









Architectural Design for Enhancing Remote Patient Monitoring in Heart Failure: A Case Study of the RETENTION Project

Ourania Manta¹^a, Nikolaos Vasileiou¹^b, Olympia Giannakopoulou¹^c, Konstantinos Bromis¹,
Ioannis Kouris¹, Maria Haritou¹^d, Lefteris Koumakis², George Spanoudakis², Irina E. Nicolae³^e,
C. Septimiu Nechifor³^f, Miltiadis Kokkonidis⁴, Michalis Vakalelis⁴, Yorgos Goletsis⁵,
Maria Roumpi⁵, Dimitrios I. Fotiadis⁵, Heraklis Galanis⁶, Panagiotis Dimitrakopoulos⁶,
George K. Matsopoulos¹^g and Dimitrios D. Koutsouris¹^h

¹Biomedical Engineering Laboratory, Institute of Communication and Computer Systems,
National Technical University of Athens, 15773 Athens, Greece

²Sphynx Technology Solutions AG, 6300 Zug, Switzerland

³Configuration Technologies, Data Analytics and Artificial Intelligence, Siemens Technology, 500097, Braşov, Romania

⁴AEGIS IT Research GmbH, 38106 Braunschweig, Germany

⁵Biomedical Research Institute, FORTH, University of Ioannina, Ioannina, Greece

⁶Datamed SA, Athens, 15124, Greece


Keywords: Clinical Site Backend, Data Analysis, Global Insights Cloud, Heart Failure, Integration, Machine Learning, Patient Edge, Personalised Interventions, Retention Platform, Testing.


Abstract: This paper introduces the RETENTION Platform, an integrated healthcare data management system meticulously crafted to support personalised interventions, thereby enhancing outcomes for heart failure (HF) patients. Comprising three fundamental components—the Global Insights Cloud (GIC), the Clinical Site Backend (CSB), and Patient Edge (PE)—the platform coordinates a sophisticated array of functions. The GIC facilitates data analysis and machine learning model training, while the CSB enables daily patient check-ups, data gathering, and intervention application. The Patient Edge enables continuous monitoring and feedback collection from patients. The system is deployed using virtual machines (VMs) and Docker containers on a cloud-based infrastructure. Integration and testing procedures are outlined to safeguard system functionality. This paper provides a comprehensive overview of the RETENTION Platform's architecture and highlights its potential for improving healthcare delivery through personalised interventions.


1 INTRODUCTION


Chronic diseases are long-lasting conditions that require ongoing medical attention and may limit daily activities (Bernell & Howard, 2016). Heart failure


(HF) is a prevalent chronic disease and a significant global health burden (Smith et al., 2012). HF is characterised by symptoms and signs resulting from cardiac abnormalities, leading to reduced cardiac output and elevated intracardiac pressures. Despite advancements in prevention, diagnosis, and


^a <https://orcid.org/0000-0003-2071-1144>


^b <https://orcid.org/0009-0009-5486-6508>


^c <https://orcid.org/0000-0003-4473-2070>

^d <https://orcid.org/0000-0003-1136-8209>

^e <https://orcid.org/0000-0002-9346-8467>

^f <https://orcid.org/0000-0001-5727-6081>

^g <https://orcid.org/0000-0002-2600-9914>

^h <https://orcid.org/0000-0003-1205-9918>

treatment, HF remains a leading cause of disability and premature death worldwide (The Global Cardiovascular Disease Pandemic, Current Status and Future Projections, 2015). It affects a substantial portion of the population, with estimates suggesting around 15 million Europeans and 5.8 million Americans suffer from HF (Braunschweig et al., 2011). The prevalence of HF is particularly high among older individuals, reaching over 10% in those over 70 years of age (Ponikowski et al., 2016). HF is associated with a poor five-year survival rate compared to other conditions like myocardial infarction and certain cancers (Ponikowski et al., 2016). Co-morbidities, including various diseases and mental disorders, often accompany HF, influencing its management and treatment (Ponikowski et al., 2016), (Calmette & Clauser, 2018), (Reiss et al., 2018). The economic burden of HF is substantial, with significant healthcare costs attributed to hospitalisations and the growing elderly population (Ayyadurai et al., 2019).

