Early Intervention to Promote Cardiovascular Health of Mothers and Children (ENRICH) Multisite Clinical Centers (Collaborative UG3/UH3 Clinical Trial Required) RFA HL 22-007, and Resource and Coordinating Center (U24) RFA HL 22-008

Pre-Application Webinar
April 12, 2021
12:00 pm -1:00 pm ET

National Heart, Lung, and Blood Institute

Webinar Best Practices

- Please turn off VPN. You are muted
- Ask questions using the Q&A box only
- Refrain from using the Chat Box
- Responses to questions unanswered during the webinar will be available in the FAQ links in the RFAs
- The URLs in this presentation will be listed in the FAQ link in the FOAs.
  - https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-007.html
  - https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-008.html
- Slides will be available in the FAQ link shortly after the webinar

Webinar Outline

- Introduction
  - Administrative Details
    - Important dates
    - Eligibility
- Overview of ENRICH
  - Key points for both RFAs (HL 22-007; HL 22-008)
- Questions and Answers
- Concluding Remarks and Resources

Introduction

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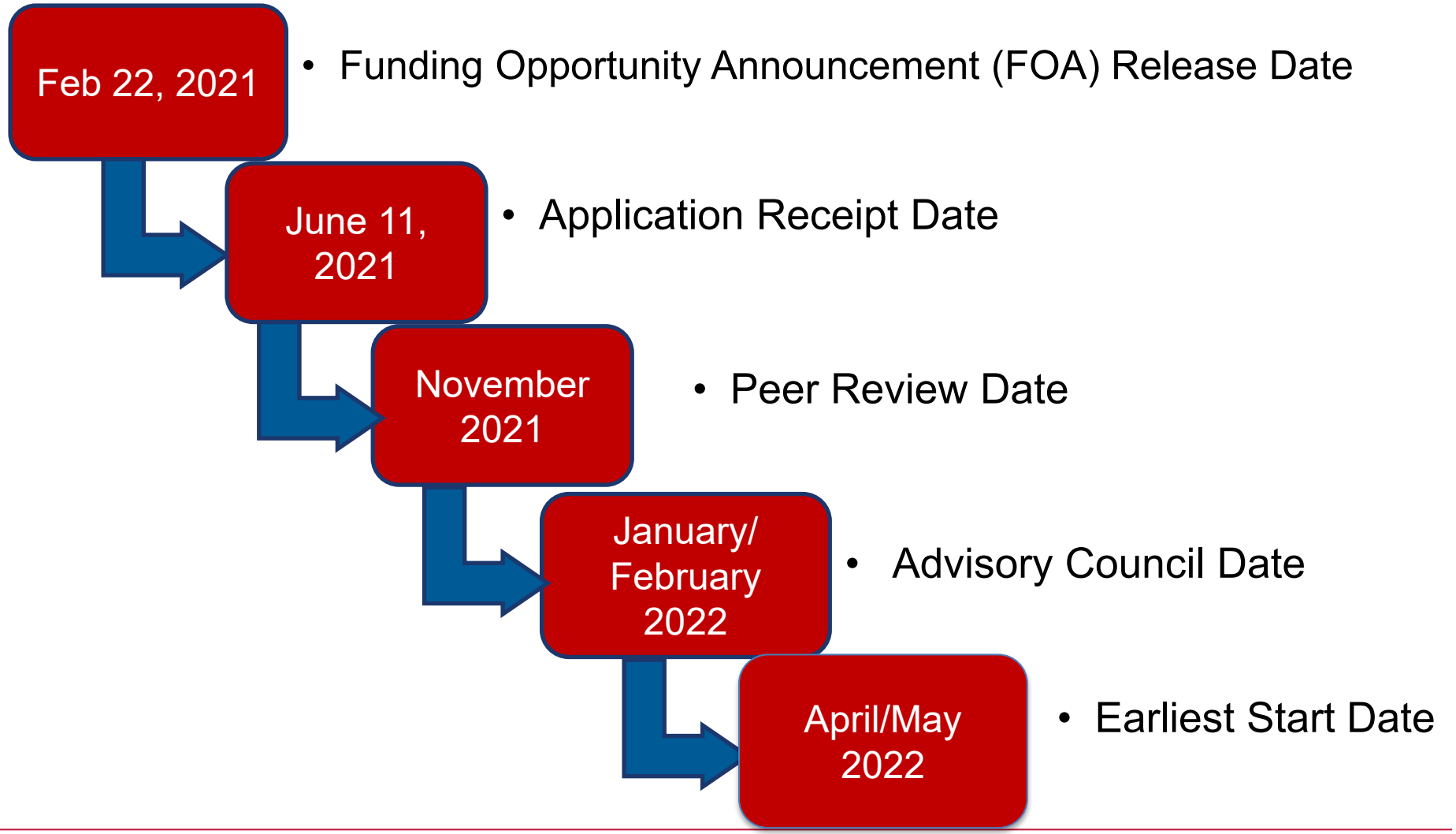
Timeline


Feb 22, 2021
• Funding Opportunity Announcement (FOA) Release Date
June 11, 2021
• Application Receipt Date
November 2021
• Peer Review Date
January/ February 2022
• Advisory Council Date
April/May 2022
• Earliest Start Date

