Pre-Application Webinar for
Funding Opportunity Announcement
RFA-CA-22-051

UG1 Clinical Sites for the HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

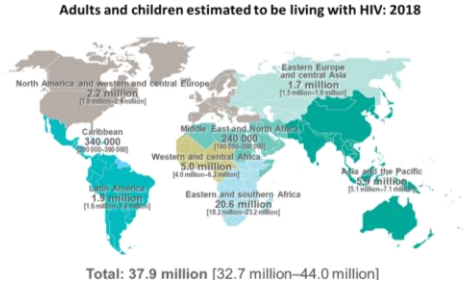
NIH NATIONAL CANCER INSTITUTE

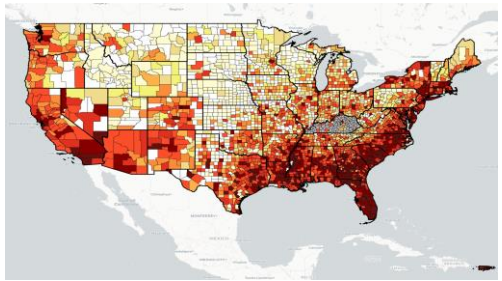
Vikrant V. Sahasrabuddhe
Division of Cancer Prevention, NCI/NIH

HIV/AIDS and Cervical Cancer: Intersecting Epidemics of High Public Health Significance

HIV/AIDS

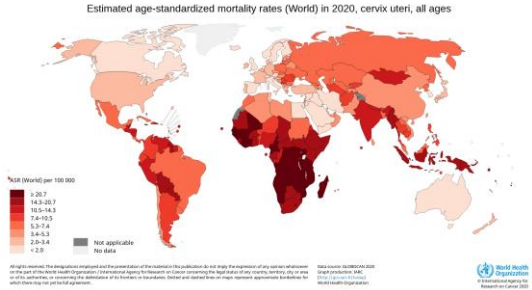
- Globally: >37 mill. persons, >18.8 mill. women with HIV
- US: >1.2 mill. persons, >250,000 women with HIV

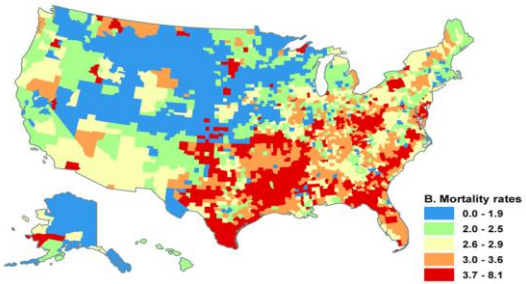




Cervical cancer

- Globally: >604,000 cases and >340,000 deaths *annually*
- US: >13,000 cases and >5,700 deaths *annually*





Refs: UNAIDS, 2018; AIDSVu 2020; IARC-WHO 2020; Horner et al 2011

HPV-mediated Cervical Carcinogenesis in the Context of HIV

Higher burden of HPV and cervical cancer among women with HIV

- accentuated by immunosuppression
- refractory to antiretroviral therapy

Cervical cancer among women living with HIV

- younger age at cancer diagnosis
- more aggressive clinical course
- less responsiveness to treatment

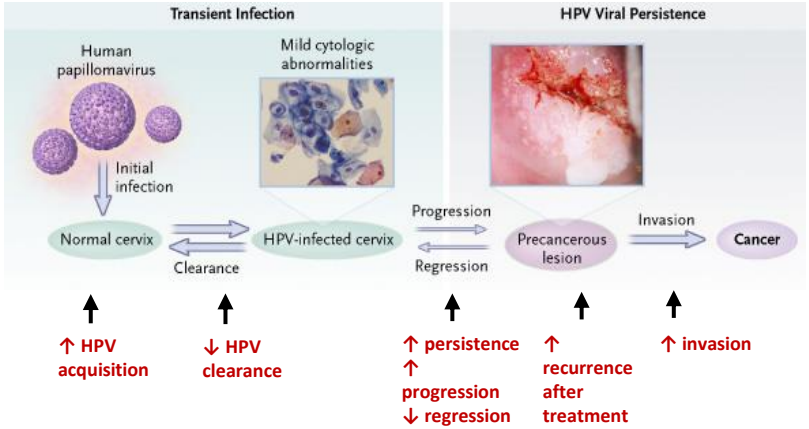
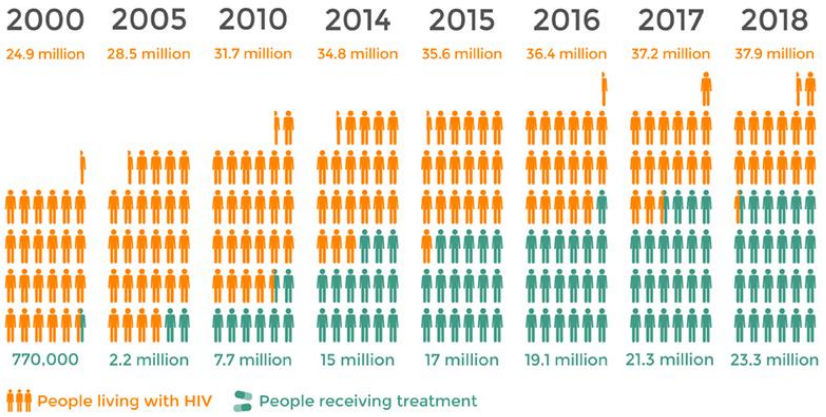


Figure ref: Wright & Schiffman, NEJM 2003

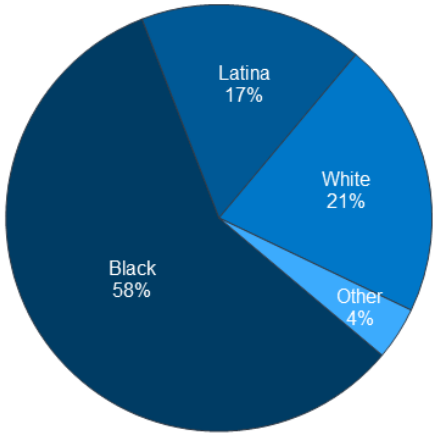


Ref: https://www.avert.org/global-hiv-and-aids-statistics

Why Should---and How Could---We Let Women With HIV Die Due to Lack of Effective Cervical Cancer Prevention Services after Extending their Lives with Antiretroviral Therapy?

