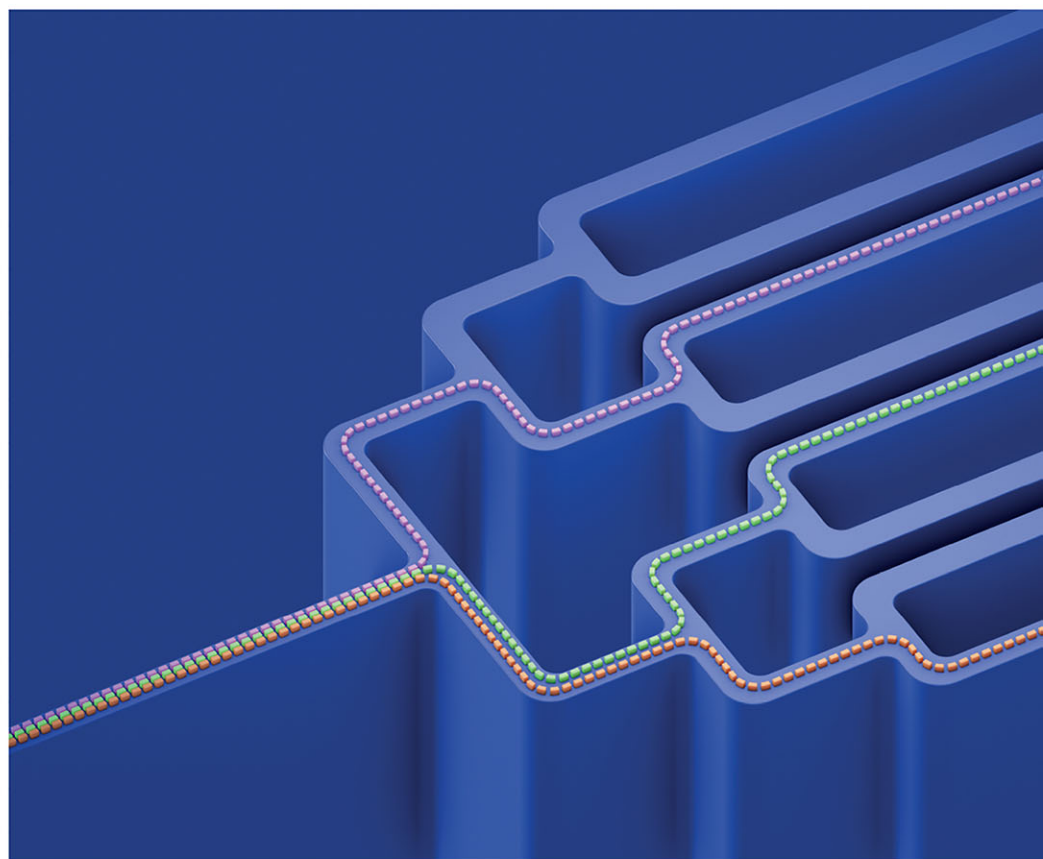


Explainable Artificial Intelligence in Medical Decision Support Systems

Edited by

**Agbotiname Lucky Imoize, Jude Hemanth,
Dinh-Thuan Do and Samarendra Nath Sur**



Explainable Artificial Intelligence in Medical Decision Support Systems

IET Book Series on e-Health Technologies

Book Series Editor: Professor Joel J.P.C. Rodrigues, College of Computer Science and Technology, China University of Petroleum (East China), Qingdao, China; Senac Faculty of Ceará, Fortaleza-CE, Brazil and Instituto de Telecomunicações, Portugal

Book Series Advisor: Professor Pranjal Chandra, School of Biochemical Engineering, Indian Institute of Technology (BHU), Varanasi, India

While the demographic shifts in populations display significant socio-economic challenges, they trigger opportunities for innovations in e-Health, m-Health, precision and personalized medicine, robotics, sensing, the Internet of things, cloud computing, big data, software defined networks, and network function virtualization. Their integration is however associated with many technological, ethical, legal, social, and security issues. This book series aims to disseminate recent advances for e-health technologies to improve healthcare and people's wellbeing.

Could you be our next author?

Topics considered include intelligent e-Health systems, electronic health records, ICT-enabled personal health systems, mobile and cloud computing for e-Health, health monitoring, precision and personalized health, robotics for e-Health, security and privacy in e-Health, ambient assisted living, telemedicine, big data and IoT for e-Health, and more.

Proposals for coherently integrated international multi-authored edited or co-authored handbooks and research monographs will be considered for this book series. Each proposal will be reviewed by the book Series Editor with additional external reviews from independent reviewers.

To download our proposal form or find out more information about publishing with us, please visit <https://www.theiet.org/publishing/publishing-with-iet-books/>.

Please email your completed book proposal for the IET Book Series on e-Health Technologies to: Amber Thomas at athomas@theiet.org or author_support@theiet.org.

Explainable Artificial Intelligence in Medical Decision Support Systems

Edited by

Agbotiname Lucky Imoize, Jude Hemanth,
Dinh-Thuan Do and Samarendra Nath Sur

The Institution of Engineering and Technology

Published by The Institution of Engineering and Technology, London, United Kingdom

The Institution of Engineering and Technology is registered as a Charity in England & Wales (no. 211014) and Scotland (no. SC038698).

© The Institution of Engineering and Technology 2022

First published 2022

This publication is copyright under the Berne Convention and the Universal Copyright Convention. All rights reserved. Apart from any fair dealing for the purposes of research or private study, or criticism or review, as permitted under the Copyright, Designs and Patents Act 1988, this publication may be reproduced, stored or transmitted, in any form or by any means, only with the prior permission in writing of the publishers, or in the case of reprographic reproduction in accordance with the terms of licences issued by the Copyright Licensing Agency. Enquiries concerning reproduction outside those terms should be sent to the publisher at the undermentioned address:

The Institution of Engineering and Technology
Futures Place
Kings Way, Stevenage
Hertfordshire SG1 2UA, United Kingdom

www.theiet.org

While the authors and publisher believe that the information and guidance given in this work are correct, all parties must rely upon their own skill and judgement when making use of them. Neither the author nor publisher assumes any liability to anyone for any loss or damage caused by any error or omission in the work, whether such an error or omission is the result of negligence or any other cause. Any and all such liability is disclaimed.

The moral rights of the author to be identified as author of this work have been asserted by him in accordance with the Copyright, Designs and Patents Act 1988.

British Library Cataloguing in Publication Data

A catalogue record for this product is available from the British Library

ISBN 978-1-83953-620-5 (hardback)

ISBN 978-1-83953-621-2 (PDF)

Typeset in India by MPS Limited

Printed in the UK by CPI Group (UK) Ltd, Croydon

Cover Image: Jorg Greuel / Photodisc via Getty Images

Contents

About the Editors	xv
Preface	xix
Acknowledgments	xxi
1 Explainable artificial intelligence (XAI) in medical decision systems (MDSSs): healthcare systems perspective	1
<i>Oluwafisayo Babatope Ayoade, Tinuke Omolewa Oladele, Agbotiname Lucky Imoize, Joseph Bamidele Awotunde, Adetoye Jerome Adeloye, Segun Omotayo Olorunyomi and Ayorinde Oladele Idowu</i>	
1.1 Introduction	2
1.2 Overview of HMDSSs	4
1.2.1 MDSSs in healthcare system	5
1.2.2 Basis of HMDSS	7
1.2.3 Characterizing and categorizing HMDSS	8
1.3 Case study of XAI enabled with MDSSs in various infectious diseases	13
1.3.1 SCD	13
1.3.2 Diabetes mellitus (DM)	20
1.3.3 Hypertensive retinopathy (HR)	22
1.3.4 Carcinoma	24
1.3.5 COVID-19 pandemic	26
1.4 XAI research trends and open issues	29
1.4.1 XAI perspective in healthcare	30
1.5 Conclusion and future directions	31
Acknowledgment	31
References	32
2 Explainable artificial intelligence (XAI) in medical decision support systems (MDSS): applicability, prospects, legal implications, and challenges	45
<i>Joseph Bamidele Awotunde, Emmanuel Abidemi Adeniyi, Sunday Adeola Ajagbe, Agbotiname Lucky Imoize, Olukayode Ayodele Oki and Sanjay Misra</i>	
2.1 Introduction	46
2.1.1 Chapter organization	48
2.2 MDSS overview in healthcare systems	48
2.2.1 Importance and prospects of MDSSs	50
2.2.2 The challenges and pitfalls of MDSS	54

