



HOKKAIDO UNIVERSITY

Title	Assessing the current utilization status of wearable devices in clinical research
Author(s)	Miyakoshi, Takashi; Ito, Yoichi M.
Citation	Clinical Trials, 21(4), 470-482 https://doi.org/10.1177/17407745241230287
Issue Date	2024-03-14
Doc URL	https://hdl.handle.net/2115/93735
Rights	Miyakoshi T, Ito YM. Assessing the current utilization status of wearable devices in clinical research. Clinical Trials. 2024;21(4):470-482. Copyright © 2024 by The Society for Clinical Trials. DOI: 10.1177/17407745241230287
Type	journal article
File Information	revice_manuscript20231205.pdf



1 **Assessing the current utilization status of wearable devices in clinical research**

2 Running title: Wearable devices in clinical research

3 Takashi Miyakoshi^{1*}; Yoichi M. Ito, PhD²

4 ¹Department of Health Data Science, Hokkaido University Graduate School of Medicine,

5 Kita 15, Nishi 7, Kita-ku, Sapporo 060-8638, Japan; ORCID: 0000-0002-7952-862X

6 ²Data Science Center, Promotion Unit, Institute of Health Science Innovation for Medical

7 Care, Hokkaido University Hospital, Kita 14, Nishi 5, Kita-ku, Sapporo 060-8648, Japan;

8 ORCID: 0000-0001-5073-0827

9 *Corresponding author

10 mi_taka_1112@huhp.hokudai.ac.jp

11 Word count: 3953 words

Abstract

Background/Aims: Information regarding the use of wearable devices in clinical research, including disease areas, intervention techniques, trends in device types, and sample size targets, remains elusive. Therefore, we conducted a comprehensive review of clinical research trends related to wristband wearable devices in research planning and examined their applications in clinical investigations.

Methods: As this study identified trends in the adoption of wearable devices during the planning phase of clinical research, including specific disease areas and targeted number of intervention cases, we searched ClinicalTrials.gov—a prominent platform for registering and disseminating clinical research. Since wrist-worn devices represent a large share of the market, we focused on wrist-worn devices and selected the most representative models among them. The main analysis focused on major wearable devices to facilitate data analysis and interpretation, but other wearables were also surveyed for reference. We searched ClinicalTrials.gov with the keywords “ActiGraph,” “Apple Watch,” “Empatica,” “Fitbit,” “Garmin,” and “wearable devices” to obtain studies published up to August 21, 2022. This initial search yielded 3,214 studies. After excluding duplicate National Clinical Trial studies (the overlap was permissible among different device types except for wearable devices), our analysis focused on 2,930 studies, including simple, time-series, and type-specific assessments of various variables.

Results: Overall, an increasing number of clinical studies have incorporated wearable devices since 2012. While ActiGraph and Fitbit initially dominated this landscape, the use of other devices has steadily increased, constituting approximately 10% of the total after 2015. Observational studies outnumbered intervention studies, with behavioral and device-based interventions being particularly prevalent. Regarding disease types, cancer and cardiovascular diseases accounted for approximately 20% of the total. Notably, 114 studies adopted multiple devices simultaneously within the context of their clinical investigations.

Conclusions: Our findings revealed that the utilization of wearable devices for data collection and behavioral interventions in various disease areas has been increasing over time since 2012. The increase in the number of studies over the past three years has been particularly significant, suggesting that this trend will continue to accelerate in the future. Devices and their evaluation methods that have undergone thorough validation, confirmed their accuracy, and adhered to established legal regulations will likely assume a pivotal role in evaluations, allowing for remote clinical trials. Moreover, behavioral intervention therapy utilizing apps is becoming more extensive, and we expect to see more examples that will lead to their approval as programmed medical devices in the future.

Keywords: ActiGraph, Apple Watch, Empatica, Fitbit, Garmin, wearable device, disease area, intervention, clinical trial, observational study

1. Introduction

Wearable devices are information and communication technology terminals designed to be worn on various parts of the body, such as the wrist, head, or as eyeglasses. These devices encompass a wide range of types of devices, including watches, wristbands, rings, and even shoe-shaped devices for monitoring infants.¹ Some of these wearables are specifically designed for tracking vital signs such as body temperature, sleep patterns, heart rate, and movements.^{2,3} Moreover, textile-based solutions are available to continuously monitor health parameters, such as heart rate and electrocardiograph;^{4,5} these solutions include clothing⁶ and sticker tattoos⁷ that prioritize ease of use. In the healthcare sector, the utilization of wearable devices has grown considerably. These devices play a crucial role in delivering effective services for disease prevention, healthcare, and wellness promotion. They achieve this by collecting biological data from the individuals wearing them through integrated sensors. This information is then transmitted and analyzed, with the results being sent to the cloud for further assessment and feedback.⁸

Wearable devices are beginning to be applied in the healthcare sector. Notably, the range of biological data that these devices can measure has expanded.^{9,10} Further, the accuracy of these measurements has notably improved for several key evaluation parameters.¹¹ Wristbands and watches are common types of wearable devices,¹² with ActiGraph (ActiGraph LLC, USA), Fitbit (Fitbit, Inc., USA), Garmin (Garmin Ltd., USA), Apple Watch (Apple Inc., USA), and

68 Empatica (Empatica Inc., USA) being the most preferred types, as represented by their
69 market share.

70 ActiGraph devices have specifications that are specialized for research, such as collecting
71 data on the acceleration (G) of raw data, number of activities, energy consumption, metabolic
72 rate, number of steps, physical activity intensity, activity interval analysis, sitting period,
73 position, sleep analysis parameters, ambient lighting, and heart rate R-R intervals.¹³ Studies
74 utilizing ActiGraph devices have been conducted in the area of cardiovascular disease and
75 focused on the evaluation of physical activity in randomized controlled trials of drug
76 interventions.¹⁴ In addition, studies have assessed sleep patterns alongside drug
77 interventions.^{15,16}

78 Fitbit devices have been utilized for a relatively long period as a commercial-use device.
79 Fitbit can collect data on the respiratory rate, heart rate variability, skin temperature, blood
80 oxygen wellness, resting heart rate, sleep score, menstrual cycle, health records, and stress
81 management scores.¹⁷ Studies utilizing Fitbit devices have been conducted on physical
82 activity; additionally, a meta-analysis and narrative review on intervention clinical studies
83 have been conducted.^{18,19}

84 Garmin also makes commercial-use devices that include assessing body energy levels, stress
85 levels, menstrual cycle tracking, moisture intake tracking, breath rate, sleep monitoring, heart
86 rate monitoring, breathwork (tracking stress conditions and breathing), and blood oxygen

levels.²⁰ One clinical trial utilized Garmin devices and evaluated physical activity as part of an exercise intervention study in the area of obesity research.²¹

Apple Watch is a medical commercial-use device that can measure electrocardiograms (ECG). In the United States, the Food and Drug Administration (FDA) approved the de novo application in September 2018, and determined that it fell under “Class II (General Controls and Special Controls)” regarding over-the-counter use of electrocardiograph software.²² De novo application is an application for a new medical device with a mild to moderate risk, whose safety and effectiveness are assured by general controls, as well as general and special controls, and for which no equivalent device exists.

Other measurements by Apple Watch include heart rate, physical activity, blood oxygen saturation, sleep patterns, cycle tracking (menstrual cycle), noise level measurement, and fall detection.²³

The Apple Watch was employed in a trial that utilized a digital health intervention for cardiovascular disease. This intervention involved tracking vital signs and activity.²⁴

Empatica devices are also equipped with sensors for data collection, in combination with clinically validated biomarkers, as they are CE marking and FDA-approved research instruments. They can measure the pulse rate, skin electrical activity, accelerometer, skin temperature, photoplethysmography, heart rate intervals, sleep, number of steps, and activity levels.²⁵ The company received FDA approval for seizure monitoring (for adults in August

2018; pediatrics in January 2019)²⁶ and a CE marking (March 2021) for wearable-based early symptom detection of respiratory infections, including the coronavirus disease of 2019 (COVID-19).²⁷ A study employing Empatica investigated autonomic reactivity to assess the potential of animal-mediated therapy in reducing social stressors.²⁸

Although the utilization of wearable devices in clinical research is increasing, long-term details on the status of wearable devices and their utilization in disease areas, intervention methods, trends on the type of device, and sample size target remain unknown. Therefore, this study aimed to elucidate the utilization of wearable devices during the planning phase of clinical research. We explored the trends in clinical research by analyzing data retrieved from ClinicalTrials.gov, focusing on wrist-worn devices, including ActiGraph, Fitbit, Garmin, Apple Watch, and Empatica.