Efforts have been made to predict and prevent HF decompensation episodes, improve medical therapy, and introduce new devices to reduce hospitalisations (Ayyadurai et al., 2019). Remote monitoring, such as e-health applications, has shown promise in the follow-up management of HF patients (Rosen et al., 2017), (Black et al., 2014), (Koehler et al., 2018). Technological advancements enable the collection of patient data, including vital signs, routine ECGs, and advanced monitoring parameters, which can aid in disease management (Bashi et al., 2017). Evidence-based therapies, devices, and disease management programmes have demonstrated improved outcomes for HF patients (Braunschweig et al., 2011).

However, despite these advancements, some patients progress to an advanced stage of HF, requiring mechanical support devices or heart transplants (Calmette & Clauser, 2018), (Reiss et al., 2018). Remote monitoring of device parameters and patient data can help identify complications and the need for hospital evaluation (Calmette & Clauser, 2018). Heart transplant recipients often require multiple outpatient visits for monitoring and rejection assessment.

In light of these challenges, the RETENTION project aims to implement daily remote monitoring for HF patients. The goal is to collect various clinical, behavioural, and real-world data. The project will analyse this data using novel data analytics and artificial intelligence (AI) to enhance clinical management, minimise hospitalisations, and improve

patient outcomes. It will also evaluate the potential of remote monitoring, data analysis models, and clinical interventions. This assessment will consider different health policy perspectives, addressing patient safety, quality of care, and the growing healthcare demand among the ageing population with complex conditions (Calmette & Clauser, 2018), (Reiss et al., 2018).

2 ADVANCING HEART FAILURE MONITORING

RETENTION strives to elevate remote patient monitoring for heart failure by enhancing current state-of-the-art technology across multiple dimensions. Through advancements in these areas, it seeks to enhance the quality of life, clinical management, and remote monitoring of patients with heart failure. In summary, the key contributions of RETENTION can be outlined as follows:

2.1 Artificial Intelligence in Heart Failure Management

Building a personalised decision support system that can make diagnosis, prognosis, and therapy more effective and reliable for HF patients is a complex challenge (Mielczarek, 2016). AI techniques, such as Bayesian networks, machine learning (ML) methods, and supervised learning algorithms like artificial neural networks (ANN), decision trees (DT), genetic algorithms (GA), and Support Vector Machines (SVM), have been utilised to develop risk assessments and mortality predictions (Weiss et al., 2012) using relevant medical data sources¹². The application of ML algorithms to individual patient data allows for more accurate predictions and the elimination of noisy and irrelevant features. Furthermore, the ethical dimension of AI usage in healthcare, as addressed in the new EU framework for trustworthy AI, emphasises the need for lawful, ethical, and robust decision-making processes (Khodadadi et al., 2019). RETENTION will address these requirements by conforming to GDPR, ensuring privacy management, providing insights into data analytics, and continuously evaluating security standards and machine learning model reliability factors.

¹ <https://optn.transplant.hrsa.gov/data/>

² <https://statistics.eurotransplant.org/>

2.2 Explanation and Verification in Machine Learning

Machine learning methods, including deep learning, have been utilised to analyse large amounts of data in HF research (Sung et al., 2019). Interpretability and explainability of ML models have become crucial in validating and understanding the decisions made by the models (Quaglini et al., 2015). Techniques for interpreting and understanding the learned models have been developed to shed light on complex machine learning models (Bryan & Heagerty, 2016). RETENTION will investigate model-agnostic methods for interpreting ML models to enhance the interpretability and explainability of the system.

2.3 Wearables, Smart Homes and Internet of Things Devices in Healthcare

Smart homes and Internet of Things (IoT) devices have the potential to transform traditional healthcare systems into more efficient and personalised environments (Linkous et al., 2019). These technologies can collect health data, provide real-time self-monitoring and enable remote interventions by healthcare providers. Wearable sensors, implantable devices, and smart information platforms can continuously monitor physiological indicators of heart failure patients, improving comfort and combining data from various sources (Akmandor & Jha, 2017),(Crema et al., 2015),(Tripoliti et al., 2019). RETENTION will leverage a wide gamut of inputs from smart medical devices used daily by patients at home, wearable devices, Patient Reported Outcome Measures electronic questionnaires, and real-time sensor measurements, coupled with state-of-the-art ML models offering personalised predictions, to provide a ground-breaking yet practical and patient-friendly IT-enhanced patient monitoring framework that aims to help doctors improve patient outcomes and minimise emergency room visits and hospitalisations, contributing to the effective and efficient management of HF patients.

