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BMJ Open

Synthesizing evidence on machine learning methods, applications, and economic analysis to predict heart failure hospitalization risk: a scoping review protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-083188
Article Type:	Protocol
Date Submitted by the Author:	13-Dec-2023
Complete List of Authors:	Seringa, Joana; NOVA University Lisbon NOVA National School of Public Health; NOVA National School of Public Health, Public Health Research Centre, Comprehensive Health Research Center, CHRC, NOVA University Lisbon, Lisbon, Portugal Abreu, João; NOVA University Lisbon NOVA National School of Public Health Magalhaes, Teresa; NOVA University Lisbon NOVA National School of Public Health; NOVA National School of Public Health, Public Health Research Centre, Comprehensive Health Research Center, CHRC, NOVA University Lisbon, Lisbon, Portugal
Keywords:	Heart failure < CARDIOLOGY, Hospitalization, eHealth, Health Services

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Synthesize evidence on machine learning methods, applications, and economic analysis to predict heart failure hospitalization risk: a scoping review protocol

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Word count: 1745

ABSTRACT

Introduction Machine Learning (ML) has emerged as a powerful tool for autonomously extracting knowledge from extensive datasets without explicit programming. This capacity to discern patterns and generate new information has revolutionized various domains, including the medical field. In cardiology, ML applications have shown promise in predictive risk assessment and phenotypic classification of Heart Failure (HF) patients, a chronic condition with a global prevalence exceeding 64 million individuals. HF imposes significant morbidity, mortality, and economic burden, necessitating innovative approaches for management. This scoping review aims to comprehensively evaluate the potential integration of ML techniques in the management and treatment of HF, to enhance patient outcomes and alleviate the associated economic strain.

Methods and Analysis This scoping review will use the approach described by Arksey and O'Malley [1]. The process consists of five phases: (1) defining the research questions, (2) identifying relevant studies, (3) selecting eligible studies, (4) organizing the data, and (5) compiling, summarizing, and reporting the results. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) was used in this protocol and the PRISMA extension for scoping reviews will be used to present the results. Databases searched are PubMed, SCOPUS, and Web of Science. The database was last searched in November 2023.

Ethics and dissemination This review does not require ethics approval. The dissemination strategy includes peer review publication, conference presentations, and to relevant stakeholders.

Keywords: Scoping Review Protocol; Machine Learning; Heart Failure; Hospitalization

Strengths and limitations of this study

A scoping review is a type of literature review that aims to provide an overview of existing research on a particular topic to identify gaps in the literature. While scoping reviews are valuable in many research contexts, they have several limitations. In this specific review, we identified the following limitations (1) the heterogeneity of the studies, which can make it challenging to draw comparisons or conclusions; (2) the fact that we will not include grey literature (e.g., unpublished studies and conference abstracts), which can result in an incomplete picture of the available evidence; (3) the subjectivity in data extraction, which can introduce researcher bias; (4) as a static study, it may not capture the most recent developments in a rapidly evolving field, as it's the case.

Despite these limitations, scoping reviews are valuable tools for mapping the literature and identifying research gaps.

INTRODUCTION

Machine Learning (ML) refers to the capacity of a system to autonomously acquire, integrate, and subsequently generate knowledge from extensive datasets, further extending this acquired knowledge by uncovering new information, all without the need for explicit programming.[2]

The learning process begins with the acquisition of observations or empirical data, comprising instances, firsthand experience, or instructional input, aiming to discerning patterns within the dataset.[3]

Machine Learning applications have proven to be successful across multiple areas, such as financial, security, industrial, marketing, environmental, and medical areas.[4–7] In the medical area, the application of ML has been particularly transformative and revolutionary, and it has fundamentally changed how healthcare is delivered, leading to improved diagnostics, personalized treatment plans, and enhanced patient outcomes.[7] Some practical examples in the medical area are medical imaging, genetic information, drug combinations, population-wide patient health outcomes, and natural language processing of existing medical documentation.[6,7]

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In cardiology, ML has applications in predictive risk assessment, classification, and identification prognostic phenotypes among patients with Heart Failure (HF).[8,9] Heart Failure is a chronic medical condition where the heart is unable to pump enough blood to meet the body's needs.[10] It's not a sudden stoppage of the heart but rather a progressive condition that can develop over time.[10] Additionally, HF is a complex and life-threatening syndrome marked by substantial morbidity and mortality, diminished functional capacity and quality of life, as well as elevated costs stemming from decompensation and subsequent hospitalization.[11] This condition affects more than 64 million people worldwide and the global economic burden of HF is estimated at \$108 billion per annum.[12]

Considering the global burden of HF, its related economic implications, and the successful exponential growth of ML, it is imperative to conduct this scoping review to comprehensively assess the potential integration of ML techniques in the management and treatment of heart failure, ultimately aiming to enhance patient outcomes and alleviate the economic strain associated with this condition.[11–13] Previous endeavors, such as those by Mpanya al.[14] and P. M. Croon et al.[15], have sought to explore similar avenues. However, their analyses, limited to data up to 2021, have not encompassed a thorough evaluation of the cost-effectiveness of employing ML models. As the landscape of ML applications continues to evolve, it becomes increasingly crucial to not only extend the temporal scope but also to incorporate a nuanced examination of the cost-benefit dynamics. This study endeavors to bridge this gap, providing a more comprehensive understanding of the role ML can play in mitigating the challenges posed by heart failure, not only from a clinical perspective but also from an economic standpoint.

