Request for Proposal

Augmented Intelligence in Medicine and Healthcare Initiative (AIM-HI)

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Section 1: Point of contact

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Section 2: Project introduction, objective, and background

While many reports detail promising performance of healthcare AI/ML algorithms in silico, there is still a critical evidence gap in demonstrating that the bedside use of such tools is actionable and effective in real-world clinical settings. Without high-quality studies evaluating the outcomes of AI/ML tools implemented for diagnostic decision-making, there is potential for poor execution, unsustainable implementation, or unfounded expectations of AI/ML tools in practice. On the other hand, rigorously designed AI/ML effectiveness studies can highlight key opportunities and best practices that produce equitable, safe, and sustainable strategies for AI/ML in healthcare.

With support from the Gordon and Betty Moore Foundation, the Kaiser Permanente Division of Research (KP-DOR) Augmented Intelligence in Medicine and Healthcare Initiative (AIM-HI) is pleased to announce a Request For Proposals (RFP) in 2023 to support research that evaluates the implementation of existing Artificial Intelligence/Machine Learning algorithms that enhance diagnostic decision-making to achieve the following objective:

To advance research methods, identify best practices for scalability, and build capacity for effectively implementing and rigorously evaluating the use of AI/ML algorithms for diagnostic decision-making in real-world settings.

This AIM-HI RFP is designed to provide 2-3 years of funding for 3 to 5 proposals of prospective AI/ML implementation-effectiveness studies in U.S. health systems with a total budget of up to $750,000 for each project. KP-DOR will serve as the Coordinating Center for this portfolio over the funding period working under the
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guidance of a National Advisory Committee on selecting funded proposals, assessing project progress, leading domain working groups, and disseminating best practices to build the capacity for effective AI/ML implementation in healthcare.

To promote diversity in health system representation, smaller health care systems and organizations are strongly encouraged to submit Letters of Intent for consideration. Additionally, larger health care systems or academic medical centers are encouraged to partner with community health care systems to demonstrate the generalizability of AI/ML implementation. The AIM-HI Program seeks to achieve a balanced funding portfolio that reflects current real-world AI/ML capabilities in US healthcare across diverse settings and systems.

Interested research applicants can submit a 3-page Letter of Intent (LOI) due on June 30, 2023. Drawn from the LOI proposals, up to 12 applicant teams will be invited to submit a 12-page full application due on October 13, 2023.

Background

The past decade has seen a rapid expansion in the availability of large-scale health data, powerful computing platforms, and innovative Artificial Intelligence and Machine Learning (AI/ML) algorithms, heralding the emerging age of AI/ML in healthcare. Yet, while an ever-growing number of research studies describe the excellent performance of AI/ML algorithms in retrospective in silico experiments, only a limited number of studies have demonstrated that these AI/ML algorithms can be implemented sustainably into clinical workflows and drive robust improvements in patient outcomes. Thus, today, there remains a persistent evidence gap related to examples of AI/ML applied prospectively and effectively to healthcare.

Beyond individual examples of high-quality AI/ML integration in healthcare, there is also a substantial knowledge gap about the programmatic approaches (e.g., best practices, implementation design, oversight/governance) that can facilitate safe and sustainable use of AI/ML at the bedside. Challenges universal to the implementation of novel technologies (e.g., change management, technical infrastructure, end-user engagement) impact AI/ML use. In addition, other unique challenges present potential barriers to effective AI/ML use, including: end-user trust and engagement, fairness and bias tradeoffs, ongoing algorithmic performance monitoring, model generalizability and customization, and patient data considerations. While guidelines and regulatory frameworks continue to be developed in these domains, best practices need to be designed to facilitate a future with effective, equitable, safe, and sustainable use of AI/ML in healthcare. Uncertainties about the generalizability of algorithms across new datasets and settings also highlight the need to promote collaborative evaluations of AI/ML tools across diverse settings.

While there are many potential applications of AI/ML in healthcare, the specific area of focus for this program is in diagnostic decision-making. Studies estimate that millions of Americans are subjected to medical errors each year, with too many suffering devastating consequences as a result. While the source of these errors is diverse, diagnostic error has been identified as the major contributor. With its ability to rapidly gather insights from large and complex data, AI/ML algorithms offer a uniquely powerful capability to enhance diagnostic excellence by improving clinician diagnostic risk stratification, decision-making, diagnostic testing approaches, and intervention. Clinical areas domains including cancer, acute vascular events, and acute infection are subject to diagnostic challenges, and have been noted as a priority area for the Moore Foundation.
Section 3: RFP objective, research methodology, and proposal criteria

Objective
The KP AIM-HI Request For Proposal (RFP) is designed to select 3 to 5 competitive research proposals for funding that conduct 2-3 year prospective studies to provide rigorous evidence of how already developed AI/ML algorithms can effectively improve diagnostic decision-making in clinical practice across diverse settings. These proposals will be embedded within a larger program whose goals are to advance methods, identify best practices, and build capacity for effectively implementing and rigorously evaluating the use of AI/ML algorithms for diagnostic decision-making in real-world settings.

