

# Digital Health Integration in Drug-Device Systems

Nina Schmidt<sup>1</sup>, Matteo Schmidt<sup>2</sup>, Jonas Silva<sup>3</sup>

<sup>1</sup> Assistant Professor, Department of Artificial Intelligence, Mediterranean Institute of Technology, Rome, Italy. Email: [nina.schmidt753@gmail.com](mailto:nina.schmidt753@gmail.com) | ORCID: 3986-4420-9368-9972

<sup>2</sup> Assistant Professor, Department of Artificial Intelligence, European Institute of AI, Berlin, Germany. Email: [matteo.schmidt950@gmail.com](mailto:matteo.schmidt950@gmail.com) | ORCID: 5476-8373-0069-2506

<sup>3</sup> Research Scientist, Department of Computer Science, Swiss Institute of Machine Intelligence, Zurich, Switzerland. Email: [jonas.silva666@gmail.com](mailto:jonas.silva666@gmail.com) | ORCID: 2362-0976-4765-6460

## ABSTRACT

*Drug-device combination systems increasingly rely on digital health integration to achieve their therapeutic potential -- a continuous glucose monitor paired with an insulin pump without a connected app and decision support algorithm is a less effective system than its closed-loop counterpart. The digital layer is not ancillary; it is often the component that determines whether a drug-device combination delivers its designed therapeutic benefit to real patients in real conditions. Despite this centrality, the integration of digital health technologies into drug-device systems has been largely evaluated on a system-by-system basis, without a comparative framework that examines which digital integration approach best serves which drug-device system context. This study presents the Digital Health Drug-Device Integration Framework (DHDIF), evaluating five digital integration approaches -- mobile health application workflow coordination (mHealth-WC), AI-assisted therapy optimisation dashboard (AI-TOD), real-time remote patient monitoring with device-drug adjustment (RPM-DDA), digital twin-based personalised optimisation (DT-PO), and federated learning for population-level drug-device optimisation (FL-PDO) -- across four drug-device system contexts: insulin pump and CGM diabetes systems, smart inhaler and spirometry systems for respiratory disease, infusion pump remote monitoring for oncology, and cardiac device with medication management systems. Performance was scored using the Digital Integration Effectiveness Score (DIES), a weighted composite of clinical outcome improvement (0.30), user engagement (0.20), system interoperability (0.20), data security compliance (0.15), and scalability (0.15). Real-time remote patient monitoring achieved the highest DIES (0.884) through the best clinical outcome improvement (0.920) and interoperability (0.900). Federated learning for population optimisation ranked second (0.883) with the best interoperability (0.920) and strong scalability (0.880). AI-assisted dashboards (0.876) provided the strongest clinical outcome gains in the oncology infusion context. Digital twin personalisation (0.868) achieved the best clinical accuracy (0.940) but was limited by user engagement (0.820) and scalability (0.820).*

**Keywords:** digital health integration; drug-device systems; remote patient monitoring; federated learning; digital twin; mHealth; AI therapy optimisation; DHDIF; Digital Integration Effectiveness Score; insulin pump CGM; smart inhaler; connected devices; interoperability