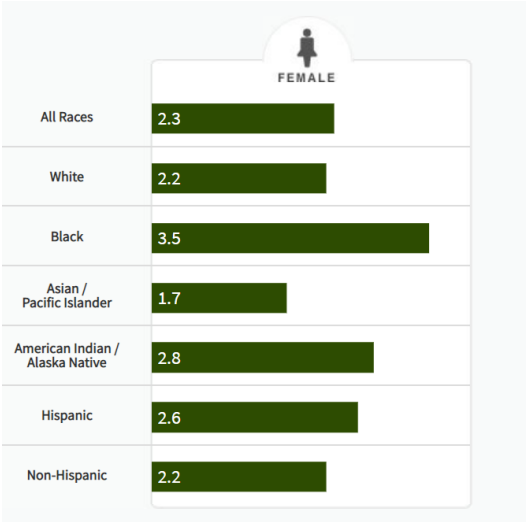
Racial and Ethnic Disparities are a prominent feature influencing the burden of both HIV/AIDS and Cervical Cancer in the United States

HIV/AIDS Diagnoses among Women in the US



Source: Kaiser Family Foundation 2018
https://www.kff.org/hivaids/fact-sheet/women-and-hivaids-in-the-united-states

Cervical Cancer Mortality Rates



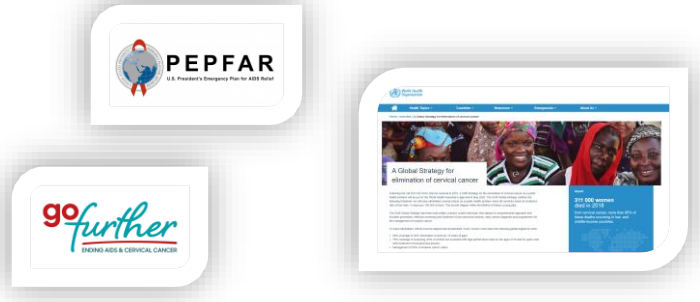
Source: NCI SEER Cancer Fact Sheets
https://seer.cancer.gov/statfacts/html/cervix.html

Rationale for the ‘CASCADE’ Clinical Trials Network

- **Acceleration in key catalytic technologies and regulatory pathways**:
  - HPV self-sampling approvals (‘Last Mile’ Initiative)
  - Development of point-of-care visual/diagnostic approaches
  - Multiple portable ablative/excisional devices in late-trials




- **Renewed impetus on bilateral and multilateral initiatives for cervical cancer screening and treatment**:
  - PEPFAR ‘Go Further’ HIV-Cervical Cancer Partnership expansion
  - World Health Organization’s Global Cervical Cancer Elimination Initiative



The **HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network**

will conduct **pragmatic clinical trials evaluating the effectiveness of clinically-proven interventions in intended-use settings** with a goal to optimize the cervical cancer screening and pre-cancer treatment cascade for women living with HIV

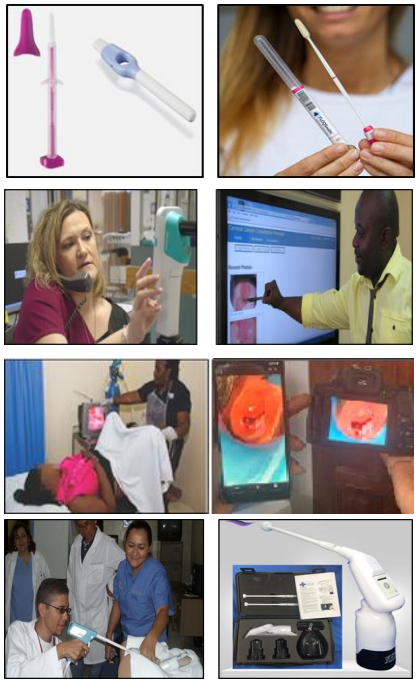
‘CASCADE’ Clinical Trials Network: Focus Areas and Study Designs

Clinical Trial Focus Areas

- **Increasing Screening Uptake**
- **Improving Management of Screen Positives**
- **Facilitating Precancer Treatment Access**
- **Optimizing Precancer Treatment**

Sites of Clinical Trials

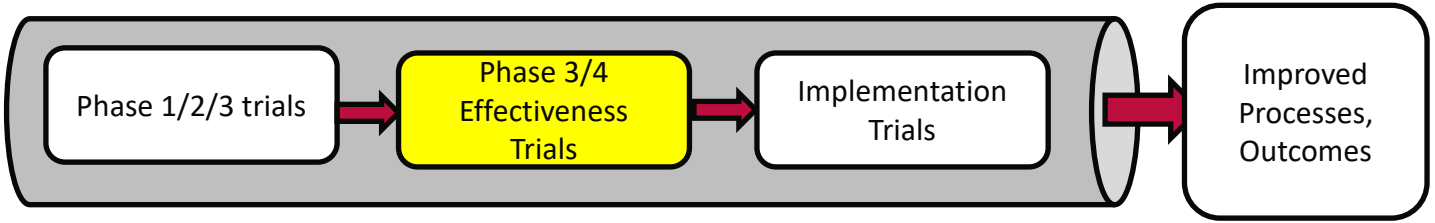
- Resource constrained settings in **Low- and Middle-Income Countries (LMICs)**
- Settings with high disease-burden and health disparities within the **United States**

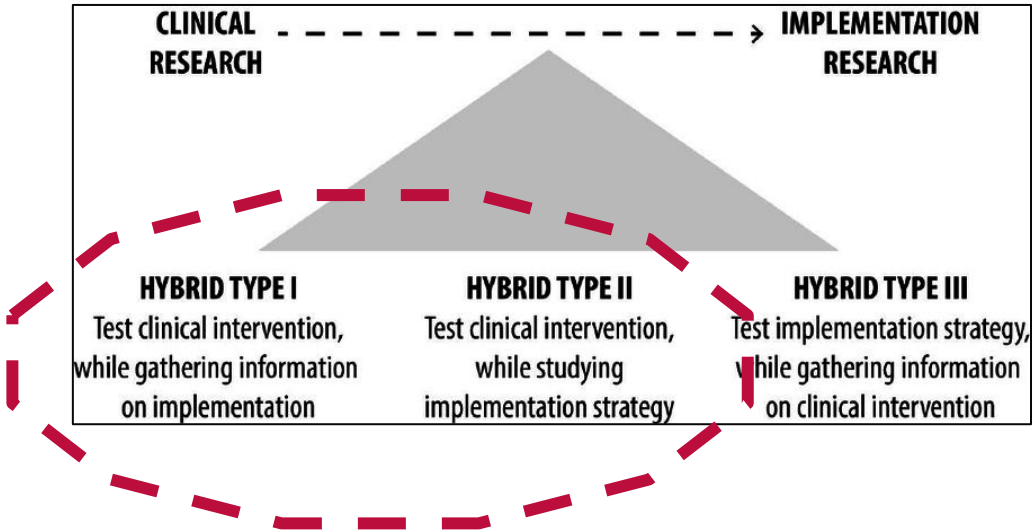


Pragmatic Phase 3/Phase 4 Clinical Trials with ‘Hybrid’ Effectiveness-Implementation Designs

- ***Clinical effectiveness outcomes***
  - Rates of HPV detection/precancer detection
  - Rates of post-treatment HPV/precancer recurrence
  - Rates of appropriate referrals
- ***Information to inform future implementation and scale-up***
  - Rates of uptake of intervention and reductions in attrition rates
  - Costs, acceptability, and implementation fidelity

‘CASCADE’ Clinical Trials Network: Scope of Clinical Trials





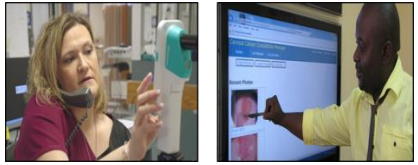
Ref: Conceptual Framework from Curran et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care 2012;50:217-26.