2.4 Big Data Management and Analytics

Big data analytics (BDA) platforms have evolved to address the challenges of complex correlations of heterogeneous, open, public, and private big data in a cost-effective, safe, and user-friendly manner (Assunção et al., 2015). RETENTION will adopt a

model-driven approach to designing and implementing big data infrastructures, aiming for modularity, reusability, and automation. Interpretability and explainability of data analytics will be crucial in validating the results and ensuring evidence-based interventions (Sparks et al., n.d.),(Du et al., 2018).

2.5 Personalised Human-Computer Interactions

Human-Computer Interaction (HCI) plays a vital role in delivering digital technologies to the healthcare sector (Blandford, 2019). User needs and usability factors, such as health literacy, age-related conditions, and the visualisation of complex health data, need to be considered in the design of user interfaces (Patel et al., 2015),(Groenvold et al., 2006). RETENTION will adopt a user-centric approach, involve users in the iterative design process, and develop adaptive visualisations and interfaces for healthcare practitioners and patients.

2.6 Security, Privacy, and Trust in Healthcare and IoT Systems

IoT applications in healthcare face security and privacy challenges, including mutual authentication, encryption, and data integrity (Salah & Khan, 2017). Cryptographic techniques, such as privacy-preserving encryption and differential privacy, have been proposed to preserve data confidentiality. Proper identity and authorisation management, along with access control policies, are essential for protecting user privacy (Hassija et al., 2019), (Li et al., 2018). RETENTION will combine novel and standardised technologies to provide lightweight and usable mechanisms for authentication, authorisation, privacy preservation, and secure communications. Continuous security and privacy assurance will be ensured through monitoring and evaluation tools (Li et al., 2018).

3 ARCHITECTURAL DESIGN OF THE RETENTION PLATFORM

3.1 RETENTION Project Overview

The architectural design of the RETENTION project follows a comprehensive approach aimed at enhancing remote patient monitoring in heart failure. To summarise, the primary objective of the

RETENTION initiative is to develop and implement a groundbreaking platform that facilitates advanced clinical monitoring and interventions with the aim of enhancing the management of patients suffering from chronic HF. This entails reducing mortality and hospitalisation rates while concurrently improving their overall quality of life, safety, and well-being.

The RETENTION platform will effectively aid clinical decision-making and provide evidence-based personalised interventions for HF patients by employing the following methods:

- Continuously monitoring and aggregating an extensive range of medical, clinical, physiological, behavioural, psychosocial, and real-world data pertinent to HF patients;
- Utilising cutting-edge model-driven big data analytics, statistical analysis, artificial intelligence, and machine learning techniques to analyse these data;
- Identifying patterns in the progression of HF and evaluating the patients' quality of life through a thorough examination of the collected data;
- Thoroughly cross-referencing and validating these findings against existing clinical literature; and
- Fostering transparent, comprehensible, and verifiable decision-making capabilities that leverage the evidence generated by the underlying data analysis, thereby bolstering clinical studies targeting HF and other cardiovascular diseases.

The RETENTION approach and its platform will be validated through a clinical study involving 450 HF patients recruited by six different hospitals in four different EU countries, within which there is some diversity in the management of such patients.

3.2 RETENTION Conceptual and System Architecture

The purpose of the system architecture activities was to define a coherent, comprehensive solution to the RETENTION platform based on principles, concepts, and properties that are related and functional to each other in a logical way. In this section, a detailed description of the architecture of the RETENTION system is provided, outlining the conceptual model and descriptions of the main components that constitute it. The RETENTION platform is architected with privacy considerations in mind and avoids unnecessary concentration of patients' personal data on, say, a cloud infrastructure beyond the patient's or hospital's control. But at the same

time, it allows ML model training across the data collected from multiple hospitals' patients. It does so through a carefully designed architecture that pays particular attention to privacy protection while allowing direct access to the medically relevant patient data collected from the clinical sites, as enhanced through RETENTION's enhanced patient monitoring outside the hospital. It is expected that the RETENTION Platform will attain a level of human-machine interaction of the highest standards to enable user-friendly interactions for handling the complexity of workflows and their outputs, coping with the output of complex models, the verification of those via the visualisation of the knowledge encoded, and the presentation of interventions.

