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Landscape of Regulatory Clinical Investigations Status of Traditional and Digital Medical Devices in Republic of Korea (2003–mid 2024)

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ABSTRACT

This study analyzed 1,556 clinical investigation plan approvals granted by the Ministry of Food and Drug Safety (MFDS) in the Republic of Korea by integrating regulatory databases and comparing the clinical investigation characteristics of traditional and digital medical devices (2003–mid 2024). Indicators included clinical investigation purpose, device classification, number of participating institutions, design characteristics, annual approval trends, major product categories, and time required from plan approval to marketing authorization. According to the Korean MFDS four-class medical device classification system (Classes 1–4), digital medical devices, predominantly concentrated in Class 2 and 3 software, exhibited a high proportion of Pivotal clinical investigations (68%); traditional medical devices, distributed among high-risk Class 3 and 4 devices, had a relatively higher proportion of exploratory investigations. The number of plan approvals for digital medical devices surpassed that of traditional devices for the first time in 2023; cognitive therapy and diagnostic assistance software constituted the major product categories. The mean time from approval to marketing authorization was significantly shorter for digital medical devices than for traditional medical devices.

Keywords

Traditional medical devices; Digital medical devices; Clinical investigations; Ministry of Food and Drug Safety

I. INTRODUCTION

Clinical investigations are an important approach used to demonstrate the safety and clinical performance of medical devices, particularly for novel devices without substantial equivalence or for higher-risk devices that require clinical evidence for regulatory authorization. Conducted in accordance with international standards such as ISO 14155:2020, clinical investigations of medical devices are strategically designed as either exploratory or pivotal studies depending on the device's risk classification, intended use, and stage of development. To meet regulatory requirements, rigorous statistical design elements—including randomization, blinding, and controlled comparisons—are applied, and based on the clinical evidence generated through these processes, regulatory authorities worldwide grant market access for pre-market medical devices.

In the Republic of Korea, a clinical investigation plan (CIP) must be approved by the Ministry of Food and Drug Safety (MFDS) prior to enrolment of human participants, and the investigation must be conducted at one of the institutions formally designated by the MFDS¹. As part of the CIP approval review, the MFDS evaluates the technical documentation to confirm that the investigational device meets the safety and performance requirements for clinical use, and the investigation title is required to clearly state the objective of demonstrating the safety and performance of the investigational device². Because these non-clinical elements are already verified at the CIP approval stage, only the clinical evidence generated under the approved CIP is additionally reviewed during the subsequent marketing authorization process, a structure that tends to shorten the overall regulatory timeline. Pre-market regulatory pathways are stratified by risk class: Class 1 and 2 devices are subject to listing or certification by the National Institute of Medical Device Safety Information (NIDS), whereas Class 3 and 4 high-risk devices require marketing authorization from the MFDS; notably, Class 2 devices for which clinical data are

required are also licensed by the MFDS rather than through third-party certification³. Information on cleared CIPs and on listed, certified, or approved medical devices is made publicly available through the MFDS Medical Device Safety Information Portal and the Public Data Portal^{4,5}.

The diversification in clinical investigation designs is closely associated with structural shifts in the medical device industry. As the field has rapidly expanded from hardware-based devices to software-driven technologies, the methodological approaches used in clinical investigations have correspondingly evolved. In particular, AI/ML-enabled software can be evaluated using retrospective clinical data, necessitating fundamentally different design strategies compared with those applied to traditional hardware medical devices.

To address these regulatory and technological transitions, the Digital Medical Product Act, the first global legislation of its kind, was enacted in the Republic of Korea in 2025. Article 2 of the Act defines “digital medical products” as an umbrella category encompassing digital medical devices, digital convergence drugs, and digital medical and health-support devices. Digital medical devices refer to products incorporating digital technologies, such as artificial intelligence, software as a medical device (SaMD), robotics, virtual reality, and high-performance computing, including in vitro diagnostic (IVD) devices⁶.

Before implementing this novel regulatory framework, understanding the distinctions between traditional hardware-based and digital medical devices is essential to enhance the acceptance of the Act’s intent and its practical implementation. However, studies that systematically analyze the regulatory differences between these two categories remain limited. Lim et al. reviewed approval and certification cases of AI/ML-enabled medical devices in Korea⁷ but provided only descriptive statistics and did not compare the regulatory characteristics of the two device types. Hong et al.

examined domestic and international regulatory systems primarily for digital therapeutics and proposed potential policy improvements⁸. Nevertheless, that study also focused on a specific subgroup of digital medical devices and, therefore, did not extend to a comprehensive comparative assessment of traditional hardware and digital medical devices.

The status of CIP approvals serves as an administrative record of regulatory procedures and an indicator of which technologies and product categories are actively preparing for market entry. Analysis of the characteristics of clinical investigations provides insights into the structural trends and directional shifts within the medical device industry. Nonetheless, comparative analyses of CIP approvals between traditional and digital medical devices are limited. Key indicators, including the number of approvals, study design characteristics, device-type distribution, and time required from the approval of a CIP to marketing authorization, reflect the industry's developmental stage and its regulatory alignment; however, systematic academic evaluations of these parameters are scarce.

Hong conducted a broad review of the Korean medical device industry, regulatory approvals, and clinical investigation activity⁹. However, given the time of publication, this study did not adequately capture the contemporary environment shaped by digital medical technologies and did not provide a quantitative comparison of clinical investigation approval patterns. Moreover, previous studies have primarily focused on individual technologies or single device categories, limiting their capacity to holistically assess structural changes across the medical device sector. Huh et al. examined clinical evidence for digital therapeutics¹⁰, but this work similarly centered on a specific type of digital technology, constraining its contribution to comparative analyses across the broader medical device landscape.

This study comprehensively analyzes the status of CIP approvals for medical devices in the Republic of Korea by integrating publicly available regulatory data from the Public Data Portal⁵ and the MFDS electronic public service system⁴. The study compares and analyzes the approval information for clinical investigations involving traditional and digital medical devices subject to regulations prior to the implementation of the *Digital Medical Products Act*. The analysis encompasses clinical investigation characteristics (exploratory vs. Pivotal investigations, classification, number of study centers, and study design), annual approval trends, distribution by device category, and the time required from CIP approval to marketing authorization. Through this approach, this study elucidates recent structural changes in the medical device industry and their associated clinical and regulatory implications.