2.3	AI in MDSS	57
2.3.1	The basis of AI in healthcare systems	59
2.3.2	The role of AI in MDSS	60
2.3.3	Related work of AI in MDSS	63
2.3.4	AI weakness in healthcare system	65
2.4	XAI	66
2.4.1	The basis of XAI	67
2.4.2	The role of XAI in MDSSs	69
2.5	Ethical effects and implications	72
2.5.1	XAI weaknesses in medicine	75
2.6	Conclusion and future directions	75
	Acknowledgment	76
	References	76
3	Explainable Artificial Intelligence-based framework for medical decision support systems	91
	<i>Joseph Bamidele Awotunde, Oluwafisayo Babatope Ayoade, Panigrahi Ranjit, Amik Garg and Akash Kumar Bhoi</i>	
3.1	Introduction	92
3.1.1	Key contributions of the chapter	94
3.1.2	Chapter organization	94
3.2	Applicability of XAI in MDSSs	94
3.3	The challenges in the applicability of XAI in MDSSs	97
3.4	The proposed DeepSHAP enabled with DNN framework	100
3.4.1	The pre-processing stage	100
3.4.2	The hyper-parameters and DNN	101
3.4.3	The Shapley additive explainable (SHAP)	101
3.5	Experimental design for cancer prediction	102
3.5.1	The Wisconsin breast cancer (WBCD) dataset	102
3.5.2	The performance evaluation metrics	103
3.6	Experimental results	104
3.6.1	The comparison of the proposed model with existing methods	105
3.6.2	The local explanation results	106
3.7	The future research direction of XAI in healthcare systems	106
3.8	Conclusion and future scopes	107
	References	108
4	Prototype interface for detecting mental fatigue with EEG and XAI frameworks in Industry 4.0	117
	<i>Martín Montes Rivera, Luciano Martinez, Alberto Ochoa Zezzatti, Alan Navarro, Jesús Rodarte and Néstor López</i>	
4.1	Introduction	118
4.1.1	Measurement of mental fatigue	119
4.1.2	EEG in mental fatigue	119
4.1.3	Acquisition with brain-machine interface (BCI)	121
4.1.4	EEGNET	122

4.2	Related work	123
4.3	Materials and methods	124
4.3.1	Selection of computer equipment for mental fatigue detection	125
4.3.2	Generation of the dataset for training	126
4.3.3	Training of EEGNet	127
4.3.4	Graphical interface and control of communication with the trained model	128
4.4	Results and discussions	128
4.4.1	Results	128
4.4.2	Discussions of results	129
4.5	Conclusions	134
	References	134
5	XAI for medical image segmentation in medical decision support systems	137
	<i>Abasiama Godwin Akpan, Flavious Bobuin Nkubli, Victoria Nnaemeka Ezeano, Anayo Christian Okwor, Mabel Chikodili Ugwuja and Udeme Offiong</i>	
5.1	Introduction	138
5.1.1	Contributions of the current study	139
5.1.2	Chapter organization	139
5.2	Related work	139
5.2.1	Concept of XAI	139
5.2.2	Framework for XAI	140
5.2.3	Explainability in healthcare	140
5.2.4	DL concept and applications	142
5.2.5	Computer vision tasks	142
5.2.6	Convolutional neural networks (CNNs)	144
5.2.7	Medical image segmentation	145
5.2.8	Medical image segmentation techniques	146
5.2.9	Medical imaging modality	146
5.2.10	Summary of related works	149
5.3	Analysis of the proposed system	152
5.3.1	Analysis of algorithm for proposed system	154
5.3.2	Advantages of the hybrid system	158
5.3.3	Disadvantages of the system	158
5.3.4	Justification of the system	160
5.4	Conclusion	160
	References	161
6	XAI robot-assisted surgeries in future medical decision support systems	167
	<i>Aishat Titilola Rufai, Kenechi Franklin Dukor, Opeyemi Michael Ageh and Agbotiname Lucky Imoize</i>	
6.1	Introduction	168
6.2	Related work	169
6.2.1	Current applications of AI in the healthcare systems	169
6.2.2	Limitations of AI in the medical field	171

6.2.3	XAI	172
6.2.4	XAI in healthcare	172
6.2.5	How explainability works—bridging the AI gap	174
6.2.6	Benefits of XAI for the medical field	175
6.3	Medical robots	176
6.3.1	History of robotic surgery	178
6.3.2	Current and future use of medical robots and devices	179
6.3.3	Robotic surgery and AI	179
6.3.4	Current application of AI in robotic surgery	180
6.3.5	Current application of AI in emerging robotic systems	181
6.3.6	XAI robot-assisted surgeries for MDSS	183
6.3.7	Current limitations of XAI and robotic surgery for MDSS	183
6.4	Explanation methods	184
6.4.1	Explanation methods in robotics	185
6.4.2	SHAPs	186
6.4.3	Layer-wise relevance propagation	186
6.4.4	LIMEs	187
6.5	Conclusion	187
	Acknowledgment	188
	References	188
7	Prediction of erythemato squamous-disease using ensemble learning framework	197
	<i>Efosa Charles Igodan, Olumide Olayinka Obe, Aderonke Favour-Bethy Thompson and Otasowie Owolafe</i>	
7.1	Introduction	197
7.2	Related literature review	200
7.3	Materials and methods	200
7.3.1	Data collection	203
7.3.2	Dataset analysis	203
7.3.3	Feature selection	203
7.3.4	Multi-filter-based feature selection approach	204
7.3.5	Multi-embedded-based feature selection approach	205
7.3.6	An ensemble multi-feature selection (EMFME-FS) approach	208
7.3.7	Machine learning classifiers	209
7.3.8	Ensemble methods	210
7.4	Experimental results and discussion	213
7.5	Conclusion	222
	References	223
8	Security-based explainable artificial intelligence (XAI) in healthcare system	229
	<i>Hüseyin Gürüler, Naveed Islam and Alloud Din</i>	
8.1	Introduction	230
8.1.1	XAI	232
8.1.2	Model-based explanation	232

8.1.3	Post-hoc XAI	232
8.1.4	Model-specific explanation	233
8.1.5	Model-agnostic explanation	233
8.1.6	Global explanation	233
8.1.7	Local explanation	233
8.2	Literature review	234
8.2.1	XAI and AI	234
8.2.2	Explanation meaningfulness and veracity	235
8.2.3	ML in healthcare	236
8.2.4	Intelligibility and explainable systems research in HCI	237
8.3	Methodology	238
8.3.1	Explainable video action recognition system	238
8.3.2	TL	238
8.3.3	Model architecture	239
8.3.4	Freeze model	240
8.3.5	Fine-tune model	241
8.3.6	Pre-trained model followed by a new classifier	241
8.3.7	Pre-trained CNNs implementation	243
8.4	Experimental result	243
8.4.1	Human action dataset	243
8.4.2	ResNet50 visual explanations	245
8.4.3	VGG16 visual explanations	245
8.4.4	VGG19 visual explanations	246
8.4.5	Final discussion	250
8.5	Conclusion and future scope	252
	Acknowledgment	252
	References	253
9	Explainable dimensionality reduction model with deep learning for diagnosing hypertensive retinopathy	259
	<i>Micheal Olaolu Arowolo, Hadassah Oluwadamilola Olumuyiwa, Ruth Omorinsola Adesina, Royal Afonime, Mobayonle Ayodeji Ajayi and Paul Adeoye Omosebi</i>	
9.1	Introduction	260
9.2	Overview and related works	262
9.2.1	Hypertension	262
9.2.2	Machine learning	262
9.2.3	Related works	264
9.3	Materials and methods	271
9.3.1	Data description	271
9.3.2	Data preprocessing	271
9.4	Results and discussions	273
9.4.1	Importing the dataset	273
9.4.2	Resizing and converting the images to array	275
9.4.3	Data splitting	275

9.4.4	Pre-processing the data with LDA	275
9.4.5	Training the ANN model with and without LDA	275
9.4.6	Plotting the scattered plot and confusion matrix for the ANN model with and without LDA	275
9.4.7	Comparison with previous works	277
9.5	Conclusions	279
	References	280
10	Understanding cancer patients with diagnostically influential factors using high-dimensional data embedding	285
	<i>Ameer Sohail Syed, Hajderanj Laureta, Kun Guo and Daqing Chen</i>	
10.1	Introduction	286
10.2	Literature review	287
10.3	Dimensionality reduction methods	290
10.3.1	Projection	290
10.3.2	Manifold learning	290
10.3.3	PCA	291
10.3.4	<i>t</i> -SNE	291
10.3.5	SDD	291
10.4	Methodology	292
10.4.1	Procedure	293
10.4.2	Data used	293
10.4.3	Performance assessment metrics	293
10.5	Experiments	294
10.6	Discussion of results	303
10.7	Concluding remarks and future work	306
	References	306
	Appendix	307
11	Explainable neural networks in diabetes mellitus prediction	313
	<i>Solomon Chiekezi Nwaneri, Chika Yinka-Banjo, Ugochi Chinomso Uregbulam, Oluwakemi Ololade Odukoya and Agbotiname Lucky Imoize</i>	
11.1	Introduction	314
11.2	Related work	315
11.3	Methodology	317
11.3.1	Key implementation requirements and strategies for xDNNs	317
11.3.2	DNN architecture	319
11.3.3	Activation function	319
11.3.4	Procedures for xDNN model implementation	319
11.3.5	Model parameters and hyper-parameters	324
11.3.6	Evaluation and explainability metrics	324
11.4	Results and discussion	327
11.4.1	Results for DNN models	327
11.4.2	Results for neural network models	327