METHOD AND ANALYSIS

Study design

The scoping review follows the approach outlined by Arksey and O'Malley [1], which involves five key stages: (1) defining the research question, (2) identifying relevant studies, (3) selecting eligible studies, (4) organizing the data, and (5) collecting,

summarizing, and reporting the findings. The protocol was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P), and we will employ the PRISMA-ScR extension [16] specifically designed for scoping reviews when presenting the results.

Stage 1: Defining the research question

The main research question is, "What machine learning models are used to predict hospitalization risk in individuals with heart failure, and what are the economic analyses conducted to assess the cost-effectiveness and economic impact of implementing these predictive models in clinical practice?"

The following specific objectives will guide the review:

1. To identify the ML models used for predicting hospitalization risk in individuals with heart failure;
2. To determine the data sources and variables utilized;
3. To identify the predictive performance of these ML models;
4. To summarize the key findings in the literature regarding the application of machine learning in heart failure hospitalization risk prediction;
5. To identify the economic analysis conducted to determine the cost-effectiveness and economic impact of implementing these models;
6. To provide recommendations for the development and application of ML models to predict HF hospitalizations.

Stage 2: Identifying relevant studies.

The databases will include PubMed, SCOPUS, and Web of Science. The database was last searched in November 2023. Articles will be included if they meet the inclusion criteria. The search terms will be ("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR "Readmission" [tiab] OR "Worsening" [tiab]) AND "Artificial Intelligence" [Mesh] AND ("Heart Failure" [Mesh] OR "Heart Failure, Diastolic" [Mesh] OR "Heart Failure, Systolic" [Mesh] OR "Heart Failure, Chronic" [tiab] OR "Heart Failure, Acute" [tiab]) OR ("Cost-Benefit Analysis" [Mesh] AND ("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR

"Readmission" [tiab] OR "Worsening" [tiab]) AND ("Artificial Intelligence" [Mesh] OR "Machine Learning" [Mesh] OR "Deep Learning" [Mesh]) AND ("Heart Failure" [Mesh] OR "Heart Failure, Diastolic" [Mesh] OR "Heart Failure, Systolic" [Mesh] OR "Heart Failure, Chronic" [tiab] OR "Heart Failure, Acute" [tiab])).

The search results will be exported into a Word document for data management, including removing duplicated articles.

Stage 3: Selecting eligible studies

After eliminating duplicates, data will be exported into Rayyan software. One reviewer will do title and abstract screening to select studies related to our Machine Learning, Population, Identification, Crosscheck, and Outcomes (ML-PICO) [17] format.

The full-text screening phase is the second step. Two independent reviewers will choose the studies that fit the inclusion criteria. During this screening phase, studies that might fit the inclusion criteria will be retrieved in full text. Studies in full text that do not fit the inclusion criteria will be eliminated, and the final report will include the rationale behind the omission. Data will be extracted by two separate reviewers, and inter-rated reliability will be evaluated and discussed in relation to the themes. The complete report on the search results will be included in the final report along with a PRISMA flow diagram. Disagreements between the reviewers will be settled by conversation or by consulting a third reviewer. If a study has several publications, the most current one will be kept. The language is limited to English.

Stage 4: Organizing the data

Critical information will be collected from the relevant studies: title, publication year, country and context, design, methods, sample size, variables, ML algorithms, performance metrics, applications, and the economic analysis performed and results.

Two researchers will extract the data, and disagreements will be discussed to reach a consensus among the team members.

Stage 5: Collecting, summarizing, and reporting the findings

During this phase, we will gather, condense, and present the data obtained from the scoping review. We'll conduct a descriptive analysis, consolidate related data segments, extract deductive codes aligned with the results, and assess interrater reliability. The information gathered from the studies included in the review will be organized into tables. Analysis of the data collected will provide recommendations to guide the development and implementation of machine learning models for predicting the risk of hospitalization by patients with heart failure.

ETHICS AND DISSEMINATION

This review does not require ethics approval. Our dissemination strategy includes peer review publications, presentations at conferences, and to relevant stakeholders.