The following figure illustrates all the high-level components of the system. Components are mainly interconnected via REST API interfaces to facilitate integration. As can be seen, the architecture is based on a 3-layer model (arising from a structured IoT architecture, modified for the RETENTION project):

- the Global Insights Cloud (GIC);
- the Clinical Site Backend (CSB); and
- the Patient Edge (PE)

These layers interact to facilitate data collection, analysis, and personalised interventions. The diagram featured in Figure 1 provides a comprehensive depiction of the RETENTION architecture, illustrating the various actors that operate within each respective layer.

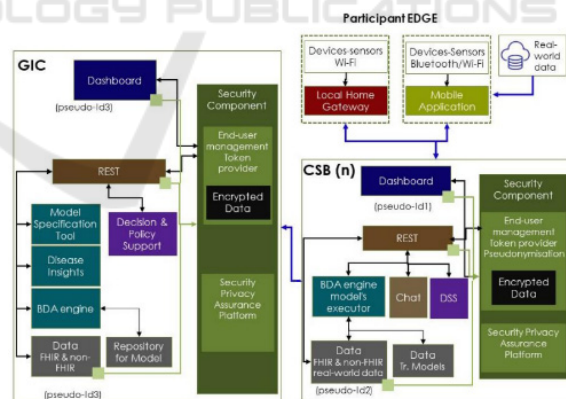


Figure 1: RETENTION Architecture: (Global Insights Cloud (GIC), Clinical Site Backend (CSB), and Patient Edge (PE).

The Global Insights Cloud (GIC) serves as the central repository for big data analytics. The GIC layer encompasses several sub-components, including the GIC Dashboard, Federated RW Data Repository and Repository for Models, BDA Engine, Model Specification Tool, Disease Insights, Decision and Policy Support, Security Component, and GIC

Rest API. It collects anonymised patient data from all sites, enabling global data analytics and insight generation. The GIC hosts the analytics engine and provides tools for data scientists, clinical experts, and healthcare policymakers to make informed decisions about HF disease management. Additionally, the GIC supports incremental data analysis and model refinement, ensuring evidence-based interventions.

The Clinical Site Backend (CSB) operates at each clinical site and is responsible for patient data management and local analytics. It comprises sub-components such as the CSB Dashboard, FHIR³ (Fast Healthcare Interoperability Resources) and Non-FHIR Repository, BDA Engine Models Executor, Decision Support System (DSS), Security Component, and CSB Rest API. It allows clinicians to monitor their patients, gather medical and usage data, and make informed decisions. The CSB facilitates the execution of personalised interventions based on trained machine learning models. It also ensures pseudonymisation of patient data. This protects privacy while granting clinicians access to pertinent information.

The Patient Edge (PE) encompasses a mobile application and a home gateway. It enables continuous monitoring of patients and the collection of real-world data. The mobile application serves as an interface for patients to report symptoms, record adherence to medication regimes, and report health metrics in a user-friendly, semi-automated manner. It collects and aggregates data from the patient's smartwatch and smart medical devices (blood pressure metre, oximetre, weigh scales) that the patient uses on a daily basis, transmitting it to the CSB of the hospital monitoring the patient's health. The home gateway also contributes by aggregating and transmitting to the CSB data from sensors in the patient's indoor home environment, as well as relevant weather open data capturing the external environmental conditions of the patient's home.

For the storage of medical data, a FHIR database was utilised. Healthcare terminologies and coding systems like SNOMED CT, LOINC, and ICD-10 were integrated into the FHIR standard to provide standardised codes and terminologies for representing clinical concepts, laboratory observations, and disease classifications, enhancing interoperability and allowing for consistent and meaningful exchange of healthcare information across different systems and applications that adhere to the FHIR standard.

