American Academy of Allergy Asthma & Immunology

A Framework for Augmented Intelligence in Allergy and Immunology Practice and Research—A Work Group Report of the AAAAI Health Informatics, Technology, and Education Committee

Paneez Khoury, MD, MHSc[a], **Renganathan Srinivasan, MD**[b], **Sujani Kakumanu, MD**[c], **Sebastian Ochoa, MD**[d,e], **Anjeni Keswani, MD**[f], **Rachel Sparks, MD**[d,g], **and Nicholas L. Rider, DO**[h] *Bethesda, Md; Vancouver, Wash; Madison, Wisc; Washington, DC; and Houston, Texas*

Artificial and augmented intelligence (AI) and machine learning (ML) methods are expanding into the health care space. Big data are increasingly used in patient care applications, diagnostics, and treatment decisions in allergy and immunology. How these technologies will be evaluated, approved, and assessed for their impact is an important consideration for researchers and practitioners alike. With the potential of ML, deep learning, natural language processing, and other assistive methods to redefine health care usage, a scaffold for the impact of AI technology on research and patient care in allergy and immunology is needed. An American Academy of Asthma Allergy and Immunology Health Information Technology and Education subcommittee workgroup was convened to perform a scoping review of AI within health care as well as the specialty of allergy and immunology to address impacts on allergy and immunology practice and research as well as potential challenges including education, AI governance, ethical and equity considerations, and potential opportunities for the specialty. There are numerous potential clinical applications of AI in allergy and immunology that range from disease diagnosis to multidimensional data reduction in electronic health records or immunologic datasets. For appropriate application and interpretation of AI, specialists should be involved in the design, validation, and implementation of AI in allergy and immunology. Challenges include incorporation of data science and bioinformatics into training of future allergists-

[a]Laboratory of Allergic Diseases, NIAID, Bethesda, Md
[b]The Vancouver Clinic, Vancouver, Wash
[c]Division of Allergy, Pulmonary and Critical Care Medicine, University of Wisconsin School of Medicine and Public Health and the William S. Middleton Veterans Memorial Hospital, Madison, Wisc
[d]National Institutes of Infectious and Allergic Diseases, Bethesda, Md
[e]Laboratory of Clinical Immunology and Microbiology, NIAID, Bethesda, Md
[f]Division of Allergy/Immunology, George Washington University School of Medicine and Health Sciences, Washington, DC
[g]Laboratory of Immune System Biology, NIAID, Bethesda, Md
[h]Section of Immunology, Allergy and Retrovirology and the William T. Shearer Center for Human Immunobiology, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas

The work was funded in part by the Division of Intramural Research, National Institutes of Allergic and Infectious Diseases, National Institutes of Health.
Conflicts of interest: P. Khoury has received research grant funding from Consortium of Eosinophilic Gastrointestinal Researchers/National Center for Advancing Translational Sciences and American Partnership For Eosinophilic Disorders. S. Kakumanu has received royalties from UpToDate and federal grant funding from VA HSR&D. N. L. Rider receives grant funding from the National Institutes of Health (1R21AI164100-01A1), The Jeffrey Modell Foundation, Takeda Pharmaceuticals, and Pharma Healthcare; is a consultant to Horizon Therapeutics, Takeda Pharmaceuticals, and Pharming Healthcare; and receives royalties for topic contributions to UptoDate from Wolters Kluwer. The rest of the authors declare that they have no relevant conflicts of interest.
Received for publication July 16, 2021; revised January 19, 2022; accepted for publication January 20, 2022.
Available online March 15, 2022.
Corresponding author: Paneez Khoury, MD, MHSc, National Institutes of Health, 10 Center Dr, Building 10, 12C103, Bethesda, MD 20892. E-mail: khouryp@nih.gov.
2213-2198
Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology
https://doi.org/10.1016/j.jaip.2022.01.047

Abbreviations used
AAAAI- American Academy of Asthma Allergy and Immunology
AI- Augmented intelligence
AI-CONSORT- Artificial Intelligence Consolidated Standards of Reporting Trials
ANN- Artificial neural networks
BDD- Breakthrough device designation
CDS- Clinical decision support
DL- Deep learning
EHR- Electronic health record
EoE- Eosinophilic esophagitis
EP- Electronic phenotyping
FDA- Food and Drug Administration
HITE- Health Informatics Technology and Education
IEI- Inborn errors of immunity
ML- Machine learning
NLP- Natural language processing
PID- Primary immunodeficiency disorder
SaMD- Software as a Medical Device
SVM- Support vector machine

immunologists. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2022;10:1178-88)

Key words: *Artificial intelligence; Asthma; Primary immunodeficiency; Atopic dermatitis; Augmented intelligence; Clinical decision support; Electronic health records; Equity; Machine learning; Natural language processing; Medical education*

Artificial intelligence, augmented intelligence (AI), and machine learning (ML) are gaining traction in health care with the promise of providing assistance to clinicians in interpreting complex datasets, improving disease diagnosis, and facilitating clinical decision support (CDS).[1] AI enables computers to imitate human intelligence with its ability to observe, problem solve, and learn, whereas ML, and the related area of deep learning (DL), is the ability of systems to learn, extract patterns, and refine performance over time.[2] AI leverages ML to enable actionable use of data in contrast to autonomous replacement of human intellect. For example, artificial neural networks (ANN) are a type of DL model that uses a series of layers to analyze data inputs for prediction or regression via a nodal structure that mimics the human brain.[3] These and other DL algorithms allow for analysis of high-dimensional and complex data that are being used widely in research settings.

The mechanics of AI center on analysis of machine-readable elements assembled for the purpose of predicting an outcome (ie, classification or regression) of interest.[4] The use of AI algorithms in health care depends on the construction of validated datasets derived from structured and unstructured data of relevance.[5] If validated datasets are maintained with appropriate governance, they may be amenable for algorithmic mining and model development.

Expenditure on health care AI is projected to increase from $2B in 2018 to $34B by 2025.[6] The National Academy of Medicine has emphasized the "quadruple aim" of improved outcomes, reducing cost, and improving patient and physician/provider experience in health care delivery. AI has the potential to positively impact these aims[2] while advancing professional development and medical education (Figure 1).

Specialties such as cardiology, oncology, and radiology were early AI adopters, whereas allergy and immunology is beginning to incorporate the use of AI. AI and ML appear to be well suited for the field of allergy and immunology where large, high-dimensional datasets are common. The use of big data approaches for infectious disease outbreak[7] prediction, asthma tracking,[8,9] and immunologic modeling from vaccination[10] are contemporary examples of use of AI. Similar to the push for adoption of evidence-based medicine in medical education, awareness of the data sources being used in models, application to CDS, and assessment of quality, transparency, reproducibility, and transferability are new areas for trainee education.[11]

This American Academy of Asthma Allergy and Immunology (AAAAI) workgroup report aims to develop a framework for understanding specialty-specific issues relevant to AI. Using search terms and Medical Subject Headings (MeSH) across the AI, ML, data science, data governance, and systems biology landscape along with common allergic conditions (eg, "asthma," "food allergy," "drug allergy," "immunodeficiency," "atopic dermatitis"), literature was reviewed via PubMed to understand the current status and potential impact of AI on clinical practice and research in allergy and immunology. Readers should note that the AAAAI does not have a formal position on AI use and implementation at this time, and this workgroup report is a summary of recent and relevant literature across the AI spectrum as assembled by membership of the AAAAI Health Informatics, Technology and Education (HITE) committee. In addition, opportunities for using AI, exploring potential areas for standardization including operational difficulties that might impact adoption of AI in allergy and immunology will be explored. We will delve into impacts of AI on research and the need for development of a framework for AI in allergy and immunology before broad adoption or implementation.