Administrative Details

- Letter of Intent (Not Binding): Due Date: May 11, 2021
- Page limitations- follow SF424
- Letters of support required
- FAQs and answers are available in the FOAs and also in this link:
  - https://grants.nih.gov/grants/guide/notice-files/NOT-HL-21-004.html
- FOAs:

https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-007.html

https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-008.html

Administrative Details

- RFAs
  - Cooperative Agreement; NIH, HRSA, ACF staff involvement
  - Both RFAs are one-time announcements; no resubmissions.
- Reviews
  - Pay particular attention to required attachments
  - Review criteria --see Section V of the FOAs.
  - Project management plan and clinical trial experience (See other clinical trial-related attachments)
  - Reviews by NHLBI Special Review Panel

Eligibility

- FOAs are open to all eligible.
  - Women and underrepresented individuals in biomedical research
  - Institutions in states with high maternal morbidity and mortality rates are encouraged to apply.
- Institutions may apply using both RFAs. Recommend not having the same PI for both RFA applications
- Applications that are ineligible:
  - Study population not those listed in FOA
  - Interventions not delivered via home visiting or combination with virtual delivery
  - Applications that do not use hybrid effectiveness/implementation intervention designs.
  - Single site clinical trials
  - Epidemiologic or observational studies
  - Animal studies
- Foreign institutions are ineligible.

Eligibility: Evidence-based home visiting (eHV) programs

Both HRSA funded and non-funded MIECHV (Maternal, Infant and Early Childhood Home Visiting) programs are eligible.

- Partner with at least one home visiting program and an expert in CVH interventions
- Partner with models, states, agencies, etc.
  - have desired sample size
- Gain approval for adaptations and/or enhancements of eHV model from the home visiting model developer

(see Section 1 of the RFA HL-22-007)

Eligibility

Can home visiting models not meeting HHS criteria for evidence of effectiveness participate?

- Yes, adhere to the established evidence-based criteria below:
  - Evidence of HHS support of home visiting staff to implement interventions in the home
  - Assessed as moderate or high-quality impact using evidence-based criteria
  - Favorable impact on primary and secondary health outcomes as defined by Home Visiting Evidence of Effectiveness (HomVEE) review (https://homvee.acf.hhs.gov/)
  - Favorable sustained impacts >1-year post program inception on maternal or child health outcomes
  - Favorable impacts on maternal or child health that have been replicated
- Applicants must provide compelling justification for their proposed inclusion
- Obtain approval from supporting agencies along with a commitment of in-kind support.

(see Section 1 of the RFA HL-22-007)

Where Can I Find Home Visiting Evidence of Effectiveness?

List of models that have met HHS criteria for evidence of effectiveness are available here: https://homvee.acf.hhs.gov/

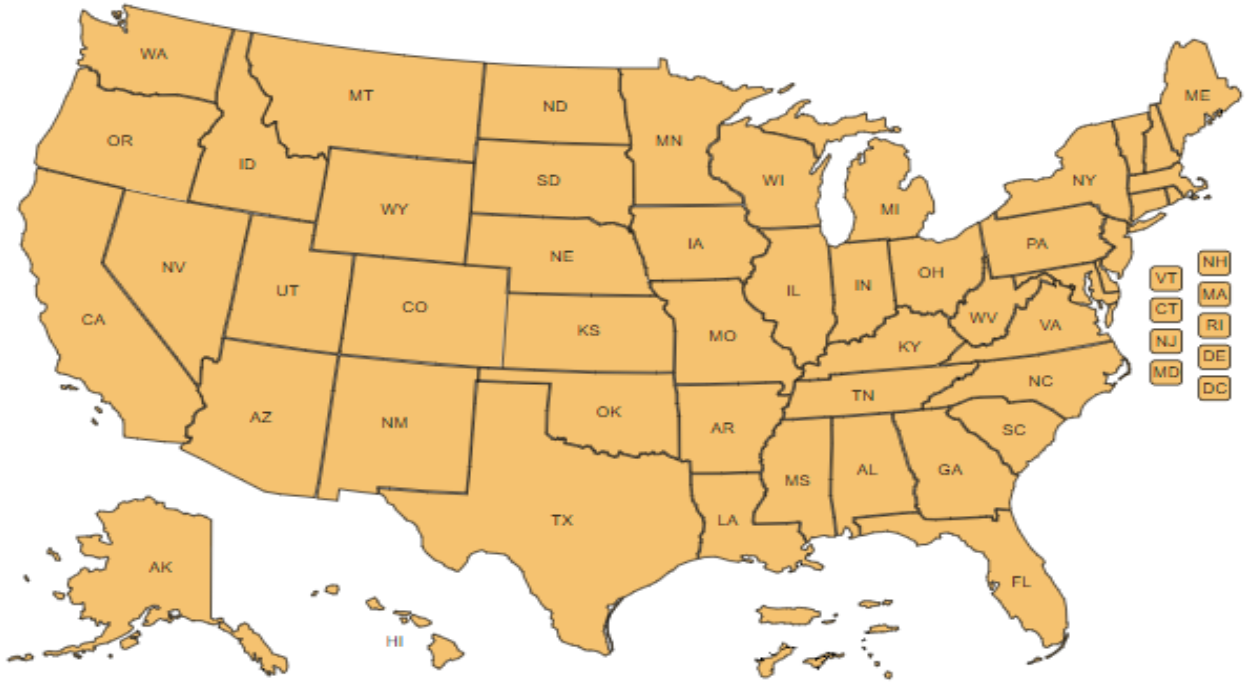
Where Can I Find Evidence-Based Home Visiting Programs in My State?