II. Result

Comparison of Clinical Investigation Characteristics

Table 1 presents the clinical investigation characteristics of traditional and digital medical devices approved by the MFDS.

Among the 1,398 clinical investigations (including 343 undefined cases), Pivotal investigations accounted for 35% (490/1,398), and exploratory investigations accounted for 40% (565/1,398). For digital medical devices (including undefined cases), the proportion of Pivotal investigations was 68% (194/287)—most studies were conducted with the objective of regulatory submission. Conversely, for traditional medical devices (including undefined cases), exploratory investigations were more prevalent, accounting for 44% (484/1,111), reflecting a greater emphasis on early-stage safety and performance evaluation. The proportion of Pivotal vs. Exploratory investigations differed significantly between digital and traditional medical devices among records with defined phase ($p < 0.001$). These findings demonstrate a clear distinction in clinical investigation patterns. Digital medical devices are predominantly evaluated through Pivotal investigations aimed at market entry, whereas traditional medical devices are primarily assessed through exploratory investigations during the development phase.

As shown in Table 1, digital medical devices were predominantly concentrated in Class 2 (57%), followed by Class 3 (34%), with no Class 4 high-risk devices included. Traditional medical devices exhibited a broader distribution across risk classes: Class 3 constituted the largest proportion (40%), followed by Class 2 (28%) and Class 4 (23%). Class 1 devices were rarely included in either digital or traditional medical device investigations (0% and 1%, respectively).

because their low-risk profiles typically exempt them from clinical investigation requirements. The overall distribution of risk classification differed significantly between digital and traditional medical devices ($p < 0.001$).

Among all clinical investigations, 67% (940/1,398) were conducted at a single center.

This trend was similar across device types, with 63% (180/287) of digital medical device clinical investigations and 68% (760/1,111) of traditional medical device clinical investigations conducted as single-center studies. Most multicenter clinical investigations involved two centers (17%), while investigations including three or more centers were less common—20% (58/287) for digital medical devices and 15% (160/1,111) for traditional medical devices. The distribution of investigation sites did not differ significantly between digital and traditional medical devices ($p = 0.054$).

Randomization was implemented in 41% of all clinical investigations, occurring more frequently in traditional medical devices (44%) than in digital medical devices (31%, $p < 0.001$). Blinding was applied in 40% of the investigations, also more common in traditional medical devices (44%) compared with digital medical devices (26%, $p < 0.001$). Single-arm study designs were more prevalent in digital medical devices (26%) than in traditional medical devices (14%, $p < 0.001$). Similarly, control groups were included in 49% of traditional medical device investigations but in only 22% of digital medical device investigations ($p < 0.001$). The proportion of prospective designs was comparable between the two groups (digital 26% vs. traditional 28%, $p = 0.590$), whereas retrospective designs were markedly more common in digital medical devices (55%) than in traditional medical devices (3%, $p < 0.001$).

Annual Characteristics of Clinical Investigations

In the early years of the study period, the classification of investigation phases based solely on publicly available titles was often not possible because of the lack of clear regulatory definitions, resulting in a notable number of undefined cases. In Fig. 1, clinical investigation approvals for traditional medical devices peaked in 2016, whereas digital medical devices received almost no approval before 2012, followed by a continuous increase. Most notably, in 2023, the total number of clinical investigation approvals for digital medical devices exceeded that for traditional medical devices for the first time, indicating a significant turning point in regulatory approval trends. However, data for 2024 include approvals recorded only up to mid-2024; therefore, the observed decline for that year reflects partial-year data rather than a full annual dataset.

Major Approved Product Categories

Fig. 2 illustrates the distribution of clinical investigations according to medical device nomenclature, separately for digital (Fig. 2a) and traditional (Fig. 2b) medical devices. For digital medical devices (Fig. 2a), the highest number of approvals was observed for "cognitive therapy software" (Class 2) with 36 approvals, followed by "neural image, computer-aided detection/diagnosis software" (Class 3; 24 approvals). Most top-ranked categories belonged to SaMDs, except for "robotic-guidance rehabilitation system" (Class 3).

For traditional medical devices (Fig. 2b), the most frequently approved category was "graft/prosthesis, biomaterial" (Class 4) with 114 approvals, followed by "brain electrical stimulation system, psychiatric therapy" (Class 3; 69 approvals), "dressing, adhesion barrier" (Class 3; 55 approvals), and "IVD reagents for infection disease" (Class 3; 45 approvals). Overall, approvals for traditional medical devices were primarily concentrated in hardware-based equipment and instruments.

Time from Clinical Investigation Approval to Market Authorization

In Fig. 3, the average time from CIP approval to market authorization was: 542.2 days (SD: 381.4) for traditional medical devices (n=101) and 361.7 days (SD: 190.9) for digital medical devices (n=71). The minimum–maximum range was 49–1,780 days for traditional medical devices and 119–1,223 days for digital medical devices. The median approval time for digital medical devices was significantly shorter than that for traditional medical devices, with a statistically significant difference between the two groups (Hodges–Lehmann median difference = –105 days, 95% CI: –182 to –34; $p < 0.005$).

III. Discussion

The findings of this study indicate a sustained increase in CIP approvals for digital medical devices in recent years, accompanied by a tendency toward faster market entry compared with traditional medical devices. This trend reflects the shorter safety verification processes typically required for digital medical devices, which are primarily designed to support or augment clinical decision-making and therapeutic procedures. Consequently, these devices can progress more rapidly to Pivotal clinical investigations than invasive traditional devices.