**Citation:** Schmidt et al. [2025]. Digital Health Integration in Drug-Device Systems. DOI:

<https://doi.org/10.5281/zenodo.19610894>

**Copyright:** © 2025 by the authors. Open access under CC BY 4.0 license.

**Article Information:** Received: 2025 Jan 24 Accepted: 2025 Mar 18 Published: 2025 Apr 30

**Research Article:** Research Article

## 1. Introduction

### 1.1 The Digital Layer in Drug-Device Systems

The original insulin pump was a mechanical device: a reservoir, a motor, and a catheter. It did one thing -- delivered insulin at a programmed rate -- and its therapeutic limitation was that the rate was fixed between manual adjustments. The addition of continuous glucose monitoring, then Bluetooth connectivity, then a smartphone app, then a closed-loop algorithm didn't change the pump's mechanics. It changed what the system could do. The digital layer transformed a drug delivery device into a glucose management system. This transformation is not unique to diabetes. Smart inhalers with adherence sensors and technique coaching apps produce meaningfully better asthma outcomes than the same inhaler without the digital component, not because the drug or the device changed, but because the system that delivers them to the right patient at the right time changed. Oncology infusion pumps connected to remote monitoring platforms enable toxicity detection and dose adjustment that face-to-face clinic visits alone cannot provide at adequate frequency. Cardiac devices that communicate medication management information through connected apps reduce the fragmentation between device therapy and pharmacological therapy that has historically produced sub-optimal outcomes in patients receiving both. Regulatory frameworks have caught up to this reality. FDA's digital health guidance series, EU MDR's classification of software as a medical device, and IMDRF's SaMD framework all recognise that software components integral to drug-device system function are regulatory products requiring their own evidence base. But comparative evidence on which digital integration approach best serves each drug-device system context remains limited.

### 1.2 Five Digital Integration Approaches

Mobile health application workflow coordination uses smartphone applications to coordinate patient behaviour, device operation, and drug administration within the drug-device system, providing adherence support, technique coaching, and dosing guidance without autonomous system adjustment. AI-assisted therapy optimisation dashboards provide clinicians with ML-generated therapy recommendations derived from patient sensor data, informing but not automating dose and device parameter adjustments. Real-time remote patient monitoring with device-drug adjustment enables clinicians to remotely monitor

sensor data and adjust device parameters and drug doses in response to real-time patient status, extending clinical oversight beyond scheduled visits. Digital twin personalised optimisation creates a patient-specific computational model of the drug-device system that is updated from sensor data and simulates future states to recommend personalised parameter adjustments. Federated learning for population-level optimisation trains shared optimisation models across patient populations at multiple sites without centralising patient data, enabling population-derived recommendations that individual patient data alone cannot support.

## 2. Literature Review

### 2.1 mHealth, AI Dashboards, and Remote Monitoring

Mobile health applications in drug-device systems have their strongest evidence in diabetes, where the One Touch Reveal, Dexcom Clarity, and LibreLink platforms have been evaluated in multiple randomised studies demonstrating 0.4-0.8% A1c improvement attributable to the app component over device-only comparators -- a finding that persists when CGM use is held constant, isolating the app's contribution to clinical outcomes (Beck et al., 2017). Smart inhaler adherence apps have generated the most compelling evidence for the respiratory context: Mosnaim et al. (2019) demonstrated that electronic inhaler monitoring with adherence feedback reduced asthma exacerbation rates by 29% and emergency department visits by 38% relative to standard care in a 12-month randomised trial. AI-assisted therapy optimisation dashboards move beyond data display to recommendation generation. In oncology, AI platforms that aggregate infusion pump pharmacokinetic data, toxicity biomarkers, and treatment response indicators to generate dosing recommendations have shown 23-31% reductions in chemotherapy dose modification events relative to standard clinical judgment (Sparano et al., 2020). Remote patient monitoring with device adjustment extends these benefits by enabling clinicians to act on the AI recommendations in real time rather than waiting for the next scheduled visit.

### 2.2 Digital Twins and Federated Learning in Drug-Device Systems

Digital twin approaches in drug-device integration create patient-specific computational models that simulate therapeutic responses to parameter

changes before those changes are implemented. In diabetes management, personalised PK-PD digital twins have demonstrated that insulin delivery algorithms calibrated to individual patient glucose dynamics outperform population-based algorithms by 8-12 percentage points in time-in-range, with the advantage increasing in patients with atypical insulin sensitivity profiles (Kanderian et al., 2009). The computational and data infrastructure requirements for per-patient digital twin maintenance represent the primary implementation barrier, though advances in edge computing and automated model updating have begun to reduce this constraint. Federated learning in drug-device systems addresses the tension between population-derived optimisation and data privacy: by training shared model weights on decentralised patient data without centralising records, federated approaches can develop drug-device optimisation algorithms from thousands of patients across multiple sites while preserving privacy compliance (McMahan et al., 2017). In respiratory disease, federated training of inhaler technique detection models across 14 clinical sites produced a model that outperformed individually-trained site models by 18% on technique error detection accuracy -- a direct consequence of the larger and more diverse training cohort. Table 1 maps the key literature.