Home Visiting Program: State Fact Sheets

In FY 2019, HRSA-supported Maternal, Infant, and Early Childhood Home Visiting Programs served **154,000 parents and children in 1,005 U.S. counties**.

Select a state or use the drop-down menu to view a fact sheet (PDF - 300 KB) explaining how the Maternal, Infant, and Early Childhood Home Visiting Program works to improve family stability, child health and safety, and school readiness.

Select a state Go

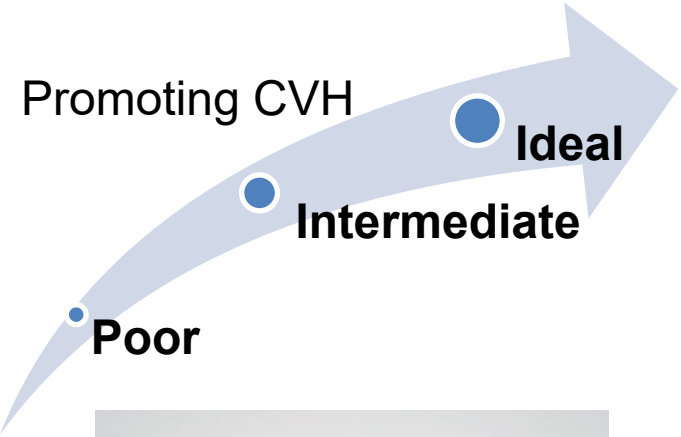


https://mchb.hrsa.gov/maternal-child-health-initiatives/home-visiting/home-visiting-program-state-fact-sheets

Overview of ENRICH

African Americans, AI/AN, and age >40: High maternal mortality

Seeking applications to test the effectiveness of an implementation-ready intervention at multiple sites in the U.S. to determine if a cardiovascular health (CVH) module can enhance maternal and child CVH. The intervention must be delivered within the context of an evidence-based home visiting program.



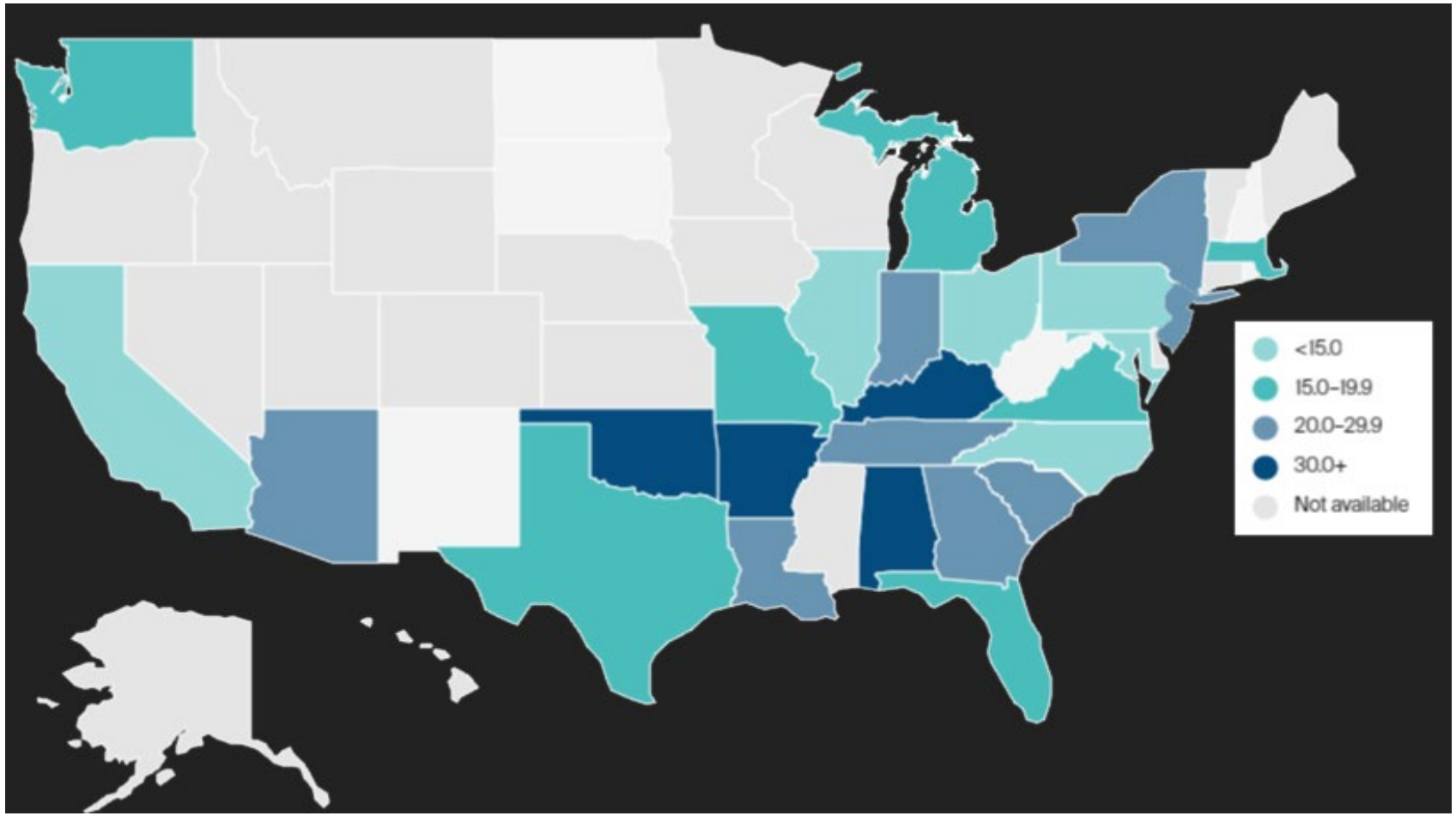
Mother: Diet, Physical Activity (PA)/sedentary behavior, smoking exposures, weight/ht/BMI; blood pressure, glucose, lipids. (CVH Score)
Infant and early childhood: Trajectories of change in growth (Weight/length/ht), sleep, smoking exposures, diet (breast/bottle/solid foods), sedentary behavior/PA, biomedical indices (see AAP guidelines; Bright Futures). **Both**: Social determinants of health & psychosocial factors, chart reviews, home contextual factors, and implementation assessments