2. Methods

2.1. Clinical research selection criteria

To determine the utilization of wearable devices in clinical research, including type of device, type of intervention, disease area, and number of studies, we examined wrist-worn watches such as ActiGraph, Apple Watch, Empatica, Fitbit, and Garmin. We selected widely available and commonly utilized devices, such as Apple Watch, Fitbit, and Garmin. In addition, we included ActiGraph and Empatica, which are rarely utilized for general purposes but are commonly used in research. Other wearable devices were also examined, including

wristband- and non-wristband-type wearable devices. We used the following search terms: “ActiGraph,” “Apple Watch,” “Empatica,” “Fitbit,” “Garmin,” and “wearable devices.” As this study identified trends in the adoption of wearable devices during the planning phase of clinical research, including specific disease areas and targeted number of intervention cases, we searched ClinicalTrials.gov—a prominent platform for registering and disseminating clinical research. Since wrist-worn devices represent a large share of the market (about 90%),²⁹ we focused on wrist-worn devices and selected the most representative models among them. The main analysis focused on major wearable devices to facilitate data analysis and interpretation, but other wearables were also surveyed for reference. We incorporated the results into our database without undertaking eligibility screenings. Search terms were adapted to the full text as well as titles and keywords. All studies that mentioned the search terms even briefly were included. We observed a minimal occurrence of missing data, with only two instances found in the enrollment variable. No corrective actions were taken to address these missing data points.

We retrieved 3,214 studies that focused on wearable devices as of August 21, 2022, as follows: ActiGraph, 1,218 studies; Apple Watch, 96; Empatica, 59; Fitbit, 833; Garmin, 113; and other wearable devices, 895 studies. Duplicate National Clinical Trial studies were excluded, and 2,930 studies were included in our analysis. As 114 studies used multiple devices in the same clinical trial (S-Figure 1), we allowed for overlap among devices other

than wearable devices and included 3,048 studies in the analysis based on the type of device (ActiGraph: 1218 studies, Apple Watch: 96 studies, Empatica: 59 studies, Fitbit: 833 studies, Garmin: 113 studies, and other wearable devices: 729 studies).

2.2. Analysis

We used a database downloaded from ClinicalTrials.gov and aggregated the study type, interventional type, device type, and conditions. The study type was categorized as either interventional or observational. Interventional studies were defined as arms or groups related to the investigational product.

For example, to categorize the variables, such as “Behavioral: Functional Training,” only the “Behavioral” component was considered; and we further classified them into categories such as behavioral, device, drug, dietary supplement, diagnostic test, and procedure. Studies with device-based interventions included those using electrical and magnetic stimulators, device training, spectacle-type phototherapy devices, and other devices.

Device type was categorized based on the search terms found on ClinicalTrials.gov, including ActiGraph, Apple Watch, Empatica, Fitbit, Garmin, and other wearable devices.

Conditions refer to the diseases, disorders, syndromes, or illnesses under investigation. This variable was used to classify clinical research into categories, such as cancer, cardiovascular disease, obesity, physical activity, sleep, and other diseases. As 61 categories were retrieved, those with fewer than 40 trials were grouped under the “other” category.

The variable StartDate was defined as the estimated start date of participant recruitment for the clinical trial or actual date when the first participant was enrolled. This value was used to calculate time-series data, specifically the percentage change or cumulative change by category.

Enrollment refers to the estimated total number of participants intended to be enrolled (the target number) or actual total number of participants who were enrolled in the clinical study. This variable was used to calculate the number of participants enrolled.

A mosaic map was created as an analysis based on the type of device for the top six areas of conditions and intervention to compare the condition–intervention type percentages.

Additionally, we conducted an analysis to compare the mean values of enrollment (planned number of cases) based on the type of device. Moreover, the relationship between the annual enrollment and trial number over time was confirmed by utilizing a 2D scatterplot. These analyses were performed by utilizing the JMP Pro 16.10 (SAS Institute, Cary, NC), Microsoft Excel for Mac version 16 (Microsoft).

3. Results

3.1. General description

3.1.1. Simple aggregations

The results of simple aggregations with regards to the study types, interventions, devices, and conditions are presented in S-Figures 2–5. Regarding the study type, we retrieved 2,411

interventional and 519 observational studies (S-Figure 2). The top six intervention types were behavioral (1,218 registered trials), device (740 registered trials), drug (132 registered trials), dietary supplement (61 registered trials), diagnostic test (61 registered trials), and procedure (38 registered trials; S-Figure 3).

ActiGraph was utilized in 1,218 instances, Fitbit in 833, Garmin in 113, Apple Watch in 96, Empatica in 59, and other wearable devices in 729 instances (S-Figure 4). A total of 114 studies employed multiple devices within the same research study. The breakdown is presented in S-Figure 1.

Conditions included 294 registered trials of cancer, 267 registered trials of cardiovascular diseases, 257 registered trials of physical activity, 240 registered trials of obesity, 167 registered trials of sleep (i.e., its use in sleep areas), and 158 registered trials of diabetes. The devices were also utilized with patients with various other disease areas, including 138 registered trials of psychiatric disorders, 111 registered trials of respiratory disorders, 94 registered trials of pain, and 79 registered trials of cerebrovascular diseases (S-Figure 5).

3.1.2. Comparison by device type

The mean results of the comparison by device type are presented in Figure 1 and S-Table 1. For ActiGraph (n = 1,216), there were an average of 167 participants; Apple Watch (n = 96) exhibited an average of 21,880 participants; Empatica (n = 59) exhibited an average of 1,837.4 participants; Fitbit (n = 833) exhibited an average of 808 participants; Garmin (n =

113) had an average of 1,039 participants, and other wearable devices ($n = 729$) exhibited an average of 2,219 participants.

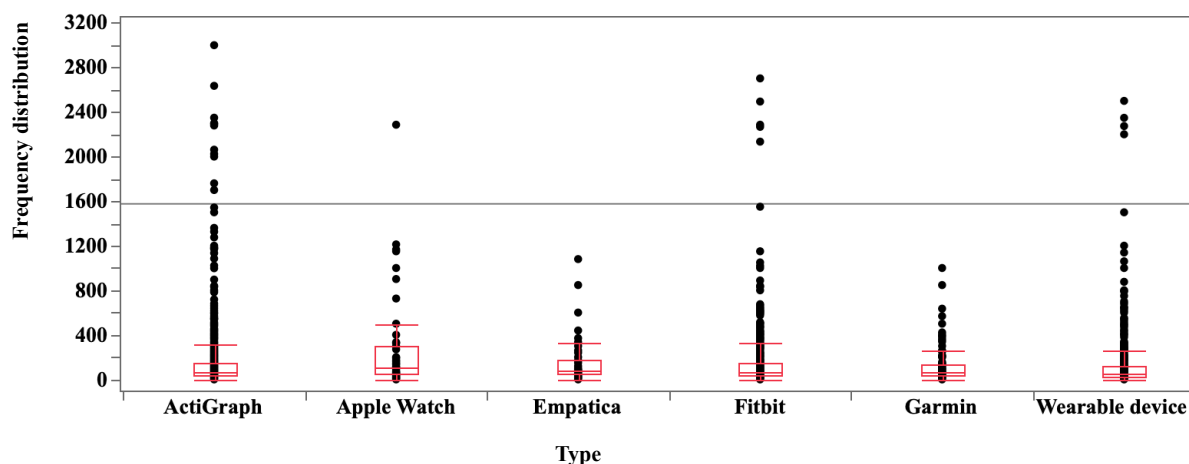


Figure 1. Mean of enrollment comparison based on the type of device

3.2. Results of change over time

3.2.1. Annual time-series aggregation

The results of the annual time-series aggregations of study types, interventions, devices, and conditions are presented in S-Figures 2–5. The number of studies exhibited an increasing trend over time since 2012 (S-Figure 2). The annual trend of the intervention demonstrated that the proportion of devices was approximately 50% in 2012 and 2013; however, since 2014, it has been between approximately 20% and 30%. Approximately 30% were behavioral studies in 2012 and 2013; however, since 2014, this percentage has increased to between 40% and 50% (S-Figure 3).

In the study type's annual time-series between 2012 and 2015, ActiGraph and Fitbit dominated; however, since 2015, Apple Watch, Garmin, and Empatica have been utilized in

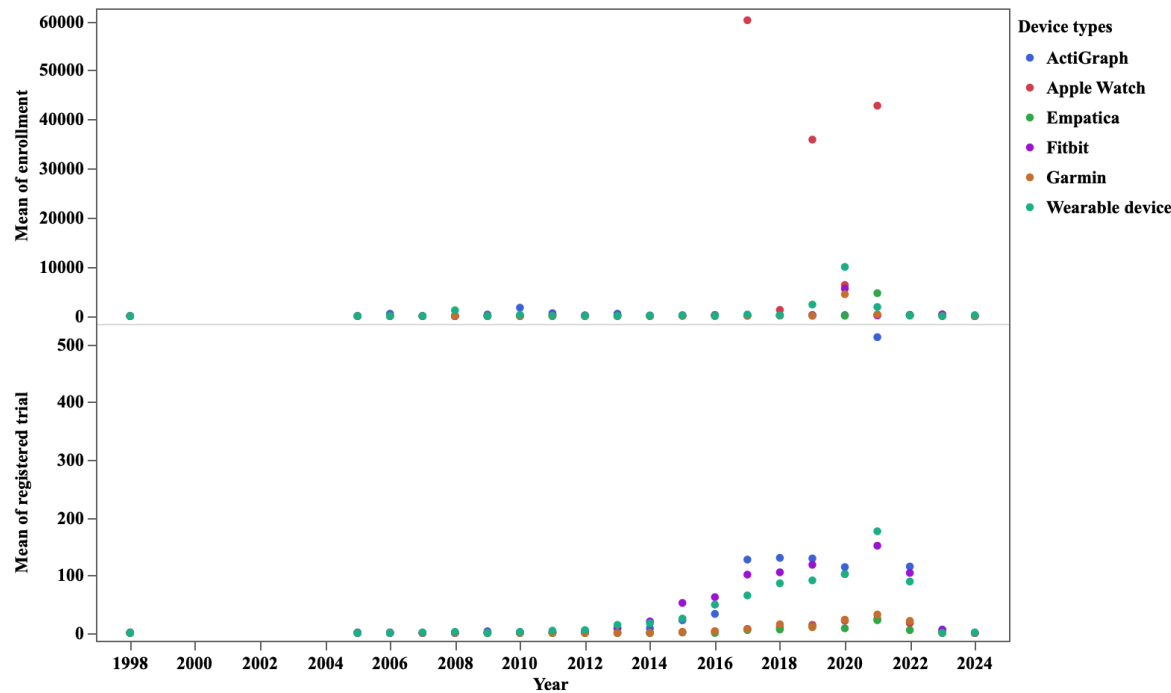
clinical studies. Their percentages have gradually increased, although they continue to comprise less than 10% of the total percentage (S-Figure 4).