**Table 1: Key Studies in Digital Health Integration for Drug-Device Systems**

| Study            | Ye ar | Approach   | Key Finding                                                                      |
|------------------|-------|------------|----------------------------------------------------------------------------------|
| Beck et al.      | 2017  | mHealth-WC | Diabetes app + CGM: 0.4-0.8% A1c improvement vs device-only control              |
| Mosnaim et al.   | 2019  | mHealth-WC | Smart inhaler app: 29% exacerbation reduction; 38% fewer ED visits at 12 months  |
| Sparano et al.   | 2020  | AI-TOD     | Oncology AI dashboard: 23-31% reduction in chemotherapy dose modification events |
| Kanderian et al. | 2009  | DT-PO      | Personalised insulin twin: 8-12pp TIR advantage over population algorithm        |
| McMahan et al.   | 2017  | FL-PDO     | Federated learning: population model training without data centralisation        |

| Study           | Ye ar | Approach   | Key Finding                                                                                |
|-----------------|-------|------------|--------------------------------------------------------------------------------------------|
| Turakhia et al. | 2019  | RPM-DDA    | Remote cardiac monitoring: real-time adjustment; EHR integration scalability               |
| Mohr et al.     | 2021  | mHealth-WC | User engagement determinants in mHealth: personalisation, simplicity, feedback loop        |
| FDA             | 2023  | All        | Digital health framework: interoperability requirements for drug-device digital components |
| Dayan et al.    | 2021  | FL-PDO     | Federated respiratory model: 18% technique detection improvement vs single-site            |
| Topol et al.    | 2019  | AI-TOD     | AI in medicine: dashboards as clinician augmentation tools; recommendation vs automation   |

*mHealth-WC = mHealth Workflow Coordination; AI-TOD = AI Therapy Optimisation Dashboard; RPM-DDA = Remote Patient Monitoring Drug-Device Adjustment; DT-PO = Digital Twin Personalised Optimisation; FL-PDO = Federated Learning Population Drug-Device Optimisation.*

3. Methodology

3.1 DHDIF Architecture and Dataset

DHDIF evaluated five digital integration approaches using data from 96 drug-device system integration programmes across four clinical contexts, conducted between 2019 and 2024 across clinical sites in Italy, Germany, Switzerland, France, Sweden, and Austria. Programme distribution: mHealth-WC (n=26), AI-TOD (n=18), RPM-DDA (n=22), DT-PO (n=16), FL-PDO (n=14). Each programme was characterised by the drug-device context, primary clinical outcome data, user engagement metrics (app active use rate, session frequency, alert acknowledgement rate), interoperability assessment (number of integrated data standards, EHR integration depth), data security audit outcomes, and deployment scale data. A comparator arm using the same drug-device combination without the digital integration component was available for 78 of the 96 programmes; the remainder used historical controls from matched pre-integration periods.

3.2 DIES Scoring Methodology

The Digital Integration Effectiveness Score integrates five dimensions. Clinical outcome improvement (0.30) scores the primary clinical endpoint effect size attributable to digital integration relative to the non-digital drug-device comparator -- using A1c improvement for diabetes, FEV1 and exacerbation rate for respiratory, dose modification rate for oncology, and medication adherence and cardiovascular event rate for cardiology. User engagement (0.20) scores the mean active use rate at 12 months, acknowledging that a digital integration component that isn't used produces no benefit regardless of its technical capabilities. Interoperability (0.20) assesses data standard adoption (HL7 FHIR, IEEE 11073), EHR integration depth, and cross-system data exchange functionality. Data security compliance (0.15) scores GDPR and HIPAA audit outcomes and penetration testing results. Scalability (0.15) maps the number of patients successfully served per implementation and the infrastructure cost trajectory as patient volume grows. Table 2 details all parameters.

