

POLICY CORNER

Development Pipeline and Geographic Representation of Trials for Artificial Intelligence/Machine Learning-Enabled Medical Devices (2010 to 2023)

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Received: July 13, 2023; Revised: September 19, 2023; Accepted: September 29, 2023; Published: November 9, 2023

Abstract

A high number of artificial intelligence/machine learning (AI/ML)-enabled medical devices are currently in development. To understand the development pipeline and worldwide geographic distribution of clinical trials for AI/ML-enabled medical devices that may enter the market in the upcoming years, we analyzed the trends in registration of clinical trials for AI/ML-enabled medical devices between 2010 and 2023 as well as their geographic distribution. We aggregated all registered trials initiated between January 1, 2010, and August 31, 2023, through the World Health Organization's International Clinical Trials Registry Platform and included all clinical studies for AI/ML-enabled medical devices in our study cohort. Among the 710,800 registered clinical trials in this time period, 2669 clinical trials for AI/ML-enabled medical devices were identified and included in our study cohort. Of these, 2517 clinical trials provided information on the locations where the trial was conducted. Most of the trials were conducted for the medical specialties of radiology, general hospital, gastroenterology, and urology. Almost all were national trials; 1095 were conducted in China, followed by the United States (196), Japan (162), India (139), and Korea (118). The countries with the most enrolled patients in clinical trials per 100,000 inhabitants were mainly smaller countries in Asia and Europe. More international trials should be encouraged — including the involvement of low- and middle-income countries — to improve equality and ensure that the algorithms perform well across populations. (Funded by the Swiss National Science Foundation.)

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Introduction

The number of approved artificial intelligence/machine learning (AI/ML)-enabled medical devices and those in development have increased in recent years.¹ This trend is expected to continue.²

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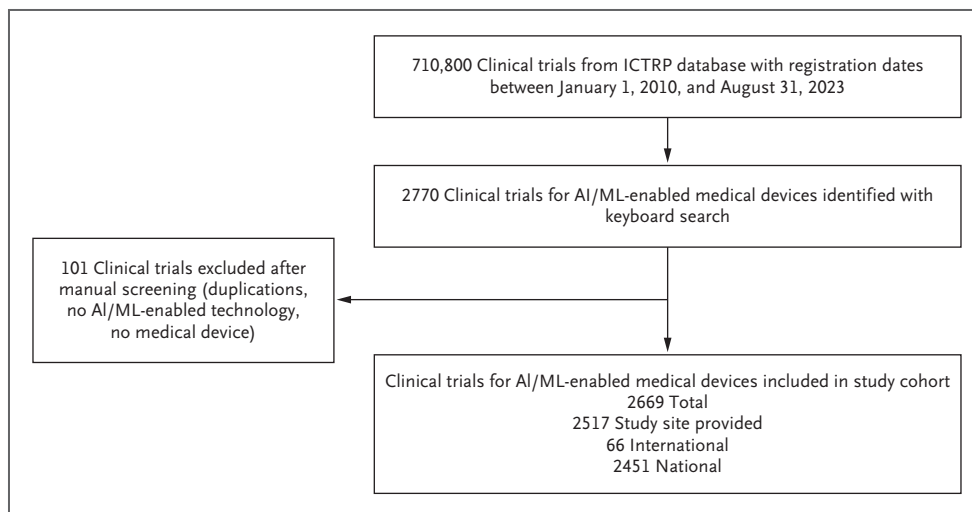


Figure 1. Flow Chart.

AI/ML denotes artificial intelligence/machine learning; and ICTRP, International Clinical Trials Registry Platform.

Previous studies have highlighted the importance of a diverse population representation in clinical studies in order for AI/ML-enabled medical devices to be applicable broadly to patients across health systems.³⁻⁷

To understand the development pipeline and worldwide geographic distribution of clinical trials for AI/ML-enabled medical devices that may enter the market in the upcoming years, we analyzed the trends in clinical trials for AI/ML-enabled medical devices registered between 2010 and 2023.