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

Scientific Areas of Focus

Increasing Screening Uptake

Improving Management of Screen Positives



Facilitating Precancer Treatment Access

Optimizing Precancer Treatment

https://prevention.cancer.gov/cascade

‘CASCADE’ Clinical Trials Network: Areas of Focus: Area 1

Area 1: Increasing Screening Uptake

Given the complexity and evolution in clinical care delivery for women with HIV, there is a need for developing innovative approaches that balance the need for maximizing the sensitivity for precancer detection while balancing costs and efficiency in screening.

Potential Designs

Compare HPV self-sampling strategies vs. standard of care (VIA/cytology)

- **Linked to HIV clinic visits**
- **Targeted outreach (navigators/mHealth)**
- **Camp-based approach**
- **Door-to-door ‘campaign’ coverage**

Potential Outcomes

- **Screening uptake and precancer detection rates**
- **Costs, acceptability, HIV-related stigma**
- **System-level barriers and facilitators**

Area 2: Improving Management of Screen Positives

Women with HIV have high cervical HPV prevalence, emphasizing the need for better methods to triage HPV-positive results to differentiate those with clinically important HPV infections (i.e., those that are associated with or will develop into cervical precancer and cancer) versus benign HPV infections destined to clear.

Potential Designs

Compare management strategies:

- **Same-visit ablation of all HPV positives (except visible cancers) without intermediate biopsy**
- **Triage with molecular biomarkers or visual approaches (same vs. deferred-visit)**

Potential Outcomes

- **Post-treatment HPV/ precancer recurrence rates**
- **Reduction in attrition through cascade**
- **Harms/risks of treatment**
- **Costs and acceptability**

‘CASCADE’ Clinical Trials Network: Areas of Focus: Area 3

Area 3: Facilitating Precancer Treatment Access

In many regions globally, a dearth of well-trained healthcare providers is a key constraint in implementing successful clinical and public health screening programs. Innovative ‘task shifting' models have relied on nurses and non-physician healthcare providers, while remote/telemedicine are being widely adopted globally, emphasizing the need for evaluating the comparative effectiveness of these approach

Potential Designs

Compare clinical decision-making strategies:

- **Independent decision-making by primary providers (‘Task shifting’)**
- **Telemedicine-based specialist consultations**

Potential Outcomes

- **Post-treatment HPV/ precancer recurrence rates**
- **Rates of appropriate referrals**
- **Reduction in attrition through the clinical care cascade**

‘CASCADE’ Clinical Trials Network: Areas of Focus: Area 4

Area 4: Optimizing Precancer Treatment

Variations in definitions of treatability of lesions, directly lead to variable performance and therefore affect the risk of precancer recurrence. Additionally, the multifocal nature of anogenital disease and the relative immunosuppressive state in women with HIV affects post-treatment recurrences. Evaluation of strategies comparing variations in treatment algorithms can provide evidence to optimize implementation for preventive therapy interventions among WLWH.

Potential Designs

Compare ‘screen-and-treat’ strategies with variations in:

- **Portable ablation vs. portable excision devices**
- **Treatability thresholds by cervical squamocolumnar junction involution status**

Potential Outcomes

- **Post-treatment HPV/ precancer recurrence rates**
- **Costs, acceptability**
- **Reduction in attrition through the clinical care cascade**

‘CASCADE’ Clinical Trials Network: design outline of a potential clinical trial

Clinics offering cervical cancer screening and treatment services to women with HIV

Clinic-level Cluster Randomization

Same-visit ablation of HPV positives (except visible cancers) without intermediate biopsy

Same-visit or deferred-visit ablation after triage with molecular biomarkers or visual approaches

Follow-up after 12 and 24-months

Follow-up after 12 and 24-months

Outcomes

- Post-treatment HPV/ precancer recurrence rates
- Reduction in attrition through cascade
- Harms/risks of treatment
- Costs and acceptability

The 'CASCADE' Clinical Trials Network will fill a gap in the spectrum of NCI-supported clinical and translational research on HPV/cervical cancer prevention