In this study, Pivotal clinical investigations accounted for 68% of all clinical investigations of digital medical devices, reflecting their structural focus on regulatory approval and verification of clinical performance. In particular, AI/ML enabled SaMDs typically undergo an internal exploratory and model optimization phase during development, involving repeated training, validation, and testing using large-scale datasets¹¹. At this stage, analytical performance thresholds for the developed AI models and other digital medical devices can be established without additional exploratory clinical investigations. Consequently, further exploratory research is

generally unnecessary during the clinical investigation phase, and the primary aim is to demonstrate the clinical performance levels required by regulatory authorities. Furthermore, clinical investigations of digital medical devices are generally based on retrospective study designs and are conducted using pre-existing clinical data with a focus on prespecified performance metrics¹². Under this data structure, there is limited scope for clinical exploration, allowing investigators to directly assess clinical validity using objective performance metrics such as accuracy, sensitivity, specificity, and the area under the receiver operating characteristic curve (AUC)¹³. These features suggest that even without preceding exploratory clinical investigations, it is possible to define justified success criteria in clinical investigation protocols by setting clinically and statistically significant threshold values. Conversely, for traditional medical devices, when designing clinical investigations, success criteria intended to ensure clinical (and statistical) significance can be set with reference to prior studies or published literature when such evidence is available; however, in many cases, the empirical basis is judged to be established through exploratory clinical investigations.

For traditional medical devices to proceed to clinical investigation, the essential safety requirements specified by international standards and regulatory authorities—electrical and mechanical safety¹⁴, electromagnetic compatibility¹⁵ and biological safety¹⁶—must be satisfied, and a greater number of performance and preclinical (including animal) evaluations are required compared with digital medical devices. Consequently, a stepwise approach involving exploratory clinical investigations is often necessary before conducting Pivotal clinical investigations to verify the initial safety and clinical performance of the product.

An examination of the classification status of the product groups showed that SaMDs designed to detect or support the diagnosis of malignant tumors were classified as Class 3, whereas

SaMDs intended for the detection or diagnostic support of noncancerous conditions were generally categorized as Class 2. Additionally, as Class 4 did not exist for software medical devices under the MFDS notification¹⁷, digital medical devices are structurally limited to Classes 1–3. This regulatory characteristic may explain why the proportion of high-risk products observed in the clinical investigations of digital medical devices remains relatively low.

Another reason clinical investigations of digital medical devices are predominantly conducted for Class 2 devices (57%) is the difficulty in demonstrating substantial equivalence. Under MFDS regulations, clinical data must be submitted when a device cannot be substantially equivalent to an already approved or cleared product. However, for AI/ML-enabled SaMDs, it is often challenging to establish technical equivalence with previously approved or cleared devices because critical technological components—algorithmic architecture, dataset composition, training and validation procedures, and model update cycles—are continuously evolving. Consequently, even among Class 2 devices, exemptions from clinical investigations based on predicate products are limited, and independent clinical performance evidence is frequently required. These characteristics ultimately contribute to the relatively high proportion of clinical investigations of Class 2 digital medical devices.

Conversely, the classification of traditional medical devices is primarily determined by their intended use, mode of application to the human body, and potential risks. As many of these devices are implantable or invasive, their inherent risk levels tend to be relatively high. Nevertheless, their physical structure and intended purpose are generally well defined, and numerous previously approved or cleared predicate devices exist. Consequently, a substantial proportion of Class 2 traditional medical devices can be exempt from clinical investigations by demonstrating

substantial equivalence. Thus, clinical investigations on traditional medical devices tend to be concentrated in higher-risk products, particularly those classified as Class 3 or 4.

Although multicenter investigations are essential for enhancing the reliability and generalizability of clinical evidence, more than 60% of medical device clinical investigations in the Republic of Korea, including digital and traditional medical devices, have been conducted at a single center, indicating the limited scalability of multicenter network-based research. This contrasts with the clinical investigations for PMA approval in the United States, where multicenter participation is common¹⁸.

Single-center investigations may be associated with several factors, including cost structures and administrative burdens related to multicenter studies. Clinical investigations of medical devices require repeated fixed expenditures across institutions, including installation of equipment, establishment of the operating environment, training of personnel for operation, monitoring and statistical analysis, equipment calibration, and development of data management systems. In the Republic of Korea, outsourcing clinical investigations to contracted research organizations (CROs) typically incurs an average cost of approximately 250 million KRW (approximately 170,742 USD)¹⁹. In multicenter investigations, institutional differences in test environments must be standardized, and additional burdens related to quality control (QC), cross-site data integration, and independent review board approval must be imposed at each site, substantially increasing both operational costs and administrative workload. Consequently, most developers prefer to conduct limited-scale studies at a single institution owing to cost-efficiency considerations and simplified procedures, contributing to the predominant reliance on single-center clinical investigations in Korea. Furthermore, unlike the United States, where racial, demographic, and institutional heterogeneity is significant, Korea has a relatively homogeneous population. Therefore, single-

center clinical investigations may be sufficient to assess the safety and effectiveness of certain medical devices. However, for AI/ML-enabled SaMD, concerns remain regarding performance degradation owing to shifts in data distributions and model drift. Thus, for devices classified in higher-risk categories, expansion of clinical investigation sites to secure external validation should be considered necessary²⁰.

The low proportion of randomization, blinding, and control group designs observed in clinical investigations of digital medical devices, along with the high prevalence of single-arm studies, is primarily attributable to the fact that such studies are generally conducted to validate model performance and assess accuracy. Formal between-group comparisons confirmed that prospective designs did not differ significantly between digital and traditional medical devices (26.1% vs. 27.7%; $p = 0.590$), whereas retrospective designs were markedly more prevalent among digital medical devices (55.1% vs. 3.4%; $p < 0.001$). This pattern reflects the established methodological landscape of AI/ML evaluation, in which retrospective designs are particularly common at the discovery and challenge stages of medical imaging device assessment because they allow investigators to control disease prevalence and case spectrum and to obtain a sufficient number of diseased cases with smaller total sample sizes than prospective designs require²¹. While randomized clinical trials remain the methodological gold standard for demonstrating clinical effectiveness, RCTs are not always the most practical or informative design for every AI/ML system, and non-randomized retrospective evaluations and diagnostic performance studies can be more reasonable designs in many clinical scenarios²².

