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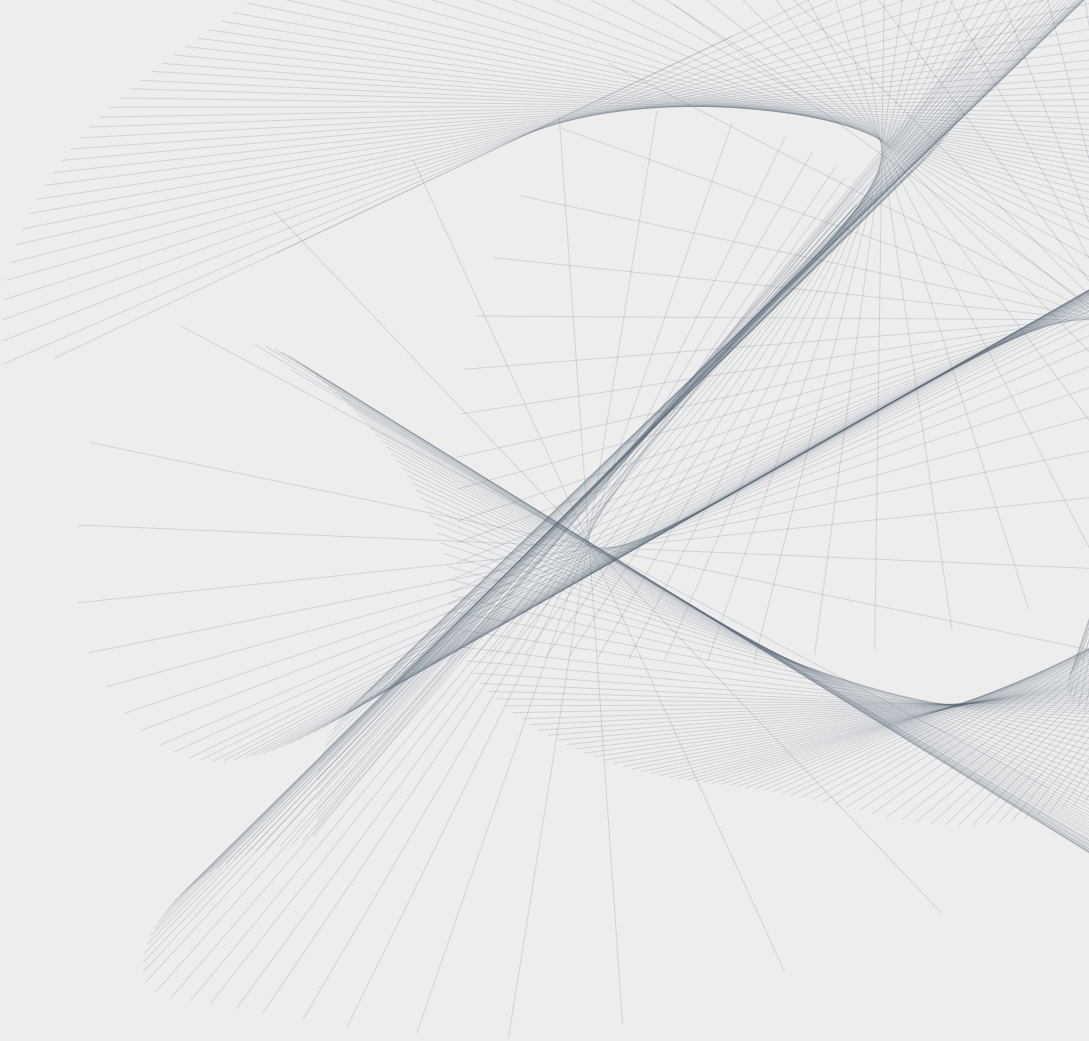

Digital Health Trends 2024

IMPLICATIONS FOR RESEARCH AND PATIENT CARE

DECEMBER
2024

Introduction

Digital health companies have faced headwinds over the past few years. Startups have seen reduced funding inflows while companies with approved products have struggled to grow revenue and expand their user base. Some have gone bankrupt. However, innovation has remained strong and new digital health products to diagnose, treat and remotely monitor patients are now launching into a more mature global marketplace with an expanding number of approval and reimbursement pathways that offer improved chances of future success. Developers are also combining individual product types into "solutions" with both patient and physician-facing interfaces that increase the case for health system adoption. In the research space, biopharma companies have been using wearable sensors and digital measures in drug trials to better understand drug benefits and reduce risk.

This report examines trends across various segments of the digital health market, which are becoming increasingly defined. We examine digital diagnostics alongside maturing therapeutic product segments like digital therapeutics (DTx) and digital care (DCs) and look at consumer apps and non-prescription digital therapeutics that aim to reduce health symptoms. We also examine how life sciences companies are strategically deploying wearable sensors and other patient monitoring tools in research.

While past IQVIA Institute digital health reports have focused mostly on consumer-facing digital health technologies, this report also explores provider-focused solutions, like digital diagnostics, clinical decision support tools, remote patient monitoring tools and AI-informed digital platforms that are now helping providers globally improve outcomes for patients with chronic diseases. For the first time, we also examine the uptake of these solutions in the marketplace drawing on various IQVIA data sources.

A follow-up to this report, to be released in early 2025, will then look across segments to examine how business strategies are shifting in the pursuit of revenue, the pathways digital products are taking to reach the market and gain reimbursement, and how payer evidence requirements and government policies are shifting globally and may influence adoption.

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Overview

THE LANDSCAPE OF DIGITAL HEALTH

While the past two years have been challenging for many players in the digital health field, they have also yielded many new products that better meet the needs of stakeholders and are more commercially viable. As the scope of digital health continues to expand — fueled by advances in technology and artificial intelligence — and more defined segments of innovation have emerged, developers have also been combining these individual product types into "solutions" with both patient and physician-facing interfaces. Their applications now span the full patient journey. Both digital therapies and new health assessment tools like digital diagnostics offer to speed care and close care gaps to improve health outcomes, are better fitting into existing care pathways, and are establishing sustainable business modals that will bring benefits to more segments of patients and health systems.

CONSUMER APP TRENDS

Since app stores first emerged in 2008, over 1 million consumer digital health apps have been created. However, two thirds of these apps are no longer marketed. Amid the cycle of app creation and elimination, the topline number of consumer health apps has remained above 300,000 since 2017 and 337,000 are currently available. More proactive removal of low-quality apps and fewer new app releases on Google Play have led app numbers to decline by 4% since 2021.

Disease-specific apps continue to grow in number, with many supporting mental health and patients with diabetes and cardiovascular diseases. Recently-launched apps also help those with visual impairments, auditory issues and dermatologic conditions. With increased competition in most categories and continued commercial headwinds, new health app entrants face challenges to grow and differentiate themselves in the market. Even for high quality apps uptake is relatively slow. While some notable consumer apps attain 420,000 installs on average after five years, disease management apps see only about 90,000 installs, although newer apps appear to be growing more quickly. Apps with stronger clinical evidence have seen higher rates of use and more rapid uptake, indicating that evidence generation is now increasingly important for consumer adoption and commercial success.

As the FDA unwinds COVID-19 emergency use authorizations, some non-prescription digital therapeutics that had been available to consumers to support mental health have been required to undergo regulatory approval as prescription products. At the same time, some disease management apps with demonstrated health benefits are now used exclusively within digital care programs for commercial reasons. Both trends have caused direct consumer access to high-quality health apps to disappear as they shift to gated commercial models with no cash-pay options, such that the promise of digital solutions to democratize health has diminished. However, this trend may gradually reverse if more prescription digital therapeutics are able to switch to over-the-counter dispensing.

Both digital therapies and new health assessment tools like digital diagnostics offer to speed care and close care gaps to improve health outcomes, are better fitting into existing care pathways, and are establishing sustainable business models that will bring benefits to more segments of patients and health systems.

DIGITAL THERAPEUTICS AND THEIR USE IN CARE

Over 360 software-based therapeutic tools are now commercially available with some products available to consumers with or without a prescription and others used by providers to enhance clinical and digital care. As regulatory and reimbursement pathways proliferate and proof of clinical utility and cost savings increase, digital therapeutics intended for patient use at home have notably grown in number with 140 granted market access through national regulatory and reimbursement pathways. As of early 2024, 42 were also available as non-prescription digital therapeutics — many directly available to patients for self-management — and 222 digital therapies were commercially available for use by providers in their clinics or within digital care programs.

As developers have progressed their global commercialization strategies, some digital therapeutics are now available in multiple geographies. Germany continues to lead in the approval and reimbursement of DTx with 56 patient-facing prescription digital therapeutics currently granted reimbursement, followed by the United States where 37 are available (46 including outpatient dosing apps). In the United Kingdom 20 have been endorsed for use by NICE along with other therapeutic digitally enabled therapies.

Since 2021, 87 digital therapeutics have gained new approvals or market access globally. Recently approved DTx include apps to treat visual impairments and chronic diseases like diabetes and hypertension, though mental health still predominates as a focus. The types and mechanisms of action for DTx have also expanded beyond widely used cognitive behavioral therapy apps. The use of biofeedback and virtual reality have grown, aiding in musculoskeletal and neurological rehabilitation, treating visual impairments, reducing various types of pain, and addressing PTSD and phobias through exposure therapies. Some have gained FDA breakthrough device designation having shown potential to address unmet medical needs through nonpharmacological treatments.

With a growing number of DTx incorporating virtual care wraparounds to overcome provider adoption issues, digital care is becoming the predominant channel for the use of digital therapeutics and over 180 digital care programs are now commercially available. Patient demand for obesity drugs has driven payer endorsement of digital care weight management programs, some of which use mobile apps to shift behavior prior to initial drug use or encourage adherence. Some countries also appear to prefer digital therapies be used within the bounds of traditional care, as “blended therapies”, resulting in digital therapeutics being marketed as a standalone DTx in one country but as a digital care solution in another.

Digital therapeutics intended for patient use at home have notably grown in number with 140 granted market access through national regulatory and reimbursement pathways.

SENSOR-BASED DIGITAL MEASURES

Through the use of digital sensors and wearables, nuanced aspects of health and patient experience are becoming traceable and measurable in daily life. In patient care and in clinical development programs for innovative medicines, sensor-based measures, including digital biomarkers and clinical outcome assessments, are proving valuable to remotely monitor patients, demonstrate the effects of therapeutic interventions and track outcomes.

Life sciences companies have incorporated digital measures into their clinical trials and have invested in the creation and validation of new digital endpoints, with some even building molecule-to-market digital strategies that overlay their drug development programs.
By offering higher quality of data capture, more consistent measurements and increased sensitivity than traditional methods, some digital endpoints have optimized clinical development, allowing trial sponsors to reduce clinical trial enrollment and they further promise to reduce trial duration and the need for patients to travel to trial sites.

The FDA and EMA have also begun to approve (or "qualify") digital endpoints for use in clinical trials, with the first ones using wearables to assess COPD, Duchenne muscular dystrophy and atrial fibrillation. While some digital endpoints may eventually replace existing methods, others may serve as objective measures alongside more subjective clinical outcome assessments within combination endpoints to give a clearer picture of patient experience.

Using AI, algorithms, image matching and other approaches, mobile health assessment tools span the patient journey with consumer-facing apps helping to identify potential causes of symptoms, consumer wearables screening undiagnosed patients for signs of disease, and digital diagnostics enabling providers to diagnose and monitor patients remotely.

DIGITAL DIAGNOSTICS AND OTHER HEALTH ASSESSMENT TOOLS

Software-based deivces that process signals from sensors have rapidly opened new routes to assess disease risk, speed diagnosis and monitor patient health and at least 103 such digital diagnostics are now commercially available. Conditions now detectable using these tools include autism spectrum disorders, sleep apnea, atrial fibrillation, skin cancers, epilepsy and sepsis, among others. Many of these devices are enabled by artificial intelligence and machine learning, and in the United States, around 75 of these AI/ML enabled mobile and point-of-care tools have been approved by the FDA. This fits in within a broader development trend towards using AI to improve diagnostic equipment and as of June 2024 801 distinct AI/ML enabled devices — mostly large-footprint radiology equipment or image analysis software used in hospitals — had received approval.

Using AI, algorithms, image matching and other approaches, mobile health assessment tools span the patient journey with consumer-facing apps helping to identify potential causes of symptoms, consumer wearables screening undiagnosed patients for signs of disease, and digital diagnostics enabling providers to diagnose and monitor patients remotely. Digital solutions that speed and improve diagnosis notably offer to expand the population recognized to require treatment and allow for early intervention. Among these, risk screening tools built on consumer smartphones and wearables offer great ability to speed diagnosis and democratize health assessment by reaching global patient populations and when they provide a negative result, may reduce the number of patients unnecessarily referred to specialist care.

Remote patient monitoring tools such as wearables and symptom-tracking apps are being combined into broader clinical "platform" solutions for providers to monitor disease progression or response to therapy, detect recurrence and even predict future health changes to triage patients in greatest need of care. This has enabled the creation of hospital-at-home solutions that continuously detect and predict adverse events, thereby speeding patient discharge from hospital settings and improving quality of life for patients being treated with advanced therapies and medicines with higher risk profiles.

The line between consumer grade devices and clinical grade devices has also begun to blur as medical device companies develop consumer wearables aimed at wellness and lifestyle optimization and conversely, medical-grade sensors begin to be added to consumer products, making in-home health and chronic condition management increasingly a part of daily life.

UPTAKE AND USE OF DIGITAL HEALTH TECHNOLOGIES

The use of digital technologies can be examined in various ways based on how they are prescribed, dispensed, distributed, billed, and reimbursed. Multiple data sources show that patients and health systems are increasingly relying on innovative digital solutions to close care gaps across the patient journey, with more rapid growth in some geographies than others. Digital tools are also being used to care for patients with a broad range of diseases, but notably for high-risk chronic conditions, including hypertension, diabetes, heart failure, and sleep disorders.

The use of digital health assessment tools for remote patient monitoring and management has grown most rapidly, driving some countries to establish reimbursement pathways. In the United States, provider billing for remote physiological monitoring increased five-fold in the past three years, and use of new codes for remote therapeutic monitoring nearly quadrupled in the year ending September 2023. Apps for obesity and weight management have gained significant use, with around 1.5 million installs on average, although mental health apps are more widely available and collectively are more widely used than weight management apps. Musculoskeletal digital care solutions are notably gaining traction in the employer benefit market, with charged medical claims growing.

Multiple data sources show that patients and health systems are increasingly relying on innovative digital solutions to close care gaps across the patient journey, with more rapid growth in some geographies than others.

Use of digital therapeutics has been growing in Germany, while commercialization challenges in the United States have contributed to the insolvency of some companies. Many early entrants into the U.S. market with pharmacy-dispensed DTx are no longer in business today — their uptake notably limited by lack of reimbursement forcing patients to pay out of pocket to receive access. However, the new cohort of DTx entering a more mature market may fare better. In Germany, where 56 digital therapeutics are currently eligible for reimbursement and the DiGA directory doubles as a centralized repository of clinical evidence on each to inform providers, prescription volume has been increasing overall.

The landscape of digital health

+ **The past two years have marked a period of retrenchment in digital health, with some established companies becoming insolvent and many shifting and diversifying their business models to survive.**
+ **After a near continuous decline in digital health venture funding since early 2021, a Q2 2024 increase offers hope for a rebound, although the number of digital health deals remain at its lowest since 2019.[1,2]**
+ **In a typical innovation cycle after such periods of disillusionment, new products come to market that better meet the needs of stakeholders and are more commercially viable — just as we see now with digital health products evolving to better fit into existing care pathways.**
+ **The scope of digital health continues to expand with more defined segments of innovation and developers combining these individual product types into "solutions" with both patient and physician-facing interfaces.**
+ **Digital solutions now assist patient and physicians across the full patient journey from preventative self-care to risk assessment, triage, diagnosis, treatment, and monitoring — offering to accelerate this journey and improve outcomes.**
+ **Physician-focused solutions are a key area of interest to life sciences companies and include tools to support clinical decision-making and remotely monitor patient outcomes in clinical research and care.**

INVESTMENT IN DIGITAL HEALTH

Digital health can be defined in many ways. The FDA describes digital health technologies (DHTs) broadly as "systems that use computing platforms, connectivity, software, and/or sensors, for health care and related uses."[4] In this report, we focus more narrowly on the use of mobile devices (such as multi-use smartphones, tablets, virtual reality devices, consumer wearables, and in-home virtual assistants) intended to improve health, along with their associated apps, biometric sensors, connected devices, analytic algorithms, and software platforms.

The value of mobile tools derives from their ability to extend patient care and health assessment beyond their traditional settings into the home, to the point-of-care or to primary care settings. They are now used across the patient health journey for disease diagnosis, prevention, symptom management, therapy, and monitoring. To deliver their benefits, they may record and analyze data including biometric measures of health, communicate information, and deliver health interventions (sometimes as games and visual experiences) and thereby influence an individual's health behaviors or disease self-management, or a provider's clinical decision-making.

As is common in the world of emerging technologies and innovation, an initial period of excitement and high expectation is often followed by a period of retrenchment where some companies fail and the mood of stakeholders levels off or turns pessimistic.[3] Over the past few years, as regulatory and commercial pathways evolved, a diverse array of new digital health technologies and products entered the market. However, attaining success in that young market has not been straightforward, and even groundbreaking companies in digital therapeutics such as Pear Therapeutics have gone bankrupt, as has Babylon for digital care, Kiio for musculoskeletal care, and Better Therapeutics (whose diabetes digital therapeutic was launched months prior to its demise). Others, including Akili, struggled to turn a profit, and sought "strategic business alternatives"[5] or have been acquired, dampening the mood significantly and impacting funding.

Indeed, the past two-and-a-half years have seen continuous declines in the number of digital health deals and total digital health investment close to 2019 levels (Exhibit 1).[1,2] Following a peak period post COVID-19 where healthcare rapidly digitized and 2021 annual venture funding rose to $59.3Bn, it then fell to half that, or $22.8Bn, in 2023 with fewer deals and lower average

deal sizes.[1,2] Although topline quarterly funding and number of digital health deals remained at recent lows as recently as Q1 2024, the second quarter has offered hope for a rebound, showing higher total funding and higher average deal values.[2]

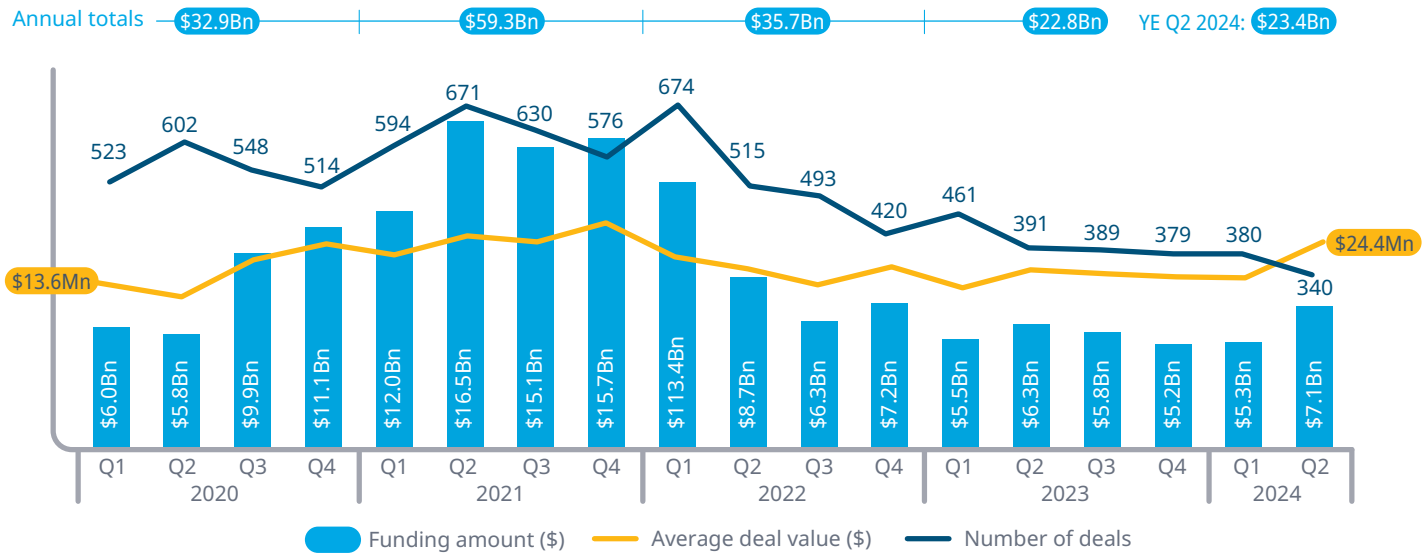
Outside of the venture capital landscape, life sciences companies have continued to invest in digital health in ways that will influence both patient care and research. Physician-focused solutions that support diagnostic and therapeutic decision-making have been a key area of interest, however, investments span applications. They include the use of sensors to capture digital endpoints in drug development trials, the development of digital therapeutics to improve patient health, digital health assessment tools to support and accelerate diagnosis (and treatment), and remote patient monitoring tools to help clinicians and investigators improve patient outcomes — all discussed in different sections of this report.

Finally, more positive news comes from typical phases of the "innovation cycle." Following periods of disillusionment with hot new technologies and lessons learned, new products typically come to market that better meet the needs of stakeholders and are more commercially viable. In the case of digital health, developers now better understand market pitfalls and are increasing their appeal with next-generation products. Physicians, having gained prior exposure, are also likely to better understand how new products can fit into or improve their business and patient care.[3]

Already we are seeing product developers gravitate to alternate business models with clearer commercial prospects and lower regulatory and reimbursement barriers. This enables them to obtain revenue earlier in their lifecycle while they refine their products over time. They are also horizontally and vertically integrating with other companies to build suites of products that fit better into existing care pathways to solve user pain points.

For instance, to overcome issues of marketing a single standalone product or point solution, some of the digital therapeutic products affected by bankruptcies have already been repurposed as tools used within digital care;[6] or have been acquired to broaden therapeutic platforms and product offerings.[7,8] Developers have also merged forces with other companies working in the same therapeutic area or category (such as serious games, virtual reality or rehabilitation tools).[9] All of these approaches have aimed to bring more appealing solutions to the market, including the employer space.

Exhibit 1: Quarter over quarter digital health funding history, $Bn



Source: Galen Growth. The Global Digital Health Ecosystem Turns a Corner: H1 2024 Key Trends & Insights. Jul 1, 2024. Available from: https://www.galengrowth.com/h1-2024-digital-health-funding-reaching-the-turning-point/.
Notes: Reprinted with permission. Displays global venture capital funding and deal values. Annual totals are from published values.

SEGMENTS OF INNOVATION

Digital health tools have expanded and diversified over the past few years, evolving into more defined areas of innovation (Exhibit 2). These areas can be segmented by whether the digital product employed is primarily software, such as apps, or a measurement tool that analyzes signals from biosensors; whether it supports patients, providers, or telemedicine and telemonitoring care interaction between the two; and by its intended health purpose (e.g., self-care, diagnosis, treatment, monitoring, research, etc.).

While health apps were initially developed for mobile phones and tablets, a growing number of solutions are now being created for virtual reality headsets, such as immersive digital therapies, "serious games" and rehabilitation apps. There has also been an explosion of innovation using biometric sensors that has opened new ways to assess patient health remotely. Indeed, by analyzing signals from sensors (i.e., digital measures), digital tools now aid in patient diagnosis and remotely monitor patients within clinical trials and care.

Tools for providers

Although the rise of mobile health has been driven by the creation and use of consumer-facing digital apps for wellness and self-care, other segments now serve healthcare providers directly (Exhibit 2). These include a growing number of tools that aid clinical decision-making such as "clinical decision support tools" that providers use as apps on their smartphones or are embedded within clinical workflow, mobile software-based medical devices that process signals from sensors to assess disease, and software platforms for clinical care or research.

Notable among these are a growing number of algorithm-, model- and AI-based digital diagnostics (Dx) that analyze data from biometric sensors to help clinicians detect and characterize disease. Using these devices, primary care doctors that might lack expertise in rare or specialty diseases can better assess patient risk and determine whether to refer patients to higher levels of care, or even provide a Dx-supported diagnosis.

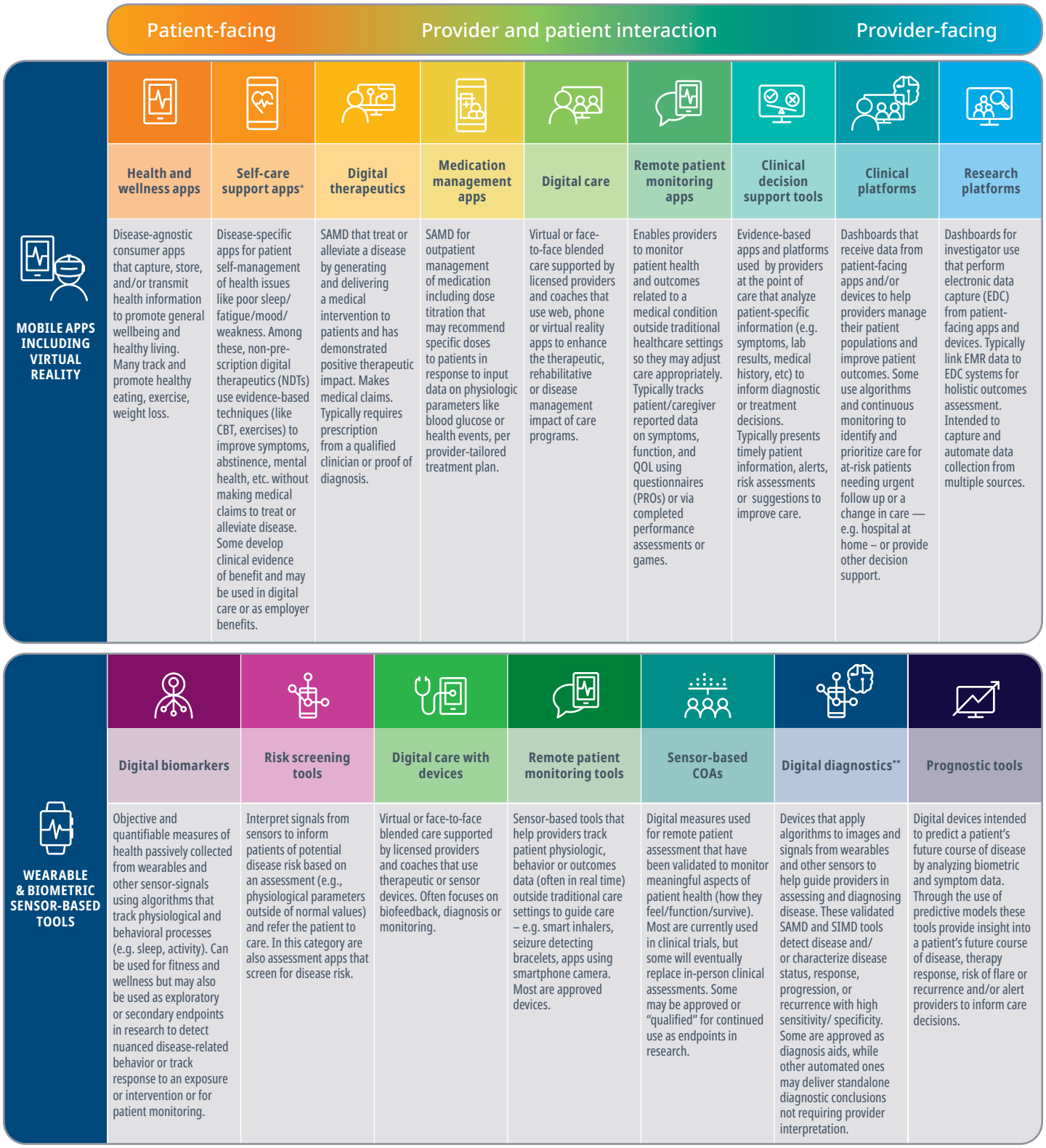
Other provider facing tools such as clinical and research platforms now serve as the conduit to bring benefits from a panoply of digital health innovation into the hands of physicians by receiving, displaying, and analyzing data from patient-facing apps and devices. Among these are remote patient monitoring (RPM) platforms that may tie to wearable devices capable of continuous measurement and monitoring of physiological data, digital biomarkers and COAs, to smart devices that track behavior or medicine use, and/or to apps that enable patients to self-report symptoms or perform clinical assessments (remote patient monitoring apps). Their inputs generate the ability for physicians to monitor their patients for disease risk or shifts in health status (progression, recurrence, exacerbation), often through the addition of built-in AI-enabled algorithms.

Tools for patients

Many apps that support patient health are available through app stores, regardless of their intended use. These include health and wellness apps, but also self-care support apps that aid in patient self-management of diseases, health issues and symptoms by providing educational resources and recommendations on self-care.[10] Among these are non-prescription digital therapeutics (NDT), which may use evidence-based wellness techniques, exercises, reminders, and education to help patients address their symptoms (like poor sleep/fatigue/low mood/ weakness) or to change their behavior (like medication adherence), without making medical claims to treat or alleviate disease.

However, the segment that has received the most attention in recent years has been digital therapeutics — software devices prescribed to patients to treat disease and supplement outpatient care — and many countries have created new approval and reimbursement pathways to accelerate their use. While nearly all of these are patient-facing, some are intended for use at home, while others delivery therapy in-clinic to make face-to-face care more effective, and these have seen increased adoption by the U.S. Veterans Administration and the U.K. NHS alike. Another segment, prescription medication management apps," provide dose adjustment recommendations based on a provider-determined treatment plan.

Exhibit 2: Segments of digital health and their use by stakeholder



Source: IQVIA Institute, Nov 2024; Adapted from Digital Therapeutics Alliance, Guidance to Industry Classification of Digital Health Technologies, Jun 5, 2023.
Notes: *Care support is defined by Digital Therapeutics Alliance as "Patient-facing digital health solutions intended to support patient self-management of a specific diagnosed medical condition through educational resources, recommendations, and/or reminders." **Digital diagnostics span health assessment applications including screening, diagnosis, monitoring and prediction/prognosis but here we split these categories by application. Biometric measuring technologies (BioMeTs) include smartphone gyroscopes and cameras. Quality of Life (QOL). Cognitive Behavioral Therapy (CBT). Software as a medical device (SAMD). Software in a medical device (SIMD). Patient reported outcomes (PROs). Telemedicine apps are excluded as they use video chat but no other digital tools.

Finally, sluggish adoption of digital therapies by providers is being overcome by their increasing use in practice by dedicated digital care providers (alternately called virtual care, hybrid care or blended care) that market innovative outpatient care services that combine telemedicine with one or more standalone digital tools. Driven by patient need for more continuous behavioral support in the treatment of chronic conditions, obesity, mental health, and physical and neurological rehabilitation, such digitally supported disease management programs are emerging to serve patients, payers and employers.

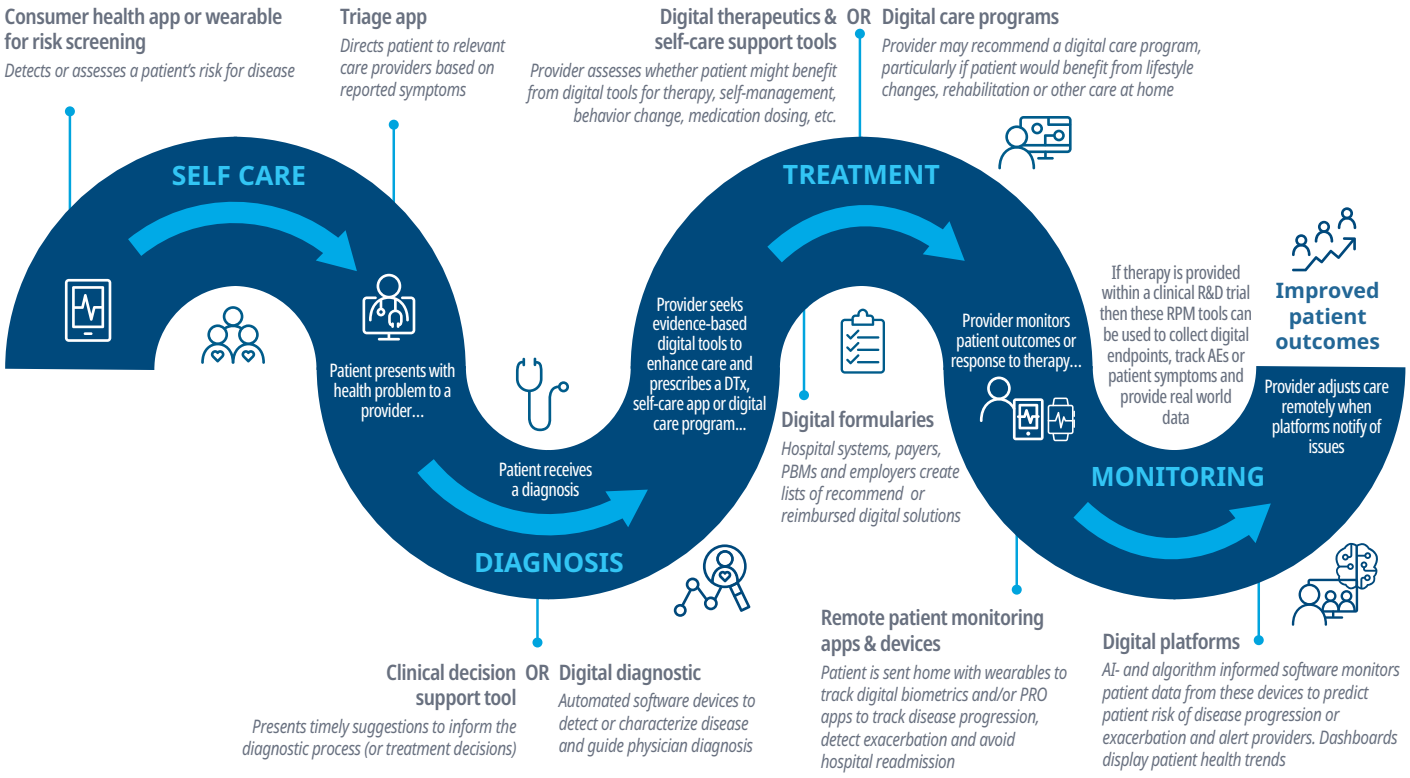
Platform solutions

As segments have grown more defined, companies are increasingly combining them into more holistic clinical platform solutions for care providers that increase the case for health system adoption, and research platforms for investigators. Developers that once offered wearables or self-care apps to patients to track their symptoms are now tying these together with provider-facing portals that pull in data from devices and allow clinicians to monitor and manage their patient and clinical trial populations. Many of these platforms use sophisticated algorithms and AI capabilities to provide clinical decision support, dose management, therapeutic guidance, and sometimes provide alerts when patient values or patient-reported outcomes fall out of a specified range to better identify patients that need their care adjusted.

DIGITAL TOOLS WITHIN CARE

With the proliferation of digital solutions, they now assist patient and physicians across the full patient journey from preventative self-care to risk assessment, triage, diagnosis, treatment, and remote patient monitoring — offering to both accelerate this journey and improve outcomes (Exhibit 3). Each of these applications will be addressed in different sections of this report.

Exhibit 3: Diagnosis, treatment and monitoring in the digital world



Source: IQVIA Institute, June 2024

Notes: Remote patient monitoring (RPM); Adverse events (AEs); Pharmacy benefit manager (PBMs); patient reported outcome (PRO).

Consumer app trends

+ **Over 1 million digital health apps have been created to date but two-thirds of these are no longer marketed.**
+ **The number of health apps available to consumers has declined by 4% since 2021 to around 337,000, as fewer new apps are released on Google Play.**
+ **Disease-specific apps continue to grow rapidly with new arrivals addressing vision and auditory issues and dermatologic conditions, although most focus on mental health, diabetes, and cardiovascular diseases.**
+ **Apps with stronger clinical evidence are installed more frequently and gain more endorsements from professional societies, government agencies, and patient organizations, suggesting that evidence generation is now increasingly important for adoption and commercial success.**
+ **Health app uptake is relatively slow, and while notable consumer apps may attain over 400,000 installs after five years, disease management apps see less than one-fourth of that on average, or around 90,000 installs.**
+ **Recently released health apps appear to be growing more quickly than in the past, with disease management apps achieving triple the uptake versus earlier cohorts.**
+ **With the FDA unwinding COVID-19 emergency use authorizations, some non-prescription digital therapeutics are now required to undergo regulatory approval and others are shifting into digital care for commercial reasons, causing direct consumer access to disappear.**
+ **As disease-specific therapeutic apps shift to gated commercial models with no cash-pay options, the promise of digital solutions to democratize health has diminished, although this trend may reverse if more prescription digital therapeutics are able to switch to over-the-counter dispensing.**

APP GROWTH

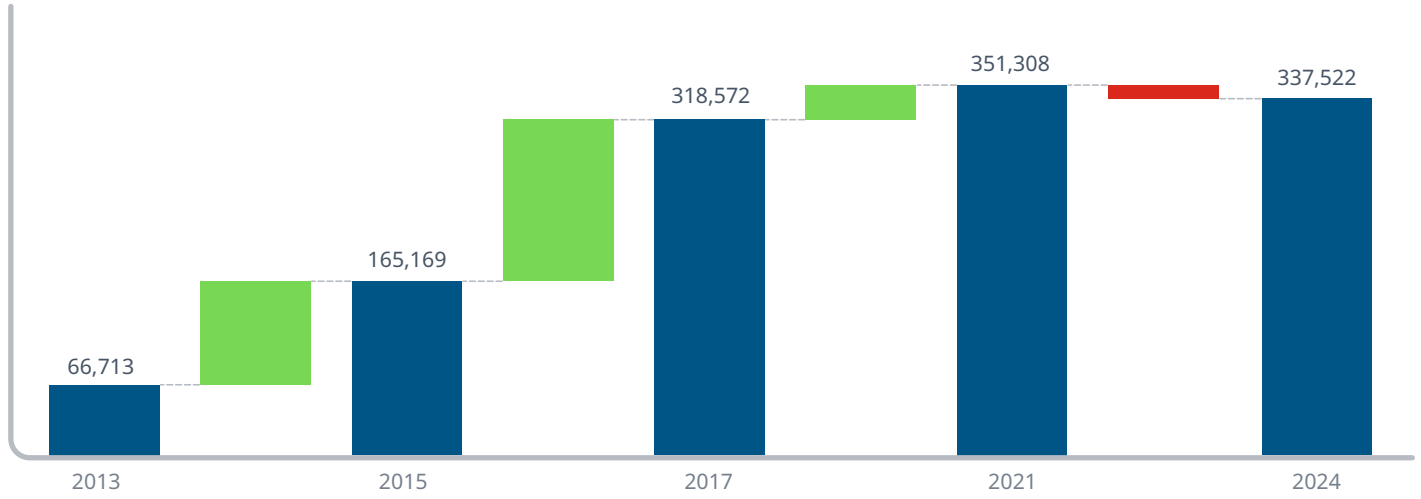
Mobile app stores are a key distribution channel for developers of health apps that allow their software to be installed and run on mobile smartphones and tablet devices. The apps launched on these platforms span digital health segments, with individuals able to install wellness and fitness apps, apps for disease self-management, digital therapeutics, and even risk screening apps from app stores, while physicians can obtain clinical decision support tools or apps approved as digital diagnostics, among others.