Author Contributions

JS conceived the idea for the scoping review and led the design of the protocol and methodology. JS and JB wrote the first draft of the manuscript. TM provided inputs and critically revised the manuscript. All authors provided valuable inputs to the research questions and subject matter.

Acknowledges

The authors are grateful to Isabel Andrade and Joana Pires.

Funding

This publication was funded by Fundação Ciência e Tecnologia, IP national support through the Comprehensive Health Research Centre (UIDP/04923/2020).

Competing interests statement

None declared.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

References

- 1 Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol*. 2005;8:19–32.
- 2 Sen J, Mehtab S, Sen R, *et al*. *Machine Learning: Algorithms, Models, and Applications*. 2022. <https://doi.org/10.5772/intechopen.94615>
- 3 Abraham Iorkaa A, Barma M, Muazu H. Machine Learning Techniques, methods and Algorithms: Conceptual and Practical Insights. *Int J Eng Res Appl*. 2021;11:55–64.
- 4 Rivara FP, Fihn SD, Perlis RH. Advancing Health and Health Care Using Machine Learning: JAMA Network Open Call for Papers. *JAMA Netw Open*. 2018;1:e187176–e187176.
- 5 De Mauro A, Sestino A, Bacconi A. Machine learning and artificial intelligence use in marketing: a general taxonomy. *Italian Journal of Marketing*. 2022;2022:439–57.
- 6 Toh C, Brody JP. Applications of Machine Learning in Healthcare. doi: 10.5772/intechopen.92297
- 7 Shehab M, Abualigah L, Shambour Q, *et al*. Machine learning in medical applications: A review of state-of-the-art methods. *Comput Biol Med*. 2022;145. doi: 10.1016/J.COMPBIOMED.2022.105458
- 8 Seetharam K, Balla S, Bianco C, *et al*. Applications of Machine Learning in Cardiology. *Cardiol Ther*. 2022;11:355–68.
- 9 Cuocolo R, Perillo T, De Rosa E, *et al*. Current applications of big data and machine learning in cardiology. *J Geriatr Cardiol*. 2019;16:601.
- 10 Inamdar AA, Inamdar AC. Heart Failure: Diagnosis, Management and Utilization. *J Clin Med*. 2016;5. doi: 10.3390/JCM5070062
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- 12 Lesyuk W, Kriza C, Kolominsky-Rabas P. Cost-of-illness studies in heart failure: A systematic review 2004-2016. *BMC Cardiovasc Disord*. 2018;18:1–11.
- 13 Precedence Research. Machine Learning Market Size To Surpass USD 771.38 Bn By 2032. <https://www.precedenceresearch.com/machine-learning-market> (accessed 7 October 2023)
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- 15 Croon PM, Selder JL, Allaart CP, *et al*. Current state of artificial intelligence-based algorithms for hospital admission prediction in patients with heart failure: a scoping review. *European heart journal Digital health*. 2022;3:415–25.
- 16 Tricco AC, Lillie E, Zarin W, *et al*. PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. *Ann Intern Med*. 2018;169:467–73.

17 Liu X, Anstey J, Li R, *et al*. Rethinking PICO in the Machine Learning Era: ML-PICO. *Appl Clin Inform*. 2021;12:407.

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BMJ Open

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Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-083188.R1
Article Type:	Protocol
Date Submitted by the Author:	20-Mar-2024
Complete List of Authors:	Seringa, Joana; NOVA University Lisbon NOVA National School of Public Health; NOVA National School of Public Health, Public Health Research Centre, Comprehensive Health Research Center, CHRC, NOVA University Lisbon, Lisbon, Portugal Abreu, João; NOVA University Lisbon NOVA National School of Public Health Magalhaes, Teresa; NOVA University Lisbon NOVA National School of Public Health; NOVA National School of Public Health, Public Health Research Centre, Comprehensive Health Research Center, CHRC, NOVA University Lisbon, Lisbon, Portugal
Primary Subject Heading:	Health services research
Secondary Subject Heading:	Health informatics, Public health, Cardiovascular medicine
Keywords:	Heart failure < CARDIOLOGY, Hospitalization, eHealth, Health Services, Machine Learning

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Machine learning methods, applications, and economic analysis to predict heart failure hospitalization risk: a scoping review protocol

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ABSTRACT

Introduction Machine Learning (ML) has emerged as a powerful tool for uncovering patterns and generating new information. In cardiology, it has shown promising results in predictive outcomes risk assessment of Heart Failure (HF) patients, a chronic condition affecting over 64 million individuals globally.

This scoping review aims to synthesize evidence on machine learning methods, applications, and economic analysis to predict heart failure hospitalization risk.

Methods and Analysis This scoping review will use the approach described by Arksey and O'Malley. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) was used in this protocol, and the PRISMA extension for scoping reviews will be used to present the results. PubMed, SCOPUS and Web of Science are the databases that will be searched. Two reviewers will independently screen full-text studies for inclusion and extract the data. All the studies focusing on ML models applied to predict the risk of hospitalization from HF adult patients will be included.