Methods

We aggregated all registered trials initiated between January 1, 2010, and August 31, 2023, through the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP).⁸

To identify all AI/ML-related trials, we searched the database ICTRP for trials with these keywords: *artificial intelligence OR machine learning OR deep learning OR artificial neural network OR neural network model OR convolutional neural network OR recurrent neural network OR supervised learning OR unsupervised learning OR natural language processing OR generative model OR generative ai OR conversational ai OR large language model OR generative pre trained transformer OR chatgpt*.

We extracted all trials that included at least one of the keywords in the trial's title or description. For each identified clinical trial we then extracted the following information, if available: title of the clinical trial, description of the clinical trial, study sites, and number of patients enrolled. We manually screened all the identified clinical trials and included all clinical trials in our study cohort that included an AI/ML technology and featured a medical device. We determined the medical specialty for each clinical trial using the Food and Drug Administration (FDA) classification as a guidance.⁹

To compare trials for AI/ML-enabled medical devices with non-AI/ML-enabled medical devices, we extracted all clinical trials for medical devices from the database ICTRP.

Descriptive statistics were performed using R, version 4.2.2 (R Foundation for Statistical Computing, Vienna).

Results

OVERVIEW

Among the 710,800 clinical trials registered between January 1, 2010, and August 31, 2023, 2669 clinical trials for AI/ML-enabled medical devices were included in our

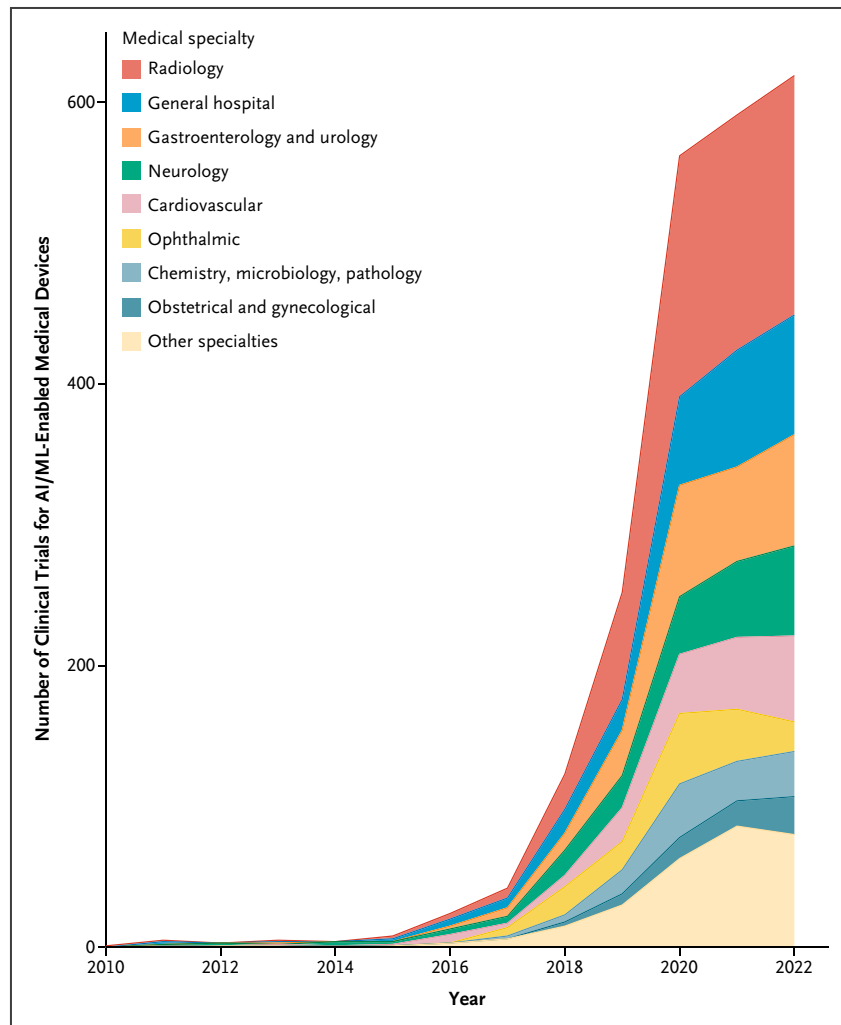


Figure 2. Temporal Trends for Clinical Trials by Medical Specialty.