11.5 Conclusion and future scope	328
Acknowledgment	328
References	328
12 A KNN and ANN model for predicting heart diseases	335
<i>Sulaiman Olaniyi Abdulsalam, Micheal Olaolu Arowolo, Enobong Chidera Udofot, Ayodeji Matthew Sanni, Damilola David Popoola and Marion Olubunmi Adebisi</i>	
12.1 Introduction	336
12.2 Overview of the literature	337
12.2.1 Heart diseases	337
12.2.2 Machine learning	338
12.2.3 Related work	341
12.3 Materials and methods	344
12.3.1 Standard scalar	345
12.3.2 ANNs	345
12.3.3 K-nearest neighbor	346
12.3.4 Performance metrics	346
12.4 Results and discussions	347
12.4.1 Comparison with previous work	350
12.5 Conclusions	352
References	352
13 Artificial Intelligence-enabled Internet of Medical Things for COVID-19 pandemic data management	357
<i>Agbotiname Lucky Imoize, Peter Anuoluwapo Gbadega, Hope Ikoghene Obakhena, Daisy Osarugue Irabor, K.V.N. Kavitha and Chinmay Chakraborty</i>	
13.1 Introduction	358
13.2 Related work	361
13.3 IoMT for COVID-19 pandemic data management	362
13.3.1 Architecture of IoMT	363
13.3.2 Applications of the IoMT in COVID-19 data management	366
13.4 Reducing the workload of the medical industry	369
13.4.1 Applications of AI-enabled IoMT	370
13.4.2 Applications of AI-enabled IoMT for drug repurposing	370
13.5 Privacy-aware energy-efficient framework using AIoMT for COVID-19	372
13.6 Open research issues	372
13.6.1 Security and privacy	372
13.6.2 Energy efficiency	372
13.6.3 Integration of emotion-aware abilities	373
13.6.4 Interoperability	373
13.6.5 AI in IoMT	373
13.6.6 Ethical issues	374

13.7 Conclusion	374
Acknowledgment	374
References	375
14 A deep neural network for the identification of lead molecules in antibiotics discovery	381
<i>Michael Idowu Oladunjoye, Olumide Olayinka Obe and Olufunso Dayo Alowolodu</i>	
14.1 Introduction	381
14.1.1 DNN and its architecture	383
14.1.2 Lead identification techniques	384
14.2 Literature review	384
14.3 Materials and methods	388
14.3.1 Dataset preparation and preprocessing	388
14.3.2 Model development	391
14.3.3 Model evaluation	392
14.4 Results and discussion	393
14.5 Conclusion	396
References	396
15 Statistical test with differential privacy for medical decision support systems	401
<i>Yuichi Sei, Akihiko Ohsuga and Agbotiname Lucky Imoize</i>	
15.1 Introduction	401
15.2 Related work	403
15.2.1 Chi-squared hypothesis test	403
15.2.2 Privacy model	404
15.2.3 ϵ -Differentially private Chi-squared test	405
15.2.4 Adversarial model	408
15.2.5 Other privacy models	408
15.3 Proposed algorithm	409
15.3.1 Outline	409
15.3.2 Global sensitivity of Chi-squared value	410
15.3.3 Differentially private hypothesis testing	418
15.3.4 Complexity analysis	420
15.4 Evaluation	420
15.4.1 Significance results	421
15.4.2 Power results	422
15.4.3 Results of real datasets	424
15.5 Discussion	425
15.6 Conclusion	427
Acknowledgment	427
References	427

16 Automated decision support system for diagnosing sleep diseases using machine intelligence techniques	435
<i>Santosh Kumar Satapathy, Bidita Khandelwal, Amik Garg and Akash Kumar Bhoi</i>	
16.1 Introduction	436
16.2 Related work	439
16.3 Experimental dataset	442
16.4 Proposed automatic sleep stage detection method	447
16.5 Classification	447
16.5.1 SVM	447
16.5.2 Random Forest (RF)	451
16.5.3 Gradient boosting decision tree (GBDT)	452
16.5.4 eXtreme gradient boosting (XGBoost)	452
16.5.5 Stacking ensembling learning	452
16.6 Experimental discussion	452
16.6.1 Feature screening results	453
16.6.2 Sleep staging performance with ISRUC-Sleep subgroup-I dataset	453
16.6.3 Automated decision on sleep staging using the ensemble learning stacking algorithm	455
16.7 Conclusion	462
References	463
17 XAI methods for precision medicine in medical decision support systems	471
<i>Abasiama Godwin Akpan, Flavious Bobuin Nkubli, Jeremiah Chinonso Mbazor, Geofery Luntsi and Offiong Udeme</i>	
17.1 Introduction	471
17.1.1 Contributions of the current study	472
17.1.2 Chapter organization	473
17.2 Related works	473
17.2.1 Measurement of XAI in precision medicine	473
17.2.2 Concept of explainability and interpretability	474
17.3 Explainable models in MDSS: opportunities and challenges	481
17.4 Conclusion	482
References	483
18 The psychology of explanation in medical decision support systems	489
<i>Vitalis Afebuame Iguoba and Agbotiname Lucky Imoize</i>	
18.1 Introduction	490
18.1.1 Categories of AI	491
18.1.2 Artificial narrow intelligence	491
18.1.3 Artificial broad intelligence	492
18.1.4 Artificial general intelligence	492
18.1.5 Artificial super-intelligence	493

18.2	Recent development of XAI in MDSS	494
18.2.1	AI in clinical practice	495
18.2.2	AI in biomedical research	496
18.2.3	AI for public and global health	496
18.2.4	AI in healthcare administration	496
18.3	Potential benefits of XAI in MDSS	497
18.3.1	Radiology	497
18.3.2	Early diagnosis	497
18.3.3	Emergency medicine	498
18.3.4	Risk prediction	498
18.3.5	Chatbots	498
18.3.6	Virtual nursing assistance	499
18.3.7	Precision medicine	499
18.3.8	Administrative workflow assistance	499
18.4	Key challenges of XAI in MDSS	499
18.4.1	Patient harm due to AI errors	499
18.4.2	Misuse of medical AI tools	500
18.4.3	Risk of bias in medical AI	501
18.4.4	Lack of transparency	501
18.4.5	Privacy and security issues	502
18.5	The future of XAI in MDSS	502
18.6	The research trend of XAI in MDSS	503
18.7	The future directions and recommendations	503
18.8	Conclusions and future scope	504
	Acknowledgment	504
	References	504

Index	507
--------------	------------

Chapter 1

Explainable artificial intelligence (XAI) in medical decision systems (MDSSs): healthcare systems perspective

*Oluwafisayo Babatope Ayode¹,
Tinke Omolewa Oladele², Agbotiname Lucky Imoize^{3,4},
Joseph Bamidele Awotunde², Adetoye Jerome Adeloye²,
Segun Omotayo Olorunyomi⁵ and
Ayorinde Oladele Idowu¹*

Abstract

The healthcare sector is very interested in machine learning (ML) and artificial intelligence (AI). Nevertheless, applying AI applications in scientific contexts is difficult due to explainability issues. Explainable AI (XAI) has been studied as a potential remedy for the problems with current AI methods. The usage of ML with XAI may be capable of both explaining models and making judgments, in contrast to AI techniques like deep learning. Computer applications called medical decision support systems (MDSS) affect the decisions doctors make regarding certain patients at a specific moment. MDSS has played a crucial role in systems' attempts to improve patient safety and the standard of care, particularly for non-communicable illnesses. They have moreover been a crucial prerequisite for effectively utilizing electronic healthcare (EHRs) data. This chapter offers a broad overview of the application of XAI in MDSS toward various infectious diseases, summarizes recent research on the use and effects of MDSS in healthcare with regard to non-communicable diseases, and offers suggestions for users to keep in mind as these systems are incorporated into healthcare systems and utilized outside of contexts for research and development.

¹Department of Computing and Information Science, School of Pure and Applied Sciences, College of Science, Bamidele Olumilua University of Education, Science and Technology, Nigeria

²Department of Computer Science, Faculty of Information and Communication Sciences, University of Ilorin, Nigeria

³Department of Electrical and Electronics Engineering, Faculty of Engineering, University of Lagos, Nigeria

⁴Department of Electrical Engineering and Information Technology, Institute of Digital Communication, Ruhr University, Germany

⁵Ekiti State Data Center, Old Governor's Office, Nigeria

Keywords: Explainable artificial intelligence; Healthcare medical decision support systems; Non-communicable diseases; Sickle cell disease; Diabetes mellitus; COVID-19 pandemic

1.1 Introduction

The healthcare industry is increasingly utilizing big data, cloud techniques, Internet of Things (IoT), and artificial intelligence (AI)-based technology for a range of applications, including clinical automations, automated medical diagnostics, precision medicine, and individualized healthcare [1]. The application and usability of these systems in the medical field are thought to be of greater interest to nurses, hematologists, and other healthcare professionals than patients, despite the fact that performance and accuracy metrics of these technologies and AI-based systems may be of interest to recipient of the health facilities. Nevertheless, medical doctors and other healthcare workers might not have the requisite training to fully understand some of these technologies and other AI-based systems [2,3].