AAP= American Academy of Pediatrics

Maternal Mortality Rates by State, 2018

U.S. Maternal Mortality Rate 17.4 per 100,000

State	Rate per 100,000 live births
Arkansas	45.9
Kentucky	40.8
Alabama	36.4
Oklahoma	30.1
Georgia	27.7
New Jersey	26.7
Tennessee	26.0
South Carolina	24.7
Louisiana	25.2
Indiana	24.5



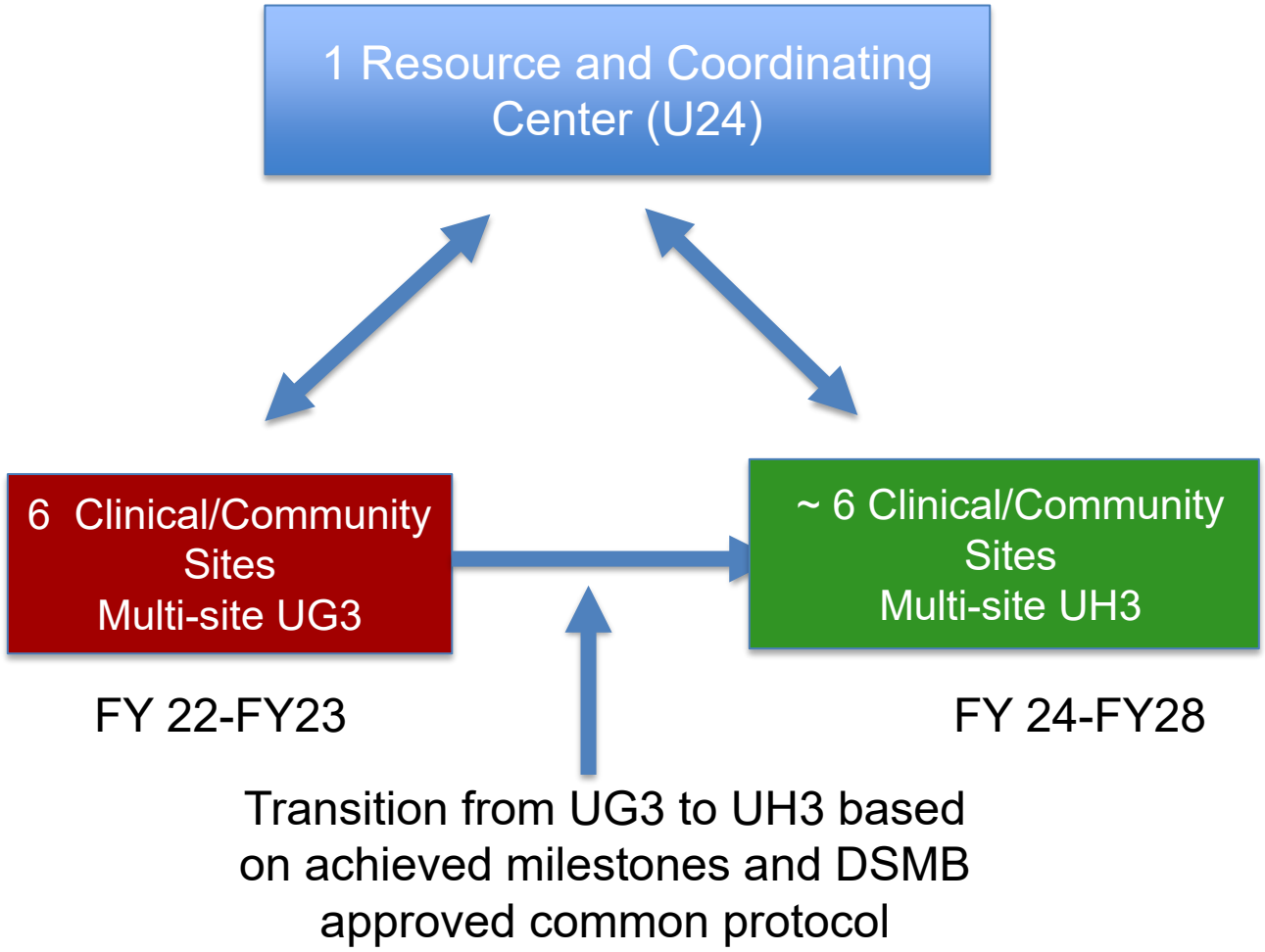
Source: CDC/NCHS, National Vital Statistics System

Funding Opportunity Announcements (FOAs)