Research methodology
This RFP is designed to support prospective evaluations of existing AI/ML algorithms in diagnostic decision-making for clinical settings. Competitive applications will focus on rigorous evaluation designs, including those that incorporate randomization assigned at the patient-, provider-, and/or medical center/unit-levels. These approaches can include traditional randomized controlled trial designs as well as extensions of applied to health system evaluation including randomized stepped wedge, cluster randomization, crossover designs, and others. As appropriate for the AI/ML tool and its clinical context, other robust study designs that do not include randomization will be considered.

Criteria for proposal review
Letters of Intent and full Proposals will be reviewed by research scientists, clinical/content experts, biostatisticians, and data scientists at the KP-DOR Coordinating Center, external expert reviewers and will be guided by the National Advisory Committee. To avoid conflicts of interest, proposals from Kaiser Permanente entities or researchers in primary roles will not be eligible for funding. Table 1 details key criteria that will be used to judge the quality of proposal submissions.
Table 1. Details of key criteria in proposal review:

| Significance | - How important is the clinical/diagnostic scenario for which the AI/ML tool has been developed?  
|             | - If successful, what is the anticipated impact that the AI/ML tool implementation will exert on meaningful patient outcomes?  
|             | - What are the generalizable contributions of the proposal’s findings on enhancing the future use of AI/ML tools?  
|             | - How well aligned is the proposal with key interest areas in diagnostic excellence (i.e., acute vascular events, cancer, infection)?  
|             | - If successful, how will the AI/ML tool be generalized and scalable to new settings?  
| Innovation  | - How innovative is the AI/ML algorithm or the implementation-evaluation design?  
|             | - What other similar AI/ML algorithms exist and what is the advantage of the proposed tool compared with existing diagnostic workflows?  
|             | - What is the potential that the proposed AI/ML tool’s integration and evaluation will shift current research or clinical paradigms by highlighting novel concepts, methods, or interventions?  
|             | - What existing barriers to the use of AI/ML tools will the proposal address and overcome?  
| Approach    | - What are the existing AI/ML tool performance metrics and key indicators (e.g., peer-reviewed publication, accuracy, calibration, etc.) for the proposal algorithm?  
|             | - What is the anticipated or existing implementation process and key indicators (e.g., completed retrospective validation on local data, prospective silent validation, workflow integration, user interface, etc.)?  
|             | - What evaluation has been completed, or is planned, with respect to fairness and bias of the AI/ML tool in the originating data source, the algorithm, as well as the proposed clinical intervention?  
|             | - What evaluation has been completed, or is planned, for clinician acceptance and intelligibility?  
|             | - How robust is the evaluation design and will the design impact the rigor of the findings?  
|             | - Do power calculations support the study feasibility?  
|             | - Is the proposal feasible within the allotted time frame and budget?  
| Investigators | - Does the team demonstrate the track record and qualifications to successfully execute the proposal?  
|             | - What is the evidence that the proposed team has successfully collaborated?  
|             | - What is the current governance/oversight structure for AI/ML implementation in the proposed study setting?  
|             | - Does the team include adequate multidisciplinary representation in key domains: AI/ML, technical instantiation, operational/clinical integration, health system evaluation, and regulatory/risk/bias considerations?  
|             | - Does the proposal’s principal investigator or key team member have the qualifications to lead one of the program’s working groups (see Domain Working Group Section below)?  
| Environment | - How well does the proposal represent implementation and evaluation across diverse US health settings or systems, including non-academic, community-based, and/or rural healthcare settings?  
|             | - What are the strengths of the proposed health system environment or setting in which the research will be conducted?  
|             | - What is the existing evidence of clinician or executive/sponsor support for the proposed research?  
|             | - What organizational resources will support implementation and evaluation outside of the RFP funding?  
|             | - What is the evidence that the health system is investing in partnerships and/or opportunities for generalizability of algorithms or learnings beyond the initial setting?  
|             | - Does the environment demonstrate adequate experience to successfully deploy and evaluate the AI/ML algorithm within the study period?  