As a result, there is a situation that prevents the use of cutting-edge technology that may automate labor-intensive repetitive analysis tasks, on the first hand, and while, on the other hand, precludes the benefits of linked productivity. It also restricts the quantity of information that may be utilized to assist the development, validation, and iteration of AI-based systems for the delivery of healthcare solutions in conjunction with particular healthcare activities. Medical decision support systems (MDSSs) and the models that underpin them are the subject of a research area known as explainable AI (XAI), which focuses on techniques and approaches that make it simpler to understand and communicate how these technologies operate [4].

Researchers have contributed to the study in a variety of fields as a result of the advancement and widespread usage of technology, with the majority of studies focusing on how it is used in focused areas such as business, healthcare, and education. In line with this, researchers must examine the link between the works articulating these benefits and the reality of technology implementation in real-world settings in order to assess the benefits of integrating new technologies in healthcare [2–5].

The increasing use of various AI-based technologies and the resulting legal constraints have increased interest in XAI research in the healthcare industry. The shift from an information technology-based economy to a digital economy is a subject that is actively being debated when looking at contemporary structural management prototypes [6,7]. In a high-tech, astonishingly swift information environment, a corporation is being formed to handle the issue of the digital economy. This ecosystem enables the development of goods that may be personalized for customers and provide value for manufacturers. Information technology addresses the information-based strategy for the present and upcoming operations of the firm [8].

The development of novel resources like big data, the IoT, AI, and machine learning (ML), as well as the possibility of their analysis and construction based on

interpretation technologies and endwise business processes, are what is paramount in this situation [8,9]. AI and big data examples include their capacity to classify unrelated things utilizing a range of sign, classification, and explanatory systems, change and exist in real time, as they come from several sources, etc. It is possible to forecast seasonal diseases and establish prescription supply levels using data on the patterns of explicit healthcare demand in online apothecaries. In order to replace the conventional method of developing research-based medical information systems, a new business model has been developed. This approach makes good use of IT services. As a result, scientific research and medical decision-making are linked to the usage of AI, ML, and big data in the healthcare industry [2,10,11].

Healthcare MDSS (HMDSS), often referred to as evidence-adaptive decision support system (DSS), is one of the numerous examples of descriptive technologies for decision making. HMDSS assist medical personnel with understanding medical research and data so that they can draw conclusions from it [12,13]. These initiatives seek to enhance the way medical information is presented so that it can be applied more effectively in a range of situations. They achieve this by focusing on actual medical decisions and fusing the expertise of medical professionals with computerized medical data. The center of interaction of hematologists, geneticists, biomedical science, healthcare organizations, physicians, etc. is where a body of knowledge concerning effective MDSSs (HMDSS) for healthcare is continually growing [14].

Given that each individual has a different genetic makeup and set of physical characteristics, it is evident that care must be given while selecting the right treatments for both communicable and non-communicable diseases. The knowledge base needs to be updated frequently because medical conditions, diagnosis, recommendations, and treatment algorithms are always evolving. Furthermore, it is undeniable that personalized medicine is on the increase and will improve as a result of sophisticated information technology [15]. Instead of being a set of rules in this case, the knowledge base with HMDSS is a particular software solution that uses cloud and classified-explanatory technologies. The disparity between HMDSS research, its relationship with other fields like XAI, its application by medical personnel, and its beneficial contribution to the effectiveness of the healthcare sector are all areas that have received little attention in healthcare settings notwithstanding the depth of study on multi-criteria decision-making techniques, healthcare procedures, and related domains [14–16].

Complete electronic medical record (EMR) systems with features and resources that facilitate outcome and sharing of information are crucial elements of healthcare. When used properly, HMDSS can support patient-specific decisions that are made in accordance with professional medical guidance [17]. After these benefits and in spite of spending vast sums of money on technical deployment, most of the African countries are still having problems embracing EMR, in contrast to other developed nations. A key barrier to the introduction and adoption of the HMDSS as a component of EMR in various African countries is the poor adoption of EMR and personalized medicine as sources of medical data. How can the branch succeed if the HMDSS source fails in its utilization? [18–20]

Consequently, to support healthcare decision-makers in their future deliberations over non-communicable disorders and delivering archived ready-made transcriptions of HMDSS in the healthcare sector to academic academics, this chapter presents an overview of healthcare MDSSs (HMDSS), XAI, and the usage of single or combined HMDSS with the support of XAI.

1.2 Overview of HMDSSs

The majority of human acts are decided upon throughout the day. Optimal decision-making is seen to be an art. According to studies, the majority of individuals act weaker than they should. One may argue that all human events and activities, regardless of the area of life, are the outcome of decision-making processes [19]. Today, decision-making is acknowledged as a problem-solving activity since it is a process that is linked to problem-solving. In other words, a person experiences mental difficulties when their desired situation departs from their current reality. In such a case, the person first tries to alter the position or state they are in, and then they are willing to modify the surroundings around them in order to attain their goals [21,22].

Given the importance of making an informed decision at the right time, the availability of a system to aid people in making judgments is highly significant. DSSs are systems that take part in even the most fundamental corporate decision-making processes in addition to providing information. DSS is a computer-based information processing system that was primarily developed to address managerial and commercial needs. Several authors claimed that DSSs may be used to any system that supports decision-making [22,23]. DDSs may also be thought of as information systems that assist with administrative, institutional, likewise corporate processes that are somehow related to decision-making. In situations when things are changing fast and it is challenging to forecast or foretell what will happen in the future, DSSs are essential [13].

One of the main issues in public health is medical mistakes, which are seen as dangers to the safety of patients. In healthcare, patient security plays a significant role. Information technology advancements have been proposed by researchers as a viable technique to enhance the caliber of healthcare services and patients' health. Medical decision support systems (HMDSSs) are among the most significant and practical information systems. Medical decision-making is, in reality, a wonderful area of DSS deployment [22–24].

Currently, the field of health encompasses a vast body of knowledge that genuinely calls for expert advice and assistance, particularly in light of the ongoing expansion of medical knowledge across various facets of the healthcare system. All three phases of primary, secondary, and tertiary prevention are covered by these features, which also encompass diagnosis, medication, treatment, and follow-up [16]. Medical decision support system (HMDSS) is interactive software built on the foundation of expert systems to help and support the decision-making of doctors, healthcare professionals, and other staff members working in more generalized

areas of health-care systems. It should be mentioned that HMDSS links health observations with health information to enhance healthcare practitioners' decision-making. The use of AI in both public and private health-care systems is demonstrated by the HMDSS [12,25].

HMDSSs are regarded as active systems of knowledge that produce patient-specific medical recommendations utilizing two or more categorization orders. This proves that HMDSS is a DSS that focuses on knowledge management in health-care matters to arrive at a medical recommendation based on a limited number of difficulties. The primary objective of developing modern HMDSSs is to support medical professionals, including doctors, nurses, geneticist, at various points throughout professional care systems. As a result, the healthcare professionals and personnel must actively interact with HMDSS to make the best possible diagnosis and analysis based on patient data [25].

Earlier guidelines and convictions of HMDSS were based on using it to diagnose patients with a medical doctor. In the past, medical doctors would only act in line with HMDSS results after giving it information and waiting for it to reach the correct decision. The modern methodology for using HMDSS forces medical doctors and healthcare professionals to interact with HMDSS and simultaneously uses both knowledge to better analyze patient data and arrive at a more accurate diagnosis and more accurate healthcare services, in contrast to earlier methods that only used these two. Usually, HMDSS categorizes and provides doctors and healthcare personnel with suggestions as well as a list of desired outputs. In this vein, doctors and other healthcare professionals explicitly choose pertinent data and reject unhelpful system recommendations [13].

Healthcare workers are only seen as a support for medical sciences experts, healthcare services, healthcare personnel, diagnosis, and treatment in HMDSSs, which are not intended to replace medical doctor. These technologies make it easier to provide particular diagnoses, prescriptions, and treatment. They also eliminate the need for expert consultation, which considerably lowers healthcare system costs and improves the quality of healthcare services [26].

In light of this, the use of information technology, such as the HMDSS, will surely help and support healthcare administrators, policy makers, staff members, and medical professionals. Several components of the healthcare system are using HMDSS to improve their services and cut down on medical error rates. This chapter research's goal is to spread awareness of HMDSS, its theoretical foundations, and its health-related benefits.

1.2.1 MDSSs in healthcare system

Computerized tools called MDSSs were developed to help nurses, hematologists, geneticists, doctors make decisions about their patients, such as those involving diagnosis and treatment. HMDSSs, which are computer applications, are developed to assist healthcare professionals in making scientific decisions regarding certain patients [22,26,27]. In other words, MDSS are active knowledge systems that provide suggestions for a given case based on at least two patient data points. These

software programs help doctors make better decisions about things like preventative, acute, and chronic care, diagnostics, ordering specialist tests, and prescribing procedures. They accomplish this by using pertinent medical and scientific data, rules from a knowledge base, and applicable information [25].