A potentially counterintuitive feature of our dataset — the apparent co-occurrence of "Randomization" and "Retrospective" labels among digital medical device CIPs — warrants explicit clarification. This co-occurrence is not an internal inconsistency but reflects a

methodologically distinct concept of randomization that is explicitly recognized by Korean regulatory guidance. The MFDS guideline on the design of clinical investigations for AI-enabled digital medical devices²³ specifies that the test dataset in retrospective clinical investigations may be selected by random sampling from a pre-specified population of subject data, establishing data-level random sampling — rather than participant-level random allocation — as a recognized form of "randomization" in the regulatory documentation of retrospective AI/ML evaluations. This regulatory position is consistent with international methodological practice. In retrospective Multi-Reader Multi-Case (MRMC) reader studies, which are widely employed in the regulatory evaluation of AI/ML-enabled imaging devices, randomization is applied at the level of cases, readers, and reading sessions to minimize bias²⁴. Related data-level randomization procedures — such as the random partitioning of datasets into training, validation, and independent test sets — are also widely used in the development and evaluation of AI/ML medical devices, although these procedures address internal validity rather than generalizability to geographically and temporally independent data²⁵.

In conventional clinical investigation designs, randomization and blinding are applied at the levels of the participants, investigators, and assessors. However, in retrospective studies involving artificial intelligence, it is challenging to apply these concepts in their traditional definitions because random sampling from a dataset does not constitute a random allocation of participants²⁶. Consequently, even when analogous procedures are employed, these methodological characteristics may not be explicitly described in the investigation design. Conversely, clinical investigations of traditional medical devices aim to verify their therapeutic effectiveness and safety, leading to a higher proportion of controlled studies that employ randomization and blinding among subjects, investigators, and evaluators. Therefore, these differences reflect the inherent

distinction between retrospective and prospective clinical investigations, rather than the methodological limitations in clinical investigations of digital medical devices.

In 2023, the number of clinical investigation approvals for digital medical devices surpassed those for traditional medical devices. This trend may have been influenced by multiple factors, including accelerated technological advancements, changes in the healthcare environment during and after the COVID-19 pandemic²⁷, and policy efforts to support the digital medical device industry²⁸. As the pandemic emerged in 2020, the demand for non-face-to-face medical services increased substantially²⁹, which facilitated the accelerated initiation of clinical investigations for digital medical devices, such as remote monitoring systems and AI-based decision support tools, showing a continuous upward trajectory except for the initial pandemic year. Conversely, traditional medical devices experienced delays or suspension of clinical investigations owing to intensified infection control measures, restrictions on patient recruitment, and limitations in equipment availability³⁰. These environmental constraints have contributed to a temporary decline in clinical investigation approvals in 2021, along with a slower recovery compared with digital medical devices.

The Korean government recently expanded its regulatory and financial support to the digital medical device industry. The MFDS has secured dedicated budgets and reinforced its authorization and review infrastructure to promote regulatory support for digital medical devices and innovative medical technologies²⁸. Considering this policy environment, the number of development activities and clinical investigation approvals for digital medical devices is expected to continue to increase over the mid- to long-term.

Among digital medical devices, cognitive therapy software has received the highest number of clinical investigation approvals as digital therapeutics (DTx) have rapidly emerged as a new treatment paradigm designed to complement the limitations of conventional pharmacotherapy. Unlike pharmacological agents, DTx can develop within a shorter time frame, has minimal adverse effects, and provides patient-centered treatment without spatial or temporal constraints³¹. These advantages have contributed to the shift in care delivery from hospital-centered systems to self-management and remote care, addressing unmet medical needs and reducing healthcare costs. Therefore, frequent clinical investigation approvals for cognitive therapy software reflect technological innovation and a paradigm shift toward improving efficiency and accessibility in healthcare service delivery.

However, despite the markedly higher number of clinical investigation approvals compared to AI/ML-enabled SaMD and the continuous publication of indication-specific regulatory guidelines by the MFDS, fewer than ten DTx products have been approved to date in Korea. This discrepancy indicates the ongoing challenges in translating clinical investigations into regulatory approaches. DTx devices, similar to traditional medical devices, require prospective clinical investigations and depend on sustained and periodic patient engagement, as patients operate the devices directly rather than by clinicians. Such strong patient–device interactions can complicate the demonstration of consistent clinical benefits during Pivotal investigations. Namgung et al. reported a case in which DTx demonstrated success during exploratory investigations but failed to achieve Pivotal endpoints, partially because of learning transfer effects that resulted in performance improvement in the control group despite robust randomization, multicenter participation, and efforts to reduce sampling bias³². Conversely, Canonico et al. reported successful outcomes attributable to high participant motivation and strong adherence to treatment

sessions³³. Consequently, for DTx clinical investigation approvals to translate into market approvals more successfully, broader dissemination of best practices and systematic analyses of failure factors are required.

Clinical investigation approvals for traditional medical devices have predominantly focused on high-risk devices that directly affect the human body, such as tissue-repair materials (e.g., tissue fillers), electrical stimulation systems, and ultrasonic surgical units. This pattern arises because such devices pose substantial potential risks or exert physical effects on the body, making clinical evidence of their safety and effectiveness essential. Among the traditional devices, tissue-repair materials account for the largest number of CIP approvals. Under current regulations, when the intended use, raw materials, or method of application of a tissue-repair product are not essentially equivalent to previously approved or cleared devices, the submission of clinical data is required.

Dermal fillers fall within this category and are classified as either “Graft/prosthesis, biomaterial” or “Graft/prosthesis,” depending on whether the raw material is biologically derived, and are assigned to the highest risk Class 4 category under MFDS regulatory classification. Although raw materials may be identical across products, the safety and effectiveness of the finished product can vary considerably depending on the manufacturing process. In particular, the intrinsic viscosity, molecular weight, presence or absence of crosslinking, type and concentration of crosslinkers, degree of crosslinking, particle size, particle morphology, concentration and volume of the primary component, and the inclusion of pharmaceutical additives can significantly affect the safety and effectiveness of the final product. Therefore, the MFDS requires the submission of clinical data to verify the product safety and effectiveness. In practice, this means that when manufacturers differ, independent clinical investigations are typically required for each

product, which accounts for the relatively high number of CIP approvals observed for dermal fillers³⁴.

Under the MFDS regulations, medical device manufacturers must provide non-clinical evidence demonstrating safety and performance at the CIP approval stage, and such documentation is equivalent to what is required for market authorization. Therefore, in addition to the clinical data generated during the clinical study, all necessary safety and performance information had undergone a regulatory review prior to the initiation of the investigation. Consequently, once a Pivotal clinical investigation is approved, traditional and digital medical devices complete regulatory reviews for all parameters other than clinical evidence.