The results of the annual time-series aggregations of condition types, in 2012, accounted for approximately 40% for obesity and 20% for diabetes; however, since 2013, the disease area became subdivided. Since 2014, the proportion of the top six items has been approximately 40%–50% (S-Figure 5).

3.2.2. Relationship between annual enrollment and trial number over time

Figure 2 presents a 2D scatterplot. For the enrollment average, Apple Watch had 60,210 participants in 2017, 35,914 participants in 2019, and 42,819 participants in 2021. These numbers were greater than those of other device types at the same points in time.

226



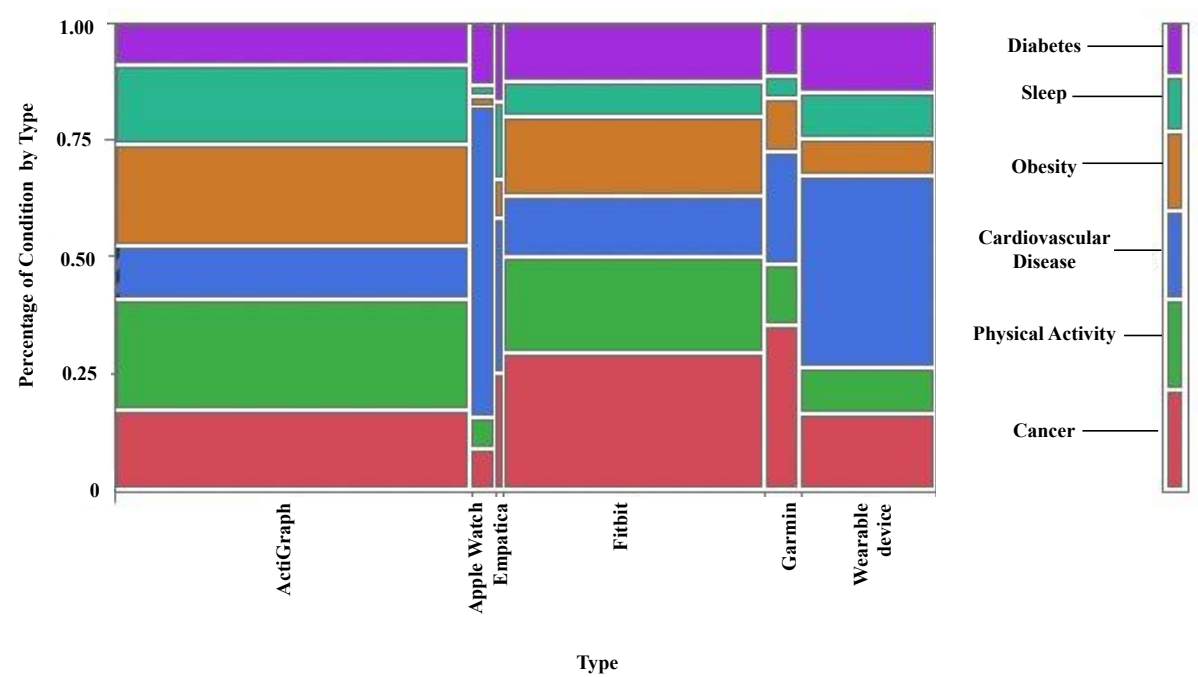
227

228 **Figure 2.** 2D scatterplot of relationship between annual enrollment and trial number over
229 time

230 **3.3. Results by condition type**

231 The contingency table was analyzed for each type of condition. The mosaic diagrams of
232 conditions are presented in Figure 3 and S-Table 2. We also compared the percentages by
233 device types (up to the top six items).

234



235

236 **Figure 3. Mosaic diagram of conditions**

237 Regarding physical activities, the percentage was high for ActiGraph and Fitbit. Regarding

238 sleeping patterns, ActiGraph and Empatica had the highest percentages. Regarding the

239 conditions of cancer, Garmin and Fitbit had high percentages. Regarding cardiovascular diseases, Apple

240 Watch and Empatica had the highest percentages. Regarding obesity, the percentage was highest for

241 ActiGraph and Fitbit. The percentage was also highest for Empatica and Apple Watch regarding diabetes.

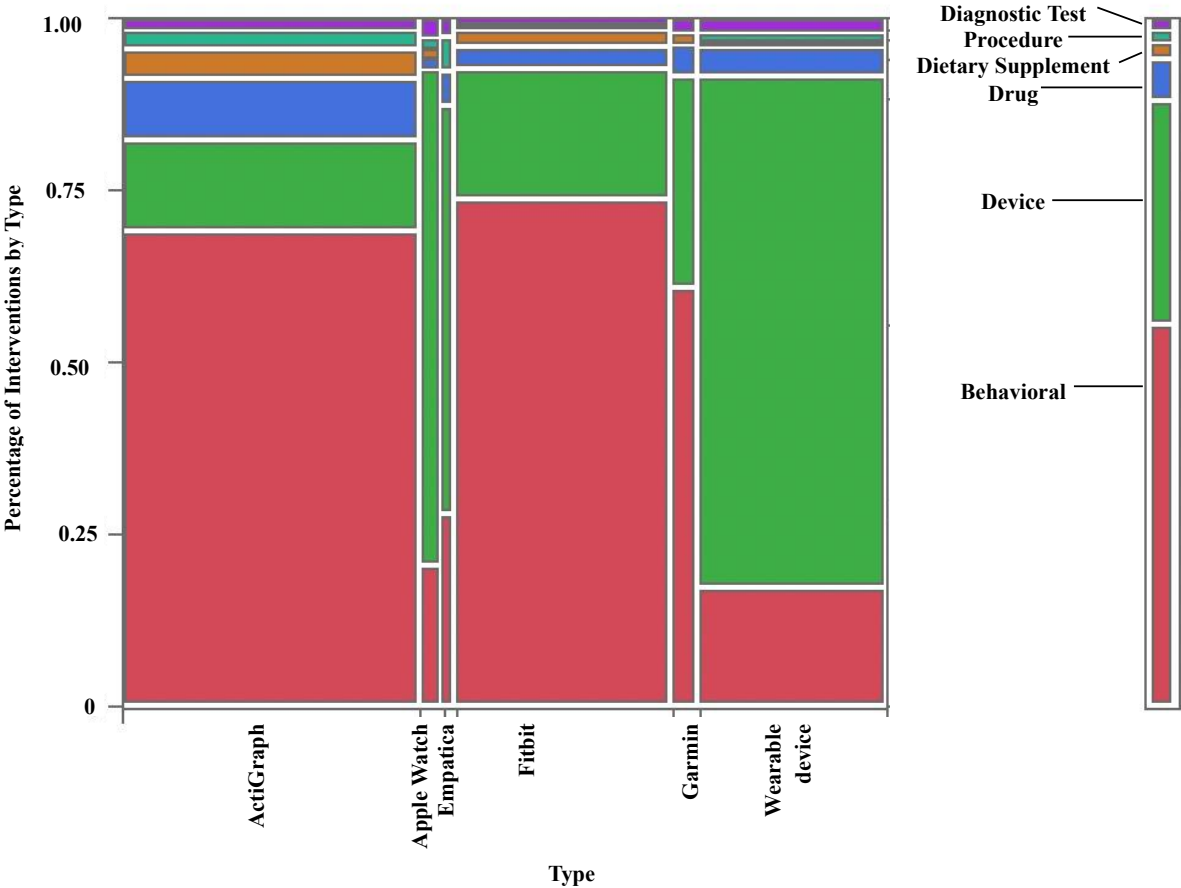
242 **3.4. Results by intervention type**

243 The contingency table was analyzed for each type of intervention. The mosaic diagrams of

244 interventions are presented in Figure 4 and S-Table 3. We also compared the percentages by

245 device types (up to the top six items).