More than 337,000 digital health apps (classified as "health and fitness" or "medical") are currently available to consumers, patients, and physicians worldwide through the Apple Store and Google Play app stores (Exhibit 4). In the past few years, there has been a leveling-off in app growth and periodic declines in the topline number of consumer health apps.

As of October 2024, 4% fewer apps were available than in 2021, likely driven by fewer new health apps being released on Google Play and the continued removal of low-quality apps. Since August 2023, when a recent high of 4,002 health apps were released in on Google Play, monthly releases dropped 54% and were only 2,171 in August 2024, likely due to new testing and quality requirements.[11,12] Although monthly app releases have remained steady on the Apple Store, both app stores have become more proactive about ensuring the quality of apps, speeding the removal of lower quality ones and those that are not updated by developers.

The total number of health apps ever created has now topped 1 million; however, due to a continuous dynamic of app creation and removal from the market, two-thirds

Exhibit 4: Number of digital health apps 2013–2024



Source: IQVIA AppScript Digital Health Database, Oct 2024, Jun 2021, Jul 2017, Jun 2015, Jun 2013. Data 2017 onward sourced from 42 Matters and from Mevvy prior.
Notes: Includes digital health apps that are publicly available to consumers and categorized as "Health & Fitness" or "Medical" apps, as well others outside this category included in the Appscript catalog. Apps that have been removed from stores are not included.

of these or ~717,000 have ceased to be marketed and are no longer available in stores (as of October 2024). Only 12% of apps released prior to 2019, for instance, are still available for download.

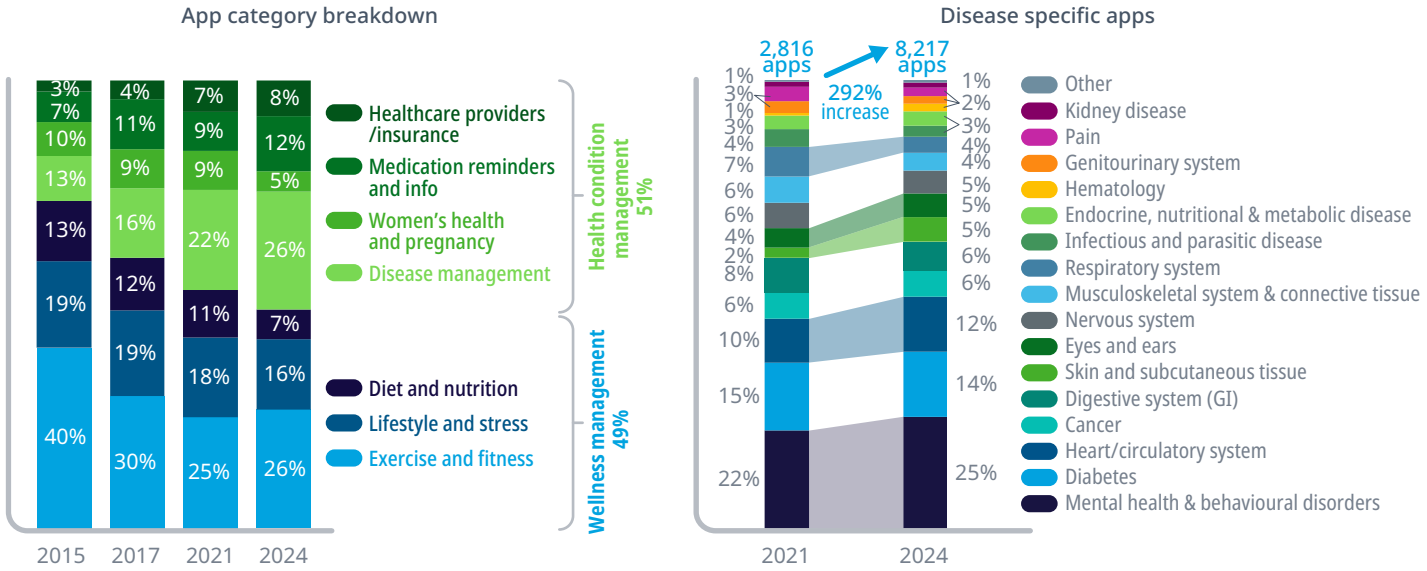
From 2021–2023, around 85,000 digital health apps were created and released each year in app stores — an average of 233 apps per day — but only 54,000 have been released to date in 2024. If this lower rate of release continues, around 20,000 fewer apps will be released in 2024. Apps are also disappearing from app stores more rapidly than ever. Already 41% of apps released in 2022 and 20% of apps released in 2023 were gone by October 2024 — some pulled by their developers due to sluggish uptake or commercial factors, while others were eliminated by app stores.

Although topline app numbers have remained at somewhat similar levels, a different picture emerges when the set of notable health-focused apps included in IQVIA's AppScript Catalog — representative of the most widely used digital health apps by consumers — are examined (Methodology). Apps present in this database were analyzed by use category to understand the current landscape of higher-quality apps likely to impact patient self-care and treatment (Exhibit 5).

Across the patient journey, digital health apps can be divided into two main categories: those focused on "wellness management," which facilitate tracking and modification of fitness behaviors, lifestyle, stress, and diet, and those that specifically focus on "health condition management," which may treat disease, supply information to patients to help them self-manage diseases or conditions, enable access to care, or support treatment such as through medication reminders. The mix of apps has shifted continually toward health condition management since 2015, and as of June 2024, more than half of all apps (51%) were focused in this area, up from 28% in 2015. In the wake of the pandemic, exercise and fitness apps experienced renewed interest and rose briefly to 27% of apps in mid-2023, but growth is already moderating again.

There has been a significant increase in the number of apps focused on specific diseases since 2021 — having nearly tripled in number to 8,217 apps — and they now account for 26% of notable apps. Mental health and

Exhibit 5: Digital health apps by category and disease state



Source: IQVIA AppScript Digital Health Database, Jun 2024; IQVIA Institute, Jun 2024.
Notes: Numbers may not sum due to rounding. View shows percentage of app categorizations. Left side 2024 data includes 34,394 apps with 34,011 categorizations.

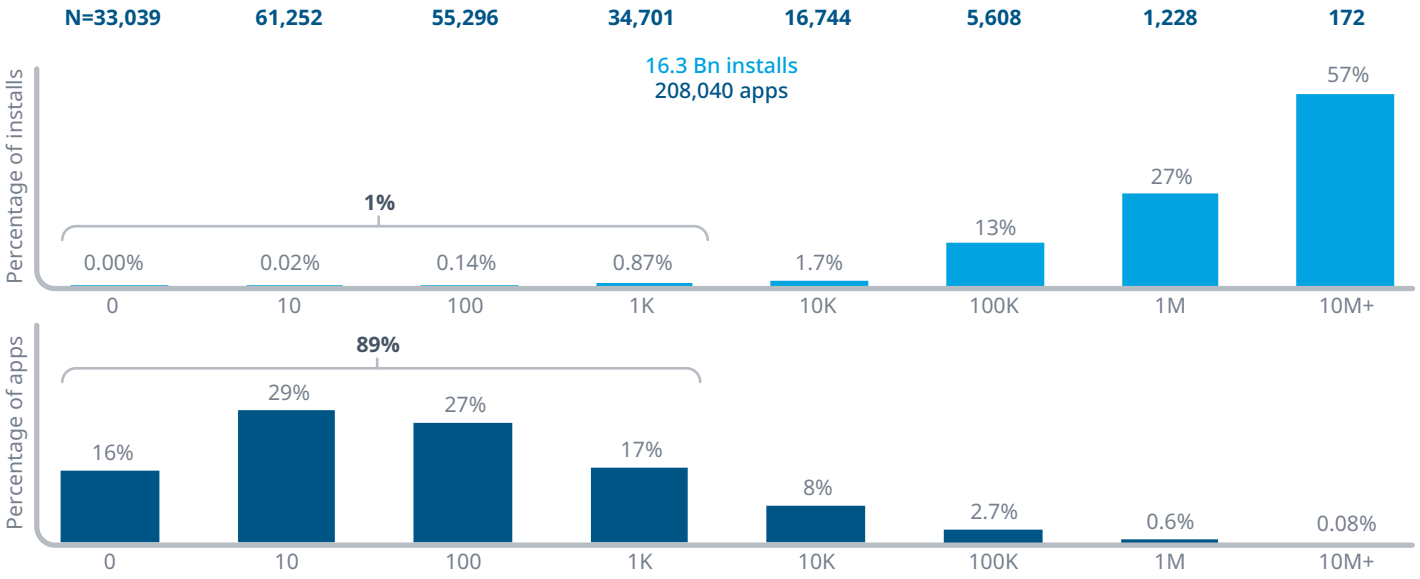
behavioral disorders — where digital therapeutics have demonstrated the ability to influence patient behaviors and treat disease symptoms — remains the largest segment, accounting for a quarter of all disease specific apps. Along with diabetes and cardiovascular diseases — which are supported by disease self-management apps, medication management apps, and remote patient monitoring sensors — these three areas now account for approximately half of disease-specific apps.

There are also several new areas of focus. There has been a notable increase in apps focusing on ocular concerns — predominantly relating to vision, such as myopia, amblyopia, and glaucoma — as well as auditory issues such as tinnitus. There has also been a rise in dermatology apps, with around 22% using artificial intelligence and 18% relating to psoriasis. Not surprisingly, post-pandemic there has also been a drop in the number of respiratory apps.

FACTORS INFLUENCING APP UPTAKE

Producing a health app that appeals to consumers is not an easy task and requires multiple phases of development and investment. As the field has become more competitive with popular and frequently installed apps in most categories, even after an app is released it has become increasingly important to continue to refine its function. While the 172 most popular health apps may have attained over 10 million installs each and now account for 57% of all installs (Exhibit 6), 89% of apps are emerging players with fewer than 10,000 installs that collectively have gained only 1% of installs (167.3 million total) and are seeking ways to stand out in their segment. In between these extremes there is now a dynamic set of nearly 17,000 apps beginning to gain traction and currently in the 10–100K range, and nearly 7,000 more that are already in the 100K–10M range.

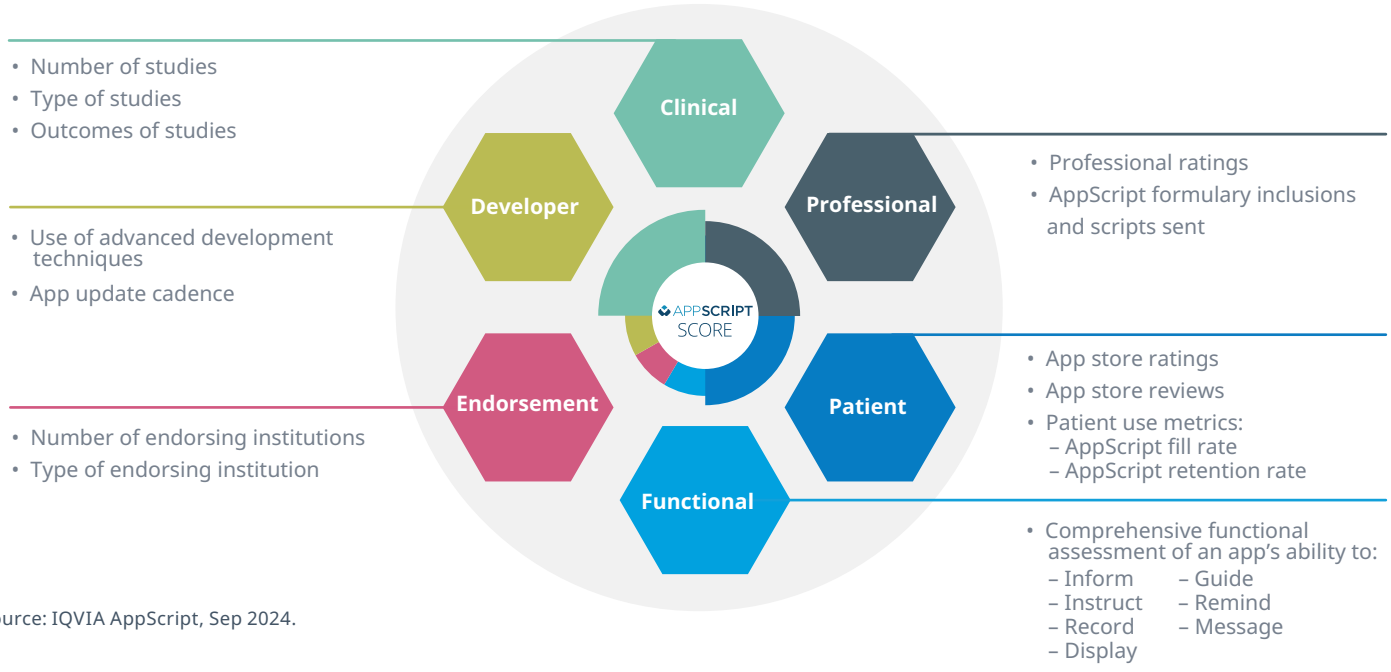
Exhibit 6: Percentage of digital health apps in each install band and their collective uptake



Source: IQVIA AppScript Digital Health Database, Left, Jan 2024; Right, Oct 2023; IQVIA Institute, Jan 2024.
Notes: Install data shown is from the Google Play app store only. Apple Store install data is unavailable. Install segments beginning with 1x (e.g., 10K) include the next 5x band (e.g., 50K). Install value shown is the minimum install value of each band.

With highly established apps in most categories, developers look to distinguish their emerging apps by improving quality along various dimensions reflected in the AppScript Score (Exhibit 7). They may adjust aspects of the user interface that influence whether a patient likes the app and wants to use it (Patient Score); what the apps do (Functional Score); update the app regularly or apply advanced development techniques (Developer Score); build evidence supporting the app's health benefit (Clinical Score); and work to gain endorsement by professional and

Exhibit 7: IQVIA AppScript Score is a way to measure the quality of apps across various domains



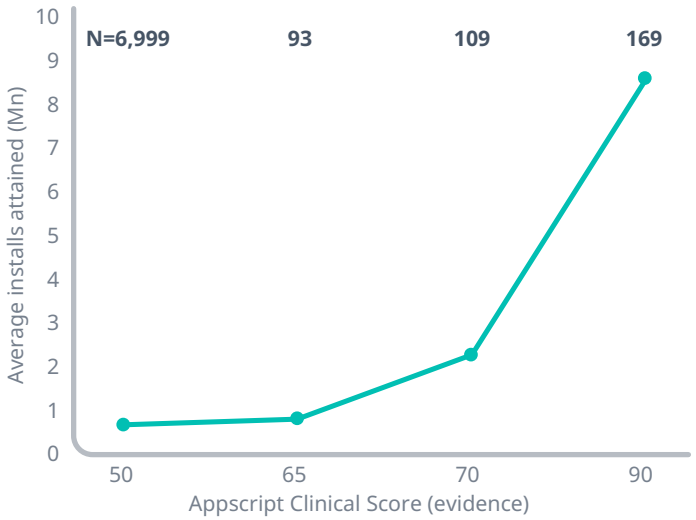
Source: IQVIA AppScript, Sep 2024.

government bodies (Endorsement Score). As developers invest in each area over time, it causes the relevant AppScript Component Scores to increase, and these improvements lead to greater adoption.

Although building success as a small app is increasingly challenging in a competitive field with popular frequently installed apps, those that have developed clinical evidence and have higher AppScript Clinical Scores as a result perform notably better in the market and achieve higher installs on average (Exhibit 8). This suggests that multiple stakeholders in the community — individuals, providers, and payers — now have quality expectations, evidence requirements, and other criteria for apps that all influence their adoption.

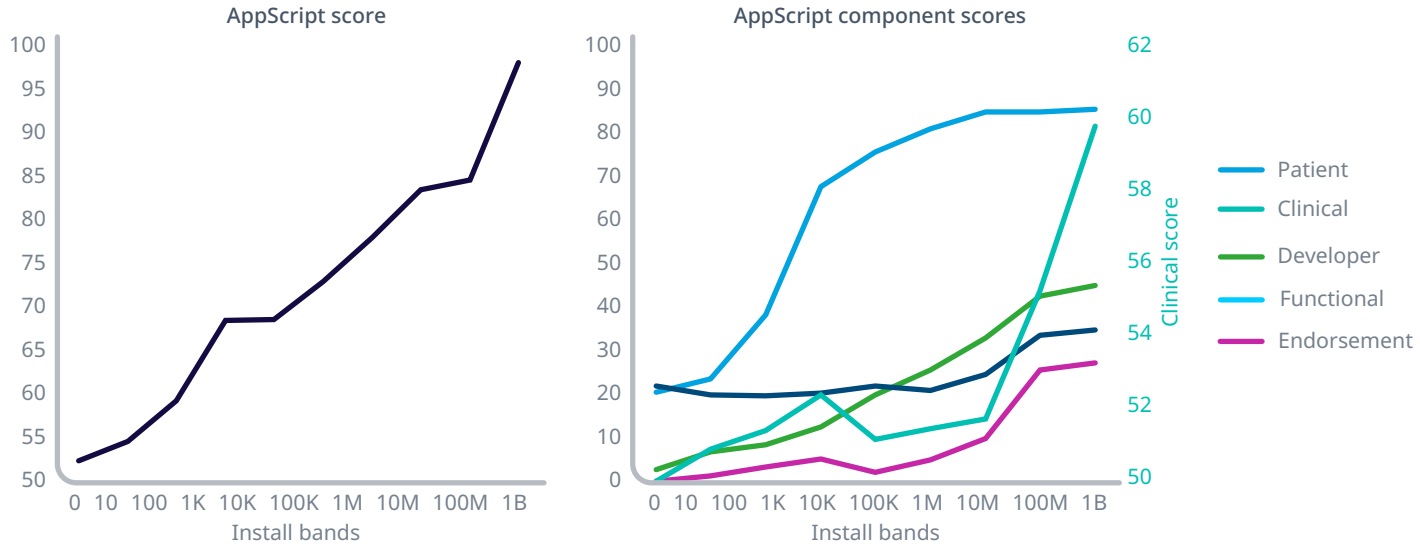
The importance of investing in each quality domain also appears to shift over time (Exhibit 9). Early in their journey (low install bands), developers appear to gain traction by building a patient-friendly product that people like and want to use (i.e., rising Patient Score), and only after they have a user-base, focus increasingly on updating the app at a cadence to improve upon performance (Developer Score). Beyond that, they seem to make further functional improvements, run potentially costly clinical studies, and build evidence of efficacy (Clinical and Functional Scores), thereby avoiding investing too early in a product unlikely to succeed. It is those later investments that also seem to be the route to gaining endorsements by medical/professional societies, government agencies, patient organizations, and other

Exhibit 8: Evidence as a key driver of uptake



Source: IQVIA AppScript Digital Health Database, Oct 2023; IQVIA Institute, Jan 2024.
Notes: Install data shown is from the Google Play app store only. Apple Store install data is unavailable.

Exhibit 9: Average AppScript Score and component scores by product install band



Source: IQVIA AppScript Digital Health Database, Oct 2023; IQVIA Institute, Oct 2023.
Notes: Install data shown is from the Google Play app store only as Apple Store install data is unavailable. Install value shown is the minimum install value of each band. Install segments beginning with 1x (e.g., 10K) include the next 5x band (e.g., 50K) and are averaged with them with no impact on overall trend.

bodies, as they rise in tandem. Although this data view pertains to health apps made available to consumers through app stores, these success factors likely apply broadly to digital therapeutics and other product types.

It is also worth noting that not all apps will be able to attain or intend to serve such a broad audience as those few that have gained a million downloads. For higher quality health apps and disease specific apps, installs mostly fall at the low end of this range at 10,000 installs and very few gain more than 1 million installs (Exhibit 10).

Among the high-quality apps that have attained more than 5 million installs are blood pressure and glucose tracking apps, apps related to COVID-19, some weight-management/obesity apps such as Noom, and mental health-focused apps such as Headspace. Several AI-based chatbots applying cognitive behavioral therapy techniques have also attained over 1 million installs (i.e., between 1–5 million) including Wysa, Youper, and Sintelly, along with others in the mental health space like Rootd and Sanvello for anxiety.

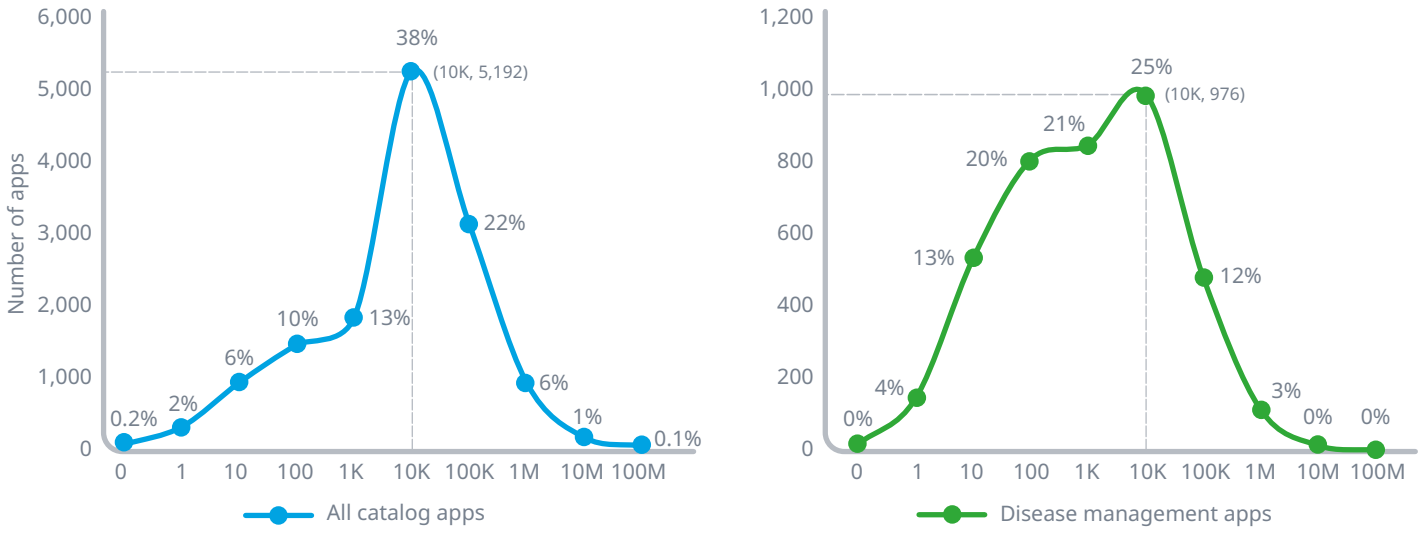
Outside the mental health space, some digital diagnostic and risk screening apps have also attained millions of installs, marking the rising importance and use of software-based health assessment tools such as those that detect cardiac arrhythmias (Kardia and Fitbit ECG App); assess the risk of skin cancer (SkinVision); aid in mental health self-assessment, like PsyTests; or provide eye exams. Exercise apps for back pain, musculoskeletal pain and Kegel exercises also have attained over 1 million installs.

BENCHMARKING APP UPTAKE OVER TIME

The uptake of health apps can be relatively slow (Exhibit 11). Based on Google Play install data available for consumer apps in the AppScript catalog, it can take nearly seven years (84 months) to build momentum in app downloads, with the number of installs attained varying by product type and quality.

While the extremely rapid adoption trend for COVID-19 apps is clearly an anomaly, with millions of downloads even in the first year, across all health and wellness apps in the AppScript catalog, the story is different. Even after five years, a typical uptake on Google Play would be around 420,000 installs (based on trendline projections)

Exhibit 10: Distribution of AppScript catalog apps and a disease management subset across install bands



Source: IQVIA AppScript Digital Health Database, Dec 2023; IQVIA Institute, Jan 2024.
Notes: Displays apps from the AppScript Catalog with install data from the Google Play app store. Apple Store install data is unavailable. Includes 13,681 catalog apps and 3,898 disease management apps. Displays values as of Dec 31, 2023. Install value shown is the minimum install value of each band. Install segments beginning with 1x (e.g., 10K) include the next 5x band (e.g., 50K) and are averaged with them with no impact on overall trend. Lines have been smoothed.

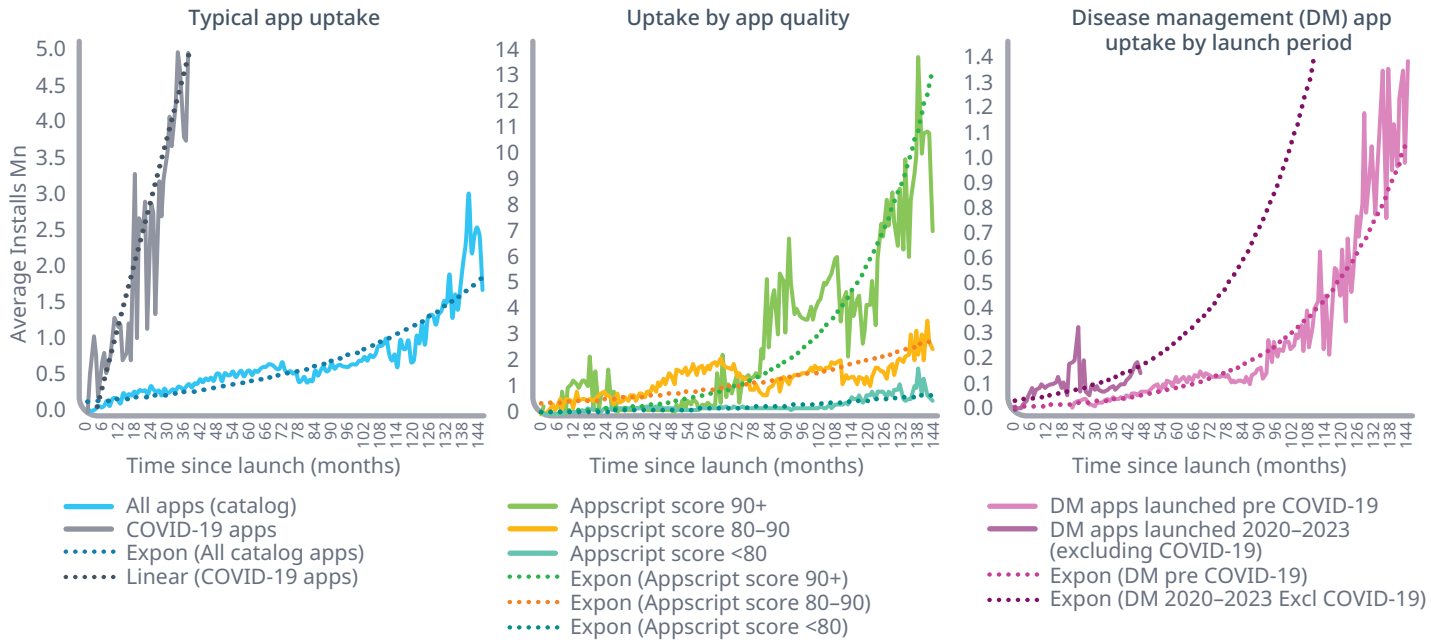
but less than one-fourth of that, or 90,000 installs, for disease management apps (see Methodology).

High quality apps, which tend to have robust clinical scores seem to fare better, and those apps with AppScript scores over 90 had more rapid uptake, accelerating after five years and installs rising rapidly from 700,000 to 1.6 million by year seven on Google Play (based on trendline projections). Only the top exercise, fitness and diet apps saw over 10 million installs after 10+ years. Quality app in the middle range of AppScript scores between 80–90 also performed very well, attaining over a million installs on average by year 7, while those apps with a score below 80 had only around 300,000 installs by that time.

Most of the apps that are likely to significantly impact patient health are considered disease management apps where growth has been much more tepid. These apps had an average of only 30,000 installs at two years on Google Play, 90,000 at five years, and 525,000 at ten years (based on trendline projections). Although the business models of disease management apps may not be solely tied to per-app download fees and instead derive from larger reimbursement amounts for care provision in some cases, this is still an important measure of consumer demand and product viability in the marketplace.

Newer disease management apps appear to be growing more quickly, with apps released from 2020–2023 achieving nearly triple the number of installs per period than earlier cohorts. Other health apps released in the past six years, and ones with AppScript scores between 80–90 are similarly achieving levels of installs above the established trendline. While some newly released apps may be successors to earlier launched versions and therefore already have traction, it may also indicate a larger consumer base actively browsing and seeking out new health apps, leading to earlier adoption.

Exhibit 11: Typical app uptake from initial release to 12 years, by app quality and type (Google Play)



Source: IQVIA AppScript Digital Health Database, Dec 2023; IQVIA Institute, Jan 2024.
Notes: Displays apps from the AppScript Catalog and install data from the Google Play app store. Uses the "Installs min" value per app at each timepoint assessed, which is the lower value of each install band range and may therefore underestimate uptake speed. Time since launch is normalized by app release date. Includes only apps currently in the app store at each normalized time point and therefore apps removed from the store may result in visible drops or increases in the average, compounded in later periods by declining n# over time. All trendlines displayed use the exponential trendline method in Excel except for the left chart COVID-19 line which is linear.

"GATED" APP STORE DISPENSING AND DIGITAL CARE ACCESS[13]

Like all apps available on the store, some health apps are free — made available by life sciences companies, patient organizations, or health systems — and some require payment or a subscription to use them. Therapeutic apps also may have "gated" access that allows use only by those holding a code, which may be given to patients by a provider, pharmacy, payer, or employer as a token validating patient eligibility to use the app and serve to control app dispensing and limit use to intended patient populations.

Eligibility may be determined by receipt of a prescription (for PDTs and other prescription digital tools), by physician referral, or other proof of clinical applicability or diagnosis. The granting of the code to unlock access to the app may further be contingent on payment for the app, such as through reimbursement by a payer, direct authorization or payment by an employer, or cash pay by a patient. For non-prescription digital therapeutics and/or their associated digital care programs, clinically validated screening questionnaires may be used to determine whether a patient qualifies for the therapy or an "authorized clinical protocol" may be established by a healthcare decision-maker to authorize automatic patient access when necessary qualification requirements are met.[13]

Because gated apps are not clearly identified on app stores, consumers may download a free app that is gated but soon delete it when they realize they are unable to access the app without a prescription or code. To combat the loss of potential interested digital therapeutic customers, many prescription apps now have an option to connect with digital care providers to obtain a prescription or provide information that facilitates connection to prescribers.

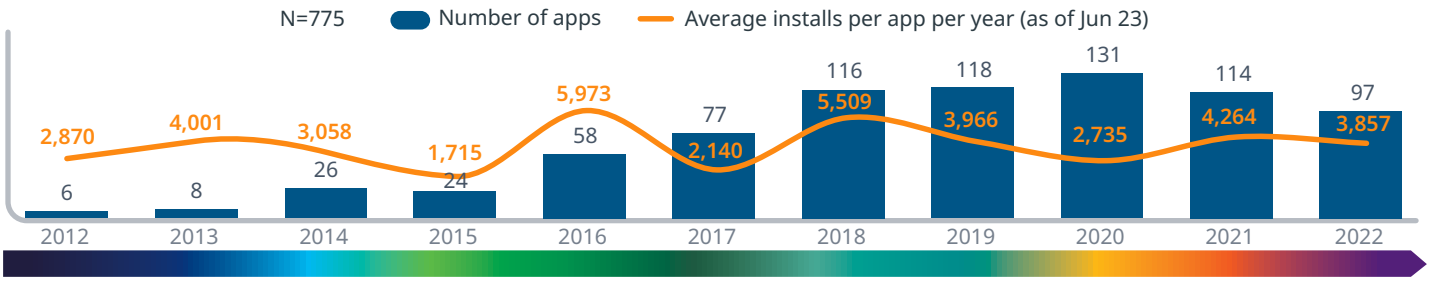
> *"DTx prescription products have been viewed as the only gated patient access path; however, that is not the case. Nearly all patient access to DTx today—including prescription and non-prescription products—involves vetting by a third-party to ensure the right patients have access to the right products."*[13]
>
> *— Digital Therapeutics Alliance*

LIFE SCIENCES COMPANY INVESTMENTS

Some consumer apps available on app stores were created by life sciences companies or were driven by their investment. These include a variety of mobile apps to help patients live better with disease and improve patient treatment, adherence, and outcomes. From 2011–2022, biopharma, medical device and even consumer health companies were involved in the creation of 775 apps, with one of the earliest being Zyrtec AllergyCast (Johnson & Johnson), an app that leveraged local pollen count data to help allergy sufferers assess daily medications needs.

The number of digital health apps launched by life sciences companies peaked in 2020 and has since declined (see Exhibit 12). On average, these apps were installed on devices between 1,700 and ~6,000 times

Exhibit 12: App investment and innovation by life sciences companies over time



Diaries Helpful information Risk self-assessment	Behavior tracking Consumer products Medical information	Rare diseases & education Symptom tracking Medication adherence GPS use in apps	Dosing apps Disease screening Info Sharing Medication Monitoring	Insulin Adjustment Augmented reality Behavior control Clinical trial apps	Quality of Life (PRO tracking) Remote monitoring & platforms Digital care programs	Non-prescription DTx (NDT) Exercise for disease Women's health Adherence tracking	Rare/Care communities Clinic-linked apps Therapy engagement Dermatology apps	Digital Therapeutics Sensor-based assessment Clinical decision support Cancer wellbeing Virtual reality COVID-19	Mental health Sensor tracking Health assessment in R&D Trial improvement Diagnosis support	Serious games for kids Gamified monitoring Care coordination
Glucolog Lite, Menarini to track and trend glucose from a glucometer **AsthmaApp**, GSK to monitor asthma control/ risk & provide local allergen info **Knowledge Genie**, Abbott medical info for physicians **Diabetes Risk**, Faes Farma — to assess diabetes risk, prevention tips **Zyrtec AllergyCast (2011)**, J&J–pollen count and allergy map to predict symptom severity	**Behavior tracking:** **Gluci-Chek**, Roche Carbohydrate counting for diabetes **Consumer products:** **Johnson's Bedtime**, J&J sleep tracking, tips and white noise to help babies fall asleep **Aquafresh Brush Time**, Haleon to help kids learn to brush **Medical information:** **GBR Guide** Viatris - Generic Brand Reference **Medical Information Novartis** **Colonoscopy Guide**, Ferring	**Provider education:** **IPF Sound Challenge**, BI to help clinicians learn to identify rare lung disease IPF **Symptom tracking:** **Acrotracker**, Pfizer for acromegaly **SymTrac MS**, Novartis **Medication tracking and adherence:** **MyStelara**, Janssen-Cilag **Hizentra App**, CSL Behring **GPS use:** **ViaOpta Daily and Nav** Novartis GPS for those with visual impairment **CED Dokumentation und Tipps IBD Crohn's and UC**, Abbvie - GPS for patients to find toilets	**Dosing apps:** **Dose Certa**, GSK HCP dose calculator **Accu-Check Connect**, Roche patient-facing app with bolus advice **Screening/ assessment** **Narcolepsy Screener**, Jazz uses clinical rating scales **Nutrition HCP App** Abbott for malnutrition **Sharing** **ViaOpta Simulator** Novartis explain eye conditions to loved ones **Monitoring** **Propeller** smart device and app for asthma adherence for BI and GSK devices **Dexcom Share & Follow** for CGM data	**Insulin adjustment & diabetes management:** **My Dose Coach**, Sanofi/ **Go Dose**, Lilly **OneTouch Reveal** Lifescan **One Drop and Contour Diabetes app** Bayer **Augmented reality (AR):** **VertiGo Exercise**, Abbott AR vestibular exercises for vertigo **Behavior control:** **MyQuit**, Haleon for smoking cessation **Clinical Trial Apps:** **Bayer Oncology Trial Finder**, Bayer **myStudy-Companion myTrialConnect** Roche	**Improving QOL:** **LivingWith** Pfizer for cancer support **Hemophilia Travel Guide** Takeda care info to enable EU travel **SymTrac Psoriasis** Novartis patients track disease impact on QOL. **Remote monitoring and platforms:** **mySugr - Diabetes Tracker Log** Roche (acquired 2017)* to link to Accu-Chek Connect Online platform **myDiabby** Lilly/ myDiabby Healthcare — diabetes management platform care platform **myMerlin** Abbott heart rhythm monitor that sends info to doc platform **Digital care:** **Pivot** Carrot /J&J Innovation/ smoking cessation program	**Exercise for functional improvement:** **Aby** and **Cleo** Biogen MS **onStEPs** Merck MS **Parkinsounds** Teva music to improve walking **MyMedicoach** Pfizer exercise for back pain **Women's Health:** **Pillenalarm** Bayer — female contraception **Fertiléa**, Merck for infertility treatments **Magic Tree for Breast Cancer** Celgene games educate kids about cancer **Digital adherence tracking:** **MyCite** Otsuka first digital medicine pill with ingestible sensor for Abilify	**Rare/Care community apps:** **SMA Community**, Roche **Clinic-linked apps:** **DigiBete**, Novo Nordisk — NHS diabetes community platform in the UK **Care4Today Education and Kneetiative app** J&J helps hospitals ready patient for hip/ knee surgery/ rehab **Behavioral science and gamified adherence:** **my a:care**, Abbott connected devices and visual feedback for chronic disease **myAir by** ResMed for CPAP therapy progress **Dermatology apps:** **der.me** GSK **Living with Eczema**, Alliance Pharma **Elidoll** Viatris Atopic Dermatitis **iControl Eczema+** Hyphens Pharma	**DTx investment:** **sinCephalea**, Perfood/BI Venture Fund for migraine **Digital/sensor assessment:** **Floodlight MS** Roche R&D tool for patient self- assessment and function monitoring in MS using tests and wearable sensor **Decision support/diagnosis:** **eROL** Sanofi Lebanon app with medical diagnostic algorithms to diagnose Gaucher disease, Fabry, Pompe, MPS-1) **axSpA ID Tool**, Novartis advises what imaging to use for axial spondyloarthritis diagnosis **Cancer wellbeing:** **ByYourSide** Pfizer, **Wikiboop** Roche, **Mi momento** Amgen **Virtual reality:** **Sickle Cell Virtual Experience** Novartis HCPs education on vaso-occlusion **COVID-19 test result apps:** **NAVIFY Pass** Roche/ **Navica Verifier** Abbott	**Mental Health DTx:** **Selfapy - Mental Health App** Medice depression **Sensor Tracking:** **SMAbility tracker** Biogen pairs with wearable devices to track aspects of SMA **Quantified R&D outcome and disease progression tracking:** **Roche PD Mobile Application Roche/MJFF** sensor monitoring and tests to track Parkinson's progression **Konectom Suite Biogen** assesses ambulation, dexterity and cognition, wearable data **myVisionTrack mVTx Roche** tests to detect vision changes in AMD, eye diseases **Trial improvements:** **tMate Roche** to reduce participant and clinical site burden in R&D **DAQ Teva** tracks and improves inhaler use in trials to improve outcomes **Diagnosis CDS:** **Wound Compass Smith & Nephew** helps non-wound specialists treat wounds	**Serious games and physiotherapy apps for kids:** **TinyTrainers**, Roche PT exercise game for children with Spinal Muscular Atrophy (SMA) **Flexterity**, Novartis PT exercises for kids with NMD **Gamified monitoring:** **BeCare MS Link**, Biogen gamified remote monitoring of MS disease progression using validated assessments of neurologic, cognitive data. PROs **Care coordination:** **acare India Abbott** connected patient ecosystem for doctors and health coaches to manage health outcome for adherence, lifestyle, education. **Care4Today 2.0 Pro J&J** allows HCPs to connect, educate and support patients through their care pathway

Source: AppScript Digital Health Database, Jun 2023; IQVIA Institute, Jun 2023. Summaries drawn from app store descriptions.