The shorter time required for digital medical devices to obtain market authorization, compared with traditional medical devices, can be explained by the characteristics of the clinical investigations conducted. A substantial portion of digital medical device investigations are retrospective in design and rely on existing clinical datasets to verify device performance. Thus, there was no need for new participant recruitment, installation of clinical-use equipment, or long-term follow-up. Additionally, clinical procedures, such as software operation, data input, and performance evaluation, are performed in a digital environment, allowing rapid execution. Conversely, clinical investigations of traditional medical devices typically involve their direct use in human subjects, requiring participant management, preparation of the clinical environment, and verification of procedural safety, ultimately leading to longer regulatory review timelines. These differences reflect the fundamental distinctions in clinical investigation methodologies and data utilization structures between traditional and digital medical devices.

This study had several limitations. First, the classification of the clinical investigations relied on limited publicly available information, including study titles and brief summaries, which may not fully capture the technical characteristics of each medical device. Second, the duration from CIP approval to market authorization is affected by multiple variables beyond the regulatory review process, such as resubmission after withdrawal, changes in regulatory requirements, and variations in the workload of the reviewing bodies. These factors limit the interpretation of authorization timelines as a direct measure of regulatory efficiency. Third, with the *Framework Act on the Development of Artificial Intelligence and Establishment of Trust* scheduled for enforcement in Korea in January 2026—conceptually aligned with the European Union Artificial Intelligence Act—the current regulatory framework for medical devices is expected to undergo structural changes. Consequently, the continuity of current trends in digital medical device regulation remains uncertain, and future regulatory transitions may impact overall review timelines and evaluation processes. Fourth, the publicly available CIP summaries from the MFDS portal record categorical labels such as "Randomization" without further specifying the level at which randomization was applied. As discussed above, in retrospective AI/ML-enabled SaMD investigations, "randomization" may refer to participant-level random allocation, case-level random sampling from a pre-specified subject population²³, or reader- and reading-session-level randomization within MRMC designs²⁴. Our dataset does not allow further disambiguation among these distinct procedures, and we therefore retain the original "Randomization" label as recorded in the regulatory documentation. This granularity limitation should be considered when interpreting the cross-tabulation of randomization status against retrospective and prospective designs in Table 1.

Despite these limitations, this study is the first to systematically compare the clinical investigation characteristics of traditional and digital medical devices in Korea and assess the regulatory timelines from CIP approval to market clearance. Furthermore, by analyzing nationwide CIP approval data, this study provides valuable insights for regulatory science research focused on the evolving landscape of medical device development. Ongoing monitoring will be necessary to determine whether these patterns have shifted following the implementation of the Digital Medical Products Act and other emerging regulatory frameworks.

This study provides meaningful insights by systematically analyzing the differences between traditional and digital medical devices using clinical investigation approval data from the Republic of Korea. CIP approvals serve as outcomes of regulatory procedures and key indicators reflecting the pace of technological advancement and market entry dynamics within the medical device industry. Digital medical devices have exhibited a continuous increase in clinical investigation approvals in recent years, surpassing traditional medical devices during certain periods. Furthermore, the time required for market authorization is generally shorter for digital medical devices than for traditional devices—digital technology-based products may undergo clinical performance verification more efficiently than conventional devices. To sustain this growth trend, the continuous improvement of regulatory frameworks is necessary to ensure alignment with the technological characteristics and development cycles of digital medical devices. Additionally, related policy measures should carefully account for the inherent differences in regulatory timelines between digital and traditional medical devices.

IV. Methods

Data collection and processing

In this study, the unit of analysis was each approved CIP, and the dataset represents all clinical investigations approved by the MFDS between 2003 and mid-2024, regardless of whether the investigated devices were subsequently authorized for market entry. In this study, the definitions of the study subjects were first established to clarify the conceptual distinction between traditional medical devices and digital medical devices. Medical devices to which digital technologies such as artificial intelligence are applied were classified as "digital medical devices," while conventional general medical devices and in vitro diagnostic medical devices to which digital technologies are not applied were collectively defined as "traditional medical devices (TMDs)" (see Supplementary material). Based on this classification framework, clinical investigation plan (CIP) approval data collected from the Public Data Portal and the MFDS electronic public service system were integrated and analyzed. Data on CIP approval issued by the MFDS were comprehensively collected from the Public Data Portal and the MFDS Medical Device Information Portal, yielding 1,556 records (Fig. 4). Data were collected from January 2003 to June 2024, and data processing was performed using Python(ver. 3.11) and Pandas(1.5.3). The datasets were consolidated to create a unified dataset because the two sources provided different information fields.

The data inclusion process is illustrated in Fig. 5. In the Identification and Screening process shown on the left, stepwise data refinement was performed on a total of 1,556 collected records. Two records were removed owing to missing values (NaN) in the device nomenclature field ($n=1,554$), and an additional 16 records were excluded owing to missing values in the clinical investigation

title field (n=1,538). Subsequently, 29 records lacking information on the primary clinical investigation site were excluded (n=1,509), and 56 records were further removed through cross-verification of consistency among the investigation title, clinical investigation site, and device nomenclature (n=1,453). Finally, 55 records were excluded through updating of device nomenclature and removal of items for which such updates were not feasible, yielding a final analytical dataset of 1,398 records.

In the classification process shown on the right, digital medical devices were identified based on the definition set forth in the Digital Medical Product Act of the Republic of Korea: devices were classified as digital medical devices only when digital technologies — such as artificial intelligence-based systems, Software as a Medical Device (SaMD), intelligent robotics, high-performance computing, and virtual convergence technologies — constituted the primary functional component of the device, whereas devices in which digital components served only supportive or secondary functions were not classified as digital medical devices. This classification was operationalized through keyword searches on the device nomenclature and clinical investigation title fields, applying four search categories: software (artificial intelligence and DTx; 260 records), robotics (25 records), virtual/augmented reality (VR/AR; 10 records), and u-Health (2 records). After removing 10 duplicate or erroneously matched records, the final analytical dataset comprised 287 digital medical device clinical investigations and 1,111 traditional medical device clinical investigations.

Throughout this process, two researchers (E.C. and J.S.) reviewed the records, and any disagreements or ambiguities were resolved through adjudication by C.L. The corresponding analytical results were subsequently re-verified by another independent researcher (E.J.).