IMPACT ON ALLERGY AND IMMUNOLOGY CLINICAL PRACTICE

The clinical practice of allergy and immunology encompasses a variety of health care practitioners such as physicians, allied-health practitioners, nurses, as well as researchers, and laboratory technologists. In addition, policy makers and payers intersect with health technology such as electronic records and telemonitoring to create a complex network of stakeholders involved in assuring patient safety and quality, appropriate and timely diagnosis of diseases, and appropriate selection of treatments. Because the immune system is extraordinarily complex, this intersectionality is not well addressed in the current health care system. Although AI seems well poised to address some of the challenges, there are as yet several limitations on its implementation and use. In the next section, we will highlight some of the nascent and potential applications of AI that are applicable to allergy and immunology research and practice.

Disease diagnosis

Health care datasets, such as electronic health records (EHRs), and pathology images (eg, eosinophils in eosinophilic gastrointestinal disease biopsies) present unique challenges and opportunities for data extraction.[6] A major focus of AI in health care is automated disease detection[12] where electronic phenotyping (EP) of patients with distinct clinical features can enable machine-readable information and detection.[13] Development of precise EPs has proven useful for searching and ascertainment of large datasets to identify disease entities.[14] Similar approaches

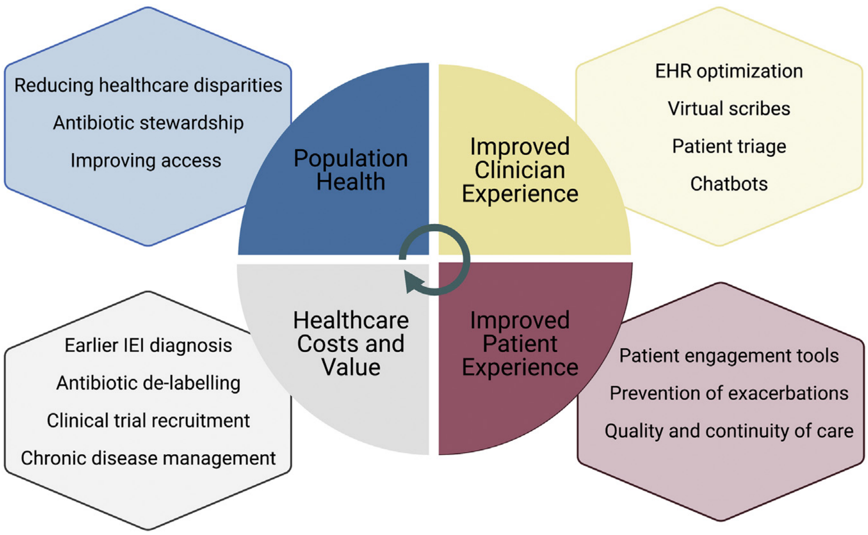

FIGURE 1. Quadruple aim of augmented intelligence applied to allergic and immunologic disorders. *EHR*, Electronic health record; IEI, inborn errors of immunity.

could be applied for allergic and immunologic diseases and will be discussed in this AAAAI workgroup report.

Within the field of allergy and immunology, an unmet need includes detection of patients at risk for primary immunodeficiency disorders (PIDs) or inborn errors of immunity (IEI) before fatal infection or organ damage. Claims data have been modeled for disease detection as one approach, and ML has been applied to available laboratory data such as calculated globulin fraction to detect hypogammaglobulinemia.[15,16] In addition, diagnoses from EHRs have been used to determine risk and provide guidance about the most likely International Union of Immunological Societies category of IEI.[17] These examples of structured health data mining show the possibilities of applying AI systems within learning health systems to improve diagnostic rates for patients with rare disease within the context of allergy and immunology. Figure 2 illustrates how undiagnosed PIDs or IEIs benefit from iteratively updated clinical data with ongoing disease characterization. Data extracted and housed in a digital learning repository may be processed and

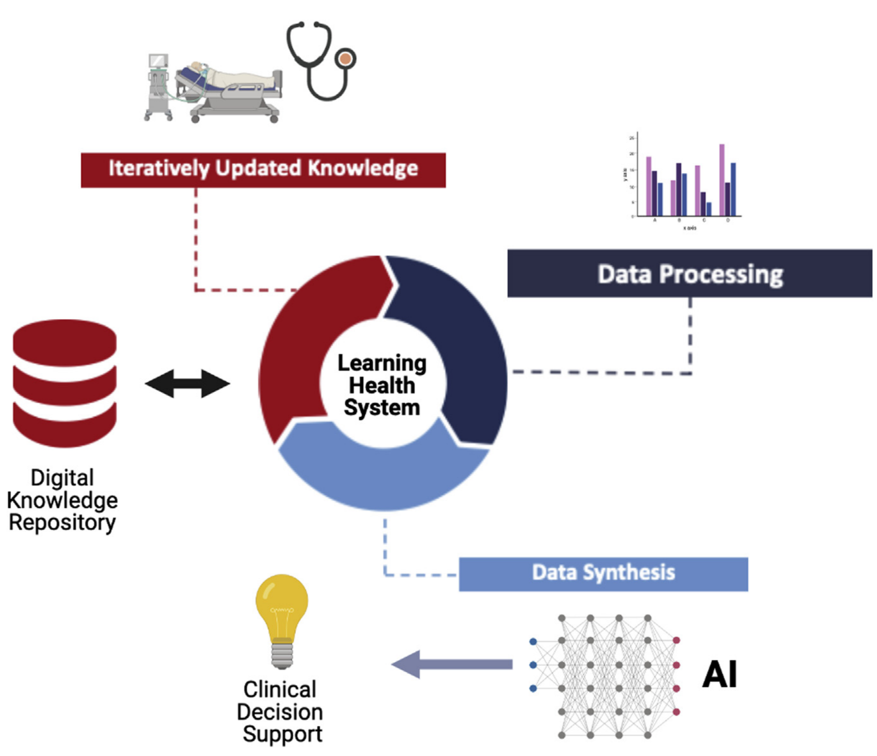

FIGURE 2. Augmented intelligence (AI) workflow in a learning health system.

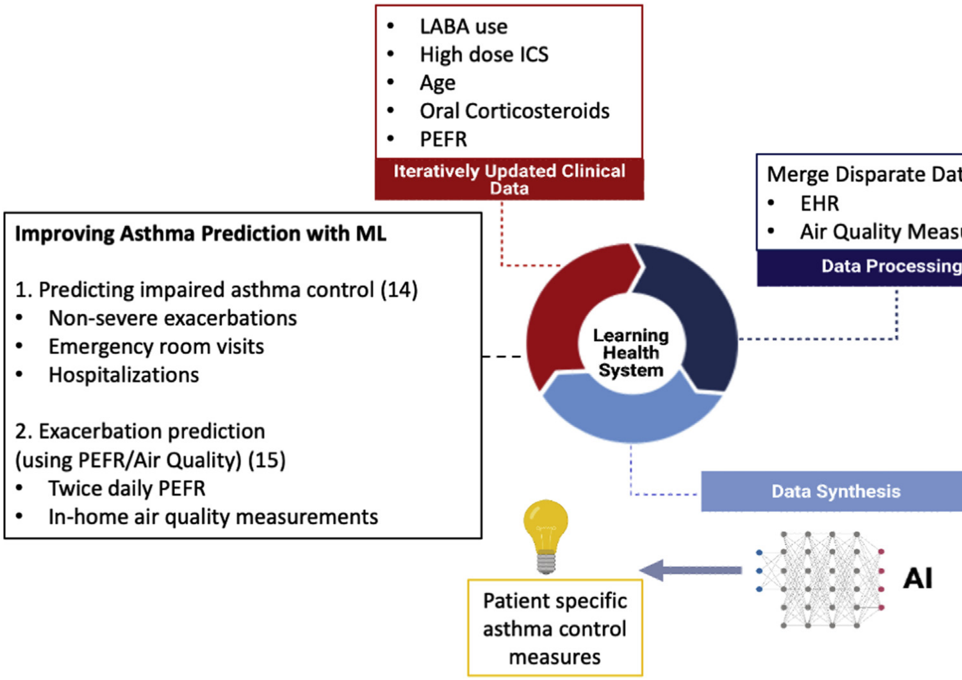

FIGURE 3. Recent examples of machine learning (ML) approaches for asthma prediction and control. *AI*, Augmented intelligence; *EHR*, electronic health record; *ICS*, inhaled corticosteroid; *LABA*, long-acting β-agonist; *PEFR*, peak expiratory flow rate.