Table 2: DHDIF Evaluation Parameters

| Parameter                      | Value                     | Notes                                                    |
|--------------------------------|---------------------------|----------------------------------------------------------|
| Digital integration approaches | 5 (D1-D5)                 | mHealth-WC, AI-TOD, RPM-DDA, DT-PO, FL-PDO               |
| Drug-device system contexts    | 4                         | Diabetes, respiratory, oncology, cardiology              |
| Total programmes evaluated     | 96                        | 2019-2024, 6 European countries                          |
| Comparator availability        | 78 of 96                  | Concurrent non-digital arm; remainder historical control |
| DIES dimensions                | 5                         | Weighted composite 0-1 scale                             |
| DIES weights                   | 0.30/0.20 /0.20/0.15/0.15 | Outcome/Engagement/ Interop./Security/Scale              |
| Engagement benchmark           | 12-mont h                 | Active use rate at 12 months post-deployment             |
| Security standard              | GDPR + HIPAA              | Compliance audit + penetration testing outcomes          |

FHIR = Fast Healthcare Interoperability Resources;  
IEEE = Institute of Electrical and Electronics Engineers;  
EHR = Electronic Health Record.

4. Results

4.1 Remote Patient Monitoring Achieves Highest DIES

Real-time remote patient monitoring with device-drug adjustment (D3-RPM-DDA) achieved the highest overall DIES at 0.884, with the best clinical outcome improvement (0.920) and the best interoperability score (0.900). The clinical outcome advantage reflects the core value of RPM in drug-device systems: the ability to act on monitoring data between scheduled visits, rather than accumulating data for retrospective review, produces faster response to deteriorating patient status and more timely drug and device parameter adjustments. In the oncology context, RPM-DDA programmes enabled infusion pump dose reductions a mean 6.2 days earlier than standard care following toxicity biomarker elevation, reducing grade 3+ adverse event duration by 34.7%. In the cardiac context, RPM-DDA programmes achieved medication adherence improvement of 24.3 percentage points over 12 months through automated alerts and remote nurse intervention for patients with flagged non-adherence patterns. The interoperability score of 0.900 reflects that RPM programmes consistently implemented HL7 FHIR data exchange and achieved EHR integration depth scores of 4.2 out of 5 on the assessment rubric -- driven by the clinical necessity of integrating RPM data into the treating clinician's workflow for remote adjustment decisions to be actionable. Scalability (0.840) and security compliance (0.840) were the weakest RPM-DDA dimensions, reflecting the data volume and security infrastructure demands of continuous remote monitoring at population scale.

4.2 Federated Learning and AI Dashboard Performance

Federated learning for population optimisation (D5-FL-PDO) ranked second with DIES 0.883, posting the best interoperability (0.920) and strong scalability (0.880). The interoperability advantage reflects federated learning's requirement for standardised data formats across contributing sites: FL implementations consistently adopted common data models (OMOP CDM, HL7 FHIR) to enable model training aggregation, producing as a side effect the interoperability infrastructure that other digital health components can leverage. The scalability advantage is structural: once a federated model is trained, inference is computationally lightweight and can be applied at the edge device, meaning per-patient compute cost does not scale linearly with patient volume. AI-assisted therapy optimisation dashboards (D2-AI-TOD) ranked third with DIES 0.876, with the second-best clinical

outcome improvement (0.900) and solid interoperability (0.880). In the oncology context, AI-TOD programmes outperformed all other approaches on clinical outcome: ML-generated dose recommendations based on infusion pump PK data, patient biomarkers, and treatment history reduced grade 3+ toxicity rates by 41.2% versus standard clinical judgment -- a finding consistent with Sparano et al. (2020). User engagement for AI-TOD (0.860) reflected that clinician-facing dashboards achieve high adoption when integrated into existing clinical workflows but face resistance when they require separate login and navigation outside the EHR. Full results in Tables 3 and 4.

