-V-related knowledge (H6a), self-efficacy for HPV-V promotion (H6b), and larger decrease in fear of negative consequences from promoting the HPV-V (H6c).

The three mediators will be measured repeatedly via a provider survey. Measurement timing is as follows: a) for providers in the intervention condition (n=10-11 clinics), the provider survey will be administered at *three timepoints*: immediately pre-training (T1), immediately post-training (T2, to capture knowledge gained from training), and at 6 months post-training (T3, to capture both long term knowledge retention, and the full effect of the intervention following a practice period). Note that T1 and T2 occur at the beginning and end of a single training session, so they are measured within 60 mins of one another; b) for providers in the UC condition (n=10-11 clinics), the provider survey will be administered at *two timepoints, yoked to the assessment periods in (a)*, i.e., at time periods consistent with T1 and T3. Assessment at T2 is not applicable to UC, because no intervention occurs during the intervening 60 minutes.

In Aim 6, we will test whether there is differential change from T1 to T3 by study arm in three pre-specified mediators. Because clinics are randomized and the outcome varies by provider over time, general linear mixed-model regression with an identity link and normal error distribution will be used to test the effect of the intervention in the general model specified below. While the endpoints are expected to be approximately normally distributed, the suitability of alternate error distributions and link functions in generalized linear mixed models will be assessed if distributions depart from expectations. The Aim 6 general model specification is:

$$ProviderEndpoint_{jit} = \gamma_{000} + \gamma_{100}StudyArm_j + \gamma_{001}Time_t + \gamma_{101}StudyArm_j*Time_t + [v_{j00} + u_{ji0} + e_{jit}]$$
$$j=clinic,\ i=provider,\ t=time\ (pre/post)$$

The endpoint variables (ProviderEndpoint) for Aim 6 are mean HPV/HPV-V-related knowledge score (H6a), mean self-efficacy for promoting HPV-V score (H6b), and mean fear of negative consequences score (H6c), gathered from provider surveys before training and six months following intervention implementation. The endpoints are predicted in separate equations by a fixed effect study arm term ($StudyArm_j$) contrasting intervention and usual care clinics, pre- or post-intervention survey (Time), and their interaction ($StudyArm_j*Time_t$). A random intercept for clinics (v_{j00}) accounts for the clinic-level randomization. A statistically significant study arm by time interaction (alpha=.05) and pre- to post-intervention contrasts by study arm in the expected direction will support the H6a, H6b, and H6c predictions stated for Aim 6. A sensitivity analysis will predict post-intervention endpoints from the pre-intervention measurement of the endpoint, study arm, stratification factors used in the clinic randomization, and provider type.

Analytic approach, Aim 7: *H7* posits that**:** that dental providers in the intervention arm compared to UC arm will have larger increases when comparing their pre- to post-intervention implementation scores on HPV/HPV-V-related knowledge (H6a), self-efficacy for HPV/HPV-V promotion (H6b), and larger decrease in fear of negative consequences from promoting the HPV-V (H6c), plus accompanying increases in HPV-V promotion for each of these mechanistic pathways**.** Building on Aim 6, in Aim 7 we will estimate the effects of change in potential *mediators* on change in provider HPV-V promotion to assess whether the intervention effects follow any of the hypothesized mechanistic pathways. Next, we will quantify and test estimates of total and individual indirect effects to understand the extent to which the relationship between the intervention and change in HPV-V promotion efforts are mediated by changes in provider HPV/HPV-V knowledge, self-efficacy for HPV-V promotion, and fear of negative consequences for HPV-V promotion. Latent Change Score (LCS) Structural Equation Modeling (SEM)[75-77] will address potential mediators of the relationship between study arm assignment to the intervention and change in provider HPV-V promotion by change in three mediators: provider knowledge of HPV/HPV-V-related knowledge, self-efficacy for promoting HPV-V, and fear of negative consequences from HPV-V promotion. The LCS SEM framework enables flexible specification (e.g., ANCOVA, difference score, residualized change) of two-wave models with various levels of constraints in model parameters.[78]

Manifest variables (considered measured without error) in the model will include a single study-arm binary exposure (intervention vs. UC) and provider-level percentage of eligible visits at which HPV-V promotion occurred in the pre- and post-intervention time periods. Multiple items in the provider survey may be used to measure change in each of the three hypothesized behavioral mechanisms. Therefore, the adequacy of the measurement model for the mediators can be addressed and each of the three potential mediator variables will be assessed as changes in latent constructs from baseline to 6-months following intervention implementation.

Following quantification of relationships between intervention exposure and primary outcome (change in HPV-V promotion), intervention exposure and behavioral mechanisms (aka mediators), and mediators and primary outcome (change in HPV-V promotion), the LCS SEM model will produce an estimate of total and individual indirect effects for the three mediators and standard errors and will assume non-causal associations among mediators. A sensitivity analysis will use the interventional effects method to estimate individual indirect effects[79,80] which is appropriate when the structural dependence between the multiple mediators is not well-understood. The analysis of Aim 7 will utilize Mplus 7.[81]

E.4 Sample size justification and power.

Aim 5. The analytic sample for Aim 5 consists of index dental encounters for patients (the first dental encounter within the pre- or post-intervention period) who are eligible for HPV vaccination but have not initiated - or have initiated but not completed, HPV vaccination. For the H5 analysis dental encounters are accrued in a 12-month pre-intervention period and 12-month post-intervention period that follows a 6-month intervention run-in. To estimate dental encounter volume a data pull in 2021 for patients age 11-26 indicates there are 3870 (1858 F + 2012 M) index encounters over one year for patients age 11-26 who have not initiated HPV vaccination, and 4259 (2221 F + 2038 M) index encounters for patients age 11-26 who have initiated but not completed the HPV vaccination series. The combined sample of 8129 (3870 + 4259) post-intervention index encounters at which provider actions are assessed plus a similar count (assumed to be 8129) in the 12 months prior to intervention (N=16,258 total) forms the denominator for the analysis of H5. With 21 clinics randomized to 2 conditions, 8129 index dental encounters in the pre- and post-intervention periods, and an intraclass correlation coefficient (ICC) assumed of .01-.03, this analysis has 80% power to detect an absolute difference of 5-10% in HPV-V promotion in intervention compared to UC clinics (e.g., 15% intervention versus 10% usual care for ICC=.01, 30% intervention vs. 20% UC for ICC=.03). This assumption is based on other intervention studies showing an increase of HPV-V between 10-20%.

Aim 6 (H6a, H6b, H6c). The analytic sample of n=131 dental providers for Aim 6 consists of n=47 general and pediatric dentists, n=79 registered dental hygienists and n=5 dental therapists. Based on prior surveys of dentists in this care system we expect 70% (n=92) will complete both surveys. Providers will be surveyed prior to the intervention training and 6 months following the start of the intervention. For the power analysis, the endpoints for Aim 6 are assumed to be approximately normally distributed so that general linear mixed models will be utilized. The clinic-level ICC for the Aim 6 endpoints is not known but assumed to be in the range of .01-.03. With 21 clinics randomized to 2 conditions, and 92 providers (4-5 per clinic) completing both surveys, this study has 80% power (alpha=.05, two-sided tests) to detect a minimum detectable standardized effect of 0.63-0.67 change in the Aim 6 endpoints in the intervention compared to UC condition.

Aim 7. The planned mediation analysis is expected to include surveys from n=92 providers at each of two time periods and their associated HPV-V promotion activities linked to approximately 8,000 dental encounters at each of two time periods. To address mediation questions with such data, models will all be conducted at the level of the provider, with aggregation of dental encounters to the provider level, disaggregation of study arm assignment to the provider level, and will utilize parameter constraints as feasible to simplify models. Evidence of estimation problems such as convergence, inadmissible solutions, or unstable parameter estimates may require specification of single-mediator models or further model simplification.

Patient/parent/guardian survey. Results from this survey (n=200 completed surveys expected per study arm) will provide an indication of how effectively dental providers were able to communicate HPV-V messages to their patients and the perceived strength of these messages. Analyses will also descriptively contrast surveys completed by patients and parents/guardians.

E.5 Secondary and Exploratory analyses. Potential disparities in intervention delivery will be addressed via exploratory analyses examining the heterogeneity of the effects of the intervention on HPV-V promotion activity in pre-specified subgroups: patient age (11-15, 16-20, 21-26), sex, and race/ethnicity, as feasible. The Aim 5 analytic model will incorporate interaction terms of patient factors and study arm by time fixed effects and utilize contrasts to estimate parameter estimates and standard errors within these subgroups. Patient-level exploratory endpoints by study condition include a binary indicator of receipt of HPV-V within 30 days of the eligible visit. These exploratory endpoints are consistent with current US HPV-V recommendations.[82]

E.6 Missing data. Any HPV-V promotion activity will be captured in the CDS during eligible visits and utilized for the analysis in Aim 5. The absence of a record of HPV-V promotion at any eligible visit will be assumed to indicate that HPV-V promotion was not delivered at that visit. In sensitivity analyses, the patient report of

receipt of HPV-V promotion will augment a missing indication from the provider. The mixed-model likelihood-based estimation used in the analysis of repeated survey data in Aim 6 will allow use of all provider survey data. Likelihood-based ignorable methods ensure accurate parameter estimates assuming data are missing at random (MAR). A sensitivity analysis will utilize an inverse probability weighting approach using information from the baseline survey and administrative data to differentially weight provider survey data. Visit eligibility is based on patient age and vaccination status which emanates from any of several state vaccination registries, which historically have relatively low rates of incomplete or missing vaccination information.

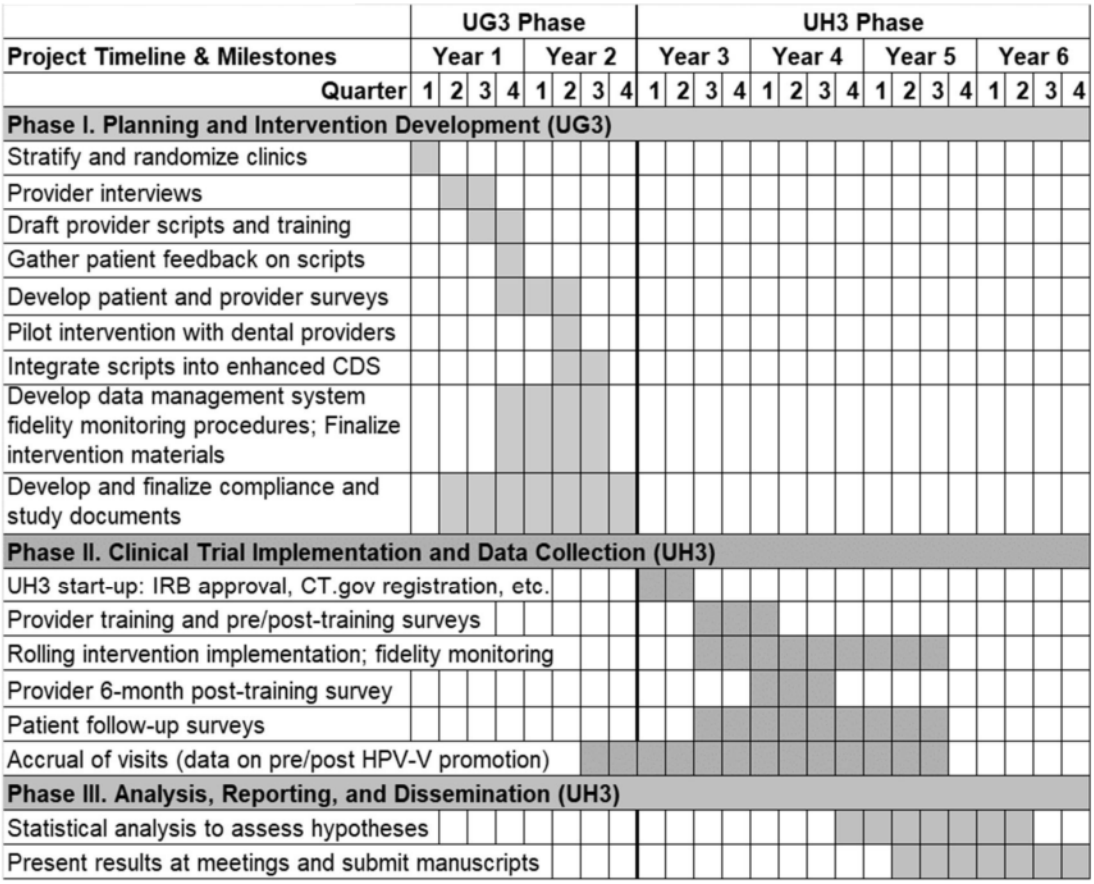
F. Strengths and Limitations.