Subsequent analyses included the following: (1) characteristics of clinical investigations, (2) annual approval trends, (3) distribution by device category, and (4) the time interval from CIP approval to market authorization. This study used only publicly available, fully de-identified regulatory records released by the MFDS through the Public Data Portal and the Medical Device Safety Information Portal. As the analysis did not involve human participants, identifiable personal data, or biological specimens, ethics committee review and informed consent were not required.

Statistical Method

Descriptive statistics were presented as means and standard deviations. Normality was assessed using the Shapiro–Wilk test, and the Mann–Whitney U test was used for comparative analyses. The Hodges–Lehmann estimator was used to quantify the median difference between groups, with 95% confidence intervals derived from the distribution of pairwise differences based on the normal approximation. Categorical variables were compared between digital and traditional medical device groups using Pearson’s chi-square test of independence (without continuity correction). For the comparison of clinical investigation stage, the test was performed on the 2×2 contingency table of Pivotal versus Exploratory stage among records with defined stage, with records of Undefined stage excluded because this category reflects an administrative artifact of 2003-2015 regulatory documentation rather than a substantive phase classification (see Supplementary Table S4 for sensitivity analyses across alternative inclusion criteria). Fisher’s exact test with Monte Carlo simulation (10,000 iterations) was applied to the medical device classification variable because two cells contained zero observations and the minimum expected cell count was 1.85, falling below the conventional threshold (≥ 5) for the validity of the asymptotic

chi-square approximation. Statistical significance was set at $p < 0.05$. Statistical analyses were performed in Python (version 3.11) using the SciPy library (version 1.10.1). To assess the robustness of the comparison of pivotal versus exploratory phase share to differential missingness in the Type variable (25% of records categorized as Undefined), five pre-specified sensitivity analyses were conducted, as detailed in Supplementary Table S4.

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Competing interests

The authors declare no competing financial or non-financial interests.

Data availability

The main data supporting our results in this study are available in the manuscript and supplementary information file.

Author contributions

C.L. and K.K. designed study; E.C. and C.L. collected data; C.L., J.S., and E.C. performed the analysis; E.J. re-verified the data; E.J., E.C. and J.S. drafted the manuscript. All authors reviewed the final version of the manuscript and approved the final version of the manuscript. C.L. and K.K. are equally contributed as the corresponding author.

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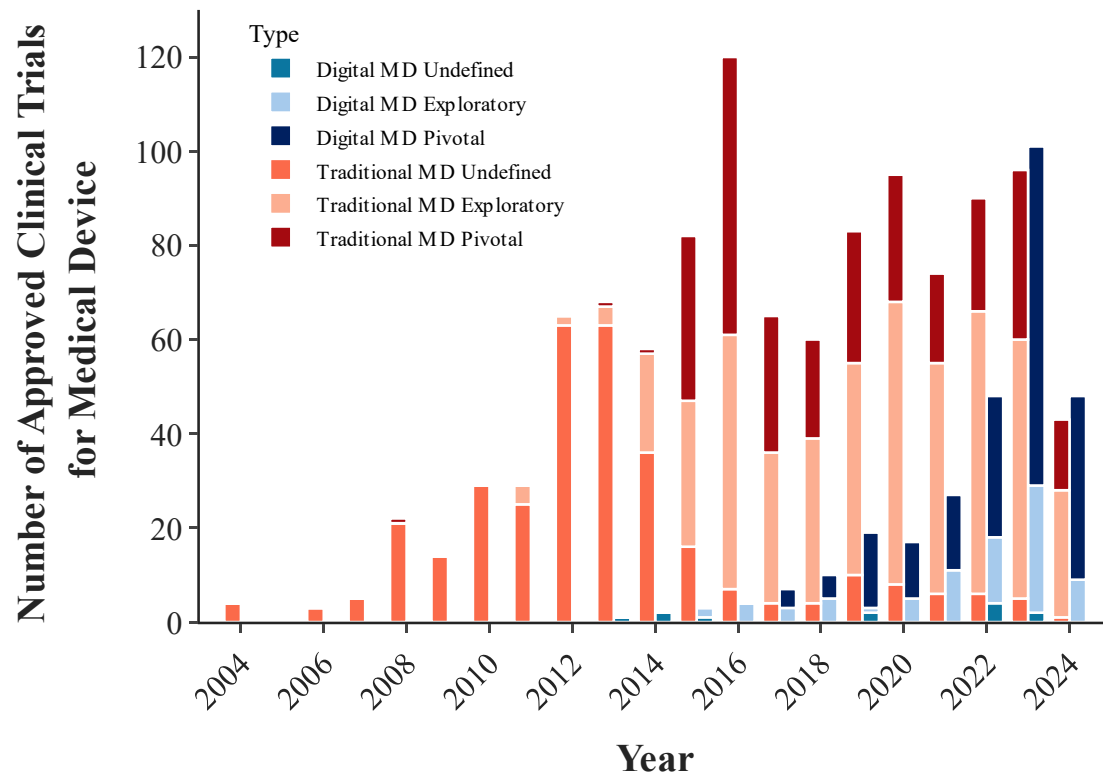
Figure