246



247

248 **Figure 4. Mosaic diagram of intervention**

249 Regarding behavioral interventions percentages, Fitbit, ActiGraph, and Garmin exhibited the
250 highest percentages. In the case of device-based interventions, Apple Watch and Empatica
251 had the highest percentages. ActiGraph dominated in drug-related interventions, while dietary
252 supplements exhibited the highest percentage with ActiGraph. Procedures had the highest
253 percentages with Empatica and ActiGraph. Diagnostic tests exhibited the highest percentages
254 with Apple Watch and Empatica (Figure 4 and S-Table 3).

255 **4. Discussion**

4.1. General summary

The ClinicalTrials.gov database was analyzed to determine the status of the clinical research conducted in the healthcare field for wearable devices, including type of device utilized, type of intervention, disease area, and number of studies. Clinical studies of wearable devices included more intervention than observational studies, and ActiGraph and Fitbit were utilized more frequently than other devices. These findings are consistent with the results of a systematic review of medical studies that utilized wearable activity trackers.³⁰

Regarding disease areas, the utilization of wearable devices was particularly high for cancer and cardiovascular disease. A survey of existing literature in these areas revealed several umbrella reviews, systematic reviews, and literature reviews focused on cancer,^{31–34} as well as several systematic reviews in the cardiovascular disease area using digital health interventions, including wearable devices. Therefore, these previous results demonstrate active research pursuits within these domains.^{35–38}

An umbrella review of systematic reviews on interventions to reduce sedentary behavior in patients with cancer and cancer survivors considered 26 studies. The interventions primarily included strategies such as electronic, wearable health technology-based, and behavior change techniques.³⁴

Although behavioral interventions constituted a significant percentage of interventions as exemplified in case studies related to cancer and cardiovascular disease,^{31–38} several digital

health studies have incorporated behavioral research.³⁹ This observation, when considered alongside the current results, underscores the prominent role of behavioral research in clinical investigation involving wearable devices.

Further, several studies have used multiple devices in the same study.^{40–42} For instance, a study focused on characterizing COVID-19 and influenza infections utilized individually generated health data collected from commercially available wearables. It used the Achievement Studies platform (Evidation Health, Inc, San Mateo, CA, USA), which facilitates web-based participant recruitment and data collection through various wearables.^{42,43} These developments suggest that the utilization of web-based wearable devices, particularly with such versatile platforms, is likely to become popular in the future.

4.2. Results of change over time

Regarding temporal trends, the number of studies has exhibited a consistent upward trajectory since 2012. This aligns with similar findings from a survey of the broader scientific literature in the field of wearable health monitoring, which covers the period from January 2010 to February 2019, and exhibits an increasing trend.⁴⁴

We also utilized a 2D scatterplot to examine the relationship between annual enrollment and trial numbers over time. Over several years, Apple Watch was utilized significantly more, by percentage, than any other type of device. From the distribution of enrollment (S-Figure 12), we inferred that the higher mean of enrollment for Apple Watch was the result of four large-

scale studies with over 100,000 participants that were conducted utilizing the Apple Watch devices: (1) an app-based study to determine if it could detect influenza-like illnesses and other diseases (Fitbit and Garmin devices were also utilized in this study);⁴⁵ (2) a study to determine if an ECG and symptom data obtained from Apple Watch were of sufficient quality to guide individual care;⁴⁶ (3) an Apple Heart study to examine the positive predictive value of atrial fibrillation;⁴⁷ and (4) a study to examine the factors that could cause a decline in the capacity to exercise and heart function.⁴⁸

A large-scale trial with over 100,000 participants used Empatica to monitor seizure events, such as systemic tonic-clonic seizures, in patients with epilepsy.⁴⁹ A large-scale study used Fitbit Heart to verify the atrial fibrillation software.⁵⁰

Large-scale clinical studies utilizing commercially available wearable devices have analyzed data collected both inside and outside medical institutions, and have obtained medical findings.^{47,50–55} In some cases, such large-scale trials have been conducted with participants who own such wearable devices, as in the Apple Heart study described above.^{45,47–50,52,53,56} Further, large-scale trials have been conducted as verification trials for the approval of the wearable devices and their accompanying applications as medical devices.^{47,49,50}

Regarding sponsors of the 100,000 large trials, we discovered that two out of the four trials involving the Apple Watch were sponsored directly by Apple.^{47,48} Additionally, one Fitbit trial⁵⁰ and one Empatica trial⁴⁹ were sponsored by Fitbit Inc. and Empatica Inc., respectively.

This suggests a notable trend in which manufacturers of wearable devices are actively engaging in large-scale trials, likely driven by their interest in advancing the capabilities and functionalities of these devices.

4.3. Results by condition type

A comparison of utilization percentages by disease area and device model revealed that the use of wearable devices exhibited unique patterns depending on both factors. For instance, in the context of physical activity, ActiGraph and Fitbit displayed notably high percentages of use. To delve deeper into this distinctiveness, we conducted a detailed analysis. We examined the mosaic diagram representing the top six disease areas studied utilizing wearable devices, identifying interventions with high utilization percentages based on the type of device and for each disease area. We then investigated each case included in this study. The results are presented in Table 1.

This analysis demonstrated that the specific features of wearable devices, such as their measurable parameters, domains of expertise (e.g., Apple Watch: cardiovascular disease area with ECG function; ActiGraph: sleep area with illuminance meter), and the type of intervention methods (e.g., behavioral intervention, device intervention) were influential in shaping their usage patterns within each disease area.

Except for cardiovascular disease and diabetes, behavioral interventions were used in a high percentage of cases, while device interventions were used in a high percentage of

cardiovascular disease and diabetes cases. In the area of cardiovascular disease, studies have been conducted in individual cases to compare the accuracy of a device's heart rate and ECG detection capabilities with the accuracy of a more accurate ECG.⁵⁷⁻⁶² Additionally, a large study was conducted using the Apple Watch,⁴⁷ which resulted in FDA approval of the ECG function.²² As for diabetes, clinical research is underway, including the development of an application for insulin administration and diet management for Type 1 diabetes.⁶³⁻⁷¹ Meanwhile, an automated insulin administration mobile application Tidepool Loop, based on algorithms first designed and developed by users of the Apple Watch, was FDA-approved in January 2023.^{72,73} It was inferred that the high number of device interventions in the areas of cardiovascular disease and diabetes was due to this type of research.

4.4. Results by intervention type

A comparison of the percentages by device type for each intervention revealed the unique characteristics of each device model. Therefore, we identified individual clinical research utilization cases and intervention types associated with the highest percentages. The results are presented in Table 2.

Behavioral interventions were implemented in the areas of cancer, obesity, physical activity, and sleep. Numerous systematic reviews have been conducted, including those using Fitbit, Garmin, and Actigraph, which have extensive physical activity measurement capabilities,^{32,34,74,75} and the results were consistent with the present findings. In addition, ActiGraph had

a high percentage of drug and dietary supplement interventions. We speculated that this was related to the fact that the ActiGraph has been used in many evaluations, including randomized controlled clinical trials,^{76–89} because it has a more reliable accelerometer and sleep monitor than commercial devices for research study purposes. The measurable items of wearable devices based on the type of model and usage by disease area may be associated with the characteristics of the intervention methods.

4.5. Future utilization of wearable devices in clinical research

Clinical trials are moving away from those that rely on visits to medical institutions and toward online clinical trials that do not require visits to medical institutions or that combine online and in-person clinical trials.^{90–98}

The purpose of remote clinical trials is to improve access to clinical trials, such as by reducing the impact of COVID-19 and the burden of patient visits. A shift is observed from medical institution-centered clinical trials premised on patient visits to medical institutions to patient-centered clinical trials conducted without patients visiting medical institutions in accordance with patient needs, such as when it is difficult to visit owing to a disease. In a conventional clinical trial, each process, from participant recruitment to the completion of this study, is conducted by visiting the site of the implementing medical institution. Remote clinical trials are implemented by collecting data with a wearable device and electronic patient-reported outcomes, receiving delivery of study drugs, and so forth.⁹⁹

We anticipate that the utilization of wearable devices as tools for remote clinical trials will increase after devices and applications are verified, evaluation methods for utilizing wearable devices are established, laws and regulations are developed, and devices, applications, as well as clouds that satisfy these requirements are implemented.

4.5. Limitations

This study had several limitations. First, the database used to search for applicable studies was limited to ClinicalTrials.gov. Second, only major wristwatch and wristband types of wearable devices (ActiGraph, Apple Watch, Empatica, Fitbit, and Garmin) were examined. Third, this study identified trends, such as disease areas and target number of intervention cases, during the planning stage of clinical studies involving wearable devices. No screening of study eligibility was conducted; consequently, the database comprises not only completed clinical studies but also incomplete, discontinued, or suspended studies. Additionally, the database includes completed clinical studies for which the study results have not been published. Consequently, while this study identified trends in the use of wearable devices in clinical studies, it could not evaluate the results of the analysis with a high degree of accuracy.

5. Conclusions

Our findings revealed that the utilization of wearable devices for data collection and behavioral interventions in various disease areas has been increasing over time since 2012.