The real-world study setting is a strength - an integrated healthcare system with an established EHR-based CDS platform that can be leveraged to deliver provider-directed interventions. EHRs are widely used in dentistry and the proposed intervention demonstrates the utility of linking EHRs with state vaccine registries. Our intervention is portable into any electronic record system, and the intervention components thought to be primarily responsible for its effects – provider training and tailored scripts, which we test here – are suitable for delivery outside of an electronic system. A potential limitation of our work is that HPV-V promotion is designed to be delivered during *preventive* dental visits only, not all visits. We believe that ensuring patient comfort is paramount to the intervention's success. Preventive care visits seem ideal as the patient's attendance is not motivated by a pressing health concern and their preventive nature aligns with cancer prevention education. A second limitation is that the size of our patient population, which is ample for detecting intervention effects on the primary intervention target (provider HPV-V promotion), it is too small to draw conclusions on the full array of purported behavioral mechanistic pathways. So, to invoke sufficient statistical power, we opted to restrict our mediation analyses to three candidate behavioral mechanisms. While advantageous, our real-world setting introduces the reality that providers work in multiple clinics, making UC vs intervention clinic distinctions less clear. To mitigate this, we will limit eligible study visits to those in the providers' home clinic and track clinic crossover in the analyses.

G. Timeline

Figure 2 and the attached milestones document depict the timeline for major study activities. The intervention will be developed during the 2-year UG3 phase. The UH3 phase includes an 18-month intervention period for each clinic.

Figure 2. Study Timeline



PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001

Expiration Date: 09/30/2024

Use of Human Specimens and/or Data

Does any of the proposed research in the application involve human specimens and/or data *	○ Yes ● No
Provide an explanation for any use of human specimens and/or data not considered to be human subjects research.	
Are Human Subjects Involved	● Yes ○ No
Is the Project Exempt from Federal regulations?	○ Yes ● No
Exemption Number	❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8
Other Requested Information	

Human Subject Studies

Study#	Study Title	Clinical Trial?
1	Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings	Yes

Section 1 - Basic Information (Study 1)

1.1. Study Title *

Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings

1.2. Is this study exempt from Federal Regulations * ○ Yes ● No

1.3. Exemption Number ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	○ No
1.4.b. Are the participants prospectively assigned to an intervention?	● Yes	○ No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	● Yes	○ No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	● Yes	○ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 1)

2.1. Conditions or Focus of Study

- human papillomavirus (HPV)
- HPV vaccination

2.2. Eligibility Criteria

Providers: General and pediatric dentists, dental hygienists, and dental therapists who work full- or part-time within HealthPartners Dental Group clinics who treat patients ages 11 to 26 years of age for routine dental care.

2.3. Age Limits	Min Age: 18 Years	Max Age: N/A (No limit)
2.3.a. Inclusion of Individuals Across the Lifespan	Inclusion Across Lifespan.pdf	
2.4. Inclusion of Women and Minorities	Women and Minorities.pdf	
2.5. Recruitment and Retention Plan	Recruitment Retention.pdf	
2.6. Recruitment Status	Not yet recruiting	
2.7. Study Timeline	Study Timeline and Milestone Plan.pdf	
2.8. Enrollment of First Participant	03/01/2023	Anticipated

2.3.a. Inclusion of Individuals Across the Lifespan

The primary population of focus for this study is dental providers. All eligible providers are at least 18 years of age. There is no upper limit for provider age.

The targeted patient population consists of individuals 11-26 years of age, and therefore will include children as well as adults. When the patient is under the age of 18 years, providers will be instructed to direct discussions about HPV risk and vaccination to the parent or guardian. In addition, surveys will be conducted with the parent/guardian of those patients under 18 years. The study targets those ages 11-26 years to ensure consistency with the most recent Advisory Committee on Immunization Practices (ACIP) guidelines.

2.4 Inclusion of Women and Minorities

The primary population of focus for this study is dental providers employed by HealthPartners Dental Group (HPDG). Specifically general and pediatric dentists, dental hygienists, and dental therapists who work in the 21 participating HPDG clinics will be eligible to participate. Based on the current composition of eligible dental providers within HPDG, we estimate that the provider population will be approximately 59% female, 72% White/Caucasian, and 5% Hispanic/Latino. Please see the provider planned enrollment report for additional demographic details.

All women and minorities who meet eligibility criteria will be included in the study. Patient participation by women and minorities will be determined by the population demographics served by HealthPartners Dental Group. Based on preparatory data, we estimate that the eligible patient population will be approximately 54% female, 46% White/Caucasian, and 12% Hispanic/Latino. Please see the patient planned enrollment report for additional demographic details. We are planning additional analyses to examine if the intervention effect varies by subpopulations including low socioeconomic groups.

2.5 Recruitment and Retention Plan

We will continue to engage with HealthPartners Dental Group (HPDG) leadership to ensure the active participation of HPDG clinics. HPDG leadership supports this project, as evidenced in the letter of support from HPDG Director Dr. David Gesko, and ensures the participation of the dental clinics. In addition, HPDG providers have a strong track record or participation in research including involvement in the National Dental Practice-Based Research Network and studies conducted within HealthPartners. Our experience conducting research in real-world settings has led to important lessons learned that will be applied to this study.

Patients 11 to 26 years of age seen for preventive care dental visits in HPDG clinics and who have either not initiated or not completed the HPV vaccine series will be eligible and automatically enrolled on the basis of data recorded in the electronic health record (EHR). A subset of patients (or parents/guardians for those under age 18) will be contacted by phone 1-3 days after the dental visit and invited to participate in a survey. Ongoing involvement is not required from patients and therefore, no additional recruitment or retention activities are planned. Vaccine data following the dental care visit will be retrieved by the programmer from the EHR. We anticipate contacting 800 individuals to collect 400 completed surveys.

All HPDG general and pediatric dentists, dental hygienists and dental therapists who work full- or part-time in one of the participating HPDG clinics will be included in the study. All providers in the intervention clinics will receive training. The study team will train new staff as needed due to staff departures for retirement or other reasons. During the UG3 phase, providers will be invited to participate in interviews and pilot testing through email, phone, or in-person recruitment by the study team. During the UH3 phase, online surveys will be conducted prior to training, upon completion of the training and after exposure to the intervention for 6 months. The study team has extensive experience and strong relationships with the HPDG provider resulting in high levels of provider participation. Their involvement will be facilitated by providing continuing education credits and related incentives for participation. We will work with HPDG leadership and the Institute’s Center for Evaluation and Survey Research to ensure the smooth implementation of surveys.

Study Timeline and Milestone Plan

UG3 Phase

Milestones to be initiated and completed in the UG3 phase are described below and depicted in the timeline.

- **IRB submission and approval for initial UG3 activities (Complete by end of Y1Q2)**
  The team will submit an application to the HealthPartners IRB for UG3 human subjects research activities including provider interviews, patient surveys and piloting.
- **Stratification and Randomization of Clinics (Complete by end of Y1Q2)**
  A total of 21 HealthPartners Dental Clinics will be stratified as described in the research strategy and randomly assigned to intervention or usual care. This timing allows us to deliver pilot training only to clinic staff in the intervention arm, thereby avoiding contaminating staff in usual care clinics with the intervention.
- **Provider Interviews (Complete by end of Y1Q3)**
  Qualitative interviews with dentists and hygienists will be conducted to inform development of the provider training. Interviews will focus on attitudes about and perceived barriers to HPV vaccine (HPV-V) promotion, vetting potential interventions to help overcome these barriers, providers' fear of negative consequences from HPV vaccine promotion and acceptability of potential study interventions/procedures.
- **Develop draft intervention materials, including scripted messages and provider training (Complete by the end of Y1Q4)**
  Insights from provider interviews and behavioral science literature will be used to develop provider training materials and scripts to guide providers in discussing HPV vaccination with patients and/or their parents.
- **Gather patient feedback on tailored scripts (Complete by end of Y1Q4)**
  HealthPartners' online patient/member panel (MyVoice) will be surveyed to gain feedback on the scripted messages and ensure that messages meet patients' expectations for communications within a dental setting.
- **Pilot Intervention materials and procedures with providers (Complete by end of Y2Q2)**
  Preliminary provider scripts will be developed for pilot testing in Year 2, and further refinements will be made based on results. Providers in the pilot will be surveyed to assess if the intervention affected the targeted behavioral mechanisms (knowledge of HPV and HPV vaccination, self-efficacy to promoted HPV vaccination and fear of negative consequences of promoting HPV vaccination). The pilot will also be used to assess the acceptability of the intervention and study procedures among providers.
- **Develop and test survey instruments (Complete by end of Y2Q2)**
  The study team will develop the patient and provider surveys for the UH3 phase in collaboration with the Institute's Center for Evaluation and Survey Research. Behavioral health experts Drs. Patricia Mabry and Meghan JaKa will lead the development of the provider survey, drawing from existing and validated tools, to ensure that the targeted behavioral mechanisms can be accurately measured.
- **Integrate Intervention Content into the existing Clinical Decision Support (CDS) Platform (Complete by end of Y2Q3)**
  Once finalized, the scripts will be integrated into the existing electronic health record (EHR) embedded CDS platform and the team will prepare to implement this enhanced CDS within clinics assigned to the intervention. The system will also include adding any data fields for providers to record their recommendations and other actions regarding HPV-V promotion during visits with eligible patients.
- **Finalize the fidelity monitoring plan (Complete by end of Y2Q3)**
  Drs. Rindal, Mabry, and JaKa will work together to finalize the fidelity monitoring plan to ensure to track provider participation on trainings and the use of intervention materials once implemented in the UH3 phase.
- **Finalize data management system (Complete by end of Y2Q3)**
  Drs. Rindal and Mabry with work with the statistician (Mr. Asche) and the programmer/analyst to ensure that the data management system is ready for the UH3 phase and will have a written plan describing where various data elements are stored and how they will be linked and secured.