AI/ML denotes artificial intelligence/machine learning.

study cohort. Of these, 2517 clinical trials provided information on the location(s) where the trial was conducted: 2451 (97%) were conducted in a single country and 66 (3%) were international collaborations ([Fig. 1](#)).

The number of clinical trials for AI/ML-enabled medical devices increased from 1 in 2010 to 619 in 2022.

MEDICAL SPECIALTIES

Among the 2669 included clinical trials, most targeted the medical specialty radiology (724, 27%), followed by general hospital (341, 13%), gastroenterology and urology (331, 12%), neurology (264, 10%), and cardiology (228, 9%) ([Fig. 2](#)).

However, differences were observed between countries and their focus on the medical specialties in their clinical trials. For example, most of the clinical trials for AI/ML-enabled medical devices conducted in China focused on radiology (382 clinical trials), followed by gastroenterology and urology (157 clinical trials), whereas in the United States, most clinical trials were attributable to general hospital (52 clinical trials), followed by neurology (37 clinical trials) and both radiology (31 clinical trials) and cardiology (31 clinical trials) ([Fig. 3](#)).

GEOGRAPHIC DISTRIBUTION

When analyzing the geographic distribution of the 2451 clinical trials for AI/ML-enabled medical devices conducted in single countries, most of them were conducted

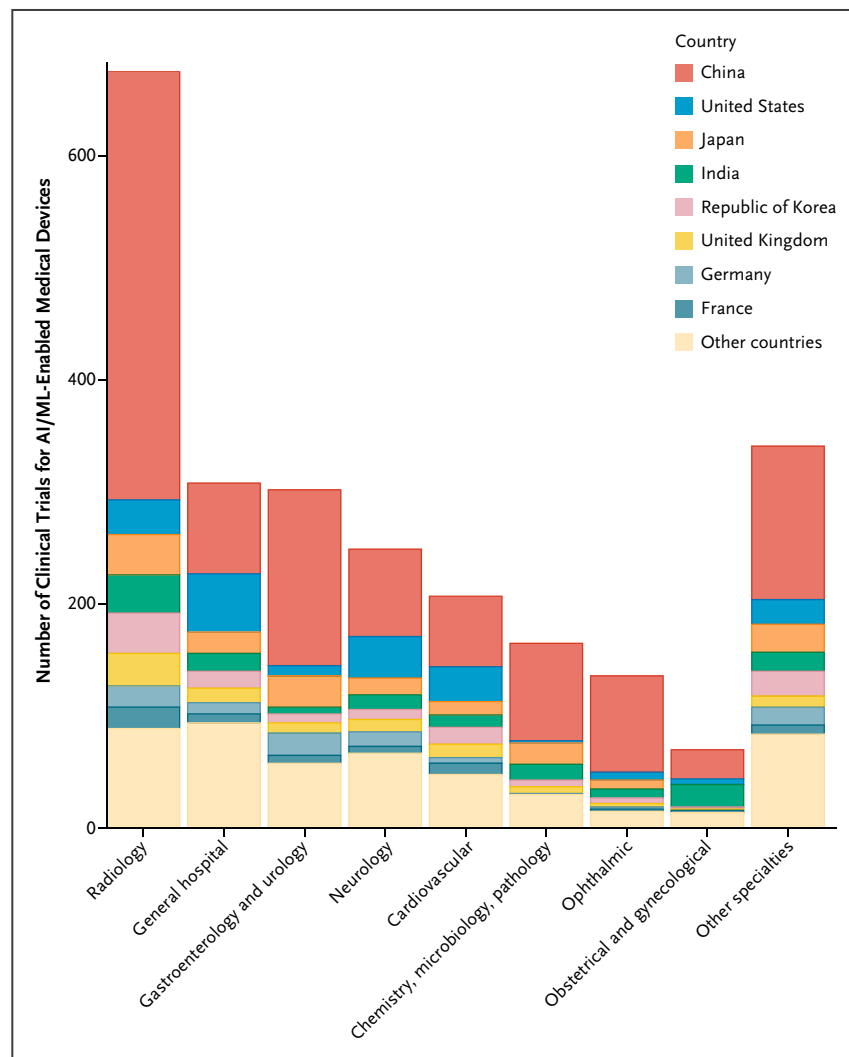


Figure 3. Distribution of Trial Locations by Medical Specialty.