Security and privacy are paramount in the RETENTION architecture. The Security Component of the RETENTION project is responsible for authentication, authorisation, and data protection during transit and storage. This component plays a pivotal role in ensuring the secure management of personal data in compliance with GDPR regulations. It facilitates secure data handling, distribution, and presentation to authorised users while safeguarding data privacy. This component is present in both the GIC and CSB instances and encompasses various mechanisms, including API management, role-based access control (RBAC), data encryption, API logs, device management, and RETENTION pseudonymisation. API management ensures data security and protection for exposed APIs, while RBAC restricts access to authorised roles and registered end-users. Data encryption safeguards personal and identifiable information. API logs monitor activity for potential security threats, and device management allows efficient technical support without compromising sensitive identification. The Security Component employs pseudonymisation as a measure of minimising the risk of data subjects' identification. Data residing in GIC is anonymised.

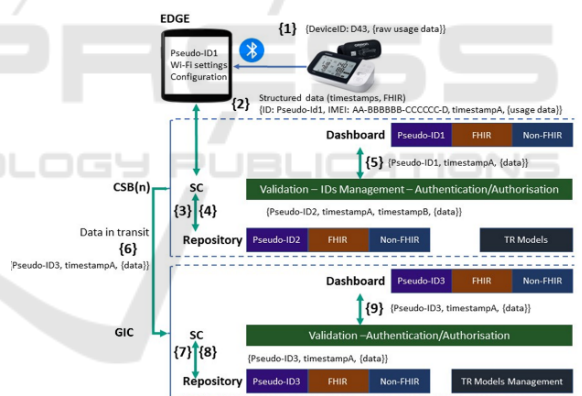


Figure 2: Transmission of data between PE, CSB and GIC.

Overall, the RETENTION system architecture will facilitate data-driven decision-making, personalised interventions, and secure data management. It supports multiple user roles, including system administrators, clinicians, patients, data scientists, and healthcare policymakers. By leveraging the capabilities of the GIC, CSB, and PE, the architecture will enable comprehensive monitoring and management of patients with heart failure, ultimately improving their clinical outcomes.

³ <https://ecqi.healthit.gov/fhir>

3.3 Integration and Testing of the RETENTION System

The integration and testing phases of the RETENTION system were crucial for its successful development and completion. These phases involved the installation of the main components, the confirmation of software quality, and ensuring the functionality and performance of the system.

Software quality assurance included creating scenarios, entering test data, and controlling procedures to confirm the "quality" of the software product. The integration process followed a staged approach, which started with the installation and customisation of software components. Docker containers were used for deploying system components (dashboard, security component, DSS, data repositories) and integrating modules such as GIC, CSB, and PE.

Testing encompassed various stages, including unit tests, application tests, integration tests, system tests, and user acceptance tests. Unit testing verified the individual subsystems, while application testing focused on checking the business logic. Integration testing ensured successful communication and system reliability. System testing guaranteed that the system met operational requirements. User acceptance tests validated system functionality and performance.

During the deployment phase, two distinct stages will be undertaken. The first stage will involve data collection, allowing AI models to be trained. In the second stage, the system will be fully available to support clinical teams and their respective patients.

Deployment will guarantee the availability, security, and operational support of the RETENTION system. It will adhere to GDPR regulations to ensure the protection of sensitive data. The integration and testing phases ensure the functionality, reliability, and readiness of the RETENTION system for real-world implementation.

4 DISCUSSION

The RETENTION platform presents a significant advancement in the field of HF management through enhanced remote patient monitoring. The discussion section below elaborates on several key points and implications arising from the architectural design and conceptual framework of the RETENTION project.

The core objective of the RETENTION initiative is to significantly improve HF management by reducing mortality and hospitalisation rates while

simultaneously enhancing the overall quality of life for HF patients. Through continuous data collection, state-of-the-art data analytics, and machine learning, the platform aims to provide personalised interventions based on robust evidence. This approach has the potential to revolutionise the way HF is managed and significantly impact patient outcomes. By leveraging a structured IoT architecture, the RETENTION platform sets a new standard for patient monitoring in chronic diseases.

The use of big data analytics and artificial intelligence in HF management is pivotal. Machine learning models, including Bayesian networks, ANN, and SVM, hold promise for improving risk assessments and mortality predictions. However, these models must meet ethical standards and data protection regulations, as emphasised by GDPR. The RETENTION project's commitment to lawful, ethical, and robust decision-making processes is essential for ensuring the platform's trustworthiness and compliance.