Notes: Exhibit trends consumer apps available in any geography including ones that have been removed. Install data is from Google Play only as Apple Store install data is unavailable, and therefore, total average installs per product are understated and exhibit should be considered a view of directional growth. Healthily and *mySugr - Diabetes Tracker Log excluded from install totals as initial creation in 2013 was non-Pharma related. Exhibit provides examples within in each year representative of new app types released in each period and is non-exhaustive. IPF = idiopathic pulmonary fibrosis (IPF). GlaxoSmithKline (GSK), Johnson & Johnson (J&J), Boehringer Ingelheim (BI). Multiple sclerosis (MS). Neuromuscular disease (NMD). Healthcare provider (HCP). Quality of life (QOL) Hereditary Angioedema (HAE). Michael J. Fox Foundation (MJFF).

each per year, depending on their annual cohort. While it generally takes time for an app to build market recognition and a user base, new apps released by life sciences companies in the past few years have rapidly attained install levels on par with earlier cohorts, adding support the idea that health app adoption may be accelerating broadly. This more rapid initial uptake may also suggest sponsored apps are now viewed as more helpful or useful by the public.

Life sciences companies have created apps to support patients and to support clinicians, with both types becoming more sophisticated over time as they leveraged new approaches and capabilities. For instance, patient-focused apps shifted from ones simply providing information (drug information, demonstration videos, disease education) and those intended to keep patients engaged and adherent (using diaries, behavior tracking, reminders),[14] to apps with more advanced functions such as non-prescription digital therapeutics (NDTs) and disease support apps (some of which act as a conduit to care or supportive patient communities).

For instance, Aby and Cleo (Biogen) and onStEPs app (Merck) released in 2018–2019 tailored exercise recommendations to the needs of patients with multiple sclerosis. Other NDT-like apps followed suit and used exercise to address conditions like MyMedicoach (Pfizer supported) for back pain, HaemActive (Novo Nordisk) for hemophilia, CF Physio (Vertex) for cystic fibrosis (2021) and VertiGo Exercise (Abbott) to help vertigo using use evidence-based vestibular rehabilitation exercises and augmented reality. Within the domain of "wellness", other therapeutic approaches have also been used to yield a positive health impact such as Parkinsounds (Teva, Takeda) which uses music to "support smooth walking" in Parkinson's patients (similarly to MedRhythms recently FDA-authorized InTandemRx digital therapy).

Some newer disease support apps such as the Brisa app (Roche/Temedica) have also begun to use AI to personalize self-care recommendations. By analyzing symptom tracking data, the app identifies areas for improvement and helps multiple sclerosis patients better manage their condition — thereby creating a closed care loop.[15]

On the physician side, life sciences companies have increasingly created solutions that support clinical decision-making and remote monitoring in patient care and research. For instance, in 2020, apps to support diagnosis were launched, such as eROL (Sanofi Lebanon), which used medical diagnostic algorithms to diagnose Gaucher disease, and Fabry, Pompe, MPS, and axSpA ID Tool (Novartis) helped suggest imaging techniques to use for axial spondyloarthritis diagnosis. Many of the most innovative apps were also not launched originally in English but rather in French, German, Spanish, and Portuguese, indicating that innovation occurred around the world and the mandate to innovate with apps at life sciences companies was a global one. Remote patient monitoring apps launched by industry have also helped providers to track patient symptoms (via surveys and PROs questionnaires) or by pulling biometric data from connected devices, wearables or auto-injectors. Within research, for instance, the Reva app (Otsuka) digitized paper-based clinical workflow to help track adverse events among participants in clinical trials.

Life sciences companies have created apps to support patients and to support clinicians, with both types becoming more sophisticated over time as they leveraged new approaches and capabilities.

Although clinical decision support tools have been a key focus of investment in recent years, industry has also sought approval for apps as medical devices. For instance, they have gained regulatory approval for prescribable insulin dosing calculators like MyDose Coach (Sanofi, 2016) and apps that personalize drugs levels, such as myPKFit for Hemophilia patients (Shire/Takeda, 2017).

Since at least 2020, life sciences companies have also supported the development of digital diagnostic and therapeutic tools, forming strategic partnerships with developers to build bespoke solutions and conduct validation studies. For instance, Boehringer Ingelheim Venture Fund invested in Perfood's sinCephalea that launched in 2020 to prevent migraine,[16] Medice led the finance round in 2022 for Selfapy which developed digital therapeutics for mental illness now approved and reimbursed in Germany under Digitale Gesundheitsanwendungen (DiGA),[17] and Selfapys for Chronic Pain (sponsored by Pfizer) launched in April 2023. This year, Otsuka's partnership with Click Therapeutics also yielded an FDA approval of Rejoyn, a digital therapeutic to treat major depressive disorder.[18]

Patient organizations and advocacy groups have played a notable role shaping many of these life sciences apps, influencing the creation of Biogen's apps for multiple sclerosis,[19] the SMA Community App for spinal muscular atrophy (SMA Australia/Roche Australia)[20] and Celgene's Magic Tree for Breast Cancer app helping kids to understand their mom's cancer diagnosis using games, among others.[21,22] Magic Tree also represents another innovative trend being used by industry to create games for serious purposes, or "serious games" that has grown over the past five years.

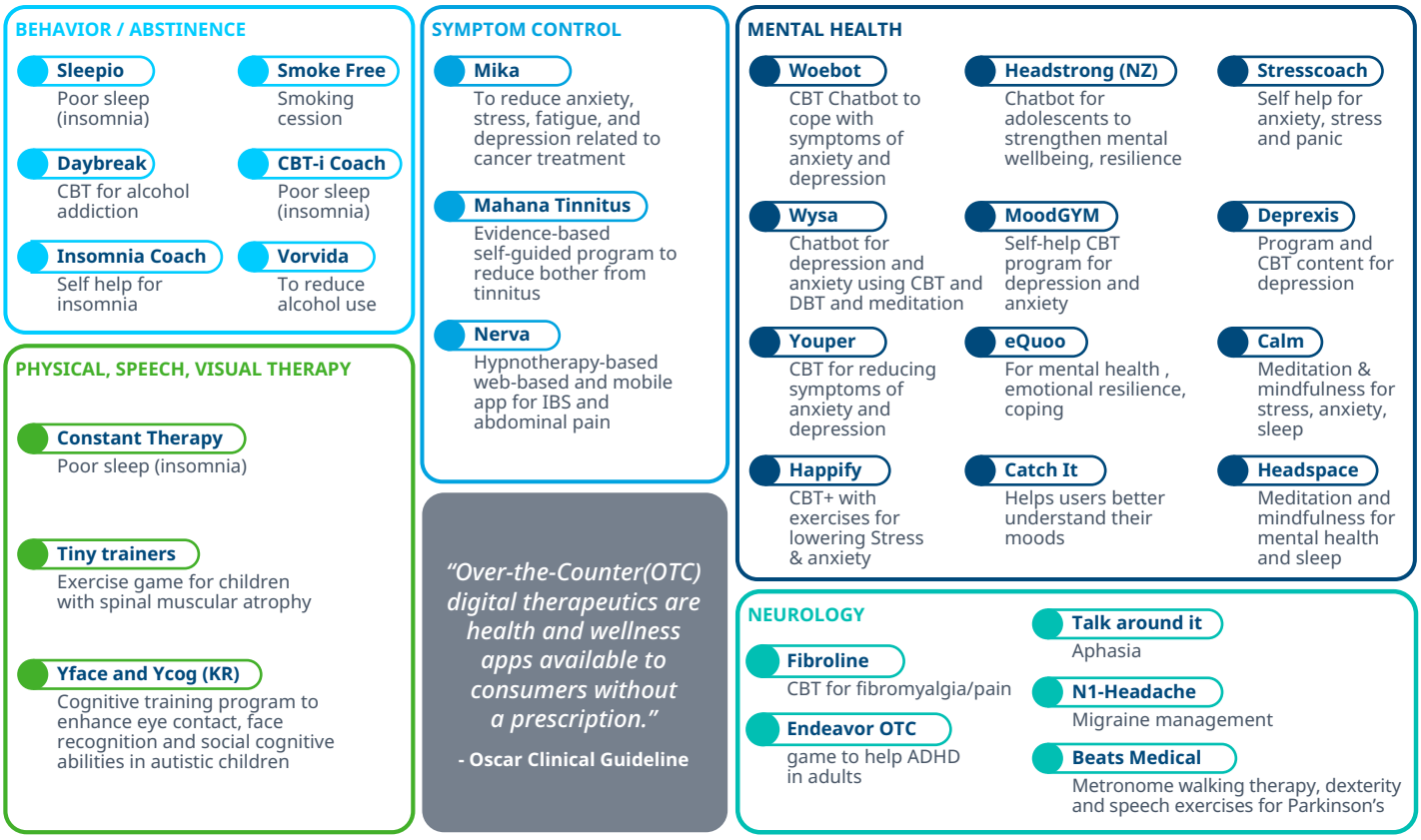
NON-PRESCRIPTION DIGITAL THERAPEUTICS

Some consumer apps that fall under FDA enforcement discretion have been shown to improve patient health and outcomes even without directly delivering a formal therapeutic intervention and are commercially available through app stores or as web-based software programs. These "care support" apps "help patients better manage their care of a specific disease or medical condition"[23,24] but do not claim treat the disease itself. They often provide educational content, serve as digital courses, or employ evidence-based approaches to help patients prevent and manage symptoms commonly associated with disease. They may deliver reminders, motivational guidance, offer tips and educational material to shift behaviors (e.g., support wellness behaviors such as exercise and abstinence) and generally improve patient self-management or help patients develop coping skills through training.

Oscar Clinical Guidelines call such apps "over-the-counter (OTC) digital therapeutics" and describes them as "health and wellness apps available to consumers without a prescription."[25] They are more commonly known as non-prescription digital therapeutics (NDTs) as they are exempt from regulatory approval and are either directly available to consumers or used within the bounds of digital care programs (Exhibit 13).

A total of 42 non-prescription digital therapeutics that fell under enforcement direction and pandemic guidance were available in the United States through early 2024, and many of them were directly available to patients for self-management. In the past few years, these have included mental health apps and AI-chatbots (like Woebot, Wysa, and Youper), and post-COVID-19, have been increasingly used to maintain mental well-being. Many of these use evidence-based methods like cognitive behavioral therapy (CBT) or acceptance and commitment therapy (ACT) or other "low intensity" approaches (CT, REBT, DBT) where users are provided with self-help materials.[26]

Exhibit 13: Non-prescription digital therapeutic apps and courses available to consumers in 2023



Source: IQVIA Institute, Jul 2024. Quote taken from: Oscar Clinical Guideline: Prescription Digital Therapeutics (PG142, Ver. 1).
Notes: Based on company websites that indicate consumers can purchase directly. Due to rapid changes in the market, some of these may use gated models only by the time of publication. Attempts to include only non-prescription digital therapeutics available to users outside of digital care.
Content non-exhaustive and based on company web sites.

"We have found that people have the best experience when our products are delivered under the supervision of a healthcare provider, which is why we partner with health plans and systems as well as employers to make Woebot available to the people they serve. Woebot is only available to new users in the United States who are part of a study or who have an access code from their provider, employer or other Woebot Health partner."

— Woebot Website, Sep 2024

However, many of these categories of apps have recently fallen from FDA enforcement discretion as the FDA unwinds COVID-19 emergency use authorization and direct consumer access to NDTs seems to be slowly disappearing. Most self-help NDT apps are now either being incorporated into gated digital care and employer benefit models (e.g., Sanvello CBT+ app for stress, anxiety, and depression symptoms is now AbleTo; and Mahana Tinnitus shifted from a consumer NDT to a gated program available through providers, just prior to the company becoming insolvent).[27,28] In these cases, there may be minimal up-front contact with trained practitioners to gain access to the app, while others may be offered within a full digital care wrap-around with ongoing support from mental health professionals. This shift may be helping some retain FDA enforcement discretion, which extends to apps that "provide or facilitate supplemental clinical care, by coaching or prompting, to help patients manage their health in their daily environment, without providing specific treatment or treatment suggestions."[29]

Other companies have sought FDA approval for these now-regulated apps as prescription digital therapeutics (PDTs) like recently approved Sleepio and Daylight. Still others have spun off new PDT apps that explicitly treat disease using their platform technologies (like Woebot, Feel Therapeutics) at the same time as they have shifted their consumer technologies into digital care.

For apps that can remain available as NDTs, formal clinical studies, and evidence generation (peer-reviewed publications demonstrating benefit and/or cost savings) have become the key route to increase their appeal to employers and gain use as digital care benefits. Sometimes these studies have been performed on patients with specific diseases and build evidence that they can cite, although the product may claim to help only symptoms — e.g., NDTs have in the past claimed to treat low mood though clinical studies were run on patients with depression.

As disease management apps and non-prescription digital therapeutics shift to gated (non-consumer) commercial models, often with no cash-pay options, the promise of digital solutions to democratize health has diminished. However, this trend may begin to reverse if more prescription solutions can be authorized as OTC consumer products. Endeavor OTC for ADHD, for example, marks the movement of digital therapeutics through the FDA approval process and back into the non-prescription consumer realm. It is likely that more PDTs will seek this route as increasingly app developers are realizing that pursuing a single route to market was not commercially viable in this early marketplace, and now pursue multiple commercial models in parallel — as PDTs or NDTs, gated employer solutions, digital care tools, OTC apps, research tools, etc.

As disease management apps and non-prescription digital therapeutics shift to gated (non-consumer) commercial models, often with no cash-pay options, the promise of digital solutions to democratize health has diminished. However, this trend may begin to reverse if more prescription solutions can be authorized as OTC consumer products.

Digital therapeutics and their use in care

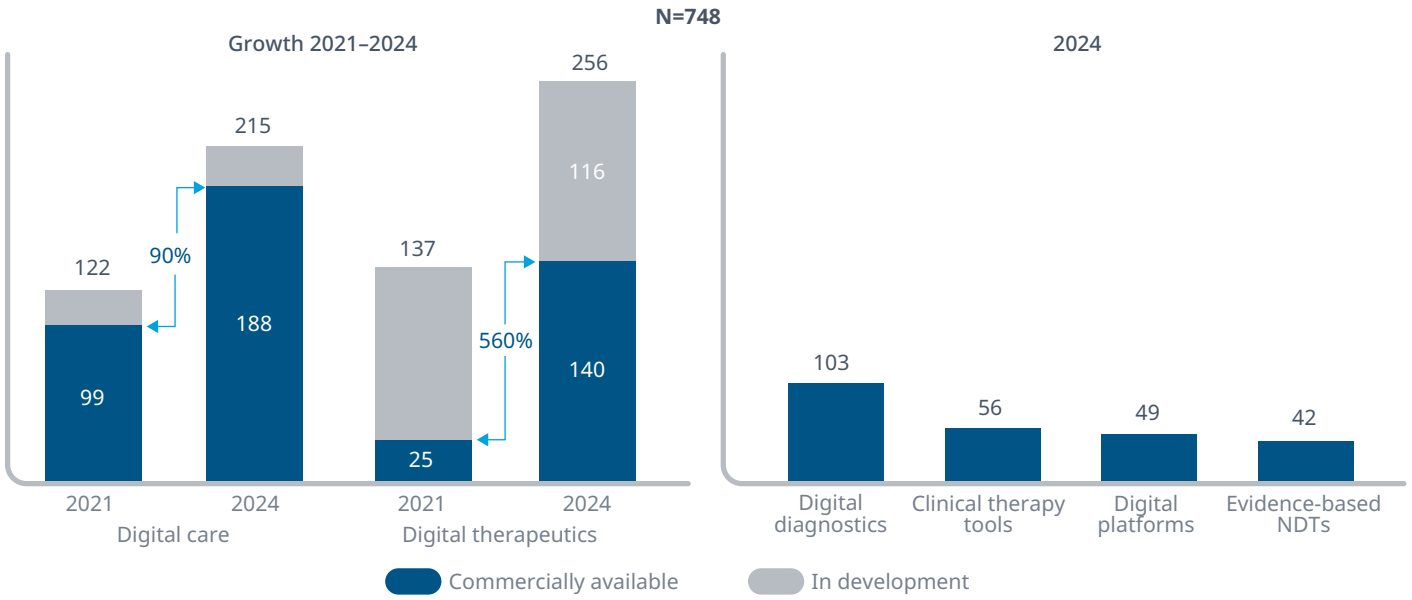
+ **Over 360 software-based therapeutic tools are now commercially available with some products available to consumers with or without a prescription and others used by providers to enhance clinical and digital care.**
+ **Prescription digital therapeutics, which use software to treat or alleviate disease, are growing in number with 140 granted market access through national regulatory and reimbursement pathways.**
+ **As of early 2024, 42 were also available as non-prescription digital therapeutics in the U.S. — that fell under FDA enforcement direction and pandemic guidance — with many directly available to patients for self-management.**
+ **Provider-focused digital therapy tools have also proliferated, with over 220 commercially available for use by providers in their clinics or used within digital care programs.**
+ **Germany continues to lead in the approval and reimbursement of prescription digital therapeutics with 56 granted reimbursement, followed by the United States where 37 are available (46 including outpatient dosing apps) and the United Kingdom where 20 have been endorsed for use by NICE along with other digitally enabled therapies.**
+ **Digital therapeutics increasingly use biofeedback and virtual reality to reduce various types of pain, treat visual impairments, support post-stroke neurological rehabilitation, and treat PTSD and phobias.**
+ **Digital care is becoming the predominant channel for use of digital therapeutics with over 180 digital care programs commercially available and many DTx building virtual care wraparounds to overcome provider adoption issues.**
+ **Patient demand for obesity drugs has driven payer endorsement of digital care programs that may use mobile apps to shift behavior prior to drug trials or encourage adherence.**
+ **At least 38 digital products have gained FDA breakthrough device designation with potential to address unmet medical needs and 14 have been approved to date, offering nonpharmacological treatments for some indications and new methods to diagnose and monitor health.**

Beyond the world of wellness apps are digital products that use software to help treat, diagnosis and monitor patients (Exhibit 14). To treat specific diseases or conditions, patients may now be prescribed a digital therapeutic — health software that delivers a medical intervention — or they may be referred to digital care (DC) providers that use digital tools to enhance their treatment, prevention, or disease management programs.

The availability of these therapeutic solutions has notably grown since 2021 with a five-fold increase in the number of commercially available prescription digital therapeutics and the number of marketed digital care programs almost doubling. Some evidence-based self-care support apps have also been validated through clinical studies to have positive health impacts and reduce the symptoms of disease and are available as non-prescription digital therapeutics (NDTs) or used within health programs.

Digital products for healthcare providers to use in their clinics or at the point of care have also proliferated. These include clinical therapy tools that enhance face-to-face therapy and rehabilitation, digital diagnostics that assess or remotely monitor patient health status, and digital platforms used alongside patient-facing apps and devices to help providers remotely monitor and manage patients.

Exhibit 14: Digital therapeutics, digital care programs and other tools commercially available or in development in 2024



Source: IQVIA Institute, Sep 2024; IQVIA AppScript Digital Medicine Database, Apr 2024.

Notes: Digital Therapeutics include outpatient medication management and dosing apps. Clinical therapy tools include digital therapies intended for use in clinics, such as VR and rehabilitation therapies. Diagnosis tools include digital diagnostics and health assessment tools. Digital Platforms are predominantly used for remote monitoring and overlap other categories. NDTs includes evidence-based therapy apps subject to enforcement discretion. Values may underestimate the number of EU CE Marked devices that haven't gone through established reimbursement processes. Other products are likely under-represented in the data. NDTs are incompletely populated due to their overlap with wellness products.

APPROVALS OF DIGITAL THERAPEUTICS

Most digital therapeutics are regulated as medical devices. To gain market authorization and reimbursement they must demonstrate a positive therapeutic effect in a narrow clinical indication and generate evidence supporting that effect by running clinical trials and other studies. Many are also dispensed via prescription and have therefore commonly become known as prescription digital therapeutics (PDTs). In some countries where low-risk therapeutic apps and online courses may be exempt from regulation, those that have generated evidence of improved patient outcomes have come to be known as non-prescription digital therapeutics (NDTs), though access to most are now "gated."

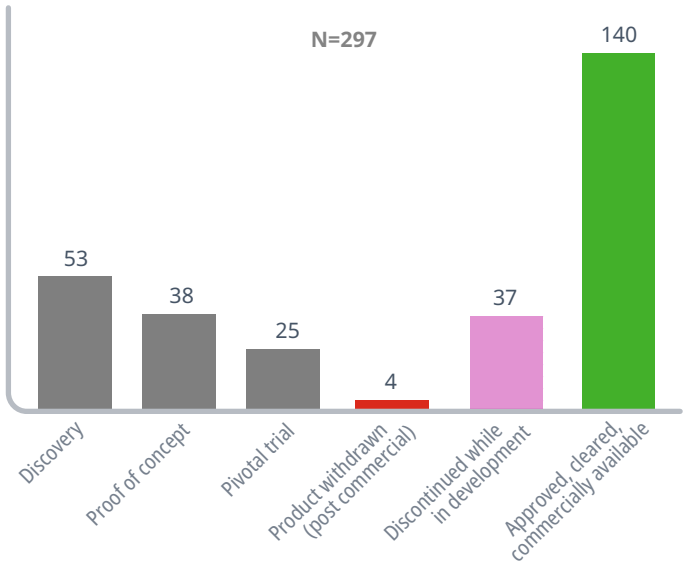
While digital therapeutics often treat patients at home as standalone or adjunct treatments, other digital therapies support traditional face-to-face therapeutic care in a clinic or improve remote home-based rehabilitation and disease management digital care programs. In total, over 360 software-based therapeutic tools are now commercially available across these product types — including PDTs, evidence-based NDTs, regulated apps for outpatient medication management, clinical therapy tools, and those used within digital care.

Prescription digital therapeutics are slowly gaining traction in the health sector as regulatory and reimbursement pathways proliferate and clinical utility increases. They are also growing in number.

DIGITAL THERAPEUTICS (DTx)

"Health softwares intended to treat or alleviate a disease, disorder, condition, or injury by generating and delivering a medical intervention that has a demonstrable positive therapeutic impact on a patient's health."[23]

Exhibit 15: Prescription digital therapeutics by phase



Source: IQVIA Institute, Oct 2024; IQVIA AppScript Digital Medicine Database, Apr 2024. Data updated manually through Oct 2024.

Notes: Prescription digital therapeutics here include outpatient medication management and dosing apps. Excludes remote patient monitoring tools, digital diagnostics and other types of tools that may flow through these pathways. Excludes products that are temporarily or permanently withdrawn due to company closure. DTx products with CE mark and/or UKCA marks only and no other endorsements are likely underrepresented.

In total, 256 DTx have been identified, of which 140 currently have gained market access through various formal regulatory and reimbursement pathways (Exhibit 15) and at least 116 of which are in development, making the pipeline for digital therapeutics robust.

Since bringing PDTs to the market requires significant resources and research, and some products fail to prove a therapeutic effect, at least 37 DTx development projects have been discontinued, and 4 products that have reached the market have subsequently been withdrawn due to company bankruptcy. Several other products have been acquired post-bankruptcy for use within digital care or to repurpose their intellectual property.

Approval and reimbursement pathways

Regulatory and reimbursement pathways for digital tools — particularly prescription digital therapeutics (PDTs) — have proliferated as stakeholders gain a better understanding of their clinical utility and potential cost savings. Countries have recognized PDTs as low-risk therapies that can address unmet needs, give providers new tools to improve care and outcomes, and close care gaps caused by limited availability of care providers. This has led to a proliferation of national reimbursement pathways to speed the use of digital therapeutics and, in some countries, pathways providing accelerated regulatory consideration for innovative technologies such as Integrated Review and Assessment System (IRAS) in Korea (Exhibit 16).

Germany continues to lead in its approval and reimbursement of digital therapeutics with 56 patient-facing prescription digital therapeutics listed on its Digitale Gesundheitsanwendungen (DiGA) directory, while 37 are currently available in the United States (46 including outpatient dosing apps) and 20 have been endorsed for use by NICE in the United Kingdom.[30] Other countries have also begun to approve digital therapeutics including Japan, South Korea, Brazil, Australia, Canada, Singapore and UAE (Exhibit 17).[31]

Both prescription digital therapeutics and digital care programs focus on the treatment mental health issues, some of which arise as comorbidities of other diseases like diabetes and cancer (Exhibit 18). They also address a diverse range of neurological diseases, helping patients overcome chronic pain or functional impairments, and aid behavior modification across a range of diseases such as diabetes and musculoskeletal issues.

However, the therapeutic focus of digital therapeutics and digital care solutions differ slightly. While DTx have now expanded to address genitourinary conditions and visual impairments, digital care programs continue to focus more heavily on conditions that may require multimodal therapy and management, such as cancer and metabolic diseases like diabetes and obesity — where they are playing an increasing role in facilitating access to medications. The active involvement from providers or coaches in digital care programs also helps to personalize digital content to individual needs and provide more holistic care solutions for these conditions.

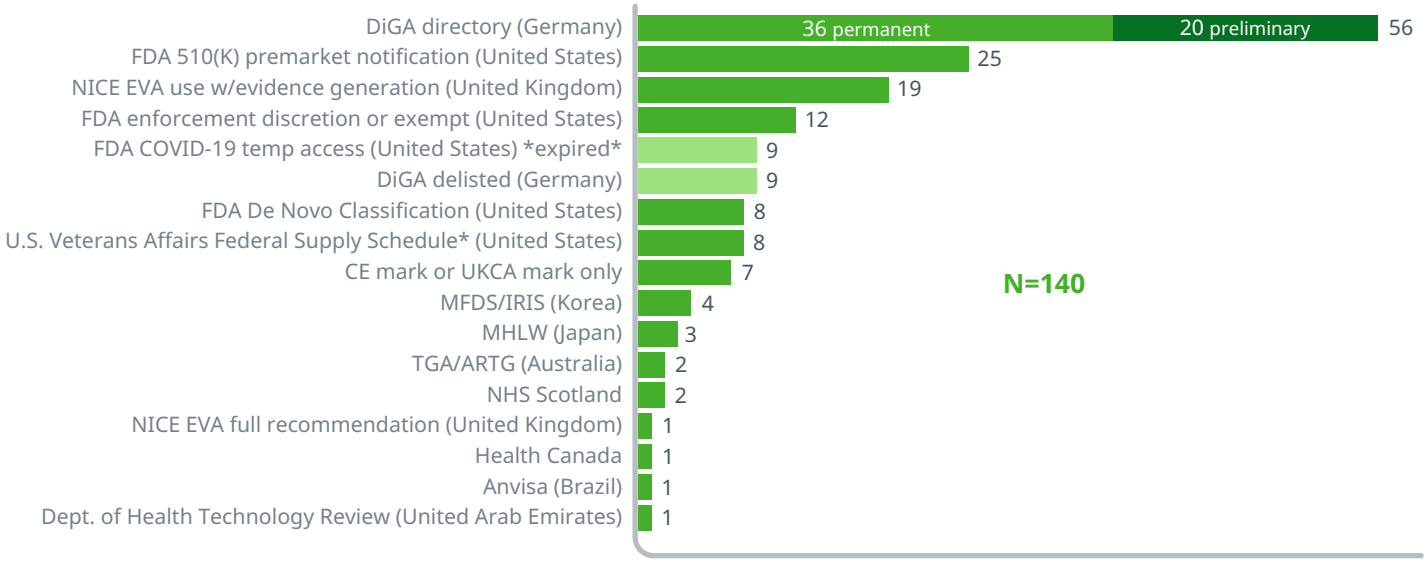
Exhibit 16: National regulatory and reimbursement pathways for digital therapies

	REGULATORY BODY	REGULATORY PATHWAYS	NATIONAL REIMBURSEMENT PATHWAYS
UNITED STATES	FDA	510(k) Premarket Notification De Novo classification FDA 510K exempt (registration /listing) Enforcement discretion	CMS (Medicare /Medicaid) US Veterans Affairs Federal Supply Schedule (FSS)
UNITED KINGDOM	MHRA	UKCA mark CE mark (MDR issued CE mark accepted until June 2030)	NICE EVA, MTG, DG (also NHS Talking Therapies, ICS/ICB Regional)
GERMANY	EC	MDR (CE mark)	DiGA and DiPA
FRANCE	ANSM	MDR (CE mark)	PECAN; LATM, LPPR (HAS, CNEDiMTS)
BELGIUM	FAMHP	MDR (CE mark)	mHealth Belgium
JAPAN	MHLW (review by PMDA)	Todokede (pre-market submission) Ninsho (pre-market certification) Shonin (pre-market approval)	MHLW / Chuikyo
BRAZIL	ANVISA	ANVISA Cadastro (Class I/II)	CONITEC
SOUTH KOREA	MFDS	MFDS Medical Device approval (KiFDA System) IRAS	IRAS HIRA NECA-nHTA (via MOHW)
AUSTRALIA	TGA	TGA software based medical devices ARTG	MSAC / MBS
UAE	MOHAP Drug Control Dept	Product registration	Department of Health Technology Review
CANADA	Health Canada	MDL (per Medical Devices Regulations)	CADTH
CHINA	NMPA	Medical Device Registration Certificate (MDRC)	
SINGAPORE	HSA	Registration with ACRA Immediate, Expedited, Abridged, Full SMDR listing	ACE
INDIA	CDSCO SLA	CDSCO Registration MD 9 License (Class C&D) MD 15 Import License MD 5 License (Class C&D)	

Source: IQVIA Institute, June 2024. Multiple public sources including Digital Therapeutics Alliance summaries of national reimbursement pathways available from: https://dtxalliance.org/understanding-dtx/dtx-by-country/

Notes: Food and Drug Administration (FDA); Centers for Medicare & Medicaid Services (CMS); VA Federal Supply Schedule Service (VA FSS); Medicines and Healthcare products Regulatory Agency (MHRA); Federal Institute of Drugs and Medical Devices (BfArM); European Commision (EC); Agence nationale de sécurité du médicament et des produits de santé (ANSM); Federal Agency for Medicines and Health Products (FAMHP); Ministry of Health, Labour and Welfare (MHLW); Brazilian Health Regulatory Agency (ANVISA); Ministry of Food and Drug Safety (MFDS) formerly Korea Food and Drug Administration (KFDA); Health Insurance Review and Assessment Service (HIRA); National Evidence based Healthcare Professional Collaborating Agency (NECA); New Medical Technology Evaluation Committee (nHTA); Korea Ministry of Health and Welfare (MOHW); Therapeutic Goods Administration (TGA); Australian Register of Therapeutic Goods (ARTG); Medical Service Advisory Committee (MSAC); UAE Ministry of Health and Prevention (MOHAP); The Canadian Agency for Drugs and Technologies in Health (CADTH); National Medical Products Administration (NMPA); Accounting and Corporate Regulatory Authority (ACRA); Singapore Medical Device Register (SMDR); State Licensing Authority (SLA); Diagnostics Guidance (DG); Medical Technologies Guidance (MTG); Early Value Assessment (EVA); Integrated Review and Assessment System (IRAS).

Exhibit 17: Prescription digital therapeutics by select regulatory and reimbursement pathways



Source: IQVIA Institute, Oct 2024; IQVIA AppScript Digital Medicine Database, Apr 2024, updated manually through Oct 2024.

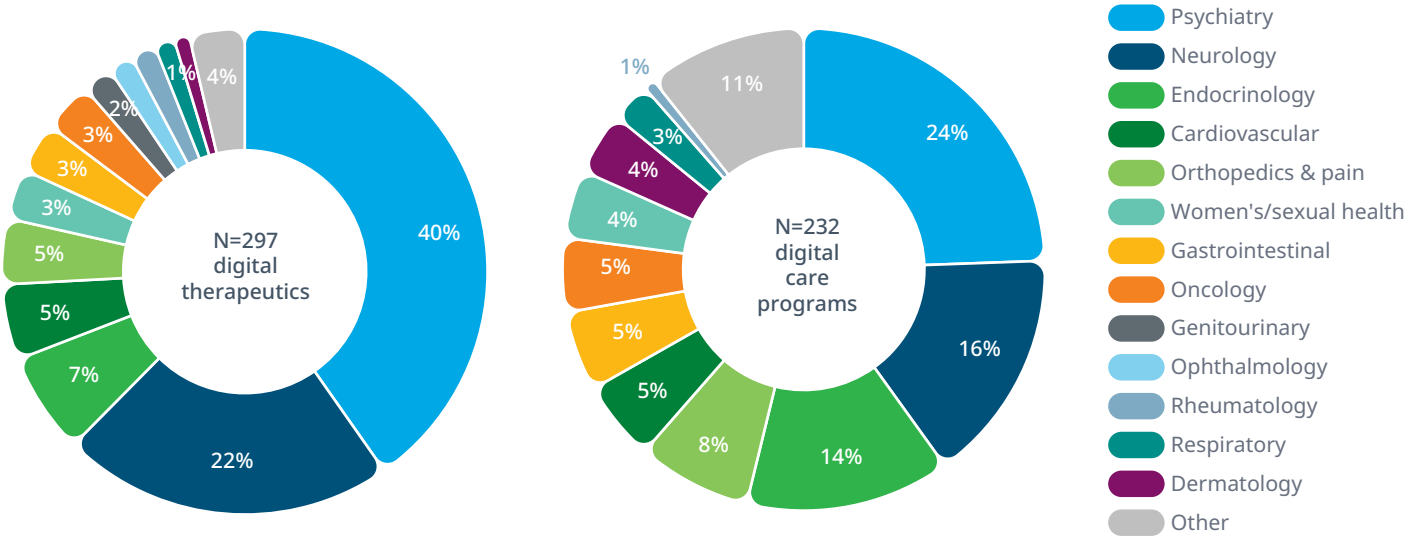
Notes: Prescription digital therapeutics here include outpatient medication management and dosing apps. Excludes remote patient monitoring tools, digital diagnostics and other types of tools that may flow through these pathways. Excludes products that are temporarily or permanently withdrawn due to company closure. DTx products with CE mark and/or UKCA marks only and no other endorsements are likely underrepresented.

Many digital care programs are also functional rehabilitation programs. They treat orthopedic/musculoskeletal issues using feedback from computer-vision technologies and customize physical therapy and rehabilitation programs to patients with cancer, neuromuscular disorders, and other specific needs. DCs also aid in rehabilitation for neurological and respiratory diseases, and dermatologic conditions like psoriasis.

Recent approvals and new mechanisms of action

Since May 2021, at least 94 PDTs gained new approvals and/or market access globally, including 51 in Germany alone (Exhibit 19). However, among these, five products that were provisionally listed on the DiGA directory in Germany have since lost their temporary reimbursement status and two others are no longer available due to company bankruptcies. The result has been 87 net new product additions: 46 in Germany and 41 elsewhere.

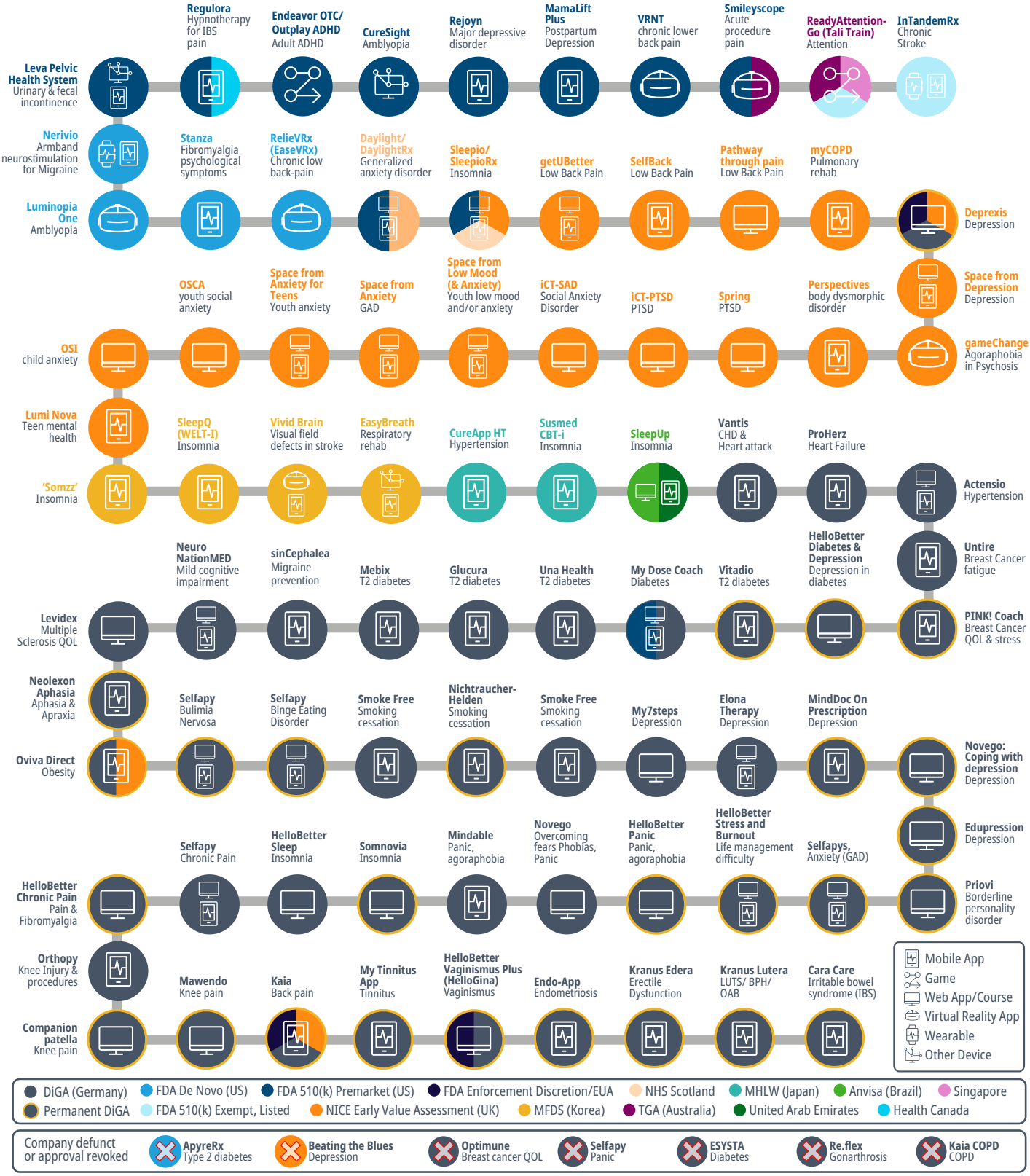
Exhibit 18: Therapeutic focus of digital therapeutics and digital care, all time



Source: IQVIA Institute, Apr 2024; IQVIA AppScript Digital Medicine Database, Apr 2024.