TABLE I. Potential clinical and laboratory applications of AI in allergy and immunology

Area of allergy and immunology	Unmet need	Potential application of AI
Inborn errors of immunity/immune dysregulatory disorders	Early diagnosis, phenotyping, prognosis	Mining EHR information and classification
Adverse reactions to drugs or vaccines	Identifying causative drug, alternate drug tolerance prediction Identifying reaction type	Time series analysis/deep learning Phenotyping
Asthma	Prediction of exacerbations, endotypes, and response to therapy Biomarker identification	Time series analysis/deep learning Unsupervised learning
Food allergy	Biomarker identification for prognosis, tolerance	Unsupervised learning
Eosinophilia and EGIDs	Diagnosis, phenotyping, endotyping, prognosis prediction, response to therapy	Mining EHR information and phenotyping
COVID19-related disease	MIS-C prediction Contact tracing/disease spread prediction	Mining EHR information and classification Clustering/geospatial analysis
Laboratory immunology	Biomarker identification Disease correlations	Unsupervised learning Deep learning
Drug discovery	Drug repositioning	Deep learning, support vector machines

AI, Augmented intelligence; *EGID*, eosinophilic gastrointestinal syndrome; *EHR*, electronic health records; *MIS-C*, multisystem inflammatory syndrome—COVID.

analyzed with a resultant AI algorithm that assists with more accurate disease diagnosis for future cases.

Clinical practice and diagnostic decision support

Allergy and immunology patients may present with significant complexity requiring analysis of both structured and unstructured EHR data for optimal information use. Natural language processing (NLP) is an AI subdomain that may be applied to allergy and immunology through extraction of unstructured concepts (eg, disease symptoms) from free text entered in clinical notes. NLP is proposed as a mechanism for predicting patient outcomes (eg, exacerbations or hospitalization for asthma) that enable targeted interventions for improving outcomes in at-risk individuals. ML and NLP models have been built using EHR data and remote monitoring to classify asthma severity using features such as medications, symptoms, lung function, and comorbid conditions.[18-20] In addition, some ML models have predicted asthma exacerbations from telemonitoring data in adult patients requiring ER evaluation and hospital admission with high sensitivity, specificity, and accuracy.[21,22] Further, validation efforts using balanced population data will be required to further validate these data. The ability to aggregate data into AI models from various data streams (eg, EHR, claims data, wearables, and immunologic data) remains a challenge; however, 2 recent

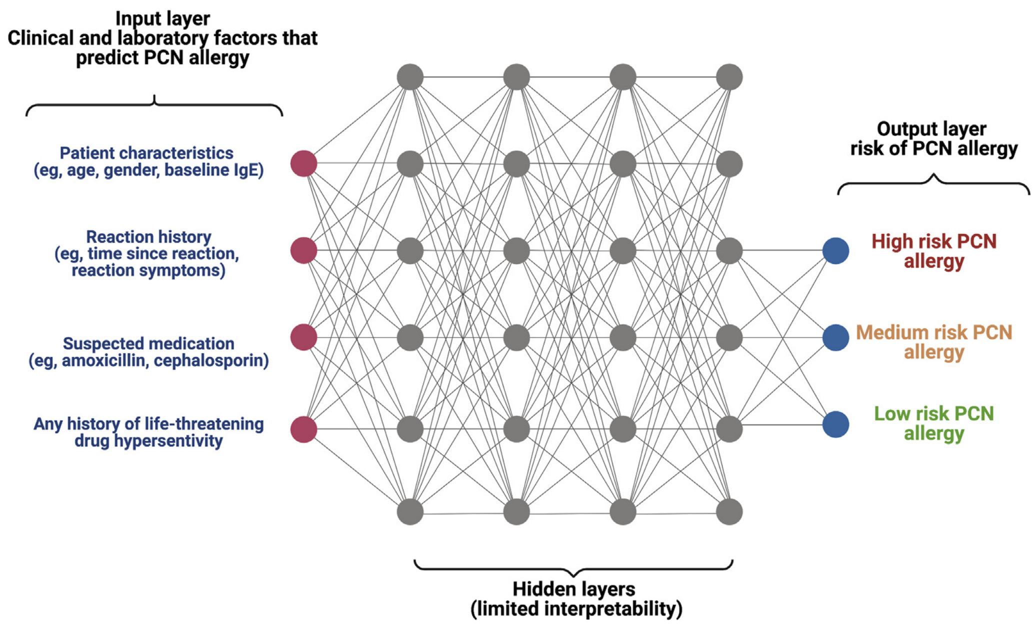

FIGURE 4. A beta-lactam artificial neural network to predict risk of reactions. This neural network takes parameters (eg, patient age, duration or location of drug rash, suspected culprit medication, etc), represents them as numbers, and uses them as "inputs" to the neural network. Nonlinear mathematical formulas are used to pass the information between the nodes in the hidden layers of the neural network, ultimately resulting in an "output prediction" for a given set of input parameters. In the case of a drug allergy prediction algorithm as shown, the output could be a probability of high, medium, or low risk of developing a reaction (eg, $P > .8$ = high risk, $P < .20$ = low risk, and between is medium). Neural networks are initially "trained" using data for which the output is known. For example, it may be a dataset containing information about a large group of patients who have been evaluated and challenged for penicillin allergy. The neural network takes this known data, passes the inputs through the model, and "tunes" the mathematical formulas in the hidden layers to maximize the prediction accuracy of the model. Then a new set of parameters (eg, for a new patient being evaluated for drug allergy) is input into the model to generate a prediction of the likelihood of PCN allergy. *PCN*, penicillin.

studies indicate that it may be possible[23,24] to use AI models for asthma prediction. In the context of asthma, EHR extracted data such as peak expiratory flow rate, long-acting β-agonist, and inhaled corticosteroid use are processed and analyzed for asthma prediction and assessment of disease control (Figure 3). The quality, size, and diversity of the datasets influence accuracy and scalability to diverse patient populations. Furthermore, there are an increasing number of stakeholders in AI, and the liability of clinical decision software vendors and practitioners remains unresolved.[25] Beyond asthma, many other diseases may benefit from assistive technologies including drug allergy, IEI and immunodysregulatory disorders, and food allergy (Table I).

Drug allergy and toxicity

The use of ML to supplement CDS for clinical applications in real time is particularly appealing for applications such as best practice alerts and smart order sets. CDS can be used to identify patients at higher risk for allergic diseases and/or to predict the optimal choice of drug as influenced by patient characteristics, drug-drug interactions, and available formulary choice. ML models showed superior predictive accuracy as compared with logistic regression in predicting patients at future risk of beta-lactam allergic reactions in adults.[9,26] Some studies used predictive modeling for non−IgE-mediated side effects such as drug-induced hepatotoxicity using molecular structure, lipophilicity, and other pharmacokinetic characteristics.[27,28] These studies used published datasets available through the US Food and Drug Administration (FDA) Adverse Reporting System, the European Union Adverse Drug Reaction reports, and the Observational Medical Outcomes Partnership.[29] As datasets for molecular descriptors and toxicogenomics increase, ML models such as ANN (Figure 4) may be used to predict adverse drug effects or risk for allergy in drug development, research,[3] and postmarketing surveillance.