Ethics and dissemination Ethical approval is not required for this review. The dissemination strategy includes a peer-reviewed publication, conference presentations, and dissemination to relevant stakeholders.

Keywords: Scoping Review Protocol; Machine Learning; Heart Failure; Hospitalization

Strengths and limitations of this study

- The heterogeneity of the studies can make it challenging to draw comparisons or conclusions;
- This scoping review will not include grey literature (e.g., unpublished studies and conference abstracts), which can result in an incomplete picture of the available evidence;
- As a static study, the study may not capture the most recent developments in a rapidly evolving field, as is the case.
- Despite the limitations, this scoping review will be a valuable tool for mapping the current literature on ML methods, applications, and economic analysis to predict heart failure hospitalization risk, drawing recommendations, and identifying research gaps.

INTRODUCTION

Machine Learning (ML) refers to the capacity of a system to autonomously acquire, integrate, and subsequently generate knowledge from extensive datasets, further extending this acquired knowledge by uncovering new information, all without the need for explicit programming.[1]

The learning process begins with acquiring observations or empirical data, comprising instances, firsthand experience, or instructional input, aiming to uncover patterns within the dataset.[2]

Machine Learning applications have proven successful across multiple areas, such as financial, security, industrial, marketing, environmental, and medical.[3–6] In the medical area, the application of ML has been particularly transformative and revolutionary, and it has fundamentally changed how healthcare is delivered, leading to improved diagnostics, personalized treatment plans, and enhanced patient outcomes.[6] Some practical examples in the medical area are medical imaging, genetic information, drug combinations, population-wide patient health outcomes, and natural language processing of existing medical documentation.[5,6]

In cardiology, ML has applications in predictive risk assessment, classification, and identification of prognostic phenotypes among patients with Heart Failure (HF).[7,8] Heart Failure is a chronic medical condition where the heart is unable to pump enough blood to meet the body's needs.[9] It's not a sudden stoppage of the heart but rather a progressive condition that can develop over time.[9] Additionally, HF is a complex and life-threatening syndrome marked by substantial morbidity and mortality, diminished functional capacity and quality of life, as well as elevated costs stemming from decompensation and subsequent hospitalization.[10] This condition affects more than 64 million people worldwide, with a global economic burden estimated at \$108 billion per annum.[11]

Considering the global burden of HF, its related economic implications, and the successful exponential growth of ML, it is imperative to conduct this scoping review to synthesize evidence on machine learning methods, applications, and economic analysis to predict heart failure hospitalization risk aiming to reduce unplanned hospitalizations, enhance patient outcomes and alleviate the associated financial strain associated with this condition.[10–12] Previous endeavours, such as those by Mpanya al.[13] and P. M. Croon et al.[14], have sought to explore similar avenues. However, their analyses, limited to data up to 2021, have not considered the cost-effectiveness of employing ML models. As the landscape of ML applications continues to evolve, it becomes increasingly crucial to extend the temporal scope but incorporate a nuanced examination of the cost-benefit dynamics. This study aims to bridge this gap, providing a more comprehensive understanding of current ML models applied to predict heart failure hospitalization risk, from a clinical and technical perspective but also from an economic standpoint.

METHOD AND ANALYSIS

Study design

The scoping review follows the approach outlined by Arksey and O'Malley [15], which involves five key stages: (1) defining the research question, (2) identifying relevant studies, (3) selecting eligible studies, (4) organizing the data, and (5) collecting,

summarizing, and reporting the findings. The protocol was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P), and we will employ the PRISMA-ScR extension [16] specifically designed for scoping reviews when presenting the results.

Stage 1: Defining the research question

The main research question is, "What machine learning models are used to predict hospitalization risk in individuals aged 18 years or older with heart failure, and what economic analyses are conducted to assess the cost-effectiveness and economic impact of implementing these predictive models in clinical practice?"

The following specific objectives will guide the review:

1. To identify the ML models used for predicting hospitalization risk in individuals with heart failure;
2. To determine the data sources and variables utilized;
3. To identify the predictive performance of these ML models;
4. To summarize the key findings in the literature regarding the application of machine learning in heart failure hospitalization risk prediction;
5. To identify the economic analysis conducted to determine the cost-effectiveness of these models;
6. To provide recommendations for developing and applying ML models to predict HF hospitalizations.

Stage 2: Identifying relevant studies.