Notes: Digital therapeutics and digital care products that treat multiple therapy areas are counted in each therapy area.

Exhibit 19: Prescription digital therapeutic market authorizations since May 2021



Source: IQVIA AppScript Digital Medicine Database, Jul 2024; IQVIA Institute, Jul 2024; Updated with known recent approvals Oct 2024. DiGA Directory from the Federal Institute for Drugs and Medical Devices (BfArM).
Notes: For Europe, only displays products both market authorized and qualified for reimbursement. Only DTx with NICE full approval or EVA approval for use in practice are included and excludes those with current "research only" status. Social anxiety disorder (SAD). Post traumatic stress disorder (PTSD). Generalized anxiety disorder (GAD). Includes home-based solutions only. Online Social anxiety Cognitive therapy for Adolescents (OSCA). Online Support and Intervention for child anxiety (OSI). Internet-delivered cognitive therapy (iCT). Virtual Reality Neuropsychological Therapy (VRNT).

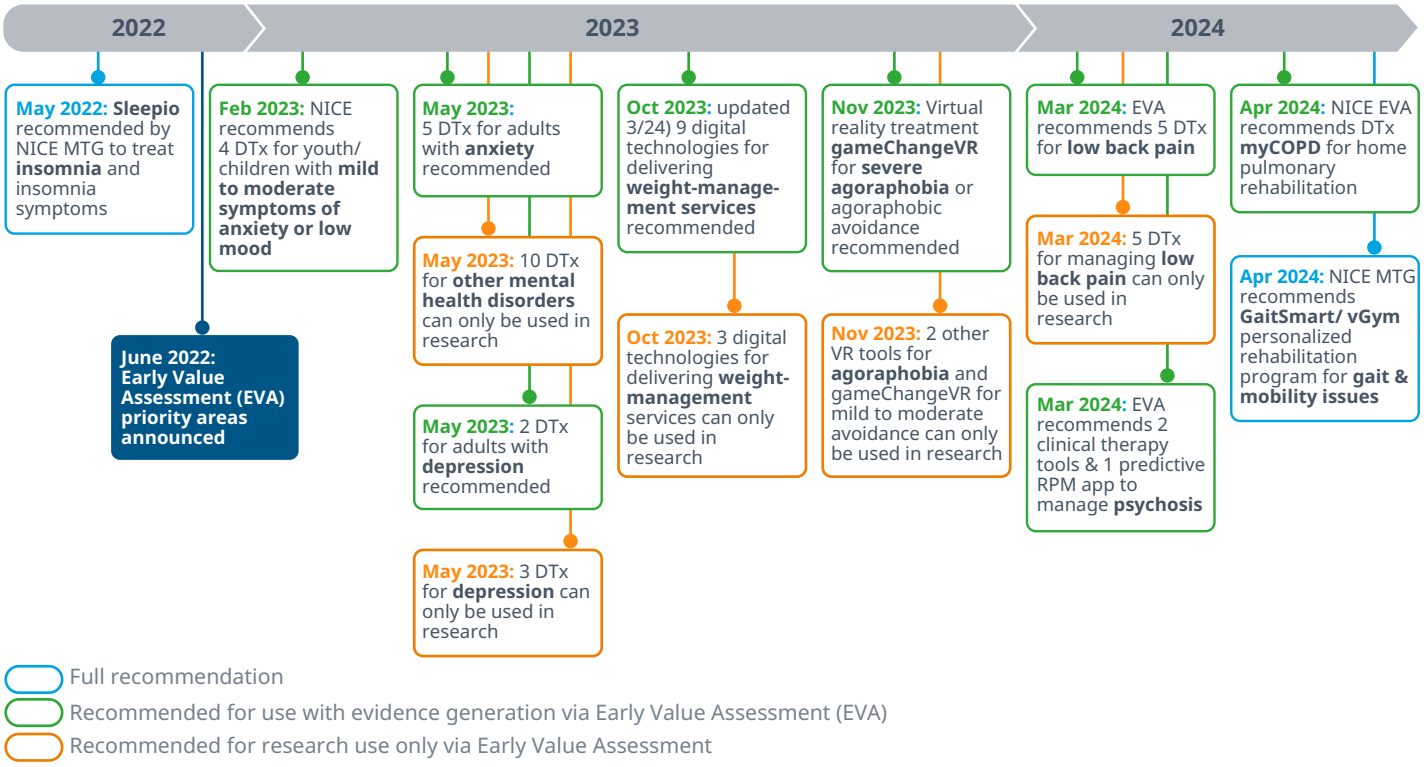
Mental health

Post COVID-19 pandemic, there has been a significant increase in anxiety and depression and other mental health issues, resulting in long waits for therapists.[32,33] This has created opportunity for digital therapeutics — both PDTs and the NDTs that became available under emergency use authorization — to fill the gap in care. In Germany, apps for behavioral and mental health now account for 50% (28/56) of the current the DiGA available, followed by ones for metabolic diseases and musculoskeletal issues (each around 15%).[30,34] While in Germany DiGA are accessible to diagnosed patients and those receiving a prescription, in October 2021, Scotland became the first country to make some low risk mental health/wellness and behavioral DTx available for free to their entire adult population — and now offer Sleepio to treat insomnia, Daylight to treat anxiety or stress, and SilverCloud for mental wellbeing.[35,36]

In the United Kingdom, where NICE has begun to recommend some digital solutions including DTx for use in practice by the NHS, many of its first Early Value Assessments (EVA), which were intended to fill a national unmet need, have also focused on digital mental health treatments for both youth and adults, in addition to musculoskeletal issues, obesity and pulmonary rehabilitation (Exhibit 20).[37–39] These EVA technology assessments serve a purpose similar to the PECAN and DIGA pathways in France and Germany of bringing innovative digital devices into use while also enabling further evidence generation.

With NICE's recommendation of GameChange (RealizedCare formerly OxfordVR), a virtual reality therapy program to treat severe agoraphobia in individuals with psychosis, digital therapeutics are now available in multiple countries to treat agoraphobia, panic

Exhibit 20: Digital therapies recommended by NICE in the U.K. for use by the National Health Service (NHS)



Source: IQVIA Institute, Apr 2024. NICE Early Value Assessments (EVAs) and Medical Technologies Guidance (MTG).
Notes: Includes centralized decisions by NICE pertaining to digital therapeutics, app-linked digital health solutions including digital or blended care programs, and digitally enabled therapies (DET) which deliver a substantial portion of therapy online but are designed to be used with therapist assistance.

disorder or social phobia. These notably allow patients to treat their fears at home and overcome barriers to care for those who face anxieties venturing outside for treatment. In Germany, HelloBetter Panic, Velibra and Invirto (which uses virtual reality), are now permanently listed in the DiGA directory and Novego Overcoming Fears and Mindable have preliminary listing.[40] Mental health applications also continue to expand in the United States, where it first DTx to treat Major Depressive Disorder (MDD), Rejoyn, was approved, along with MamaLift Plus to treat Postpartum Depression and Stanza to treat psychological symptoms of Fibromyalgia.

Treating chronic disease

Digital therapeutics that impact chronic diseases have also been launched in several countries. In the metabolic space, two PDTs have been shown to reduce HbA1c in diabetes patients — Vitadio in Germany and AspyreRx, in the U.S. (now withdrawn from the market when BetterTherapeutics ceased operations)[8] — and three provisionally listed DiGAs Mebix, Glucera and Una are running pivotal trials to prove similar effects in diabetes. For patients requiring insulin, My Dose Coach is also available to support insulin dose titration and medication adherence in the U.S. and Germany, and Zanadio and Oviva Direct support weight loss in obesity — with Oviva recommended by NICE in the U.K. in the form of a multidisciplinary weight management program (digital care).

Cardiovascular diseases are also a growing target with CureApp HT approved in Japan and Actensio in Germany approved to treat hypertension. CureApp HT, which was the second DTx approved in Japan, guides lifestyle self-modification and lowered systolic blood pressure in trials by 2.4 mmHg. Several other cardiovascular DTx in Germany are provisionally-listed including Vantis, which continues to build evidence of systolic blood pressure reductions to help patients with coronary heart disease and ProHerz to improve therapy adherence and self-management in patients with health failure, such as the recording of vital parameters.

Virtual reality approvals

In addition to app-based mobile DTx, a range of immersive digital therapeutics using virtual reality have emerged — both as approved patient-facing PDTs and as clinical therapy tools. The immersive nature of virtual reality provides safe environments in which to deliver behavioral therapies, exposure therapies and visual therapies. Approved apps now treat visual disorders, pain and a range of mental health issues including post-traumatic stress disorder (PTSD) and phobias like agoraphobia. They are also being used to minimize pain.

Two VR immersive-therapies have been approved in the United States so far by the Food and Drug Administration (FDA) for different types of pain. The first is RelieVRx (formerly EaseVRx) an eight-week therapy which earned breakthrough device designation in 2020 to treat chronic low back pain (CLBP) and showed a 42% reduction in pain intensity and ~50% reductions in pain's interference with activity, sleep, mood and stress in its pivotal trial.[42]

The other is Smileyscope, a prescription VR device used to minimize pain and stress during medical procedures by creating a positive virtual reality overlay to real-world events — something known as "procedural choreography". The Smileyscope headset reduces pain and anxiety among children undergoing needle procedures, like a blood draws and vaccination, and is also approved for use in Australia by the TGA. It creates "positive visual stimuli" in virtual reality of an underwater adventure where the approaching needle appears to be a fish that then nibbles a clinician-selected body part corresponding to the procedure site. In clinical trials with pediatric patients, the tactic reduced the pain children reported by 60% and their anxiety by 40%, and notably reduced caregiver distress and the need for restraints.[43]

Biofeedback

Another growing segment of DTx employs device biofeedback where therapy may be guided by an app. For instance, recently launched Leva Pelvic Health System treats urinary and fecal incontinence through pelvic floor muscle training. A motion sensing wand helps patients train and strengthen pelvic floor muscles by showing them the extent of their lifting and squeezing motions visually on screen. Earlier-launched DTx like Freespira also used biofeedback to normalize dysregulated breathing, and in the digital care space, JOGO runs digital care programs that use an EMG biofeedback device, JOGO-Gx, to treat multiple conditions.

Visual impairments and amblyopia

Several recently approved DTx treat visual impairments. Two digital therapeutics approved in the United States treat amblyopia, or lazy eye as an alternative to conventional eye-patching — Luminopia One and CureSight — and another, VIVID Brain (Nunaps), approved in Korea in 2024 treats visual field defects resulting from stroke or other brain damage using "visual perceptual learning (VPL) and virtual reality."[44]

Both Luminopia One and CureSight improve visual acuity through treatment sessions where each eye sees a different image and software algorithms modify streaming video to encourage use of the weak eye. They blur images for the dominant eye and send clearer images to the lazy eye. Luminopia One (Luminopia) uses a binocular virtual reality headset, while with CureSight (NovaSight) kids use red-blue glasses to view video on a computer and images at the center of their vision are blurred using eye-tracking technology.[45] As is the case now with most DTx, both products have associated provider platform software to allow the prescribing provider to monitor patient compliance and progress.

These two products also elucidate another distinction in the world of DTx: not all digital therapeutics can be installed on commercially available consumer devices that patients already own. Some digital therapeutics are only available on dedicated devices that must be purchased or rented, or have special device components, and therefore the patient must receive a kit containing a device and/or an iPhone with only one installed-app. Such is the case with Curesight (and also Nightware) while others may be installed by a patient onto their personal devices via a consumer platform (like Luminopia One, which is used with Samsung Gear VR) or are online web applications that patients can sometimes access on smartphones or computers alike.

Music therapy

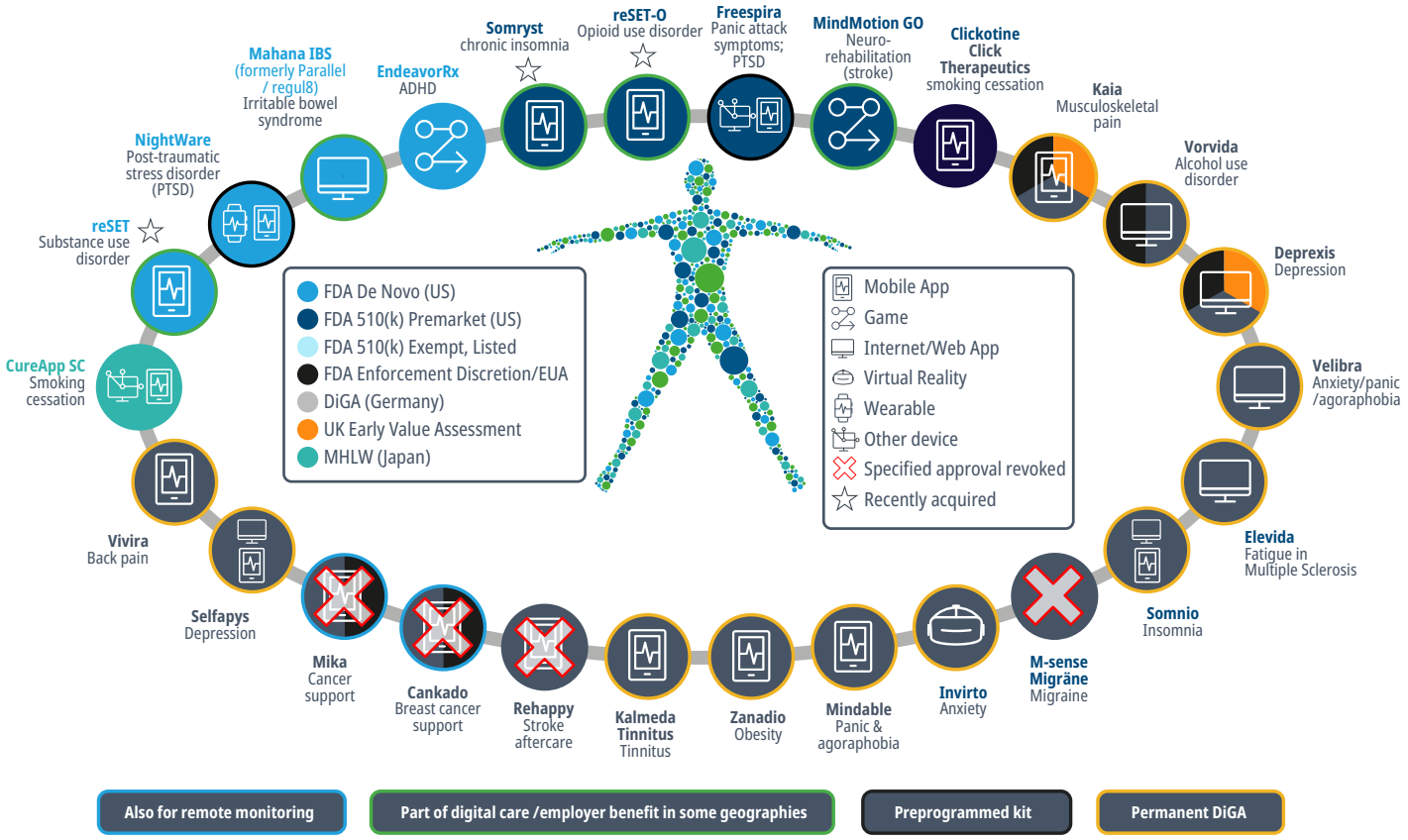
Finally, in the neuromuscular disease and movement disorders (CNS) space, there are several new emerging approaches that use musical patterns. For instance, MedRhythms' recently approved InTandem for stroke, is intended to increase patient gait by having them walk to a musical beat and uses a shoe-located sensor to modulate the rhythm. This strategy may also be useful in MS, Parkinson's, and other conditions. Others in development like Lucid Therapeutics' Resonance Rx aim to treat anxiety, pediatric stress and Alzheimer's dementia using music, while MediMusic aims to use music and biofeedback to treat pain and anxiety.[46]

Status of previously approved DTx

The set of digital therapeutics that gained market access prior to May 2021 have experienced both success and challenges commercially (Exhibit 21). The majority of those listed on the DiGA directory in Germany have been able to show clinical benefit and did gain permanent listing (yellow rings). Several have also been able to gain additional global approvals: Kaia and Deprexis were recommended by NICE in the United Kingdom and Vorvida and Deprexis now fall under FDA's enforcement discretion in the United States rather than COVID-19 emergency use.[47] At least five of these therapies have also gained reimbursement in the United States under the US Veterans Affairs Federal Supply Schedule (FSS) including Freespira, Nightware, Mahana IBS, Deprexis and Vorvida.[48,49]

Other commercial shifts, however, have been driven by tough market conditions. For instance, Akili Interactive

Exhibit 21: Current status of digital therapeutics that gained market authorization before May 2021



Source: Digital Health Trends 2021 - Innovation, Evidence, Regulation and Adoption. Report by the IQVIA Institute for Human Data Science.
Notes: SAMD through May 14, 2021 have been updated to current status.

(now Virtual Therapeutics) successfully filed an adult over-the-counter (OTC) version in the U.S. of its serious game for ADHD, Endeavor, that saw limited uptake as an Rx product, and is now currently available as Outplay ADHD for $130/year (and also FSA/HSA eligible).[50] Approval of the OTC version may also be a positive sign for developers that, over time, the FDA may become increasing comfortable allowing more lower risk digital devices and PDTs to be available OTC to consumers without physician oversight.

> *"For a product to be an OTC DTx, efficacy, safety, and usability data is necessary to ensure a medical product will not be abused or cause harm to a patient"*
>
> *— Digital Therapeutics Alliance[13]*

Three of these digital therapeutic products were also affected by the bankruptcy of Pear Therapeutics and were ultimately acquired by digital care companies. Somryst, was immediately acquired by sleep-care company, Nox Health, adding to the company's digital toolbox and enabling its use within digital care for sleep in its SleepCharge program provided to employers and health plans.[6,51,52] However, two other Pear products, reSET and reSET-O, were temporarily lost from the market after its bankruptcy. Both were then acquired

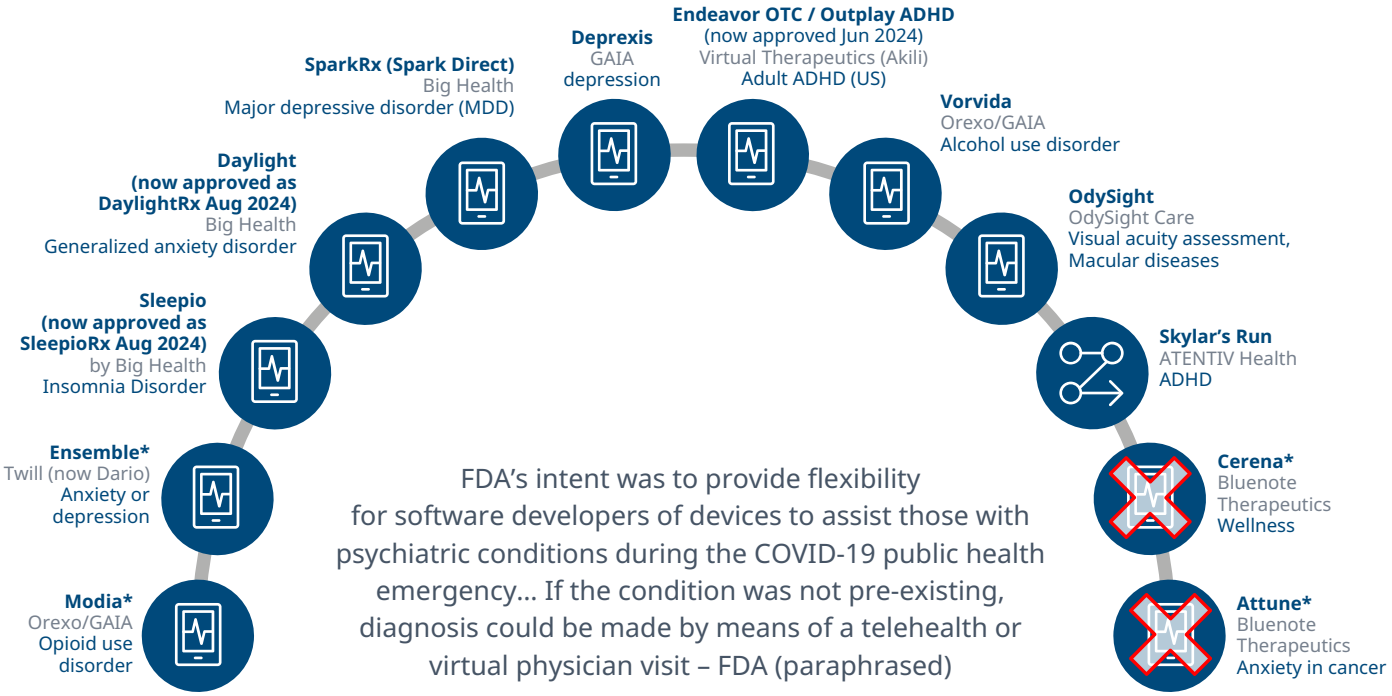
in August 2024, by PursueCare, a digital addiction treatment provider, and similarly relaunched within the bounds of digital care.[53] Like Pear, Mahana also recently faced financial challenges and was reported as insolvent,[54] meaning yet another of the first companies with FDA authorized PDTs may be at risk of ceasing operations,[55] and Mahana IBS and its other assets, Cara Care and Mahana Tinnitus, could potentially be sold to other companies.

Finally, four provisionally-listed DTx were removed from the DiGA directory: two due to weak evidence (Cankado PRO-React and Rehappy) and two upon the manufacturers request (Mika and M-sense Migraine) because requirements for permanent listing couldn't be met in the specified timeframe.[56] In total, since the start of the DiGA directory in September 2020, nine provisionally listed DTx have been removed from the directory. Two among these, Cankado PRO-React and Mika, which record cancer patient symptoms (and PROs) and support patient care appear to have repositioned themselves commercially: Cankado as a patient monitoring tool focusing on data collection in clinical research as well as connected patient care platform, and Mika as a patient support app with self-tracking and data collection.[57,58] Both remain as approved CE-marked medical devices and fall under FDA enforcement discretion.

Unwinding of pandemic guidance for DTx available during COVID-19

Quite a few other digital therapeutics were initially able to enter the U.S. healthcare market during the pandemic without approval under its COVID-19 public health emergency policy. The FDA waived some regulatory requirements to allow digital health devices treating psychiatric disorders (or "computerized behavioral therapy devices") as well as ophthalmologic assessment and monitoring devices (such as for remote visual acuity testing) to market their products during this period (Exhibit 22).

Exhibit 22: Digital therapeutics and diagnostics initially made available under COVID-19 Emergency Use Authorization



Source: IQVIA Institute, Apr 2024. Quote adapted from FDA, Enforcement Policy for Digital Health Devices For Treating Psychiatric Disorders During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency - Guidance for Industry and Food and Drug Administration Staff, April 2020. Available from: https://downloads.regulations.gov/FDA-2020-D-1138-0068/attachment_1.pdf. A Playbook for Employers Prescription Digital Therapeutics. National Alliance of Healthcare Purchaser Coalitions, Sep 2023. Available from: https://www.nationalalliancehealth.org/wp-content/uploads/NationalAlliance_PDT-Playbook_L-FINAL.pdf

However, as these policies expired in 2023, some affected products were at risk of losing market access. While some like Deprexis, Vorvida and Spark Direct appear to still fall under FDA enforcement discretion as self-care support apps, and Modia is now available as a clinical therapy tool within the bounds of Medication- Assisted Treatment programs,[59] other ones were required by the FDA to formally submit for market authorization (but retained market access during FDA review).[60–62] This policy shift has already led to U.S. approvals this year of Sleepio for insomnia, Daylight for anxiety and EndeavorOTC for ADHD in adults as Rx products, and Blue Note Therapeutics went bankrupt when Attune was rejected by the FDA.[63] It is unclear whether Ensemble became part of the Dario Mind digital care program, with Dario Health's recent acquisition of Twill.[64]

MEDICATION MANAGEMENT APPS

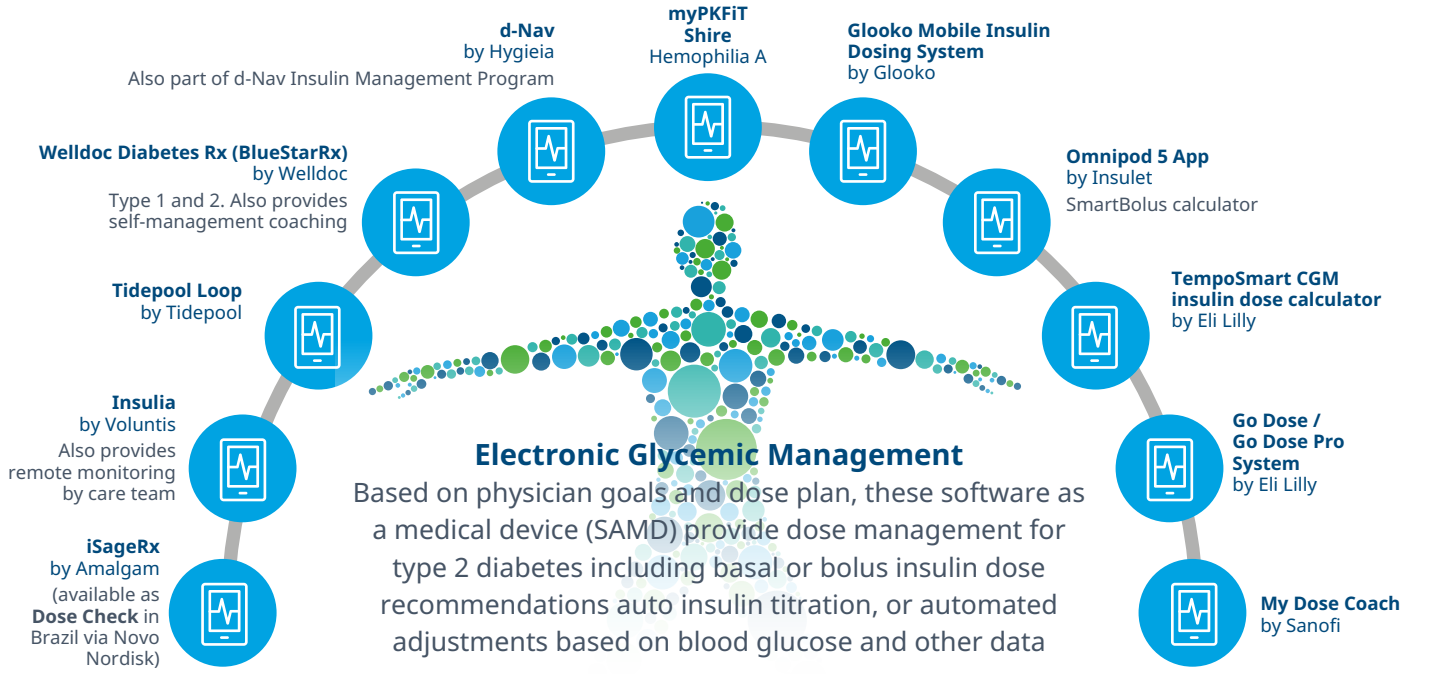
In additional to digital therapeutics that deliver interventions, several software-based medication management apps have also been FDA cleared for outpatient therapeutic dose management (Exhibit 23).

They may provide dose adjustment recommendations, are in some cases have been grouped with digital therapeutics since they are SAMD and influence therapy, however, most do not treat disease themselves or do so by providing care support.

Such mobile prescription dose calculator apps for diabetes medication were some of the first SAMD approved and help patients manage their medication, providing auto insulin control or predicting future glucose levels to adjust levels to target. Versions of these have also been approved globally, such as iSageRx, which is available as DoseCheck in Brazil.

While most SAMD have proven very safe, last year one of these medication management products experienced the first Class I recall for a therapeutic digital tool, demonstrating that some software devices may have risks, just like other therapeutics devices. In this case, a version of the Omnipod 5 mobile app with integrated SmartBolus calculator (distributed between April and December 2023) experienced a software error that made it fail to recognize a decimal point if a patient entered it

Exhibit 23: Software FDA cleared for outpatient dose management in diabetes or other diseases



Source: IQVIA Institute, July 2024. Compiled from multiple published sources. Some of these apps also aid patient self-management. Content is non-exhaustive.

"Insulet Corporation recalled the Omnipod 5 App for compatible Android smartphones due to a software error... When the user enters a bolus amount less than one unit without putting a leading zero before the decimal point... the SmartBolus calculator does not register the decimal point if it is the first character entered. For example, if a user enters ".2" intending to request a 0.2 units insulin bolus, the app would not register the decimal point and would display 2 units as the requested insulin bolus instead.
Or if a user enters ".20" units, the app could display 20 units as the requested insulin bolus instead. This failure to recognize the decimal point ...may lead to the app giving too much insulin, anywhere from 10 times to up to 100 times the intended amount."[65]

without a leading zero. As a result, the app could give anywhere from 10–100 times the intended amount of insulin if the user didn't catch the error and confirmed the erroneous dose. While the issue was rectified and Insulet Corporation sent affected customers and health care providers an urgent Medical Device Correction notice, this episode called attention to the fact that software updates risk changing product function.[65]

BREAKTHROUGH PRODUCTS AND PIPELINE NOTABLES

Some of the most novel digital innovations have been granted breakthrough device designation by the FDA, including at least 38 mobile digital products with potential to address unmet medical needs in life-threatening or irreversibly debilitating diseases (Exhibit 24). At least 14 have also been formally approved to date while some other are exempt, used in clinical or digital care, or still in development. Some offer the first nonpharmacological prescription treatments in their indications and others offer new methods to diagnose and monitor health. Still, five companies that received the award are now apparently defunct indicating the status neither ensures product nor commercial success.

On the part of DTx developers, a key focus has been to improve care for undruggable or under-treated diseases. Breakthrough products seek to improve cognitive function in neurological disease like Alzheimers, improve speech and aphasia as a result of stroke (Speech Therapy ST-App) or autism (Floreo VR), while others treat a range of debilitating mental health conditions like agoraphobia, schizophrenia and postpartum depression. Quite a few products also rely on sensor-based detection devices for diagnosis and patient management including the approved, Empatica's Embrace and Ceribell for seizures, Biofourmis's Biovitals platform, Cognoa's CanvasDx ASD Diagnosis Aid and dedicated point-of-care devices like Dermasensor for detecting skin cancers (3DermSpot).

The breakthrough designation also makes some of these products eligible to participate in the FDA's Total Product Life Cycle (TPLC) Advisory Program (TAP) intended to advise on and speed commercialization of breakthrough devices early in development that haven't yet run a pivotal study. Although FDA had enrolled 46 devices in TAP as of July 1, 2024, it is unclear how many among these are mobile digital products, through Floreo VR for autism is among them.[66]

Exhibit 24: Approved and emerging digital health technologies granted FDA breakthrough device designation

Jan 26, 2018 **Empatica** **EMBRACE** Seizure monitoring	Dec 10, 2018 **Pear Therapeutics (now PursueCare)** **reSET-O** Opioid use disorder	Nov 3, 2020 **Cognoa** **Cognoa ASD Diagnosis Aid** Autism spectrum disorder diagnosis aid	Nov 6, 2020 **NightWare** **NightWare** Post-traumatic stress disorder (PTSD)	Jul 29, 2021 **Biofourmis** **BiovitalsHF** **Heart failure** Everion and Apple Watch+ mobile app to direct dosing of heart failure meds	Oct 2, 2021 **NeuroSync** **Eye-sync** **Concussion diagnosis aid** VR assessment that records and analyzes eye movement as an aid to concussion diagnosis	Nov 16, 2021 **AppliedVR** **RelieVRx (EaseVRx)** Severe chronic low back-pain	
Jun 8, 2022 **EarliTec Diagnostics** **Earlipoint System** Autism Spectrum Disorder Diagnosis Aid	Jun 30, 2022 **Renovia** **Leva Pelvic Health System** **Urinary and fecal incontinence** Pelvic floor biofeedback	Nov 22, 2022 **Cala Health** **Cala Kiq** **tremor** Upper limb electrical stimulation	May 9, 2023 **Swing Therapeutics** **Stanza** Fibromyalgia depression & anxiety	May 23, 2023 **Ceribell** **Ceribell Status Epilepticus Monitor** Seizure monitoring	Jul 6, 2023 **MedRhythms** **InTandem** **Chronic Stroke** DTx for walking impairment w/rhythmic auditory stimulation	Jan 18, 2024 **Dermasensor** **DermaSensor** Skin cancer diagnosis using optical spectroscopy	
Dec 18, 2019 **Eko/Mayo Clinic** **Low Ejection Fraction Algorithm** **Heart Failure** Detection from ECG For Eko DUO digital stethoscope	Jan 7, 2020 **Digital Diagnostics 3DermSpot** **Skin Cancers** Autonomous AI to detect melanoma, squamous cell carcinoma, and basal cell carcinoma from skin images	Feb. 24, 2020 **Altair Medical Respmeter** **Opioid overdose detection** Chest-worn wireless sensor to detect opioid-induced respiratory depression	Apr 14, 2020 **Constant Therapy Health** **Speech Therapy (ST) App** **Stroke** Cognitive, speech and language therapy for stroke patients	Jan 12, 2021 **Cognito Therapeutics** **CogTx-001** **Alzheimer's** non-invasive light & sound therapy for cognitive/ functional symptoms in Alzheimer's	May 12, 2021 **Wysa** **Wysa Dtx** **Chronic musculoskeletal pain depression and anxiety** AI and CBT mental health conversational agent	May 26, 2021 **Woebot Health** **WB001** **Postpartum depression** CBT and IPT to reduce the symptoms of postpartum depression	Feb 22, 2022 **DynamiCare Health Inc** **DCH-001** **Perinatal smoking cessation** PDT using contingency mgmt. breath carbon monoxide monitor, saliva nicotine tests
March 31, 2021 **Sana Health** **Sana Device** **Fibromyalgia** Audio-visual stimulation and neuromodulation	July 2021 **Altoida Predictive ML algorithms** **Mild Cognitive Impairment (MCI** Performance based motor and AR task digital biomarkers	Jun 22, 2022 **OxfordVR gameChange** **Psychosis with agoraphobic avoidance** Clinician led CBT therapy	Dec 16, 2022 **Click Therapeutics** **CT-132** **Episodic migraine** Adjunctive preventive treatment using multiple cognitive and neurobehavioral approaches	Apr 12, 2023 **DynamiCare Health Inc** **DCH-002** **Alcohol use disorder** PDT app using contingency mgmt. breathalyzer, CBT modules	April 2023 **HelloBetter** **HelloBetter Panic** **Panic disorder and associated agoraphobia** CBT-based PDT	May 2, 2023 **JOGO Health (DC)** **JOGO-CLBP** **Chronic low back pain (CLBP)** EMG biofeedback	Dec 12, 2023 **Floreo** **Floreo VR** **Autism/ASD** Immersive games to teach social and communication skills
Jan 4, 2024 **Click and Boehringer Ingelheim** **CT-155 PDT** **Negative symptoms of schizophrenia**	Nov 22, 2021 **Pear Therapeutics** **reSET-A** **Alcohol use disorder**	Jan 22, 2022 **Blue Note Therapeutics** **DreAMLand (inpatient PDT)** **Acute myeloid leukemia related anxiety and depression**	Jun 2020 **Blue Note Therapeutics** **Attune** **Cancer-related anxiety and depression**	Feb 20, 2024 **Better Therapeutics** **Liver Disease DTx** **MASH (NASH)** CBT-based treatment	Aug 24, 2018 **Dthera Sciences** **DTHR-ALZ** **Alzheimer's agitation and depression** "Reminiscence Therapy"	Apr 22, 2021 **Nēsos** **Rheumatoid Arthritis DTx** Electrical pulses to the auricular branch of the vagus nerve via earbuds to control immune response	Mar 19, 2024 **Alex Therapeutics & Vicore Pharma** **Almee** **Anxiety related to pulmonary fibrosis** CBT-based treatment

Approved | In development or available in clinic | Company no longer operating

Source: IQVIA Institute, Apr 2024. Internet press releases and CDRH and CBER Breakthrough Device Marketing Authorizations data as of December 31, 2023, Available at: https://www.fda.gov/medical-devices/how-study-and-market-your-device/breakthrough-devices-program#list.
Notes: For products in development, dates reflect either date breakthrough device status was granted or date publicly reported. For approved products date is that of FDA approval.

DIGITAL CARE

A growing number of digital therapies are now provider-focused, with 222 used within digital care programs or available for use by providers in their clinics. While any provider may adopt digital tools into their practice to create a form of blended care, digital care providers are those that own software-based tools and use them within commercially marketed physician- and/or coach-supported disease management programs. These programs span health purposes — prevention, diagnosis, treatment, disease self-management and monitoring — and while care is almost always delivered virtually, this arrangement differs from pure telehealth in that and the software itself plays a fundamental role in improving health outcomes.

Provider-focused digital therapies are generally intended to make a clinical therapy or rehabilitation program more effective — such as by increasing engagement (e.g. VR games to support rehabilitation) — and/or may act as an extension to treatment by giving patients tools to take home with them after they have been customized in a care setting. For instance, patients may be assigned exercises on digital apps or be given apps that support daily self-care or disease management and address lifestyle-habits to reduce symptoms. Digital care tools also span product types, with some formally approved as therapeutic devices, but many others exempt from premarket notification or under enforcement discretion. Unlike standalone DTx, which may deliver a specific intervention or recommendations, the therapeutic tools used within digital care often enable providers to personalize treatment to patient needs.