The importance of interpretability and explainability in machine learning models cannot be overstated. The RETENTION project's exploration of model-agnostic methods for interpreting ML models represents a significant step towards ensuring transparency in decision-making. This approach aligns with the broader trend in healthcare AI, where the ability to understand and validate model decisions is critical.

The integration of IoT devices into healthcare holds enormous potential. These technologies can provide real-time monitoring and personalised interventions, transforming traditional healthcare into a more efficient and patient-centric environment. RETENTION's use of real-time sensor measurements and personalised treatment exemplifies this potential, enhancing the management of HF patients and potentially extending to other chronic diseases.

Security and privacy are paramount in healthcare systems, especially when IoT applications are involved. The RETENTION project's approach to security, including privacy-preserving encryption and access control policies, addresses these challenges comprehensively. Ensuring the protection of user privacy while facilitating secure data exchanges is vital for the success of any healthcare platform.

The user-centric design approach adopted by the RETENTION project acknowledges the importance of considering user needs and usability factors. This perspective is particularly relevant in healthcare, where various user groups, including patients, clinicians, and data scientists, interact with the system. The emphasis on adaptive visualisations and

interfaces aligns with the broader trend of making healthcare technologies accessible to a wide range of users.

The RETENTION project's commitment to validation through a clinical study involving at least 450 HF patients across multiple EU countries is a crucial step. It ensures that the platform's benefits and effectiveness are rigorously evaluated in a real-world context with diverse patient populations and clinical settings.

In conclusion, the RETENTION platform represents a significant advancement in HF management by leveraging cutting-edge technologies and a comprehensive approach. By addressing challenges related to data analytics, explainability, IoT, security, and user-centric design, the project paves the way for more effective, personalised, and secure healthcare solutions. The clinical study will provide valuable insights into the platform's real-world impact and its potential for broader applications in healthcare data management and personalised interventions.

5 CONCLUSIONS

Overall, this paper provides a comprehensive understanding of the RETENTION system, focusing on its technical aspects and the modules comprising it. Specifically, the architecture for the RETENTION Platform is presented, which encompasses the Global Insights Cloud (GIC), Clinical Site Backend (CSB), and Patient Edge (PE) components. The GIC serves as the hub for data analysis and ML model training, providing evidence-based personalised interventions. The CSB supports daily patient check-ups, data gathering, and the application of ML models for interventions. The PE enables continuous patient monitoring and feedback collection. The infrastructure supporting the RETENTION system is based on virtual machines (VMs) and Docker containers, with a cloud-based deployment. Integration and testing procedures were crucial to ensuring the system's functionality and performance. The presented reference architecture lays the foundation for further development and implementation of the system to improve healthcare data management and personalised interventions.

ACKNOWLEDGEMENTS

The RETENTION project was financed by the European Union's Horizon 2020 Research and

Innovation Programme, Grant Agreement Number 965343.