- **Finalization of all provider intervention materials. (Complete by end of Y2Q3)**
  All intervention materials, including provider trainings, patient informational materials, will be finalized. Case report forms will also be finalized.
- **Finalization of clinical protocol and other regulatory documents (Completed by end of Y2Q4)**
  In collaboration with NIDCR, the study team will finalize the study protocol with anticipated finalization by Year 2, Quarter 3. We also plan to finalize the clinical quality management plan and data management plan at this time.

The commitment and resources needed to implement the trial in HealthPartners dental clinics have already been secured (see letter of support from HPDG Dental Director David Gesko, DDS and Chair of Pediatrics Andrea Singh, MD), and therefore the following milestone is not applicable: Finalization of agreements for use of resources available within CTSAs, practice-based research networks, patient registries, etc. Drs. Rindal and Mabry will engage with organizational stakeholders throughout the UG3 phase to ensure their ongoing collaboration in intervention development activities to ensure that the intervention and study procedures are acceptable and feasible to dental providers.

UH3 Phase
Following successful completion of milestones during UG3 phase and approval of the transaction package, milestones to be initiated and completed in the UH3 phase are described below and summarized below in Table 2.

- **IRB submission and approval for UH3 activities (Completed by end of Y3Q2)**
  Upon finalization of the protocol, we will seek final approval from the HealthPartners IRB for UH3 activities.
- **Registration of clinical trial in ClinicalTrials.gov (Complete by end of Y3Q2)**
  Once the protocol has been accepted by NIDCR, we will register the trial in ClinicalTrials.gov and make updates as the trial proceeds into the UH3 phase.
- **Provider Baseline (Pre-/Post-Training) Surveys (Complete by end of Y4Q1)**
  Over the course of a 9-month roll-out period, providers in intervention clinics will receive training and be asked to complete brief pre- and post-training online surveys on the same day as the receive training. Providers in usual care clinics will be asked to complete an online baseline survey. This survey will be used to assess the targeted behavioral mechanisms.
- **Site Activation – Clinic Training and Enhanced Clinical Decision Support Go Live (Complete by end of Y3Q4)**
  Site activation will happen through clinic trainings over approximately nine months, starting Y3Q3 and ending by the end of Y4Q1. The enhanced clinical decision support will be turned on in intervention clinics on a rolling basis, once each clinic has received training.
- **Intervention Initiation (Complete by end of Y3Q4)**
  Providers will be instructed to begin delivering the intervention to patients during eligible visits once they have been trained (no later than Y3Q4). Patients seen by providers during study eligible visits (or their parents or guardians) will be contacted 1-3 days after the visit and asked to respond to a survey pertaining to the care they received at that visit.
- **Completion of eligible study visits (Y5Q3)**
  The intervention will run for 27 months, with eligible visits expected to occur relatively evenly throughout this period:
  - Completion of 50% of study visits (Year 4, Quarter 4)
  - Completion of 100% of study visits (Year 5, Quarter 3)
- **Data cleaning and creation of an analytic dataset (Complete by end of Y6Q1)**
  This time is needed for data cleaning and merging data sources for analyses so that that all planned analyses can start in Y6.
- **Complete primary study analyses, manuscripts prepared, and results disseminated (Complete by end of Y6Q4)**
  Initial analyses will begin by the end of Year 3, and primary study analyses will be completed by the end of the first quarter of Year 6, to allow time for results dissemination.
- **Completion of annual study reports (Complete by end of Y6Q4)**
  Study reports will be completed annually at the end of each year and filed with NIH for review by NIDCR program officials. The final study report will be completed and provided to NIDCR by the end of Year 6, Quarter 4.

	UG3 Phase								UH3 Phase															
Study Timeline	**Year 1**				**Year 2**				**Year 3**				**Year 4**				**Year 5**				**Year 6**			
Quarter	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Ongoing Project Activities																								
Weekly study team meetings led by Drs. Rindal and Mabry																								
Quarterly Reports to NIDCR																								
Data Safety and Monitoring Board (DSMB) or Medical Monitor Reporting																								
Phase I. Planning (UG3)																								
IRB submission and approval (Initial application for UG3 research activities)																								
Stratify and randomize clinics																								
Provider interviews to inform development of training and intervention																								
Develop preliminary intervention materials (tailored scripts & provider training)																								
Gather patient feedback on tailored scripts (MyVoice survey)																								
Develop patient and provider surveys for UH3 phase																								
Pilot Intervention materials and procedures with dental providers																								
Integrate provider scripts into Clinical Decision Support (CDS)																								
Develop fidelity monitoring procedures																								
Refine and finalize intervention procedures and materials																								
Develop and finalize data management system																								
Develop and finalize clinical trial protocol, clinical quality management plan, data quality management plan, finalize data management system, consent/assent forms, and any other documents required for NIDCR and submit IRB application																								
Phase II. Clinical Trial Implementation and Data Collection (UH3)																								
Finalize IRB approval for UH3 activities; Registration in ClinicalTrials.gov																								
Ramp-up/planning activities (Schedule trainings, engaging clinic leadership, etc.)																								
Provider pre-training survey, provider training, post-training survey*																								
Rolling intervention implementation; fidelity monitoring																								
Provider 6-month post-training survey																								
Patient follow-up surveys																								
Accrual of visits (data on pre/post HPV-V promotion)							**	**	**	**														
Phase III. Analysis, Reporting, and Dissemination (UH3)																								
Data cleaning and creation of analytic dataset																								
Statistical analysis to assess hypotheses																								
Present results at meetings and submit manuscripts																								
Completion of annual study reports																								

*The immediate post-training survey will be given only to providers from clinics assigned to the intervention who will receive training.

**Retrospective data to assess HPV-V promotion prior to intervention implementation will be pulled during the UH3 phase. The timeline reflects the retrospective view of this data, not when it will be pulled.

2.9. Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
Study 1, IER 1	Domestic	HealthPartners Dental Group Clinics
Study 1, IER 2	Domestic	HealthPartners Dental Clinics

OMB Number: 0925-0770

Expiration Date: 09/30/2024

Inclusion Enrollment Report 1

1. Inclusion Enrollment Report Title* : Dental Providers

2. Using an Existing Dataset or Resource* : ❍ Yes ● No

3. Enrollment Location Type* : ● Domestic ❍ Foreign

4. Enrollment Country(ies): USA: UNITED STATES

5. Enrollment Location(s): HealthPartners Dental Group Clinics

6. Comments:

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	8	4	0	0	12
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	6	5	0	0	11
White	48	38	5	3	94
More than One Race	10	4	0	0	14
Total	72	51	5	3	131

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

OMB Number: 0925-0770

Expiration Date: 09/30/2024

Inclusion Enrollment Report 2

1. Inclusion Enrollment Report Title* : Dental Patients

2. Using an Existing Dataset or Resource* : ❍ Yes ● No

3. Enrollment Location Type* : ● Domestic ❍ Foreign

4. Enrollment Country(ies): USA: UNITED STATES

5. Enrollment Location(s): HealthPartners Dental Clinics

6. Comments:

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	15	10	6	6	37
Asian	473	365	11	10	859
Native Hawaiian or Other Pacific Islander	4	3	2	2	11
Black or African American	901	764	53	44	1762
White	1886	1576	341	239	4042
More than One Race	525	450	231	212	1418
Total	3804	3168	644	513	8129

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

Section 3 - Protection and Monitoring Plans (Study 1)

3.1. Protection of Human Subjects	Human Subjects.pdf
3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	○ Yes ● No ○ N/A
Single IRB plan attachment	
3.3. Data and Safety Monitoring Plan	DSMB plan.pdf
3.4. Will a Data and Safety Monitoring Board be appointed for this study?	○ Yes ● No
3.5. Overall structure of the study team	Study Team Org.pdf

3. Protection and Monitoring Plans

3.1 Protection of Human Subjects

1. Risks to Human Subjects

a. Human Subjects Involvement, Characteristics, and Design

This is a study to develop a theory-based behavioral intervention to support dental providers in promoting the HPV-V to their patients (UG3). We will also examine the intervention's behavioral mechanisms of action and test its real-world efficacy in a clinic-randomized trial (UH3). The intervention will be designed to address identified barriers to dental providers' promotion of HPV-V: HPV-related knowledge, self-efficacy in HPV-V promotion, and fear of adversely affecting the patient-provider relationship. A total of 21 clinics in the HealthPartners Dental Group (HPDG) practice will be randomly assigned to the usual care (UC) or intervention arm. The intervention will consist of provider training and tailored scripts address knowledge, barriers, and fears to discussing and promoting HPV vaccination to eligible patients. The intervention will be delivered in the context of an electronic health record (EHR)-based Clinical Decision Support (CDS) platform. All general and pediatric dentists, hygienists, and dental therapists who see age-eligible patients will receive the interventions.

The provider-delivered HPV vaccine promotion will be delivered at eligible visits defined as meeting all of the following criteria:

1. Patient is age 11-26 at time of visit.
2. Visit takes place at a HealthPartners Dental Clinic.
3. Patient is seen for routine preventive care visit.
4. Patient has either not initiated or not completed the HPV-V series, as indicated by their HPV-V status in the EHR.

We expect that during the 18-month study period approximately 8,000 qualifying visits will occur with HPV unvaccinated patients and 3,000 qualifying visits will occur with partially HPV-vaccinated patients.

All study activities will be performed within HealthPartners, with collaboration between the HealthPartners Institute study team and the HealthPartners Dental Group (HPDG) care providers. There are no collaborating clinical sites or investigators outside of HealthPartners.

b. Study Procedures, Materials, and Potential Risks

Dental providers: During the trial's UG3 planning phase, a limited number of dentists and hygienists will be interviewed to determine knowledge gaps and barriers to HPV vaccine promotion. These same individuals will be engaged in piloting the test intervention to determine if the planned intervention targets the behaviors of interests and to assess the feasibility and acceptability of the intervention and clinic procedures. Interview information will be recorded by study investigators. PHI will not be collected from these select providers. During the UH3 trial phase, pre- and post-intervention survey information will be collected from all participating providers. As part of these surveys, we will collect information about provider type (dentist, pediatric dentist, dental therapist, and hygienist) and the providers' age, gender, years in clinical practice and race and ethnicity. Given the number of providers in our system, the collection of these variables could enable one to identify specific individuals. These data, however, will not be reported except in aggregate to minimize the risk of loss of privacy. Individual survey results will not be shared with non-study personnel. Provider activity during the intervention period (tracking of HPV-related discussions and vaccine recommendations) will be tracked during the study period but these results will not be shared outside the study team. These protections of research subjects will be strictly adhered to in accordance with HealthPartners IRB policies and oversight. No biospecimens will be collected from providers. The organization has policies in place that limit access to patient records by the provider's supervisor. More importantly we will not alert a provider's supervisor if a provider is not promoting the HPV vaccine. To further minimize that risk, the study investigators will not have access to provider identifiers.

Patients: Data to determine patient eligibility and to assess the impact of the provider-delivered intervention will be derived from HealthPartners EHR (Epic) and HealthPartners claims data.

Limited clinical data from the EHR will be used to determine eligibility for the study, including age, gender, having a scheduled preventive dental care visit, and vaccination status. These data, along with patient-level details (i.e., name and contact information) are needed to contact a random subset of patients (or parents/guardians if patients are less than 18 years of age) for the survey will be obtained.