AI/ML denotes artificial intelligence/machine learning.

in China (1095 clinical trials), followed by the United States (196 clinical trials), Japan (162 clinical trials), India (139 clinical trials), and Republic of Korea (118 clinical trials) ([Fig. 4A](#)).

This order changed when analyzing the number of all national clinical trials for AI/ML-enabled and non-AI/ML-enabled medical devices (113,815 clinical trials) between January 1, 2010, and August 31, 2023. Most of these clinical trials were conducted in the United States (21,323), followed by China (9809) ([Fig. 4B](#)).

China had a total enrollment of approximately 12 million patients in the AI/ML-related trials, followed by Germany (5.5 million), the United Kingdom (3.7 million), the

Republic of Korea (1.3 million), Japan (1.1 million), Australia (1.03 million), the United States (441,282), New Zealand (402,534), India (369,323), and Taiwan (265,756) ([Fig. 4C](#)). New Zealand, followed by Germany, the United Kingdom, Australia, the Republic of Korea, Sweden, Hong Kong, Denmark, Taiwan, and Switzerland, was the country with the highest patient enrollment in clinical trials per 100,000 inhabitants ([Fig. 4D](#)).

On the continental level, Asia and Europe had the largest increase in the number of trials for AI/ML-enabled medical devices between 2010 and 2022. In total, Asia accounted for 68.8% of all clinical trials, Europe for 17.8%, North America for 9.4%, Australia and Oceania for 2.3%, South America for 0.9%, and Africa for 0.8% of the