Digital care is rapidly becoming the predominant channel for digital therapeutic use with 188 commercially available DC programs available from around 145 companies, and many more rapidly emerging.

Some digital care providers also now offer programs for several conditions that may respond to similar digital interventions and techniques. To date, DC programs have been heavily focused on mental health, musculoskeletal/orthopedic conditions that affect people with a range of diseases including cancer, and a diverse range of neurological diseases. While many early providers used apps that rely on cognitive behavioral therapy (CBT) or physical therapy apps with computer vision to effect behavioral change, the use of biofeedback devices and virtual reality (VR)-based immersive exposure therapies have grown (Exhibit 25). Many of the digital tools used also fall in FDA exempt care support of health and wellness categories.

There are several drivers for this trend. As standalone digital therapeutics have seen limited profit, this appears to have driven developers of many digital therapeutics — both PDTs and NDTs — to rapidly build care wraparounds for their solutions, with the aim of overcoming challenges in gaining provider adoption. They have done so by forming partnerships with provider groups, merging with digital care companies, and by building video calling into their platform. At the same time, many have also shifted exclusively to employer and health plan-mediated digital care models — perhaps finding them more lucrative — and as a result, most digital care that once gave patients direct-to-consumer access to NDT solutions are now "gated," requiring permission or referral from a provider, payer, or employer, although a few still do allow patient self-enrollment, and cash pay.

From a provider standpoint, acquiring digital tools allows them to position their care as cutting-edge, and possibly more effective, while they also aren't reliant on the digital tools as their primary revenue source. For instance, by partnering with MindMotion GO, a virtual reality game for neurological rehabilitation that helps stroke patients recover physical movement,

DIGITAL CARE (DC)

Digital care, which is also known as blended care, combines face-to-face clinician- or coach-directed care (sometimes in-person and sometimes virtual) with mobile devices, apps and online courses.

Mount Sinai created an innovative digitally enabled program extending into the home setting: Mount Sinai's MindMotion GO telerehabilitation program.[67]

And from a payer, prescriber and regulator standpoint some conditions simply are too high-risk to be removed from the safety wrapper of face-to-face or telemedicine-enabled care where patient wellbeing can be closely monitoring, such as in cancer and some mental health conditions. For instance, in the United Kingdom, where there is a national health system, blended care seems clearly preferred. Digital therapies for some mental health conditions are expected to use a therapist-guided model of care and mirror NICE-recommended therapy to be recommended by IAPT expert panels.[68] And, digital therapeutic programs may then be further tailored to be supported with NHS staff.[69] To respond to this trend, as developers progress their global commercialization plans, some digital products that are now approved in multiple geographies may be offered as a standalone DTx in one country, and a digital care solution in another, per country preference (e.g. Oviva Direkt in Germany versus Oviva's NHS Digital Weight Management Programme in the U.K.).

Several blended therapies have also been endorsed formally by NICE in the United Kingdom via its early value assessments (EVA). For instance, SlowMo therapy was recommended and is a blended digital therapy for paranoia, that helps users identify alternative, less distressing explanations for perceptions motivating their fears and augments face-to-face therapy with an interactive 'webapp' and a mobile app for daily home practice.[71]

Exhibit 25: Digital care and blended therapy programs using digital therapies and disease management tools

Mental health	Women's health	Musculoskeletal pain & physical therapy	Diabetes & chronic conditions	Device biofeedback & monitoring	Weight loss
Tali Train (TGA) attention in children with brain injury/ neurodegeneration	**Carrot Fertility** Fertility care and family-building support	**Hinge Health** (EVA) computer vision and AI to guide exercise therapy for joint or muscle pain	**Oviva** Type 2 diabetes prevention, management	**JOGO-Gx** (FDA) EMG-biofeedback with app to treat migraine, stroke, pelvic health, chronic pain, movement disorders, etc.	**Vida Health**
RethinkCare/Whil for stress, anxiety, sleep	**HelloGina** vaginismus and painful sex	**Sword Health** motion sensors and computer vision for PT	**Omada** chronic conditions, diabetes, hypertension, MSK	**Propeller Health** smart sensors on asthma and COPD inhalers for coaching on use, adherence tracking, support, monitoring	**Noom**
AVATAR Therapy (EVA) avatar voiced by therapist for auditory hallucinations	**Maven Clinic** maternity, newborn care, parenting, menopause	**Kaia MSK** computer vision and AI for PT sessions, corrective feedback	**Livongo** diabetes/ prevention, hypertension, weight management	**Podimetrics** SmartMat monitors foot temperature to detect diabetic foot complications	**Wondr**
SlowMo (EVA) web app helps slow distressing thoughts in psychosis	**Substance abuse** (alcohol, smoking)	**Vigo Health:** CBT chatbot & gamification for home stroke recovery	**Lark Health** prediabetes prevention and weight loss using smart scale and activity monitor	**Symptom control**	**Season Health**
gameChangeVR (EVA) severe agoraphobic avoidance in psychosis	**Pelago**		**Welldoc** (Bluestar Rx/OTC) Type 1 and 2 diabetes, hypertension, heart failure, prediabetes,		**Welldoc weight management solution**
Feel DTx MDD and GAD	**Daybreak**		**Onduo** T1 and T2 diabetes and hypertension	**Kaia Breathe** pulmonary rehab for COPD	**Oviva's NHS Digital Weight Management Programme** (EVA)
Lyra Health Employee mental health	**DynamiCare**	**Heart Health**	**Sleep**	**Mymee** MS Emilyn app for autoimmune diseases	**CheqUp** (EVA)
AbleTo (Sanvello) uses CBT+ app for stress, anxiety, and depression	**Affect Therapeutics**	**Hello Heart** hypertension	**Nox SleepCharge**	**Oto Tinnitus** for auditory symptoms	**Gro Health W8Buddy** (EVA)
Headspace Care (Ginger)	**Pivot Program** using breath sensor				**Juniper** (EVA)
	Ascure Smoking Cessation Program available in Japan				**Liva** (EVA)
					Roczen (EVA)
					Second Nature (EVA)
					Counterweight (EVA)
					Weight Loss Clinic (EVA)

Source: IQVIA Institute, Jul 2024. Multiple public sources including company websites and payer assessments.
Notes: Physical therapy (PT). Market authorization and endorsement information is incomplete but noted where possible. FDA listed or exempt products and products with CE mark are not noted here.

> *"A blended model of care is psychological therapy that is provided online or through mobile applications, with the support of a fully trained therapist. In this approach much of the learning to be achieved through patient self-study, reinforced, and supported by suitably trained therapists."*
>
> *— IAPT FAQs[70]*

For prescription digital therapeutics and even pharmaceutics alike, partnering with telehealth teams has also become a strategy to not lose interested patients who visit a product's website. To facilitate initial prescribing, telehealth providers are hired to review individual cases and prescribe their solutions when appropriate.[72] For instance, with the newly launched Leva Pelvic Health System, its owner Axena Health partnered with UpScriptHealth telehealth clinicians/prescribers in July 2024 to evaluate women's incontinence symptoms and, if appropriate, prescribe Leva.[73]

Digital care for obesity

Patient demand for obesity drugs has notably driven payer endorsement of digital care programs that may use mobile apps to shift behavior prior to drug trials or encourage adherence. Digital care programs in the obesity space tend to be holistic lifestyle-change programs bringing together various digital approaches and specialists to provide guidance on diet, physical activity/exercise as well as behavioral/psychological support.[74] With the rise of highly successful GLP-1 drugs to treat obesity, a large number of patients have sought access to these medicines. However, a lack of providers to see and/or screen them all, plus the high cost for these drugs has put digital care programs on stakeholder's radar in unique ways, creating a niche for them to help triage patient, manage costs, and ensure treatment success.

It has also increased the appeal and adoption of DCs across stakeholders,[75] with some public payers in the U.S. and U.K (NICE) endorsing digital care providers for weight loss, and even obesity drug manufacturers like Lilly, now referring patients to virtual providers. While the intent of drug manufacturers is to facilitate access to the drugs via virtual providers, payers have made endorsements in part to manage the use and cost of obesity drugs — as digital care providers may use mobile apps to shift behavior prior to recommending drug trials or encourage drug adherence among treated patients.

While there is strong evidence that GLP-1 drugs offset health costs for severely obese patients above 35BMI,[76] and benefit many others with BMI below that, not all patients seeking care are severely obese. In those cases, payers may aim to limit access to costly medicines without the patient first trying lower-cost options, such as those focused on behavior change such as digital care programs for obesity.

For instance, in the United Kingdom, where 7.6 million patients were on waiting lists for traditional visits in Aug 2023,[77] four digital care programs — Gro Health W8Buddy, Oviva, Roczen and Second Nature — have been picked up by NICE as a means to triage patients to various levels of care, with this use being codified in a draft guidance, and a fifth provider Liva was recommended for tracking weight-management medicine.[77,78]

In the United States, payers and employers appear similarly interested in avoiding patients going directly to these medicines as a first-line option. For instance, Connecticut's state employee health plan requires employees to first use Intellihealth's clinical lifestyle management program called Flyte, which offers online tools for weight management and personalized care plans, to avoid an expected spend of $30 million for its 265,000 employees.[79] Such required use may be thought of as a means of prior authorization (requiring patients to first leverage digital care with relatively lower treatment costs, which could then refer them to drug therapy).

To capitalize on the opportunity, many virtual diabetes and weight loss digital care programs have shifted their business model to be able to prescribe medicines including Noom, Ro and Weightwatchers, which purchased a telehealth startup called Sequence, and Welldoc expanded their offerings to weight loss.[80–82]

Clinical therapy tools in practice

While digital therapeutics are an area of investment for multiple stakeholders, traditional face-to-face providers (both hospital- or office-based), practices and health systems have begun adopting and developing commercially available digital therapeutics and disease management tools into their practice to improve and differentiate their care. This trend has been facilitated by the increasing number of digital tools intended for provider use in clinic and for patient use at home supervised by a care provider through provider platforms that may feed data back into EHR systems.

> *"Digital weight-management technologies … provide weight-management programmes that prescribe or monitor treatment… [and] will particularly benefit people who do not have access to specialist weight-management services in their area or who are on a waiting list"*
>
> *— NICE*

Government adoption of hardware-based products via the VA Federal Supply Schedule

In the U.S., devices using VR for rehabilitation appear to have made inroads. In government agencies, several have been listed for use and reimbursement through the U.S. Veterans Affairs Federal Supply Schedule (FSS) for medical equipment and supply contracts, which makes these therapies available to the federal healthcare system, such as the Veterans Health Administration, the Department of Defense (DOD), Indian Health Service and other federal government agencies. Use of immersive technology by Department of Veteran's Affairs (VA) expanded from 240 medical centers and facilities in 2021 to over 2,000 member centers in 2023, spanning all states and territories.[83] The VA has also deployed over 1,200 headsets throughout the United States for immersive virtual/extended reality therapies ranging from creative art therapies to physical rehabilitation, the management of phantom limb pain and mental health therapies to help decrease pain, stress, anxiety, boredom, and restless behaviors.[84] A 2023 Veteran's Affairs guide to immersive technologies mentions the use of at least 21 extended reality software platform technologies.[84]

For instance, Bravemind immersive virtual reality has been used to treat soldiers with PTSD and AppliedVR with its FDA-approved RelieVRx, a VR-based digital therapy for chronic low back pain, recently partnered with Lovell Government Services to broaden its reach into the federal healthcare system.[85] Contracts also extend to Strolll Augmented Reality and Reality DTx home use headset for rehabilitation and the VA has partnered with Penumbra to develop custom DTx for VR neurorehabilitation and chronic condition management, to ensure veterans can receive needed care from any location.[86]

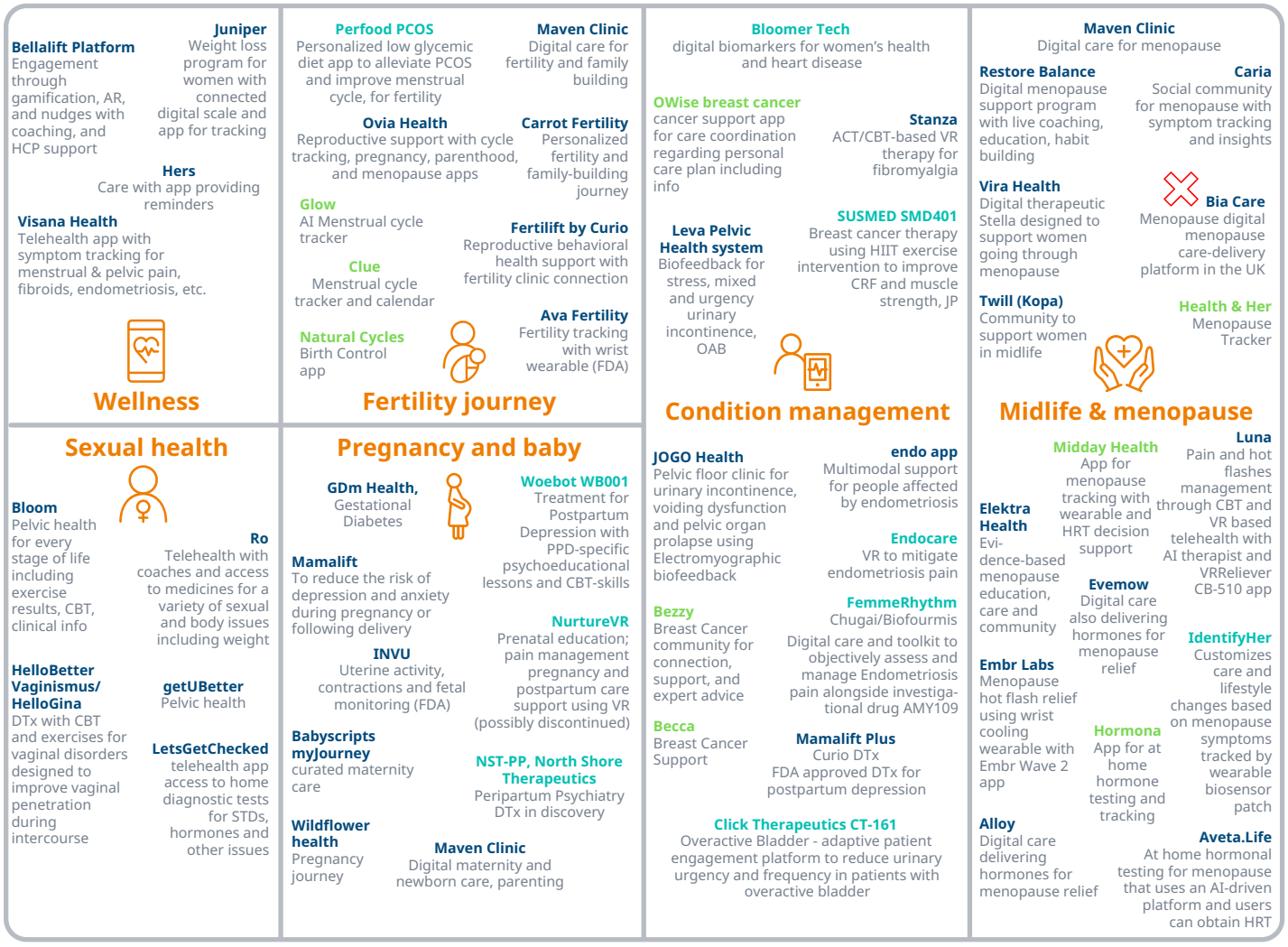
Outside of the VR space, the federal government also began reimbursing digital therapies like Deprexis by Orexo under the FSS in July 2022, making the therapy available to ~15 million people receiving healthcare from the federal government by going through their federal healthcare providers, and Modia and Vorvida were added to the FSS in January 2024.[49,87] Durable medical equipment products focused on PTSD like Freespira and Nightware have been able to gain use by government agencies, as well as MedRhythms' InTandem for veterans with stroke-related walking impairment.[88] These and many more examples demonstrate how government agencies have become increasing comfort with these innovative approaches.

FemTech as a focus

Among the panoply of digital tools and care solutions that have emerged, many are in the area of Women's Health, including some for sexual health (Exhibit 26). Such solutions offer a greater sense of privacy for personal issues, and overcome a lack of OB-GYN staff in some cases, and now support female wellness, sexual health, fertility, pregnancy, and menopause. Some also treat conditions that exclusively or more commonly affect women like pelvic floor dysfunctions, incontinence, endometriosis, fibromyalgia, postpartum-depression and breast cancer.

One of the first digital health assessment tools to gain device approval was the Natural Cycles mobile app, which uses algorithms to calculate fertile periods as a means of contraception and was approved by the FDA via the DeNovo pathway in 2018.[89] However, since then a number of DTx have been approved including Leva for urinary incontinence, MamaLift Plus for postpartum depression, Stanza for fibromyalgia and HelloBetter/ HelloGina for vaginismus, though many other NDTs and devices are used within the bounds of digital care.

Exhibit 26: Examples of women's health apps and digital care programs in the Femtech space



Source: IQVIA AppScript Digital Medicine Database, Jun 2024; IQVIA Institute, Nov 2024.
Note: Some apps noted as available from app stores may used within digital care programs. Hormone replacement therapy (HRT)

Digital care formularies

In the United States, one of the main ways patients currently access digital care programs are through employer benefit programs. With employers increasingly looking at and incorporating digital care programs into their benefits —some providing 4–9 digital health solutions to their employees[90] — this has led benefits companies, payers and PBMs to offer suites of digital health solutions via digital formularies to employers and patients (Exhibit 27). Most programs offered are digital or virtual care solutions and these span treatment areas. For instance, UHC had a network of 22 partners within its UHC Hub as of Jan 2024, of which 17 appeared to have a digital care component.[91]

These players are also seeking to make digital care programs more straightforward for employers to use by ensuring they are integrated into a broader data and care ecosystem, with pre-vetted legal and procurement contracts, privacy and security protections, standard PBM or payer billing, and sharing of summarized outcomes data. The ability to provide care to a patient within days of them showing interest is also critical since the time when patients investigate care options is typically when they have highest motivation to address health issues. Despite competition, formularies have also created a route for developers to gain traction. Big Health, for instance, has found partnerships with CVS Caremark and Cigna's Evernorth formularies, among others to expand access to Sleepio and Daylight.[92]

Exhibit 27: Treatment areas where digital solutions are offered by U.S. payers via formularies

TREATMENT AREA	United	Cigna	Aetna	Kaiser	CVS	Walgreens	Navitus
Behavioral health/ Addiction Sleep, Nicotine Dependence and Cessation		●		●●	●●	●●●	
Mental health Depression, Anxiety, Insomnia	●●	●●●	●●●●●	●	●●	●●●●	
Diabetes care Pre-diabetes prevention T1&2 diabetes, obesity	●●●●	●●●	●	●	●	●	●
Muskuloskeletal / PT Chronic muscle and joint pain/PT	●●	●●●	●●		●	●●●	●
Cardiovascular care/ HPT	●			●	●●	●	
Weight management/ Prevention Healthier choices, lifestyle changes, nutrition, behavior	●●	●	●		●●	●	●●
Pulmonary care Asthma & COPD		●					●
Women's health Family planning, pregnancy, post-partum	●●	●	●		●	●	
Gastrointestinal (IBS etc)		●				●	
Cancer & medication management Injectables, side effects and adherence	●●●	●			●	●	
Caregiver Care Caregiver scress and wellness	●	●			●		

● Digital solution

Source: IQVIA Institute, May 2024. Cigna includes Evernorth.
Notes: Excludes pure telehealth providers. Content non-exhaustive and based on company web sites.

Sensor-based digital measures

+ **Digital sensors and wearables are making nuanced aspects of health and the patient experience of disease traceable and measurable in daily life.**
+ **Validated digital measures to assess patient health status and outcomes provide new ways to demonstrate the effects of therapeutic interventions and are proving valuable in clinical development.**
+ **Life sciences companies have invested in the creation of digital endpoints using data from clinical-grade wearables and built molecule-to-market digital strategies to overlay their drug trials.**
+ **By offering higher quality of data capture, more consistent measurements and increased sensitivity than traditional methods, some digital endpoints have optimized clinical development, allowing trial sponsors to reduce clinical trial enrollment and further promise to reduce trial duration and the need for patients to travel to trial sites.**
+ **The FDA and EMA have begun to approve ("qualify") digital endpoints for use in clinical trials, with the first using wearables to assess COPD, Duchenne muscular dystrophy and atrial fibrillation.**
+ **Objective sensor-based COAs are likely to be used alongside traditional clinical outcome assessments to gain a more holistic understanding of the patient experience, and some may eventually replace traditional methods.**

It has always been possible to describe human behavior and experience subjectively, but assessing and measuring it objectively has been a challenge. Disease assessment scales, patient questionnaires, performance tests and other tools have been created to measure changes in an individual's behavior, health status, clinical outcomes and experience. However, some of these traditional methods and tools still rely on subjective observation of a behavior — by a clinician or a patient — and may therefore deliver variable results and values based on how a test is individually conducted.

The promise of digital measures derives from their ability to open the various domains of human function to objective measurement and assessment. With the emergence of sensor-based digital health technologies, it is now possible to track an individual's movements and behaviors in a consistently measurable way — whether they are performing rehabilitative exercises at home or taking a puff from an inhaler — thereby making changes in patient behavior more meaningful in both research and care. Some digital measures also promise more sensitivity and specificity versus traditional methods of measurement and are measured non-invasively, offering benefits to multiple stakeholders.

Notably, novel uses of digital measures are beginning to optimize clinical trials, speed diagnosis, and improve the continuity of patient care. As stakeholders become increasingly comfortable with the ability of wearable devices to track meaningful measures of health, they have discovered ways to benefit from digital measures and in some cases are beginning to view them as a best-practice necessity. Regulators speak to their ability

DIGITAL BIOMARKERS AND MEASURES

A digital measure is an objective, quantifiable measure of physiology and/or behavior derived from digital signals collected using digital tools. When a digital measure is used to indicate the presence of "normal biological processes, pathogenic processes, or responses to an exposure or intervention" including therapeutic interventions, it is considered a digital biomarker,"[93,94] and its clinical meaning is established by showing a reliable relationship to an existing, validated endpoint.[95]

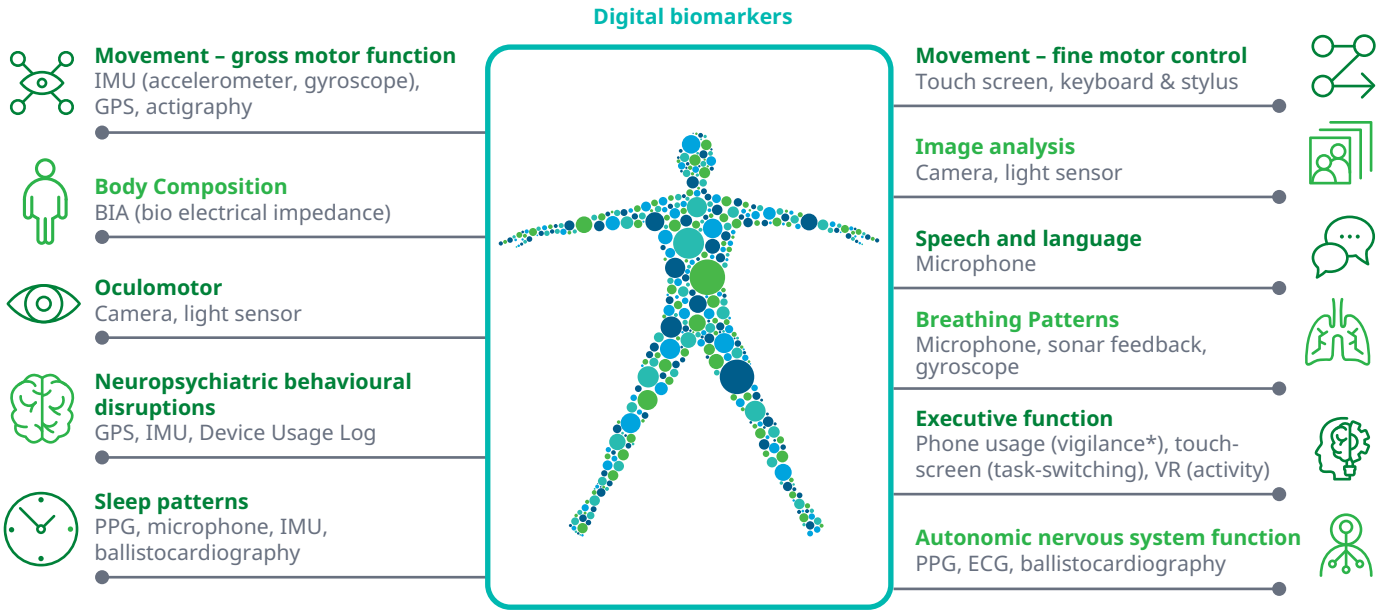
to improve evidence quality and gain a more accurate understanding of patient response to investigational therapies. Life sciences companies see them as a way to better demonstrate the value of their therapies and reduce clinical trial complexity (duration and enrollment) and have therefore invested in the development of digital endpoints. And healthcare providers are finding remote measurement gives them new abilities to assess patient health at home, screen for or diagnose disease, and remotely monitor patients with chronic conditions or after hospitalization (see Digital Diagnostics chapter).

Such objective digital measures are therefore likely to be used alongside traditional measures to gain a more holistic understanding of the patient experience, and some may eventually replace traditional measures. The potential benefits of this shift have made the development of digital measures an area of significant activity and investment.

The creation of digital biomarkers has been enabled by the wide range of sensor components now included on wearables and mobile devices. Both consumer devices (like smartwatches and fitness trackers) and clinical-grade devices (like actigraphs) can collect physiologic and behavioral data on a continual (or repeat) basis requiring little effort from an individual. As new types of sensors have been added over time to these devices, a wide range of signals can now be tracked passively by these devices. These signals can then be interpreted by algorithms, mathematical formulas, and other formal methods (like ECG) to allow them to measure physiological processes and behavior (Exhibit 28). As a result, digital biomarkers now shed light on nuanced human movements, actions, performance ability and patterns and their measurement has yielded value to nearly every medical specialty.

For instance, wrist-worn accelerometers and activity monitors might be used to track scratching behavior in atopic dermatitis[96] or tremor in Parkinson's disease; foot-worn wearables might track aspects of gait and mobility in neuromuscular diseases; smartphone microphones might measure coughing in infectious disease; and cameras might be used to make facial measurements that indicate if someone is smiling to shed light on psychological states.

Exhibit 28: Sensors, signals and methods enabling the creation of digital biomarkers



Source: Adapted from IQVIA Breaking New Ground with Digital Biomarkers. Mar 2021. Available from https://www.iqvia.com/library/white-papers/breaking-new-ground-with-digital-biomarkers; IQVIA Institute, Nov 2024.
Notes: *Vigilance refers to the ability to sustain attention on a task and is a measure of overall attention. Inertial measurement unit (IMU), photoplethysmography (PPG) for health rate, electrocardiogram (ECG), global positioning system (GPS) for geopositioning, ballistocardiogram (BCG), virtual reality (VR), bioelectrical impedance analysis (BIA) used for people on obesity medications lean muscle mass.

SENSOR-BASED COAs

Healthcare stakeholders including provider organizations, life sciences companies, and device developers themselves have sought ways to leverage sensor-based data to improve both patient care and research. However, for the health community to make use of digital measures, they need to be proven reliable, accurate, sensitive to change and clinically relevant to the individual whose health is affected.

Digital measures that are validated to signify meaningful health outcomes — defined as how patients feel, function, or survive — are considered digital clinical outcome assessments (or COAs). By describing how a patient's mental' or physical function or quality of life are affected, they shed new light on patient experience and outcomes. Since COAs already have accepted value in the health system, this potentially facilitates acceptance of new categories like AI-generated Clinical Outcome Assessments (AI-COA) and DHT-Passive Monitoring COAs once they are validated.

DIGITAL ENDPOINTS

As the complexity of clinical trials has increased, efforts to apply digital tools to research and development to de-risk development have proliferated. AI-based solutions have been used for patient matching and clinical trial recruitment, speeding enrollment or used to assess study feasibility, while research platform technologies that electronically source data from mobile devices and software systems (eSource, EDC) have been deployed to improve and simplify data collection.

Digital measures, and especially sensor-based COAs are increasingly finding use as endpoints in clinical trials, deployed to better assess the effects of drugs. However, for digital measures to be used in the realm of research and development, they need to be accepted by regulators as either **primary endpoints**, which establish the efficacy and safety of the drug and are used to conclude whether the study met its objective; as **secondary endpoints** to extend understanding of primary endpoint's clinical effect, safety or provide evidence of another clinical benefit;[97] or as **exploratory endpoints**, which may be included to explore new hypotheses or inform additional research. Separate **safety endpoints** may also be used to identify specific safety signals or trigger participant discontinuation. While only sensor-based COAs can be used as a primary endpoint for drug labeling, digital biomarkers can be used as secondary or exploratory endpoints.

SENSOR-BASED CLINICAL OUTCOME ASSESSMENTS

A sensor-based clinical outcome assessment (also known as digital COA) is a quantifiable tool used to measure how patients feel, function, or survive that is derived from a digital measure through either active performance-based assessment (e.g., software-based visual or movement games and exercises) or passive monitoring of patient behavior or performance (e.g., via medical grade and consumer-facing biometric sensors). Their clinical meaning is established de novo,[95] such as through patient research. Digital versions of traditional questionnaire-based assessments reported by a clinician, patient, or non-clinician observer also exist and are known as eCOAs and ePROs.

DIGITAL ENDPOINTS

A digital endpoint is a precisely defined variable intended to reflect an outcome of interest that is statistically analyzed to address a particular research question (such as within a clinical trial). It is derived from or includes a digital measurement and can be a COA or biomarker.[95] Efficacy endpoints are designed to reflect the intended effects of a drug and include assessments of clinical events, symptoms, measures of function, or surrogate endpoints that are reasonably likely or expected to predict a clinical benefit.[97]

FDA and other regulatory agencies may directly accept an endpoint for use in a single trial on a case-by-case basis, but for endpoints to be deemed adequate for use in research studies more generally, they need to go through a pathway to be "qualified" (or approved) for use in research. As of July 2024, 484 non-unique endpoints had been accepted for use in single trials according to the Digital Medicine Society (DiMe) Library of Digital Endpoints, but with multiple endpoints used per trial, a total of 110 clinical trials have incorporated digital endpoints into their design.[98,99]

Some digital endpoints have been approved more broadly for use in studies of specific conditions. To gain such an approval requires the endpoint's "qualification" by regulatory bodies. In the United States, for instance, they can be submitted to the FDA for acceptance as a Drug Development Tool (DDT) — sometimes via the ISTAND Pilot Program for novel technologies including AI — or as a Medical Device Development Tool (MDDT).

Qualification of endpoints

Both the FDA in the United States and the EMA Committee for Medicinal Products for Human Use (CHMP) in the European Union have now approved (or "qualified") digital endpoints for use in research and have discussed their strengths versus traditional methods. Both device developers and life sciences companies alike have sought qualification for digital endpoints validated on wearables and other sensors (Exhibit 29).

To date, at least 14 digital measures have been submitted to the two agencies with two sensor-based COAs formally qualified by the EMA and one digital biomarker measured on a consumer device — the Apple Watch — qualified by the FDA as a medical device development tool.[100,101] An additional seven endpoints have been accepted into the DDT Qualification Program by the FDA which thereby progresses them to a second step where they create a Qualification Plan, and two AI-informed COAs for drug development have been accepted into ISTAND. Two submissions have been rejected. Notably, the FDA has yet to approve a sensor-based COA.

Many of the submitted endpoints have measured aspects of physical and motor activity across disease areas including COPD, neuromuscular and movement disorders, and cardiovascular disease, while others have measured symptoms in new ways, such as quantifying the "itchiness" of skin by measuring scratching behavior in atopic dermatitis. However, stakeholders are also focusing on the development of digital endpoints in mental health and chronic diseases like diabetes and seeking new ways to leverage new speech biomarkers.

A sensor-based COA, Stride Velocity 95thCentile (SV95C), that measures the maximal speed of subject's walking strides, was the first-ever fully-digital endpoint to be qualified in July 2023 by the EMA CHMP for use in studies of Duchenne Muscular Dystrophy.[104] It also became the first to be permitted as a primary endpoint allowing it to be used for regulatory decision making and in pivotal trials.[102,103] Its use is notably expected to reduce patient travel to clinical care sites and investigational sites for clinical trials, as well as provide a more accurate understanding of patient response to therapies, and may eventually replace the six minute walk test in some cases.[104]

Another endpoint, PROActiv, was approved by EMA in 2018 for use in COPD trials, and is a combined digital-and-COA endpoint built on an actigraphy device. It uses a questionnaire-based patient reported outcome measure to capture a patient's perspective on their level of activity alongside an actigraphy device to measure the actual amount of activity — essentially measuring the same aspect both subjectively and objectively. This example shows there is not only a role for digital devices and measures to replace existing COAs but also to be used in combination alongside them. By looking at objective measures alongside more subjective measures, the data together paints a clearer picture of patient experience and how the two tie together, and ultimately may yield endpoints that hold more value to both patients and regulators.

Exhibit 29: Decisions by FDA and EMA on digital endpoint submissions

Proactiv	Apple AFib History Feature	ADAM Swallow Sensor	Scratch Sensor	CHF-SS & CHF-IS	AIDA using AI/ML	MC10 BioStamp nPoint
Daily physical activity	Atrial fibrillation burden	Swallowing function (frequency and respiratory timing	Itch intensity & persistence	Daily physical activity	Clinical event adjudcation	Progressive gait abnormality
For: **Chronic obstructive pulmonary disease** Replacing/ Complementing: **Patient-reported outcomes** **Qualified Mar 2018** Sponsored by: **COPD Consortium**	For: **Atrial fibrillation** Replacing: **Implanted cardiac monitors for AFib burden** **Qualified May 2024** Sponsored by: **Apple**	For: **Parkinson's Disease** Possibly replacing: **Endoscopic exams (FEES) and videofluoroscopy** **LOI Accepted Nov 2023** Sponsored by: **Sibel Health**	For: **Atopic dermatitis** Possibly replacing: **Patient reported outcomes** **LOI accepted Dec 2020** Sponsored by: **Sonica LLC**	For: **Chronic heart failure** Possibly replacing: **Accelerometery in a clinic** **LOI accepted May 2019** Sponsored by: **PRO Consortium**	For: **Cardiovascular disease** Possibly replacing: **Manual adjudication** **Accepted into ISTAND Pilot Program Mar 2024** Sponsored by: **AstraZeneca**	For: **Huntington's Disease** Possibly replacing: **Clinic/self assessment** **LOI not accepted** Sponsored by: **MC10, Inc**
SV95C (uses ActiMyo)	**ActiMyo**	**PAACT**	**Actibelt**	**Actibelt**	**AI-COA**	**Virtual Motor Exam Part III**
Daily motor activity (maximal walking stride speed)	Daily motor activity (walking stride variables)	Accelerometry assessment Physical activity	Change in walk speed	Change in walk speed	Automated depression & anxiety severity measure	Motor symptom severity
For: **Duchenne muscular dystrophy** Replacing/ Complementing: **6MWT** **Qualified Jul 2023** Sponsored by: **Sysnav**	For: **Duchenne muscular dystrophy** Replacing/ Complementing: **6MWT** **LOI accepted Aug 2019** Sponsored by: **Sysnav**	For: **Knee osteoarthritis** Possibly replacing: **Accelerometery in a clinic** **LOI accepted May 2018 (withdrawn Aug 2023)** Sponsored by: **ACTTION**	For: **Sarcopenia** Possibly replacing: **Clinic/self-assessment** **LOI accepted Jan 2019** Sponsored by: **Trium Analysis Online**	For: **Multiple Sclerosis** Possibly replacing: **Clinic/self-assessmentc** **LOI accepted Jan 2019** Sponsored by: **Trium Analysis Online**	For: **Parkinson's Disease** Possibly replacing: **Clinical rating scales for depression/anxiety** **Accepted into ISTAND Pilot Program Nov 2023** Sponsored by: **Deliberate AI**	For: **Parkinson's Disease** Possibly replacing: **In-clinic neurological exams** **LOI Not Accepted** Sponsored by: **Verily Life Sciences**

Accepted (Qualified) by EMA

Accepted (Qualified) via FDA MDDT as a Secondary Endpoint

Letter of Intent accepted by FDA

Accepted into ISTAND Drug Development Tool pilot

Letter of Intent not accepted by FDA

Source: IQVIA Institute, May 2024; European Medicines Agency (EMA) CHMP, Opinions and letters of support on the qualification of novel methodologies for medicine development, Available from: https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance/opinions-letters-support-qualification-novel-methodologies-medicine-development; FDA CDER & CBER Drug Development Tool Qualification Project Search, Available from: https://force-dsc.my.site.com/ddt/s/. AI-generated Clinical Outcome Assessment (AI-COA). Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION). Physical Activity Accelerometry Assessment (PAACT). Medical Device Development Tool (MDDT) . Automating Identification, Detection, and Adjudication (AIDA). Stride velocity 95th centile (SV95C).

While sponsors generally aim to take sensor-based COAs through the process of being qualified as endpoints for use in clinical trials, digital biomarkers can also be qualified as surrogate endpoints. Notably, in May 2024 the FDA qualified a digital biomarker — the Apple Watch's atrial fibrillation (AFib) history feature — for use as a secondary endpoint in medical device trials. It is the first sensor-based digital health technology ever qualified in the United States for this use.[105] The watch's linked software uses photoplethysmography (PPG) analysis to assess how frequently a user shows signs of irregular, often rapid, heartbeat associated with AFib and measures the time of onset and duration of each arrhythmia episode. It then derives estimates of AFib burden (or the duration of AFib as a percentage of the total time assessed).

While earlier studies had indicated that AFib burden may hold greater clinical significance than some traditional measures like time-to-first-recurrence of arrhythmia, in the past, inserted cardiac monitors have been required to capture the endpoint (as was done in some past trials for cardiac ablation devices and antiarrhythmic drugs).[105] With the Apple Watch being able to measure AFib burden non-invasively, the FDA's approval for use in the Medical Device Development Tools (MDDT) program will reduce patient burden for participants in trials and will allow its use as a secondary (surrogate) endpoint more broadly in clinical studies evaluating the safety and effectiveness of cardiac ablation devices.

Where the FDA and EMA have rejected endpoint submissions — or even given constructive criticism on endpoints that have had their Letter of Intent accepted — there are some come objections the agencies have voiced, including failure to: reflect measures meaningful to patients; measure the concept they were intended to measure; or prove that the measure can be correctly gathered under non-ideal conditions, such as a patient slightly mispositioning a device.