Post-dental visit surveys will be conducted on a subset of approximately 400 patients (or parents/guardians) 1-3 days following the dental visit to determine if the patient/parent/guardian received a recommendation for HPV vaccine from his/her provider, to assess the perceived strength of that recommendation and to gauge the readiness of the patient/parent/guardian to initiate or receive a follow-up dose of the vaccine. These surveys will be conducted by HealthPartners' Center for Evaluation and Survey Research (CESR), which has extensive experience conducting these types of patient surveys. Verbal consent will be obtained by CESR at the start of the call. Patient contact information will be stored securely in a RedCap database. No biospecimens will be collected from patients, parents or guardians.

3. Potential Risks.

The aims of this study are to develop and test the efficacy of an intervention targeting a dental provider's HPV-related knowledge, barriers to HPV vaccine promotion and willingness to recommend the vaccine to eligible patients. The intervention will be designed to increase promotion of the HPV vaccine as recommended by the CDC and the American Dental Association. We are simply testing an intervention to support dental providers in this activity. The intervention does not involve the use of deception or placebos.

We consider risks to providers as minimal, and principally involve the potential loss of confidentiality of study data. Information regarding the providers' performance (either on the pre- and post-intervention surveys or in terms of study activities tracked during the intervention period) will not be shared with non-study personnel. Only group aggregated data will be presented in presentations and publications. A provider's participation in or performance during the trial will not affect their employment relationship with HealthPartners Dental Group. See prior section header, Dental providers, for additional detail on how that potential risk will be addressed.

Patient risks include the possibility that the information available to the provider might result in a patient/parent/guardian receiving an erroneous recommendation for the HPV vaccine. The risk of untoward consequences from such clinical actions is considered minimal given the patient will only be referred to their medical care provider to receive a vaccination. There are minimal risks of receiving the vaccine, including soreness, redness, and minor swelling and the rare allergic reaction, but these risks will be reviewed, and separate consent will be obtained by the patient's medical care provider. Additional risks to patients are also minimal and include the loss of confidentiality/privacy.

Providers can elect not to participate in the interventions. Similarly, patients can elect not to pursue vaccination despite the recommendation of the dental care provider.

2. Adequacy of Protection Against Risks

a. Informed Consent and Assent

Providers: The study activities mirror a broader initiative supported by HealthPartners to improve HPV vaccination rates (See letter of support from Dr. Andrea Singh). Previously, our IRB has determined that the consenting of providers is generally not required for studies that explore ways to improve adherence to care guidelines, as is the case in the current proposal. We could potentially include all dental providers who provide general dental care and see patients in the target age range. That final determination will be made by the HealthPartners IRB. Dental providers who are selected for interviews will complete an informed consent process agreeing to their participation and the recording. Provider participation in the intervention training sessions will be incentivized by providing free continuing education credits.

Patients: A waiver of informed consent will be requested for the involvement of patients' information at the point of care for the following reasons: 1) All HPV-related information and vaccine recommendations will be based on current evidence and recommendations promulgated by groups such as the CDC, the HPV Roundtable, and the American Cancer Society. Therefore, the recommendations conform to current standards of care and don't present a risk to patients that exceed the risks that patients assume when they seek care within any healthcare system focused on disease prevention through vaccination promotion; and 2) This research would not be feasible without such a waiver, as recruitment at the point of care would notably bias the involvement of providers and, potentially, the response of patients. All patients seeking care at HealthPartners Clinics annually sign a HIPPA authorization form that includes the option to opt out of using the health data for research purposes. Before pulling any patient level data our programmers check the opt out list to see if their data should be excluded. In addition, patients contacted for the patient survey are explained that their health record data would be used for this study and they are given a second opportunity to opt out.

Informed Consent for Surveys: A waiver of signed informed consent will be requested for patients or guardians surveyed by phone. HealthPartners CESR personnel have completed human subjects training. All data capture will be conducted in RedCap, a secure, web-based application. The protocol for the patient telephone interviews will be developed and tested, with input from the investigative team, during the initial phase of this proposed project. We will not attempt to convince patients/parents/guardians otherwise who initially decline to participate.

Patients may elect to withdraw at any time with no impact on their relationship with their provider or the institutions involved in conducting the research. Survey participants will be mailed a $15 gift card as a thank you for their time and feedback.

b. Protections Against Risk

The study team has extensive experience in health services research and studies with human subjects, procedures to safeguard privacy and personal information, use of untraceable identification (ID) numbers, strong user login authentication on all electronic devices, and physical security for all electronic devices containing personal information. We guard against breach of subject confidentiality through a multilayered system of data protection policies, processes, staff training, software safeguards, and physical security measures for both paper and electronic data involved in research.

The following measures will be taken to protect providers and patients from the risk of breach of confidentiality. A unique study ID code unrelated to the EHR provider-ID, patient medical record number or other study subject-specific information will be assigned to each patient and provider study subject and used to link data from various sources needed for analysis. A crosswalk table linking this code number to a provider and a patient medical record number will be destroyed after completion of analyses needed to test study hypotheses. Audio files from provider semi-structured interviews will also be destroyed at study completion. All electronic study data will be maintained in a computerized database residing on a username- and password-protected file server to which only required study researchers have access. All study-related paper documents containing individually identifiable information will be maintained in locked file cabinets at HealthPartners Institute. Data will be retained in secure storage after completion of the study, in accordance with Minnesota and federal law. The written informed consent procedure (for select providers) and documentation for providers and patients will be reviewed in advance, approved, and monitored on an ongoing basis by all appropriate site IRBs.

The following measures will be taken to minimize the risk that a provider will act wrongly on the basis of information provided through support tools developed for this study. Each project-related communication to providers and patients will include a prominently placed written statement that no clinical action of any kind should be undertaken as a result of the recommendations derived from study materials or tools without review of the patient’s entire medical record and with due consideration of all aspects of the patient’s health, previous health care, current treatment, and other factors.

In additional to local site policies, HIPAA itself makes specific provision for waiver of authorization to use PHI for research recruitment purposes under specific conditions, which this study meets: “For research uses and disclosures of PHI, an IRB or privacy board may approve a waiver or an alteration of the authorization requirement in whole or in part. A complete waiver occurs when the IRB or privacy board determines that no authorization will be required for a covered entity to use and disclose PHI for a particular research project. A partial waiver of authorization occurs when an IRB or privacy board determines that a covered entity does not need authorization for all PHI uses and disclosures for research purposes, such as disclosing PHI for research recruitment purposes. An IRB or privacy board may also approve a request that removes some PHI, but not all, or alters the requirements for an authorization (an alteration).

HealthPartners Institutional Review Board is accredited by the Association for the Accreditation of Human Research Protection Programs and the manager is well-versed in human subject protection and knowledgeable about all aspects of state and federal regulations. The IRB manager works closely with HealthPartners and affiliated researchers to ensure that their research protocols are consistent with the protection of human subjects and compliant with applicable standards and regulations.

This study’s provider-directed intervention involves didactic training and the development and use of scripts that will be embedded within an existing CDS tool within the dental module of the EHR. The provider-delivered intervention involves educating patients/parents/guardians about HPV, addressing concerns and promoting the HPV vaccine. Thus, we have no study-specific plans to provide medical or professional intervention in the

event of an adverse event. Study oversight will be provided by a independent safety monitor or Data Safety and Monitoring Board as determined by NIDCR.

c. Vulnerable Subjects, if relevant to your study

All providers, being licensed and practicing dentist, dental therapists, or hygienists, are non-vulnerable adults. The provider-delivered interventions will be directed at patients 18 to 26 years of age and at parents/guardians of patients 11-17 years of age. Children of this age are included as the “target” group to align with current vaccine recommendations of the CDC’s Advisory Committee on Immunization Practices (ACIP). ACIP guidelines indicate that children as young as 9 years of age can initiate the vaccine. We will exclude 9 and 10 year old children, however, because of study design issues (see Section D. Study Approach). The study will exclude patients who do not consent to participate in this research or who have language barriers. Notably, only a randomly-selected subgroup of parents/guardians of children will be surveyed by phone. Survey information will not be sought from the children.

3. Potential Benefits of the Proposed Research to Research Participants and Others

Providers and patients will not benefit directly from participating in this research. However, the training and support tools made available to some providers may improve their clinical care by making them more comfortable discussing HPV with patients and recommending the HPV vaccine. Patients who pursue vaccination may benefit by lowering their risks for future HPV-related cancers.

4. Importance of the Knowledge to be Gained

Despite the effectiveness of the HPV vaccine in reducing the prevalence of HPV-related cancers, vaccination rates remain below US national goals and rates in other developed countries. The HPV vaccine reduces the prevalence of oncogenic strains of the virus in the oral cavity and chronic oral HPV infection is associated with oropharyngeal cancer. This research will test if an intervention delivered to dental care providers increases providers’ willingness to recommend the HPV vaccine as a means of oral cancer prevention. The risks to providers and patients participating in this research are minimal and are, in our opinion, outweighed by the potential benefits of improved HPV vaccination rates among eligible patients and the longer-term benefit of reduced oropharyngeal cancer rates.

Data Safety and Monitoring Plan

We will convene a data safety monitoring board (DSMB) if deemed necessary by the medical monitor at NIDCR. We expect that oversight by the medical monitor may be sufficient, but we understand that this determination must be made by NIDCR. We will work closely with the Program Officer to recommend potential board members, establish a schedule for in-person meetings and video or phone conferences, and establish the frequency and content of interim data reports. We label these tasks “as needed” because the study intervention is provider-directed and builds on guidelines and recommendations from a number of organizations. The study aims to develop and test an intervention aimed at improving HPV vaccine promotion in the dental setting. HPV vaccine promotion is an activity that falls within the scope of dental practice, that dentists and hygienists are interested in providing, and is something that the Centers for Disease Control and Prevention, the American Cancer Society, the American Dental Association and the American Academy of Pediatric Dentistry currently recommend that dental care providers do. We judge the risks associated with the provider intervention as minimal given that patients will be advised to adhere to a vaccination schedule recommended by government science panels and professional organizations.

To ensure the integrity of the study data, we will generate interim reports (approximately bimonthly) to monitor study activities in terms of both the intervention training, expected provider behaviors, and patient outcomes. We will generate (and distribute as dictated by NIDCR) reports that track study enrollment, intervention fidelity and clinic-level summaries of the study outcomes. The reports will also discuss any issues that arise that affect how the intervention is delivered or the study team’s ability to collect complete and quality study data from internal (EHR) or external (MN and WI state vaccine registry data) sources. These reports will summarize the number of patient encounters, and the fractions of providers and patients, by study group, with complete, partial and incomplete study data. The study PIs (Drs. Rindal and Mabry) and the statistician, Steve Asche, MA, will meet regularly to review these reports and the entire study team will meet regularly to address any concerns with data collection or quality.

Much of the study data will be collected electronically. Provider surveys will be collected via RedCap by HealthPartners’ Center for Evaluation and Survey Research (CESR) and sent electronically to the Mr. Asche. CESR has quality control procedures in place to ensure that updated patient contact information and phone survey responses are accurately recorded in the RedCap database, and that all mailings are sent to the appropriate person. Patient information will be captured from the EHR by HealthPartners’ data programmers who are well-versed and experienced in abstracting, securely storing, and de-identifying this information for analysis. Paper case report forms will not be used to collect data from providers or patients.

The proposed intervention does not include changes to practice that may harm patients. Although patients will be referred to medical care providers for HPV vaccination, risks associated with the vaccine will be reviewed by the medical care provider and not by study personnel. We will, however, track patients who were incorrectly referred for vaccination (because, for example, they had previously completed the series), whether or not they ultimately received a vaccination. Also each study provider has complete freedom to deliver the patient-directed intervention he or she believes is best for that patient.