389 The increase in the number of studies over the past three years has been particularly
390 significant, suggesting that this trend will continue to accelerate in the future. However, after
391 devices and their evaluation methods are sufficiently validated to establish accuracy and
392 regulations are implemented, wearable devices are expected to be used remotely to measure
393 and evaluate primary and secondary assessments. We anticipate that their utilization in
394 remote clinical trials will increase. Moreover, behavioral intervention therapy utilizing apps is
395 becoming more extensive, and we expect to see more examples that will lead to their
396 approval as programmed medical devices in the future.

Statements and declarations

Acknowledgments

We thank Editage (www.editage.com) for English language editing.

Funding statement

No financial support was received for this research.

Author contributions

Takashi Miyakoshi: Formal analysis, Investigation, Writing-Original Draft. Yoichi M Ito: Conceptualization, Formal analysis, Methodology, Supervision. Takashi Miyakoshi and Yoichi M Ito contributed equally to this work.

Declaration of conflicting interests

The authors have no potential conflicts to declare.

Data availability

Source data are provided in the FigShare database under Digital Object Identifier:

<https://doi.org/10.6084/m9.figshare.24464200> (Figure1 and S-Table 1),

<https://doi.org/10.6084/m9.figshare.24464203> (Figure 2),

<https://doi.org/10.6084/m9.figshare.24464272> (Figure 3, 4 and S-Table 2, 3).

<https://doi.org/10.6084/m9.figshare.24596058> (All figures and tables other than the above)

References

1. Ministry of Economy Trade and Industry. The future of living and ICT. White paper on information and communications, <https://www.soumu.go.jp/johotsusintokei/whitepaper/ja/h27/pdf/n4100000.pdf> (2015, accessed 13 May 2023).
2. Zambotti M, Rosas L, Colrain IM, et al. The sleep of the ring: comparison of the ŌURA sleep tracker against polysomnography. *Behav Sleep Med* 2019; 17(2): 124–136. <https://doi.org/10.1080/15402002.2017.1300587>
3. Anjewierden S, Humpherys J, LaPage MJ, et al. Detection of tachyarrhythmias in a large cohort of infants using direct-to-consumer heart rate monitoring. *J Pediatr* 2021; 232: 147–153. <https://doi.org/10.1016/j.jpeds.2020.12.080>
4. Ousaka D, Hirai K, Sakano N, et al. Initial evaluation of a novel electrocardiography sensor-embedded fabric wear during a full marathon. *Heart Vessels* 2022; 37(3): 443–50. <https://doi.org/10.1007/s00380-021-01939-3>
5. Kana E, Ryosuke A, Suehiro S, et al. Validation of RRI anomaly processing and calculation accuracy of temporal features of heartbeats in real-world heart rate variability analysis using a wearable electrocardiograph. In: *Multimedia, Distributed, Cooperative and Mobile Symposium*, 2018, pp. 1698–1705. https://ipsj.ixsq.nii.ac.jp/ej/?action=pages_view_main&active_action=repository_view

[main_item_detail&item_id=193673&item_no=1&page_id=13&block_id=8](#) (accessed 13 May 2023).

6. Kang SW, Choi H, Park H, et al. The development of an IMU integrated clothes for postural monitoring using conductive yarn and interconnecting technology. *Sensors* 2017; 17(11): 1–10. <https://doi.org/10.3390/s17112560>
7. Bandodkar AJ, Jia W, Wang J. Tattoo-based wearable electrochemical devices: a review. *Electroanalysis* 2015; 27(3): 562–72. <https://doi.org/10.1002/elan.201400537>
8. Ministry of Economy Trade and Industry. Document 3: Wearables and data utilization for disease and care prevention and next-generation healthcare, https://www.meti.go.jp/shingikai/sankoshin/2050_keizai/003.html (2019, accessed 13 May 2023).
9. Guk K, Han G, Lim J, et al. Evolution of wearable devices with real-time disease monitoring for personalized healthcare. *Nanomaterials* 9(6): 1–23. <https://doi.org/10.3390/nano9060813>
10. Sharma A, Badea M, Tiwari S, et al. Wearable biosensors: an alternative and practical approach in healthcare and disease monitoring. *Molecules* 2021; 26(3): 1–32. <https://doi.org/10.3390/molecules26030748>

11. Fuller D, Colwell E, Low J, et al. Reliability and validity of commercially available wearable devices for measuring steps, energy expenditure, and heart rate: systematic review. *JMIR Mhealth Uhealth* 2020; 8(9): e18694. <https://doi.org/10.2196/18694>
12. Mück JE, Ünal B, Butt H, et al. Market and patent analyses of wearables in medicine. *Trends Biotechnol* 2019; 37(6): 563–566. <https://doi.org/10.1016/j.tibtech.2019.02.001>
13. ActiGraph. <https://theactigraph.com> (accessed 13 May 2023).
14. Howard LS, Rosenkranz S, Frantz RP, et al. Assessing daily life physical activity by actigraphy in pulmonary arterial hypertension: insights from the randomized controlled study with Selexipag (TRACE). *Chest* 2023; 163: 407–418. <https://doi.org/10.1016/j.chest.2022.08.2231>
15. Santisteban JA, Stein MA, Bergmame L, et al. Effect of extended-release dexamethylphenidate and mixed amphetamine salts on sleep: a double-blind, randomized, crossover study in youth with attention-deficit hyperactivity disorder. *CNS Drugs* 2014; 28: 825–833. <https://doi.org/10.1007/S40263-014-0181-3>
16. Gringras P, Nir T, Breddy J, et al. Efficacy and safety of pediatric prolonged-release melatonin for insomnia in children with autism spectrum disorder. *J Am Acad Child Adolesc Psychiatry* 2017; 56: 948-957.e4. <https://doi.org/10.1016/j.jaac.2017.09.414>
17. Fitbit. <https://www.fitbit.com/global/us/home> (accessed 13 May 2023).

- 468 18. Ringeval M, Wagner G, Denford J, et al. Fitbit-based interventions for healthy lifestyle
469 outcomes: systematic review and meta-analysis. *J Med Internet Res* 2020; 22(10):
470 e23954. <https://doi.org/10.2196/23954>
- 471 19. St Fleur RG, St George SM, Leite R, et al. Use of fitbit devices in physical activity
472 intervention studies across the life course: narrative review. *JMIR Mhealth Uhealth*
473 2020; 22(10): e23411. <https://doi.org/10.2196/23411>
- 474 20. Garmin. <https://www.garmin.com/en-US/> (accessed 13 May 2023).
- 475 21. Frediani JK, Bienvenida AF, Li J, et al. Physical fitness and activity changes after a 24-
476 week soccer-based adaptation of the US diabetes prevention program intervention in
477 Hispanic men. *Prog Cardiovasc Dis* 2020; 63: 775–
478 785. <https://doi.org/10.1016/J.PCAD.2020.06.012>
- 479 22. US Food & Drug Administration. Notification of FDA review results of de novo
480 request for Apple Watch ECG app.
481 https://www.accessdata.fda.gov/cdrh_docs/pdf18/den180044.pdf (2018, accessed 13
482 May 2023).
- 483 23. Apple Watch. <https://www.apple.com/watch/> (accessed 13 May 2023).
- 484 24. Marvel FA, Spaulding EM, Lee MA, et al. Digital health intervention in acute
485 myocardial infarction. *Circ Cardiovasc Qual Outcomes* 2021; 14:
486 e007741. <https://doi.org/10.1161/CIRCOUTCOMES.121.007741>

- 487 25. Empatica. <https://www.empatica.com/> (accessed 13 May 2023).
- 488 26. Empatica. Embrace2 receives FDA clearance for children ages 6 and up.
- 489 <https://www.empatica.com/blog/empatica-s-2019-in-review.html> (2019, accessed 13
- 490 May 2023).
- 491 27. Empatica. Empatica receives first of its kind European CE mark for early detection of
- 492 COVID-19. [https://www.empatica.com/blog/aura-and-care-receive-ce-mark-for-early-](https://www.empatica.com/blog/aura-and-care-receive-ce-mark-for-early-detection-of-covid-19-and-other-respiratory-infections.html)
- 493 [detection-of-covid-19-and-other-respiratory-infections.html](https://www.empatica.com/blog/aura-and-care-receive-ce-mark-for-early-detection-of-covid-19-and-other-respiratory-infections.html) (2021, accessed 13 May
- 494 2023).
- 495 28. Mueller MK, Anderson EC, King EK, et al. Null effects of therapy dog interaction on
- 496 adolescent anxiety during a laboratory-based social evaluative stressor. *Anxiety Stress*
- 497 *Coping* 2021; 34: 365–380. <https://doi.org/10.1080/10615806.2021.1892084>
- 498 29. De Arriba-Pérez F, Caeiro-Rodríguez M, Santos-Gago JM. Collection and processing of
- 499 data from wrist wearable devices in heterogeneous and multiple-user scenarios. *Sensors*
- 500 (Switzerland) 2016; 16. Epub ahead of print. <https://doi.org/10.3390/s16091538>
- 501 30. Chan A, Chan D, Lee H, et al. Reporting adherence, validity and physical activity
- 502 measures of wearable activity trackers in medical research: a systematic review. *Int J*
- 503 *Med Inform* 2022; 160: 104696. <https://doi.org/10.1016/J.IJMEDINF.2022.104696>