REFERENCES

- Akmandor, A. O., & Jha, N. K. (2017). Keep the Stress Away with SoDA: Stress Detection and Alleviation System. *IEEE Transactions on Multi-Scale Computing Systems*, 3(4), 269–282. <https://doi.org/10.1109/TMSCS.2017.2703613>
- Assunção, M. D., Calheiros, R. N., Bianchi, S., Netto, M. A. S., & Buyya, R. (2015). Big Data computing and clouds: Trends and future directions. *Journal of Parallel and Distributed Computing*, 79–80, 3–15. <https://doi.org/10.1016/j.jpdc.2014.08.003>
- Ayyadurai, P., Alkhawam, H., Saad, M., Al-Sadawi, M. A., Shah, N. N., Kosmas, C. E., & Vittorio, T. J. (2019). An update on the CardioMEMS pulmonary artery pressure sensor. In *Therapeutic Advances in Cardiovascular Disease* (Vol. 13). SAGE Publications Ltd. <https://doi.org/10.1177/1753944719826826>
- Bashi, N., Karunanithi, M., Fatehi, F., Ding, H., & Walters, D. (2017). Remote Monitoring of Patients With Heart Failure: An Overview of Systematic Reviews. *Journal of Medical Internet Research*, 19(1).
- Bernell, S., & Howard, S. W. (2016). Use Your Words Carefully: What Is a Chronic Disease? *Frontiers in Public Health*, 4. <https://doi.org/10.3389/fpubh.2016.0159>
- Black, J. T., Romano, P. S., Sadeghi, B., Auerbach, A. D., Ganiats, T. G., Greenfield, S., Kaplan, S. H., & Ong, M. K. (2014). A remote monitoring and telephone nurse coaching intervention to reduce readmissions among patients with heart failure: Study protocol for the Better Effectiveness After Transition - Heart Failure (BEAT-HF) randomized controlled trial. *Trials*, 15(1). <https://doi.org/10.1186/1745-6215-15-124>
- Blandford, A. (2019). HCI for health and wellbeing: Challenges and opportunities. *International Journal of Human Computer Studies*, 131, 41–51. <https://doi.org/10.1016/j.ijhcs.2019.06.007>
- Braunschweig, F., Cowie, M. R., & Auricchio, A. (2011). What are the costs of heart failure? *Europace*, 13(SUPPL. 2). <https://doi.org/10.1093/europace/eur081>
- Bryan, M., & Heagerty, P. J. (2016). Multivariate Analysis of Longitudinal Rates of Change. *PubMed Central*, 35(28).
- Calmette, L., & Clauser, S. (2018). Von Willebrand disease. In *Revue de Medecine Interne* (Vol. 39, Issue 12, pp. 918–924). Elsevier Masson SAS. <https://doi.org/10.1016/j.revmed.2018.08.005>
- Crema, C., Depari, A., Flammini, A., Lavarini, M., Sisinni, E., & Vezzoli, A. (2015). A smartphone-enhanced pill-dispenser providing patient identification and in-take recognition. *2015 IEEE International Symposium on Medical Measurements and Applications, MeMeA 2015 - Proceedings*, 484–489. <https://doi.org/10.1109/MeMeA.2015.7145252>