AI applications to coronavirus-induced disease immune responses

AI models were vital for synthesizing vast amounts of data generated in the coronavirus-induced disease 2019 pandemic. Classifying the severe acute respiratory syndrome-coronavirus 2 genome and scaling vaccine production are two of the approaches being advanced by AI.[7,30] Use of AI and data science helped understand patterns of viral spread and which communities may be most vulnerable.[31] In addition, an unsupervised learning approach called Tracking Responders EXpanding can characterize lymphocyte subpopulations to provide early signs that herald diagnosis and enable insights into host defense mechanisms.[32] Understanding immunologic and/or vaccine responses in immunocompromised or immunodeficient patients remains an unmet need. Some are attempting use of AI/ML for multicriteria decision-making to identify patients in most need of convalescent plasma.[7] ML approaches are being leveraged to classify immune cell stress features and predict antiviral responses for drug repurposing efforts.[33,34] Lastly, ML is being coupled with reverse vaccinology to predict viral-host protein interactions and identify druggable targets and vaccine epitopes.[35]

TABLE II. Clinical and research AI applications in "omics" in allergy and immunology[41-43]

Data type	Information generated	Assay types	Clinical or research application in allergy and immunology
Genomics	Genetic sequence, to include SNPs, rearranged TCR/BCR sequences, open regions of chromatin, DNA methylation status, and the microbiome	Next-generation sequencing, microarray	Association between the methylation status of mononuclear cells and risk of asthma development
Transcriptomics	Sequence of expressed RNA transcripts, including mRNA and rRNA (often used in microbiome analysis)	Next-generation sequencing, microarray	Comparison between the skin and gut microbiome
Proteomics	Identification and quantification of proteins in biological samples	Mass spectrometry NMR spectroscopy Affinity-based methods	Evaluation of serum proteins to identify anaphylaxis phenotypes and associated protein signatures
Lipidomics	Identification and quantification of lipids in biological samples	Mass spectrometry NMR spectroscopy	Lipid profiles in third trimester pregnant women and risk of infant atopic disease
Metabolomics	Identification and quantification of metabolites in biological samples	Mass spectrometry NMR spectroscopy	Association between serum metabolites and lung function in children with severe asthma
Phenomics	Clinical diagnoses, laboratory, and radiology results in a format that can be queried	EHR data Clinical laboratory, radiographic data	Identification of trends in office PFTs and rescue inhaler use to predict likelihood of future severe asthma exacerbations
Exposomics	Exposures experienced from conception to death. Includes diet, lifestyle, climate, environmental, and occupational exposures	Questionnaires, biomonitoring data (pollution tracking), environmental or dwelling measurements	Identification of patterns between local particulate matter concentrations, local elementary school ventilation systems, and asthma exacerbations in urban areas
Cell profiling	Proteins expressed on the inside and outside of cells	Flow cytometry Mass cytometry/CyTOF	Use of mass cytometry to identify unique populations of cells found in milk-allergic children but not healthy age-matched controls

AI, Augmented intelligence; *BCR*, B-cell receptor; *CyTOF*, Cy time-of-flight; *DNA*, deoxyribonucleic acid; *EHR*, electronic health record; *mRNA*, messenger ribonucleic acid; *rRNA*, ribosomal RNA; *NMR*, nuclear magnetic resonance; *PFT*, pulmonary function tests; *SNP*, single nucleotide polymorphism; *TCR*, T-cell receptor.

Practice management

The practice and management of medicine is a target for automating and improving efficient care delivery. The administrative cost and adverse effects of EHR clinical workflow have increased[9,10] and have led to clinician burnout.[36,37] Although EHRs have served regulatory, billing, and revenue needs, prioritizing the patient-clinician interaction and user experience are aspects of the quadruple aim (Figure 1). Practice management could be significantly streamlined with AI. Potential uses include clinical order set automation[13] where NLP evaluates clinical entries to ascertain drug reactions[14,15] and uses speech-to-text for clinical documentation.[38,39] More companies are developing digital products such as "chatbots," or automated support chat features, for patient triage. Digital scribes employ NLP and speech recognition with EHR integration for outpatient clinical encounters. Other potential applications for practice management may include AI workflows for prior authorizations, billing, supply chain of extracts or vaccines, and optimizing patient triage or clinic flow.[39] AI could extract data from the EHR to streamline order sets for medication prescribing, diagnostic testing, and referrals. However, engagement of clinicians in the development of AI tools and operationalization of AI in the EHR will be crucial. Future research funding of AI in health care should focus on the impact of AI on clinician workflow, physician well-being, and clinical outcomes.

Analysis of immunologic data

During the last decade, the field of Immunology has seen an increase in the volume and complexity of biologic data that can be generated, largely driven by advances in multiplexed technologies, imaging, and genomic sequencing.[40] Frequently referred to as multi-"omics," these data include DNA sequence, gene expression/RNA sequence, and assessment of proteins, lipids, metabolites, the microbiome, and environmental/lifestyle exposures (Table II). As each data type can capture different attributes,[44] complementary and integrated approaches for immunological investigation can be employed. To process and transform such large-scale, high-dimensional data into biological and clinical insights, computational tools, including those that apply AI and ML approaches, have been implemented in both basic and clinical immunology.

Although the use of ML in common clinical practice is still nascent, researchers have already successfully developed ML tools to make significant contributions in research. So far, ML methods have been used to analyze genomics data to understand pathophysiology, define biomarkers, and dissect endotypes of allergic diseases such as asthma, atopic dermatitis, and food allergy (reviewed in the papers by Mersha et al[41] and Ghosh et al[45]). Similar approaches are being employed in clinical immunology including use of support vector machine (SVM) for candidate gene identification in IEI,[46] and ML algorithms to analyze high-dimensional mass cytometry data to identify lymphocyte subpopulations for influenza vaccine response prediction.[10]

As ML methods are increasing in the medical literature, providers must understand some of their limitations. A common pitfall is the use of data inputs of varying quality. When the data contain artifactual variations or are not representative of heterogeneity in human samples, ML algorithms can misinterpret the dataset.[47,48] Although several groups have developed AI algorithms for flow cytometry to detect specific lymphocyte subpopulations,[47] the differential process of fluorescent labeling, cytometer voltage selection, and gating strategies to define specific cell subpopulations are operator dependent, lack standardization, and have a high degree of variability such that one cell subpopulation may be defined differently by disparate groups.[47,48] These variations can affect model generalizability and performance. As such, application of ML to "real-world" biological samples requires standardizing data analysis before broad scale implementation. Other common pitfalls are reviewed in detail elsewhere.[49]

Rapid technological advances allow biological characterization at increasingly high resolution and sensitivity. Most recently, single cell profiling has accelerated the ability to identify and phenotype cell types.[50] For example, single-cell RNA sequencing can identify CD4+ T cells enriched in endoscopic biopsies of patients with active eosinophilic esophagitis (EoE) when compared with EoE in remission.[51] In addition, single molecule array digital enzyme-linked immunosorbent assay technology now allows ultrasensitive proteomic quantification, which has been used to evaluate plasma concentrations of interferon-α in patients with polygenic and monogenic interferonopathies.[52]

The ability to generate high-dimensional data using a variety of modalities allows for more comprehensive biological characterization. In AI, for example, the Mechanisms of the Development of Allergy project applied ML methods to several classes of omics data (including transcriptomics, proteomics, DNA methylation, and genome-wide association study data) to identify 2 phenotypes of IgE-associated disease ("monosensitization" vs "polysensitization") and found that those with polysensitization were more likely to have severe and persistent allergic disease[53] (reviewed in the paper by Mersha et al[41]). However, analysis of multiomic data requires computational and mathematical approaches that can process and model hundreds of thousands of measured parameters and extract those that are relevant to key biological variables. Some of the issues that come into play include: (1) evaluating the data for differences that arise from batch effects; (2) adjusting for multiple comparisons; (3) data reduction (eg, principal component analysis); and (4) determining the optimal ML model for analysis (eg, SVM or neural network).[54] Readers of studies using multiomic data should consider these and related issues when evaluating study quality and subsequent conclusions.