The databases will be PubMed, SCOPUS, and Web of Science. Articles will be included if they meet the inclusion criteria. A preliminary search to validate the appropriateness of the search terms was conducted, resulting in the identification of the following terms: ("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR "Readmission" [tiab] OR "Worsening" [tiab]) AND "Artificial Intelligence" [Mesh] AND ("Heart Failure" [Mesh] OR "Heart Failure, Diastolic" [Mesh] OR "Heart Failure, Systolic" [Mesh] OR "Heart Failure, Chronic" [tiab] OR "Heart Failure, Acute" [tiab]) OR ("Cost-Benefit Analysis" [Mesh] AND

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("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR "Readmission" [tiab] OR "Worsening" [tiab]) AND ("Artificial Intelligence" [Mesh] OR "Machine Learning" [Mesh] OR "Deep Learning" [Mesh]) AND ("Heart Failure" [Mesh] OR "Heart Failure, Diastolic" [Mesh] OR "Heart Failure, Systolic" [Mesh] OR "Heart Failure, Chronic" [tiab] OR "Heart Failure, Acute" [tiab])).

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After eliminating duplicates, data will be exported into Rayyan software. One reviewer will do title and abstract screening to select studies related to our Machine Learning, Population, Identification, Crosscheck, and Outcomes (ML-PICO) [17] format.

The full-text screening phase is the second step. Two independent reviewers will choose the studies that fit the inclusion criteria. Studies that might fit the inclusion criteria will be retrieved in full text during this screening phase. Studies in full text that do not fit the inclusion criteria will be eliminated, and the final report will include the rationale behind the omission. Two separate reviewers will extract data, and inter-rater reliability will be evaluated and discussed. The complete report on the search results will be included in the final report, along with a PRISMA flow diagram. Disagreements between the reviewers will be settled by conversation or consulting a third reviewer. If a study has several publications, the most current one will be kept. Studies will be excluded if the population is not specifically for adults with heart failure. Studies that do not include economic analysis but focus on ML models to predict HF hospitalizations will be included. The language is limited to English.

Stage 4: Organizing the data

Critical information will be collected from the relevant studies: title, authors, publication year, country and context, study design, sample size, variables, ML algorithms, performance metrics and results, applications, and economic analysis performed and results.

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174 Two researchers will extract the data, and disagreements will be discussed to reach a
175 consensus among the team members.

176 **Stage 5: Collecting, summarizing, and reporting the findings**

177 During this phase, we will gather, condense, and present the data obtained from the
178 scoping review. We'll conduct a descriptive analysis, consolidate related data segments,
179 extract deductive codes aligned with the results, and assess interrater reliability. The
180 information gathered from the studies included in the review will be organized into
181 tables. Analysis of the data collected will provide recommendations to guide the
182 development and implementation of machine learning models for predicting the risk of
183 hospitalization by patients with heart failure.

184 **Patient and public involvement**

185 Patients and/or the public were not involved in the design, or conduct, or reporting, or
186 dissemination plans of this research.

187 **ETHICS AND DISSEMINATION**

188 This review does not require ethics approval. Our dissemination strategy includes a
189 peer-reviewed publications, presentations at conferences, and dissemination to
190 relevant stakeholders.

191 **AUTHOR CONTRIBUTIONS**

192 JS conceived the idea for the scoping review and led the design of the protocol and
193 methodology. JS and JA wrote the first draft of the manuscript. TM provided inputs and
194 critically revised the manuscript. All authors approved the final manuscript.

195 **ACKNOWLEDGES**

196 The authors are grateful to Isabel Andrade and Joana Pires.

197 **FUNDING**

The present publication was funded by Fundação Ciência e Tecnologia, IP national support through CHRC (UIDP/04923/2020).

COMPETING INTERESTS STATEMENT

None declared.

REFERENCES

- 1 Sen J, Mehtab S, Sen R, *et al.* *Machine Learning: Algorithms, Models, and Applications*. 2022. <https://doi.org/10.5772/intechopen.94615>
- 2 Abraham Iorkaa A, Barma M, Muazu H. Machine Learning Techniques, methods and Algorithms: Conceptual and Practical Insights. *Int J Eng Res Appl*. 2021;11:55–64.
- 3 Rivara FP, Fihn SD, Perlis RH. Advancing Health and Health Care Using Machine Learning: JAMA Network Open Call for Papers. *JAMA Netw Open*. 2018;1:e187176–e187176.
- 4 De Mauro A, Sestino A, Bacconi A. Machine learning and artificial intelligence use in marketing: a general taxonomy. *Italian Journal of Marketing*. 2022;2022:439–57.
- 5 Toh C, Brody JP. Applications of Machine Learning in Healthcare. doi: 10.5772/intechopen.92297
- 6 Shehab M, Abualigah L, Shambour Q, *et al.* Machine learning in medical applications: A review of state-of-the-art methods. *Comput Biol Med*. 2022;145. doi: 10.1016/J.COMPBIOMED.2022.105458
- 7 Seetharam K, Balla S, Bianco C, *et al.* Applications of Machine Learning in Cardiology. *Cardiol Ther*. 2022;11:355–68.
- 8 Cuocolo R, Perillo T, De Rosa E, *et al.* Current applications of big data and machine learning in cardiology. *J Geriatr Cardiol*. 2019;16:601.
- 9 Inamdar AA, Inamdar AC. Heart Failure: Diagnosis, Management and Utilization. *J Clin Med*. 2016;5. doi: 10.3390/JCM5070062
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- 13 Mpanya D, Celik T, Klug E, *et al.* Predicting mortality and hospitalization in heart failure using machine learning: A systematic literature review. *IJC Heart & Vasculture*. 2021;34:100773.
- 14 Croon PM, Selder JL, Allaart CP, *et al.* Current state of artificial intelligence-based algorithms for hospital admission prediction in patients with heart failure: a scoping review. *European heart journal Digital health*. 2022;3:415–25.
- 15 Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol*. 2005;8:19–32.