Fig. 1. Approved Clinical Investigations for Medical Device per Year

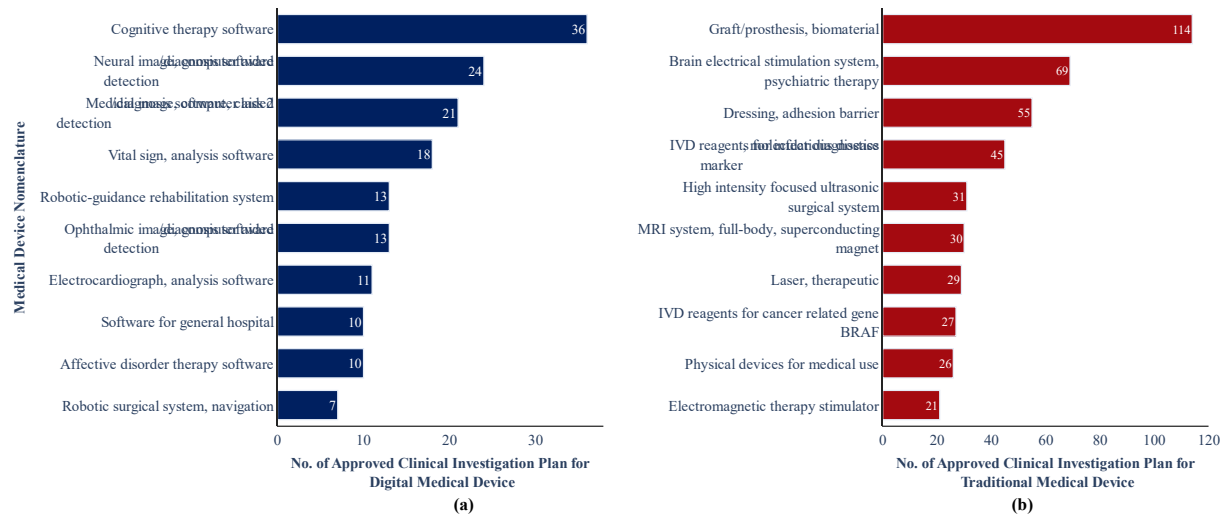


Fig. 2. Number of Clinical Investigations by Medical Device Nomenclature. (a) Digital Medical Device (b) Traditional Medical Device

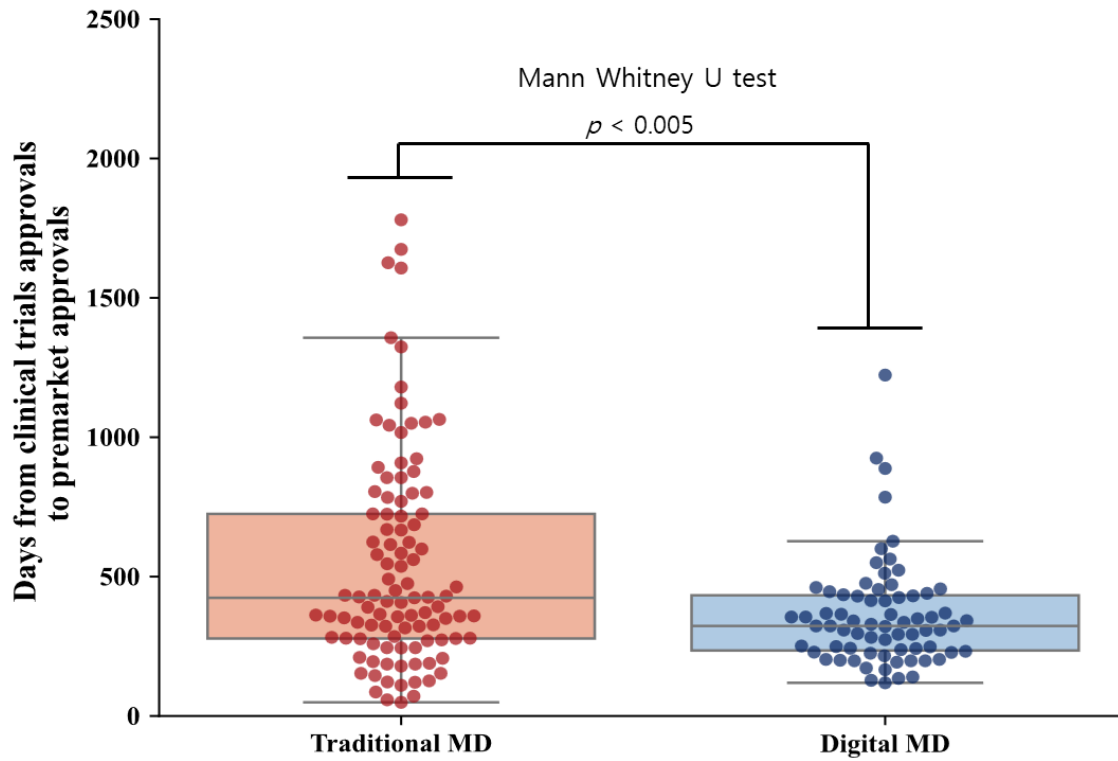


Fig. 3. Days from CIP Approval to Pre-market Approvals: Traditional vs. Digital Medical Device