- Low SES, low-resource rural or urban communities
- Diverse geographic regions of the United States with a high burden of cardiovascular disease (CVD) risk factors.
- RFA-HL-22-007-- Clinical or Community Sites
- RFA-HL-22-008--Resource and Coordinating Center (RCC)
- Multi-center group- or cluster-randomized trial
- Promote CVH and address CVH disparities in both mothers and children (0-5 years old)
  - Estimated total mother-child dyads: ~ 500-600 per awardee during the UH3 phase

ENRICH Overview and Structure

Leveraging Home Visiting Programs by HRSA & ACF



Cooperative Agreement:

Collaborating Partners include staff from NIH, HRSA & ACF

DSMB Oversight

RFA HL 22-007 Clinical or Community Sites UG3

UG3 Phase Highlights. Milestones Driven

- 2-year phase
- Planning, collaboration with EBHV organizations
- Pilot testing and feasibility studies
- Manual of Operations; Staff training
- Development of common protocol, refinement of protocol, informed consents, activation of sites
- DSMB approval
- Transition from UG3 to UH3 milestone driven
- See RFA HL 22-007 for details

https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-007.html

RFA HL 22-007 Clinical or Community Sites UH3

- Transition to UH3 Highlights
  - UG3 milestones met
  - DSMB approval
- UH3 Highlights (5 years)
  - Common protocol and its implementation across awardee sites
  - Common protocol with age specific interventions.
  - Common data elements
  - Collaboration with all awardees and RCC
  - ~3,000 mother-child dyads across all 6 awardees

- Applicants must provide detailed proposals for both for both UG3 and UH3. See the key elements in the FOA

https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-007.html

RFA-HL-22-008--Resource and Coordinating Center (RCC) – U24

Highlights of Years 1-2. Milestone Driven

- Develop a coordinating structure to support clinical center functions
- Convene clinical sites and foster collaboration and communication
- Facilitate development of a common protocol for the UH3 phase:
  - Intervention, study design, analytic plan, sample size, common data elements etc.
- Coordinate the approval of protocol by NHLBI-appointed DSMB
- Train staff on common protocol
- Facilitate pilot testing of components of the common protocol
- Develop and implement data collection procedures
- Provide skills training for Early Stage Investigators (ESIs), home-visiting staff & Other study staff

See FOA for further details: https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-008.html

RFA-HL-22-008--Resource and Coordinating Center (RCC) –U24

Some highlights of Years 3-7. Milestone Driven

- Continue with activities in years 1-2
- Facilitate the implementation of common protocol
- Develop and implement data collection, train measurement staff, etc.
- Continue to develop skills of ESIs and home visiting staff
- Facilitate integration of approved ancillary studies
- Data transfer, curation, storage and analysis
- Facilitate reporting of study data in peer-reviewed journals
- Maintain study structure- Steering committees and subcommittees; working groups
- Prepare public access data files

See FOA for further details: https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-008.html

PI (s): Clinical Trial Research Experience Table Required for both RFAs

- Column A: clinical study title
- Column B: applicant's role in the study
- Column C: a brief description of the study design
- Column D: planned enrollment
- Column E: actual enrollment
- Column F: whether the studies completed on schedule or not
- Column G: publication reference(s)

Above not to exceed 3 pages; see SF424

Expertise UG3/UH3 Clinical or Community RFA HL 22-007

- Expertise must be commensurate with expected functions
- A multi-disciplinary and diverse team with expertise in cardiovascular health, maternal and child health, home visiting intervention implementation, and statistical data analysis
- Encourage applications from all including:
  - Underrepresented racial and ethnic groups
  - Individuals with disabilities

Expertise Resource Coordinating Center RFA HL 22-008 (U24)

- Experience working with and/or leading multidisciplinary research teams
- Expertise in group- and cluster-randomized trial designs.
- Experience in clinical trial management
- Experience in working with home visiting organizations, data analytic skills, etc.
- Experience in clinical trial design, implementation and monitoring, and cardiovascular disease prevention research.
- Experience in maternal and early child health.
- Expertise in coordinating collaborative, multi-site research in low-resource and/or in diverse settings.
- Experience in data analysis across multiple sites.

Applicants must be familiar with the UG3/UH3 FOA- RFA HL 22-007

Scientific Review Highlights

Dr. Li-Smerin, SRO

- Review by Special Emphasis Panel convened by NHLBI
- Pay attention to review criteria in the RFAs (specific for the FOA)
- Reviews: Pay particular attention to
  - Required attachments
  - Review criteria --see Section V of the FOAs.
    - Significance, investigators, innovation, approach, environment
  - Include project management plan and clinical trial experience (See other clinical trial-related attachments)

- Contact: Li-Smerin@nhlbi.nih.gov (SRO)

Budget Highlights- UG3/UH3 RFA HL 22-007 (CC)

Allison Moyal, GMS, NHLBI

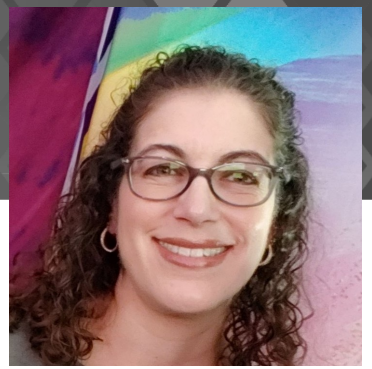
- Application need to reflect the actual needs for activities in the proposed project.