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Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-083188.R2
Article Type:	Protocol
Date Submitted by the Author:	21-Mar-2024
Complete List of Authors:	Seringa, Joana; NOVA University Lisbon NOVA National School of Public Health; NOVA National School of Public Health, Public Health Research Centre, Comprehensive Health Research Center, CHRC, NOVA University Lisbon, Lisbon, Portugal Abreu, João; NOVA University Lisbon NOVA National School of Public Health Magalhaes, Teresa; NOVA University Lisbon NOVA National School of Public Health; NOVA National School of Public Health, Public Health Research Centre, Comprehensive Health Research Center, CHRC, NOVA University Lisbon, Lisbon, Portugal
Primary Subject Heading:	Health services research
Secondary Subject Heading:	Health informatics, Public health, Cardiovascular medicine
Keywords:	Heart failure < CARDIOLOGY, Hospitalization, eHealth, Health Services, Machine Learning

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Machine learning methods, applications, and economic analysis to predict heart failure hospitalization risk: a scoping review protocol

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ABSTRACT

Introduction Machine Learning (ML) has emerged as a powerful tool for uncovering patterns and generating new information. In cardiology, it has shown promising results in predictive outcomes risk assessment of Heart Failure (HF) patients, a chronic condition affecting over 64 million individuals globally.

This scoping review aims to synthesize evidence on machine learning methods, applications, and economic analysis to predict heart failure hospitalization risk.

Methods and Analysis This scoping review will use the approach described by Arksey and O'Malley. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) was used in this protocol, and the PRISMA extension for scoping reviews will be used to present the results. PubMed, SCOPUS and Web of Science are the databases that will be searched. Two reviewers will independently screen full-text studies for inclusion and extract the data. All the studies focusing on ML models to predict the risk of hospitalization from HF adult patients will be included.

Ethics and dissemination Ethical approval is not required for this review. The dissemination strategy includes a peer-reviewed publication, conference presentations, and dissemination to relevant stakeholders.

Keywords: Scoping Review Protocol; Machine Learning; Heart Failure; Hospitalization

Strengths and limitations of this study

- The heterogeneity of the studies can make it challenging to draw comparisons or conclusions;
- This scoping review will not include grey literature (e.g., unpublished studies and conference abstracts) and systematic reviews, which can result in an incomplete picture of the available evidence;
- As a static study, the study may not capture the most recent developments in a rapidly evolving field, as is the case.
- Despite the limitations, this scoping review will be a valuable tool for mapping the current literature on ML methods, applications, and economic analysis to predict heart failure hospitalization risk, drawing recommendations, and identifying research gaps.

INTRODUCTION

Machine Learning (ML) refers to the capacity of a system to autonomously acquire, integrate, and subsequently generate knowledge from extensive datasets, further extending this acquired knowledge by uncovering new information, all without the need for explicit programming.[1]

The learning process begins with acquiring observations or empirical data, comprising instances, firsthand experience, or instructional input, aiming to uncover patterns within the dataset.[2]

Machine Learning applications have proven successful across multiple areas, such as financial, security, industrial, marketing, environmental, and medical.[3–6] In the medical area, the application of ML has been particularly transformative and revolutionary, and it has fundamentally changed how healthcare is delivered, leading to improved diagnostics, personalized treatment plans, and enhanced patient outcomes.[6] Some practical examples in the medical area are medical imaging, genetic information, drug combinations, population-wide patient health outcomes, and natural language processing of existing medical documentation.[5,6]

In cardiology, ML has applications in predictive risk assessment, classification, and identification of prognostic phenotypes among patients with Heart Failure (HF).[7,8] Heart Failure is a chronic medical condition where the heart is unable to pump enough blood to meet the body's needs.[9] It's not a sudden stoppage of the heart but rather a progressive condition that can develop over time.[9] Additionally, HF is a complex and life-threatening syndrome marked by substantial morbidity and mortality, diminished functional capacity and quality of life, as well as elevated costs stemming from decompensation and subsequent hospitalization.[10] This condition affects more than 64 million people worldwide, with a global economic burden estimated at \$108 billion per annum.[11]