Blue: not exclusively HIV focused
Red: primarily HIV-focused

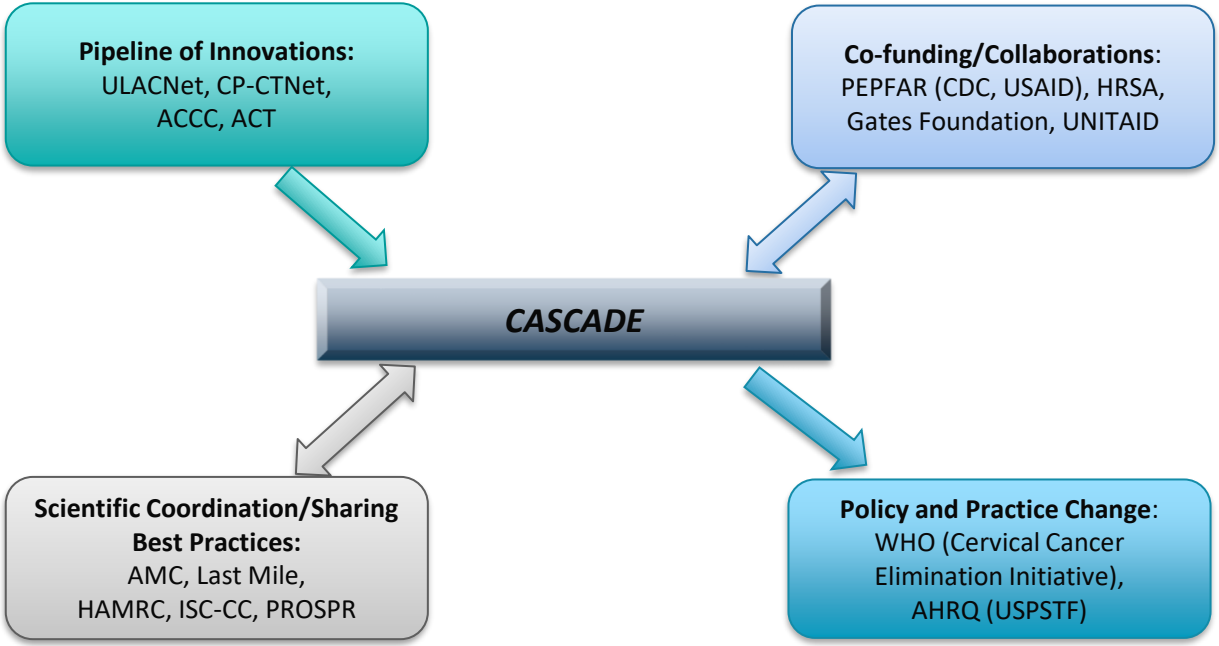
	T0 & T1	*T2*	*T2*	*T3 & T4*
	Pre-Clinical Development	***Phase 1/2/3 Clinical Trials***	***Phase 3/Phase 4 Clinical Trials***	***Dissemination & Implementation***
	Translation to Humans	**Translation to Patients**		**Translation to Practice**
Licensed HPV vaccines: dosing/uptake		CP-CTNet, ULACNet	HPV-1DT	ISC3, Impl-PLWH
Novel HPV vaccines	PREVENT, SPORE	CP-CTNet		
Licensed HPV tests: self-sampling		R01s	R01s, Last Mile, ***CASCADE***	PROSPR
Novel HPV molecular biomarkers	EDRN, ACT	ACCC, ACT, R01s, ULACNet	***CASCADE***	Impl-PLWH
Novel precancer diagnostic & imaging	EDRN, ACT	ACCC, ACT, R01s	***CASCADE***	Impl-PLWH
Novel ablative/excisional treatments		ACT	***CASCADE***	Impl-PLWH
HPV therapeutic vaccines	PREVENT	CP-CTNet, ULACNet, AMC		
Topical precancer therapeutics	PREVENT	CP-CTNet, ULACNet, AMC		
Management of invasive cancers		NCTN, NCORP, AMC	NCTN, NCORP, AMC	

ACCC: Cancer Moonshot 'Accelerating Cervical Cancer Control' initiative
ACT: Affordable Cancer Technologies Program
AMC: AIDS Malignancy Consortium
CP-CTNet: Cancer Prevention Clinical Trials Network
EDRN: Early Detection Research Network
HPV-1DT: NCI HPV vaccine One vs. Two dose trial in Costa Rica
ISC3: Implementation Science Centers for Cancer Control
Impl-PLWH: Implementation Science Research on PLWH

Last Mile: NCI Cervical Cancer 'Last Mile' Initiative
NCORP: NCI Community Oncology Research Program
NCTN: NCI National Clinical Trials Network
PREVENT: Chemoprevention Agent Preclinical Development Program
PROSPR: Population-based Research to Optimize the Screening Process
SPORE: Specialized Programs of Research Excellence
ULACNet: US Latin American Caribbean HIV/HPV-Cancer Prevention Clinical Trials Network

(Note: above listing is for illustrative purposes only, and is not an exhaustive compilation of all NCI programs)

‘CASCADE’ Clinical Trials Network: External Organizational Linkages

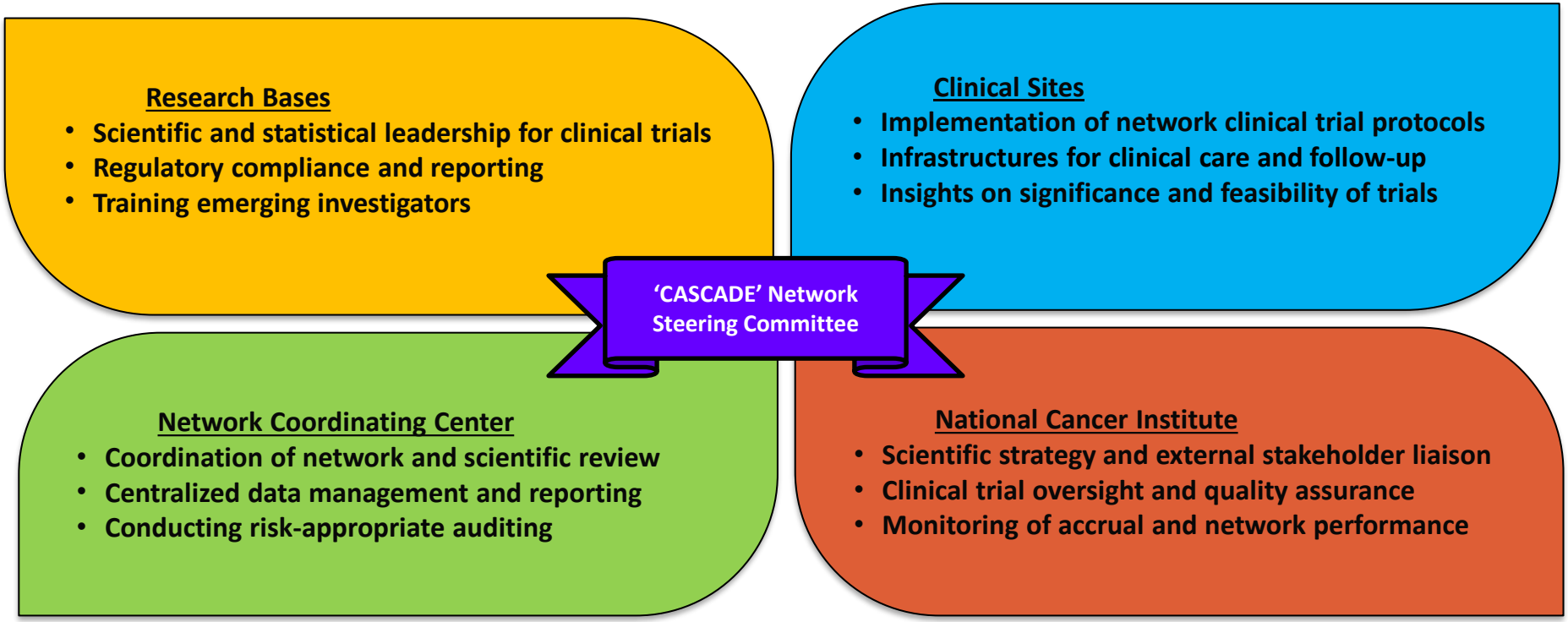


AHRQ: Agency for Healthcare Research and Quality
CDC: Centers for Disease Control and Prevention
HRSA: Health Resources and Services Administration
PEPFAR: President’s Emergency Plan for AIDS Relief
USAID: US Agency for International Development
USPSTF: United States Preventive Services Task Force
WHO: World Health Organization