Direct questions about the RFP to AIM-HI@kp.org
Desirable proposal criteria
As this RFP is designed to evaluate the impact of real-world implementation of AI/ML algorithms, model development and retrospective validation of AI/ML algorithms are expected to have been completed prior to proposal submission. Thus, the funding is not intended to support new or ongoing development of algorithms, except where used to verify performance and support evaluation in a new healthcare setting. Along with retrospective validation, proposals which provide metrics of model performance at clinically-actionable thresholds and across relevant subgroups will be viewed favorably.

Evidence of technical, clinician, and organizational integration and endorsement of the AI/ML algorithm will be viewed as a priority for funding, which may include artifacts of: existing peer-reviewed publication, availability of the algorithm for open-source or external use; ‘silent’ prospective real-time validation metrics; clinical playbooks and end-user educational materials; design of end-user interfaces to support clinical workflow; and/or resources allocated by the applicant organization to support deployment and engagement outside of this RFP funding. While these are not requirements for LOI submission, such elements support the feasibility of AI/ML evaluation within the study time period.

To achieve an AIM-HI program goal of evaluating AI/ML diagnostic decision support in diverse settings, health systems outside of academic health system settings are strongly encouraged to apply to achieve a program goal of including a diverse portfolio of funded projects. To foster demonstrations of generalizability of AI/ML algorithms across the US healthcare environment, proposals that include partnerships including diverse healthcare settings beyond that in which initial model development occurred will be viewed as a priority. Further, proposals that include implementation and evaluation occurring across two distinct health settings during the same study period will be viewed as highly competitive.

Application areas that align with existing efforts fostering diagnostic excellence in acute vascular events, cancer, and infectious disease, will be viewed favorably, although proposals addressing all diagnostic areas and modalities will be considered. Because of the broad scope of AI/ML applications in diagnostic decision-making, the final funding portfolio could include projects across domains or within a thematic focus on a specific clinical area or diagnostic challenge.
Section 4: Submission information, application timeline, eligibility

Interested research groups can submit a 3-page Letter of Intent (LOI) due on June 30, 2023.

From the LOI proposals, up to 12 research groups will be invited to submit a 12-page full application due on October 13, 2023.

The application process will be in multiple stages, beginning with a three-page Letter of Interest (LOI). The main milestones and dates are as follows:

<table>
<thead>
<tr>
<th>Timeline</th>
<th>Stage</th>
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<tbody>
<tr>
<td>May 5, 2023</td>
<td>Launch RFP with requests for LOI.</td>
</tr>
<tr>
<td>May 22, 2023</td>
<td>Information Session #1 for RFP applicants, 11:30-12:30 Pacific. Email <a href="mailto:AIM-HI@kp.org">AIM-HI@kp.org</a> for additional meeting information.</td>
</tr>
<tr>
<td>June 30, 2023</td>
<td>Close LOI; selection period for full proposal applicants.</td>
</tr>
<tr>
<td>July 21, 2023</td>
<td>Information Session #2 for full proposal applicants, 11:30-12:30 Pacific.</td>
</tr>
<tr>
<td>October 13, 2023</td>
<td>Close full proposal submission; final selection process begins.</td>
</tr>
<tr>
<td>December 15, 2023</td>
<td>RFP grantees notified.</td>
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Eligibility
Health care systems based in the United States are eligible to apply. Due to conflicts of interest, Kaiser Permanente institutions are not eligible to apply.

Section 5: Letter of Intent instructions

Description of proposed work and evaluation criteria

In a 3-page narrative describe the: (1) proposed clinical diagnostic use case; (2) AI/ML algorithm and its performance; (3) implementation and evaluation design proposed; and (4) team and health system setting collaborating in the proposal. Proposal LOIs should aim to address relevant key criteria noted in Table 1 such that reviewers can perform a comprehensive assessment to identify the highest priority teams to invite to submit full applications.

LOI reviews will be conducted by AIM-HI Coordinating Center staff, including scientists from KP Division of Research, staff from the Gordon and Betty Moore Foundation, and invited experts under the guidance of the National Advisory Committee.

Major criteria for evaluation will encompass the five domains described in Table 1: Significance, Innovation, Approach, Investigators, and Environment.

1. Assessments of Significance will aim to identify proposals that offer high potential to deploy AI/ML tools that address and overcome challenges within high-impact diagnostic scenarios. Proposals will also be gauged on their potential for advancing generalizable knowledge in improving the use of AI/ML tools for effectively and safely in diverse healthcare settings.
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2. Assessments of innovation will aim to identify proposals that offer novel approaches to diagnostic challenges, rather than those that offer incremental advances compared with existing diagnostic workflows or tools. Proposals will also be assessed for the innovation in the evaluation design, with priority towards those that advance the science of AI/ML evaluation.