Candidate selection for clinical trials

Phenotyping of clinical notes and EHR data to identify distinct clinical concepts became highly visible with the advent of the federally funded Electronic Medical Records and Genomics program[55] and other efforts within the bioinformatics community.[56] Applications such as clinical research cohort selection[57] and clinical phenotyping[58] became early and visible applications of AI. NLP was identified as an approach for overcoming clinical trial recruitment hurdles by using EHR data to identify potential research participants, where classifying asthma phenotypes[8] or atopic dermatitis severity[59] can enable trial recruitment. Similarly, mining health record information in other practice settings, such as emergency department unstructured allergy data,[60] could be a key to intelligent extraction of data across the care continuum. In a recent publication, Seol et al[61] trained and validated a custom NLP algorithm from an Olmsted County Birth Cohort and used predetermined asthma criteria to create an "asthma predictive index" to distinguish patients predicted to have asthma. Further optimizing tools such as this and developing algorithms for other disease entities could broadly improve clinical trial candidate ascertainment.

CHALLENGES FOR AI

Data procurement and modeling

There are many potential data considerations that remain as challenges for AI when applied to the allergy and immunology context. The end-to-end AI development process involves extracting appropriate data for analysis, addressing key elements of data quality, and data provenance that is a transparent description of where the data come from. Many have indicated the need for a reference card, or so-called model cards,[62] that documents relevant performance characteristics and intended use of a model. From a purely data perspective, data inputs, use cases, and data procurement are key factors that directly impact the models that are built. Governance of models to ensure optimal inputs, best practice algorithmic model development (ie, training, validation, and testing), and operationalizing the model effectively by creating a sustainment plan for tracking longitudinal performance is important. Lastly, model deployment requires regulatory oversight to ensure that ethical and equity considerations are met as well as to optimize reproducibility of AI. The details of a granular end-to-end analytics pipeline are beyond the scope of this article; however, we will discuss key elements that are widely publicized and relate to concerns about fairness and reproducibility in digital medicine.[63,64]

Ethics and equity implications

Ethical considerations must be considered at all stages of AI algorithm development but are particularly important in the stages of data procurement and model development. As AI should enhance the health care of individuals and populations, bias in algorithms is a critical concern. One study analyzed a commercial prediction algorithm to guide health decisions for US patients. Using health care utilization and spending on care, the algorithm falsely attributed better health scores to Black patients compared with sick White patients despite the fact that unequal access to care and health care disparities likely resulted in algorithmic bias.[65]

Patient safety and health equity using AI are crucial concerns. Health care practitioners must incorporate informed consent regarding diagnostic error, accountability, privacy, and cybersecurity considerations[1] when AI technology is used in their care. AI-enabled misdiagnosis is also a concern, particularly when relying solely on CDS or if inaccurate data or homogeneous populations were used to train an algorithm. Deep neural networks may be a "black box" for clinicians,[1] and over-reliance on AI may make it difficult to counter a clinical decision suggested by the AI.[66] Guidelines on how to override algorithms must be considered. Similarly, there will need to be a mechanism for reporting of safety events including misdiagnoses or inappropriate treatment decisions. Systems to address areas of conflict between ML-CDS tools and clinician judgment will need to be developed. In addition, medicolegal aspects of use of (or inability to access) AI technology for clinicians in different practice settings will need to be addressed. Engaging frontline users in the adoption of AI will be important in future applications.

There is substantial concern regarding health equity in AI. Although clinicians are not immune to racial and other biases, AI systems' ability to achieve massive scaling means these biases could be amplified more than by humans alone. In addition, some clinical trials remain insufficiently diverse in their recruitment[67]; as such, datasets may result in inadequate assessments for underrepresented populations.[66] Moreover, consideration of data inputs (such as health care utilization) may be an ineffective proxy for illness,[65] and health inequities may be exacerbated when bias is "baked-in" to AI algorithms.[62] On the other hand, disparities of patient experience of pain may be re-examined using ML as was performed in a study of knee pain.[68] In this study, an algorithmic assessment of radiographic features using a diverse patient training set showed less pain disparities by race than the radiographic scale currently used in routine practice. Because radiographic severity may impact when arthroplasty is offered to patients, ML has the potential to alter future outcomes. Clearly, both possibilities exist with AI not only having the potential to worsen bias but also having the potential to improve the understanding of diverse health outcomes and improve care for historically disadvantaged patients.

AI DEPLOYMENT

AI governance

AI clinical applications will likely be accelerated by the proposed regulatory framework of "Software as a Medical Device" (SaMD).[69] Here, SaMD is defined by the FDA as a medical device platform or virtual network that is used for medical purposes but is distinct from hardware with embedded software. Numerous consensus documents exist related to ethical AI use. The FDA and United Nations Children's Fund have implemented ML "best practices" and operational standards that enable fairness in respect to the proprietary nature of the technology and mitigate bias.[70,71] With this broad perspective for both AI impact and potential for bias, governance teams must have diverse stakeholder representation and "first do no algorithmic harm" with an intent to optimally balance utility and fairness[70] in the process of assuring algorithmic equity. To facilitate optimal development and operational practices, thought leaders and broad stakeholder groups have begun to emerge. For example, the Partnership on AI formed "About ML" that focuses on transparent ML lifecycles to improve responsible scaling of ML and define optimal ML lifecycles.[72] Although the "black box" of AI may not be fully reducible, and alternate statistical methods may be used, the Partnership on AI is focused on engaging multiple stakeholders to make AI more equitable.

Training and education

Currently, AI as a field is outside of the scope of standard training and core competencies for Allergy and Immunology. In contrast, in 2019, the American Medical Association adopted policies to bolster incorporation of AI within medical education.[73] Specifically, curricular modifications to incorporate educational modules and training on bias in assistive technologies were highlighted. As technological advances occur, medical education will increasingly be focused on ensuring that trainees have mentors in informatics and senior faculty members who can contextualize AI data applications. Applying these technologies may become important for professional development and identity formation for future allergy and immunology specialists.

AI adoption

Before adoption, AI algorithms should be rigorously validated in the context of clinical trials. To date only one comparative effectiveness study of an AI algorithm has been performed in the field of allergy and immunology.[74] Clinical utility, algorithmic explainability, and interoperability should also be considered. Safeguarding privacy of data and outlining liability concerns[75] are paramount. AI dataset governance and impacts on individual patients are similar to issues frequently discussed when considering genomic data.[76] Data sharing amongst AI applications, the EHR, and other health devices along with the impact of direct-to-consumer tools will raise further privacy and ethical concerns. Engaging policy makers and clinicians in advocacy efforts to establish privacy safeguards will be needed to preserve viable and safe AI systems. Rapid adoption may cause interoperability problems similar to rapid EHR adoption if downstream effects are not anticipated.[77] Ultimately, the value of AI for specific applications in allergy and immunology will influence the degree and magnitude of AI adoption in our specialty.