ACCC: Cancer Moonshot ‘*Accelerating Cervical Cancer Control*’ initiative
ACT: Affordable Cancer Technologies Program
AMC: AIDS Malignancy Consortium
CP-CTNet: Cancer Prevention Clinical Trials Network
ISC-CC: Implementation Science Centers for Cancer Control
Last Mile: NCI Cervical Cancer ‘Last Mile’ Initiative

NCTN: NCI National Clinical Trials Network
NCORP: NCI Community Oncology Research Program
HAMRC: HIV-Associated Malignancy Research Centers
PROSPR: Population-based Research to Optimize the Screening Process
ULACNet: US Latin American Caribbean HIV/HPV-Cancer Prevention Clinical Trials Network

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network



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HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

CASCADE Organizational Units

Organizational Unit	Principal Investigator(s)	Institution(s)	Grant No.
CASCADE Network Coordinating Center (CNCC)	Susanne Siminski, M.B.A., KyungMann Kim, Ph.D., and Anna-Barbara Moscicki, M.D.	Frontier Sciences, with University of Wisconsin and University of California, Los Angeles	U24CA275417
Research Base 1 (RB1)	Rachel Winer, Ph.D., M.P.H. and Elizabeth Brown, Sc.D., M.S.	University of Washington, with Fred Hutchinson Cancer Research Center	UG1CA275402
Research Base 2 (RB2)	Timothy Wilkin, M.D., M.P.H., Anna Giuliano, Ph.D., and Carla Chibwesha, M.D., M.Sc.	Weill Medical College of Cornell University, with Moffitt Cancer Center and University of North Carolina at Chapel Hill	UG1CA275414
Research Base 3 (RB3)	Jennifer Smith, Ph.D., M.P.H., Michael Hudgens, Ph.D., and Lameck Chinula, M.D., M.P.H.	University of North Carolina at Chapel Hill	UG1CA275403
Clinical Trials Site 1 (CS1): Uganda	Betty Mwesigwa, M.B.Ch.B., M.Sc.	Makerere University Walter Reed Project, with US Military HIV Research Program and Uganda Cancer Institute	UG1CA275412
Clinical Trials Site 2 (CS2): Kenya	Michael Chung, M.D., Ph.D., M.P.H. and Samah Sakr, M.B.Ch.B.	Emory University, with Coptic Hope Center for Infectious Diseases and Kenyatta National Hospital	UG1CA275400
Clinical Trials Site 3 (CS3): Botswana	Scott Dryden-Peterson, M.D., M.S. and Doreen Ramogola-Masire, M.B.B.S., Ph.D., M.P.H.	Brigham and Women's Hospital, with Botswana Harvard AIDS Institute Partnership	UG1CA275416

+ 5 additional Clinical Trials Sites to be funded through RFA-CA-22-051 in 2023

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Funding Opportunity Announcement (FOA)

RFA-CA-22-051

Clinical Sites to JOIN the
HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network
(UG1 Clinical Trial Required)

Funding Opportunity Announcement for Clinical Sites to join the 'CASCADE' Network

Through the Funding Opportunity Announcement (FOA) RFA-CA-22-051, NCI will be soliciting applications from institutions/organizations to participate as international and domestic Clinical Sites for the HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network. The 'CASCADE' Network was launched in Fiscal Year 2022 with three organizational components through individual FOAs: the Network Coordinating Center (funded through RFA-CA-21-045), Research Bases (three organizations funded through RFA-CA-21-046), and Clinical Sites (three organizations funded through RFA-CA-21-047).

The FOA RFA-CA-22-051 (re-issue of RFA-CA-21-047) will support five additional UG1-Cooperative Agreement-funded Clinical Sites (anticipated to be two domestic and three international sites) to join the 'CASCADE' Network.

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HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

Clinical Sites

(previously funded under RFA-CA-21-047 and new sites to be funded under RFA-CA-22-051)

Participate as implementing sites of the multicenter network of institutions/organizations by providing access to potential study participants **for enrollment in pragmatic clinical trials** in the 'CASCADE' Network.

Interact with the UG1 Research Bases by

- providing insight into clinical significance during concept development,
- identifying healthcare disparities in their local populations that could be studied,
- providing input on feasibility during protocol development in the 'CASCADE' Network,
- creating recruitment plans to achieve trial accrual goals.

Interact with the U24 Coordinating Center:

- for undertaking activities related to centralized data management activities
- for risk-appropriate clinical trials auditing in support of 'CASCADE' clinical trials.

The range of experience and expertise for UG1 Clinical Sites should encompass **at least three of the four scientific focus areas of the network.**

https://prevention.cancer.gov/cascade

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

Clinical Sites

(previously funded under RFA-CA-21-047 and new sites to be funded under RFA-CA-22-051)

In the US: the UG1 Clinical Sites should include a major focus on women with HIV covered by Medicaid, the CDC National Breast and Cervical Cancer Early Detection Program (NBCCEDP), or by the Health Resources and Services Administration (HRSA)-Ryan White HIV/AIDS Care Program funding or seen at HRSA-funded Federally Qualified Health Centers (FQHCs) including Community Health Centers, Migrant Health Centers, Health Care for the Homeless, and Health Centers for Residents of Public Housing.

Internationally, the UG1 Clinical Sites should include a major focus on women with HIV receiving clinical care services through ongoing cervical cancer prevention and control initiatives, such as that through the PEPFAR 'Go Further' HIV-Cervical Cancer Partnership in high burden countries in sub-Saharan Africa, the World Health Organization's efforts through the Global Cervical Cancer Elimination Initiative, or other national-funded and/or bilaterally/multilaterally-funded clinical care service delivery initiatives.

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HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

Research Bases
(previously funded under RFA-CA-21-046)

Provide an established organizational structure, with scientific and statistical leadership for developing, implementing, and analyzing multi-institutional pragmatic clinical trials in the primary focus areas of the 'CASCADE' Network in partnership with the 'CASCADE' Network grantees and the NCI.

- increasing screening uptake
- improving the management of screen positives
- facilitating precancer treatment access
- optimizing precancer treatment for cervical cancer prevention in women with HIV

Assume responsibility for study operations, including efficient protocol development, and compliance with US and international regulatory requirements, human subject protection requirements, and applicable NIH, NCI, and DCP policies.

Provide opportunities for expanding training and capacity-building initiatives for programmatic implementation and scale-up of cervical cancer prevention interventions in intended use settings.