3. Assessments of approach will aim to identify proposals that intend to use AI/ML tools that have been shown to exhibit promising, clinically sustainable, and operationally feasible performance when applied to the diagnostic use case. Because the AIM-HI program focuses on evaluations of AI/ML deployment, proposals that focus on algorithm development will be viewed with low priority. Careful attention will be paid to robust evaluation designs intended to rigorously demonstrate the value of the AI/ML tool in a diagnostic process.

4. Assessments of the investigator team will aim to identify proposals that include a team with multidisciplinary expertise in designing, instantiating, and deploying AI/ML tools. The Principal Investigators and co-investigators of final AIM-HI program awardees will be expected to lead and participate in quarterly workgroups addressing challenges in: algorithm development and technical instantiation, operational and clinical integration, health system evaluation, and/or mitigating regulatory, risk and bias concerns.

5. Finally, assessments of the environment will aim to identify proposals that exhibit the value of AI/ML tool implementation and evaluation in specific health system settings. Because the AIM-HI program aims to foster diversity in awardees across health system settings (e.g., academic versus non-academic, larger versus smaller, rural versus urban), proposals from all health system settings are strongly encouraged, including from those which have less experience in AI/ML tool development and deployment.

Please make sure to address the following at a high level in your LOI:

1. **Proposed internal team and partnering organizations:** Provide (brief) bios of study principal investigators, key project members, and any partnering organizations, emphasizing any internal or cross-health system collaborations. Please also provide at least one internal letter of executive support/sponsorship for this research project.

2. **Health system executive support and experience:** At a high level, describe the approach to project governance that will align the proposed project with interests of health system executive leadership, frontline clinicians, and technical teams.

3. **Health system frontline support and experience:** Describe the health system’s approach to engaging frontline clinicians in clinical AI/ML projects.

4. **Health system information system technical support and experience:** Describe this project team’s approach to successfully engaging technical teams in clinical AI/ML projects.

5. **Previous experience in design and implementation of prospective evaluation of health system interventions, clinical AI/ML algorithms, and/or randomized studies:** Describe any previous or related experience in the design and implementation of prospective evaluations of clinical algorithms (including those that might not use machine learning) and conducting randomized studies.

6. **Strength/previous experience in human-computer interaction and clinical workflow design and change management:** Describe health system’s approach to assessing and modifying clinical workflows.

7. **Data analytic maturity (including ability to test and validate algorithms on internal health system data):** Describe any previous experience in test and validation of algorithms developed within or outside of the health system.
8. **Patient engagement**: Describe the health system’s approach to engaging patients in clinical AI/ML projects.

### Letter of Interest submission instructions and checklist

<table>
<thead>
<tr>
<th>Timeline</th>
<th>Stage</th>
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</thead>
<tbody>
<tr>
<td><strong>Due date</strong></td>
<td>June 30, 2023, 11:59 PM Pacific Time</td>
</tr>
<tr>
<td><strong>Submit to</strong></td>
<td><a href="mailto:AIM-HI@kp.org">AIM-HI@kp.org</a></td>
</tr>
<tr>
<td><strong>File type and format</strong></td>
<td>PDF, 1-inch margins, single spaced, 11 point Arial or Calibri font</td>
</tr>
<tr>
<td><strong>Page limit</strong></td>
<td>Narrative should be no more than 3 pages</td>
</tr>
<tr>
<td><strong>Letter of Support</strong></td>
<td>Include one letter of support from executive sponsors confirming specific endorsement of the proposal and the goal of timely implementation to allow for adequate evaluation of resulting outcomes.</td>
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</tbody>
</table>

### LOI Submission Checklist
1. LOI Narrative
2. NIH-style bio sketches or CV for proposed investigators
3. One letter of support

### Section 6: Full application instructions

Please write a 12-page narrative outlining your vision for the implementation and prospective evaluation of a machine learning-based diagnostic decision support tool. Specifically, please make sure to address the following topics and questions:

**Overview**
- Describe the proposed clinical diagnostic use case and algorithm.
- Describe the team's internal governance and deployment structure.

**Existing alignment within health system and partner organizations**
- Describe how this project relates to existing organizational priorities and initiatives.
- How will existing infrastructure and resources support the success of this project?
- How will partnerships across collaborating institutions be implemented?