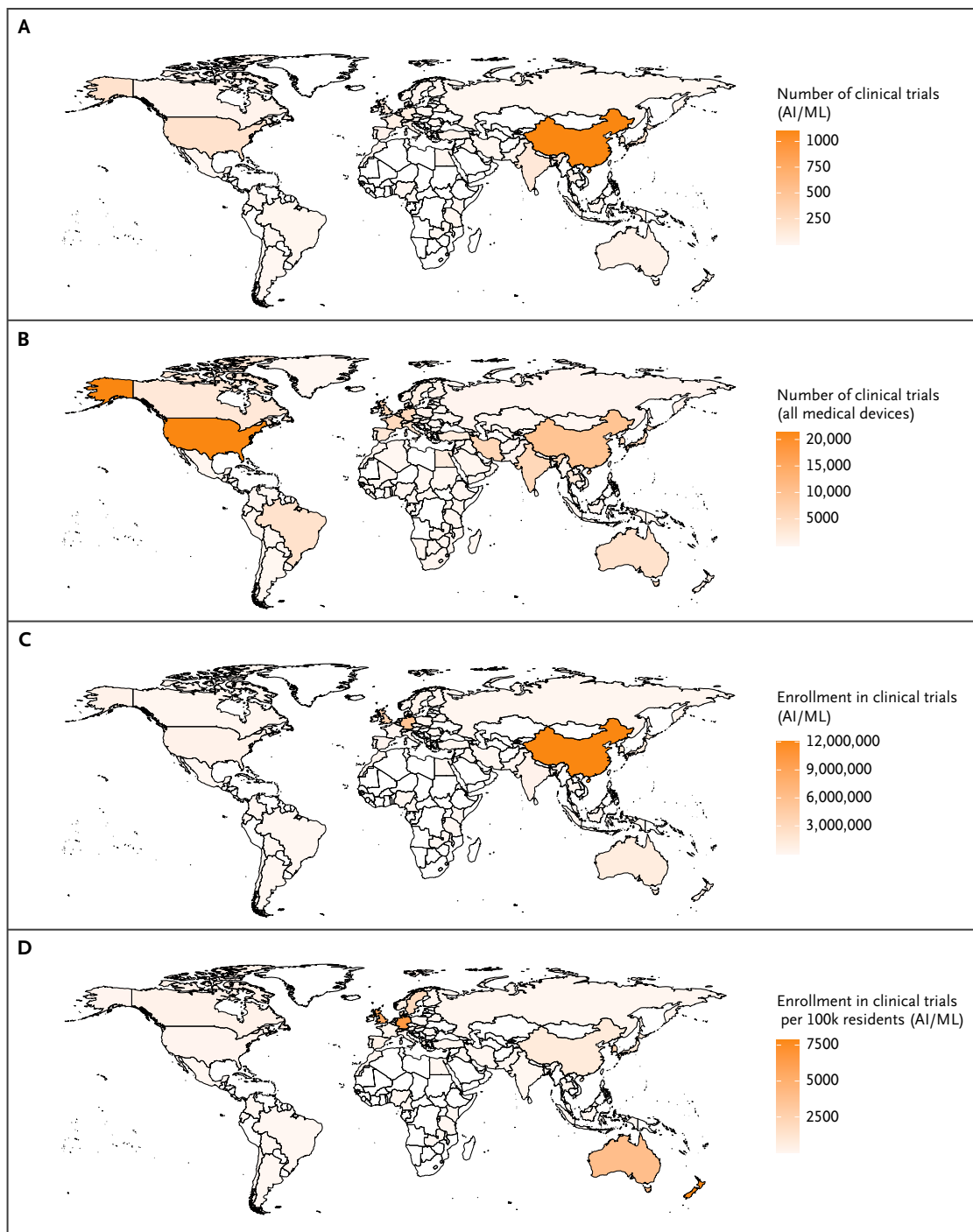


Figure 4. Geographic Distribution of Clinical Trials for AI/ML-Enabled Medical Devices.

Panel A depicts the number of clinical trials for AI/ML-enabled medical devices for each country. Panel B depicts the number of clinical trials for all medical devices. Panel C depicts the sum of enrolled patients in clinical trials for AI/ML-enabled medical devices for each country. Panel D depicts the sum of the enrolled patients in clinical trials for AI/ML-based medical devices per 100,000 inhabitants per country. AI/ML denotes artificial intelligence/machine learning.

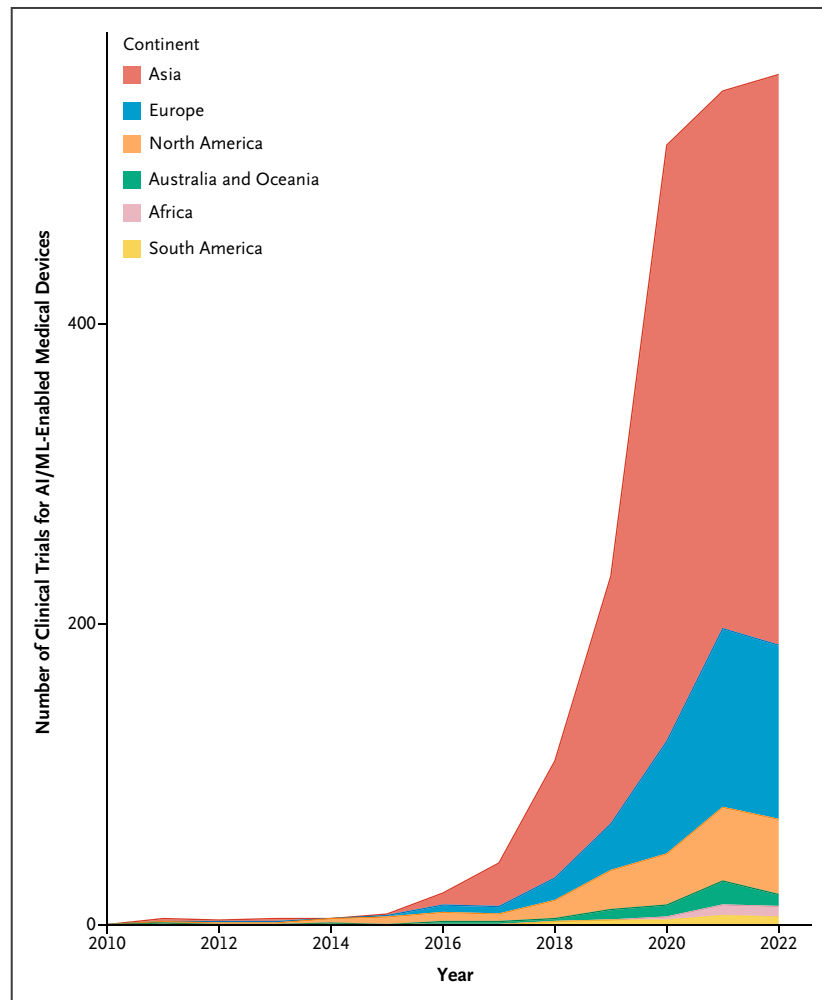


Figure 5. Temporal Trends for Clinical Trials for AI/ML-Enabled Medical Devices by Continent. AI/ML denotes artificial intelligence/machine learning.

clinical trials registered between January 1, 2010, and December 31, 2022 (Fig. 5).