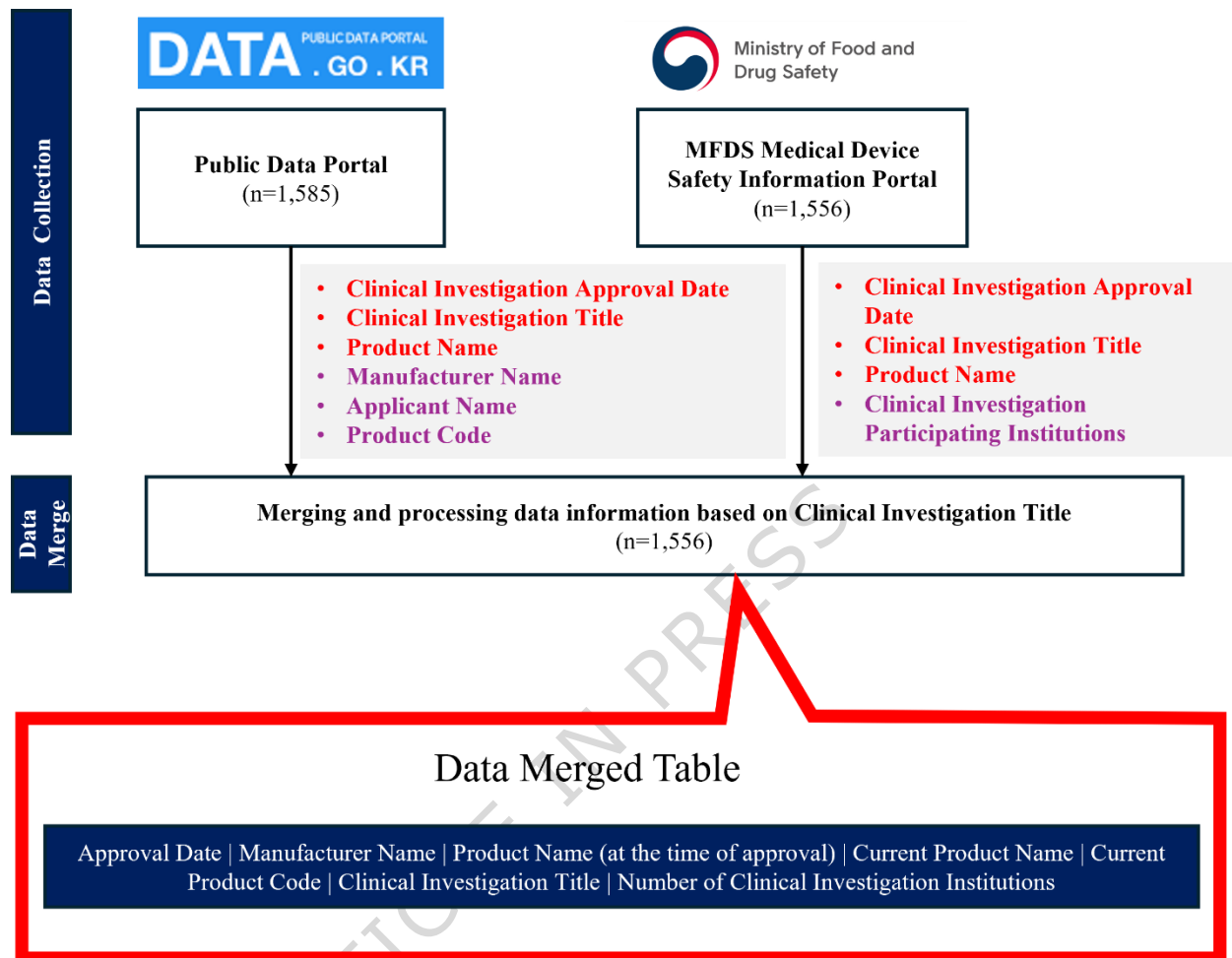


Fig. 4. Data Merged Process

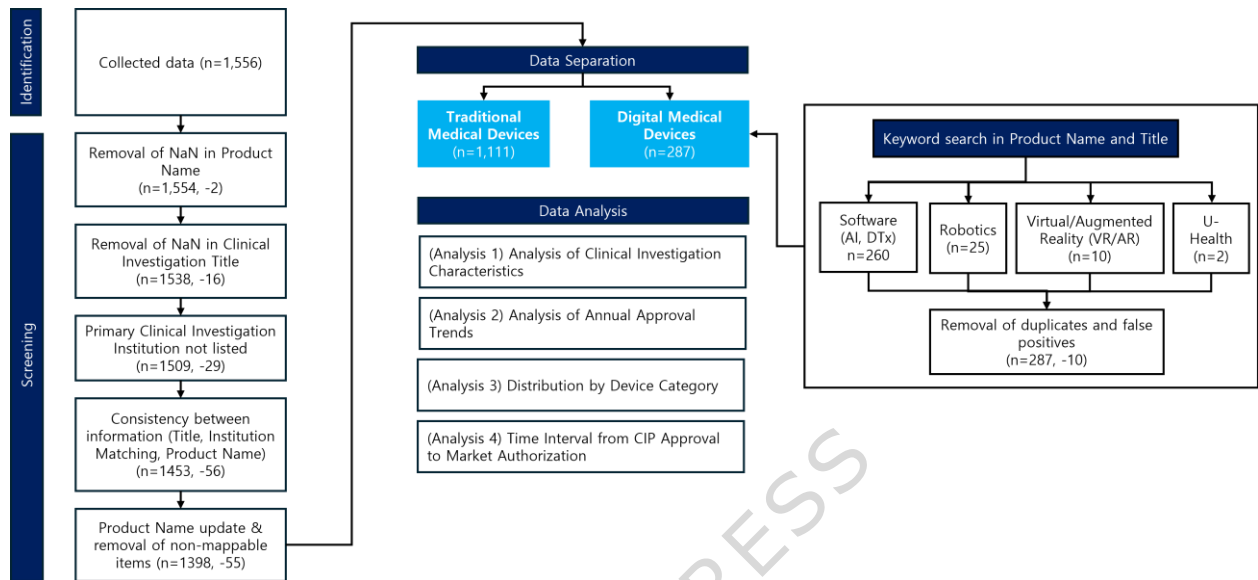


Fig. 5. Inclusion Process.

Table

Table 1. Characteristics of MFDS Approved Clinical Investigations

	Total	Digital MD	Traditional MD	p-value
Total number, n	1,398	287	1,111	
Stage, n(%)				<0.001 [†]
Pivotal	490(35%)	194(68%)	296(27%)	
Exploratory	565(40%)	81(28%)	484(44%)	
Undefined	343(25%)	12(4%)	331(30%)	Exception
Medical Device Classification, n(%)				<0.001 [‡]
Class 1	9(1%)	-	9(1%)	
Class 2	477(34%)	165(57%)	312(28%)	
Class 3	545(39%)	97(34%)	448(40%)	
Class 4	251(18%)	-	251(23%)	
Undefined	116(8%)	25(9%)	91(8%)	
Clinical Investigation Site, n(%)				0.054
Single Center	940(67%)	180(63%)	760(68%)	
Multicenter(2)	240(17%)	49(17%)	191(17%)	
Multicenter(3)	88(6%)	29(10%)	59(5%)	
Multicenter(≥4)	130(9%)	29(10%)	101(9%)	
Characteristics, n(%)				
Prospective	383(27%)	75(26%)	308(28%)	0.590
Retrospective	196(14%)	158(55%)	38(3%)	<0.001
Randomization	573(41%)	87(31%)	486(44%)	<0.001
Blind	565(40%)	74(26%)	491(44%)	<0.001
Single Arm	232(17%)	75(26%)	157(14%)	<0.001
Control	607(44%)	65(22%)	542(49%)	<0.001

[†] The Stage comparison was performed on a 2×2 contingency table of Pivotal vs. Exploratory among records with defined phase (Digital n = 275; Traditional n = 780). Records with Undefined phase (Digital n = 12; Traditional n = 331) were excluded from this test because the Undefined category reflects an administrative artifact of 2003-2015 regulatory documentation rather than a substantive phase classification

[‡] Fisher's exact test with Monte Carlo simulation (10,000 iterations) was used for Medical Device Classification (5×2) because two cells contained zero observations and the minimum expected cell count was 1.85, violating the chi-square test assumption.