31. Beauchamp UL, Pappot H, Holländer-Mieritz C. The use of wearables in clinical trials during cancer treatment: systematic review. *JMIR Mhealth Uhealth* 2020; 8(11): e22006. <https://doi.org/10.2196/22006>
32. Coughlin SS, Caplan LS, Stone R. Use of consumer wearable devices to promote physical activity among breast, prostate, and colorectal cancer survivors: a review of health intervention studies. *J Cancer Surviv* 2020; 14: 386–392. <https://doi.org/10.1007/s11764-020-00855-1>
33. Belcher BR, Kang DW, Yunker AG, et al. Interventions to reduce sedentary behavior in cancer patients and survivors: a systematic review. *Curr Oncol Rep* 2022; 24: 1593–1605. <https://doi.org/10.1007/S11912-022-01313-0>
34. Qiu L, Ye M, Tong Y, et al. Promoting physical activity among cancer survivors: an umbrella review of systematic reviews. *Support Care Cancer* 2023; 31: 301. <https://doi.org/10.1007/S00520-023-07760-0>
35. Akinosun AS, Polson R, Diaz-Skeete Y, et al. Digital technology interventions for risk factor modification in patients with cardiovascular disease: systematic review and meta-analysis. *JMIR Mhealth Uhealth* 2021; 9(3): e21061. <https://doi.org/10.2196/21061>

36. Jiang X, Ming WK, You JHS. The cost-effectiveness of digital health interventions on the management of cardiovascular diseases: systematic review. *J Med Internet Res* 2019; 21(6): e13166. <https://doi.org/10.2196/13166>
37. Hannan AL, Harders MP, Hing W, et al. Impact of wearable physical activity monitoring devices with exercise prescription or advice in the maintenance phase of cardiac rehabilitation: systematic review and meta-analysis. *BMC Sports Sci Med Rehabil* 2019; 11: 14. <https://doi.org/10.1186/S13102-019-0126-8>
38. Wongvibulsin S, Habeos EE, Huynh PP, et al. Digital health interventions for cardiac rehabilitation: systematic literature review. *J Med Internet Res* 2021; 23(2): e18773. <https://doi.org/10.2196/18773>
39. Mizuno A, Changolkar S, Patel MS. Wearable devices to monitor and reduce the risk of cardiovascular disease: evidence and opportunities. *Annu Rev Med* 2021; 72: 459–471. <https://doi.org/10.1146/ANNUREV-MED-050919-031534>
40. Thomson EA, Nuss K, Comstock A, et al. Heart rate measures from the Apple Watch, Fitbit Charge HR 2, and electrocardiogram across different exercise intensities. *J Sports Sci* 2019; 37: 1411–1419. <https://doi.org/10.1080/02640414.2018.1560644>
41. Bai Y, Hibbing P, Mantis C, et al. Comparative evaluation of heart rate-based monitors: Apple Watch vs Fitbit Charge HR. *J Sports Sci* 2018; 36: 1734–1741. <https://doi.org/10.1080/02640414.2017.1412235>

42. Shapiro A, Marinsek N, Clay I, et al. Characterizing COVID-19 and influenza illnesses in the real world via person-generated health data. *Patterns* 2020; 2(1): 100188.
<https://doi.org/10.1016/J.PATTER.2020.100188>
43. Deering S, Grade MM, Uppal JK, et al. Accelerating research with technology: rapid recruitment for a large-scale web-based sleep study. *JMIR Res Protoc* 2019; 8: e10974.
<https://doi.org/10.2196/10974>
44. Loncar-Turukalo T, Zdravevski E, da Silva JM, et al. Literature on wearable technology for connected health: scoping review of research trends, advances, and barriers. *J Med Internet Res* 2019; 21: e14017. <https://doi.org/10.2196/14017>
45. ClinicalTrials.gov. The DETECT (digital engagement, tracking for early control, and treatment) study (DETECT). <https://clinicaltrials.gov/ct2/show/NCT04336020> (accessed 13 May 2023).
46. ClinicalTrials.gov. Evaluation of ECG transmission and AI types using Apple Watch ECGs and symptoms data collected using a Mayo iPhone app.
<https://clinicaltrials.gov/ct2/show/NCT05324566> (accessed 13 May 2023).
47. Perez MV, Mahaffey KW, Hedlin H, et al. Large-scale assessment of a smartwatch to identify atrial fibrillation. *N Engl J Med* 2019; 381(20): 1909–1917.
<https://doi.org/10.1056/nejmoa1901183>

48. ClinicalTrials.gov. Apple heart and movement study.

<https://clinicaltrials.gov/ct2/show/NCT04198194> (accessed 13 May 2023).

49. ClinicalTrials.gov. Embrace: seizure characterization.

<https://clinicaltrials.gov/ct2/show/NCT03206502> (accessed 13 May 2023).

50. Lubitz SA, Faranesh AZ, Atlas SJ, et al. Rationale and design of a large population study to validate software for the assessment of atrial fibrillation from data acquired by a consumer tracker or smartwatch: the Fitbit heart study. *Am Heart J* 2021; 238: 16–26.

<https://doi.org/10.1016/j.ahj.2021.04.003>

51. Strain T, Wijndaele K, Dempsey PC, et al. Wearable-device-measured physical activity and future health risk. *Nat Med* 2020; 26(9): 1385–1391.

<https://doi.org/10.1038/s41591-020-1012-3>

52. Radin JM, Wineinger NE, Topol EJ, Steinhubl SR. Harnessing wearable device data to improve state-level real-time surveillance of influenza-like illness in the USA: a population-based study. *Lancet Digit Health* 2020; 2(2): e85–e93.

[https://doi.org/10.1016/s2589-7500\(19\)30222-5](https://doi.org/10.1016/s2589-7500(19)30222-5)

53. Hicks JL, Althoff T, Sosic R, et al. Best practices for analyzing large-scale health data from wearables and smartphone apps. *NPJ Digit Med* 2019; 2(45): 1–12.

<https://doi.org/10.1038/s41746-019-0121-1>

54. Rose SMS, Contrepois K, Kegan J, et al. A longitudinal big data approach for precision health. *Nat Med* 2019; 25(5): 792–804. <https://doi.org/10.1038/s41591-019-0414-6>
55. Goodday SM, Karlin E, Alfarano A, et al. An alternative to the light touch digital health remote study: the stress and recovery in frontline COVID-19 healthcare workers study. *JMIR Form Res* 2021; 5(12): 1–15. <https://doi.org/10.2196/32165>
56. ClinicalTrials.gov. A study to investigate if early atrial fibrillation (AF) diagnosis reduces risk of events like stroke in the real-world. <https://clinicaltrials.gov/ct2/show/NCT04276441> (accessed 13 May 2023).
57. ClinicalTrials.gov. Accuracy of the Apple Watch series 4 for detection of heart rhythm: a pilot study. <https://clinicaltrials.gov/ct2/show/NCT03798613> (accessed 13 May 2023).
58. ClinicalTrials.gov. Apple Watch heart failure study. <https://clinicaltrials.gov/ct2/show/NCT04510779> (accessed 13 May 2023).
59. ClinicalTrials.gov. Heart watch study: a pragmatic randomized controlled trial. <https://clinicaltrials.gov/ct2/show/NCT04468321> (accessed 13 May 2023).
60. ClinicalTrials.gov. A study to investigate if early atrial fibrillation (AF) diagnosis reduces risk of events like stroke in the real-world. <https://clinicaltrials.gov/ct2/show/NCT04276441> (accessed 13 May 2023).

61. ClinicalTrials.gov. Identification of arrhythmias with one-time ECG.
<https://clinicaltrials.gov/ct2/show/NCT03753139> (accessed 13 May 2023).
62. ClinicalTrials.gov. Portable measurement methods combined with artificial intelligence
in detection of atrial fibrillation (WB-AF).
<https://clinicaltrials.gov/ct2/show/NCT04917653> (accessed 13 May 2023).
63. ClinicalTrials.gov. Evaluation of meal gesture dosing in adults with type 1 diabetes.
<https://clinicaltrials.gov/ct2/show/NCT04964128> (accessed 13 May 2023).
64. ClinicalTrials.gov. Real-time reminders to decrease late or missed meal boluses (Klue).
<https://clinicaltrials.gov/ct2/show/NCT03970889> (accessed 13 May 2023).
65. ClinicalTrials.gov. The loop observational study (LOS).
<https://clinicaltrials.gov/ct2/show/NCT03838900> (accessed 13 May 2023).
66. ClinicalTrials.gov. Artificial pancreas with different stress assessments in the outpatient
setting. <https://clinicaltrials.gov/ct2/show/NCT04142229> (accessed 13 May 2023).
67. Corbett JP, Hsu L, Brown SA, et al. Smartwatch gesture-based meal reminders improve
glycaemic control. *Diabetes Obes Metab* 2022; 24: 1667–1670.
<https://doi.org/10.1111/dom.14737>
68. Wong JJ, Suttiratana SC, Lal RA, et al. Discontinued Use of the Loop Insulin Dosing
System: A Mixed-Methods Investigation. *Diabetes Technol Ther* 2022; 24: 241–248.
<https://doi.org/10.1089/dia.2021.0362>