- The budget for each application may not exceed direct costs
  - FY 2022: up to $390,000
  - FY 2023: up to $520,000
  - FY 2024 through FY 2026: up to $650,000 per year
  - FY 2027 and FY2028: up to $520,000 per year

- NIH may modify budgets on award

Contact: Allison.moyal@nih.gov (GMS)

Budget Highlights- U24 RFA HL 22-008 RCC



Allison Moyal, GMS

- Application budgets need to reflect the actual needs for activities in the proposed project.
- NHLBI intends to fund one award for 7 years
- Total Costs:
  - FY 2022 up to $1.5 million
  - FY 2023 through FY 2027 up to $1.2 million/year
  - FY 2028: $1.5 million in FY 2028
- NIH may modify budgets on award
- Only 1 application will be awarded

Contact: Allison.moyal@nih.gov (GMS)

Questions and Answers

Please use Q&A box

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Concluding Remarks

- *Connect with us at NHLBI_Enrich* NHLBI_Enrich@nhlbi.nih.gov
- Post Webinar *Frequently Asked Questions* will be at *(also in the RFAs):*
  - https://www.nhlbi.nih.gov/grants-and-training/funding-opportunities/foa-ENRICH-FAQ
- *Multisite Clinical Centers RFA*
  - https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-007.html
- *Multisite Resource and Coordinating Center*
  - https://grants.nih.gov/grants/guide/rfa-files/RFA-HL-22-008.html

Resources

- Phases of Clinical Trials- What phase is it? Phase 2 or 3 CT?
  - https://grants.nih.gov/policy/clinical-trials/glossary-ct.htm#ClinicalTrial
- What are UG3/UH3 applications? See PAR 19-329
  - https://grants.nih.gov/grants/guide/pa-files/PAR-19-329.html
- AAP Recommendations for Preventive Pediatric Health Care Bright Futures/American Academy of Pediatrics
  - https://brightfutures.aap.org/materials-and-tools/

NIH National Heart, Lung, and Blood Institute

Some Questions and Answers: U24 RCC

My University will be submitting two applications (UG3/UH3 and U24 with different PIs). Would it be a problem if there are some key personnel on the UG3/UH3 (CC) also on the U24 or vice versa?

- With respect to overlapping personnel, be careful with levels of effort and actual duties on both applications to assure that someone is not receiving funds twice for the same work to be completed.

Will the U24 application be an independent application that will not need to be accompanied by a UG3/UH3 (CC)?

- Yes. An institution can submit one or the either or both but they have to be independent of each other.

How do roles of the proposed Resource Coordinating Center (RCC, U24) relate to roles for Clinical or Community Sites?

- The roles for the RCC are distinct from the roles of the clinical centers. Data analysis is by the RCC at the UH3. Statisticians from both the RCC and the CCs will provide input in the UG3 phase and in the design of the common protocol. Data analysis of common data will come from the RCC.

Is the common database implemented in the UH3 phase the only database the RCC is expected to implement?

- Yes. The RCC must be able to transfer data collected at clinical sites into a database that holds all data for ENRICH. It is possible other databases may be discussed during the first 1-2 years. During the UH3 phase, one database by RCC should manage data for the pilot studies as well. The CCs may also analyze data in coordination with the RCC their own data if they have the resources.

Could provide examples of expected skills for ESIs and home visiting professional staff that should be fostered and that the RCC is expected to play a major role in its development?

- We expect that skills training of ESIs and Home Visiting Professional staff would include aspects of the study protocol, for examples: data collection and measurement, and intervention. In particular for ESIs, we expect the RCC to provide skills development that would support their growth as independent researchers. Examples could include clinical trial implementation and the ENRICH protocol, study design, clinical trial implementation, blinding of the study population, etc. We also expect the RCC to foster ESI career development . An example could be to encourage their first or co-authorship of peer-reviewed publications in scientific journals.

Some Questions and Answers: UG3/UH3 CC

Clarify if the ENRICH sites are expected to deliver the intervention prenatally, starting in early pregnancy.

- Yes, we expect the intervention to begin early in pregnancy and/or early postpartum. As stated in the RFA, “Many [evidence-based] home visiting models are designed to begin during pregnancy or shortly after birth and typically continue through early childhood, up to 5 years old.” Thus, we expect applicants to target pregnant women early in the pregnancy to the extent possible within their localities. In some cases, applicants may have access to mothers and children at postpartum and that is also acceptable