Coverage and reimbursement

In 2018, the FDA granted approval to an AI device for retinal fundus examinations.[78] This device, called IDx-DR, is capable of rapid autonomous retinal examination, can be used in areas of specialty shortages, and could be scalable and cost-effective.[79,80] Tools such as IDx-DR fall under the FDA category of breakthrough device designation (BDD) as novel technology, which have their own criteria and pathways to approval. However, Medicare Administrative Contractors ultimately determine coverage of BDDs according to coding, coverage, and payment rules related to medical necessity. A BDD may be eligible for new technology add-on payment, but this only applies to inpatient services. In contrast, outpatient device coverage will depend on commercial payers and provider contracts. As such, there is considerable ambiguity about how AI may be reimbursed in a comprehensive manner and whether these technologies will ultimately prove to be cost-effective. In addition, the impact of direct-to-consumer markets on the use and adoption of AI digital tools will influence cost for patients, clinicians, and the health care system. Future areas of research must investigate the feasibility, efficacy, and cost-effectiveness of AI implementation within mobile health devices, remote-patient monitoring systems, the EHR, and in assessments of population health.

AI maintenance and evaluation

As clinicians find increasing use for AI tools, clinical acumen will need to be expanded toward interpreting AI. In addition, rigorous assessment of algorithmic explainability and reporting of clinical and performance measures, including the population in which the AI was trained and the standard to which the AI was compared using one of several approaches will be important. Checklists for manuscript writing that include minimum information about clinical artificial intelligence modeling, "Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis" (TRIPOD-AI), or "Prediction model Risk Of Bias ASsessment Tool" (PROBAST-AI), or "MINimum Information for Medical AI Reporting" (MINIMAR) will be important and are reviewed elsewhere.[81] Added training will be needed to interpret appropriate construction of studies using the Artificial Intelligence Consolidated Standards of Reporting Trials (AI-CONSORT) guidance,[82] and as technology advances algorithms evaluated to ensure that they remain appropriate.

FUTURE DIRECTIONS

AI has the potential to impact the specialty of allergy and immunology in the next decade. From a data procurement perspective, advances in data systems, EHR design, and recognition of relevant inputs (eg, pollen identification[83,84] and epitope maps) hold promise for AI-based improvements. As routinely generated medical and genetic data are captured and stored more thoughtfully within EHRs, more reliable data acquisition and subsequent model development using evidence-based and best-practice algorithm training and validation will be possible. AI can be used for pathology and radiology relevant applications to improve care for patients with allergic and immunologic disorders.[85-87] In addition, postmarket surveillance of outcomes and consideration of ethical factor impact on health care disparities will be required. Fundamentally, involvement and training of allergy and immunology physicians to be stewards in the design, development, and implementation of AI will be important to define best practice use for optimal patient outcomes.

CONCLUSIONS AND RECOMMENDATIONS

This AAAAI workgroup report highlights the potential clinical implementation of AI in allergy and immunology to improve individual and population-wide health. This report serves as a high-level framework for conceptualizing AI for the practicing clinician. Limitations of this report include the inability to describe at length the process of data procurement, and model development that would help inform the practical considerations outlined throughout. Many aspects such as data quality, algorithm sharing and explainability, partnering with developers, facilitating data science competency in allergy and immunology training programs, use of AI in quality improvement, and validation of theoretical models are not discussed in sufficient depth for the experienced reader. Similarly, how and when to use AI or how to develop AI falls outside of the scope of this workgroup report. It should be noted that AI will not be the best fit for all data applications. In some cases, data scientists may determine that a rigorous statistical approach is more appropriate than an ML/AI approach, for example, when a high degree of accuracy is desired, for small datasets, or when there are a limited numbers of variables.[88] Furthermore, assuring equity dimensions and potential impact of AI on health disparities is key, and we only scratched the surface in describing some potential impacts in this workgroup report. Future impact analyses of AI on clinician workflow, health care consults, and health disparities are needed. There are several concrete recommendations that can be made as AI continues to mature and evolve:

- Engage frontline clinicians and health care systems in developing AI systems that are cost-effective, and abide by privacy and legal standards.
- Allergy and immunology specialists should be involved in the design, validation, and implementation of AI in Allergy and Immunology.
- Partnerships with various stakeholders including but not limited to local health system informaticists, clinicians, patients, data scientists, and health information technology professionals will be needed as AI in allergy and immunology is deployed.
- Payers and policy makers will have important inputs into applications of future AI.
- Clinicians engaging with AI should become trained in these domains, to optimally advance AI for allergy and immunology applications and patient care.

Acknowledgments

We would like to thank the AAAAI Leadership Institute, mentors Drs Thanai Pongdee and James Li, as well as chairs of the HITE committee for critical discussions and support and Dr Sunit Jariwala for his critical review of the manuscript. Figures 1 and 4 were created using BioRender.com.

REFERENCES

1. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nat Med 2019;25:44-56.
2. Matheny M, Israni ST, Auerbach A, Beam A, Bleicher P, Chapman W, et al. Artificial Intelligence in Health Care: The Hope, the Hype, the Promise, the Peril. Washington, DC: National Academy of Medicine; 2019.
3. Vamathevan J, Clark D, Czodrowski P, Dunham I, Ferran E, Lee G, et al. Applications of machine learning in drug discovery and development. Nat Rev Drug Discov 2019;18:463-77.
4. Witten IH, Frank E, Hall MA, Pal CJ. Data Mining Practical Machine Learning Tools and Techniques. 4th ed. Burlington, MA: Morgan Kaufmann; 2016.
5. Rider NL, Srinivasan R, Khoury P. Artificial intelligence and the hunt for immunological disorders. Curr Opin Allergy Clin Immunol 2020;20:565-73.
6. Rudrapatna VA, Butte AJ. Opportunities and challenges in using real-world data for health care. J Clin Invest 2020;130:565-74.
7. Albahri AS, Hamid RA, Alwan JK, Al-Qays ZT, Zaidan AA, Zaidan BB, et al. Role of biological data mining and machine learning techniques in detecting and diagnosing the novel coronavirus (COVID-19): a systematic review. J Med Syst 2020;44:122.
8. Himes BE, Kohane IS, Ramoni MF, Weiss ST. Characterization of patients who suffer asthma exacerbations using data extracted from electronic medical records. AMIA Annu Symp Proc 2008;2008:308-12.
9. Almonacid Sánchez C, Melero Moreno C, Quirce Gancedo S, Sánchez-Herrero MG, Álvarez Gutiérrez FJ, Bañas Conejero D, et al. PAGE study: summary of a study protocol to estimate the prevalence of severe asthma in Spain using big-data methods. J Investig Allergol Clin Immunol 2021;31:308-15.
10. Tomic A, Tomic I, Rosenberg-Hasson Y, Dekker CL, Maecker HT, Davis MM. SIMON, an automated machine learning system, reveals immune signatures of influenza vaccine responses. J Immunol 2019;203:749-59.
11. Cutillo CM, Sharma KR, Foschini L, Kundu S, Mackintosh M, Mandl KD, et al. Machine intelligence in healthcare-perspectives on trustworthiness, explainability, usability, and transparency. NPJ Digit Med 2020;3:47.
12. Bastarache L, Hughey JJ, Goldstein JA, Bastraache JA, Das S, Zaki NC, et al. Improving the phenotype risk score as a scalable approach to identifying patients with Mendelian disease. J Am Med Inform Assoc 2019;26:1437-47.
13. Banda JM, Seneviratne M, Hernandez-Boussard T, Shah NH. Advances in electronic phenotyping: from rule-based definitions to machine learning models. Annu Rev Biomed Data Sci 2018;1:53-68.
14. Pacheco JA, Rasmussen LV, Kiefer RC, Campion TR, Speltz P, Carroll RJ, et al. A case study evaluating the portability of an executable computable phenotype algorithm across multiple institutions and electronic health record environments. J Am Med Inform Assoc 2018;25:1540-6.
15. Holding S, Khan S, Sewell WAC, Jolles S, Dore PC. Using calculated globulin fraction to reduce diagnostic delay in primary and secondary hypogammaglobulinaemias: results of a demonstration project. Ann Clin Biochem 2015;52(Pt 3):319-26.
16. Rider NL, Miao D, Dodds M, Modell V, Modell F, Quinn J, et al. Calculation of a primary immunodeficiency "risk vital sign" via population-wide analysis of claims data to aid in clinical decision support. Front Pediatr 2019;7:70.
17. Pickett G, Motazedi T, Kutac C, Cahill G, Cunnigham-Rundles C, Fuleihan RL, et al. Infection phenotypes among patients with primary antibody deficiency mined from a US patient registry. J Clin Immunol 2021;41:374-81.