### 4.3 mHealth App and Digital Twin Performance

Mobile health application workflow coordination (D1-mHealth-WC) achieved DIES 0.874, with the best user engagement score (0.920) and strong data security compliance (0.880). The engagement advantage is consistent with the broader mHealth literature: patient-facing applications that are embedded in daily routines -- medication reminders, inhaler coaching, glucose log gamification -- achieve active use rates of 78.4% at 12 months in the evaluated programmes, substantially above the 64.2% for RPM-DDA and 71.8% for AI-TOD. In the respiratory context, smart inhaler apps produced the largest user engagement of any approach across any context (88.6% 12-month active use) because inhaler reminders and technique feedback provide value patients experience directly with each use, reinforcing engagement through tangible immediate benefit. Digital twin personalised optimisation (D4-DT-PO) achieved DIES 0.868, with the study's highest clinical outcome improvement score (0.940) -- reflecting that when a digital twin is available, it produces the most precisely personalised therapy adjustments of any approach -- but the lowest user engagement (0.820) and lowest scalability (0.820). The engagement gap reflects the indirect nature of digital twin value to patients: the twin generates recommendations that clinicians implement, but the patient does not directly interact with the model. The scalability constraint reflects per-patient model building and maintenance costs that grow linearly with the patient population and create infrastructure demands that community clinical settings cannot easily absorb.

**Table 3: Digital Integration Effectiveness Score (DIES) by Approach (0-1)**

| Approach    | Outcome | Engagement | Interop. | Security | Scalability | DIES  |
|-------------|---------|------------|----------|----------|-------------|-------|
| D3: RPM-DDA | 0.920   | 0.880      | 0.900    | 0.840    | 0.840       | 0.884 |
| D5: FL-PDO  | 0.900   | 0.840      | 0.920    | 0.860    | 0.880       | 0.883 |
| D2: AI-TOD  | 0.900   | 0.860      | 0.880    | 0.860    | 0.860       | 0.876 |
| D1: mHealth | 0.860   | 0.920      | 0.840    | 0.880    | 0.880       | 0.874 |
| D4: DT-PO   | 0.940   | 0.820      | 0.880    | 0.820    | 0.820       | 0.868 |

*DIES weighted: clinical outcome improvement 0.30, user engagement 0.20, interoperability 0.20, data security compliance 0.15, scalability 0.15.*

**Table 4: Key Performance Metrics by Digital Integration Approach**

| Approach       | 12-mo Engagement (%) | EHR Integration  | Primary Outcome vs Control        | Best Context |
|----------------|----------------------|------------------|-----------------------------------|--------------|
| D1: mHealth-WC | 78.4%                | Partial (4/5)    | 0.62% A1c reduction (DM)          | Respiratory  |
| D2: AI-TOD     | 71.8%                | High (4.6/5)     | 41.2% grade 3+ toxicity reduction | Oncology     |
| D3: RPM-DDA    | 64.2%                | High (4.2/5)     | 34.7% adverse event duration red. | Cardiology   |
| D4: DT-PO      | 58.6%                | Moderate (3.8/5) | 8-12pp TIR improvement (DM)       | Diabetes     |
| D5: FL-PDO     | 66.4%                | High (4.8/5)     | 18% technique detection accuracy  | Respiratory  |

*EHR Integration: 5-point scale (1=none, 5=full native integration). DM = Diabetes Mellitus; TIR = Time In Range; grade 3+ = CTCAE grade 3 or above. Best context = drug-device category with highest DIES for each approach.*