A MDSS provides a clinician with advice, assessments, and prescriptions by fusing information regarding baseline demographics with a reliable knowledge base, or help that is tailored to the patient. Patient data can be manually entered into computer systems by patients, healthcare providers, or clinic employees. Alternately, you can query EMRs to get patient characteristics (EMR). Physicians can discover and choose the optimal course of action with the aid of these decision-support technologies [12]. The decision-support services offered are built on sophisticated algorithms and outcomes evaluation methods that scour information repositories for the most recent improvements in best practice. Whatever the definition of MDSS, it is critical to recognize that the field is unregulated and expanding swiftly. Particularly in terms of the efficiency of medical personnel, the standard of treatment, and patient outcomes, MDSS has a lot of potential to be helpful. If systems are not adequately designed and tested, they run the danger of being hazardous [14].

Different types of professionals must make medical decisions on patient data with a hazy understanding of the patients' state of health. Computer technologies have been created to support both veterinary and human healthcare practitioners in this decision-making process in order to help manage this ambiguity. These technologies were created for a number of reasons, which including enhanced information retrieval, patient record analysis, and intelligent systems that directly support decision-making via ML. Some computational techniques have been developed since the 1950s. A 1979 evaluation that looked at the benefits and drawbacks of the early clinical algorithms, databanks, and mathematical models that allowed computer-based clinical decision support systems also contained documentation of these early tests [17].

Since the historical book release titled "To Err Is Human" in 2000, MDSS and computer-based physician order entry systems have been crucial in evaluating and enhancing patient care. With MDSS, it has been discovered that patient outcomes and healthcare expenses are both improved [18]. They have shown to decrease analytical errors and their diagnostic procedures have shown to enable more accurate diagnoses by warning the clinician of potentially dangerous prescription combinations. MDSS may be used in a variety of ways in clinical settings [24]. Among the principal applications are the following:

- (i) supporting the patient's decision-making;
- (ii) deciding on the best treatment plans for certain individuals;
- (iii) assisting overall health strategies by calculating the clinical and financial results of various therapy approaches;
- (iv) calculating therapeutic effects in situations when unmethodical studies are either not feasible or not possible.

For instance, according to [23] as cited by [24], a study of 100 patient studies was undertaken, and the results showed that MDSS improved diagnosis in 64% and patient outcomes in 13% of the studies examined. In the same year, decision support systems considerably enhanced medical practice in 68% of all trials, according to a thorough analysis of 70 separate instances undertaken by Duke University. The success of the two analyses was due to the MDSS properties listed below:

- (i) seamless incorporation into the clinical process;
- (ii) nature of electronic medical reports;
- (iii) not before or after the patient participation, but at the time and place of therapy, decision assistance should be offered;
- (iv) substitution of indicated care for care evaluation.

In two areas of healthcare, the pharmacy and diagnostic (out-patient departments – OPD) sectors, MDSS have had a particularly significant influence. Batch-based order checking systems are being used more often by pharmacies to check orders for potentially hazardous drug interactions and notify the patient's ordering physician about them. OPDs have used MDSS to evaluate both likely treatment trajectories and common medicare conditions in order to develop treatment plans that achieve the perfect balance among patient care, medication prescriptions, and financial expenses.

1.2.2 Basis of HMDSS

Healthcare professionals, staff, patients, and other people can benefit from expertise and skillfully selected facts about a single person and given at the right times to enhance medical care and wellness. The Ministries of Health of various countries has long expressed concerns about the quality of healthcare in African nations and has long promoted the use of health information technology (IT), such as electronic MDSS (e-health), to raise medical standards [28]. The governments of several African nations have also supported the use of EMRs, and adoption of electronic health records has been modest but growing (e-health). However, it is crucial to keep in mind that these health IT systems are merely a tool, not a goal in and of itself, to enhance the quality of treatment [28–30].

An alternative viewpoint on MDSS, commonly referred to as evidence-adaptive DSSs, assists users in making selections informed on medical evidence and research. These systems emphasize on medical judgments in real-world settings by merging electronic medical data with physicians' discretion, enhancing how medical knowledge is presented so that it can be applied more effectively. Even though decision-making technologies, its multi-criteria (MC) techniques, in such domains, and medical approaches, the discrepancy between MDSS research and the practical application of end users and its contribution to organizational performance has received little attention [30].

In this instance, a number of MDSS strategies may have avoided the pharmaceutical interaction. These instruments could include pop-up warnings about

possible drug interactions when a new prescription is provided, risk assessment standards for the patient’s painkiller, clinical recommendations for the treatment of sickle cell disease (SCD), or requests for timely follow-up. This hypothetical example demonstrates how EMRs are the foundation for raising patient safety and the caliber of healthcare, but MDSS is necessary for completely achieving these objectives [31,32].

1.2.3 *Characterizing and categorizing HMDSS*

MDSSs come in a very wide variety of styles across the healthcare industry. Throughout the last 10 years, there has also been a substantial change in the fundamental principles of architecture and strategy. A variety of healthcare MDSS qualities are linked to or directly impacted by the scientific effectiveness, functionality, error avoidance, possibility of acceptability in the medical community, system portability, cost-efficiency, and other characteristics of health sector. As a result, it is essential to explain HMDSSs in a way that makes it easy for us to understand the range of decision support systems. Understanding categorization and the earlier mentioned common healthcare decision-making processes offer a powerful collection of foundational assumptions that are beneficial to the creators and reviewers of HMDSSs. As a result, having defined HMDSSs in varieties of phenomenon, this chapter will attempt to categorize HMDSS by fusing a number of resources to produce a thorough categorization that captures important aspects of HMDSS strategy and purpose with regard to non-communicable illness in healthcare.

According to Figure 1.1, Refs. [33,34] asserted that the five axes of DSS – context axes, knowledge axes, decision support axes, information delivery axes,

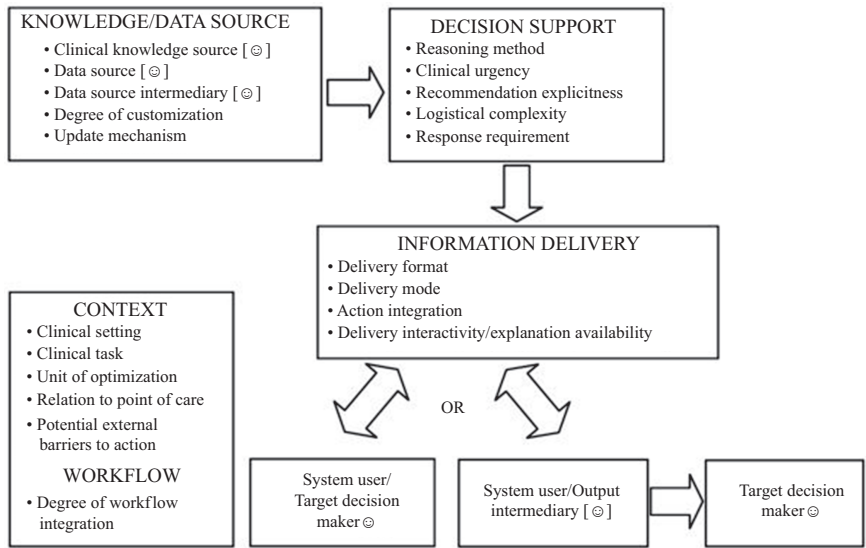


Figure 1.1 *Outline of MDSS taxonomy axes*

and workflow – may be used to classify the HMDSS. Each of them has a unique subpart that contributes to the system’s development. From the figure, the smileys notations ☺ and |☺| symbols represent humans and possible human roles within the systems, respectively. The following are thorough explanations of them.