The range of experience and expertise for each UG1 Research Base encompass ***at least two of the four scientific focus areas*** of the 'CASCADE' Network

https://prevention.cancer.gov/cascade

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

Network Coordinating Center
(previously funded under RFA-CA-21-045)

Network-wide coordination and scientific review of clinical trial concepts and protocols

- overall network coordination: administrative support, program and logistical coordination.
- scoring system framework for review of clinical trial concepts and protocols
- organize, support, and coordinate activities of a network-wide data safety monitoring committee
- support standardized receipt and bidirectional secure distribution of protocol and review documents

Provision of centralized data management support for network clinical trials

- 'fit-for-purpose' centralized clinical data management system (cloud-based and offline, facility and remote/field-based).
- data management policies for quality data collection to ensure adequacy, integrity, and legitimacy of data
- routine and ad-hoc reporting of clinical trials data using pre-designed and custom formats.
- develop appropriate web-services as per industry best practices for system-to-system data exchange of clinical trial data.

Conduct of independent risk-appropriate auditing of network clinical trials

- Independent risk-appropriate auditing activities (remote/virtual and on-site) of UG1 Research Bases and UG1 Clinical Sites, as per GCP and applicable regulatory requirements, federal regulations, and NIH/NCI/DCP policies.
- Collaboratively identifying areas for systemic and policy-level improvements in order to increase both efficiency and compliance, ensure the protection of human subjects, and enhance the quality and integrity of 'CASCADE' clinical trials.

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HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

'CASCADE' Network Steering Committee

- Governing body of the 'CASCADE' Network
- Seek to integrate the efforts of all network recipients
- Permit collaborative interactions with the NCI
- Provide joint oversight of network activities.
- Reviewing and prioritizing clinical trial concepts and making recommendations about selection of study implementation sites after balancing competing considerations around scientific focus, geographic distribution of studies across the network, trial accrual targets, protocol implementation complexity, and strategic partnership opportunities.

Composition

- Two representatives from each network award recipient (i.e., from each UG1 Research Bases, each UG1 Clinical Sites, and the U24 Coordinating Center), one of whom must be the PD/PI: **one vote for each award** they represent.
- NCI representation: **one vote for NCI**: Project Scientist (voting member), Program Official (non-voting member).
- Additional non-voting members may be added to the committee as needed.

https://prevention.cancer.gov/cascade

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network
Protocol Teams and Program Operations

Protocol Teams:

- Protocol Chair(s): UG1 Research Bases
- Protocol Statisticians: UG1 Research Bases
- Site Principal Investigator #1: UG1 Clinical Site #1
- Site Principal Investigator #2: UG1 Clinical Site #2
- Site Principal Investigator #3: UG1 Clinical Site #3
- Site Principal Investigator #4: UG1 Clinical Site #4
- …
- NCI Project Scientist(s)

Research Support:

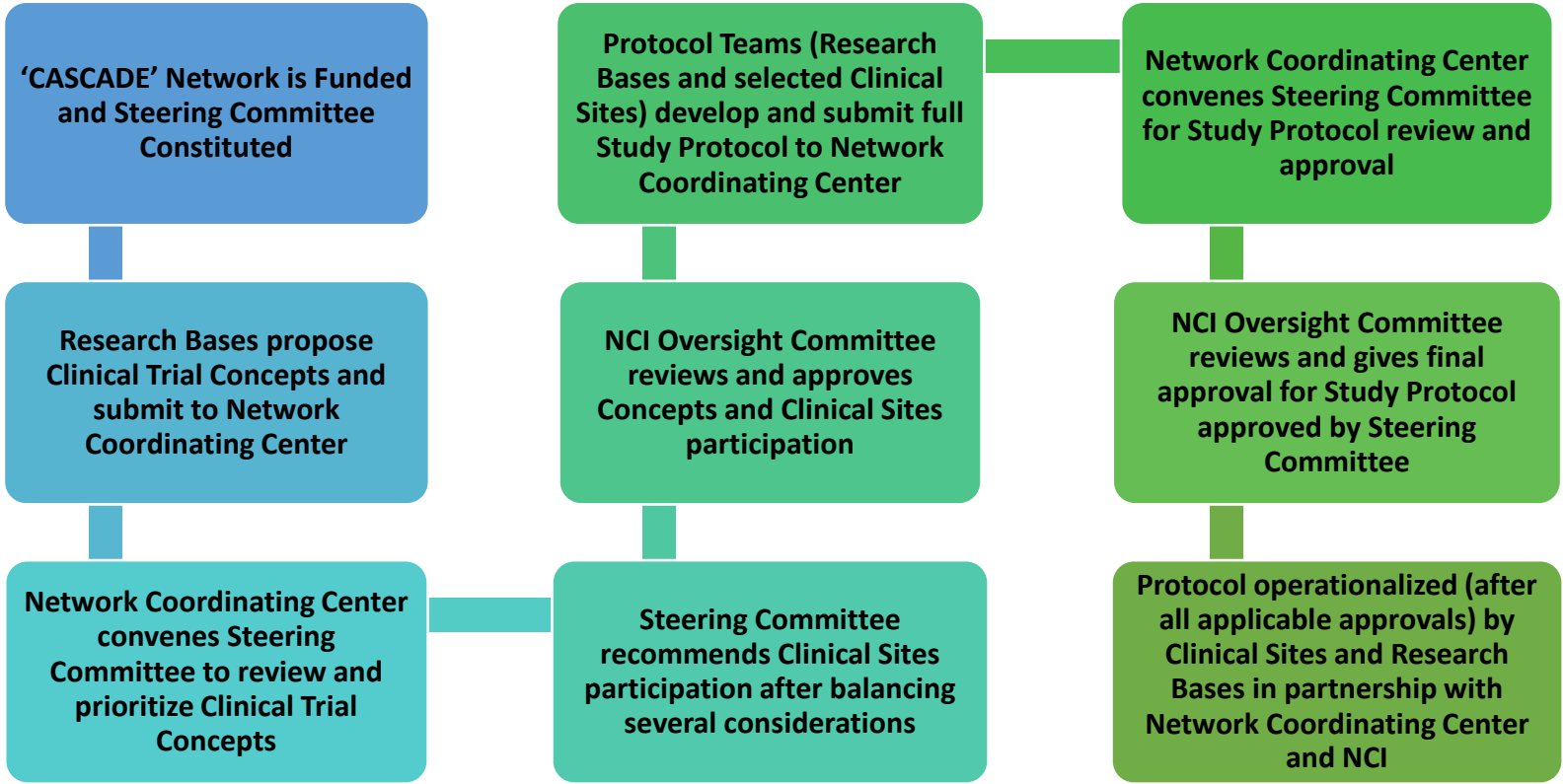
- Oversight, Compliance: UG1 Research Base Admin Staff
- Local Site Clinical Support: UG1 Clinical Site Clinicians
- Local Site Operations Support: UG1 Clinical Site Research Staff