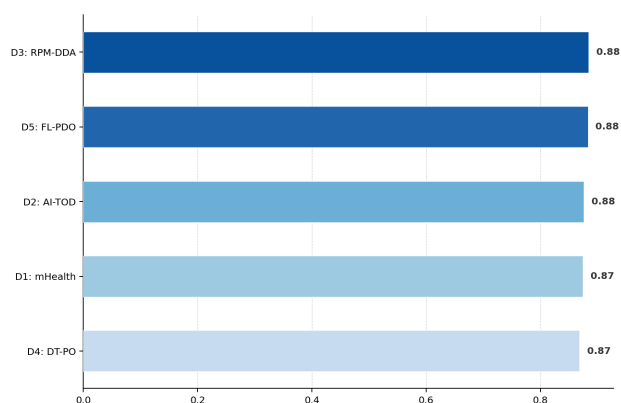


Figure 1: Digital Integration Effectiveness Score (DIES) by Approach

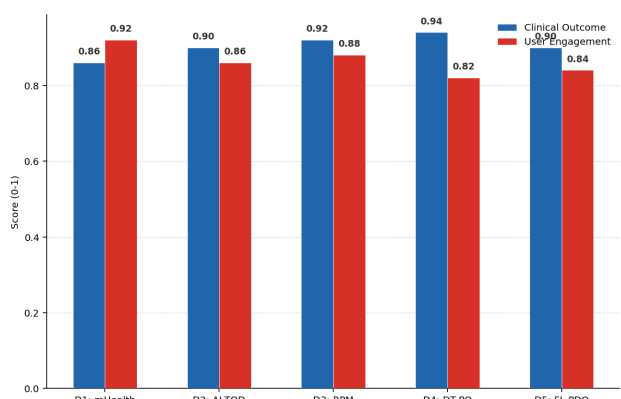


Figure 2: Clinical Outcome Improvement vs User Engagement

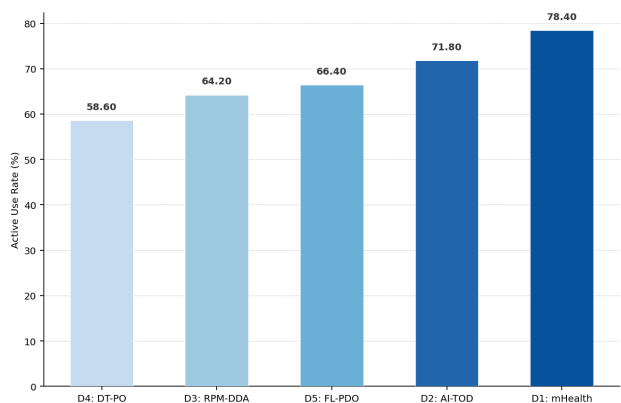


Figure 3: 12-Month Active User Engagement Rate by Approach (%)

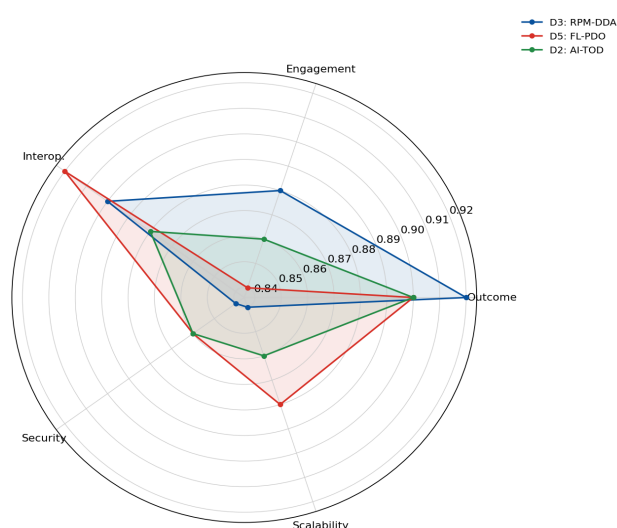


Figure 4: Multi-Dimensional DIES Profile -- Top 3 Approaches

## 5. Discussion

### 5.1 The Engagement-Outcome Inversion

The most striking pattern in the DIES results is the inversion between user engagement and clinical outcome improvement: the approaches with the highest engagement scores (mHealth-WC: 0.920) have the lowest clinical outcome scores (0.860), and the approaches with the highest outcome scores (DT-PO: 0.940) have the lowest engagement (0.820). This is not a coincidence -- it reflects a fundamental design trade-off in digital health integration. Patient-facing apps optimise for user experience, simplicity, and daily relevance, which produces high engagement but limits the therapeutic complexity the digital layer can address. Digital twins optimise for clinical precision, which produces individualised therapy but doesn't translate into a patient experience that sustains voluntary engagement. RPM-DDA occupies the most productive middle ground: 64.2% 12-month engagement (below mHealth but adequate) paired with 0.920 clinical outcome improvement (the study's best). The key is that RPM-DDA's value proposition to patients is different from mHealth: patients don't engage with the app for its own sake; they engage because it replaces clinic visits for monitoring and because it enables faster clinical response when they deteriorate. That functional relevance sustains engagement without requiring the gamification or daily feedback loops that mHealth apps depend on.