CLINICAL TRIAL OPTIMIZATION

Efforts to develop digital endpoints stem from the understanding that capturing continuous data in the real world or home settings offers benefits compared with snapshot clinical assessments. These include a more accurate and nuanced understanding of patient response to therapies, lower burden on trial participants and greater sensitivity than provided by traditional endpoints, and are beginning to optimize clinical trials for sponsors and patients alike.

CONSUMER DEVICES FOR DIGITAL ENDPOINTS[105]

It was a surprise to many in the field that a digital biomarker, rather than a sensor-based COA or "true endpoint" became the first-ever qualified digital health measure by the FDA, but no less surprising was that this biomarker used a consumer device. Most of the investment and use to date of digital endpoints has been on medical-grade devices such as those for actigraphy. However, the achievement of FDA's approval of AFib burden from the Apple Watch's atrial fibrillation (AFib) history feature underscores the growing importance of consumer wearable technology in healthcare, particularly for monitoring heart health. It reflects the FDA's assessment that the Apple Watch was accurate enough to measure AFib Burden as a surrogate endpoint, potentially paving the way for other consumer devices to be similarly qualified in the future. In this case, the value of AFib Burden was already established using inserted cardiac monitors, so FDA's approval focused on demonstrating that the device is fit-for-purpose. It represents an important initial step toward approving more novel and innovative digital measures.[105]

Reduced trials size and study time

Some new digital endpoints have been shown to be more sensitive than the endpoints they are replacing, opening the door to reduce trial durations and the number of participants needed to show statistical improvements in outcomes.

For example, Bellerophon Therapeutics' used a primary actigraphy endpoint to measure changes in moderate-to-vigorous physical activity (MVPA) in a trial of its INOpulse treatment for patients with pulmonary hypertension and fibrotic Interstitial Lung Disease (fILD). The FDA endorsed the endpoint's use based on results of a Phase II trial where MVPA (which used an wearable actigraphy device to capture data continuously) was compared to the gold standard 6 Minute Walking Test (6MWT) and found to have improvements in both the quality of data capture and increased sensitivity (or a greater effect size).[106,107]

Use of the more sensitive endpoint allowed the company to reduce the sample size of its Phase III trial from ~300 patients to 140 patients — a significant decrease that would likely have impacted the estimated cost of the trial and time to completion.[107] Use of the traditional 6MWT alone would have been less sensitive and required a larger sample size. Although results of the PIII trial were negative due to a failure of the drug, the effective use of a digital endpoint to reduce complexity in a clinical trial was a milestone.

Improved understanding of patient outcomes

Digital endpoints are also proving to be more clinically meaningful to patients, offering a more accurate understanding of patient response to therapies and the patient experience. Although patients are often assessed with one-time clinical assessments in both research and care settings, patients may have 'good days' and 'bad days' or even "sick days" that can skew results, or they may become tired due to the travel to care locations.[104]

In the case of stride velocity 95th centile (SV95C) in ambulatory Duchenne Muscular Dystrophy, for instance, the EMA recognized in its qualification opinion that by allowing continuous monitoring over relatively long periods in a home-setting the measure is "less sensitive to the timing of the assessment (e.g., day and time of test) and relies less on patient motivation or subjective assessment as compared with established tests."[104] It was also approved because the measure was noted to be "highly correlated" to the 6MWT gold standard endpoint, and yet proved to be more sensitive to change and was considered more representative of the patient's real ambulatory capabilities — thereby making it a better alternative. Ultimately it is clear that in some cases, actigraphy measures offer benefits in trials that will eventually allow the replacement of gold-standard measures with lower sensitivity, such as the 6MWT.

More consistent measurement

Digital endpoints also offer greater consistency in their measurement that helps de-risk development. For companies running multi-site and global clinical trials, there has always been the risk with traditional endpoints and assessments that they may be subjective — tied to the clinician — and could be run/tested differently from country to country. The shift to more objective and standardized endpoints may make for more optimized clinical trials and evidence. The EMA has noted this as a potential benefit saying, "using a wearable device and system is likely to also overcome variations in practice encountered across different centers/countries, which also has a significant impact on the reliability of results, particularly in global studies."[104]

Improved patient quality of life in clinical and trial settings

For patients, approvals of digital endpoints also offer to reduce the burden on them to participate in clinical research. For instance, with the qualification of SV95C, the ability to assess the abilities of patients with Duchenne Muscular Dystrophy remotely or in the real

world may help to reduce the need to travel to clinical sites during the study. Such benefits are also likely in the future to carry over into care settings. While qualification is specific to research use, the validation and acceptance of SV95C as a measurement by regulators is likely to encourage providers to eventually choose to use it to detect ambulatory decline in a care setting to inform treatment decisions and reduce clinic visits. Approval of AFib burden as a digital endpoint may also improve patient quality of life by enabling patients to avoid an implant procedure for a cardiac monitor through its ability to measure AFib burden non-invasively.

The future

While the data submitted for SV95C were recorded on the ActiMyo device, the approval of this digital clinical measure was device agnostic "provided accuracy and reliability of measurement are established" for digital wearable devices or systems.[104] This opens up the possibility that other consumer wearable devices will eventually be able to measure these type of sophisticated disease-correlated measures in the future. It also means wearables are likely to become more valuable to patients over time for disease screening, progression tracking or prognosis, and become more trusted and accepted by the clinical community.

> *"This achievement [with SV95C] is the result of a 14-year collaboration between many stakeholders across the DMD community, including technology developers, academia, the pharmaceutical industry, caregivers, and most importantly patients and families living with DMD."*[108]
>
> *— SYSNAV Healthcare*

Digital diagnostics and other health assessment tools

+ **Digital diagnostics — software-based devices that process signals from sensors — have rapidly opened new routes to assess disease risk, speed diagnosis and monitor patient health and at least 103 are commercially available.**
+ **In the United States, 801 medical devices enabled by artificial intelligence and machine learning received 952 approvals as of June 2024, and include around 75 mobile tools that assess patient health and detect disease.**
+ **Digital tools that speed diagnosis are a growing focus for investment as they expand the population recognized to need treatment and allow early intervention.**
+ **Risk screening tools built on consumer smartphones and wearables offer to democratize health assessment by reaching global patient populations, while physician-facing ones offer to reduce the number of patients unnecessarily referred to specialist care.**
+ **Clinical "platform" solutions that draw data from wearable sensors and symptom-tracking apps are now enabling providers to remotely monitor, manage and triage patients in greatest need of care to improve health outcomes.**
+ **The proliferation of such digital tools to remotely monitor patient health has spurred the creation of reimbursement pathways like Germany's DiPA and France's PECAN pathways.**
+ **In clinical trials, remote monitoring devices improve participant safety by speeding investigator response to adverse events and help regulators assess drug safety and efficacy.**
+ **Hospital-at-home programs, a type of digital care that continuously monitors patients to detect and predict adverse events, may speed patient discharge from hospital settings and improve quality of life for patients treated with CAR-T therapies and other drugs with higher risk profiles.**
+ **The line between consumer-grade and clinical-grade wearables is blurring, as medical device companies develop consumer wearables supporting wellness in healthy individuals and medical-grade sensors are added to consumer products, making condition management a part of daily life.**

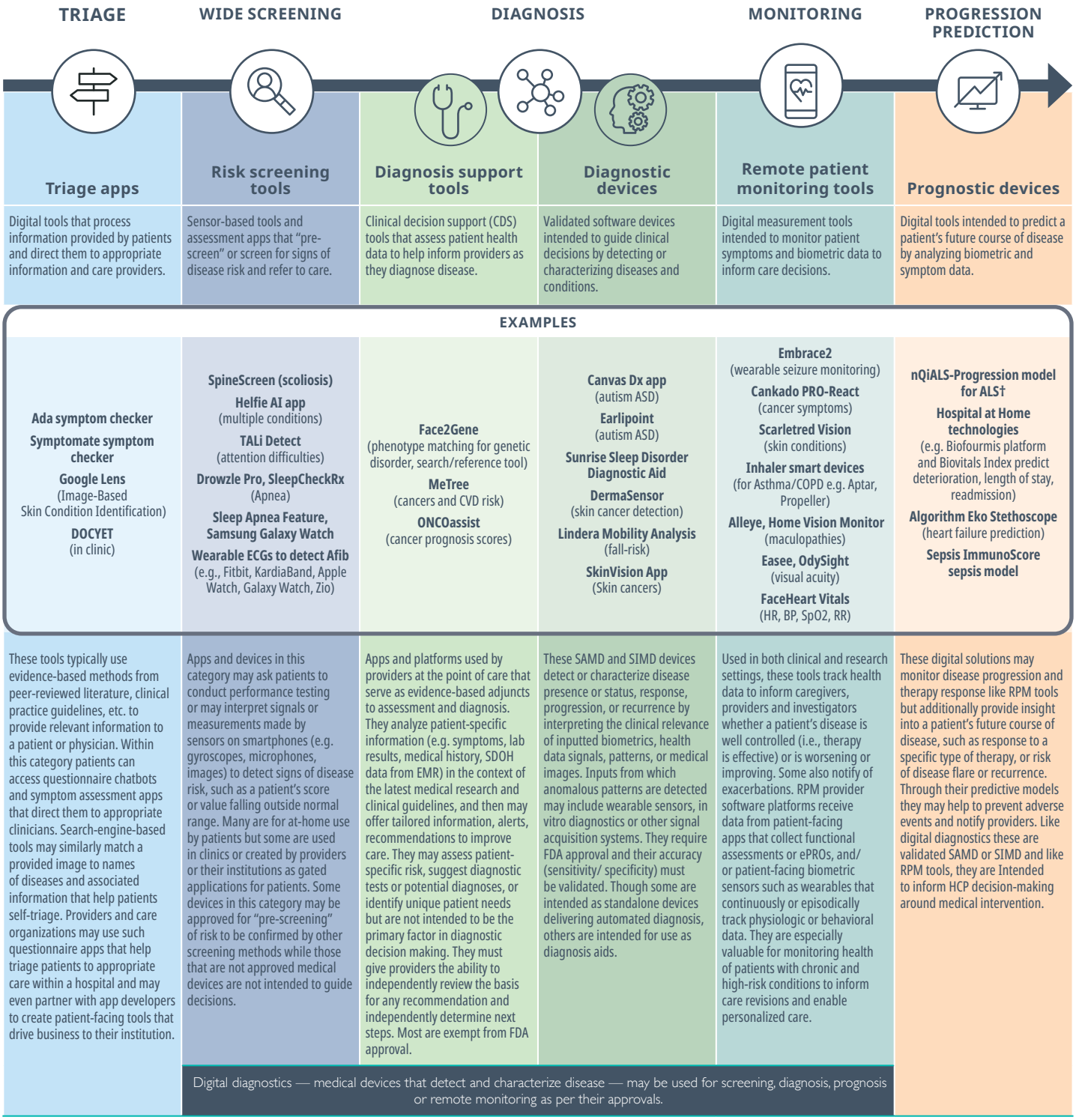
HEALTH ASSESSMENT ACROSS THE PATIENT JOURNEY

To arrive at a diagnosis, clinicians must gather and synthesize multiple pieces of information about a patient's health.[109] They conduct medical examinations where they listen to sounds from the patient's body, lay hands, conduct performance assessments, and use imaging and other diagnostic tools. However, such decisions can be complex and rely on clinicians to assimilate many sources of information, as well as decide which tests are relevant to run.

A wide range of digital tools now help to simplify this process, supporting health assessment across the entire patient journey and accelerating diagnosis. They help individuals identify potential causes of symptoms they may be experiencing, aid in triage, disease screening and diagnosis, and enable providers to monitor a patient's disease progression or response to therapy. They sometimes even predict future health changes (Exhibit 30).

While most of these tools analyze data from sensor-based devices that gather digital measures associated with the presence of a disease, others analyze patient-reported data or big data to yield clues to a patient's health status. For instance, AI-based triage chatbots may

Exhibit 30: Digital tools supporting disease assessment and diagnosis



Source: IQVIA Institute, Aug 2024; Digital Therapeutics Alliance, Guidance to Industry Classification of Digital Health Technologies, Jun 5, 2023; Grim E. The Doctor is In: A Guide to Clinical Decision Support Apps. Pepid Pulse. Feb 12, 2024.

Notes: Software as a medical device (SAMD). Software in a medical device (SIMD). Remote Patient Monitoring tools (RPM). Social determinants of health (SDOH) * May overlap other categories. Algorithmic analysis of ECG to detect Afib includes multiple technologies including Kardia Mobile, Apple Watch, Fitbit Irregular Rhythm Notifications. patient reported outcomes (PROs). These technologies can also be used in diagnosis and remote monitoring.

ask patients to respond to questionnaires while some patient-monitoring apps may ask users to conduct digital performance assessments.

This rapidly expanding new area of health assessment offers yet another way that digital tools can support health equity: broadening the reach of disease screening through consumer devices and empowering primary care physicians globally with tools to help them detect specialty conditions and rare diseases they may not typically encounter.

DIGITAL DIAGNOSTICS

Devices that use software to process signals from sensors and/or other data have rapidly opened new routes to assess disease risk, aid and speed diagnosis, and monitor patient health. While digital biomarkers use sensor signals to indicate health processes are occurring and measure them, digital devices that go further and interpret the meaning of such signals (or other information acquired digitally), draw conclusions about a patient's health status or risk, and offer information, guidance, and insights to either providers or patients are known as "**digital diagnostics (Dx)**."

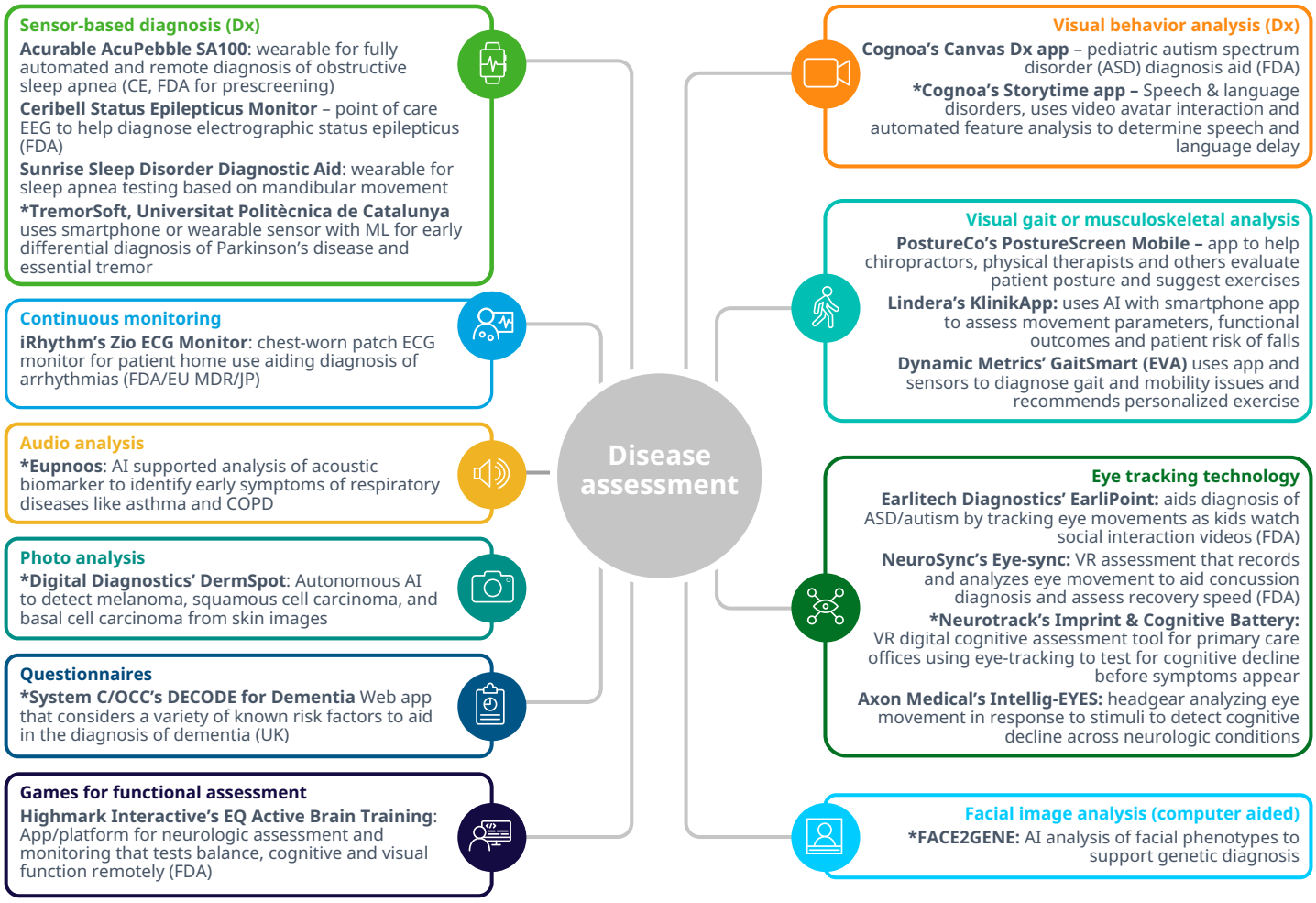
At least 103 digital diagnostic devices are commercially available globally. Like standalone digital therapeutics that treat patients, digital diagnostics are regulated medical devices. This is because in the United States and elsewhere, software that processes and analyses medical images or signals from sensor-based technologies (e.g., signal acquisition systems and in vitro diagnostic device) are subject to regulation and evidence requirements. Most such tools are thereby considered classified as Software as a Medical Device (SaMD) or Software in a Medical Device (SiMD) which both rely on analytic software such as algorithms and models.

Based on their clinical validation studies and regulatory approvals, medical devices that assess disease can often be used for disease screening, diagnosis, and monitoring. Many of these tools themselves interpret (e.g. detect/assess/characterize) a patient's health, whereas pure remote monitoring tools collect health data like vitals but transmit them to a healthcare professional for analysis."[10,110] Digital tools now use a range of approaches to assist physicians in diagnosing, characterizing, and monitoring conditions (Exhibit 31). Many of these devices also use "artificial intelligence (AI) or machine learning (ML) to achieve their intended medical purpose" or are "AI-enabled."[111]

Devices that use software to process signals from sensors and/or other data have rapidly opened new routes to assess disease risk, aid and speed diagnosis, and monitor patient health.

DIGITAL DIAGNOSTICS (Dx)
"A digital diagnostic is a validated tool for detecting disease and/or characterizing disease status, response, progression, or recurrence based on inputted biometrics."[93]

Exhibit 31: Tools assisting clinicians in diagnosing, assessing, and monitoring conditions



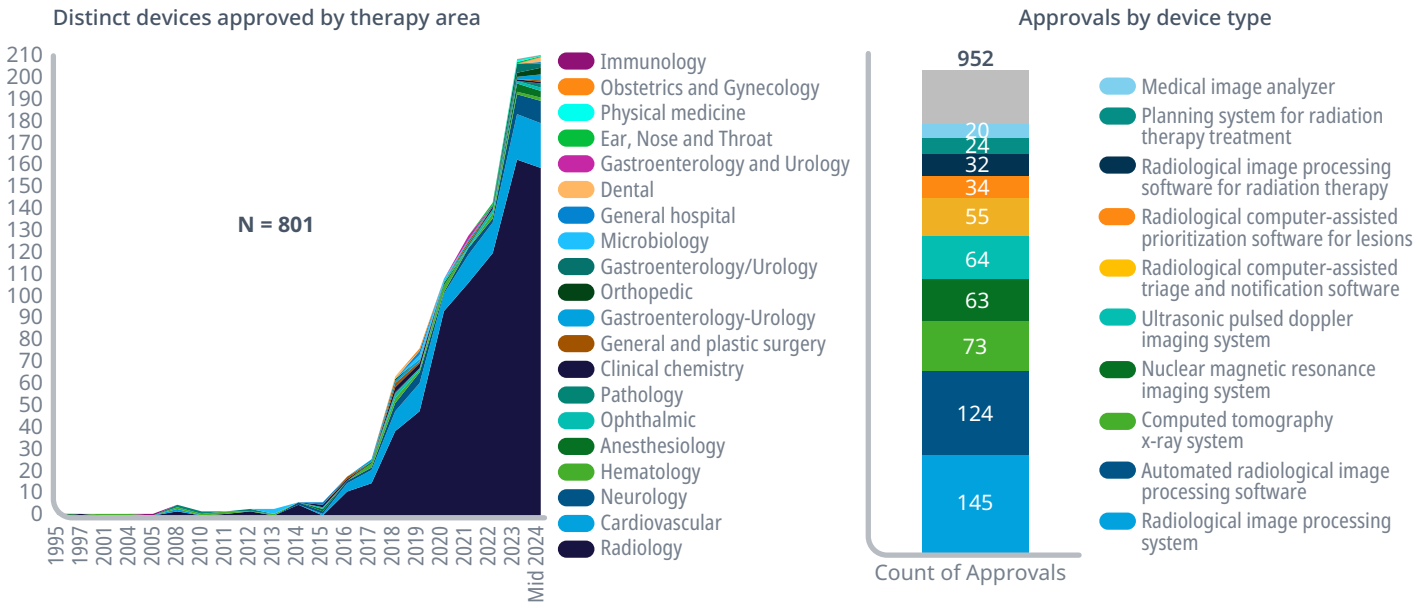
Source: IQVIA AppScript Digital Medicine Database, May 2024; IQVIA Institute, July 2024; Company websites and other public sources.
Notes: Exhibit provides examples within in each category only and is non-exhaustive.

AI/ML-ENABLED DEVICES

The recent explosion of innovation using biometric sensors comes, in part, from the rise of AI/ML, which has sped the creation of analytic algorithms and models and helped to bring meaning to digital signals and given rise to a new term AI as a Medical Device (AIaMD). In the United States, a rapidly increasing number of AI/ML enabled devices have found applied use across disease screening, diagnosis and monitoring, with more than 801 individual SAMD and SIMD tools now cleared by the FDA (Exhibit 32).[112] Some of these devices have gained multiple approvals, such that a total of 952 AI/ML approvals have been granted through June 2024. Approvals have also been accelerating, with a total of 210 new AI/ML devices approved in 2023.

The most sizable segment among these AI-enabled technologies are those used in the radiology space, including large-footprint ultrasound, CT, X-Ray and other imaging machines with AI-supported analytic software purchased for use in hospitals (SIMD), and hospital medical software that provides additional AI/ML interpretation of images collected by other devices (SAMD).[113] However, mobile AI-tools can be further parsed from the larger group of AI-enabled digital devices.

Exhibit 32: FDA-approvals of artificial intelligence and machine learning enabled medical devices



Source: IQVIA Institute, Oct 2024; Artificial intelligence and machine learning (AI/ML)-Enabled Medical Devices | FDA. Aug 7, 2024. Last entry dated 6/25/2024.
Notes: Displays devices approved with a total of 952 approvals gained for those devices through to 2024. *Mid 2024 displayed is a rolling year ending Jun 25.

Mobile tools are typically intended for home-based use by consumers or for point-of-care use by physicians to better detect, diagnose, or assess the risk of health issues. Among the 103 identified digital diagnostics, around 75 mobile tools have been approved by the FDA as AI/ML enabled devices and now help to assess patient health either remotely or at point-of-care (Exhibit 33). Some of these software devices process signals from multi-purpose consumer devices like smartphones, tablets, and wearables (as apps or features), but most are single-purpose office-based devices that add informative value versus their traditional counterparts.

For instance, in the case of two recently approved Autism diagnosis aids, one uses a patient-facing smartphone app alongside provider inputs to enable home-based or remote diagnosis (e.g., Cognoa's Canvas Dx) — potentially enabling primary care providers to confidently diagnose — while the other is a single-purpose device geared more for in-clinic assessment and diagnosis by specialists (e.g., Earlipoint test for autism which runs on a dedicated Microsoft Surface Pro with a custom eye-tracking component).[114]

Digital point-of-care devices used in doctors' offices, such as automated or remote stethoscopes and digital diagnostic aids now help to guide healthcare professionals as they make clinical diagnoses or treatment decisions. For instance, in the cardiovascular space, the Eko Stethoscope is used like a normal stethoscope but also amplifies its signal, cancels noise, and links to an app that detects/identifies arrhythmias like tachycardia, brachycardia and atrial fibrillation.[115] Such value-added analytics help to make patient exams more objective and quantitative and increase the likelihood that an issue is accurately detected. These devices may also be more convenient. Rather than using traditional ECG devices that require wires, patches or gels and potentially skilled support staff to run the test, software like Alivecor's KardiaStation app and its AI/ML enabled InstantQT service process ECG data from a highly portable wireless sensor that can more easily be used in clinics to detect a dangerous heart condition associated with QT prolongation.[116]

Exhibit 33: FDA approved AI/ML enabled mobile tools by type and number of approvals

N = 75 Devices with 82 Approvals as of June 2024

CARDIOVASCULAR

Cardiac monitoring platforms

AliveCor Kardia AI & AliveCor QT Service
Biofourmis RhythmAnalytics
Implicity IM007
iRhythm Technologies ZEUS System, Zio Watch, Zio AT ECG Monitoring System, Zio ECG Utilization Software
Medicalgorithmics DeepRhythmAI & DeepRhythmAI platform

Reduced ejection fraction notification software (heart failure risk or status)

Ventric Health's Vivio LVEDP System wearable for HF monitoring and diagnosis
Anumana Low Ejection Fraction AI-ECG Algorithm to detect risk of heart failure
Eko Health, Eko Low Ejection Fraction Tool (ELEFT)

Irregular heart rhythm detection OTC PPG or ECG Analysis

Apple Atrial Fibrillation History Feature, Irregular Rhythm Notification Feature (IRNF), ECG app
Fitbit Irregular Rhythm Notifications
Samsung ECG Monitor w/Irregular Heart Rhythm Notification (OTC ECG Software)

Cardiac ECG remote monitoring devices

Qompium NV FibriCheck
Verily Life Sciences Study Watch and Irregular Pulse Monitor (+home use)
VivaQuant RX-1 Rhythm Express
Kestra Medical Technologies' ASSURE Wearable ECG
Rooti Labs Rooti Rx ECG Event Recorder, Rooti Link APP Software
Withings Scan Monitor 2.0
PhysIQ Heart Rhythm and Respiratory Module
Peerbridge Peerbridge Cor System
Laerdal Medical NeoBeat Mini Newborn heart monitor

Predictive Cardiovascular Indicators

Edwards Lifeciences Acumen Hypotension Prediction Index (HPI) and Global Hypoperfusion Index (GHI) Algorithm
Implicity SignalHF1 (IM008) (Heart failure algorithm)

Arrhythmia Detection or Alarms

Preventice Tech. Bodyguardian Remote Monitoring System for arrhythmias
Eko Devices' Eko Analysis Software/Sensora

RESPIRATORY

Electronic Stethoscopes For detecting heart and lung problems

AusculThing AusculThing ACC
CSD Labs eMurmur Heart Ai and EMurmur ID
Eko Devices Eko Murmur Analysis Software
M3DICINE Stethee Pro 1/ Pro Software System
Stratoscientific Steth IO
Tyto Care, Tyto Stethoscope & SAMD Lung Sounds Analyzer

Obstructive Sleep Apnea Detection Ventilatory Effort Recorder

Appian Medical SnoreSounds
EnsoData Aurora
Belun Tech. Belun Sleep System wearable ring
Zephyr Sleep Technologies MATRx Plus
Compumedics Sleep Monitoring System

Diagnostic spirometer

NuvoAir's Air Next Heart and lung care

Abnormal Breath Sound Device

Tyto Care Tyto Insights for Wheeze Detection

NEUROLOGY

Diagnosis aids for Autism

Cognoa Canvas Dx ASD Diagnosis Aid
EarliTec Diagnostics EarliPoint System and Device

Tremor Transducers for Parkinson's

New Touch Digital's NeuroRPM

Seizure Monitoring & event detection EEG or Physiological signals

Ceribell Ceribell Status Epilepticus Monitor
Epitel REMI AI Discrete Detection Module/ Vigilenz AI for ambulatory monitoring
Empatica Embrace and EpiMonitor

Sleep Staging & Event Detection via EEG

Neumetry Medical SomnoMetry
Beacon Biosignals Dreem 3S and SleepStageML
EnsoData EnsoSleep

Brain Injury Adj. Interpretive Oculomotor Assessment Aid

Oculogica's EyeBOX concussion vs. brain hemorrhage (portable device)
SyncThink, EYE-SYNC

VITALS MONITORING

Multivariate Vital Signs Index

Biofourmis' Biovitals Analytics Engine
VGBio (DBA PhysIQ) Personalized Physiology Analytics Engine Software
Spry Health's Loop System for remote patient monitoring

Optical/Camera Measurement of Heart Respiratory Rates/Function

Oxehealth's Oxehealth Vital Signs Software (DeNovo)
FaceHeart, FaceHeart Vitals Software Development Kit
Continuse Biometrics Gili Biosensor System

ENDOCRINE/DIABETES

OTC Blood Glucose Monitoring System

AgaMatrix One Drop Blood Glucose Monitoring System
LabStyle Innovations Dario Blood Glucose Monitoring System

Apps tied to Infusion Pump (Infusion Pump Accessories)

WellDoc WellDoc BlueStar

Insulin Pump Therapy Adjustment Calculator for HCPs

DreaMed Diabetes' DreaMed Advisor Pro Software Algorithm (Glooko)

ONCOLOGY

Adjunctive diagnosis device for skin cancer

DermaSensor cancer detection for non-dermatology providers)

ORTHOPEDICS

Optical contour sensing device

Momentum Health, Momentum Spine (scoliosis)

INFECTIOUS DISEASE

Prediction and diagnosis aid for sepsis

Prenosis' Sepsis ImmunoScore

VISION

Diagnosis support and ID of visual tracking impairment

RightEye's Vision System

Source: IQVIA Institute, Oct 2024. Artificial intelligence and machine learning (AI/ML)-Enabled Medical Devices | FDA. Aug 7, 2024 update. Last entry dated 6/25/2024.
Notes: Includes products assessed to be mobile consumer products or intended for use at point-of-care as a portable/mobile device.

These mobile assessment tools most notably allow care to shift to alternative locations like the home or less intensive levels of care — for instance helping primary care doctors diagnose conditions usually identified by specialists. As many of these devices can be used cross-purposes for screening and monitoring, similar ECG-based wearable devices have been approved both for non-invasive ambulatory cardiac monitoring by physicians and OTC home use by patients to detect abnormal heart rhythms.

DIGITAL TOOLS SPEEDING DISEASE ASSESSMENT AND DIAGNOSIS

The use of digital health assessment tools now spans the full patient journey (Exhibit 30). For instance, some detect the presence of a disease or medical condition while others help to triage patients to care, assess physiologic parameters, symptom data, or other data sources like medical records to assess patient risk or inform clinical decision-making, such as determining if patients would benefit from further diagnostic tests.

Patient-focused triage

Patient-facing triage tools may process information provided by app users through questionnaires or submitted images and help refer patients to appropriate primary or specialty care. While some triage tools have been approved in Europe, in the United States some fall under FDA enforcement discretion as general wellness products providing patients access to reference information. Although the intent of this type of tool is to provide information and direct patients to care, in some cases patients perceive these as a means to self-diagnose.

Apps in this category include evidence-based symptom checkers and search-engine tools that use image-matching to identify related conditions and help patients self-triage.[117] Symptom checking chatbots like Ada (Ada Health), Symptomate, and Buoy AI Assistant, ask patients a series of questions about their health and then use AI to assess their symptoms and direct them to appropriate care. They may provide information on associated conditions, what type of doctors to consult, or what treatments might be available. Some developers have also partnered with provider organizations[118] and life science companies to embed these as tools on their websites to help link patients directly to their partnered virtual or in-person care providers. Other similar tools, like Docyet, are used in care settings by providers to triage patients or obtain a set of differential diagnoses. However, not all players in this space have been successful and the AI-powered symptom checker company Babylon recently shut down.[119]

Another type of digital triage tool is search-engine based and provides image-based condition identification. Google Lens, for instance helps patients self-triage for skin conditions by taking a photo of their skin, hair or nail conditions and providing visual matches along with their linked condition names, aiding them to describe their condition and better self-screen. Google's related investments in AI image recognition for skin conditions[120] include one tool presented at a conference in 2021, which demonstrated the ability to recognize 288 different skin, hair, and nail conditions, and present the correct condition in the top three suggestions 84 percent of the time.[121,122]

Risk screening tools

Digital screening tools use patient-facing sensors (e.g. gyroscopes, microphones, images) or assessment apps to detect signs of disease risk (such as a patient's score or value falling outside normal range). Of all digital tools, these may have the greatest impact to speed diagnosis through their ability to reach patient populations broadly using consumer tools they already may own and use and may help to democratize care by reaching patients globally.

Some smartwatches now act as screening devices that notify undiagnosed individuals of newly identified disease risk, having been granted various device approvals. For instance, the Sleep Apnea Feature of Samsung Galaxy Watch notifies users if it detects a risk of sleep apnea by monitoring breathing patterns during sleep.

Other devices/features have also been given OTC approval to detect atrial fibrillation, such as on the Apple Watch and Fitbit (and other Wearable ECGs) which notifies patient of an irregular rhythm or pattern via its FDA approved Irregular Rhythm Notification Feature.

In the dermatology space, the AI-based SkinVision app detects skin cancers including melanoma from a smartphone photo with up to 95% sensitivity (TGA approval and CE mark) and provides a risk assessment that suggests whether a patients should be seen by a provider.[123,124] When put in the hands of primary care providers, such risk screening devices offer potential to reduce the number of patients referred to specialist care. This potential benefit may partly have prompted NICE in the United Kingdom to issue an innovation briefing on these technologies (including SkinVision, nomela by Moletest Scotland, DERM by Skin Analytics, and Moleanalyzer pro by FotoFinder Systems).

"Dermatologists have been overwhelmed in the past by the number of referrals they have received from GPs who were looking for a specialist to decide if skin lesions needed some further investigation... Because GPs are not specially trained in spotting potentially malignant marks on a patient's skin, they basically had to send every potential case for analysis."

— Dr. Janusz Kulon, University of South Wales[125]

In its analysis, NICE suggested the most appropriate place for these tools was likely to be in primary care, helping doctors to triage suspected melanoma for referral to a specialist, though they are also helping to create community diagnostic hubs for community screening.[126,127] NICE also noted that their signal processing and artificial intelligence (AI) capabilities have proven to result in improved accuracy in detecting melanoma versus standard of care dermatoscope examination. Already one of these products, DERM, has been used across NHS pathways to analyze >60,000 cases.[127] However, repeating a common theme seen with digital therapeutics, NICE also said more RCTs and further testing in practice were needed, as well as more testing on rare skin cancers and people with darker skin.

While most available tools for risk-screening are now regulated medical devices that have gained approvals, historically, some were made available to the general population on app stores by providers or their institutions to alert patients to consult a physician. For example, Shriners Hospitals for Children initially released the SpineScreen app in 2017 to help parent's check their child's spine for "possible signs of scoliosis" using their phone's gyroscope to detect curvature when the phone is run along a child's back.[128] However as it has become clearer that apps that process signals from sensors fall under FDA regulation, this app and many others are no longer available to the general public via app stores or have been repurposed as monitoring tools. Other scoliosis assessment apps have recently been given formal 501K clearance by the FDA for monitoring including Momentum Spine, which uses image-based contour sensing and is approved for OTC use, and NSite Scoliosis Assessment App for provider use.[129,130]

Some tests approved by the FDA in this category have also officially been approved for "pre-screening" only (such as Drowzle Pro and SleepCheckRx for Apnea) and are intended to be confirmed by other screening methods. This seems to suggest that digital technologies may fall short of the accuracy of gold-standard screening methods, or concern remains about potential user-error, but are still recognized by the FDA to play a valuable role reaching patients at home.

Other apps and devices in this category may ask patients to conduct performance testing. For instance, risk screening tools used by providers to assess their patients include TALi Detect, a serious game to detect attention difficulties that may link to ADHD, and CognICA a digital test for dementia, where users rapidly identify images as animal or non-animal.[131] A subset of clinically validated health assessments are also made available to consumers through apps available. For instance, in the iPhone Health app, users can take age-appropriate standardized mental health assessments (often used by clinicians) for depression or anxiety and determine if they should seek care.[132]

The ubiquity of smartphones may also be a driving force for the future development of risk screening tools using only a smartphone camera or plugin attachments. Among those under development are the BiliScreen app to detect jaundice from a photograph of the eye, and several other apps to screen for Retinoblastoma (an eye cancer) since using flash photography can cause a milky white color instead of "red-eye" that can be detected.

Clinical decision support tools

An area of keen interest for life sciences companies and other stakeholders has been clinical decision support (CDS) software that inform evidence-based clinical decision making as providers diagnose, treat, or prevent diseases and conditions. Their appeal lies partly due to FDA's guidance that has declared them exempt from regulatory approval if they meet exemption criteria as a CDS, and their ability improve the quality of the diagnostic process and care.

For instance, a CDS used to inform diagnosis (diagnosis support tool) might apply an analytic model to patient-specific information in the medical record — like reported symptoms, family history, demographics and test results — to inform the provider of related evidence based best practices. It might help the provider determine whether the patient should be evaluated via diagnostic testing or recommend running specific diagnostic tests, while allowing the provider to maintain full autonomy in decision making. In practice, a notification might be presented to the provider within workflow while the patient is being examined, alerting him/her of a patient-specific health risk detected in the EHR data, and recommend running specific diagnostic tests.[134] The ONCOassist app, for instance, serves a number of functions including providing access to prognostic scoring systems that use patient data for risk stratification and to predict survival at the time of diagnosis to guide therapeutic decisions.[135] Another notable tool in this space is Face2Gene, which uses AI and facial image-matching like a search-engine to aid in differential diagnosis of rare genetic syndromes.

CDS may be apps for smartphones or tools that plug into clinical workflow systems, many of which are powered by AI analysis of big data. However, to avoid regulatory review they cannot acquire, process, or analyze medical images or signals, as this would make them medical devices. Their purpose is instead to make medical information about a patient or evidence-based best practices and guidelines rapidly available to providers to facilitate diagnostic or treatment decisions for the individual patient. The recommendations can enhance, inform, or influence decision-making but cannot substitute for a provider's judgment… and therefore they must enable the provider to independently review the basis for the recommendations presented rather than have him/her rely on it to make a clinical diagnosis or treatment decision. They often do so by displaying the patient specific variables that contributed to the recommendation with hyperlinks to relevant data within the patient chart to encourage the provider to independently evaluate.[136]

Diagnostic tools

To help overcome challenges in assessing complex diseases, automated digital diagnostics (Dx) and diagnosis aids are being developed that detect and characterize disease and guide clinical decisions.[24,110] Unlike CDS, these regulated devices often analyze medical images and signals and apply predictive AI models to data. Like other health assessment tools, some aid primary care physicians to diagnose patients

with conditions typically seen by specialists (e.g. rare diseases, dermatology) or help them to determine if a patient should be referred to higher levels of care.