- 613 69. Suttiratana SC, Wong JJ, Lanning MS, et al. Qualitative Study of User Experiences
614 with Loop, an Open-Source Automated Insulin Delivery System. *Diabetes Technol*
615 *Ther* 2022; 24: 416–423. <https://doi.org/10.1089/dia.2021.0485>
- 616 70. Lum JW, Bailey RJ, Barnes-lomen V, et al. A Real-World Prospective Study of the
617 Safety and Effectiveness of the Loop Open Source Automated Insulin Delivery System.
618 *DIABETES Technol Ther* 2021; 23: 367–375. <https://doi.org/10.1089/dia.2020.0535>
- 619 71. Kesavadev J, Srinivasan S, Saboo B. The Do-It-Yourself Artificial Pancreas : A
620 Comprehensive Review. *Diabetes Therapy* 2020; 11: 1217–1235.
621 <https://doi.org/10.1007/s13300-020-00823-z>
- 622 72. Downey L, Donnell SO, Melvin T, et al. A European Regulatory Pathway for Tidepool
623 Loop Following Clearance in the United States ? Author Affiliations.
624 <https://doi.org/10.1111/dme.15246>.
- 625 73. Braune K, Hussain S, Lal R. The First Regulatory Clearance of an Open-Source
626 Automated Insulin Delivery Algorithm. *J Diabetes Sci Technol* 2023; 17: 1139–1141.
627 <https://doi.org/10.1177/19322968231164166>
- 628 74. Mercer K, Li M, Giangregorio L, et al. Behavior change techniques present in wearable
629 activity trackers: a critical analysis. *JMIR Mhealth Uhealth* 2016; 4(2): e40.
630 <https://doi.org/10.2196/mhealth.4461>

75. Brickwood KJ, Watson G, O'Brien J, et al. Consumer-based wearable activity trackers increase physical activity participation: systematic review and meta-analysis. *JMIR Mhealth Uhealth* 2019; 7(4): e11819. <https://doi.org/10.2196/11819>
76. ClinicalTrials.gov. Exogenous melatonin in intensive care unit chrono-disruption (EMIC). <https://clinicaltrials.gov/ct2/show/NCT03708341> (accessed 13 May 2023).
77. ClinicalTrials.gov. Repurposing low-dose clonidine for PTSD in veterans. <https://clinicaltrials.gov/ct2/show/NCT04877093> (accessed 13 May 2023).
78. ClinicalTrials.gov. Effects of ranolazine and exercise on daily physical activity trial (EREDA). <https://clinicaltrials.gov/ct2/show/NCT01948310> (accessed 13 May 2023).
79. ClinicalTrials.gov. Ambulatory oxygen effects on muscles in COPD (OM-COPD). <https://clinicaltrials.gov/ct2/show/NCT01722370> (accessed 13 May 2023).
80. ClinicalTrials.gov. The effect of prebiotic fibers on weight loss in an overweight and obese population (MNGII). <https://clinicaltrials.gov/ct2/show/NCT03135041> (accessed 13 May 2023).
81. ClinicalTrials.gov. The impact of cranberries on the microbiome and the brain in healthy ageing study (COMBAT). <https://www.clinicaltrials.gov/ct2/show/NCT03679533> (accessed 13 May 2023).
82. ClinicalTrials.gov. Multi-nutrient supplement to improve physical performance in older adults. <https://clinicaltrials.gov/ct2/show/NCT04454359> (accessed 13 May 2023).

650

651 83. Taibi DM, Vitiello M V., Barsness S, et al. A randomized clinical trial of valerian fails
652 to improve self-reported, polysomnographic, and actigraphic sleep in older women with
653 insomnia. *Sleep Med* 2009; 10: 319–328. <https://doi.org/10.1016/j.sleep.2008.02.001>

654 84. Camargos EF, Louzada LL, Quintas JL, et al. Trazodone improves sleep parameters in
655 Alzheimer disease patients: A randomized, double-blind, and placebo-controlled study.
656 *American Journal of Geriatric Psychiatry* 2014; 22: 1565–1574.
657 <https://doi.org/10.1016/j.jagp.2013.12.174>

658 85. Madsen MT, Hansen MV, Andersen LT, et al. Effect of Melatonin on Sleep in the
659 Perioperative Period after Breast Cancer. 12. <https://doi.org/10.5664/jcsm.5490>

660 86. Willis LH, Slentz CA, Johnson JL, et al. Effects of Exercise Training With and Without
661 Ranolazine on Peak Oxygen Consumption, Daily Physical Activity, and Quality of Life
662 in Patients With Chronic Stable Angina Pectoris. *American Journal of Cardiology* 2019;
663 124: 655–660. <https://doi.org/10.1016/j.amjcard.2019.05.063>

664 87. Hess AL, Benítez-Páez A, Blædel T, et al. The effect of inulin and resistant
665 maltodextrin on weight loss during energy restriction: a randomised, placebo-
666 controlled, double-blinded intervention. *Eur J Nutr* 2020; 59: 2507–2524.
667 <https://doi.org/10.1007/s00394-019-02099-x>

88. Tessier AJ, Levy-Ndejuru J, Moyen A, et al. A 16-week randomized controlled trial of a fish oil and whey protein-derived supplement to improve physical performance in older adults losing autonomy-A pilot study. *PLoS One* 2021; 16: 1–18.
<https://doi.org/10.1371/journal.pone.0256386>
89. Camargos EF, Louzada LL, Quintas JL, et al. Trazodone improves sleep parameters in Alzheimer disease patients: a randomized, double-blind, and placebo-controlled study. *Am J Geriatr Psychiatry* 2014; 22: 1565–1574. <https://doi.org/>
90. Rogers A, de Paoli G, Subbarayan S, et al. A systematic review of methods used to conduct decentralized clinical trials. *Br J Clin Pharmacol* 2021; 88(6): 2843–2862.
<https://doi.org/10.1111/bcp.15205>
91. Price J, Goodson N, Warren EJ, et al. Resilient design: decentralized trials recovered faster from the impact of COVID-19 than traditional site-based designs. *Expert Rev Med Devices* 2021; 18(sup1): 1–4. <https://doi.org/10.1080/17434440.2021.2014818>
92. Naik H, Palaniappan L, Ashley EA, Scott AS. Digital health applications for pharmacogenetic clinical trials. *Genes* 2020; 11(11): 1261.
<https://doi.org/10.3390/genes11111261>
93. van Norman GA. Decentralized clinical trials: the future of medical product development? *JACC Basic Transl Sci* 2021; 6(4): 384–387.
<https://doi.org/10.1161/circheartfailure.120.007767>

- 687 94. Spertus JA, Birmingham MC, Butler J, et al. Novel trial design: CHIEF-HF. *Circ Heart*
688 *Fail* 2021; 14(3): e007767. <https://doi.org/10.1161/circheartfailure.120.007767>
- 689 95. de Brouwer W, Patel CJ, Manrai AK, et al. Empowering clinical research in a
690 decentralized world. *NPJ Digit Med* 2021; 4(1): 1–5. [http://dx.doi.org/10.1038/s41746-](http://dx.doi.org/10.1038/s41746-021-00473-w)
691 [021-00473-w](http://dx.doi.org/10.1038/s41746-021-00473-w)
- 692 96. Coert RMH, Timmis JK, Boorsma A, et al. Stakeholder perspectives on barriers and
693 facilitators for the adoption of virtual clinical trials: qualitative study. *J Med Internet*
694 *Res* 2021; 23(7): 1–12. <https://doi.org/10.2196/2021.07.14.21260523>
- 695 97. Lee JL, Cerrada CJ, Vang MKY, et al. The DiSCover project: protocol and baseline
696 characteristics of a decentralized digital study assessing chronic pain outcomes and
697 behavioral data. *medRxiv*. 2021; 22: 1–23.
698 <https://doi.org/10.1101/2021.07.14.21260523>
- 699 98. Sommer C, Zuccolin D, Arnera V, et al. Building clinical trials around patients:
700 evaluation and comparison of decentralized and conventional site types in patients with
701 low back pain. *Contemp Clin Trials Commun* 2018; 11: 120–6. <https://doi.org/10.1016/j.conctc.2018.06.008>
- 702 <https://doi.org/10.1016/j.conctc.2018.06.008>
- 703 99. Japan Pharmaceutical Manufacturers Association. Study for introduction and utilization
704 of clinical trial methods that do not depend on visits to medical institutions. 2020,
705 Available at

https://www.jpma.or.jp/information/evaluation/results/allotment/lofurc0000005jr6-att/tf3-cdt_00.pdf (2020, accessed 13 May 2023).

100. ClinicalTrials.gov. eHealth weight loss program in African American breast cancer survivors. <https://clinicaltrials.gov/ct2/show/NCT02699983> (accessed 13 May 2023).

101. ClinicalTrials.gov. Weight management and health behavior intervention in lowering cancer risk for BRCA positive and lynch syndrome families.

<https://clinicaltrials.gov/ct2/show/NCT04125914> (accessed 13 May 2023).