We do not plan to conduct an interim analysis to assess study futility or early success. Thus, we do not plan to develop stopping rules, unless required by NIDCR or the DSMB. We will, however, track and report serious concerns about patient or provider safety, inadequate performance (low intervention fidelity), or rate of provider or patient enrollment. The intervention period is only 18 months in duration. The programmer will work with Mr. Asche to finalize all datasets for analysis.

3.5 Overall Structure of the Study Team

Co-Principal Investigators, D Brad Rindal, DDS and Dr. Patricia Mabry, PhD, will provide oversight of all study activities, study staff and study teams described below. Drs. Rindal and Mabry will work closely with the project manager to ensure the coordination and timely completion of all study activities. They will consult with the HealthPartners Dental Group (HPDG) leadership, including HPDG Director Dr. David Gesko and leaders from the 21 dental clinics enrolled in the study. Throughout the study, they will convene weekly meetings to ensure ongoing collaboration among all members of the study team.

Intervention Development and Implementation Team

The intervention development and implementation team will develop the provider training, scripts, and related components of the intervention during the UG3 phase and work together to roll out the intervention in HPDG clinics during the UH3 phase. Drs. Patricia Mabry and Meghan JaKa will help develop the provider training and scripts for discussing HPV vaccination with patients, ensuring integration of behavior theory to target the hypothesized mechanisms of behavior change. Dr. Elyse Kharbanda, as an expert in HPV vaccine safety, will also contribute to the development of provider trainings and scripts, and will help the project manager deliver trainings during the UH3 phase. Dr. Rindal and the project manager will ensure all relevant intervention components are integrated into the existing CDS platform and piloted tested, so it functions as planned. The programmer completes the technical components of this integration with the input of Drs. Rindal and Worley to ensure that the intervention functions as planned.

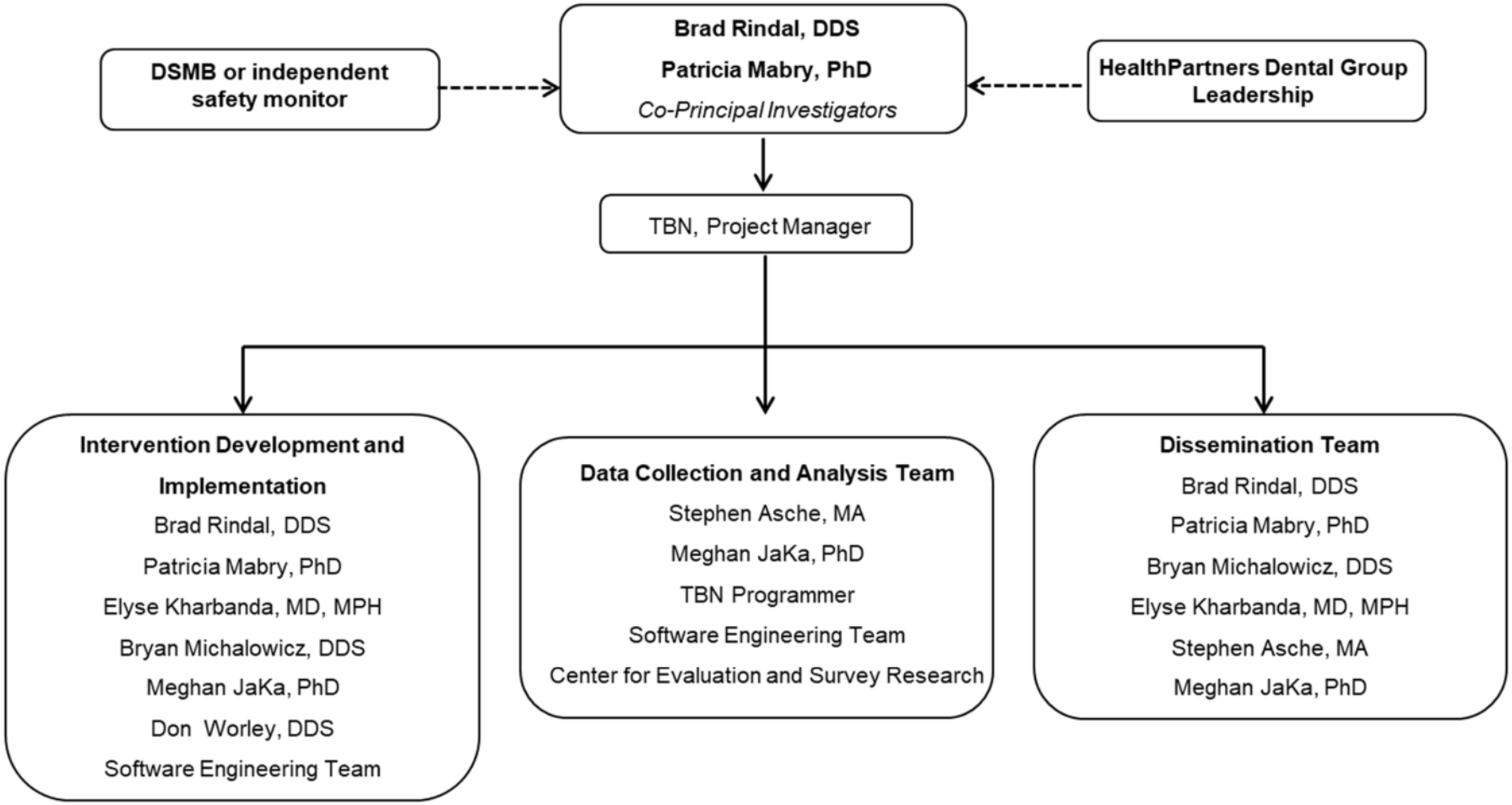
Data Collection and Analysis Team

Stephen Asche, MA will lead all quantitative analyses while Dr. JaKa will lead qualitative analyses. The Institute's Center for Evaluation and Survey (CESR) will lead the collection of all survey data from providers and patients, and will assist Dr. JaKa with interviews or dentists and hygienists. All other data will be extracted by the programmer from administrative and electronic health record (i.e., Clarity) databases. The programmer will work with Mr. Asche and CESR to clean and compile data files for analysis.

Dissemination & Implementation Team

Drs. Rindal and Mabry along with co-investigators will contribute to the dissemination of findings through local and national presentations as well as manuscripts to peer-reviewed journals. In addition, the Drs. Rindal and Worley will share results with the HealthPartners Dental Group and Dr. Kharbanda and Rindal will share results with HealthPartners leaders from primary care and pediatrics.

Organizational Chart



Section 4 - Protocol Synopsis (Study 1)

4.1. Study Design

4.1.a. Detailed Description

Study design overview. We will utilize a 2-arm, parallel, cluster(clinic)-randomized controlled trial design with baseline measures and will balance and randomly allocate 21 clinics in a 1:1 ratio to either intervention or usual care (UC). The real-world efficacy of the full intervention will be assessed by comparing intervention clinics to UC clinics on the primary outcome: pre-to post-intervention change in percentage of eligible visits with HPV-V promotion (Aim 5). The effect of the intervention on purported mechanisms of behavior change (aka mediators, i.e., provider HPV knowledge, provider self-efficacy for HPV vaccine promotion, and provider fear of negative consequences from HPV vaccination promotion) will be examined in Aim 6.

Provider Intervention Delivery. With support of HPDG Director David Gesko, DDS, we will work with clinic managers and leaders on a plan to deliver the interventions. Providers will receive continuing education credits for their participation. The intervention (education, scripts and enhanced CDS functionality) will be delivered in a manner that will allows for scheduling flexibility so we can reach all intervention arm providers. Based on past experience we anticipate developing a training video that will standardize the training and delivered either in person or virtually utilizing study staff to answer questions and provide any additional training as needed.

Provider Eligibility

General and pediatric dentists (n=47), dental hygienists (n=79) and dental therapists (n=5) who work full- or part-time within HPDG intervention clinics will be trained to deliver the intervention. Other dental specialists will not participate because they either do not routinely see adolescents or young adults in their practice or do not examine patients during preventive care visits. Because many US states do not have dental therapists, we will analyze data including and excluding patient encounters with therapists.

Eligible Study Visits

An eligible visit is defined as the first dental visit during the study period at which preventive care is delivered for any patient aged 11 to 25 years of age who has neither initiated nor completed the HPV-V dosing series.

4.1.b. Primary Purpose — Health Services Research

4.1.c. Interventions

Type	Name	Description
Behavioral (e.g., Psychotherapy, Lifestyle Counseling)	Usual Care	Dental providers in usual care clinics will receive: 1. HPV patient education brochures about HPV, its sequelae and HPV vaccination 2. Clinical decision support containing patients' HPV vaccination status and alert, standard scripts (no tailoring), and vaccine order functionality
Behavioral (e.g., Psychotherapy, Lifestyle Counseling)	Dental HPV Vaccine Promotion Intervention	Dental providers in intervention clinics will receive all components of usual care plus: 1. Provider training (didactic instruction) to increase knowledge about HPV and HPV vaccination 2. Tailored scripts delivered via clinical decision support, for various patient/parent/guardian responses, to guide providers in promoting HPV vaccination.

4.1.d. Study Phase — Phase 3

Is this an NIH-defined Phase III Clinical Trial? ● Yes ○ No

4.1.e. Intervention Model — Parallel

4.1.f. Masking ○ Yes ● No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.1.g. Allocation — Randomized

4.2. Outcome Measures

Type	Name	Time Frame	Brief Description
Primary	Promotion of the HPV vaccination	At each eligible patient visit	The primary outcome for the intervention is the percentage of eligible visits at which HPV-V was promoted over a 12-month period. The occurrence of HPV-V promotion at eligible visits will be operationalized using a binary composite measure: If the provider pushes a toggle switch in the CDS indicating that they promoted HPV-V at the visit and/or the provider invokes the CDS quick-scheduling capability to refer the patient to a vaccine scheduler, the visit will count as one at which HPV-V promotion did occur. Otherwise, HPV-V will be presumed to have not occurred at that visit. The main comparison for Aim 5 is the differential pre- to post-intervention change by study arm in the percentage of eligible visits at which HPV-V promotion occurred. HPV-V promotion is assessed in the 12 months pre-intervention and 12 months post-intervention, following a 6-month run-in period.
Secondary	Provider HPV/HPV vaccine-related knowledge	Measured immediately prior to intervention delivery and following a 6 months post-intervention run-in period	Provider surveys developed in Aim 1 will be used to assess between-groups differences in pre- to post-intervention change in Provider HPV/HPV vaccine-related knowledge (H6a).
Secondary	Provider self-efficacy for HPV vaccine promotion	Measured immediately prior to intervention delivery and following a 6 months post-intervention run-in period	Provider surveys developed in Aim 1 will be used to assess between-groups differences in pre- to post-intervention change in provider self-efficacy for HPV vaccine promotion (H6b).
Secondary	Providers' fear of negative consequences from promoting HPV vaccination	Measured immediately prior to intervention delivery and following a 6 months post-intervention run-in period	Provider surveys developed in Aim 1 will be used to assess between-groups differences in pre- to post-intervention change in providers' fear of negative consequences from promoting HPV vaccination (H6c).
Secondary	Parent/Patient/Guardian perceptions of HPV-V promotion delivery	Measured 1 to 3 days following the eligible visit	To determine if provider HPV vaccine promotion is being effectively communicated to the intended recipients, in a random subset of approximately 400 patients with eligible study visits, we will measure patient/parent/guardian reports of HPV vaccine promotion activity. Sampled patients/ parents/guardians will be contacted by phone 1 to 3 days following the eligible visit and asked if their provider promoted HPV vaccination.