Regulatory agencies assess these diagnostics in the same way as their non-digital counterparts,[137] with requirements that their diagnostic accuracy (sensitivity and specificity) must be validated. Some approved devices and diagnostic tests like Cognoa's ASD Diagnosis Aid (CanvasDx) and Sunrise Sleep Disorder Diagnostic Aid have gone through the DeNovo pathway as first-in-class novel technologies,[138] and notably allow patients to be assessed at home. In the case of childhood diseases like autism and ADHD, development of digital tools have been an early area of innovation, offering ways for children to be screened remotely without having to travel to see a specialist and speeding diagnosis since treatment for developmental issues has been linked to better outcomes including higher IQs and better social skills.

Prognostic tools

Finally, predictive and prognostic abilities added on top of digital assessment tools bring additional value. When combined with AI, predictive algorithms or models, digital tools can be used to predict a patient's future course of disease by analyzing biometric and symptom data. They can be used to predict exacerbations, readmissions, poor prognoses, or even predict when patients are coming down with an illness days before symptoms — thereby potentially reducing the spread of contagious disease.[139] They may also be able to predict treatment response early.

AI-enabled predictive abilities are already available on some remote monitoring platforms like Biofourmis' Hospital-at-Home platform which uses the Biovitals Index to predict deterioration, length of stay and readmission. However, digital tools may also be used to support assessment at the point of care. For instance at Cedars Sinai, an AI-based tool under development to assess cardiac CT test images could assess coronary artery plaque buildup and narrowing to predict heart attack risk within five years.[140]

However, not every attempt has proven successful. For instance, an AI-based model to predict sepsis introduced by EPIC in 2022 was later withdrawn when it was shown to miss cases and falsely alert clinicians — an issue which has since been resolved by FDA asserting oversight over such predictive technologies.[141,142] Since then, another model for the prediction and diagnosis of sepsis, Prenosis' Sepsis ImmunoScore, has been approved by the FDA via the DeNovo pathway in April 2024 for use on its Immunix acute care platform.

Digital care using digital diagnostics

Just as therapeutic digital care companies have emerged to create innovative care models using digital therapeutics, some developers of digital diagnostics now offer remote health-assessment-as-a-service. For instance, Easee, a digital diagnostic eye test that assesses visual acuity and both spherical and cylindrical refractive errors is an eye test approved in Europe for use at home where optometrists validate the tests results in a form of digital or blended care.[143]

The creation of such screening and diagnostic "digital-first" care services, where the results provided by a digital tool are subsequently reviewed by a provider, may help patients gain access to care in disease areas where there is a shortage of specialists and reduce the number of patients referred unnecessarily from primary care to specialists, reducing workload.

Even digital tools that are not themselves digital diagnostics like mobile MDDS (Medical Device Data Systems) that store, transfer, convert, or display medical device data, can help accelerate screening and diagnosis by shifting the site of care. Spect, for instance, is a hardware attachment that enables smartphone cameras to take retinal images and is being used to enable remote retinal exams and screening in the community by partnering with DocGo, a mobile health services company.[114]

Digital diagnostic laboratories and orderable tests — integrating into workflow

Some companies that have created AI-based algorithms and models to diagnose disease or detect progression have begun to offer diagnosis- or monitoring-as-a-service. Instead of selling software that needs to live on a health system's or provider's software systems, or even is accessible in the cloud as a separate application that providers would need to learn to use, some companies have become a laboratory where a provider can prescribe device-based services or send captured images or signal data to a "centralized" lab and bill for the application of AI algorithms as a test.

For example, in addition to AliveCor's digital care wraparounds for its OTC devices (KardiaCare), it has also set up AliveCor Labs as an independent diagnostic testing facility (IDTF) that offers monitoring devices with services. Readings from the devices are sent to AliveCor Labs for monitoring, analysis and reporting by certified technicians, and provides end-of-study reports to help providers diagnose conditions or adjust treatment.[145] For developers, this strategy allow the company to bill directly for cardiac monitoring services, including the use of device like KardiaMobile 6L and offer end-to-end diagnostic and monitoring support.[146]

REMOTE PATIENT MONITORING

Tools for remote patient monitoring (RPM), also known as telemonitoring and digital nursing in some countries, are now being used to improve patient care in healthcare settings and in clinical trials. They use a range of methods such as tracking physiologic or behavioral data from sensors and collecting electronic patient reported outcomes (ePROs) via apps, and sometimes provide additional alerts and risk analysis to aid in population management, chronic condition management and enable personalized care (Exhibit 34). While some remote monitoring tools transmit raw data to a healthcare professional for their analysis and interpretation[10] — and may therefore be exempt from regulatory approvals — devices in this category have increasingly added sophisticated analytic and predictive capabilities and are being approved as devices.

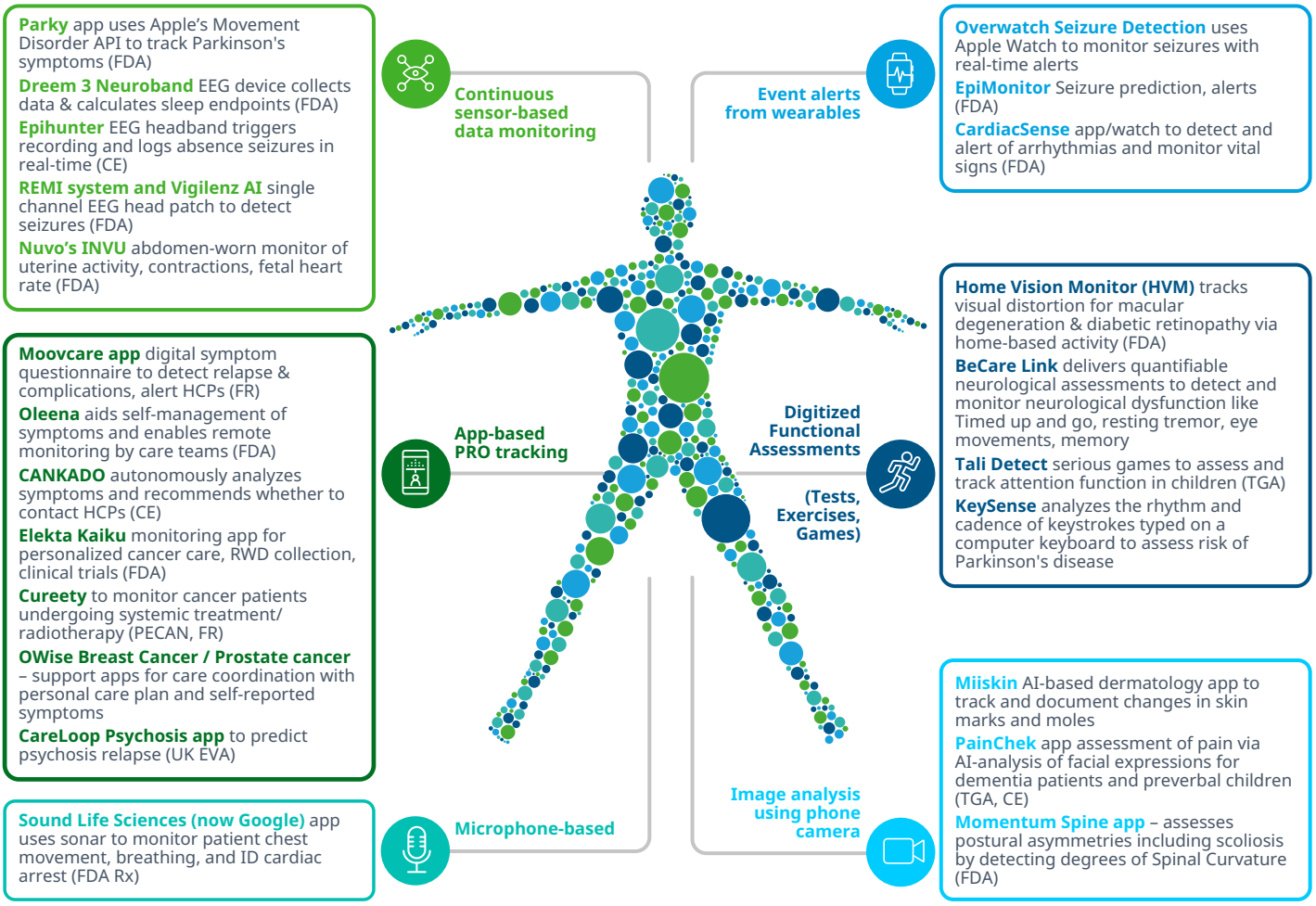
RPM tools typically have two components: a patient-facing app or wearable for data collection, and a provider-facing software platform to present the data for analysis. Although some patient-facing wearables and symptom-tracking apps were originally created solely for self-monitoring and had the ability to share data via email with a provider or caregiver, developers are now adapting many of these to add a provider visualization platform or tool, with formal medical reporting and billing functions.

Monitoring tools have rapidly proven themselves valuable to track patient outcomes in a real-world environment, allowing providers to remotely follow the health of patients with chronic and high-risk conditions, and enable them to adjust and personalize their care. By giving providers and investigators the ability to see whether a patient's disease is worsening or well controlled (i.e., therapy is effective) and sometimes notifying them of exacerbations, they offer to improve patient health outcomes by enabling timely care decisions.

PATIENT MONITORING TOOLS

Patient Monitoring products are intended to accurately monitor patient data related to a diagnosed medical condition and relay this data to healthcare professionals to inform their clinical management of specific diseases, medical conditions, or health outcomes. They use validated methods to collect disease-specific data (biometrics, PROs, digital biomarkers) and typically present them for interpretation by a healthcare professional,[93,10] although multi-feature monitoring solutions are now supplemented by validated and approved algorithms that interpret monitored data, such as to predict patient risk and detect disease.

Exhibit 34: Patient facing mobile apps and sensors for remote patient monitoring



Source: IQVIA AppScript Digital Medicine Database, May 2024; IQVIA Institute, July 2024; Company websites and other public sources.
Notes: Exhibit provides examples within in each category only and is non-exhaustive.

Some leaders in this area started out as digital care providers and created disease management programs using these technologies. However, many now also make their sophisticated platforms available to health systems to use to create their own programs, using their own care teams.

Among patient-facing devices are wearables that providers can prescribe to track patient symptoms or adverse events and monitor disease progression, such as tremor transducers for Parkinson's like NeuroRPM, and the Parky App that tracks tremor and dyskinesia using the Apple Watch.[147] Others use a microphone to pick up breathing or use vocal biomarkers. For instance, the Sound Life sciences (now Google) app uses sonar pulses reflected back to the smartphone microphone to monitor breathing and indicate possible cardiac arrest — potentially useful for patients with respiratory disorders or congestive heart failure.

Apps collecting ePROs or otherwise tracking patient symptoms are on the other end of the spectrum, lacking the use of sensor-based devices but similarly informing providers of changes in patient outcomes. Among these are some software-based medical devices for patient remote monitoring and symptom management such as Moovcare, Cankado Pro-React Onco, and Oleena, which diary or track the emergence and severity of symptoms

in cancer patients with the intent of guiding care team interaction.[148] Some like Oleena may also close the loop to provide personalized symptom recommendations based on data that providers are invited to input.[149]

The proliferation of such tools for remote monitoring has spurred the creation of accelerated reimbursement pathways for remote patient monitoring tools like Germany's Digitale Pflegeanwendungen (DiPA) pathway for "nursing applications" and France's PECAN (Prise en charge anticipée) pathway. These solutions are likely to benefit from the creation of these new and accelerated pathways, but to do so they must demonstrate health benefits such as improved patient health outcomes.

Platforms for patient management and population health

Developers are increasingly combining RPM tools like wearables and symptom-tracking apps into broader clinical "platform" solutions that have provider-facing portals for clinicians to monitor and manage their patient populations and triage patients in greatest need of care adjustments. Many of these platforms use sophisticated algorithms and AI capabilities to provide clinical decision support, dose management, offer therapeutic guidance, and sometimes provide alerts or customized recommendations when patient values or patient-reported outcomes fall out of a specified range. Diagnostic and prognostic algorithms also allow provider solutions to span potential uses.

As increasingly sophisticated RPM platforms are built, this has given rise to new emerging digital care segments (and terminology) such as Virtual Wards or Hospital-at-Home programs (Exhibit 35) which typically conduct multi-parameter ambulatory monitoring of vital-signs using mobile medical grade devices and are combined with rounding medical staff as a form of digital care. Data from these solutions are also being integrated into EHRs (like EPIC), enabling clinical platforms to pull information from patient records and feed new data back holistically to close the care loop. Some of these segments are also gaining endorsements by payers and are likely to gradually become standard of care. For instance, in October 2023 NICE in the United Kingdom issued an EVA guidance recommending virtual ward platform technologies for acute respiratory infections.[150]

Such physician platforms are a notable focus of solution-building, with newer players:

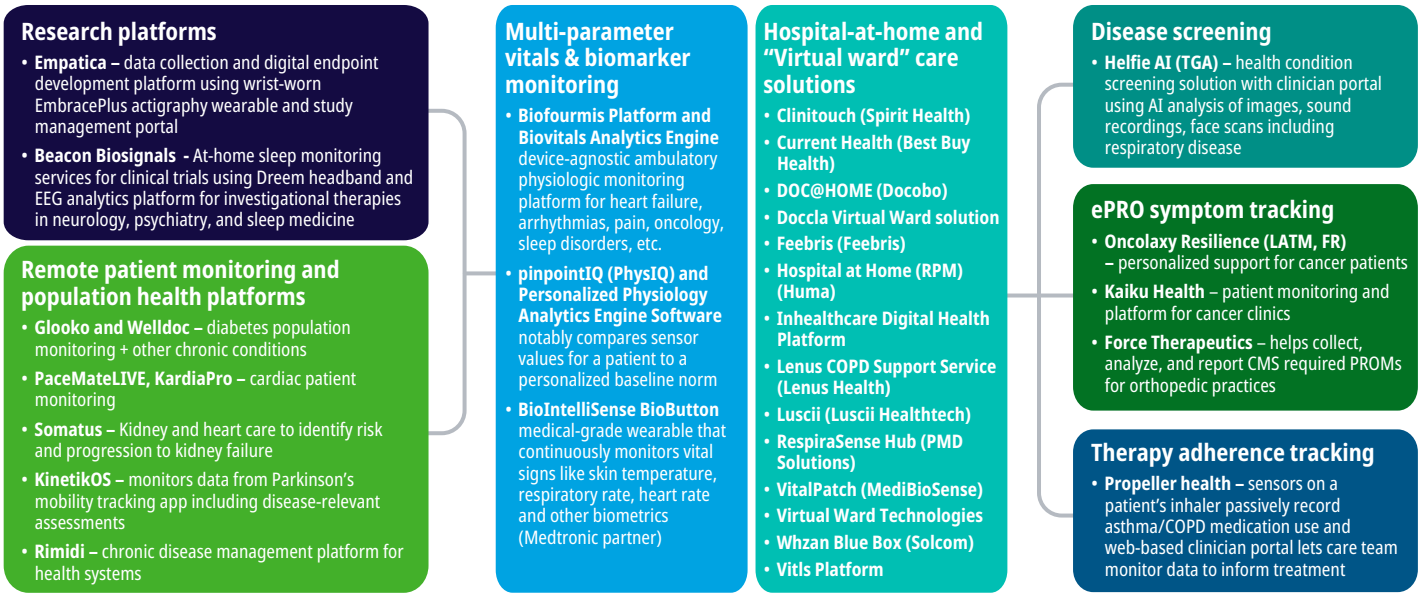
- Creating diagnosis-to-treatment platforms for a specific health condition that may act as closed-loop solutions. For instance, developers have been acquiring sets of digital tools to screen for, monitor and treat a single issue like poor sleep (e.g. SleepUp, Nox Health) or digestive health (Mahana Therapeutics, now reported to be insolvent)[151,152]
- Creating cross-therapy area monitoring platforms like hospital-at-home/ virtual ward solutions by amassing tools to monitor vital signs, biomarkers, COAs
- Building platforms for specific provider types like a "neurology platform" for Neurologists (Neuroventis — e.g. epilepsy, migraine, etc.) by bringing together innovative point solutions

Continuous glucose monitors available to consumers

Innovation in health monitoring devices has also continued in the patient self-monitoring space. With consumer-grade wearable devices gaining adoption, some companies with medical-grade monitoring devices are now moving into the consumer market, developing OTC versions of their devices for lifestyle optimization and wellness. Adaptation of medical-grade devices for use in the nascent wellness tracking market is a trend likely to make the use of digital health wearables more meaningful and help elevate the trust in these technologies.

For instance, in the past few years, continuous glucose monitoring (CGM) systems, which were primarily developed for patients with diabetes mellitus, began to be used off-label by providers for wellness, fitness and prevention in healthy individuals. These include applications in sports to optimize nutritional strategies pre-, during, and post-exercise, in digital care for nutrition helping users understand how daily habits affect glucose metabolism, and in CGM-assisted weight management to confirm achievement of glucose target levels following GLP-1 initiation 15300

Exhibit 35: Examples of remote patient monitoring (RPM) platforms and solutions



Source: IQVIA Institute, Nov 2024.
Notes: Shows examples only within each category. Many companies active within one segment also have product offerings in other segments. Electronic patient-reported outcome (ePRO).

Seeing the popularity of digital care providers in the nutrition and "tech-enabled weight loss" space such as ZOE, Zone.health, and glucare.health in Dubai, manufacturers of CGMs saw an opportunity to broaden their indication to prediabetic and at-risk patients for early detection of abnormal glucose regulation or even to healthy populations in the context of exercise programs.[153] Both Dexcom and Abbott[154] pursued broader applications for their CGM platforms and gained approval this year in the U.K. and U.S. for new OTC consumer-friendly sensors: Dexcom's Stelo and Abbott's Lingo (able to sense glucose, ketones, alcohol and lactate) and Libre Rio Biowearables, as counterparts to their medical grade Dexcom G7 and Freestyle Libre, respectively.[155,156]

Lingo, for instance, with its approval extending to healthy consumers trying to improve their health and wellness, has been made available in the U.K. and elsewhere with an optional digital coaching component (HelloLingo) to help guide lifestyle changes to eating and drinking habits and manage weight through data.[157] In addition to aiding in lifestyle change, users tracking glucose levels with CGMs have also shown greater compliance with obesity medicines.[158]

Conversely, the addition of medical-grade sensors to consumer products is also occurring, making in-home health and chronic condition management increasingly a part of daily life. For instance, a smart scale by Withings, the"Body Scan Connected Health Station," was cleared by the FDA in 2023 to detect atrial fibrillation using a six-lead ECG and also sensors to track skin conductance and sweat gland activity in the feet and provide daily assessment of small nerve activity, making it able to detect signs of peripheral neuropathy complications in diabetes.[159]

Device use for patient safety, surveillance, and REMS

As clinicians and drug developers become more comfortable with the ability of wearable digital health sensors to yield actionable clinical-grade information, this has opened avenues for the use of digital monitoring devices to guard against health exacerbations in clinical trials and beyond to potentially fulfill post-marketing obligations and surveillance requirements under REMS (Risk Evaluation and Mitigation Strategy) drug safety programs.[160]

In recent years, drugs with higher risk profiles have been able to come to market by offsetting the risk of adverse events by meeting regulatory requirements

for REMS data collection and patient monitoring to assure safe use. Remote patient monitoring solutions, including Hospital-at-Home virtual wards, may make life significantly easier for patients by allowing them to be closely monitored on an outpatient basis.

For instance, in oncology, as investment continues in promising cell and gene therapies such as CAR-T, where patient post-surgical monitoring may need to continue for weeks to catch the emergence of cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS), etc., digital health has emerged as a route to shift the site of post-surgical monitoring out of the hospital and perhaps to outpatient and home-based settings. Wearable devices that monitor vital signs like blood pressure, oxygen levels, and temperature, have been shown to detect cytokine release syndrome and fevers several hours earlier than standard care after CAR-T therapy in multiple myeloma, making outpatient release more feasible post-infusion, and potentially functioning as early warning systems for adverse events or solutions to fulfill obligations under REMS.[162,163]

DEVICE USE IN CLINICAL TRIALS

Within clinical trials, continuous monitoring of vitals is also expected to increase over time, with regulatory agencies beginning to suggest it be used to assess and reduce health risks of investigational drugs. This would allow identified risks to be managed with appropriate label warnings. For instance, in draft guidance for clinical trials, the FDA recommended measurement of ambulatory blood pressure (ABPM) to assess the effects of drugs intended for long-term or chronic use on blood pressure, as prolonged use of drugs that elevate blood pressure has been associated with increased risk of cardiovascular events.[164] In this guidance, the FDA noted that ABPM provides more accurate measurements of blood pressure effects throughout the day and can detect increased nocturnal blood pressure especially systolic blood pressure, which has recently been recognized as an important predictor of risk. Other benefits mentioned by the FDA were that it is more precise and capable of detecting small but potentially relevant blood pressure effects (3mmHg increase in 24-hour average systolic blood pressure); that its ability to collect multiple measurements over a 24-hour period is more informative than assessment at a single time point; and its use reduces investigator bias where BP values may be rounded up or down.

During the pandemic, life sciences companies sought to mitigate the risk to their clinical development programs through fully decentralized and hybrid trials. Driven in part by higher costs of home-based nursing visits as well as preferences of patients post-COVID to return to in-clinic visits, companies have gradually shifted back to site-based studies but have retained some of the most helpful elements of decentralized trials such as the use of technology.

Monitoring technologies that emerged partly to enable remote care within trials have continued to grow in use. Ambulatory monitoring of patient vitals and outcomes are performed using clinical grade wearables and other devices, and apps collect ePROs and adverse event data within the bounds of traditional and hybrid trials alike. Use of wearable technologies in clinical development trials is also increasing since analysis of their remotely collected data can lead to the development of endpoints (new digital biomarkers/sensor-based COAs) and yield new insights. Research platforms are used to simplify data collection from these tools and related workflow.

As the ability to conduct health assessments and gather digital endpoints using clinical grade wearables continue to grow, these technologies deliver similar benefits to decentralized trials. This notably includes the ability to reduce the number of clinic visits and conduct measurements without the need for implanted or complicated devices, which is likely to reduce the burden of participating in clinical trials on participants, and potentially reduce dropout rates. Additionally, because more continuous data collection can yield more precise endpoints, primary endpoints may be met more rapidly thus resulting in better, faster, cheaper trials.

While the addition of remote assessment tools to clinical trials is the most common, hybrid and decentralized trials continue to find a niche in certain therapy areas. For instance, these continue in rare diseases or other conditions where patients might have comorbidities or mobility challenges, or where trial burden is often significant such as in obesity, Alzheimer's, multiple sclerosis, epilepsy, gout and other rheumatic conditions. In these areas decentralized trials still offer to improve recruitment and expand the patient pool when it is hard to find participants.

DEVICE STRATEGY IN DRUG DEVELOPMENT TRIALS

Devices are used in clinical trials for three key reasons all of which relate to evidence generation. They are used in drug development to collect data on the safety and efficacy of a drug, in device development to gather additional data to validate performance of the device itself or the digital biomarkers and measures it collects, or as a means to create and validate new biomarkers and measures related to a drug. In the final case, device and AI/ML teams may collaborate to create new biomarkers for life sciences companies that can be tracked in clinical trials. They identify a sensor to track the data, pull data from that sensor for analysis, and determine ways to track the intended measure of the safety and efficacy of a drug.

Increasingly, as companies become more adept with using digital data collection to shed new light on drug benefits, they are starting early in clinical development to add extra sensor devices to their trials. For instance, in Phase I and II they may include new devices to gather data or validate newly created measures, in essence building a molecule-to-market digital strategy that overlays their drug trials. They may run a device proof-of-concept POC trial in Phase I with a wearable to assess whether a patient is comfortably able to wear the device and assess its performance, and then in Phase II, continue with that device, exploring multiple measures to determine if there is a link to health outcomes or gather data for building evidence. Ultimately, this may enable their use as digital endpoints in Phase III pivotal trials.

> *"Now we see companies bringing their device strategy early in drug development trials as they go molecule-to-market and integrating that into their development plan. They build a device into Phase I to experiment early, test it, and gather data to determine if the customer can wear the device, for instance and then progress into Phase II pulling through the device… using early trials as their experiment to see if there is a link to health outcomes and see if it can replace gold standard measures."*
>
> *— IQVIA Connected Devices Expert*

Uptake and use of digital health technologies

+ **Patients and health systems are increasingly relying on innovative digital solutions to close care gaps across the patient journey.**
+ **The use of digital diagnostics and other tools for remote patient assessment and monitoring is growing rapidly along with medication management apps for diabetes.**
+ **Consumer apps for obesity and weight management have gained significant use, with around 1.5 million installs on average, although mental health apps are more widely available and have collectively gained 30% more installs.**
+ **Digital therapeutics — software to treat or alleviate disease — are gaining traction more rapidly in some geographies than others as regulatory and reimbursement pathways proliferate and their clinical utility is recognized.**
+ **Nearly all developers that entered early into the U.S. market with pharmacy-dispensed digital therapeutic have faced commercial challenges and some are no longer in business today. However, the new cohort of PDTs entering a more mature market may fare better.**
+ **In Germany, where 56 digital therapeutics are currently eligible for reimbursement and the DiGA directory doubles as a centralized repository of clinical evidence on each, prescription volume has been increasing overall.**
+ **In the United States, provider billing for remote physiological monitoring increased five-fold in the past three years from May 2020 to September 2023, and new remote therapeutic monitoring codes first issued in January 2022 nearly quadrupled in the year ending September 2023.**
+ **Devices and digital tools to evaluate, monitor and treat patients are being used across a broad range of diseases, but notably for high-risk chronic conditions (hypertension, diabetes, heart failure) and sleep disorders.**
+ **Musculoskeletal digital care solutions are gaining traction as employer benefit offerings, with charged medical claims growing.**

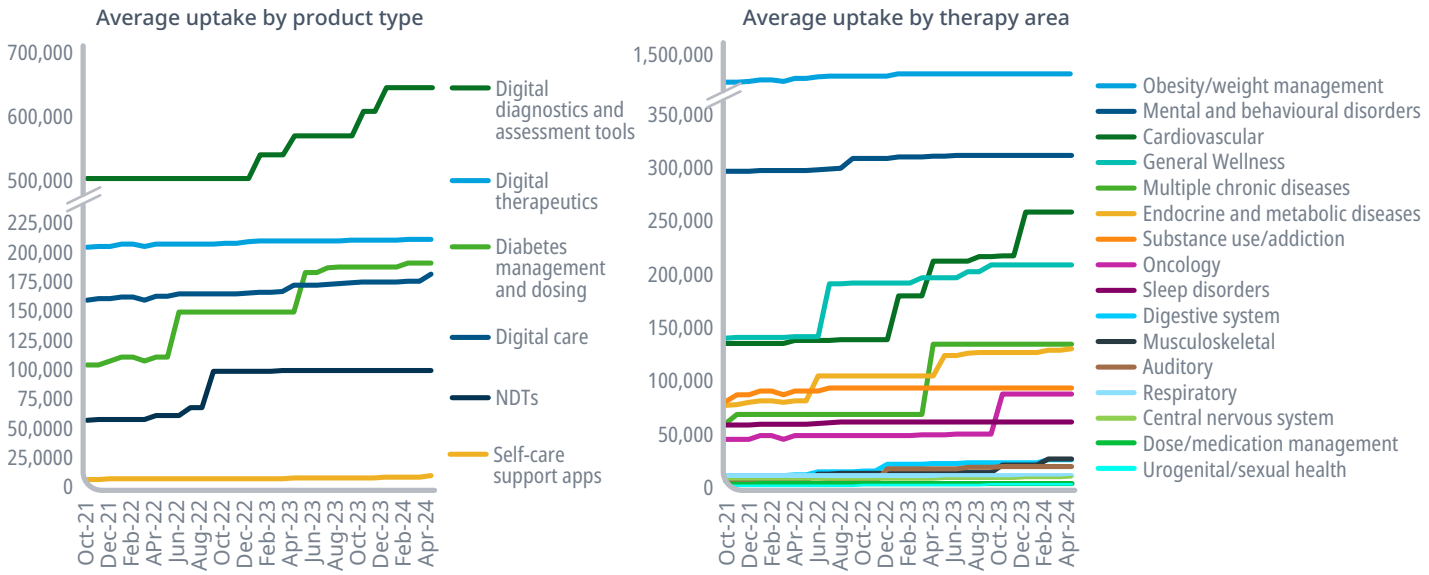
Like medicines, the use of digital technologies can be examined in various ways depending on data showing how they are prescribed, dispensed, distributed, billed, and reimbursed. This data shows that patients and health systems are increasingly relying on innovative digital solutions to close care gaps across the patient journey, with the most rapid growth seen in the use of tools for remote patient assessment and monitoring. For digital therapeutics, growth can be observed in Germany, while the commercialization challenges in the United States have contributed to the insolvency of many companies.

APP INSTALLATION ACROSS PRODUCT TYPES

Regardless of the geographies they serve and their health purposes, both standalone apps and those linked to wearables or other devices may be dispensed through consumer app stores including the Apple Store and Google Play. Google Play provides data on app installation in the form of ranges. Examining this data provides a way to compare the adoption of various apps, and by grouping apps by product type and therapy area, it also provides a way to compare the success of various segments (Exhibit 36).

Examining the average installs gained collectively by various product types helps shows the relative uptake and success that each has achieved over time. Health assessment tools like digital diagnostics, symptom checking chatbots and measurement tools for remote monitoring — like Ada, Alleye, Canvas Dx, FibriCheck,

Exhibit 36: Installs as a measure of uptake for digital health apps by product type and therapy area (Google Play)



Source: IQVIA AppScript Digital Health Database, May 8, 2024.

Notes: Displays apps from the AppScript Catalog and install data shown is from the Google Play app store only. Apple Store install data is unavailable, and therefore total average installs per product is understated and exhibit should be considered a view of directional growth in each segment. Uses the "Installs min" value per app at each timepoint assessed, which is the lower value of each install band range and may therefore underestimate uptake speed. Due to install data being available only at the install band level, jumps are seen when individual products advance into the next band. Includes only apps in the app store at each time point and therefore apps removed from the store may result in visible drops or increases in the average.

Fitbit ECG App, Kardia, Lindera Mobility Analysis, SkinVision and others — have collectively achieved the highest average installs, indicating that where patients are given the ability to assess their health using OTC or prescribed devices to check on their health concerns, there may be opportunity for rapid adoption. This segment has also continued to grow, indicating strong commercial opportunities. Total installs for this category however (not shown), which speak to the prevalence of each product type globally, lag digital therapeutics and care, similarly suggesting there is whitespace in this emerging area.

CAVEATS ON APP DATA AND EXHIBIT 36

To better understand this exhibit showing average installs as a measure of uptake, it is worth noting that since the data provided by Google Play is in the form of an install range rather than discrete values, a line will jump if a product within the set advances into the next installation range and drop when a product is removed from the app store. Also, since ranges widen as a product grows (e.g. 1–5 versus 10,000–50,000) they provide greater detail for apps at the beginning of their adoption journey than at later phases, therefore making lines smoother for sets of recently-launched solutions. Finally, values will underrepresent total global installs since some apps are available on both platforms but only Google Play makes installation data available. Furthermore, data in this exhibit includes only a select set of apps within the AppScript Catalog available on Google Play. It is also worth noting that some apps will be counted as installed even if they have been rapidly uninstalled by a user, for instance where a downloaded product was found to be gated and inaccessible and then deleted.

Some of the digital therapeutic apps available by prescription, like app-based DiGAs, are ultimately downloaded for use from app stores. These PDTs have seen the next highest level of adoption on average after digital assessment tools, however their average uptake is only one third of that seen by digital diagnostics and assessment tools. Growth has also been more muted in recent years, and it appears these stand to be outpaced by apps for outpatient therapeutic dosing and management of diabetes, which are growing more rapidly, and even potentially by apps that support digital care, where providers have already made a decision to incorporate these tools into their practice and physician adoption is less of an issue. As an example of uptake in disease assessment space, Dexcom's Stelo, a wearable OTC glucose biosensor-linked app for prediabetics, which was released in August after this analysis was performed, gained over 5,000 installs in the month after its release and had over 10,000 downloads a month later.[165]

Finally, standalone NDT apps that help patient manage their health and do not require a prescription have also been growing, suggesting that it may be more important for developers to build evidence of efficacy and cost savings than to gain approval if they fall in an exempt category… although this category admittedly appears to be shrinking or moving into digital care.

Perhaps not surprisingly, obesity and other weight management apps have also gained significant use, with around 1.5 million installs on average, although total installs, which speaks to the prevalence of each product type globally, show that mental health apps have collectively gained around 30% more installs than the obesity category. Notable growth and adoption has also been seen by cardiovascular apps and those for chronic and endocrine diseases like diabetes. There has been rapid growth among new entrants in the musculoskeletal, digestive disease, and auditory space (likely tinnitus), and notably steady but slow growth among central nervous system apps.

PHARMACY DISPENSING OF DTx IN THE UNITED STATES

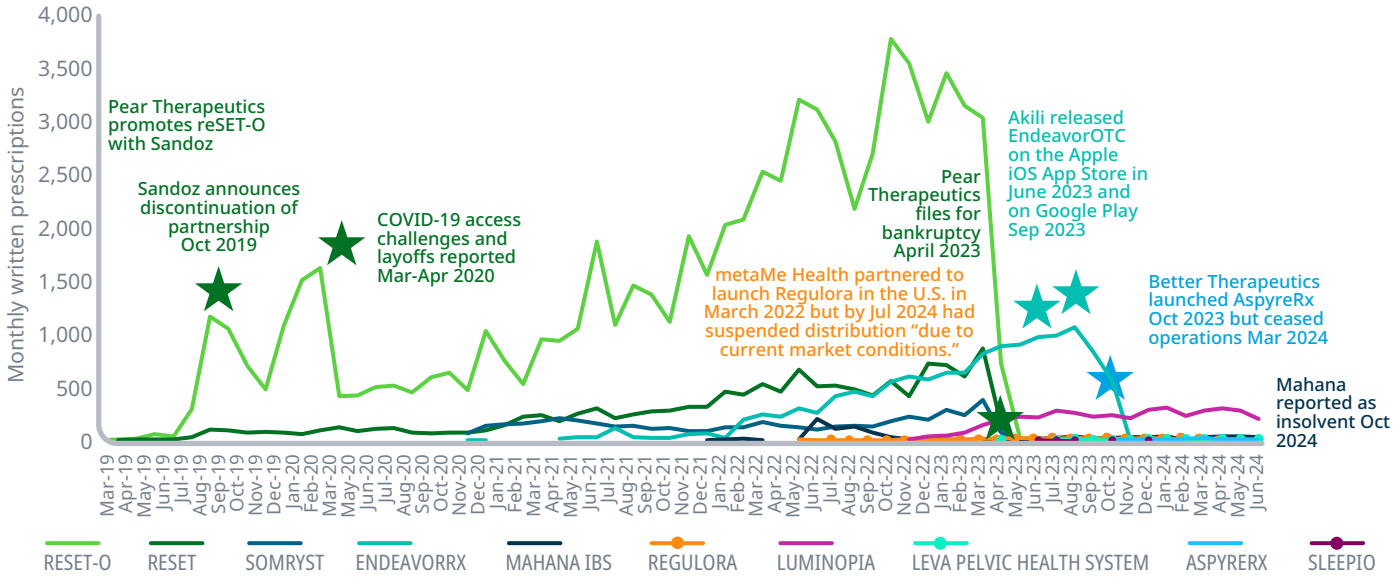
Many digital product developers that entered the U.S. market early have faced commercial challenges, failing to earn enough money from their initial go-to-market strategy, and some are no longer in business today. This has been true for nearly all companies that marketed initially as a prescription DTx through the pharmacy channel in the U.S., which faced sluggish adoption or reimbursement, and one among them, EndeavorRx, is shifting to OTC distribution to enable broader consumer-driven adoption (Exhibit 37). While this data trend should be considered directional due to unknown capture in this unique market, where single-pharmacy dispensing is the norm, it seems apparent that little PDT prescription volume is now flowing through this channel. However, new PDTs are now emerging that may fare better in the marketplace, including Luminopia, Leva Pelvic Health System, SleepioRx and, more recently, Rejoyn was launched to treat Major Depressive Disorder (MDD). To date though, to date the number of prescriptions for these newer PDTs remains very low.

PRESCRIBING TRENDS FOR DTx IN GERMANY

Despite tepid uptake for PDTs in the U.S., in Germany, where there are quite a few approved DTx eligible for reimbursement via listing on the DiGA directory (a centralized repository that includes clinical evidence summaries), prescription volume for digital therapeutics has been increasing overall, the largest being therapies for pain, tinnitus, obesity, depression and impotence. Among newer apps, Oviva for obesity, NeuroNation Med for mild cognitive impairment and Mebix for Type 2 diabetes are notably growing (Exhibit 38, which displays unprojected data representing around 4.5% total use, see Methodology)

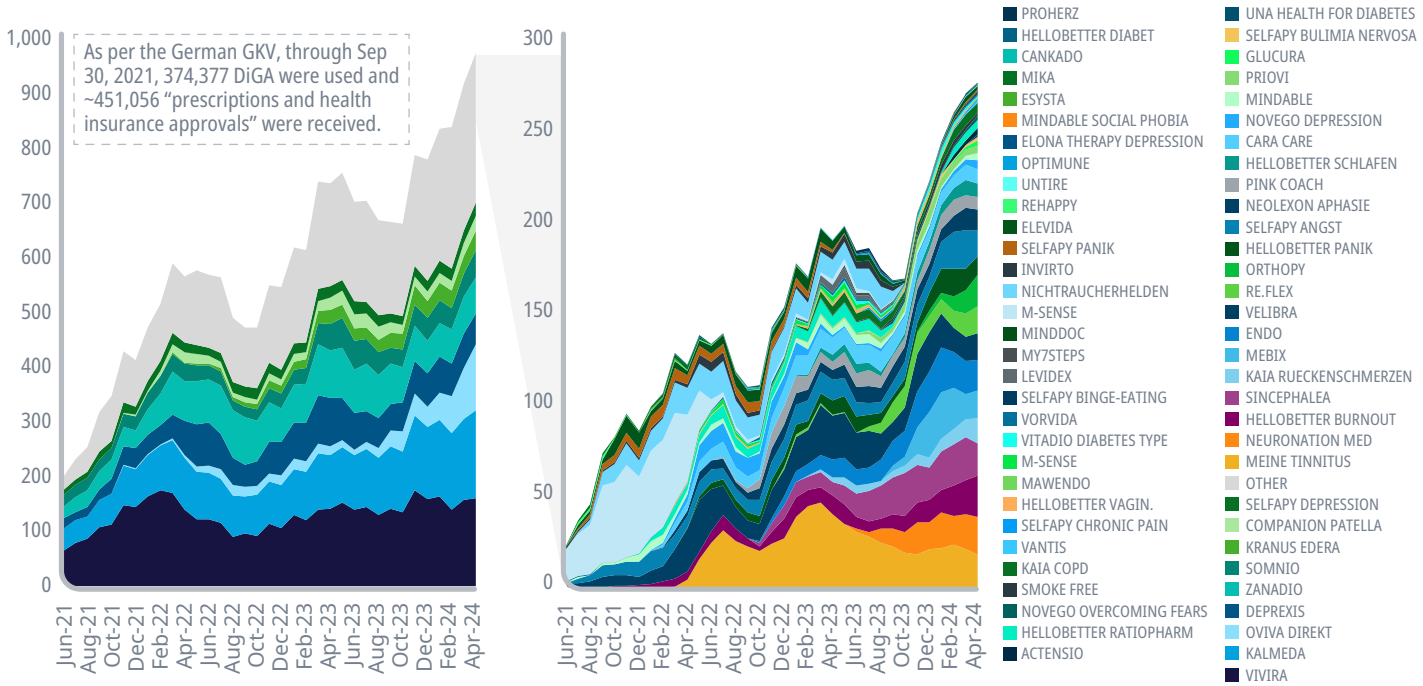
The German government-regulated public health insurance system known as the Gesetzliche Krankenversicherung or GKV reports that from September 2020 to through Sep 30, 2021, 374,000 DiGA were used by insured persons. They also report

Exhibit 37: Number of monthly prescriptions for pharmacy-dispensed digital therapeutics written in the United States



Source: IQVIA Institute, Aug 2024; IQVIA Longitudinal Prescription Data, data through week of Feb 2024 extracted Apr 11, 2024.
Notes: Includes all "Digital Therapy Applications." IQVIA likely has limited capture of this data. MetaMe reports they have suspended U.S. marketing of Regulora "due to current market conditions" but continues to sell in Canada [website accessed Jul 15, 2024].

