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

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Keywords:	Heart failure < CARDIOLOGY, Hospitalization, eHealth, Health Services



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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 costeffectiveness 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

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"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

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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.

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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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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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29 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.

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

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

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9 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;

- 55 As a static study, the study may not capture the most recent developments in a 66 rapidly evolving field, as is the case.
- 57 Despite the limitations, this scoping review will be a valuable tool for mapping 58 the current literature on ML methods, applications, and economic analysis to 59 predict heart failure hospitalization risk, drawing recommendations, and 70 identifying research gaps.
- 71

72 INTRODUCTION

73 Machine Learning (ML) refers to the capacity of a system to autonomously acquire, 74 integrate, and subsequently generate knowledge from extensive datasets, further 75 extending this acquired knowledge by uncovering new information, all without the need 76 for explicit programming.[1]

77 The learning process begins with acquiring observations or empirical data, comprising 78 instances, firsthand experience, or instructional input, aiming to uncover patterns within 79 the dataset.[2]

30 Machine Learning applications have proven successful across multiple areas, such as 31 financial, security, industrial, marketing, environmental, and medical.[3-6] In the 32 medical area, the application of ML has been particularly transformative and 33 revolutionary, and it has fundamentally changed how healthcare is delivered, leading to 34 improved diagnostics, personalized treatment plans, and enhanced patient 35 outcomes.[6] Some practical examples in the medical area are medical imaging, genetic 86 information, drug combinations, population-wide patient health outcomes, and natural 37 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.

⁵⁰ 51 113 METHOD AND ANALYSIS

114 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, o Page 5 of 9

1 2 **BMJ** Open

ne findings. The protocol was based on the Preferred c Reviews and Meta-Analysis Protocols (PRISMA-P), and R extension [16] specifically designed for scoping reviews	-
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3 4	118	summarizing, and reporting the findings. The protocol was based on the Preferred
5 6	119	Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P), and
7	120	we will employ the PRISMA-ScR extension [16] specifically designed for scoping reviews
8 9	121	when presenting the results.
10 11 12	122	Stage 1: Defining the research question
13 14	123	The main research question is, "What machine learning models are used to predict
15 16	124	hospitalization risk in individuals aged 18 years or older with heart failure, and what
17	125	economic analyses are conducted to assess the cost-effectiveness and economic impact
18 19 20	126	of implementing these predictive models in clinical practice?"
20 21 22	127	The following specific objectives will guide the review:
23 24	128	1. To identify the ML models used for predicting hospitalization risk in individuals
25 26	129	with heart failure;
27 28	130	2. To determine the data sources and variables utilized;
29 30	131	3. To identify the predictive performance of these ML models;
31 32	132	4. To summarize the key findings in the literature regarding the application of
33 34	133	machine learning in heart failure hospitalization risk prediction;
35 36	134	5. To identify the economic analysis conducted to determine the cost-
37 38 39 40	135	effectiveness of these models;
	136	6. To provide recommendations for developing and applying ML models to
41 42 43	137	predict HF hospitalizations.
44 45	138	Stage 2: Identifying relevant studies.
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48	139	The databases will be PubMed, SCOPUS, and Web of Science. Articles will be included if
49 50	140	they meet the inclusion criteria. A preliminary search to validate the appropriateness of
51 52	141	the search terms was conducted, resulting in the identification of the following terms:
53 54	142	("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR "Readmission" [tiab] OR
55	143	"Worsening" [tiab]) AND "Artificial Intelligence" [Mesh] AND ("Heart Failure" [Mesh] OR
56 57	144	"Heart Failure, Diastolic" [Mesh] OR "Heart Failure, Systolic" [Mesh] OR "Heart Failure,
58 59 60	145	Chronic" [tiab] OR "Heart Failure, Acute" [tiab]) OR ("Cost-Benefit Analysis" [Mesh] AND

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"Worsening" [tiab]) AND ("Artificial Intelligence" [Mesh] OR "Machine Learning" [Mesh]
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151 The search results will be exported into a Word document for data management,152 including removing duplicated articles.

153 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,
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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.

51 169 Stage 4: Organizing the data
52

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 a175 consensus among the team members.

176 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.

184 Patient and public involvement

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

187 ETHICS AND DISSEMINATION

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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.

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- 197 FUNDING

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The present publication was funded by Fundação Ciência e Tecnologia, IP national support through CHRC (UIDP/04923/2020). **COMPETING INTERESTS STATEMENT** None declared. REFERENCES Sen J, Mehtab S, Sen R, et al. Machine Learning: Algorithms, Models, and Applications. 2022. https://doi.org/10.5772/intechopen.94615 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. 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. 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. Toh C, Brody JP. Applications of Machine Learning in Healthcare. doi: 10.5772/intechopen.92297 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 Seetharam K, Balla S, Bianco C, et al. Applications of Machine Learning in Cardiology. Cardiol Ther. 2022;11:355-68. 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. Inamdar AA, Inamdar AC. Heart Failure: Diagnosis, Management and Utilization. J Clin Med. 2016;5. doi: 10.3390/JCM5070062 Savarese G, Becher PM, Lund LH, et al. Global burden of heart failure: a comprehensive and updated review of epidemiology. Cardiovasc Res. 2023;118:3272-87. 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. 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) Mpanya D, Celik T, Klug E, et al. Predicting mortality and hospitalization in heart failure using machine learning: A systematic literature review. IJC Heart & Vasculature. 2021;34:100773. 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. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol. 2005;8:19–32.