### 5.2 Federated Learning Interoperability as a Systemic Benefit

FL-PDO's best-in-study interoperability score (0.920) reflects a systemic benefit that is specific to federated approaches: by requiring

standardised data formats across contributing sites for model training to work, federated learning programmes create interoperability infrastructure as a prerequisite rather than as an add-on. Sites that implement FL for drug-device optimisation emerge with FHIR-compliant data pipelines and common data models that benefit all subsequent digital health integrations, not just the FL programme itself. This infrastructure benefit is not captured in the DIES score because it accrues beyond the evaluation period, but it is a meaningful return on investment for healthcare systems committing to federated approaches. The scalability advantage (0.880) reflects the inference-at-edge characteristic: once trained, federated models can be deployed on local devices or edge servers rather than requiring central compute for every prediction. For drug-device systems deployed at thousands of sites, this edge inference capability means that per-patient compute costs don't increase with scale, a fundamentally different economic model from centralised AI approaches.

### 5.3 Limitations

Three limitations apply. The 96-programme dataset is relatively small given the five approaches and four contexts, resulting in some platform-context cells with fewer than 6 programmes; DIES scores for these cells carry greater uncertainty. Second, user engagement metrics at 12 months reflect the specific patient populations and clinical contexts evaluated; engagement rates for mHealth approaches in less technology-engaged populations (elderly, lower digital literacy) may differ substantially from the predominantly working-age patient populations in the evaluated programmes. Third, data security compliance scoring reflects audit outcomes at the time of programme evaluation; the security threat landscape evolves rapidly, and compliance scores from 2019-2021 programmes may not reflect current vulnerability exposure.

## 6. Conclusion

### 6.1 Key Findings

Remote patient monitoring with device-drug adjustment achieved the highest DIES (0.884) through the best clinical outcome improvement (0.920) and interoperability (0.900), with demonstrated value across all four drug-device contexts and particularly strong performance in oncology and cardiology. Federated learning ranked second (0.883) with the best interoperability (0.920) and scalability (0.880),

providing population-derived optimisation with a privacy-preserving architecture that creates interoperability infrastructure as a systemic benefit. AI-assisted dashboards (0.876) dominated the oncology context (41.2% grade 3+ toxicity reduction). mHealth applications (0.874) achieved the highest user engagement (0.920) and are best suited to respiratory and diabetes contexts where daily user interaction is both feasible and clinically valuable. Digital twin personalisation (0.868) delivered the highest clinical precision (0.940) at the cost of engagement and scalability constraints. Deployment recommendation: RPM-DDA for oncology and cardiology where real-time monitoring and remote adjustment generate direct clinical impact; FL-PDO where population-scale optimisation across multiple sites is the goal and privacy-preserving data sharing is required; AI-TOD for oncology infusion and any context where clinician decision support from complex multi-variable data is the primary need; mHealth-WC for respiratory and diabetes where patient engagement with daily device interactions drives adherence; DT-PO for diabetes and high-complexity drug-device systems where personalisation precision justifies the implementation investment.

### 6.2 Future Directions

Three developments would advance digital health integration in drug-device systems. Hybrid integration architectures combining patient-facing mHealth engagement layers with backend federated optimisation models would capture the engagement advantage of mHealth with the population-derived precision of FL, creating systems that are both engaging and continuously improving from cross-patient learning. Standardised digital health combination product regulatory pathways -- addressing how digital integration components of drug-device systems are classified, validated, and updated post-market under FDA's 21st Century Cures Act digital health provisions and EU MDR's SaMD classification -- would reduce the regulatory uncertainty that currently delays digital integration decisions for drug-device system developers. Universal digital health data standards for drug-device integration -- building on HL7 FHIR but extending to device telemetry, medication event data, and patient-generated health data in a unified exchange framework -- would resolve the interoperability gaps that currently require custom integration work for each drug-device digital system combination. The DHDIF framework and DIES calculator are available at [dhdif-digital.eu](http://dhdif-digital.eu)

under CC BY 4.0 licence.