Exhibit 38: Prescription trend for DiGA DTx in Germany, rolling 3-month average, unprojected



Source: IQVIA Institute, Aug 2024. IQVIA Disease Analyzer, unprojected EMR practice software data, period ending Apr 2024.
Notes: Trends is directional as counts are unprojected and is coverage is estimated at [illegible] patients directly from health insurers with proof of diagnosis, which is allowed in Germany. Based on recent GKV use data, the displayed prescription values likely reflect 4.5% of actual users, or 3.8% of all written prescriptions plus insurance approvals as not all prescribed patients go on to use the product. Market numbers are therefore likely ~22x the values shown here.

5% of providers and produce furniture like tables and chair

this value as 83% of "all medical or psychotherapeutic prescriptions and health insurance approvals received by the health insurance companies," indicating that not all patients deemed eligible to use a digital therapeutic went on to do so. This means that around 451,056 "prescriptions and health insurance approvals" were received during this period.[34] Extrapolating from IQVIA's Disease Analyzer (EMR practice software data), it seems likely that this number is now closer to 587,000 prescriptions through September 2024, though updated figures will soon be released by the GKV.

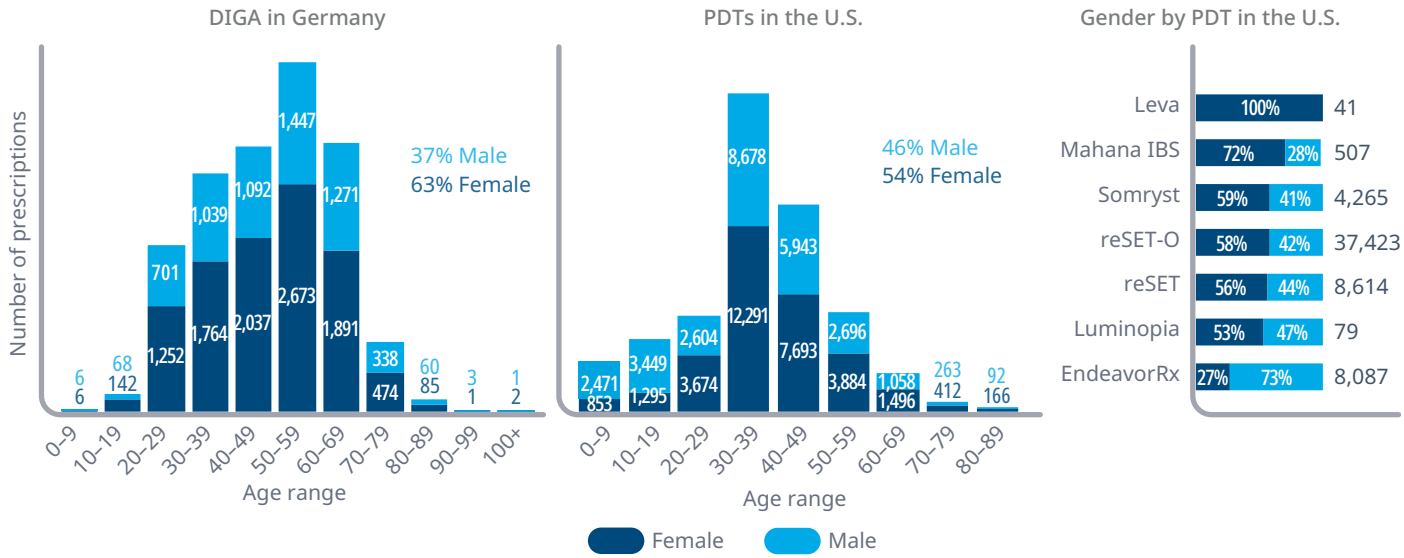
Still, one might argue that uptake in Germany continues to be slow, in part due to continued poor integration into existing supply pathways, and limited provider adoption.[34] The GKV itself has made the argument that the DiGA fast-track procedure itself, while speeding their route to market, may have had the counter-effect of reducing physician interest due to its low initial evidence requirement. Weak data at release for some apps may have failed to convince doctors of their benefit.[34]

DEMOGRAPHICS OF TREATED PATIENTS

As with any therapeutic, the age and gender of the population it serves ties to the population affected by the condition. However as digital therapeutics are still in a phase of early adoption, other factors like patient interest, willingness to try new modalities, digital savviness and preferences may also influence adoption. Notably, both in the United States and in Germany, a greater number of women than men have used DTx. And, age utilization also differs between the two countries, with use in the United States mostly by younger individuals age 30–50 and use in Germany spanning age ranges and greater use in older populations 50+ (Exhibit 39) and an average age of 45 years according to the GKV.[34]

This may be due, in part to product mix. For instance, in Germany there are DTx available for cardiovascular conditions such as proHerz, which treats heart failure, and has an average age among its users of 66. On the other end of the spectrum, a DiGA for sexual health, HelloBetter Vaginismus for anxiety, pain and discomfort related to

Exhibit 39: Use of prescription digital therapeutics by gender, age and geography



Source: Disease Analyzer, April 2024. IQVIA Rx Data, April 2024.
Note: Prescription digital therapeutics (PDTs). IQVIA likely has limited capture of this data. Includes only Pharmacy distributed PDTs in the U.S. from April 2019-Feb 2024. DIGA data covers all time periods since the DIGA directory was launched and excludes direct patient requests for DIGA coverage from payers based on diagnosis.

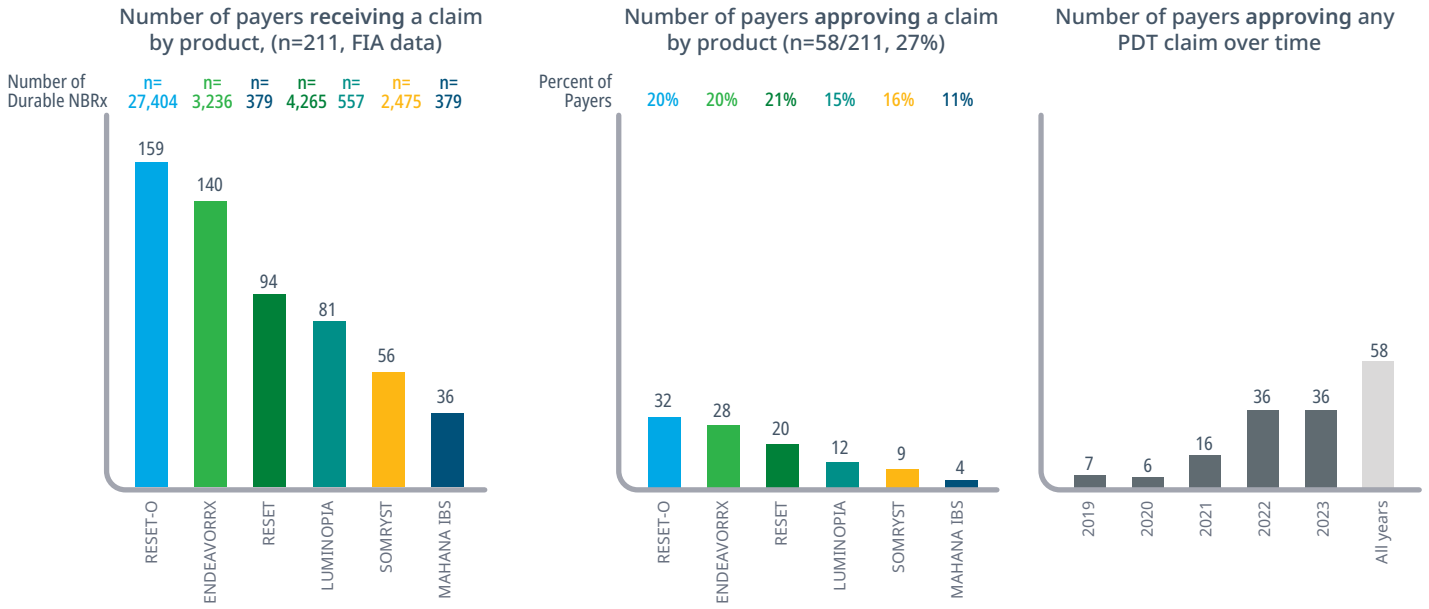
vaginal penetration, had the lowest average age of 29, while in the U.S. the EndeavorRx product to treat ADHD, is useful for young children. Differences seen by gender are also in part due to the products available in each market (right chart), since ADHD affects males more so than females, and IBS and urinary incontinence (Mahana IBS and Leva, respectively) affect women, however, the predominant use by women in Germany spans some conditions where a gender link is less common.

REIMBURSEMENT OF DTx IN THE UNITED STATES

In the U.S. where there is only a low level of prescribing, there is an even lower level of reimbursement. Despite several payers adding reimbursement of prescribed DTx beginning in 2022 (e.g. as Highmark did for FDA-cleared digital therapeutics), only 27% (n=58) of the ~211 payers (including self-insured employers) that received new prescription claims for pharmacy-dispensed digital therapeutics have approved one or more of them, with products for addiction (Reset and Reset-O) and ADHD (EndeavorRx) seeing greater traction. However, as a positive trend, the number of payers reimbursing DTx has grown over time, indicating that not only the largest of payers have begun to extend coverage, and some payers and PBMs have begun to create special plans to appeal to employers that include DTx (Exhibit 40).

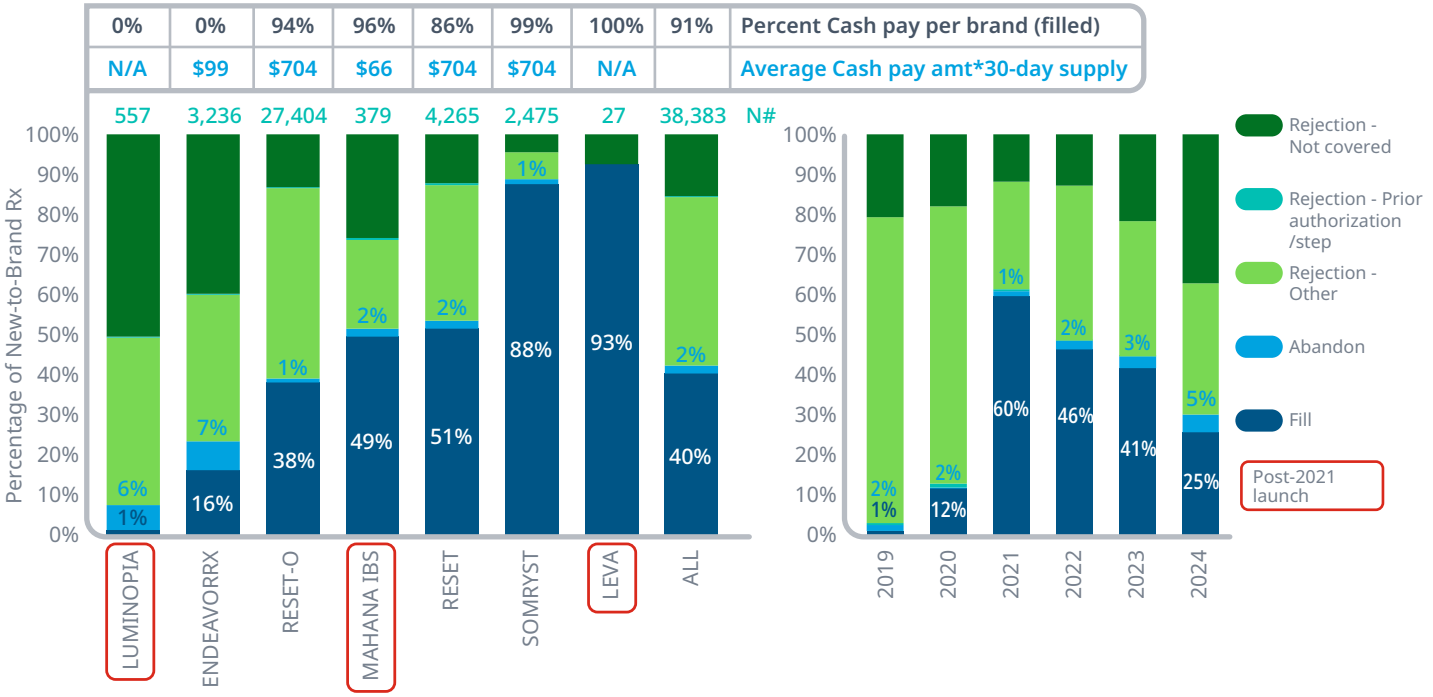
However, such poor reimbursement means that patients in the United States wind up paying cash for 91% of all filled prescriptions of pharmacy-dispensed PDTs. Fill rates have also been declining since 2021 and more prescriptions have been abandoned (Exhibit 41). Although it is too early to tell, even products launched more recently like Mahana IBS, Luminopia and Leva have seen low prescribing and are almost exclusively cash pay for those filled. This has not surprisingly contributed to Mahana's recent insolvency,[166] and earlier to the bankruptcy of Pear Therapeutics. Additionally, although newer players like Leva, Mahana IBS and Aspyrx saw fill rates increasing in the past two year, which may indicate growth in consumer demand, any enthusiasm would be tempered by the fact that two of their developers are now defunct due to lack of profitability.

Exhibit 40: Payers receiving versus approving a new-to-brand prescription for pharmacy-dispensed prescription digital therapeutics (PDTs)



Source: IQVIA Institute, Aug 2024; IQVIA Formulary Impact Analyzer data ending May 1, 2024.
Notes: Payers include distinct employers. Leva and AspyreRx were excluded on left chart due to low claims counts. Charts restricted to durable claims, which are assessed 30-days after the initial claim was prescribed for New-to-Brand (NBRx) prescriptions of pharmacy-dispensed PDTs

Exhibit 41: Fill rates for new prescriptions of pharmacy-dispensed prescription digital therapeutics (PDTs)



Source: IQVIA Institute, Aug 2024; IQVIA Formulary Impact Analyzer data ending May 1, 2024 (right chart). Notes: AspyreRx excluded as individual products due to low claims counts as of May but included in 'All'. Charts restricted to durable claims, which are assessed 30-days after the initial claim was prescribed. *Only includes data on abandoned prescriptions as none were filled via cash pay.

BILLING FOR DIGITAL CARE IN THE UNITED STATES

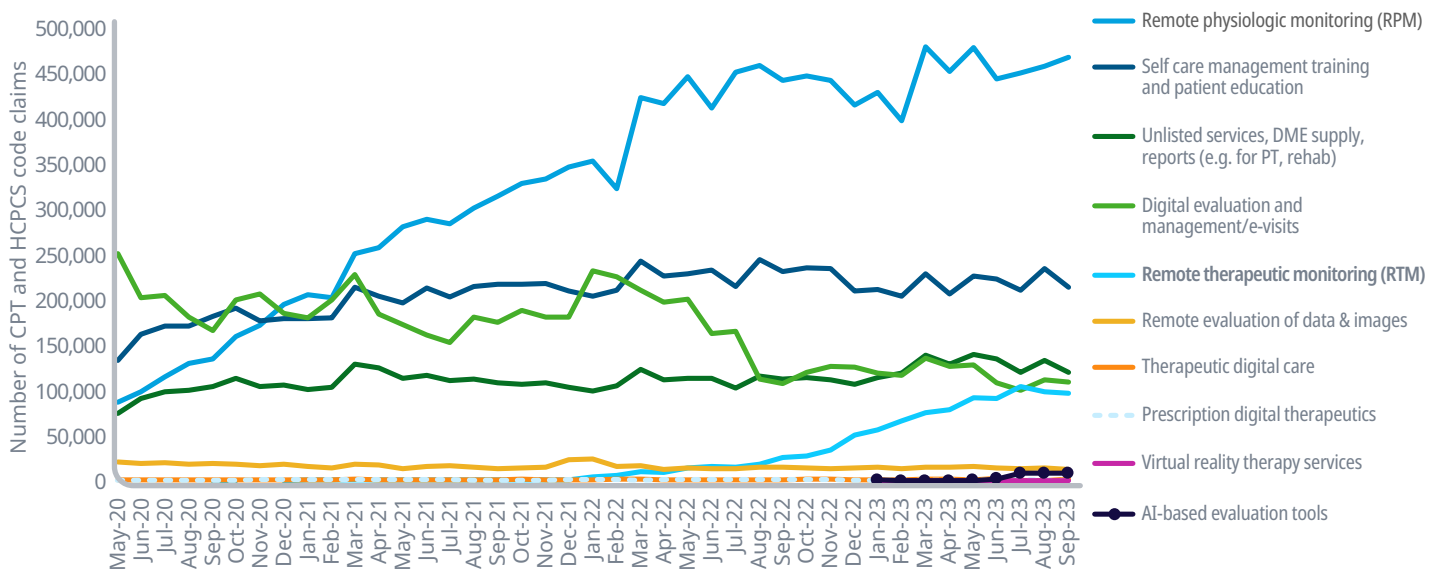
In the U.S., Centers for Medicare & Medicaid Services' (CMS) has gradually created billing codes that aid in the reimbursement of digital tools, and services providers perform relating to them. These now span digital devices for remote evaluation, monitoring, medication management, digital care and the use of DTx for therapy.

For instance, in January 2022, it published a new set of Current Procedural Terminology Codes (CPT) codes for remote therapeutic monitoring (RTM), expanding on existing codes for remote physiological monitoring (RPM). Together, these codes have created additional routes for providers to bill and be paid for time and services linked to remote patient monitoring using a variety of devices that assess disease including software-based tools.

While there has been gradual growth in medical claims for other product types, physician claims for remote monitoring have increased rapidly since new codes were released, increasing product opportunities for sensor-based devices and CBT digital therapeutics that also provide patient reporting of symptoms and medication adherence (Exhibit 42). From the period shown from May 2020 to September 2023, monthly claims from remote physiological monitoring increased 540% from 86,294 to 466,774 claims (and at a 136% CAGR the past 2 years), while use of remote therapeutic monitoring (RTM) codes (including remote monitoring of patients using CBT-based digital therapeutics) quadrupled, growing 379% in the year ending September 2023.

While RTM codes were initially purposed for reimbursing providers for monitoring patients with respiratory or musculoskeletal conditions, along with medication adherence, in 2023 cognitive based therapy was added. This has allowed providers to now bill for their time spent and digital solutions to remotely monitoring patients undergoing cognitive behavioral therapy, such those that capture and share non-physiological patient self-reported measures of cognitive and social function. This expansion, along with more qualified health professionals who can utilize them, could further widen adoption, and incentivize providers use of digital

Exhibit 42: Number of monthly CPT and HCPCS code claims by use type



Source: IQVIA Institute, Apr 2024; IQVIA Medical Claims Data, month ending Feb 2024.
Therapeutic digital care includes amblyopia, diabetes, and musculoskeletal programs for which codes are available.

solutions, though growth in the use of RTM codes to date has been driven predominantly by musculoskeletal condition monitoring.

Codes have also been created to reimburse providers for employing therapeutic digital tools within their practice (Therapeutic Digital Care), including to treat amblyopia and supporting diabetes, and musculoskeletal rehabilitation programs (PT/OT). Providers may be reimbursed for helping patients get started with the device, supervising care and interpreting data, etc. Other codes have also been added to CMS' Healthcare Common Procedure Coding System (HCPCS) to reimburse for the use of digital devices themselves including digital therapeutics for cognitive and behavioral therapy and visual therapy (such as those for amblyopia like Luminopia) and virtual reality CBT devices like RelieVRx).

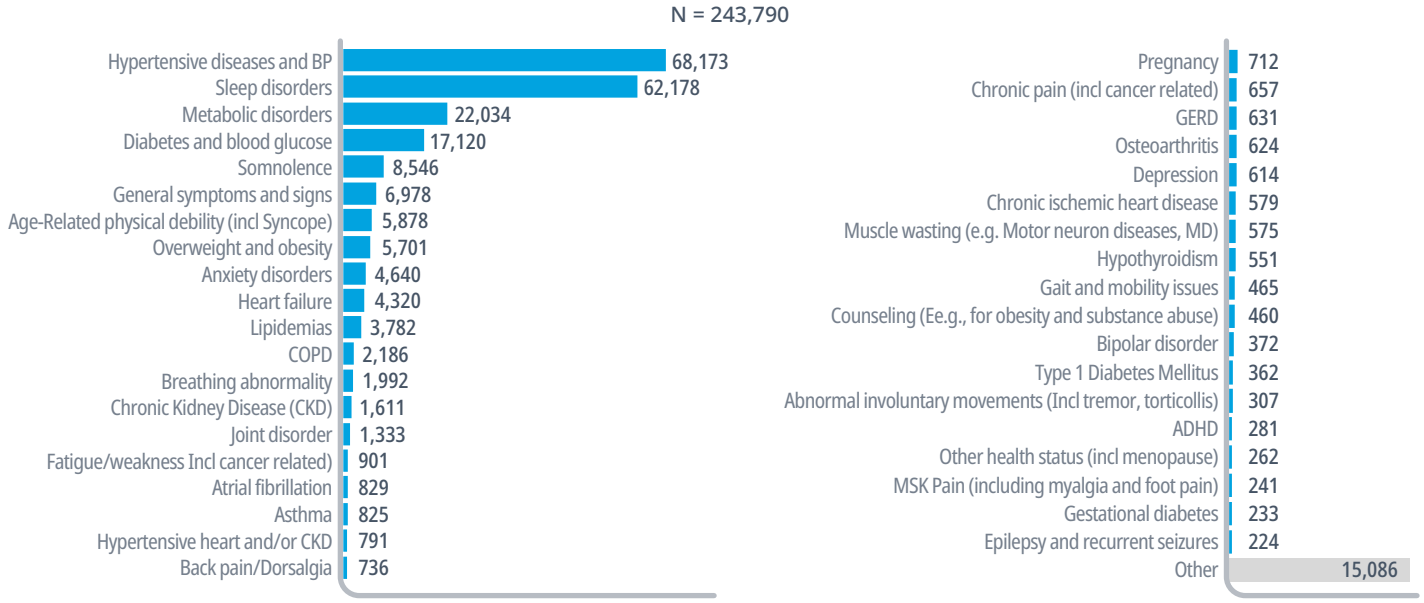
Finally, CPT codes have gradually been added for two areas of rapid device growth: mobile AI-based evaluation tools and VR-based therapeutics. AI-tools that aid in diagnosis using facial imaging (e.g. Face2Gene), assess cardiac function, and perform automated insulin dose titration (like d-NAV) now have codes to enable their reimbursement and pay physicians for device set up, educating patients to use the device, providing the software and collecting data from it. However, payers may still decline to cover these services.

As new digital solutions enter the market and wait for relevant reimbursement codes to be created, they may use general equipment codes that exist to cover services, procedures, reports and durable medical equipment. While only a few payers may choose to cover these mobile-based health management software applications, it does create routes to market for those able to negotiate effectively with payers.

Devices and digital tools to evaluate, monitor and treat patients are now being used across a broad range of diseases (Exhibit 43). By examining only those codes most closely linked to use of devices and digital tools (AI-based evaluation, PDTs, RPM and RTM codes, therapeutic digital care, VR therapy), we can see they are notably being used to treat high-risk chronic conditions (hypertension, diabetes, heart failure) and sleep disorders.

Some have suggested that employers are moving away from the digital-care-as-benefit model, feeling that there are too many digital health solutions on the market,[167] or facing challenges to measure the impact or return on investment from these programs. However, there still appears to be growth in some areas like physical therapy

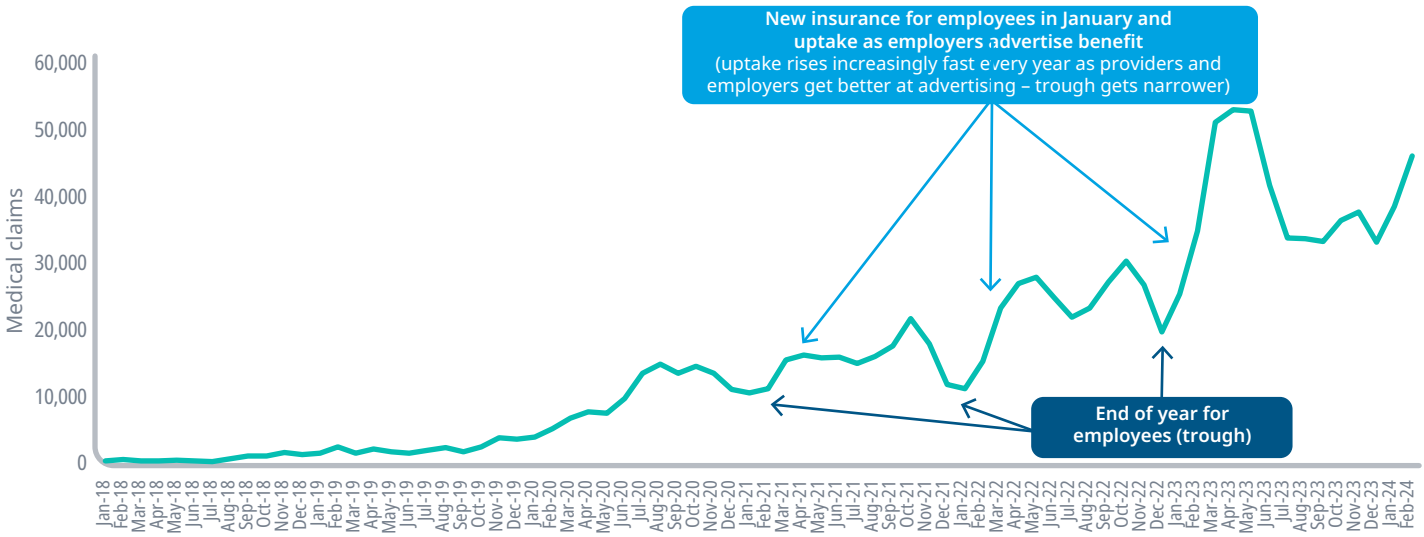
Exhibit 43: Diagnoses treated under a subset of digital-specific codes and their associated billing claims since 2021



Source: IQVIA Institute, Apr 2024; IQVIA Medical Claims Data, month ending Feb 2024.
Notes: Displays number of claims since 2021. Codes include only those for AI-based evaluation tools, digital therapeutics, remote physiologic monitoring and therapeutic monitoring codes, therapeutic digital care, VR therapy, assumed to be most closely linked to use of digital tools.

solutions for back pain (Exhibit 44). In the physiotherapy world many of these providers use apps with computer vision to analyze a patient's movements, record movement parameters and use it to guide effective exercise therapy —effectively a form of biofeedback — that has been used by Kaia, Hinge Health, Sword Health, Lindera's KlinikApp and Kemtai Care, among others. However, for those solutions that serve as employer benefits, their use may fluctuate over the course of the year based on employee benefit notification and mailings that are likely out of the hands of the developer.

Exhibit 44: Use of musculoskeletal (MSK) digital care based on number of monthly medical claims



Source: IQVIA Institute, Apr 2024; IQVIA Medical Claims Data, data extracted Apr 25, 2024, Jan 17 through period ending Feb 2024.
Notes: Includes three digital care companies in the musculoskeletal space

Notes on sources

THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW

IQVIA's LONGITUDINAL PRESCRIPTION DATA: IQVIA receives nearly 4 billion prescription claims per year with history from January 2006 with coverage over 90% for the retail channel, 60–85% for mail service, and 75–80% for long-term care. Longitudinal data derives from electronic data received from pharmacies, payers, software providers and transactional clearinghouses. This information represents activities that take place during the prescription transaction and contains information regarding the product, provider, payer, and geography. Rx data is longitudinally linked back to an anonymous patient token and is linkable to events within the data set itself and across other patient data assets.

IQVIA's MEDICAL CLAIMS DATA: Medical claims (Dx) data are pre-adjudicated claims collected from office-based physicians and specialists. These data are sourced from CMS-1500 form-based claim transactions, the standard reimbursement form for all non-cash claims. Medical claims data includes patient-level diagnosis and procedures for visits to U.S. office-based individual professionals, ambulatory and general healthcare sites. The medical claims data includes more than 205 million patients, over 1.7 billion claims and 3 billion service records obtained annually.

IQVIA's FORMULARY IMPACT ANALYZER (FIA): FIA provides key insights into the volume of paid, rejected and reversed prescription claims. Tracking the adjudication between pharmacy, payer, and patient at the point of sale, lifecycle claims are collected from retail, mail and long-term care pharmacies as well as switch clearinghouses with historical coverage beginning with 2013 and increasing over time.

IQVIA'S DISEASE ANALYZER is a database of anonymized electronic medical records (EMR) from physicians' offices in European countries including Germany and France. It contains data on diagnoses, demographic data, laboratory values and prescription and treatment information. With EMR data from general and specialized practices it offers an accurate reflection of routine clinical practice and real-world settings. Approximately 5% of all German practices are included in the Disease Analyzer data for Germany and the validity and representativeness of the dataset has been described extensively, demonstrating the suitability of the Disease Analyzer Database for the conduction of pharmacoepidemiological and pharmacoeconomic studies.

IQVIA'S APPSCRIPT DIGITAL HEALTH DATABASE: Global mobile application data sourced from 42Matters is reviewed and supplemented with primary research by IQVIA AppScript to create the curated IQVIA's AppScript Digital Health Database consumer mobile health apps. It includes app data from the Apple Store and the Google Play Store classified as "health and fitness" or "medical" as well as a manually curated set of health apps within other categories used for health purposes. As of October 30, 2024, it included data on 337,522 health apps.

IQVIA'S APPSCRIPT DIGITAL MEDICINE DATABASE: The digital medicine database includes comprehensive information on digital therapeutic apps, games, and virtual reality, as well as digital care programs across a range of diseases and digital diagnostics that span their various applications. It also captures information opportunistically on a range of digital tools used in clinical therapy, digital medicine products, and wearable-driven digital solutions. The database is updated on a quarterly basis and captures information on both pre-launch and post-launch digital medicine products including their product indications, pipeline progress, regulatory and reimbursement pathways, global approvals, dates, features, evidence generation and the companies and partnerships associated with these tools.

Methodologies

APP STORE DATA FROM THE IQVIA'S APPSCRIPT DIGITAL HEALTH DATABASE

Global mobile application data sourced from 42Matters was reviewed and supplemented with primary research by IQVIA AppScript to create the curated IQVIA's AppScript Digital Health Database consumer mobile health apps. It includes app data from the Apple Store and the Google Play Store classified as "health and fitness" or "medical" as well as a manually curated set of health apps within other categories used for health purposes.

As of October 30, 2024, when topline data was pulled, there were 337,522 health apps available with 187,203 in the Apple Store and 150,319 in the Google Play Store. There were also 221,958 apps in the Health and Fitness category and 81,293 in the Medical category, with the rest falling in other categories across the two stores. Although some apps are available in both stores, their unique instances may offer different functionality, and are therefore counted separately in this report, however at least 62,000 of these health apps have versions on both stores, placing a distinct-app count at around 275,000. Counts only of distinct apps place around 180,000 in the Health and Fitness category, 65,000 in the Medical category, and 30,000 in other categories (like Lifestyle, Sports, Education and Food & Drink).

Since app availability on these platforms simply means an app has been built to be installed and run on associated smartphone and tablet devices, these apps span health purposes and digital health segments. For instance, in addition to wellness apps, individuals can also install disease management apps, digital therapeutics and risk screening apps from app stores, while physicians can obtain clinical decision support tools like digital diagnostics. These segments are therefore also reflected in our examination of apps available on app stores, which can therefore best be thought of as a distribution channel for app developers.

APPSCRIPT CATALOG

This dataset prioritizes review of apps in the "Health and Fitness" and "Medical" categories, as well as the most downloaded apps, to define a set of the digital health apps most widely used by consumers. Under AppScript curation methods, app store apps with greater than 1,000 user ratings are prioritized for in-depth examination, as are apps that have already been reviewed and have a version or price update. A thorough examination of the content of apps enables exclusion of apps from further analysis that are considered irrelevant to normal healthcare use (e.g., salons, apps with gimmicks, etc.), or which are unavailable in English language or require an access code prohibiting access to apps for review. For the remaining apps extensive data is collected and their various quality domains are assessed. As of June 8, 2024 when catalog data was pulled, the dataset include 34,394 apps with 34,011 categorizations.

APPSCRIPT SCORE

The AppScript Score provides a comprehensive method for all stakeholders to assess digital health app quality and may be predictive of a given app's value to human health and the overall health system. The AppScript Score is derived from six sub-scores, or "ratings," across the following dimensions: Patient, Professional, Functional, Developer, Endorsement, and Clinical ratings (Exhibit 7). More than 70 individual metrics are considered across the six ratings. Some metrics leverage data from the AppScript distribution platform, which enables clinicians to electronically recommend apps, connected devices and digital content to their patients. AppScript Score components are weighted and combined to generate a consolidated score of 1–100. Apps with the highest scores typically have key quality characteristics such as exceptional patient ratings, connectivity to sensors, and rapid update cadence, thereby ensuring that apps are reliable, incorporate

the latest technologies and have endorsements from at least digital publishers and often from providers or government authorities (e.g., the FDA).

ANDROID INSTALL DATA ANALYSIS

Google Play data contained in the AppScript App Database includes information on volume of downloads which are quoted in ranges up to 1 billion and tracked over time. Examples include 100 million to 500 million; 50 million to 100 million; 10 million to 50 million descending to lower ranges such as 50 to 100; 10 to 50; 5 to 10; and 1 to 5. The median number of downloads was taken for each range, from which a total number of downloads was estimated.

BENCHMARKING APP UPTAKE ANALYSIS

This analysis displays apps from the AppScript Catalog and install data from the Google Play app store. It uses the "Installs min" value per app at each timepoint assessed, which is the lower value of each install band range and may therefore underestimate uptake speed. Time-since-launch is normalized by app release date. Because the data includes only apps currently in the app store at each normalized time point, apps removed from the store may result in visible drops or increases in the average, compounded in later periods by declining n# over time. Install values discussed in the text are based on trendline values.

GERMAN DiGA DATA

Data showing the trend in DiGA prescribing was sourced from IQVIA's Disease Analyzer, EMR practice software data, for data periods ending Apr 2024. Prescription data displayed is unprojected and coverage is estimated at 5% of providers. However, because patients in Germany can self-refer to obtain DiGA access with proof of diagnosis and gain approval for use directly from health insurers, based on recent GKV data, the displayed values likely represent ~4.5% of all product users or 3.8% of all prescriptions plus insurance approvals (as not all prescribed patients go on to use the product). Product use is therefore likely more than 22x the values shown.

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Murray Aitken is Executive Director, IQVIA Institute for Human Data Science, which provides policy setters and decisionmakers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics, now the IQVIA Institute, since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.

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Deanna is Director of Research for the IQVIA Institute for Human Data Science, leading the development of reports focused on the changing role of technology and innovation in healthcare in the United States and globally, and other shifts transforming research and patient care. She leverages both IQVIA and public data sources to perform analyses of global biopharmaceutical and healthcare trends. With a diverse background that spans from consulting and business development to market analysis and writing industry publications, she brings a unique perspective of the biopharma industry to the Institute. Deanna joined the Institute in 2013 and IMS Health in 2004. Deanna holds a B.A. in Biology from Yale University with a specialization in Neurobiology and a Certificate in International Affairs from New York University.

About the Institute

The IQVIA Institute for Human Data Science contributes to the advancement of human health globally through timely research, insightful analysis and scientific expertise applied to granular non-identified patient-level data.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved human outcomes. With access to IQVIA's institutional knowledge, advanced analytics, technology and unparalleled data the Institute works in tandem with a broad set of healthcare stakeholders to drive a research agenda focused on Human Data Science including government agencies, academic institutions, the life sciences industry, and payers.

Research agenda

The research agenda for the Institute centers on five areas considered vital to contributing to the advancement of human health globally:

- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.
- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

Guiding principles

The Institute operates from a set of guiding principles:

- Healthcare solutions of the future require fact based scientific evidence, expert analysis of information, technology, ingenuity and a focus on individuals.
- Rigorous analysis must be applied to vast amounts of timely, high quality and relevant data to provide value and move healthcare forward.
- Collaboration across all stakeholders in the public and private sectors is critical to advancing healthcare solutions.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Protecting individual privacy is essential, so research will be based on the use of non-identified patient information and provider information will be aggregated.
- Information will be used responsibly to advance research, inform discourse, achieve better healthcare and improve the health of all people.

The IQVIA Institute for Human Data Science is committed to using human data science to provide timely, fact-based perspectives on the dynamics of health systems and human health around the world. The cover artwork is a visual representation of this mission. Using algorithms and data from the report itself, the final image presents a new perspective on the complexity, beauty and mathematics of human data science and the insights within the pages.

The algorithmic art for this report cover was derived from a dataset detailing the uptake of digital therapeutics in Germany as sourced from IQVIA'S Disease Analyzer database of anonymized electronic medical records in August 2024.

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