4.3. Statistical Design and Power — Statistical Design Power.pdf

4.4. Subject Participation Duration — 18 months

4.5. Will the study use an FDA-regulated intervention? ❍ Yes ● No

4.5.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.6. Is this an applicable clinical trial under FDAAA? ❍ Yes ● No

4.7. Dissemination Plan — Dissemination.pdf

4.4 Statistical Design and Power

We will utilize a 2-arm, parallel, cluster (clinic)-randomized controlled trial design with baseline measures of dental provider HPV-V promotion activities and will balance and randomly allocate 21 clinics in a 1:1 ratio to either intervention or usual care (UC). The real-world efficacy of the full intervention will be assessed by comparing intervention clinics to UC clinics on the primary outcome: pre-to post-intervention change in percentage of eligible visits with HPV-V promotion (Aim 5). The effect of the intervention on purported mechanisms of behavior change (aka mediators, i.e., provider HPV/HPV-V knowledge, provider self-efficacy for HPV-V promotion, and provider fear of negative consequences from HPV-V promotion) will be examined in Aims 6 and 7.

Provider Eligibility. General and pediatric dentists (n=47), dental hygienists (n=79) and dental therapists (n=5) who work full- or part-time within HPDG intervention clinics will be trained to deliver the intervention. Other dental specialists will not participate because they either do not routinely see adolescents or young adults in their practice or do not examine patients during preventive care visits. Because many US states do not have dental therapists, we will analyze data two ways: including and excluding patient encounters with therapists and will compare the results to determine if inclusion of dental therapists is having an outsized effect on our results.

Eligible Study Visits. An eligible visit is defined as the first dental visit during the study period at which preventive care is delivered for any patient aged 11 to 26 years of age who has neither initiated nor completed the HPV-V dosing series.

Study Outcomes

HPV-V promotion activity (Aims 5 &7). The primary outcome for the intervention is the percentage of eligible visits at which HPV-V was promoted over a 12-month period. The occurrence of HPV-V promotion at eligible visits will be operationalized using a binary composite measure: If the provider pushes a toggle switch in the CDS indicating that they promoted HPV-V at the visit and/or the provider invokes the CDS quick-scheduling capability to refer the patient to a vaccine scheduler, the visit will count as one at which HPV-V promotion did occur. Otherwise, HPV-V will be presumed to have not occurred at that visit. The main comparison for Aim 5 is the differential pre- to post-intervention change by study arm in the percentage of eligible visits at which HPV-V promotion occurred. HPV-V promotion is assessed in the 12 months pre-intervention and 12 months post-intervention, following a 6-month run-in period. In subsequent sections, we refer to this comparison between the two timepoints as "*pre- to post-intervention*".

Intervention Impact on Behavioral Mechanisms (Aim 6). Provider surveys developed in Aim 1 will be used to assess between-groups differences in pre- to post-intervention change in targeted behavioral mechanisms, i.e., provider HPV/HPV-V-related knowledge (H6a), self-efficacy for HPV-V promotion (H6b) and fear of negative consequences from promoting HPV-V (H6c). Behavioral mechanisms will be measured immediately prior to intervention delivery and at 6 months post-intervention, to allow for an intervention run-in period.

Parent/Patient/Guardian perceptions of HPV-V promotion delivery. To determine if provider HPV-V promotion is being effectively communicated to the intended recipients, we will measure patient/parent/guardian reports of HPV-V promotion activity at a random sample of eligible visits (n=~800 of 8,000 total eligible visits). Sampled patients/parents/guardians will be contacted by phone 1 to 3 days following the eligible visit and asked if their provider promoted HPV-V. Surveys will be developed and conducted by CESR. Consistent with CESR's past experience, we anticipate a 50% response rate (400 completed surveys).

Covariates

Provider characteristics. Provider characteristics are gathered to describe the study sample and for use as covariates. Provider characteristics come from the health plan administrative data and include provider type (general dentist, pediatric dentist, hygienist, and dental therapist), gender and years in practice.

Patient characteristics. Patient characteristics will be used to describe the study sample, describe clinic case-mix for randomization, to utilize as covariates in analyses, and to define subgroups for analysis of treatment

effect heterogeneity. Patient characteristics come from the EHR and health plan administrative data and include patient age, sex, race, and insurance status.

Plan of Analysis and Analytic Methods

Analytic approach, Aim 5: H5 posits a larger increase in percentage of eligible visits at which HPV-V promotion occurred from pre-intervention to 6-months post-intervention implementation (i.e., "pre- to post-intervention" as described above) in intervention vs. UC clinics. Because clinics are randomized and the endpoint varies at the patient level, we will use generalized linear mixed-model regression with a logit link and binomial error distribution to test the effect of the interventions using the model specified below.

$$HPV\_Vaccination\_Promotion_{ji} = \gamma_{00} + \gamma_{10}StudyArm_j + \gamma_{01}Time_i + \gamma_{11}StudyArm_j*Time_i + \gamma_{02}PtCovariates_i$$

$$+ \gamma_{20}\,StratFactors_j + [u_{j0} + e_{ji}] \qquad j=clinic, i=patient$$

HPV-V promotion rates (H5) will be predicted by a fixed effect study arm term ($StudyArm_j$), an indicator for an eligible visit in the pre- to post-intervention period (Time), their interaction ($StudyArm_j*Time_i$), covariates ($PtCovariates_i$) to potentially include patient age group (11-17, 18-26), sex, and prior vaccination status (not initiated, initiated), and stratification factors used in the clinic randomization ($StratFactors_j$). A random intercept for clinics (u_{j0}) will account for the clinic-level randomization. A statistically significant interaction (alpha=.05) between study arm and time, and a pattern of pre- to post-intervention differences by study arm in the expected direction will support the H5 predictions for Aim 5.

Analytic approach, Aim 6: *H6a, H6b, H6c* posit that dental providers in the intervention arm compared to usual care arm will have larger increases when comparing their pre- to post-intervention implementation scores on HPV/HPV-V-related knowledge (H6a), self-efficacy for HPV-V promotion (H6b), and larger decrease in fear of negative consequences from promoting the HPV-V (H6c).

The three mediators will be measured repeatedly via a provider survey. Measurement timing is as follows: a) for providers in the intervention condition (n=10-11 clinics), the provider survey will be administered at *three timepoints*: immediately pre-training (T1), immediately post-training (T2, to capture knowledge gained from training), and at 6 months post-training (T3, to capture both long term knowledge retention, and the full effect of the intervention following a practice period). Note that T1 and T2 occur at the beginning and end of a single training session, so they are measured within 60 mins of one another; b) for providers in the UC condition (n=10-11 clinics), the provider survey will be administered at *two timepoints, yoked to the assessment periods in (a)*, i.e., at time periods consistent with T1 and T3. Assessment at T2 is not applicable to UC, because no intervention occurs during the intervening 60 minutes.

In Aim 6, we will test whether there is differential change from T1 to T3 by study arm in three pre-specified mediators. Because clinics are randomized and the outcome varies by provider over time, general linear mixed-model regression with an identity link and normal error distribution will be used to test the effect of the intervention in the general model specified below. While the endpoints are expected to be approximately normally distributed, the suitability of alternate error distributions and link functions in generalized linear mixed models will be assessed if distributions depart from expectations. The Aim 6 general model specification is:

$$ProviderEndpoint_{jit} = \gamma_{000} + \gamma_{100}StudyArm_j + \gamma_{001}Time_t + \gamma_{101}StudyArm_j*Time_t + [v_{j00} + u_{ji0} + e_{jit}]$$

j=clinic, i=provider, t=time (pre/post)

The endpoint variables (ProviderEndpoint) for Aim 6 are mean HPV/HPV-V-related knowledge score (H6a), mean self-efficacy for promoting HPV-V score (H6b), and mean fear of negative consequences score (H6c), gathered from provider surveys before training and six months following intervention implementation. The endpoints are predicted in separate equations by a fixed effect study arm term ($StudyArm_j$) contrasting intervention and usual care clinics, pre- or post-intervention survey (Time), and their interaction ($StudyArm_j*Time_t$). A random intercept for clinics (v_{j00}) accounts for the clinic-level randomization. A statistically significant study arm by time interaction (alpha=.05) and pre- to post-intervention contrasts by study arm in the expected direction will support the H6a, H6b, and H6c predictions stated for Aim 6. A sensitivity analysis will predict post-intervention endpoints from the pre-intervention measurement of the endpoint, study arm,

stratification factors used in the clinic randomization, and provider type.

Analytic approach, Aim 7: *H7* posits that**:** that dental providers in the intervention arm compared to UC arm will have larger increases when comparing their pre- to post-intervention implementation scores on HPV/HPV-V-related knowledge (H6a), self-efficacy for HPV/HPV-V promotion (H6b), and larger decrease in fear of negative consequences from promoting the HPV-V (H6c), plus accompanying increases in HPV-V promotion for each of these mechanistic pathways**.** Building on Aim 6, in Aim 7 we will estimate the effects of change in potential *mediators* on change in provider HPV-V promotion to assess whether the intervention effects follow any of the hypothesized mechanistic pathways. Next, we will quantify and test estimates of total and individual indirect effects to understand the extent to which the relationship between the intervention and change in HPV-V promotion efforts are mediated by changes in provider HPV/HPV-V knowledge, self-efficacy for HPV-V promotion, and fear of negative consequences for HPV-V promotion. Latent Change Score (LCS) Structural Equation Modeling (SEM)[75-77] will address potential mediators of the relationship between study arm assignment to the intervention and change in provider HPV-V promotion by change in three mediators: provider knowledge of HPV/HPV-V-related knowledge, self-efficacy for promoting HPV-V, and fear of negative consequences from HPV-V promotion. The LCS SEM framework enables flexible specification (e.g., ANCOVA, difference score, residualized change) of two-wave models with various levels of constraints in model parameters.[78]

Manifest variables (considered measured without error) in the model will include a single study-arm binary exposure (intervention vs. UC) and provider-level percentage of eligible visits at which HPV-V promotion occurred in the pre- and post-intervention time periods. Multiple items in the provider survey may be used to measure change in each of the three hypothesized behavioral mechanisms. Therefore, the adequacy of the measurement model for the mediators can be addressed and each of the three potential mediator variables will be assessed as changes in latent constructs from baseline to 6-months following intervention implementation. Following quantification of relationships between intervention exposure and primary outcome (change in HPV-V promotion), intervention exposure and behavioral mechanisms (aka mediators), and mediators and primary outcome (change in HPV-V promotion), the LCS SEM model will produce an estimate of total and individual indirect effects for the three mediators and standard errors and will assume non-causal associations among mediators. A sensitivity analysis will use the interventional effects method to estimate individual indirect effects[79,80] which is appropriate when the structural dependence between the multiple mediators is not well-understood. The analysis of Aim 7 will utilize Mplus 7.[81]

Sample size justification and power.