- Du, M., Liu, N., & Hu, X. (2018). *Techniques for Interpretable Machine Learning*. <http://arxiv.org/abs/1808.00033>
- Groenvold, M., Petersen, M. A., Aaronson, N. K., Arraras, J. I., Blazeby, J. M., Bottomley, A., Fayers, P. M., de Graeff, A., Hammerlid, E., Kaasa, S., Sprangers, M. A. G., & Bjorner, J. B. (2006). Letter to the Editor. *Palliative Medicine*, *20*(2), 59–61. <https://doi.org/10.1191/0269216306pm1133xx>
- Hassija, V., Chamola, V., Saxena, V., Jain, D., Goyal, P., & Sikdar, B. (2019). A Survey on IoT Security: Application Areas, Security Threats, and Solution Architectures. In *IEEE Access* (Vol. 7, pp. 82721–82743). Institute of Electrical and Electronics Engineers Inc. <https://doi.org/10.1109/ACCESS.2019.2924045>
- Khodadadi, M., Shayanfar, H., Maghooli, K., & Mazinan, A. H. (2019). Fuzzy cognitive map based approach for determining the risk of ischemic stroke. *IET Systems Biology*, *13*(6), 297–304. <https://doi.org/10.1049/iet-syb.2018.5128>
- Koehler, F., Koehler, K., Deckwart, O., Prescher, S., Wegscheider, K., Kirwan, B. A., Winkler, S., Vettorazzi, E., Bruch, L., Oeff, M., Zugck, C., Doerr, G., Naegele, H., Störk, S., Butter, C., Sechtem, U., Angermann, C., Gola, G., Prondzinsky, R., ... Stangl, K. (2018). Efficacy of telemedical interventional management in patients with heart failure (TIM-HF2): a randomised, controlled, parallel-group, unmasked trial. *The Lancet*, *392*(10152), 1047–1057. [https://doi.org/10.1016/S0140-6736\(18\)31880-4](https://doi.org/10.1016/S0140-6736(18)31880-4)
- Li, J., Zhang, Y., Chen, X., & Xiang, Y. (2018). Secure attribute-based data sharing for resource-limited users in cloud computing. *Computers and Security*, *72*, 1–12. <https://doi.org/10.1016/j.cose.2017.08.007>
- Linkous, L., Zohrabi, N., & Abdelwahed, S. (2019). Health Monitoring in Smart Homes Utilizing Internet of Things. *Proceedings - 4th IEEE/ACM Conference on Connected Health: Applications, Systems and Engineering Technologies, CHASE 2019*, 29–34. <https://doi.org/10.1109/CHASE48038.2019.00020>
- Mielczarek, B. (2016). Review of Modelling Approaches For Healthcare Simulation. *Operations Research and Decisions*, *26*(1), 55–72.
- Patel, V., Kannampallil, T., & Kaufman Editors, D. (2015). *Health Informatics Human Computer Interaction in Healthcare*. <http://www.springer.com/series/1114>
- Ponikowski, P., Voors, A. A., Anker, S. D., Bueno, H., Cleland, J. G. F., Coats, A. J. S., Falk, V., González-Juanatey, J. R., Harjola, V. P., Jankowska, E. A., Jessup, M., Linde, C., Nihoyannopoulos, P., Parissis, J. T., Pieske, B., Riley, J. P., Rosano, G. M. C., Ruilope, L. M., Ruschitzka, F., ... Davies, C. (2016). 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. In *European Heart Journal* (Vol. 37, Issue 27, pp. 2129–2200m). Oxford University Press. <https://doi.org/10.1093/eurheartj/ehw128>
- Quaglini, S., Sacchi, L., Lanzola, G., & Viani, N. (2015). Personalization and Patient Involvement in Decision Support Systems: Current Trends. In *Yearbook of medical informatics* (Vol. 10, Issue 1, pp. 106–118). <https://doi.org/10.15265/IY-2015-015>
- Reiss, N., Schmidt, T., Boeckelmann, M., Schulte-Eistrup, S., Hoffmann, J.-D., Feldmann, C., & Schmitt, J. D. (2018). Telemonitoring of left-ventricular assist device patients-current status and future challenges. *Journal of Thoracic Disease*, *10*(15).
- Rosen, D., McCall, J. D., & Primack, B. A. (2017). Telehealth Protocol to Prevent Readmission Among High-Risk Patients With Congestive Heart Failure. *The American Journal of Medicine*, *130*(11), 1326–1330.
- Salah, K., & Khan, M. (2017). IoT Security: Review, Blockchain Solutions, and Open Challenges. *Future Generation Computer Systems*.
- Smith, S. C., Collins, A., Ferrari, R., Holmes, D. R., Logstrup, S., McGhie, D. V., Ralston, J., Sacco, R. L., Stam, H., Taubert, K., Wood, D. A., & Zoghbi, W. A. (2012). Our time: A call to save preventable death from cardiovascular disease (heart disease and stroke). *Journal of the American College of Cardiology*, *60*(22), 2343–2348. <https://doi.org/10.1016/j.jacc.2012.08.962>
- Sparks, E. R., Venkataraman, S., Kaftan, T., Franklin, M. J., & Recht, B. (n.d.). *KeystoneML: Optimizing Pipelines for Large-Scale Advanced Analytics*. <http://www.keystone-ml.org/>
- Sung, J. M., Cho, I.-J., Sung, D., Kim, S., Kim, H. C., Chae, M.-H., Kavousi, M., Rueda-Ochoa, O. L., Ikram, M. A., Franco, O. H., & Chang, H.-J. (2019). Development and verification of prediction models for preventing cardiovascular diseases. *PLOS ONE*. *The global cardiovascular disease pandemic, current status and future projections*. (2015).
- Tripoliti, E. E., Karanasiou, G. S., Kalatzis, F. G., Bechlioulis, A., Goletsis, Y., Naka, K., & Fotiadis, D. I. (2019). HEARTEN KMS – A knowledge management system targeting the management of patients with heart failure. *Journal of Biomedical Informatics*, *94*. <https://doi.org/10.1016/j.jbi.2019.10.3203>
- Weiss, E. S., Allen, J. G., Kilic, A., Russell, S. D., Baumgartner, W. A., Conte, J. V., & Shah, A. S. (2012). Development of a quantitative donor risk index to predict short-term mortality in orthotopic heart transplantation. *Journal of Heart and Lung Transplantation*, *31*(3), 266–273. <https://doi.org/10.1016/j.healun.2011.10.004>