Discussion

The substantial increase in registered clinical trials for AI/ML-enabled medical devices over the past years indicates that the number of such devices that will be approved and applied in the clinical setting will further increase in the upcoming years. The increase may be even higher because medical devices are often approved without clinical trials.^{10,11} Whereas radiology may keep its leading position across medical specialties, other medical specialties¹ such as gastroenterology or urology could introduce more AI/ML-enabled medical devices in the clinical setting in the near future. As of August 31, 2023, only four AI/ML-enabled medical devices

for the medical specialty gastroenterology and urology have been cleared in the United States.² One example for such a device in the development pipeline is a clinical trial with 200,000 enrolled participants with the goal of evaluating the effect of AI systems used during colonoscopy for the detection of precancerous polyps in the colon (NCT05888623).

The current dominance of national trials instead of international collaborations indicates that the results of the clinical trials may lack external validity. Clinical practice standards are known to differ internationally, and trial and target populations will differ in regions where the trial was conducted.⁴⁻⁶ As previous studies and the FDA have pointed out, it is crucial that approval agencies, physicians, patients, and the public be informed about the selected data with regard to patient demographic and baseline characteristics, such as number of patients, distribution of

patients' ages, and representation of race and ethnicity as well as gender.^{2,4,12-15} This information helps to understand whether a specific AI/ML-enabled medical device is appropriate for the diagnosis or therapy of a patient in the relevant clinical setting. Furthermore, these findings indicate that a stronger collaboration between countries on clinical trials for AI/ML-enabled medical devices is desirable and should be more strongly encouraged to ensure that the algorithms perform well across representative populations.

Reports highlight the global competition between countries on the successful development of AI technologies has emerged over the past decade, with medicine at the forefront of interest.¹⁶⁻¹⁸ Findings in our study show that China, followed by the United States, dominated in terms of absolute number of trials. Smaller countries, mainly in Asia (Korea, Taiwan, and Hong Kong) and Europe (Germany, the United Kingdom, Denmark, and Switzerland), and New Zealand had the most enrolled patients per 100,000 inhabitants. With the exception of China and India, low- and middle-income countries were underrepresented. The involvement of low- and middle-income countries is challenging for different reasons, including the lack of expertise, time, and financial resources such AI/ML-enabled medical devices may require.¹⁹ Nonetheless, it is crucial that these countries also be involved in clinical trials to overcome the selection bias because the demographics of high-income countries may not match those of other countries.^{5,20} Moreover, some of these devices — for example, AI/ML-enabled optimal antibiotic treatment strategies for severe bacterial infections (NCT01338116) — would help patients suffering from these diseases with high prevalence and burden in low- and middle-income countries and thus could help to improve the health status of patients and potentially save labor and financial costs in the longer run.

LIMITATIONS

Our study has limitations. It was not always possible to determine whether a clinical trial for a medical device had an AI/ML component. Additionally, we included clinical trials for AI/ML-enabled medical devices only if they were registered at the WHO's ICTRP, which is not comprehensive for all trial registries. However, it can be assumed that the WHO's ICTRP contains the globally major and largest clinical trial registries. Furthermore, not all included medical devices in our study will be cleared and used for patients in the clinical setting. Moreover, a majority of AI/ML-enabled medical devices are cleared without a clinical trial.¹⁰ Thus, our findings are representative not of all AI/ML-enabled

medical devices but rather of those for which clinical trials were conducted.

Disclosures

Author disclosures are available at [ai.nejm.org](https://www.nejm.org).

This study was funded by the Swiss National Science Foundation (grant number 407740_197485).

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