18. Kaur H, Sohn S, Wi C-I, Ryu E, Park MA, Bachman K, et al. Automated chart review utilizing natural language processing algorithm for asthma predictive index. BMC Pulm Med 2018;18:34.
19. Ross MK, Yoon J, van der Schaar A, van der Schaar M. Discovering pediatric asthma phenotypes on the basis of response to controller medication using machine learning. Ann Am Thorac Soc 2018;15:49-58.
20. Wi C-I, Sohn S, Rolfes MC, Seabright A, Ryu E, Voge G, et al. Application of a natural language processing algorithm to asthma ascertainment. An automated chart review. Am J Respir Crit Care Med 2017;196:430-7.
21. Finkelstein J, Jeong IC. Machine learning approaches to personalize early prediction of asthma exacerbations. Ann N Y Acad Sci 2017;1387:153-65.
22. Luo G, He S, Stone BL, Nkoy FL, Johnson MD. Developing a model to predict hospital encounters for asthma in asthmatic patients: secondary analysis. JMIR Med Inform 2020;8:e16080.
23. Zein JG, Wu C-P, Attaway AH, Zhang P, Nazha A. Novel machine learning can predict acute asthma exacerbation. Chest 2021;159:1747-57.
24. Bae WD, Kim S, Park C-S, Alkobaisi S, Lee J, Seo W, et al. Performance improvement of machine learning techniques predicting the association of exacerbation of peak expiratory flow ratio with short term exposure level to indoor air quality using adult asthmatics clustered data. PLoS One 2021;16:e0244233.
25. Morley J, Machado CCV, Burr C, Cowls J, Joshi I, Taddeo M, et al. The ethics of AI in health care: a mapping review. Soc Sci Med 2020;260:113172.
26. Chiriac AM, Wang Y, Schrijvers R, Bousquet PJ, Mura T, Molinari N, et al. Designing predictive models for beta-lactam allergy using the drug allergy and hypersensitivity database. J Allergy Clin Immunol Pract 2018;6:139-148.e2.
27. Hammann F, Schöning V, Drewe J. Prediction of clinically relevant drug-induced liver injury from structure using machine learning. J Appl Toxicol 2019;39:412-9.
28. Cai J, Li C, Liu Z, Du J, Ye J, Gu Q, et al. Predicting DPP-IV inhibitors with machine learning approaches. J Comput Aided Mol Des 2017;31:393-402.
29. Ietswaart R, Arat S, Chen AX, Farahmand S, Kim B, DuMouchel W, et al. Machine learning guided association of adverse drug reactions with in vitro target-based pharmacology. EBioMedicine 2020;57:102837.
30. Cao Y, Li L, Feng Z, Wan S, Huang P, Sun X, et al. Comparative genetic analysis of the novel coronavirus (2019-nCoV/SARS-CoV-2) receptor ACE2 in different populations. Cell Discov 2020;6:11.
31. Malik YS, Sircar S, Bhat S, Sharun K, Dhama K, Dadar M, et al. Emerging novel coronavirus (2019-nCoV)-current scenario, evolutionary perspective based on genome analysis and recent developments. Vet Q 2020;40:68-76.
32. Barone SM, Paul AGA, Muehling LM, Lannigan JA, Kwok WW, Turner RB, et al. Unsupervised machine learning reveals key immune cell subsets in COVID-19, rhinovirus infection, and cancer therapy. eLife 2021;10:e64653.
33. Mirabelli C, Wotring JW, Zhang CJ, McCarty SM, Fursmidt R, Frum T, et al. Morphological cell profiling of SARS-CoV-2 infection identifies drug repurposing candidates for COVID-19. Proc Natl Acad Sci USA 2021;118:e2105815118.
34. Zhou Y, Wang F, Tang J, Nussinov R, Cheng F. Artificial intelligence in COVID-19 drug repurposing. Lancet Digit Health 2020;2:e667-76.
35. Ong E, Wong MU, Huffman A, He Y. COVID-19 coronavirus vaccine design using reverse vaccinology and machine learning. Front Immunol 2020;11:1581.
36. Bingemann T, Sharma H, Nanda A, Khan DA, Markovics S, Sussman J, et al. AAAAI work group report: physician wellness in allergy and immunology. J Allergy Clin Immunol Pract 2020;8:1224-9.
37. Erickson SM, Rockwern B, Koltov M, McLean RM. Medical Practice and Quality Committee of the American College of Physicians. Putting patients first by reducing administrative tasks in health care: a position paper of the American College of Physicians. Ann Intern Med 2017;166:659-61.
38. Saxena K, Diamond R, Conant RF, Mitchell TH, Gallopyn IG, Yakimow KE. Provider adoption of speech recognition and its impact on satisfaction, documentation quality, efficiency, and cost in an inpatient EHR. AMIA Jt Summits Transl Sci Proc 2018;2017:186-95.
39. Dymek C, Kim B, Melton GB, Payne TH, Singh H, Hsiao C-J. Building the evidence-base to reduce electronic health record-related clinician burden. J Am Med Inform Assoc 2021;28:1057-61.
40. Goodwin S, McPherson JD, McCombie WR. Coming of age: ten years of next-generation sequencing technologies. Nat Rev Genet 2016;17:333-51.
41. Mersha TB, Afanador Y, Johansson E, Proper SP, Bernstein JA, Rothenberg ME, et al. Resolving clinical phenotypes into endotypes in allergy: molecular and omics approaches. Clin Rev Allergy Immunol 2021;60:200-19.
42. Joshi A, Rienks M, Theofilatos K, Mayr M. Systems biology in cardiovascular disease: a multiomics approach. Nat Rev Cardiol 2021;18:313-30.
43. Agache I, Miller R, Gern JE, Hellings PW, Jutel M, Muraro A, et al. Emerging concepts and challenges in implementing the exposome paradigm in allergic diseases and asthma: a Practall document. Allergy 2019;74:449-63.
44. Karahalil B. Overview of systems biology and omics technologies. Curr Med Chem 2016;23:4221-30.
45. Ghosh D, Bernstein JA, Khurana Hershey GK, Rothenberg ME, Mersha TB. Leveraging multilayered “omics” data for atopic dermatitis: a road map to precision medicine. Front Immunol 2018;9:2727.
46. Keller MD, Pandey R, Li D, Glessner J, Tian L, Henrickson SE, et al. Mutation in IRF2BP2 is responsible for a familial form of common variable immunodeficiency disorder. J Allergy Clin Immunol 2016;138:544-550.e4.
47. Saeys Y, Van Gassen S, Lambrecht BN. Computational flow cytometry: helping to make sense of high-dimensional immunology data. Nat Rev Immunol 2016;16:449-62.
48. Finak G, Langweiler M, Jaimes M, Malek M, Taghiyar J, Korin Y, et al. Standardizing flow cytometry immunophenotyping analysis from the human immunophenotyping consortium. Sci Rep 2016;6:20686.
49. Teschendorff AE. Avoiding common pitfalls in machine learning omic data science. Nat Mater 2019;18:422-7.
50. Zhu C, Preissl S, Ren B. Single-cell multimodal omics: the power of many. Nat Methods 2020;17:11-4.
51. Wen T, Aronow BJ, Rochman Y, Rochman M, Kc K, Dexheimer PJ, et al. Single-cell RNA sequencing identifies inflammatory tissue T cells in eosinophilic esophagitis. J Clin Invest 2019;129:2014-28.
52. Rodero MP, Decalf J, Bondet V, Hunt D, Rice GI, Werneke S, et al. Detection of interferon alpha protein reveals differential levels and cellular sources in disease. J Exp Med 2017;214:1547-55.
53. Anto JM, Bousquet J, Akdis M, Auffray C, Keil T, Momas I, et al. Mechanisms of the Development of Allergy (MeDALL): introducing novel concepts in allergy phenotypes. J Allergy Clin Immunol 2017;139:388-99.
54. Yamada R, Okada D, Wang J, Basak T, Koyama S. Interpretation of omics data analyses. J Hum Genet 2021;66:93-102.
55. Shang N, Liu C, Rasmussen LV, Ta CN, Caroll RJ, Benoit B, et al. Making work visible for electronic phenotype implementation: lessons learned from the eMERGE network. J Biomed Inform 2019;99:103293.
56. Pathak J, Kho AN, Denny JC. Electronic health records-driven phenotyping: challenges, recent advances, and perspectives. J Am Med Inform Assoc 2013;20:e206-11.
57. Weng C, Shah NH, Hripcsak G. Deep phenotyping: embracing complexity and temporality—towards scalability, portability, and interoperability. J Biomed Inform 2020;105:103433.
58. Juhn Y, Liu H. Artificial intelligence approaches using natural language processing to advance EHR-based clinical research. J Allergy Clin Immunol 2020;145:463-9.
59. Gustafson E, Pacheco J, Wehbe F, Silverberg J, Thompson W. A machine learning algorithm for identifying atopic dermatitis in adults from electronic health records. IEEE Int Conf Healthc Inform 2017;2017:83-90.
60. Goss FR, Plasek JM, Lau JJ, Seger DL, Chang FY, Zhou L. An evaluation of a natural language processing tool for identifying and encoding allergy information in emergency department clinical notes. AMIA Annu Symp Proc 2014;2014:580-8.
61. Seol HY, Rolfes MC, Chung W, Sohn S, Ryu E, Park MA, et al. Expert artificial intelligence-based natural language processing characterises childhood asthma. BMJ Open Respir Res 2020;7:e000524.
62. Mitchell M, Wu S, Zaldivar A, Barnes P, Vasserman L, Hutchinson B, et al. Model cards for model reporting. Proceedings of the Conference on Fairness, Accountability, and Transparency—FAT* ’19. New York, NY: ACM Press; 2019:220-9.
63. Stupple A, Singerman D, Celi LA. The reproducibility crisis in the age of digital medicine. NPJ Digital Med 2019;2:2.
64. Beam AL, Manrai AK, Ghassemi M. Challenges to the reproducibility of machine learning models in health care. JAMA 2020;323:305-6.
65. Obermeyer Z, Powers B, Vogeli C, Mullainathan S. Dissecting racial bias in an algorithm used to manage the health of populations. Science 2019;366:447-53.
66. Vayena E, Blasimme A, Cohen IG. Machine learning in medicine: addressing ethical challenges. PLoS Med 2018;15:e1002689.
67. Spielman DB, Liebowitz A, Kelebeyev S, Smith TL, McKinney K, Woodard T, et al. Race in rhinology clinical trials: a decade of disparity. Laryngoscope 2021;131:1722-8.
68. Pierson E, Cutler DM, Leskovec J, Mullainathan S, Obermeyer Z. An algorithmic approach to reducing unexplained pain disparities in underserved populations. Nat Med 2021;27:136-40.