- Data Management Support: U24 Coordinating Center: Unit 2
- Risk-appropriate Auditing: U24 Coordinating Center: Unit 3

Concept and Protocol Review:

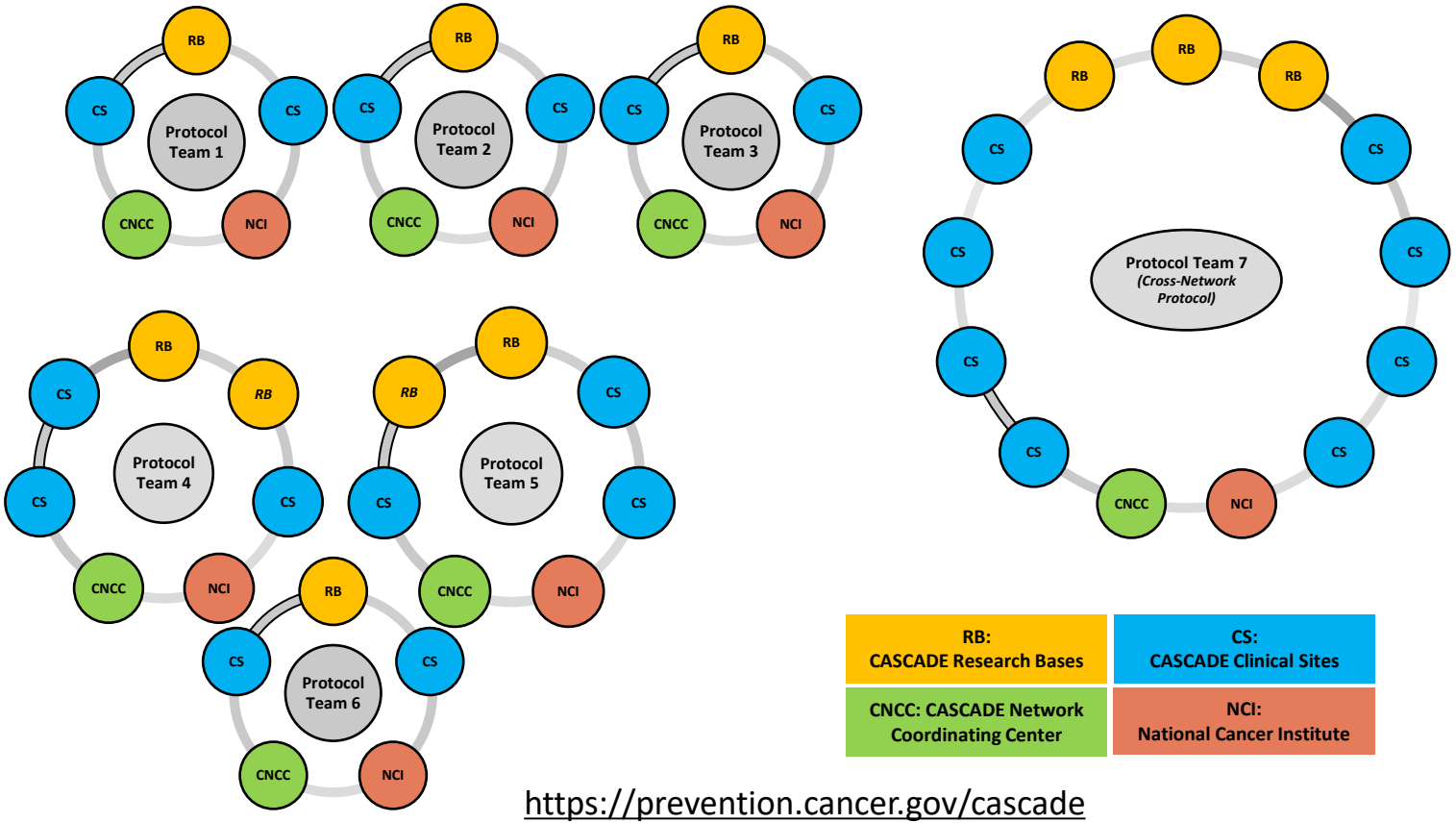
- Network Steering Committee
- NCI Oversight Committee
- Coordination/Scientific Review: U24 Coordinating Center: Unit 1

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network
Concept and Protocol Development Process



HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

'CASCADE' Protocol Teams (for illustrative purposes only)



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'CASCADE' UG1 Clinical Sites: Eligibility

	UG1 Clinical Sites
	RFA-CA-22-051
Applicants	
US Institutions	Yes
Foreign (LMIC) institutions	Yes
Components	
US Institutions	Yes
Foreign (LMIC) institutions	Yes

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network
Funding Opportunity Announcement for UG1 Clinical Sites: RFA-CA-22-051

'CASCADE' UG1 Clinical Sites: Submission Information

	UG1 Clinical Sites
	RFA-CA-22-051
Maximum Direct Costs	**$200,000 per year for 4 years**
Page Limits	
• Specific Aims	1 page
• Research Strategy	6 pages
Other Attachments	
• No. of attachments	1
• File names of attachments	'Catchment Area'

*Introduction to Resubmission and Revision Applications: 1 page

*FOA instructions for page limits supersede instructions on https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/page-limits.htm#other

'CASCADE' UG1 Clinical Sites: Submission Information

	UG1 Clinical Sites
	RFA-CA-22-051
Maximum Direct Costs	**$200,000 per year for 4 years**
Research Strategy Page Limits	6 pages*
• Sub-section A	Clinical and Research Leadership
• Sub-section B	Implementing Clinical Trials
• Sub-section C	Strategies for recruitment and retention
• Sub-section D	--

*FOA instructions for page limits supersede instructions on https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/page-limits.htm#other

'CASCADE' UG1 Clinical Sites: Budget Information

Maximum Direct Costs: $200,000 per year for up to 4 years

Key Personnel Costs:

- ***PD/PI Effort Commitment***
  - Contact PD/PI: minimum effort: 2.4 person-months (20%).
  - Multiple PD/PI: each PD/PI: minimum effort of 1.2 person-months (10%)
  - Levels cannot be reduced during the project period.
- ***Personnel for 2-4 clinical trials*** *(ranging widely in scope, geographic settings, and sample size)*
  - Clinical and scientific staff
  - Administrative and clinical research staff

'CASCADE' UG1 Clinical Sites: Budget Information

Maximum Direct Costs: $200,000 per year for up to 4 years

- **Leveraging ongoing cervical cancer prevention service delivery programs**
  - Most standard-of-care costs would be covered by service delivery programs including costs for screening tests (e.g., visual inspection-based screening) and precancer treatment equipment (e.g., portable thermal ablators or cryotherapy devices).
  - Relevant costs for implementing clinical trial-specific procedures may be included in the budget.
- **Budget line item of at least $25,000 per year under 'Other Costs'**
  - to cover various novel/experimental interventions (e.g., interventions not already covered by the current standard of clinical care activities including any novel point-of-care HPV tests, newer self-sampling devices, novel screening/imaging devices, newer precancer treatment devices, etc.)
  - details not known at the time of the application (and will be known only after the protocols are approved after site joins the network)
- **NCI may consider additional supplemental protocol-specific funding to sites:** *however, since details of protocols are not known at time of application; this possibility should not be accounted for in the budget or referenced in the application*
- **Additional Budget Instructions:**

  The following costs should ***not be*** included in the budget:
  - Costs associated with routine patient care that are reimbursable by insurance.
  - Costs for alterations and renovations

'CASCADE' UG1 Clinical Sites: Submission Information

- Applicants are ***not expected to propose specific concepts and protocols*** as part of their applications in response to the FOA.

