PRIMED-AI Analysis of External Input

The information below is a summary of the input we received from the public and research community to inform planning for the PRIMED-AI concept. It does not necessarily represent the opinion of the NIH or its staff.

Data Collection

From the RFI, we received a total of 109 responses distributed across four topics:

- Imaging and related multimodal data integration approaches (n=34)
- Developing AI-based clinical decision support tools using imaging and multimodal data integration (n=31)
- Demonstrating the clinical utility of multimodal algorithms for precision medicine (n=23)
- Other relevant comments, suggestions, or considerations (n=21)

Additionally, we conducted six informational calls with 14 subject matter experts. We collected seven hours of audio, video, transcripts, and summaries of these calls. The outcomes of the external public input (RFI + informational calls) were summarized using Large Language Models (LLMs), specifically ChatGPT-4o (version: 2024-05-13), installed on NIH Azure servers.

Analysis of PRIMED-AI RFI & Informational Calls

Input from the RFI and the informational calls (**bolded**) for each topic is divided into three paragraphs summarizing the areas of consensus, disagreement, and unique perspectives.

1. Standardization and Data Integration [This includes: Current challenges in ensuring quality and integrity of multimodal datasets; Methods for standardizing data normalization protocols across different medical imaging approaches that could improve machine learning (ML) outcomes; Best strategies for curation and integration of imaging data of the same type that originates from different vendors/sources; Curation and integration methods for datasets to best prepare them for use with multimodal AI, with specific emphasis on techniques for labeling images with ground truth; Other areas that could benefit from standardized methods and metrics that would aid in data integration].

There is broad agreement on the need for standardization across multiple methods of medical imaging and data collection. Standardized imaging protocols, such as those required for MRI sequences, and metadata retention are essential for improving the reliability and reproducibility of AI/ML models. **Quality and integrity challenges of medical imaging datasets include variations in image acquisition methods, the need for extensive expertise, high costs, and data harmonization complexities. Standardizing protocols like DICOM[1], proper curation, and integration are vital for AI model training.** This includes thorough labeling with accurate ground truth data, the use of Common Data Elements

[1] DICOM is the international standard to transmit, store, retrieve, print, process, and display medical imaging information.

(CDEs)[2], and adherence to FAIR principles[3] to ensure datasets are usable across different platforms and studies. **Key actions include developing open-source platforms for dataset integration, forming committees to govern data quality and harmonization, promoting standardized protocols through major medical societies, preserving metadata during data de-identification, funding diverse AI training data research, and fostering collaboration between labs and institutions.**

While integrating imaging data with other clinical and environmental data is seen as important for improving diagnostic and prognostic outcomes, there is significant disagreement on the best methods to achieve standardization. Some advocate for publicly available tools like DICOM, while others suggest alternative solutions like OMOP Common Data Model[4] or proprietary systems due to varying compliance across institutions.

Unique perspectives emphasize developing AI systems to handle differences in imaging data from different vendors using techniques like collaborative ML (also known as federated learning) and data linkages. Collaborative, multi-institutional data collection and curation are recommended to create large, diverse, and high-quality datasets. Concept learning methodologies[5] are suggested as a promising direction for creating more explainable and robust AI systems.

2. AI-Based Clinical Decision Support Tools [This includes: Advanced ML techniques that would be most effective for integrating multimodal data into a coherent model for clinical application; Methods for ensuring that AI/ML models are interpretable, explainable, and transparent to clinical and/or patient users; Risks and benefits to use of synthetic data in multimodal algorithms for precision medicine; Strategies for incorporating user input during development of algorithms for precision medicine; Bias identification and mitigation techniques that will ensure AI-driven healthcare tools adhere to ethical standards while also providing equitable care across diverse patient populations; Ethical considerations, such as patient privacy and data security, and methods for ensuring patient privacy and data security; Potential regulatory barriers to deploying multimodal algorithms for precision medicine in clinical settings, and strategies for addressing them].

Harmonizing AI platforms and ML software across major MRI companies like GE, Siemens, and Philips is crucial. Integrating data from multiple studies and topics is vital for inclusivity and fairness, particularly for underrepresented groups.

Addressing bias in AI systems and ensuring proper de-identification of medical imaging data are essential but contentious topics. Disagreements exist on the regulatory approach and the effectiveness of collaboration among companies. **Regulatory and ethical challenges, including unclear guidelines for AI, bias, and patient privacy concerns, are significant. Current regulations lag technological advancements, complicating management of these concerns.** Clear guidelines for AI and AI devices, along with ethical frameworks for data privacy, security, and bias mitigation, are needed.

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[2] Common Data Elements (CDEs) are standardized, precisely defined questions, paired with a set of allowable responses, used systematically across different sites, studies, or clinical trials to ensure consistent data collection.
[3] FAIR principles include findability, accessibility, interoperability, and reusability.
[4] For more information, see https://www.ohdsi.org/data-standardization/.
[5] Concept learning in ML is the task of recognizing patterns from data and using those patterns to make predictions.