1.2.3.1 Context axes

The generalized and relevance of a HMDSS are influenced by the environment in which it is used and evaluated. These are their main areas of influence on the healthcare industry:

- (a) *Clinical setting*: The healthcare facilities’ inpatient and outpatient settings are included in this. Here, the HMDSSs may be utilized in an inpatient or outpatient context or independently of any healthcare organization (e.g., a website for smoking termination). Medical students may participate in educational settings of such.
- (b) *Clinical task*: The target task of MDSSs, such as prevention or screening, diagnosis, therapy, drug dosage or prescription, and test ordering, has conventionally been the foundation for evaluation. This include chronic illness management and health-related activities (like exercises) to these tasks since MDSSs for chronic diseases may be more prone to failure. Under this category, we have the following procedures:
 - (i) *Diagnostic assistance*: The HMDSS offers likely diagnoses depending on the patient’s information and the system’s database of knowledge. It is possible to combine complicated data retrieval systems, such as electrocardiogram (ECG) with diagnostic aid. It aims to pinpoint “what is true” with relation to a specific patient.
 - (ii) *Therapy consultation and criticism*: The order-entry process used by medical doctors may contain this capability as an example. It evaluates the course of treatment, checks for faults and inconsistencies, compares possible drug interactions, and stops the prescription of allergic medications. It has been demonstrated that the therapeutic significance of HMDSSs is greatly increased by the need that a medical doctor explains a valid justification for any deviation from the guidelines. The HMDSS can offer an ideal treatment plan and support adhering to it employing patient information acquired from the EMR together with protocols and evidence-based recommendations. These HMDSSs answer the issue “what to do” with a patient and often make recommendations for more analytical analysis (i.e. which X-rays, CT scans, to tests-order, and so on) [33]. With the help of such software, you may ask more questions and give even more detailed recommendations for subsequent therapy (and diagnosis).
 - (iii) *Medication dosage or prescription*: To guarantee that a prescription conforms with guidelines and recommendations, HMDSS can lower the number of dangerous pharmaceuticals in a prescription and shorten the time it takes to maintain therapeutic control. If the system is linked to an EMR, it can prevent the administration of drugs that have negative side

effects. These systems are well accepted because they incorporate automated order input forms, electronic transmission to pharmacies, and effortless incorporation into the clinician's routine practice. One of a doctor's most common behaviors is to prescribe medication, which is also one of the clinical duties where HMDSSs are most frequently used.

- (iv) *Alerts and reminders*: Real-time auditory, visual, or tactile warnings can be sent by an expert system (e.g. e-mail, SMS, pager) that is incorporated with a monitoring equipment or healthcare information system (such as a test center information system or EMR). Reminder systems are made to prepare the medical practitioner to important chores that must be completed before a certain occurrence (like not taking drug therapy before to major surgery or fasting prior to actually endoscopy).
- (v) *Information gathering*: Locating pertinent information in large knowledge systems or on the Internet
- (vi) *Understanding and recognizing images*: Today, a portion of the interpretation of scientific pictures from CT scans, magnetic resource imaging (MRI), angiograms, etc. may be done automatically. More crucially, HMDSS can serve as a tool for mass screening in which software identifies photos that need the clinicians' specific attention.
- (vii) Others are choosing testing procedures, preventing, detecting, using a skilled laboratory system and treating lingering illnesses.

1.2.3.2 Knowledge axes

The sources, quality, and personalization of the information and data provided by the HMDSS are the topical issues of this axes. They use knowledge base techniques in relation to the following:

- (a) *Scientific sources of information*: It may come from reputable sources (including directives from national or professional societies, observational studies, and randomized supervised investigations, or by involving medical professionals who will ultimately use the software).
- (b) *Data source*: An EMR, a medical device (such as blood pressure monitor), or another data source can provide the patient-specific information. It is possible that the information will be given by a person or a paper chart. The data must then be fed through a data input intermediate into the system. This feature has a considerable impact on the likelihood that HMDSS will be used in real-world applications. It has been demonstrated that automatically sending data to the system via computers is preferable (e.g., via an EMR). A doctor who feeds data into a data source is referred to as a data source intermediate (see above). Patients themselves might serve as intermediaries.
- (c) *Data coding*: It is preferable to utilize a widely used coding scheme, such as version 10 of the International Classification of Diseases (ICD-10) or Systematized Nomenclature of Medicine (SNOMED), for a number of reasons (including financing and epidemiology). Obviously, plain text might also be used for the data.

- (d) *Personalized data*: HMDSS has a higher likelihood of being clinically relevant and beneficial the more patient-specific targeted suggestions it generates, according to age, gender, co-occurring diseases, etc.
- (e) *System updating*: As already mentioned, the knowledge base needs to be instantly created and contemporary. Both knowledge-based and knowledge-free systems are included in HMDSS. A knowledge-based system's knowledge base, inference engine, and communication mechanism make up the majority of its components. They can reason using the information they get from the many sources mentioned above because they have professional clinical knowledge of very particular facts and actions. These systems commonly employ probabilistic links between acquired knowledge and data.

The inference engine, which mixes and it links patient data to knowledge-based standards, is the brain of AI in knowledge-based systems. In essence, the inference engine makes inferences and comes to new inferences using the data. In contrast, the non-knowledge-based systems rely on the concepts of ML, such as neural networks or genetic algorithms, where computers acquire new abilities via previous experience and/or search for patterns in a patient's scientific data.

1.2.3.3 Decision support axes

The most crucial aspect of HMDSS is undoubtedly addressing an appropriate decision-making process.

- (a) *Reasoning approach*: HMDSS reasoning engines include, among others:
 - (i) *Rule-based systems*: Different expert knowledge bases are utilized by rule-based systems in the form of expressions and it can be broken down into IF-THEN rules (production rules). Such a system is an illustration of an empirical technique, whereby distinct logical claims in the form of production rules are acquired through professionals' observation, interview, and debriefing, and then merged in an effort to mimic knowledgeable thinking. This method was originally employed in the MYCIN (an AI technology designed for DSS) to choose the best antibiotic treatment for a patient.
 - (ii) *Neural networks*: A non-knowledge-based adaptive HMDSS called an artificial neural network employs ML-based models to learn from understandings and spot outlines in clinical data.
 - (iii) *Bayesian network*: The Bayesian network is a common example of a knowledge-based decision-making system, referred to as a causal probabilistic network or belief network at times. Using the Bayes theorem's conditional probability, it shows probabilistic relationships between groups of data, like disease and symptom data. In this network, the causality of the linkages is needed explicitly. The fact that clinical knowledge oftentimes struggles to express itself clearly A major barrier is "what is the impact" and "what the cause" to this network's capacity to accurately forecast how an illness will progress over time and how several diseases will interact.

- (b) *Model-based systems*: Patient-specific modeling is the most recent accomplishment.
- (c) *Logical condition*: Decisions are made using logic based on the value of a specific variable. If the value is inside or outside of the predetermined parameters, the decision-making process will provide various results.
- (d) *ML and data mining procedures*: The database of the system indicates that these strategies are based on probabilistic decision-making. Large and well-designed databases are desirable because they enable accurate retrieval of patients who are comparable to the current patient. The optimum therapy for the present patient is chosen based on an analysis of how those patients responded to various therapies.
- (e) *Genetic algorithm*: Iterative techniques are used by this non-knowledge-based approach to reorganize itself and offer the best possible outcome depending on patient data.
- (f) *Medical emergencies*: The provision of decision assistance for hastily needed choices. According to the dictum “cure first what kills first,” HMDSS should devote its resources initially to problems with a clear clinical importance. Better patient outcomes and medical doctor performance are the result of this trait.
- (g) *Emphasis on explicitness*: In-depth instructions that clearly lay out a particular course of action are more likely to be followed by end users.
- (h) *Adequate prompt responses*: It is possible to inquire about the utilizing physician’s response to the HMDSS’s suggestions. Numerous strategies can be used to do this, such as acknowledging the advice, outlining any replacement actions performed, and providing a justification for failure.

1.2.3.4 Information delivery axes

The goal of these axes is to give the user access to recently produced information. They contain the following subsections:

- (a) *Delivery format*: Using extra technical tools such as phone, pager, or e-mail, or using paper-based, electronic (online or incorporated into an EMR), or electronic methods.
- (b) *Delivery mode*: Whether it is a notification, a prompt, or a request for optimization, the ideas may be provided upon the decision-request maker’s request or alternatively, they may be provided without the decision-agreement maker’s request. The software is initially inactive since it requires the doctor to make extra effort to obtain a diagnostic or therapeutic evaluation, recognize when the advice would be beneficial, and “go to the program” to input data. The so-called “push systems,” which provide solutions autonomously, might be more advantageous, and extensively used. Because of their work in data management, they actively assist decision-making (e.g., monitoring, EMR supervision). The findings of the system’s decision analysis are provided without the need for further work on the part of the physician since system decision logic is in a sense incorporated inside the patient database that has already been compiled from a variety of sources. How to minimize “alarm

fatigue,” which occurs when a physician is too alerted to tiny anomalies that are ordinarily observed and understood, is an important issue to think about in this situation.

- (c) *Integration of actions:* The HMDSS must give the decision-maker the tools necessary to quickly implement the advised actions. For instance, the program is able to offer direct connections to order entry forms and therapy planning section of the EMR, as well as suggestions for therapeutic review. Similar to verifying a mark, the therapy adjustment activity should be completed in a few clicks. The utility and acceptance of HMDSS are clearly increased by action integration.
- (d) *The availability of justification:* In order to clarify its suggestions and give evidence, the system offers links to books, articles, or knowledge base entries.

1.2.3.5 Workflow axes

Despite the fact that HMDSS is sometimes referred to as a procedure, it actually functions more as a technology intervention at the point of care and may result in a disruption. Systems that function in unison with the institution’s workflow are more commonly used and more successful in improving practitioners’ performance.

1.3 Case study of XAI enabled with MDSSs in various infectious diseases

1.3.1 SCD

Even though the “era of data” has access to improved computer and storage capabilities, the challenges associated with understanding these enormous data sets have risen significantly. Many industries, including those in education, health, business, and organizations, are developing intelligent systems to address these issues by utilizing relevant concepts and methods including data mining, data science, ML, and even AI. One of the most active areas in computer science is AI. As a result, it imparts insight and importance to the data [35,36].