Aim 5. The analytic sample for Aim 5 consists of index dental encounters for patients (the first dental encounter within the pre- or post-intervention period) who are eligible for HPV vaccination but have not initiated - or have initiated but not completed, HPV vaccination. For the H5 analysis dental encounters are accrued in a 12-month pre-intervention period and 12-month post-intervention period that follows a 6-month intervention run-in. To estimate dental encounter volume a data pull in 2021 for patients age 11-26 indicates there are 3870 (1858 F + 2012 M) index encounters over one year for patients age 11-26 who have not initiated HPV vaccination, and 4259 (2221 F + 2038 M) index encounters for patients age 11-26 who have initiated but not completed the HPV vaccination series. The combined sample of 8129 (3870 + 4259) post-intervention index encounters at which provider actions are assessed plus a similar count (assumed to be 8129) in the 12 months prior to intervention (N=16,258 total) forms the denominator for the analysis of H5. With 21 clinics randomized to 2 conditions, 8129 index dental encounters in the pre- and post-intervention periods, and an intraclass correlation coefficient (ICC) assumed of .01-.03, this analysis has 80% power to detect an absolute difference of 5-10% in HPV-V promotion in intervention compared to UC clinics (e.g., 15% intervention versus 10% usual care for ICC=.01, 30% intervention vs. 20% UC for ICC=.03). This assumption is based on other intervention studies showing an increase of HPV-V between 10-20%.

Aim 6 (H6a, H6b, H6c). The analytic sample of n=131 dental providers for Aim 6 consists of n=47 general and pediatric dentists, n=79 registered dental hygienists and n=5 dental therapists. Based on prior surveys of dentists in this care system we expect 70% (n=92) will complete both surveys. Providers will be surveyed prior to the intervention training and 6 months following the start of the intervention. For the power analysis, the

endpoints for Aim 6 are assumed to be approximately normally distributed so that general linear mixed models will be utilized. The clinic-level ICC for the Aim 6 endpoints is not known but assumed to be in the range of .01-.03. With 21 clinics randomized to 2 conditions, and 92 providers (4-5 per clinic) completing both surveys, this study has 80% power (alpha=.05, two-sided tests) to detect a minimum detectable standardized effect of 0.63-0.67 change in the Aim 6 endpoints in the intervention compared to UC condition.

Aim 7. The planned mediation analysis is expected to include surveys from n=92 providers at each of two time periods and their associated HPV-V promotion activities linked to approximately 8,000 dental encounters at each of two time periods. To address mediation questions with such data, models will all be conducted at the level of the provider, with aggregation of dental encounters to the provider level, disaggregation of study arm assignment to the provider level, and will utilize parameter constraints as feasible to simplify models. Evidence of estimation problems such as convergence, inadmissible solutions, or unstable parameter estimates may require specification of single-mediator models or further model simplification.

Patient/parent/guardian survey. Results from this survey (n=200 completed surveys expected per study arm) will provide an indication of how effectively dental providers were able to communicate HPV-V messages to their patients and the perceived strength of these messages. Analyses will also descriptively contrast surveys completed by patients and parents/guardians.

Secondary and Exploratory analyses. Potential disparities in intervention delivery will be addressed via exploratory analyses examining the heterogeneity of the effects of the intervention on HPV-V promotion activity in pre-specified subgroups: patient age (11-15, 16-20, 21-26), sex, and race/ethnicity, as feasible. The Aim 5 analytic model will incorporate interaction terms of patient factors and study arm by time fixed effects and utilize contrasts to estimate parameter estimates and standard errors within these subgroups. Patient-level exploratory endpoints by study condition include a binary indicator of receipt of HPV-V within 30 days of the eligible visit. These exploratory endpoints are consistent with current US HPV-V recommendations.[82]

Missing data. Any HPV-V promotion activity will be captured in the CDS during eligible visits and utilized for the analysis in Aim 5. The absence of a record of HPV-V promotion at any eligible visit will be assumed to indicate that HPV-V promotion was not delivered at that visit. In sensitivity analyses, the patient report of receipt of HPV-V promotion will augment a missing indication from the provider. The mixed-model likelihood-based estimation used in the analysis of repeated survey data in Aim 6 will allow use of all provider survey data. Likelihood-based ignorable methods ensure accurate parameter estimates assuming data are missing at random (MAR). A sensitivity analysis will utilize an inverse probability weighting approach using information from the baseline survey and administrative data to differentially weight provider survey data. Visit eligibility is based on patient age and vaccination status which emanates from any of several state vaccination registries, which historically have relatively low rates of incomplete or missing vaccination information.

4.7 Dissemination Plan

In accordance with internal policy in place at HealthPartners Institute, the award will be registered and results promptly posted on ClinicalTrials.gov within specific timelines outlined by NIH policy. Posted results will include only aggregated data, and additional measures will also be taken as needed to protect patient privacy and confidentiality. Consent documents, when applicable (i.e., for patient and provider surveys) will include a specific statement relating to posting of clinical trial information on ClinicalTrials.gov.

In addition, the study team will present results at national meetings and in peer-reviewed journals, and the investigators are available for any further dissemination activities that NIDCR staff deems appropriate. As study findings become available, the team will share aggregate results with HealthPartners clinical leaders and staff of the HealthPartners Dental Group clinics involved in the study. The team will also share results with their national collaborators from the National Dental Practice-Based Research Network and the Health Care Systems Research Network. Further, the team will share the intervention materials developed as a part of this study, including provider trainings, scripts, and the rules that serve as a foundation for the clinical decision support (CDS) tool. The team will further develop a publications and presentations plan to broadly disseminate results. Potentially these results could be shared with organizations such as the American Dental Association who could assist in strategies to make the intervention components readily available through various electronic distribution methods. If efficacy is demonstrated, the team would also look for implementation funding opportunities to disseminate more broadly with a target on disparate populations with low vaccination rates.

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
The form does not have any delayed onset studies			

Multiple PI Leadership Plan

Overview

For this proposed UG3/UH3 project, we intend to utilize the multiple Principal Investigator (PI) leadership model for study leadership. D. Brad Rindal, DDS and Patricia Mabry, PhD will share leadership for this cluster-randomized trial. Both PIs will be jointly and equally accountable to the grantee organization for the overall conduct of the project. Together, Drs. Rindal and Mabry will share the authority and responsibility for directing and leading all intellectual and logistical components of the project.

Rationale for Multiple Principal Investigators

Drs. Rindal and Mabry's complementary expertise will be valuable in leading a project of this type. Specific expertise and methods include real-world clinical trials, behavior change and delivery of interventions utilizing electronic health records with embedded clinical decision support. In leveraging the complementary research strengths and interests of the PIs and the entire research team, this study will develop and test an intervention to increase HPV vaccination promotion by dental providers.

D. Brad Rindal, DDS is a board-certified dentist and researcher with a clinical focus on TMD/orofacial pain. His research focus is on practice-based research and testing new approaches to improve dental care delivery and the translation of research into daily practice. He is the Director of the Midwest Region of the National Dental Practice-Based Research Network (U19DE022516, PI: Gregg Gilbert) funded by NIDCR through the University of Alabama, Birmingham (National Dental PBRN). The network involves practicing dental providers in the development of clinically important research questions and the collection of research data. Dr. Rindal has acted as PI or co-investigator on many federally-funded projects.

Patricia Mabry, PhD is a Research Investigator at HealthPartners Institute with a doctoral degree in clinical psychology. Relevant to the proposed project, she has experience as a clinician providing direct patient care in medical settings and as researcher conducting behavioral intervention development. She has experience developing behavior change interventions (i.e., tobacco cessation, dietary and exercise interventions) and testing these interventions through research. Dr. Mabry has experience in user-centered design (smokefree.gov), leading and contributing to several federally funded grants. She currently serves as PI of a NSF-funded grant focused on to identifying and characterizing social capital accumulation pathways that may explain funding gaps in the biomedical research workforce (NSF/2122232).

Shared Leadership and Governance

The PIs will employ joint decision-making for all aspects related to leading, directing, and administering the project. The PIs will ensure that policies, procedures, and work processes are in place to guarantee institutional compliance with US laws, DHHS, and NIH policies including human research, data, infrastructure, and facilities. The PIs will also ensure the development and implementation of any new policies and procedures or adjustments in existing ones as necessary to guide proper conduct of research described in the proposal. Project decisions, requiring any re-allocation of funds or revisions to the Leadership Plan during the project period, will be made via a joint decision of the PIs and their institutions. HealthPartners Institute is the applicant institution for this proposal, and Dr. Rindal will be the contact PI responsible for submitting all necessary documents to NIH, including IRB approvals and required reports. The PIs will utilize a single shared budget with joint oversight throughout the project period. The PIs will work closely together to ensure the integrity and execution of the infrastructure, evaluation plan, the timely completion of reports, and discussion of any changes needed in the direction of the research project and the reprogramming of funds, if necessary. The PIs will provide direct supervision of key personnel and coordination of project management.

Roles and Responsibilities of PIs

Drs. Mabry and Rindal will work together with joint responsibility for this project. Both PIs will oversee all project activities for their respective aims including finalizing the study protocol and manual of procedures, establishing the research team for the clinical trial project period, supervising personnel assigned to this project, and preparing and presenting study results/progress to professional forums. Both will assume all fiscal and administrative management responsibilities, including maintaining communication among investigators and key personnel through regular meetings. They will both be responsible for overseeing project implementation, addressing the specific aims, the leadership plan, and ensuring that systems are in place to guarantee institutional compliance with US laws, DHHS, and NIH policies including biosafety, use of human subjects, human and laboratory research, data, and facilities. Both will consult with the project's statistician in matters including design, implementation, interpretation of the data, and reporting of study results.

Dr. Rindal will serve as Contact PI as the primary liaison with HPDG stakeholders, including dental group leadership and staff from participating dental clinics. He will engage with HPDG stakeholders, including leaders, providers, and clinic staff, during the UG3 phase to get input on the intervention development, and throughout the UH3 phase to ensure the successful implementation and maintenance of the intervention. Dr. Rindal will contribute his expertise in practice-based dental research and cluster-randomized clinical trials leveraging CDS and tailored scripts to all aspects of the study including protocol and intervention development, implementation, analysis and dissemination.

Dr. Mabry will Mabry will assume leadership for incorporating behavior change theory and The NIH Stage Model of Intervention Development into the development of the intervention and study design as well as the analysis and interpretation of results. She will also guide plans for measuring behavioral mechanisms via provider surveys as well as the plans for monitoring provider fidelity to the intervention. In close collaboration with the project manager, Dr. Mabry will oversee the delivery of the provider training to all relevant staff in the intervention clinics.

Both PIs will be responsible for initiating, maintaining, and documenting communications with co-investigators, consultants, and the project team. The PIs will communicate weekly through meetings and other communications as appropriate. The PIs will also jointly manage the integration of all resources needed for the project and production of reports and publications. Report writing will be shared among all project investigators. A publication plan will be established with specific details regarding publication authorship based on the relative scientific contributions of the PIs and key personnel, and on authorship and contributorship standards for manuscripts submitted to biomedical journals.

Conflict Resolution

Both PIs have been engaged in numerous successful collaborative research projects with a variety of investigators for years. While it is doubtful that conflicts will arise as this work proceeds, the PIs have discussed and documented here a plan of action for managing any conflicts. If a potential conflict develops, the PIs shall meet and attempt to resolve the dispute. If a potential conflict is not resolvable by the PIs, the appropriate co-investigators representing the PIs shall meet and attempt in good faith to settle any dispute, claim, or controversy arising out of or relating to the interpretation, performance, or breach of this disagreement. If the administrators fail to resolve the disagreement within thirty business days, then such disagreement shall be referred for resolution to a designated senior executive at the HealthPartners Institute who has the authority to settle the disagreement but who is not directly involved in the disagreement.