Innovative methods such as federated learning and generative AI[6] techniques address privacy concerns and enhance model transparency. Zero-shot learning[7] and generative AI can reduce biases and improve model fairness. **Research should focus on identifying and eliminating bias, dealing with data shift[8], and ensuring equity across diverse populations. Patient and community engagement frameworks are needed for transparency and trust. Promoting data sharing and collaboration among academia, industry, and healthcare institutions to create comprehensive datasets is essential. Aligning AI model development with clinically relevant goals and fostering communication between AI experts and clinical data scientists will enhance practical utility. Further research should focus on real-time bias detection, improving multimodal data integration, and creating scalable frameworks for patient data privacy that are secure and compliant with regulations. Engaging regulatory bodies early in the development process and integrating clinician data to guide AI/ML models are innovative approaches to improve interpretability and explainability.**

3. Demonstrating Clinical Utility of Multimodal Algorithms [This includes: Key factors for successful real-world implementation of multimodal algorithms for precision medicine, and strategies to support these factors; Methods for ensuring generalizability of algorithms for precision medicine across various clinical environments and/or patient populations; Methods for establishing effective collaborations among academic institutions, industry, and healthcare providers to accelerate development and clinical uptake of multimodal algorithms for precision medicine; Methods for measuring and demonstrating the impact of multimodal algorithms for precision medicine on patient outcomes; Regulatory frameworks to ensure the safe and ethical deployment of multimodal algorithms for precision medicine].

Enhancing the reproducibility and generalizability of algorithms in precision medicine requires diverse, high-quality datasets representing various demographics and clinical environments. Collaboration among academic institutions, industry, and healthcare providers is essential for accelerating development and clinical uptake of these algorithms. **Establishing partnerships with vendors like EPIC to facilitate seamless access to Electronic Health Records (EHR), which are vital data sources for such algorithms, is crucial. Developing standardized tools and platforms is essential for effectively handling the integration of diverse and voluminous data.** Well-designed clinical trials and real-world evidence studies are necessary to measure the clinical utility and impact of AI tools on patient outcomes.

There are differences in opinions on the best approaches to achieve these goals. Some stakeholders emphasize comprehensive sharing of code and documentation, while others focus on leveraging existing platforms and tools. There is also divergence in views on the extent of industry involvement required and the role of regulatory bodies. **To ensure the broad usefulness of AI models, they should be trained on diverse, real-world datasets, enhanced with techniques like generative AI while avoiding biases. They should also be adaptable. Early-stage validation and adherence to common standards throughout the development process are necessary for ensuring reliability. There should also be an emphasis on collaboration among academia, industry, and healthcare providers, with academic-industry partnerships enabling technology transfer and addressing financial and intellectual property considerations. Using secure federated data[9] systems can support algorithm training without**

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[6] Generative AI are AI algorithms that create new content in the form of text, images, video, audio, and more from knowledge gathered from an extremely large set of data.
[7] Zero-shot learning describes when an AI algorithm is trained to recognize and categorize objects without prior knowledge of or exposure to the categories or concepts.
[8] Data shift occurs when there is a severe mismatch between the training data and testing data. This can introduce significant bias or result in false findings.
[9] Federated data is decentralized data used in federated (collaborative) machine learning. See note 1.

compromising data privacy. Lastly, measuring the impact on patient outcomes, though challenging, is essential and involves evaluating workflow improvements, urgency prioritization, and access for non-specialist physicians.

Unique insights include using decision curve analysis to improve diagnostic capabilities and incorporating user feedback loops to enhance adaptability and real-time refinement of AI models. Federated learning is presented as a promising strategy for maintaining patient privacy while accessing diverse datasets, underscoring the importance of innovative methodologies and collaborative frameworks in advancing precision medicine.

4. Ethical Considerations for the Use of Imaging-Based, Multimodal AI Clinical Decision Support Tools
[This includes: Ethical considerations, such as patient privacy and data security, that need to be considered during development of multimodal algorithms for precision medicine, and methods for ensuring patient privacy and data security; Bias identification and mitigation techniques that will ensure AI-driven healthcare tools adhere to ethical standards while also providing equitable care across diverse patient populations; Strategies for supporting prioritization of image-centric research in multimodal data integration and precision medicine at institutes, within industry, among clinicians, etc; Regulatory frameworks to ensure the safe and ethical deployment of multimodal algorithms for precision medicine].

The importance of leveraging ML within precision medicine by integrating multiple data types, particularly medical imaging, is widely emphasized. For example, using ML to enhance lesion diagnosis and early cancer detection has the potential to significantly improve healthcare outcomes. Incorporating real-time data from wearable devices and sensors to dynamically update patient health status was also highlighted for enhancing the clinical utility and impact of AI-driven precision medicine. Bringing data together and standardizing it is crucial for ensuring the quality and integrity of multimodal datasets, facilitating reproducibility of research, and dissemination of ML algorithms across different institutions.

Disagreements arise concerning the roles and capabilities of various professionals in developing and implementing ML solutions in healthcare. Some argue that PhD scientists lack the necessary clinical understanding for meaningful healthcare ML research, advocating that only physician-scientists with extensive ML knowledge can design effective systems. Conversely, others highlight the potential of interdisciplinary collaboration, including PhD scientists, as essential for progress. There is also a divide on the necessity of interpretability in ML models, with some prioritizing higher accuracy over explainability, while others insist on the importance of interpretable models for building trust and ensuring ethical standards.

Unique and valuable perspectives include integrating prior knowledge into ML models to improve, for example, lesion diagnostics. **Public outreach and education are emphasized to encourage research participation and data sharing by diverse groups, which are crucial for developing equitable AI-driven healthcare tools. Establishing common language and data use agreements to streamline data sharing and governance are realistic approaches to overcoming barriers in data accessibility and use.**