Considering the global burden of HF, its related economic implications, and the successful exponential growth of ML, it is imperative to conduct this scoping review to synthesize evidence on machine learning methods, applications, and economic analysis to predict heart failure hospitalization risk aiming to reduce unplanned hospitalizations, enhance patient outcomes and alleviate the associated financial strain associated with this condition.[10–12] Previous endeavours, such as those by Mpanya al.[13] and P. M. Croon et al.[14], have sought to explore similar avenues. However, their analyses, limited to data up to 2021, have not considered the cost-effectiveness of employing ML models. As the landscape of ML applications continues to evolve, it becomes increasingly crucial to extend the temporal scope but incorporate a nuanced examination of the cost-benefit dynamics. This study aims to bridge this gap, providing a more comprehensive understanding of current ML models to predict heart failure hospitalization risk, from a clinical and technical perspective but also from an economic standpoint.

METHOD AND ANALYSIS

Study design

The scoping review follows the approach outlined by Arksey and O'Malley [15], which involves five key stages: (1) defining the research question, (2) identifying relevant studies, (3) selecting eligible studies, (4) organizing the data, and (5) collecting, summarizing, and reporting the findings. The protocol was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P), and

we will employ the PRISMA-ScR extension [16] specifically designed for scoping reviews when presenting the results.

The study is planned to begin at the end of March 2024 and finish by June 2024.

Stage 1: Defining the research question

The main research question is, "What machine learning models are used to predict hospitalization risk in individuals aged 18 years or older with heart failure, and what economic analyses are conducted to assess the cost-effectiveness and economic impact of implementing these predictive models in clinical practice?"

The following specific objectives will guide the review:

1. To identify the ML models used for predicting hospitalization risk in individuals with heart failure;
2. To determine the data sources and variables utilized;
3. To identify the predictive performance of these ML models;
4. To summarize the key findings in the literature regarding the application of machine learning in heart failure hospitalization risk prediction;
5. To identify the economic analysis conducted to determine the cost-effectiveness of these models;
6. To provide recommendations for developing and applying ML models to predict HF hospitalizations.

Stage 2: Identifying relevant studies

The databases will be PubMed, SCOPUS, and Web of Science. Articles will be included if they meet the inclusion criteria. A preliminary search to validate the appropriateness of the search terms was conducted, resulting in the identification of the following terms: ("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR "Readmission" [tiab] OR "Worsening" [tiab]) AND "Artificial Intelligence" [Mesh] AND ("Heart Failure" [Mesh] OR "Heart Failure, Diastolic" [Mesh] OR "Heart Failure, Systolic" [Mesh] OR "Heart Failure, Chronic" [tiab] OR "Heart Failure, Acute" [tiab]) OR ("Cost-Benefit Analysis" [Mesh] AND ("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR "Readmission" [tiab] OR

"Worsening" [tiab]) AND ("Artificial Intelligence" [Mesh] OR "Machine Learning" [Mesh] OR "Deep Learning" [Mesh]) AND ("Heart Failure" [Mesh] OR "Heart Failure, Diastolic" [Mesh] OR "Heart Failure, Systolic" [Mesh] OR "Heart Failure, Chronic" [tiab] OR "Heart Failure, Acute" [tiab])).

The search results will be exported into a Word document for data management, including removing duplicated articles.

Stage 3: Selecting eligible studies

After eliminating duplicates, data will be exported into Rayyan software. One reviewer will do title and abstract screening to select studies related to our Machine Learning, Population, Identification, Crosscheck, and Outcomes (ML-PICO) [17] format.

The full-text screening phase is the second step. Two independent reviewers will choose the studies that fit the inclusion criteria. Studies that might fit the inclusion criteria will be retrieved in full text during this screening phase. Studies in full text that do not fit the inclusion criteria will be eliminated, and the final report will include the rationale behind the omission. Two separate reviewers will extract data, and inter-rater reliability will be evaluated and discussed. The complete report on the search results will be included in the final report, along with a PRISMA flow diagram. Disagreements between the reviewers will be settled by conversation or consulting a third reviewer. If a study has several publications, the most current one will be kept. Eligible studies will be considered based on the criteria identified in Table 1.

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Studies focusing on ML models to predict the risk of hospitalization from HF patients aged 18 years and older.	Studies whose population is not of adult individuals with HF.
Studies that do not include economic analysis but focus on ML models to predict HF hospitalizations.	Studies whose cause of hospitalization is not HF.

	Grey literature (e.g., unpublished studies and conference abstracts) and systematic reviews.
	Studies in languages other than English.