102. ClinicalTrials.gov. Exercise intervention after cancer treatment for improving health in stage II-III breast cancer survivors (PACT).

<https://clinicaltrials.gov/ct2/show/NCT03523195> (accessed 13 May 2023).

103. ClinicalTrials.gov. The patterns of activity and cognition during treatment (PACT) study. <https://clinicaltrials.gov/ct2/show/NCT04562987> (accessed 13 May 2023).

104. ClinicalTrials.gov. Patient activation through counseling, exercise, and mobilization (PACE-Mobil). <https://clinicaltrials.gov/ct2/show/NCT03411200> (accessed 13 May 2023).

105. ClinicalTrials.gov. Passive sensing technology for lapse measurement.

<https://clinicaltrials.gov/ct2/show/NCT03739151> (accessed 13 May 2023).

- 723 106.ClinicalTrials.gov. Lifestyle intervention program for former elite athletes
724 (Champ4Life). <https://clinicaltrials.gov/ct2/show/NCT03031951> (accessed 13 May
725 2023).
- 726 107.ClinicalTrials.gov. Evaluation of a family intervention program for the management of
727 overweight or obese children (NEREU).
728 <https://clinicaltrials.gov/ct2/show/NCT01878994> (accessed 13 May 2023).
- 729 108.ClinicalTrials.gov. Supporting together exercise and play and improving nutrition
730 (STEP IN). <https://www.clinicaltrials.gov/ct2/show/study/NCT02724839> (accessed 13
731 May 2023).
- 732 109.ClinicalTrials.gov. Financial incentives for weight reduction study (FIReWoRk).
733 <https://clinicaltrials.gov/ct2/show/NCT03157713> (accessed 13 May 2023).
- 734 110.ClinicalTrials.gov. Sedentary behavior, cardiovascular function, and sleep (PACE).
735 <https://clinicaltrials.gov/ct2/show/NCT04137068> (accessed 13 May 2023).
- 736 111.ClinicalTrials.gov. Development and feasibility of an incentive scheme to promote
737 walking/cycling to school (RIGHT_TRACKS).
738 <https://clinicaltrials.gov/ct2/show/NCT02282631> (accessed 13 May 2023).
- 739 112.ClinicalTrials.gov. Testing the efficacy of Pokémon Go for increasing physical activity.
740 <https://clinicaltrials.gov/ct2/show/NCT03109509> (accessed 13 May 2023).

113.ClinicalTrials.gov. Physical activity promotion in children using a novel smartphone game: a pilot randomized controlled trial.

<https://clinicaltrials.gov/ct2/show/NCT04593199> (accessed 13 May 2023).

114.ClinicalTrials.gov. The BWH wellness project (B-Well).

<https://clinicaltrials.gov/ct2/show/NCT02850094> (accessed 13 May 2023).

115.ClinicalTrials.gov. STEP together: an effectiveness-implementation study of social incentives and physical activity. <https://clinicaltrials.gov/ct2/show/NCT04942535>

(accessed 13 May 2023).

116.ClinicalTrials.gov. Mind-body interventions to mitigate effects of media use on sleep in

early adolescents (Sleepazoid). <https://clinicaltrials.gov/ct2/show/NCT04550507>

(accessed 13 May 2023).

117.ClinicalTrials.gov. Efficacy of Tai Chi versus CBT-I in treating chronic insomnia in

older adults. <https://clinicaltrials.gov/ct2/show/NCT04384822> (accessed 13 May 2023).

118.ClinicalTrials.gov. M-Health administered sleep treatment to enhance recovery in

bariatric populations (MASTER). <https://clinicaltrials.gov/ct2/show/NCT04619771>

(accessed 13 May 2023).

119.ClinicalTrials.gov. Reducing sleep disparities in minority children.

<https://clinicaltrials.gov/ct2/show/NCT01301989> (accessed 13 May 2023).

- 759 120.ClinicalTrials.gov. Sleep specialty consultation: improving management of sleep
760 disorders. <https://clinicaltrials.gov/ct2/show/NCT00390572> (accessed 13 May 2023).
- 761 121.ClinicalTrials.gov. Adapting sleep and yoga interventions for maximal effectiveness in
762 low-income populations (CALYPSO). <https://clinicaltrials.gov/ct2/show/NCT03392194>
763 (accessed 13 May 2023).
- 764 122.ClinicalTrials.gov. Better sleep in psychiatric care: anxiety and affective disorders
765 (BSIP-AAD). <https://clinicaltrials.gov/ct2/show/NCT04136054> (accessed 13 May
766 2023).
- 767 123.ClinicalTrials.gov. Genetic risk-based atrial fibrillation screening (GeneAF Study).
768 <https://clinicaltrials.gov/ct2/show/NCT04932798> (accessed 13 May 2023).
- 769 124.ClinicalTrials.gov. Electrocardiogram clinical validation study.
770 <https://clinicaltrials.gov/ct2/show/NCT04842123> (accessed 13 May 2023).
- 771 125.ClinicalTrials.gov. MechSens: dose-response relationship of in vivo ambulatory load
772 and mechanosensitive cartilage biomarkers (MechSens).
773 <https://clinicaltrials.gov/ct2/show/NCT04128566> (accessed 13 May 2023).
- 774 126.ClinicalTrials.gov. Aerobic exercise on improving sleep in systemic lupus
775 erythematosus. (EFEXO). <https://clinicaltrials.gov/ct2/show/NCT02037971> (accessed
776 13 May 2023).

- 777 127.ClinicalTrials.gov. Physical fitness training in subacute stroke (PHYS-Stroke).
778 <https://clinicaltrials.gov/ct2/show/NCT01953549> (accessed 13 May 2023).
- 779 128.ClinicalTrials.gov. Level of activity in lumbar spinal stenosis patients pre- and post-
780 surgery. <https://clinicaltrials.gov/ct2/show/NCT02154191> (accessed 13 May 2023).
- 781 129.ClinicalTrials.gov. AMPLE-3: IPC plus talc vs. VATS in management of malignant
782 pleural effusion (AMPLE-3). <https://clinicaltrials.gov/ct2/show/NCT04322136>
783 (accessed 13 May 2023).

784 **Figure captions**

785 **Figure 1.** Mean of enrollment comparison by type

786 **Figure 2.** 2D scatterplot of relationship between annual enrollment and trial number over
787 time

788 **Figure 3.** Mosaic diagram of conditions

789 **Figure 4.** Mosaic diagram of intervention

790 **Tables**791 **Table 1.** Frequently used intervention types in selected studies

Type of condition	Frequently used devices	Frequently used interventions	Description
Cancer	Garmin 68.75% Fitbit: 69.23% S-Figure 6, S-Table 1	Behavioral	Dietary, exercise, and physical activity interventions to control obesity after breast cancer, increase or maintain the levels and intensity of physical function by activating patients through exercise, reduce symptoms and side effects, and improve quality of life. ^{100–104}
Cardiovascular disease	Apple Watch: 80% Empatica: 100% S-Figure 7, S-Table 2	Device	Comparing the accuracy of the device's heart rate and ECG detection functions with those of a more accurate ECG; development of smartphone applications. ^{57–62}
Obesity	ActiGraph 92.08% Fitbit 91.43% S-Figure 8, S-Table 3	Behavioral	Lifestyle, diet, and exercise interventions, such as psychological counseling and coaching, for weight loss. ^{105–109}
Physical activity	ActiGraph 93.08% Fitbit 90.59% S-Figure 9, S-Table 4	Behavioral	Exercise, physical activity, and lifestyle interventions, including incentives (e.g., points earned based on the number of steps taken per day), donations as gifts or charitable contributions, and games (e.g., “Pokémon Go”) to motivate engagement. ^{110–115}
Sleep	ActiGraph: 60% Empatica: 100% S-Figure 10, S-Table 5	Behavioral	Cognitive-behavioral therapy to promote sleep, sleep counseling, and exercise interventions, such as tai chi. ^{116–122}
Diabetes	Apple Watch 60% Empatica 50% S-Figure 11, S-Table 6	Device	Development of applications for insulin administration and dietary management of type 1 diabetes; assessment of psychological and physiological stress during the use of insulin administration systems. ^{63–66}

792

793 **Table 2.** Frequently used intervention types in clinical research

Intervention type	Device	Description
Behavioral	Fitbit, Garmin ActiGraph	Used for cancer, obesity, physical activity, and sleep. Numerous systematic reviews have been conducted on interventions promoting physical activity, ^{32,34,74,75} including those utilizing Fitbit, Garmin, and ActiGraph, and the results align with the present findings.
Device	Apple Watch Empatica	Device accuracy confirmation and application intervention studies for cardiovascular diseases and diabetes.
Drug dietary supplement	ActiGraph	Used to evaluate sleep, physical activity, and other variables for various drug administration interventions. ^{76–82}
Diagnostic test	Apple Watch Garmin	Used to quantify cognitive ability and daily activities and evaluate diagnoses of atrial fibrillation and cardiovascular disease events using ECG. ^{48,123,124}
Procedure	ActiGraph Empatica	Used to acquire data on physical activity, sleep, and stress levels, evaluate exercise therapies (e.g., training and rehabilitation), and compare multiple treatment methods. ^{125–129}

794