69. Gerke S, Babic B, Evgeniou T, Cohen IG. The need for a system view to regulate artificial intelligence/machine learning-based software as medical device. NPJ Digital Med 2020;3:53.
70. Reddy S, Allan S, Coghlan S, Cooper P. A governance model for the application of AI in health care. J Am Med Inform Assoc 2020;27:491-7.
71. Mello MM, Wang CJ. Ethics and governance for digital disease surveillance. Science 2020;368:951-4.
72. Partnership on AI. About ML. Accessed June 21, 2021. https://www.partnershiponai.org/about-ml/
73. American Medical Association. 2019 Council on Medical Education AI report. 2019 CME report; 2019. Accessed June 21, 2021. https://www.ama-assn.org/system/files/2019-08/ai-2019-cme-report.pdf
74. Seol HY, Shrestha P, Muth JF, Wi C-I, Sohn S, Ryu E, et al. Artificial intelligence-assisted clinical decision support for childhood asthma management: a randomized clinical trial. PLoS One 2021;16:e0255261.
75. McGreevey JD, Hanson CW, Koppel R. Clinical, legal, and ethical aspects of artificial intelligence-assisted conversational agents in health care. JAMA 2020;324:552-3.
76. Bonomi L, Huang Y, Ohno-Machado L. Privacy challenges and research opportunities for genomic data sharing. Nat Genet 2020;52:646-54.
77. Hernandez-Boussard T, Bozkurt S, Ioannidis JPA, Shah NH. MINIMAR (MINimum Information for Medical AI Reporting): developing reporting standards for artificial intelligence in health care. J Am Med Inform Assoc 2020;27:2011-5.
78. U.S. Food Drug Administration. Retinal diagnostic software device approval 2018 Jan. Accessed June 21, 2021. https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN180001.pdf.
79. Gibson DM. Estimates of the percentage of US adults with diabetes who could be screened for diabetic retinopathy in primary care settings. JAMA Ophthalmol 2019;137:440-4.
80. Abràmoff MD, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. NPJ Digital Med 2018;1:39.
81. Shelmerdine SC, Arthurs OJ, Denniston A, Sebire NJ. Review of study reporting guidelines for clinical studies using artificial intelligence in healthcare. BMJ Health Care Inform 2021;28:e100385.
82. Liu X, Cruz Rivera S, Moher D, Calvert MJ, Denniston AK, SPIRIT-AI and CONSORT-AI Working Group. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI extension. Nat Med 2020;26:1364-74.
83. Cordero JM, Rojo J, Gutiérrez-Bustillo AM, Narros A, Borge R. Predicting the Olea pollen concentration with a machine learning algorithm ensemble. Int J Biometeorol 2021;65:541-54.
84. Kubera E, Kubik-Komar A, Piotrowska-Weryszko K, Skrzypiec M. Deep learning methods for improving pollen monitoring. Sensors (Basel) 2021;21:3526.
85. van Leeuwen KG, de Rooij M, Schalekamp S, van Ginneken B, Rutten MJCM. How does artificial intelligence in radiology improve efficiency and health outcomes? Pediatr Radiol. Published online June 12, 2021. https://doi.org/10.1007/s00247-021-05114-8
86. Jain D, Torres R, Celli R, Koelmel J, Charkoftaki G, Vasiliou V. Evolution of the liver biopsy and its future. Transl Gastroenterol Hepatol 2021;6:20.
87. Pantanowitz L, Wu U, Seigh L, LoPresti E, Yeh F-C, Salgia P, et al. Artificial intelligence-based screening for mycobacteria in whole-slide images of tissue samples. Am J Clin Pathol 2021;156:117-28.
88. Harrell F. Road map for choosing between statistical modeling and machine learning. Statistical Thinking; 2021. Accessed September 23, 2021. https://www.fharrell.com/post/stat-ml/