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

Journal:	BMJ Open
Manuscript ID	bmjopen-2023-083188.R2
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Primary Subject Heading :	Health services research
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Keywords:	Heart failure < CARDIOLOGY, Hospitalization, eHealth, Health Services, Machine Learning

SCHOLARONE[™] Manuscripts

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29 ABSTRACT

30 Introduction Machine Learning (ML) has emerged as a powerful tool for uncovering 31 patterns and generating new information. In cardiology, it has shown promising results 32 in predictive outcomes risk assessment of Heart Failure (HF) patients, a chronic 33 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.

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

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

59 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.

72 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.

- 48 112 METHOD AND ANALYSIS
 49
- 51 113 **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 Page 5 of 9

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3 4	119	we will employ the PRISMA-ScR extension [16] specifically designed for scoping reviews
5 6	120	when presenting the results.
7 8	121	The study is planned to begin at the end of March 2024 and finish by June 2024.
9 10 11	122	Stage 1: Defining the research question
12 13	123	The main research question is, "What machine learning models are used to predict
14	124	hospitalization risk in individuals aged 18 years or older with heart failure, and what
15 16	125	economic analyses are conducted to assess the cost-effectiveness and economic impact
17 18	126	of implementing these predictive models in clinical practice?"
19 20 21	127	The following specific objectives will guide the review:
22 23	128	1. To identify the ML models used for predicting hospitalization risk in individuals
24 25	129	with heart failure;
25 26 27	130	2. To determine the data sources and variables utilized;
28 29	131	3. To identify the predictive performance of these ML models;
30 31	132	4. To summarize the key findings in the literature regarding the application of
32 33	133	machine learning in heart failure hospitalization risk prediction;
34 35	134	5. To identify the economic analysis conducted to determine the cost-
36 37	135	effectiveness of these models;
38 39	136	6. To provide recommendations for developing and applying ML models to
40 41	137	predict HF hospitalizations.
42 43 44 45	138	Stage 2: Identifying relevant studies
46 47	139	The databases will be PubMed, SCOPUS, and Web of Science. Articles will be included if
48 49	140	they meet the inclusion criteria. A preliminary search to validate the appropriateness of
50	141	the search terms was conducted, resulting in the identification of the following terms:
51 52	142	("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR "Readmission" [tiab] OR
53 54	143	"Worsening" [tiab]) AND "Artificial Intelligence" [Mesh] AND ("Heart Failure" [Mesh] OR
55 56	144	"Heart Failure, Diastolic" [Mesh] OR "Heart Failure, Systolic" [Mesh] OR "Heart Failure,

145 Chronic" [tiab] OR "Heart Failure, Acute" [tiab]) OR ("Cost-Benefit Analysis" [Mesh] AND
146 ("Hospitalization" [Mesh] OR "Decompensat*" [tiab] OR "Readmission" [tiab] OR

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"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])).

151 The search results will be exported into a Word document for data management,152 including removing duplicated articles.

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

		Grey literature (e.g., unpublished studies
		and conference abstracts) and systematic
		reviews.
		Studies in languages other than English.
167		
168	Stage 4: Organizing the data	

169 Critical information will be collected from the relevant studies: title, authors, publication 170 year, country and context, study design, sample size, variables, ML algorithms, 171 performance metrics and results, applications, and economic analysis performed and 172 results.

173 Two researchers will extract the data, and disagreements will be discussed to reach a174 consensus among the team members.

175 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.

183 Patient and public involvement

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

186 ETHICS AND DISSEMINATION

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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 Sen J, Mehtab S, Sen R, et al. Machine Learning: Algorithms, Models, and Applications. 2022. https://doi.org/10.5772/intechopen.94615 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. 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. 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. Toh C, Brody JP. Applications of Machine Learning in Healthcare. doi:

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16	229	12	Precedence Research. Machine Learning Market Size To Surpass USD 771.38
17 18	230		Bn By 2032. https://www.precedenceresearch.com/machine-learning-market
10	231		(accessed 7 October 2023)
20	232	13	Mpanya D, Celik T, Klug E, et al. Predicting mortality and hospitalization in
21	233		heart failure using machine learning: A systematic literature review. IJC Heart &
22	234		Vasculature. 2021;34:100773.
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24	236		based algorithms for hospital admission prediction in patients with heart failure: a
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