- Please note that under Section IV.2 in the 'PHS Human Subjects and Clinical Trials Information', applicants are not required to complete a study record (i.e., not expected to present details of individual trials) and are only required to indicate that 'Multiple Delayed Onset Studies' will be conducted through the 'CASCADE' Network.

- Coordination between potential applicants for the UG1 Clinical Sites and existing awardees (Research Bases, Clinical Sites, Coordinating Center) is ***not expected*** prior to application.
  - The 'CASCADE' Steering Committee, which will include the successful applicants, will review and prioritize clinical trial concepts and selection of implementation sites for individual studies.

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network
Funding Opportunity Announcement for UG1 Clinical Sites: RFA-CA-22-051

"Clinical Trials Required": Section IV.2: Study Record: PHS Human Subjects and Clinical Trials Information

- All instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions: Only choose 'Delayed Onset Study
- Study Title--use: "Multiple Delayed Onset Studies"
- Justification Attachment:
  - Applicants are not expected to propose specific concepts and protocols as part of their applications in response to these three FOAs.
  - **Only indicate** that the 'CASCADE' Network clinical trials will be designed by the UG1 Research Bases and implemented at the UG1 Clinical Sites with assistance and oversight from the U24 Coordinating Center and NCI during the Project Period. Each clinical trial concept developed will be subject to approval through the 'CASCADE' Network Steering Committee and each protocol will be subject to approval by the NCI Oversight Committee prior to activation. The Coordinating Center will participate for providing infrastructure support for scientific review and program coordination, data management, and independent risk-appropriate auditing for network clinical trials.

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- PDs/PIs of applications submitted in response to this FOA ***must not be named*** as Senior/Key Personnel or Other Significant Contributors on any teams previously funded under FOAs RFA-CA-21-045, RFA-CA-21-046, and RFA-CA-21-047.

- NCI's goal is to maximize participation of diverse institutions and permit applicants to tailor applications to their most suitable expertise/organizational elements.
  - Example:
    - Dr. XYZ is a PI/Key Personnel on an application for RFA-CA-21-046 (UG1 Research Bases) from institution A.
    - Dr. XYZ cannot be named as Key Personnel (Investigator, Other Significant Contributor) on an application to FOA RFA-CA-22-051 (UG1 Clinical Sites) from Institution B.

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UG1 Clinical Sites

- On-site implementation leadership

- LMIC Sites: led either by LMIC PI(s) or co-led by LMIC and US-based PI(s)
- US Sites: led by US PI(s).

- Self-organized consortium of clinicians and/or clinical investigators with expertise and experience in providing clinical care or cancer prevention services to patients and/or communities in collaborative, multi-institutional clinical trials.

HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network

Funding Opportunity Announcement for UG1 Clinical Sites: RFA-CA-22-051

Applications submitted to the NIH in support of the NIH mission are evaluated for scientific and technical merit through the NIH peer review system.

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 scored and additional review criteria (as applicable).

Scored Review Criteria

- Significance
- Investigator(s)
- Innovation
- Approach
- Environment

Additional Review Criteria

- Study Timeline
- Protections for Human Subjects
- Inclusion of Women, Minorities, and Individuals Across the Lifespan
- Vertebrate Animals
- Biohazards

For additional review details, please refer to the FOA

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Scored Review Criteria

Significance

Specific for this FOA:

Is there a strong scientific premise for choice of the focus areas proposed by the UG1 Clinical Site in the 'CASCADE' Network?

How likely is the proposed UG1 Clinical Site to contribute meaningfully to adequately support the research goals and focus areas of the network clinical trials?

For additional review details, please refer to the FOA

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Scored Review Criteria

Investigators

Specific for this FOA:

How well does the organizational structure at the affiliated facility-based or field-based sites support work towards the successful goals of the trials that will be conducted in the network?
Do the UG1 Clinical Site key personnel have complementary and integrated expertise and skills?
How well will the team be able to contribute unique expertise and perspectives to such joint endeavors?

For additional review details, please refer to the FOA

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Scored Review Criteria

Innovation

Specific for this FOA:

Do the proposed approaches include innovative elements, as appropriate, to facilitate efficient and effective operations?

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Scored Review Criteria

Approach

Specific for this FOA:

How well does UG1 Clinical Site application demonstrate capabilities in their specified focus areas of the 'CASCADE' Network and how well does it build on previously conducted clinical research activities?

How adequate is the UG1 Clinical Site group suited to deliver interventions to successfully conduct the pragmatic trials and provide interpretable results?

How adequate is the proposed pool of participants at the UG1 Clinical Sites for efficient accrual to the conduct of these trials?

For additional review details, please refer to the FOA

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Scored Review Criteria

Approach

Specific for this FOA:

How adequate are considerations for addressing potential ethical issues including obtaining adequate informed consent or assent? How adequately described are the UG1 Clinical Site applicant group's plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection? Is an adequate and appropriate menu of planned design and statistical approaches and methods considered for the proposed focus areas? Are overall plans to standardize, assure quality of, and monitor adherence to, the trial protocol and data collection or distribution guidelines appropriate? Does the application propose to use existing available resources, as applicable?

For additional review details, please refer to the FOA

Key Dates

- (Optional) Letter of Intent Due Date: November 28, 2022
- **Application Due Date: December 28, 2022**
- Scientific Merit Review: March 2023
- Advisory Council Review: May 2023
- Earliest Start Date: July 2023

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For additional questions, please see: https://prevention.cancer.gov/cascade

or
email cascade@mail.nih.gov

or
email
Dr. Vikrant Sahasrabuddhe, Program Director, NCI Division of Cancer Prevention,
at sahasrabuddhevv@mail.nih.gov

www.cancer.gov www.cancer.gov/espanol