Intellectual Property

The two PIs are aware of the copyright and intellectual property policies at the HealthPartners Institute. The policies are consistent in honoring the possibility for jointly held ownership of any future work that may result from this work. Rights in any pre-existing intellectual property will remain the property of the party that created and/or controls it.

Change in PI Location

If a PI moves to a new institution, attempts will be made to transfer the relevant portion of the grant to the new institution. In the event that a PI cannot carry out his duties, a new PI will be recruited as a replacement at one of the participating institutions.

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Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings

Letters of Support Table of Contents

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February 18, 2022

Brad Rindal, DDS
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Patricia Mabry, PhD
Research Investigator
HealthPartners Institute
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Dear Drs. Rindal and Mabry,

I am pleased to provide my support for your research application to the National Institute of Dental and Craniofacial Research entitled “Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings.”

As the Director of the HealthPartners Dental Group, I want to affirm my support for implementing this study within HealthPartners dental clinics. As you know, we recently worked closely with the pediatrics department to develop and implement a pilot study to increase HPV vaccine completion rates among our pediatric patients. Now, with the help of your colleagues at the Institute, the Center for Oral Health Integration is moving forward with the development of a clinical decision support (CDS) system embedded in the electronic dental record which will include alert providers when patients are due for the HPV vaccine and will allow for easy access to information on patients’ HPV vaccine status. HPV vaccination is a priority for the dental group given the link between HPV and oropharyngeal cancer and the growing calls for dental practices to actively engage in HPV vaccine promotion efforts. Your study will help us better understand how to meet this priority while building from the tools and processes that we have already developed. We therefore welcome your project and the randomized trial you have proposed.

I understand that as a part of the study, providers will be asked to participate in training on HPV vaccination and how to best talk to patients and parents about the importance of vaccination to protect against oropharyngeal cancer. Given the value that we see in this type of training, I and the rest of the dental leadership team are prepared to endorse the training and will encourage the participation of all eligible providers and support staff. Based on our experience working with you, Dr. Rindal, on similar studies, which have included provider training and clinical decision support tools with scripts integrated within the electronic dental record, I am confident that you will be able to effectively engage providers in this study and capture all necessary data. I was glad to learn that you are working with Don Worley and the Epic team to integrate the study components within the dental workflow, including the structured data fields that will be added to determine if a provider talked to his or her patient about HPV vaccination. By fully integrating the study within current workflows, you are well positioned to develop an intervention that will be well received and sustainable.

Given your complementary expertise and your research and leadership experience, I am confident that you and your team will be successful in meeting the study aims. You have assembled an impressive team of researchers with expertise in dental research, behavioral health, HPV, oropharyngeal cancer, and clinical decision support. I am pleased to support this work and will do all I can to ensure that the study is smoothly implemented in HealthPartners dental clinics. As a strong advocate of clinical research, I look forward to learning from this project and sharing the findings with our organizational leaders.

Sincerely,

David S. Gesko, DDS

David S. Gesko, DDS
Dental Director and Sr. Vice President, HealthPartners

Our mission is to improve health and well-being in partnership with our members, patients and community.

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February 9, 2022

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Dear Brad and Patty,

I am pleased to provide my sincere support for your upcoming grant proposal to the National Institute of Dental and Craniofacial Research titled: “Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings.”

The proposed engagement of dental providers in HPV vaccine promotion is innovative and strongly aligns with HealthPartners’ priority of providing comprehensive care through enhanced care integration. HealthPartners is an ideal setting for this study given our linked medical and dental electronic health records and the availability of vaccine data, including the data from the Minnesota and Wisconsin state immunization registries with which we have a bidirectional linkage. In addition, our researchers, supported by our skilled informatics team, have considerable experience developing, implementing, and evaluating clinical decision support (CDS) tools that are embedded into the Epic electronic health record and seamlessly integrated into the care delivery workflow. Many of these CDS tools that were developed as part of research studies have proven to be of great benefit to our patients and providers and have therefore continued to be used in care delivery beyond the conclusion of research. In addition, we have partnerships with a couple of regional health systems with which we have shared CDS tools and implementation strategies. Overall, our organization is prepared and well equipped with the resources needed to carry out this project.

You have convened an impressive team with exceptional expertise in oral health, HPV, and vaccine research as well as informatics and CDS tool development and implementation. I am extremely confident that you will be successful in meeting the aims of this study and I am happy to lend my strong support to this proposal. By examining how to effectively engage dental providers in HPV vaccine promotion and the mechanisms that promote this engagement, your project has the potential to help increase HPV vaccination referrals and uptake and may serve as a model for other organizations. As a leader in behavioral health research and health promotion initiatives within our organization and with partners across the country, and I would be happy to help share the results of this study with relevant stakeholders.

Best of luck on the application, and please keep me informed of how I may continue to support this important project.

Sincerely,

Nico Pronk, PhD
President, HealthPartners Institute
Chief Science Officer, HealthPartners, Inc.

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March 2, 2022

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Dear Drs. Rindal and Mabry,

I am pleased to provide my support for your research application to the National Institute of Dental and Craniofacial Research, “Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings.”

As a member and the former chair of the HealthPartners Immunization Expert Panel, I am involved in vaccination initiatives to ensure safety and optimal preventive care. Unfortunately, HPV vaccination rates lag behind those of other vaccines and there is still significant work to be done in order to bring rates up to goal levels. This is true on both a national and local level. While HealthPartners has taken steps to increase the initiation and completion of the HPV series in age-eligible individuals, there are still opportunities to better identify and address vaccine barriers such as provider inconsistencies in promoting vaccination and parent discomfort or dismissal due to the association with sexual health. Your study may help address some of these challenges by shifting the focus of vaccine messaging from sexual health to oral health and by systematically delivering tools to help providers discuss vaccination with patients and their parents through scripts within a clinical decision support platform embedded in the electronic health record. In addition, promoting vaccination at dental visits would give us another key opportunity to reach patients, and I agree that with the right messaging and approach, these gained opportunities could make a notable difference in vaccination rates.

Please do not hesitate to reach out to me as you have questions about HealthPartners vaccine initiatives, policies, and workflows. I appreciate your initiative in reaching out to partners from across the organization to ensure that the intervention you plan to develop will align with our immunization guidelines and our current efforts in HPV vaccine promotion. In addition, I am pleased that you are drawing from the expertise of Dr. Elyse Kharbanda in developing the provider training and the scripts for guiding conversations with patients and parents. It is imperative that we provide the most-up-to-date facts about HPV risk and HPV vaccination while carefully addressing both provider and patient concerns. By developing your intervention based on provider, patient, and stakeholder feedback, you stand to create a model that we can all benefit from.

I wish you the best of luck with the proposal and look forward to hearing about your progress.

Sincerely,

Poornima K. Kavathekar, MD
Immunization Expert Panel Member
HealthPartners Medical Group

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February 9, 2022

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Dear Drs. Rindal and Mabry,

I am delighted to provide this letter in support of your grant application to NIDCR titled: "Investigating Behavioral Mechanisms and Efficacy of a Provider-Directed Intervention for HPV Vaccine Promotion in Real-World Dental Settings." HPV vaccination is a key priority for our organization and I am happy to partner with your research team and HealthPartners Dental Group leadership to develop new and innovative ways to promote HPV vaccination across the HealthPartners patient population.

As the Department Chair for Pediatrics at Park Nicollet Health Services and Co-Lead of the HealthPartners Children's Health Initiative, I have been involved in numerous discussions and projects focused on improving HPV vaccination rates among our adolescent and young adult patients. It is clear that making a real and lasting impact on HPV vaccination rates will require multi-faceted efforts from partners across the healthcare community. Recently, I had the pleasure of working with leaders in the HealthPartners Dental Group on a pilot project focused on encouraging HPV vaccine completion among patients who received a first dose of the HPV vaccine but were overdue for the next dose. As part of this project, dental providers in two clinics received alerts within the electronic health record during visits with patients who were overdue for the HPV vaccine and were asked to remind the patients to get their next dose. The pilot project laid a promising foundation for future HPV vaccine promotion efforts, including your grant proposal. As you know, a key part of this pilot project was working with our Epic team to ensure that providers have access to HPV vaccination status, including state vaccination data available through the Minnesota and Wisconsin immunization registries. The work that Dr. Rindal is currently spearheading for the HealthPartners Center for Oral Health Integration which will make vaccination status readily accessible to dental providers through a clinical decision support platform builds from our pilot work and dovetails nicely with the proposed grant. By developing and testing enhanced tools and training to support dental providers in promoting HPV vaccination and examining the key behavioral mechanisms at play, your proposal will inform future efforts to better engage providers in vaccination efforts.

I was honored to be named the 2019 HPV Vaccine Cancer Prevention Champion for Minnesota by the Centers for Disease Control and Prevention and the American Cancer Society. This award represents the commitment and partnerships of people from across our organization working together to address HPV. While I am thankful for the recent progress we have made in raising awareness to this priority, there is still much work to be done to raise vaccination rates substantially. I welcome your help with this goal and look forward to learning about the results of your study. I am particularly glad to see that Dr. Elyse Kharbanda is on your investigative team to help develop and implement the provider training program. As you know, she is a board-certified pediatrician with experience working in the HealthPartners clinic system to develop provider support tools such as the one you plan to leverage in your proposed project. With her expertise in vaccine research, along with your complementary expertise in oral health and

behavioral health, I am confident that you will be successful in carrying out this study. Please let me know if there is anything additional that I or our pediatrics team can help you with in the development or implementation of your intervention.

Sincerely,

Andrea Singh, MD
Department Chair for Pediatrics, Park Nicollet Health Services
HealthPartners

Resource Sharing Plan. The goal of improving dental care delivery and improving population health is a priority to NIDCR, our health systems, and our research team. This project will be directed toward the goals of broad-scale dissemination, implementation, and improvement in dental practice via several pathways that will be pursued actively by this project team:

1. To facilitate the conduct of future research, we will create Limited Data Sets from the completed project in a manner consistent with human subjects protections and HIPAA privacy regulations. These data sets will be kept at HealthPartners Institute along with data dictionaries, coding manuals, and other documentation relevant to data collection or measurement issues. These resources will be available to the funding agency or to other approved investigators according to requirements imposed by the governing IRB and legal requirements, including HIPAA and Data Use Agreements.

2. Co-PI, Brad Rindal, DDS, is the Director of the Midwest Node of the **National Dental Practice-Based Research Network**, funded by NIDCR. Efforts will be made to make results available to all dentists in the network through its website. The investigators are also involved in the Health Care Systems Research Network (HCSRN), and have built strong bridges with affiliated large dental groups and dental plans. The team will share results with these partners.

3. We will share our findings internally with the dentists and the leadership within the HealthPartners Dental Group. Additionally, HealthPartners Institute has an active communications team that works to publicize our research results in local and national media.

4. Results from this study will be presented at national conferences and in peer-reviewed publications in aggregate form.

5. We will share the intervention materials developed as a part of this study, including provider trainings, scripts, and the rules that serve as a foundation for the clinical decision support (CDS) tool. Thus, the results of our work will provide the groundwork for broader dissemination and implementation of this intervention into other settings.