Stage 4: Organizing the data

Critical information will be collected from the relevant studies: title, authors, publication year, country and context, study design, sample size, variables, ML algorithms, performance metrics and results, applications, and economic analysis performed and results.

Two researchers will extract the data, and disagreements will be discussed to reach a consensus among the team members.

Stage 5: Collecting, summarizing, and reporting the findings

During this phase, we will gather, condense, and present the data obtained from the scoping review. We'll conduct a descriptive analysis, consolidate related data segments, extract deductive codes aligned with the results, and assess interrater reliability. The information gathered from the studies included in the review will be organized into tables. Analysis of the data collected will provide recommendations to guide the development and implementation of machine learning models for predicting the risk of hospitalization by patients with heart failure.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

ETHICS AND DISSEMINATION

This review does not require ethics approval. Our dissemination strategy includes a peer-reviewed publications, presentations at conferences, and dissemination to relevant stakeholders.

AUTHOR CONTRIBUTIONS

JS conceived the idea for the scoping review and led the design of the protocol and methodology. JS and JA wrote the first draft of the manuscript. TM provided inputs and critically revised the manuscript. All authors approved the final manuscript.

ACKNOWLEDGES

The authors are grateful to Isabel Andrade and Joana Pires.

FUNDING

The present publication was funded by Fundação Ciência e Tecnologia, IP national support through CHRC (UIDP/04923/2020).

COMPETING INTERESTS STATEMENT

None declared.

REFERENCES

- 1 Sen J, Mehtab S, Sen R, *et al.* *Machine Learning: Algorithms, Models, and Applications*. 2022. <https://doi.org/10.5772/intechopen.94615>
- 2 Abraham Iorkaa A, Barma M, Muazu H. Machine Learning Techniques, methods and Algorithms: Conceptual and Practical Insights. *Int J Eng Res Appl*. 2021;11:55–64.
- 3 Rivara FP, Fihn SD, Perlis RH. Advancing Health and Health Care Using Machine Learning: JAMA Network Open Call for Papers. *JAMA Netw Open*. 2018;1:e187176–e187176.
- 4 De Mauro A, Sestino A, Bacconi A. Machine learning and artificial intelligence use in marketing: a general taxonomy. *Italian Journal of Marketing*. 2022;2022:439–57.
- 5 Toh C, Brody JP. Applications of Machine Learning in Healthcare. doi: 10.5772/intechopen.92297
- 6 Shehab M, Abualigah L, Shambour Q, *et al.* Machine learning in medical applications: A review of state-of-the-art methods. *Comput Biol Med*. 2022;145. doi: 10.1016/J.COMPBIOMED.2022.105458

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59
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218 7 Seetharam K, Balla S, Bianco C, *et al.* Applications of Machine Learning in
219 Cardiology. *Cardiol Ther.* 2022;11:355–68.
220 8 Cuocolo R, Perillo T, De Rosa E, *et al.* Current applications of big data and
221 machine learning in cardiology. *J Geriatr Cardiol.* 2019;16:601.
222 9 Inamdar AA, Inamdar AC. Heart Failure: Diagnosis, Management and
223 Utilization. *J Clin Med.* 2016;5. doi: 10.3390/JCM5070062
224 10 Savarese G, Becher PM, Lund LH, *et al.* Global burden of heart failure: a
225 comprehensive and updated review of epidemiology. *Cardiovasc Res.*
226 2023;118:3272–87.
227 11 Lesyuk W, Kriza C, Kolominsky-Rabas P. Cost-of-illness studies in heart failure:
228 A systematic review 2004-2016. *BMC Cardiovasc Disord.* 2018;18:1–11.
229 12 Precedence Research. Machine Learning Market Size To Surpass USD 771.38
230 Bn By 2032. <https://www.precedenceresearch.com/machine-learning-market>
231 (accessed 7 October 2023)
232 13 Mpanya D, Celik T, Klug E, *et al.* Predicting mortality and hospitalization in
233 heart failure using machine learning: A systematic literature review. *IJC Heart &*
234 *Vasculature.* 2021;34:100773.
235 14 Croon PM, Selder JL, Allaart CP, *et al.* Current state of artificial intelligence-
236 based algorithms for hospital admission prediction in patients with heart failure: a
237 scoping review. *European heart journal Digital health.* 2022;3:415–25.
238 15 Arksey H, O’Malley L. Scoping studies: towards a methodological framework.
239 *Int J Soc Res Methodol.* 2005;8:19–32.
240 16 Tricco AC, Lillie E, Zarin W, *et al.* PRISMA extension for scoping reviews
241 (PRISMA-ScR): Checklist and explanation. *Ann Intern Med.* 2018;169:467–73.
242 17 Liu X, Anstey J, Li R, *et al.* Rethinking PICO in the Machine Learning Era: ML-
243 PICO. *Appl Clin Inform.* 2021;12:407.
244

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