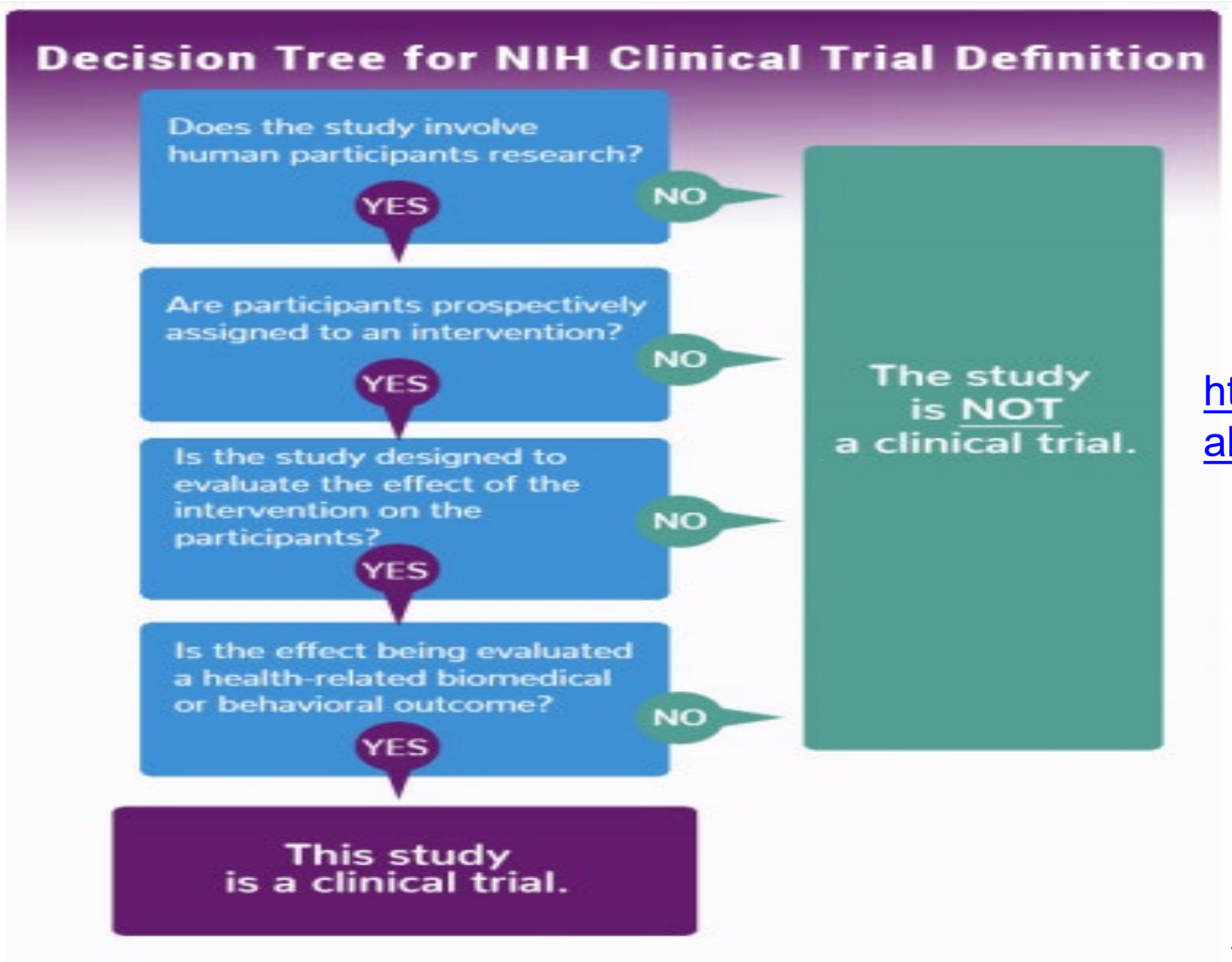
Is it appropriate for clinical centers to have expertise in interventions to promote cardiovascular health in mothers or children or is expertise for interventions for both recommended?

- Clinical center applicants must have expertise in the research that is commensurate with their intervention approach. Because both mother and child are to be intervened on, we recommend that applicants include personnel that have expertise in interventions to promote cardiovascular health in both mother and child.

Will the awardees collaborate in the UG3/UH3 phase for a sole CVH module to test- or will multiple options exist?

- As stated in the FOA (Section 1. Funding Opportunity Description) “During the UG3/UH3 phase, multiple clinical/community sites that receive the UG3 awards will work together with the RCC (RFA-HL-22-008) and project office staff to develop one common protocol (including study design, analytic plan, sample size) to be used across multiple sites in the UH3 phase. Toward that end, community/clinical sites may need to conduct pilot studies in Year 2 of this phase to refine the development of the common protocol. Applicants will be expected to submit proposals for the study design and analytic plan to be used in the UH3 to evaluate the intervention and use information gathered in the UG3 phase that would inform the analytic plan for the UH3 phase.”

What is a Clinical Trial?: NIH Clinical Trial Decision Tree



https://grants.nih.gov/policy/clinical-trials/definition.htm

What is effectiveness-implementation hybrid design?

- A study design that takes a dual focus in assessing clinical effectiveness and implementation. Hybrid designs can typically take 1 of 3 approaches: (a) testing effects of a clinical intervention on relevant outcomes while observing and gathering information on implementation; (b) dual testing of clinical and implementation interventions/strategies; (c) testing of an implementation strategy while observing and gathering information on the clinical intervention's impact on relevant outcomes.

Curran GM. *Medical Care*, 2012;50(3):217-26.

Effectiveness-implementation hybrid designs- Papers

- Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Medical Care,* 2012;50(3):217-26.
- Landes SJ, McBain SA, Curran GM. An introduction to effectiveness-implementation hybrid designs. *Psychiatry Research*. 2019;280:112513.