Ref. [36] asserts that the daily growth in data velocity and the development of digital technology result in the continuous generation of new data across a range of data collecting tactics. In the area of AI, computers help people understand data in a way that is comparable to a person. In this field of AI, computational learning and pattern recognition are included. ML, a subfield of AI, is impacted by advances in human knowledge technology. This has to do with changes made to systems that do various AI-related tasks, such as robotics, planning, prediction, analysis, and recognition [36,37].

The quantity of data and knowledge that our civilization is able to produce and retain is growing exponentially every day, but our capacity to absorb it is not keeping up [4]. It is crucial to employ current technology to balance the seemingly incompatible aims of scalability and usability in data and information interpretation in order to overcome these difficulties. According to [38], several data and information analysis techniques have been developed and used all over the world with

the intention of making them more complicated. Particularly in a number of organizational sectors, the most prominent of which is the healthcare sector, which encompasses several subsections such as genetics, human genetics, and medical genetics, humans must be involved in the early stages of data analysis and information generation. A primary objective and top priority for many governmental and commercial sector companies is to improve data analysis processes.

The need to provide new and appropriate services, as well as the need to improve productivity and adhere to rules, all have an impact on the illumination of medical data analysis. In the current digital era, healthcare systems are swamped with data, yet having access to this data and expertise is insufficient to fully capitalize on improving patient health. The ability to combine, adjust, or anonymize data from many sources, including EHRs, health surveys, administrative data, physician notes, and consultant reports, to mention a few, is therefore required by both private and public healthcare organizations. The patient would receive a complete medical assessment of their condition as a result [39]. Various patient data are combined, examined, and reported on using healthcare data analytic technologies. Additionally, healthcare organizations make wiser clinical, administrative, and financial choices that improve patient care and engagement. The importance of utilizing information and communication technology (ICT) to change patient medical data with regard to their health cannot be overstated [40].

In order to improve healthcare diagnosis, management as well as appropriate decision-making, the optimal framework for patient medical data analysis and decision support systems must be effectively managed as IT in data analysis in the health sector increases. When the healthcare industry transitions to a value-based paradigm, medical consultants, hematologists, geneticists, and others may find themselves in danger of not respecting patient decisions. As a result, reviewing medical data to guide judgments is no longer a good idea but rather a need [41–43].

SCD is a red blood cell (RBC) disorder brought on by the deficiency of oxygen. The end consequence is a group of diseases known as hemoglobinopathies, the most prevalent of which are thalassemia and sickle cell anemia (SCA). There are no additional treatment options for adults with SCD, a congenital abnormality of the hemoglobin structure, which can only be treated in infants by bone marrow or cord blood transplantation [44]. Hemoglobinopathies (abnormal Hb or anemia), according to [44], are brought on by genes that affect around 5% of the world's population. The prevalence of sickle cell gene carriers is higher compared to the prevalence of affected newborns because healthier individuals have thalassemia than SCA (who acquire just one mutant gene from their parents). In Ref. [45] it is said that among the diseases for which ML algorithms have been used to model, forecast, and diagnose include SCD, cancer, and malaria. One of the most serious medical illnesses in the world, SCD, has a variety of symptoms that can vary from moderate to catastrophic.

SCD, for instance, is one of the most prevalent genetic RBC illnesses in humans in Nigeria and affects people of all ages, resulting in hemolysis and vaso-occlusive crises. Studies show that Nigeria, where over 150,000 births occur annually, has the largest number of people with SC illness. The RBCs of patients

with SCD exhibit aberrant hemoglobin, such as hemoglobin S or sickle hemoglobin [46,47]. Hemoglobin, a protein that transports oxygen throughout the body, is found in human RBCs. SCD is a genetically based non-communicable illness that is passed on from parent to child [48]. Like Ebola, Zika, tuberculosis, or the typical cold and flu, it is not contagious. Patients with SCD have long-term acute pain [vaso-occlusive episodes (VOEs)], long-term suffering, multiple organ damage (including kidney failure, heart failure, and others), a short lifespan, bone infections, and stroke, to name a few symptoms and problems [49,50].

Apparently, a single-point mutation (glutamic acid substitution) of valine at position 6 in the hemoglobin component known as beta globin (-globin) causes sickle hemoglobin (HbS) to deform or transform, according to [45,48]. According to [48], those who have two copies of the HbS mutation are homozygous (HbSS) and have the sickle cell phenotypic form of the disease, as opposed to those who have one copy of the gene, who are heterozygous carriers (HbAS), who do not. In order to lower the mortality rate and other issues that SCD patients face, it is crucial to give medical officers, hematologists, and healthcare managers a platform to strategize on how to make life meaningful and fulfilling for these patients by integrating ML algorithms into the analysis of SCD medical datasets [51].

In order to address practical issues like significant variation, low accuracies, the presence of feature noises and biases, as well as medical doctors' decisions based on the data gathered, the involvement of healthcare MDSSs with the support of explanatory AI should be developed [52]. As a result, the availability of enormous databases containing pertinent genomic data would enable researchers to focus on developing new approaches for diagnosing and treating human genetic diseases like SCD. Due to the size and diversity of the data, it may be challenging to effectively employ genomic databases for SCD in this situation without the proper development of advanced data analysis tools [53].

In order to provide proper management and follow-up on SCDs, this section provides a review of SCD along with its correlation and the participation of explicable AI in healthcare decision support systems. The effectiveness of these explanatory AI technologies will reassure medical experts, other healthcare workers, researchers, and patients who are suffering from this condition.

1.3.1.1 Historical perspective with SCD

Doctors have found it difficult and time-consuming to correctly diagnose SCD and forecast the patient's chances of survival and life expectancy over time. According to studies, conventional or clinical tests take a long time to discover the presence of SCD or its variants. As a result, explanatory AI technologies are being employed more often to provide SCD patients with a non-clinical diagnosis. In 30–50% of cases, SCD is regarded to be avoidable [36,44]. In order to provide accurate, objective, and systematic forecasts of human blood cells, advanced computer approaches such as XAI are needed [2].

One cannot overestimate the importance of medical data analysis and medical decision support systems to any nation's economy [39]. One of the challenges faced the healthcare sector is decision-making and medical data analysis issues,

particularly in the context of non-communicable disorders like SCD. When compared to the inadequate local medical infrastructure that is appropriate for this human genetic concern in the examination of medical data, the birth rate in Africa continent is quite high and at a critical stage [54]. When learning from huge medical histories and their datasets like SCD, difficulties including missing parameter values (incompleteness), systematic or data random noise, and inappropriate parameter selection have all arisen. It will be possible to handle the difficulties that medical datasets like SCD bring using a HMDSS with support of XAI technologies [55].

1.3.1.2 Synopsis of SCD

A patient with SCD inherits mutant hemoglobin (Hb) genes from both parents and has hematological abnormalities in RBCs. SCD is a non-communicable illness. SC problems are brought on by the RBCs' lack of oxygen [44]. In Figure 1.2, some of

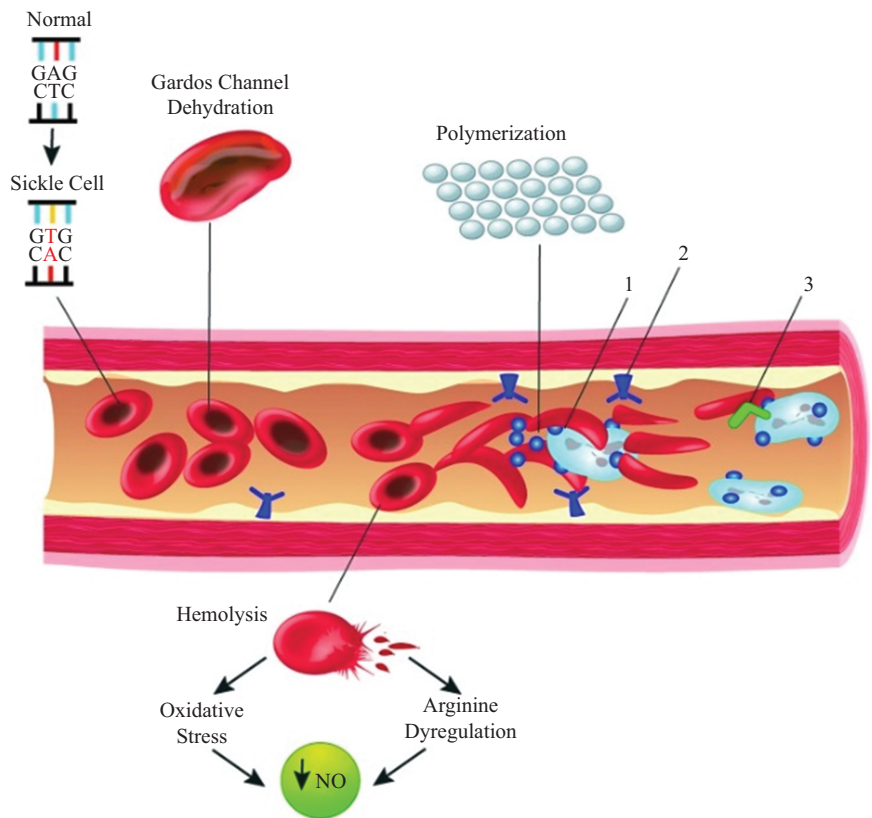


Figure 1.2 Sick erythrocytes from single gene mutation (GAG–GTG and CTC–CAC) resulting in a defective hemoglobin due to deoxygenation exposure (1: mononuclear cells and platelets {light blue and dark blue}; 2: ligands; and 3: receptors {dark green}; NO: nitric oxide) [56]