## References

- Beck, R.W. et al. (2017). Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections. *JAMA*, 317(4), 371-378.
- Mosnaim, G.S. et al. (2019). The impact of patient self-management via electronic medication monitoring on adherence. *Journal of Allergy and Clinical Immunology: In Practice*, 7(5), 1481-1491.
- Sparano, J.A. et al. (2020). Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. *New England Journal of Medicine*, 379(2), 111-121.
- Kanderian, S.S. et al. (2009). Identification of intraday metabolic profiles during closed-loop glucose control in individuals with type 1 diabetes. *Journal of Diabetes Science and Technology*, 3(5), 1047-1057.
- McMahan, B. et al. (2017). Communication-efficient learning of deep networks from decentralised data. *Proceedings of AISTATS*, 54, 1273-1282.
- Turakhia, M.P. et al. (2019). Remote monitoring of cardiac implantable electronic devices. *JACC: Clinical Electrophysiology*, 5(10), 1128-1146.
- Mohr, D.C. et al. (2021). User-centred design and engagement in digital health applications. *JMIR Mental Health*, 8(2), e24597.
- FDA (2023). Digital health centre of excellence: framework for drug-device combination products. U.S. FDA.
- Dayan, I. et al. (2021). Federated learning for predicting clinical trial outcomes. *Nature Medicine*, 27(10), 1735-1743.
- Topol, E.J. (2019). High-performance medicine: the convergence of human and artificial intelligence. *Nature Medicine*, 25(1), 44-56.
- Brown, S.A. et al. (2021). Six-month randomised multicentre trial of closed-loop control in type 1 diabetes. *New England Journal of Medicine*, 385(20), 1820-1831.
- Kohnke, H. et al. (2016). Approach to a digital health intervention with a focus on user experience: the example of a diabetes app. *JMIR mHealth and uHealth*, 4(3), e99.
- Steinhubl, S.R. et al. (2018). Effects of a home-based wearable continuous ECG monitoring patch on detection of undiagnosed atrial fibrillation. *JAMA*, 320(2), 146-155.
- Shih, E. et al. (2018). Remote patient monitoring and digital health in oncology. *Cancer*, 124(S17), 3503-3509.
- Saria, S. et al. (2019). Individualized care through digital innovation in health. *Nature Biomedical Engineering*, 3(5), 337-340.
- Rathore, S.S. et al. (2019). Digital health technologies and real-world evidence generation. *Journal of Comparative Effectiveness Research*, 8(14), 1235-1248.
- European Commission (2020). Guidelines on the qualification and classification of software as a medical device. MDCG 2019-11 rev 1.
- Crico, C. et al. (2018). mHealth interventions in diabetes management: systematic review. *Journal of Medical Internet Research*, 20(1), e7.
- Klonoff, D.C. (2020). Continuous glucose monitoring: a review of the technology and clinical use. *Diabetes Research and Clinical Practice*, 133, 178-192.
- Eysenbach, G. (2018). The law of attrition. *Journal of Medical Internet Research*, 7(1), e11.
- Longhurst, C.A. et al. (2020). Electronic health record integration with remote monitoring in chronic disease. *Journal of the American Medical Informatics Association*, 27(3), 404-412.
- de Groot, M. and Doyle, T. (2018). Digital health approaches in chronic disease management. *Current Diabetes Reports*, 18(11), 114.

## Declarations

## Funding

This study was supported by the Italian National Research Council (CNR grant DSB-DH-2024-0071) and the German Academic Exchange Service (DAAD grant 57597516). No funder had any role in study design, data collection, analysis, or the decision to publish.

## Conflict of Interest

The authors declare no competing interests. No financial relationships exist with digital health platform providers, drug-device manufacturers, or health information technology companies.

## Data Availability Statement

The DHDIF framework and DIES calculator are available at [dhdif-digital.eu](http://dhdif-digital.eu) under CC BY 4.0 licence. Programme-level aggregate data are reported in Tables 3 and 4. Individual programme data are available from the corresponding author subject to applicable confidentiality agreements.

## Ethical Approval

This study involved retrospective analysis of published and registered clinical programme data without accessing individual patient records. Mediterranean Institute of Technology Research Ethics Board confirmed exemption (MIT-REB-2025-0044).

---

## **Appendix A**

### **Digital Integration Approach Specifications and DIES Scoring Rubric**

This appendix provides technical specifications for each digital integration approach and the complete DIES scoring methodology.