Maternal Mortality by Age and Race, 2018

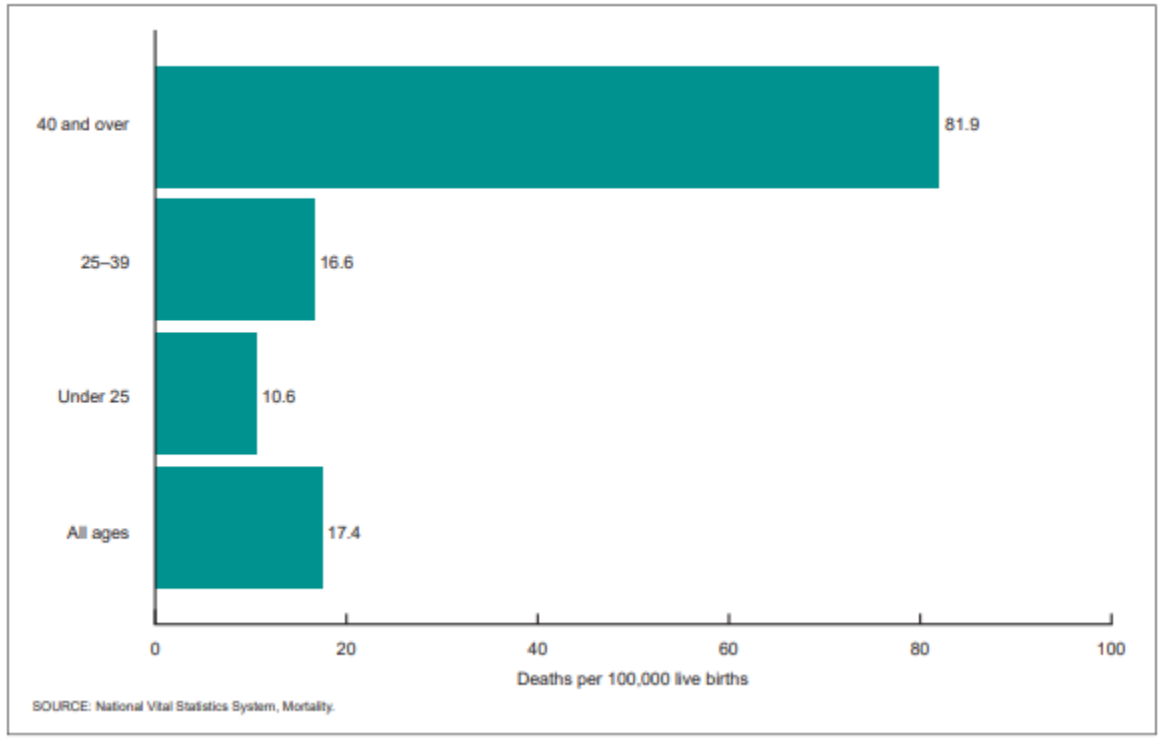


Figure 1. Maternal mortality rates, by age: United States, 2018

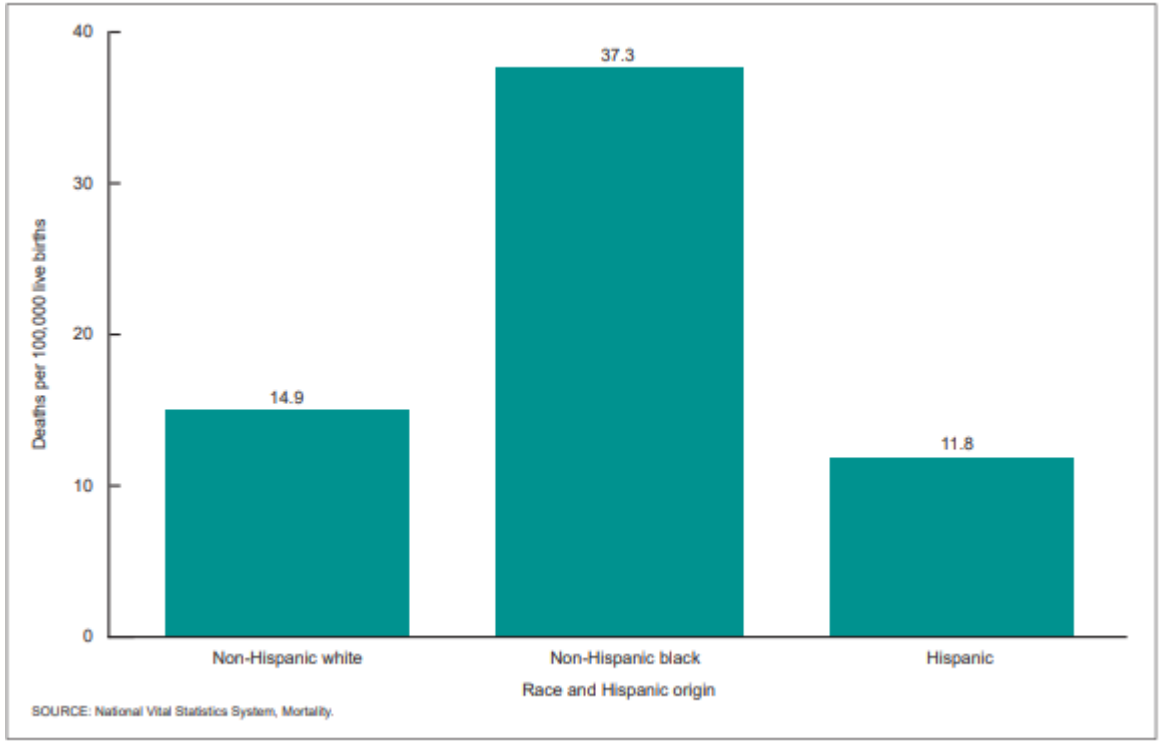


Figure 2. Maternal mortality rates, by single race and Hispanic origin: United States, 2018