**Alignment with the joint KP and Moore Foundation diagnostic priorities**
- Describe how this project relates to the stated focus areas of this call – addressing diagnosis in one or more of the following areas: acute vascular events, cancer, infection.

**Clinical impact of proposed use case**
- Describe the clinical impact of this use case on patient outcomes.

**Fairness and equity impact of proposed use case**
- Describe the process for evaluation of bias and fairness in the algorithm and its application to clinical care.

**Analytic validity**
- Describe the development, validation, and instantiation process of this algorithm.
- What published evidence supports analytic validity? What other algorithms were considered?

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- What type of evaluation design will be used and how does that impact the anticipated rigor of the findings?

Data requirements and retraining
- Describe anticipated challenges in re-training or adapting the algorithm to the health system’s population.

Understanding of workflow and implementation challenges
- Describe the existing clinical workflow used for the diagnosis in this use case.
- How will the proposed algorithm impact this workflow? What evidence exists to support the proposed new or modified workflow?

Suitability of algorithm to prospective evaluation studies
- What types of outcomes will be measured in this prospective evaluation?
- Describe anticipated challenges in collecting and analyzing this data.

Domain Working Group Expertise
- Identify 1-2 Working Groups (see below) that you would be able to lead and facilitate
- Provide evidence for your expertise in the selected domain/s

Domain Working Groups/Knowledge Hubs
The Coordinating Center is developing Domain Working Groups/Knowledge Hubs, whose membership will be comprised of Principal Investigators/co-Is from the grantee institutions, Coordinating Center leaders, as well as other invited external experts as outlined in the Table below. The PI of awarded projects will be expected to lead one Working Group. Additionally, all grantee institutions will be expected to have investigator-level team members who actively participate in monthly or quarterly Working Group sessions, including through presenting ongoing activities, evaluation design, and progress. The Working Groups are intended to further the overall aims of the effort - advance research methods, identify best practices, and build capacity for effectively implementing and rigorously evaluating the use of AI/ML algorithms for diagnostic decision-making in real-world settings.

<table>
<thead>
<tr>
<th>Working groups</th>
<th>Lead</th>
<th>Expertise of members*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AI/ML/Data Science Core</td>
<td>Grantee 1 – PI</td>
<td>AI/ML Methodologists, Biostatisticians, selected Clinical Domain Experts, Model Explainability/Interpretability scholars</td>
</tr>
<tr>
<td>Technology Enablement</td>
<td>Grantee 2 – PI</td>
<td>Computing platform architects, IT leaders, EHR experts, Human Factors experts</td>
</tr>
<tr>
<td>Operational Integration</td>
<td>Grantee 3 – PI</td>
<td>Clinical domain experts, Operational Leaders, Health System Executives, Local governance teams</td>
</tr>
<tr>
<td>Risk, Regulatory, Fairness</td>
<td>Grantee 4 – PI</td>
<td>Legal scholars, Technology Transfer Specialists, Government Relations, DEI leadership, Community representatives.</td>
</tr>
<tr>
<td>Health system evaluation and design</td>
<td>Grantee 5 – PI</td>
<td>QI/PI/Delivery Science scholars, Learning Health System Experts, Quality/Safety Leaders, Health System Evaluation Design</td>
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* National Advisory Board members may be invited to join select Working Groups

Full application submission instructions and checklist
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<td><strong>NIH-style biosketch or CV</strong></td>
<td>Required for all investigators</td>
</tr>
<tr>
<td><strong>Letter(s) of support (LOS)</strong></td>
<td>Include up to three letters of support from executive sponsors, health system leadership, and if collaborating with another institution, a required LOS from each participating institution confirming specific endorsement of the proposal and the goal of timely implementation to allow for adequate evaluation of resulting outcomes. Must include institutional acknowledgement of Facilities and Administration (F&amp;A) rates from each institution.</td>
</tr>
<tr>
<td><strong>Budget</strong></td>
<td>Use the template provided</td>
</tr>
<tr>
<td><strong>Budget Justification and Study Team</strong></td>
<td>Include a list of study team members along with expected roles &amp; responsibilities for each person</td>
</tr>
<tr>
<td><strong>Institutional information and sign-off</strong></td>
<td>Use the template provided</td>
</tr>
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**RFP Submission Checklist**
1. RFP Application Narrative
2. Appendices, if including
3. NIH-style biosketches or CV for all investigators
4. Letter/s of support
5. Budget (use template provided on AIM-HI website)
6. Budget Justification and Study Team
7. Institutional information and sign-off (use template provided)