the pathophysiologic elements of the disease are shown in a streamlined manner. The pathophysiology of the illness is described in depth in several researches. The basic assumption that sickle cells are only responsible for creating vascular blockage or vaso-occlusion is no longer correct after red cells assume the pathognomonic sickle cell form after being subjected to deoxygenation. SCD is brought on by a single gene mutation that results in complex physiologic abnormalities, whereas vaso-occlusion is essential to understanding the illness and can bring about localized hypoxia and inflammation. The illness manifests itself in many ways as a result of these alterations. In addition to vaso-occlusion, anemia, and hemolysis, it is now known that SCD is a disorder characterized by issues with arginine metabolism, increased inflammation, hypercoagulability, and oxidative stress.

According to [45], SCD is one of the most hazardous diseases in the world, with a wide spectrum of symptoms that can be anything from mild to fatal. SCD affects people of all ages, is one of the most prevalent genetic RBC illnesses in Nigeria, and causes hemolysis and vaso-occlusive crises. The sickled erythrocytes and irregularities that develop as a result of low oxygen levels in RBCs are seen in Figure 1.3. With approximately 150,000 parturitions (births) per year, African continent especially Nigeria has the highest number of individuals living with SC disease, according to studies. The survey found that hemoglobin S or sickled hemoglobin was present in the RBCs of SCD patients, along with other hemoglobin abnormalities [46,47]. Table 1.1 shows the fundamental medical signs of SCD in both children and adults, along with the many possible symptoms.

1.3.1.3 Importance of XAI support in HMDSS for SCD

In areas including patient deterioration, readmissions, mortality, improved documentation, sickness diagnosis, patient relocation, and chronic care management, predictive modeling in healthcare has been driven by digital transformation. Thanks to advancements in big data, AI, cloud computing, and the IoTs, consequently, mixing data from various sources, offer massive computing, and store shared resources are made possible by the modern technologies. Hence, connect data to one another through devices, sensors, software, and other technologies, and exchange data with them [2]. AI's success in a range of applications results in a large number of autonomous systems and accurate projections for decision support. In healthcare, predictive modeling encompasses forecasting illness states and their trajectories, hospital readmission, adverse medication responses, and drug-drug interactions, using the interrelatedness of organ dysfunctions to predict the survival of sepsis patients, and finding off-label usage of pharmaceuticals.

Healthcare predictive modeling may be challenging, counterintuitive, and frequently difficult to explain. Due to their opaque nature in the healthcare field, these traits prevent predictive solutions from being adopted widely or having much value in the clinical situation. In order to improve their capacity to be understood, predictive solutions in healthcare require a successful strategy. A greater understanding of the model, enhanced value of its output, and improved patient care outcomes may result from improving model explainability [5].

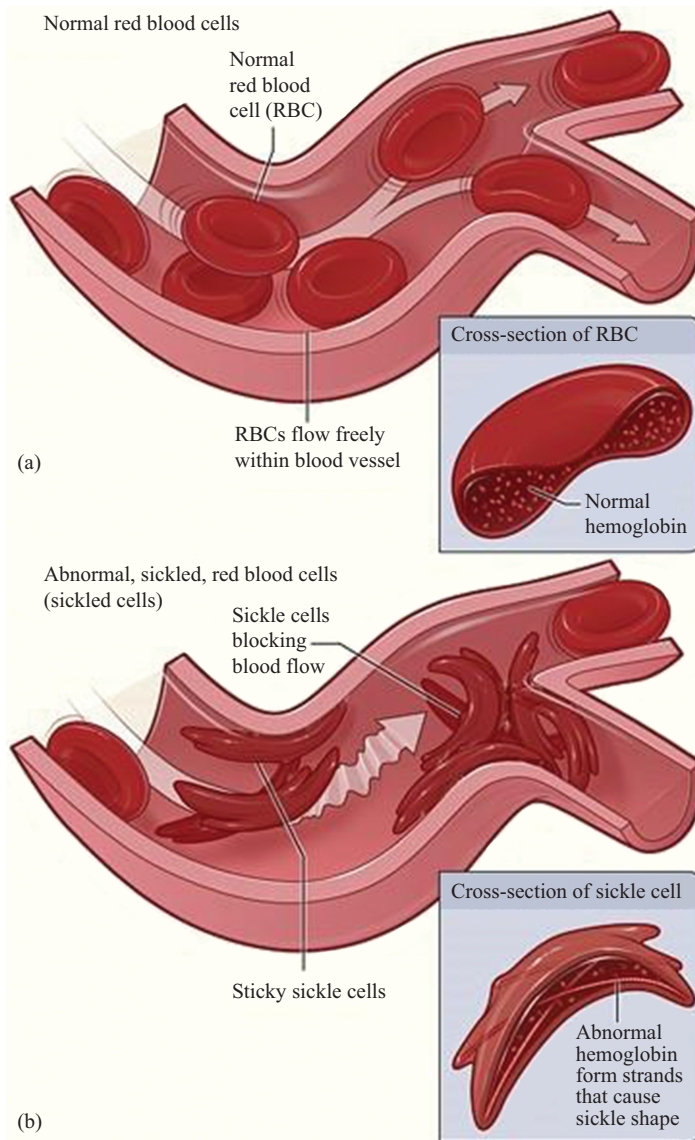


Figure 1.3 Normal and sickled erythrocytes showing abnormality forming irregular stiff rods [39]

In some functional areas of healthcare, like personalized medicine for SCD, AI can help doctors make better clinical judgments or even take the role of human judgment in some situations. With the use of pertinent clinical questions developed in collaboration with healthcare experts, cutting-edge AI algorithms like XAI may

Table 1.1 Medical indicators of children and adult SCD (adapted from [38,49])

Children with SCD		The program is able to offer direct connections to order entry forms	
Indications/symptoms			
	Infants	Children	
	Chest, stomach, and limbs/joints pain anemia, dactylitis, mild cyanosis, fever, enlarged spleen, upper respiratory infections that are common	Pain (acute or chronic), severe anemia, infections jaundice, inadequate nutrition and metabolism, failure in school, and premature puberty	significant joint pain, persistent leg ulcers, retinal disease, thromboembolic side effects, neurological problems, drug tolerance/dependence
Complications			
• CNS • Eye • Lung • Heart • Spleen • Liver • Kidney • Gall bladder • Genitals • Bones/joints • Skin	• Stroke, retinopathy caused by retinal artery blockage, ACS, and asthma • hypertrophy of the left ventricle, Cardiomyopathy, acute sequestration of the spleen, reduced immunity (such is sepsis or a viral infection) • Hyposthenia Priapism, perivascular necrosis, proteinuria-renal neurocognitive, cholelithiasis, persistent sores, usually on the ankles	• Hemorrhagic stroke and recurrent ischemic stroke Progressive retinal disease, persistent ACS, chronic pulmonary illness, pulmonary hypertension, an early form of coronary artery disease, heart attack, Auto-infarction, Asperenia with function • liver sequestration liver failure brought on by excessive transfusions of iron Nephropathy, Urinary tract infections frequently • Chronic leg ulcers, cholelithiasis, priapism, avascular necrosis, and early loss of bone density	

Keys: CNS, central nervous system; ACS, acute chest syndrome.

uncover clinically pertinent information concealed in the vast amount of healthcare data. Most clinical trials for medical research include well-defined hypotheses or particular questions. Given a collection of characteristics, the AI algorithms are taught to anticipate specific events, and via the prediction, insights may be gained [3]. Recent developments in deep learning have attracted a lot of interest. Deep learning is a neural network with numerous hidden layers that allow for the

exploration of more intricate nonlinear patterns to enhance prediction accuracy. Understanding forecasting outcomes and how AI systems function to produce predictions are challenging tasks.

This portion of the chapter discusses the numerous data sources used to support SCD predictive modeling in healthcare, along with its benefits and drawbacks. Additionally, it would include some examples of predictive modeling in healthcare. The necessity of explainability in AI for HMDSS is next discussed in order to win the confidence of medical experts in predictive modeling for SCD. To explain internal decisions, behaviors, and actions to the interacting humans, a smart AI system must include an explanation model. Additionally, the information-based and instance-based clarifications in XAI using HMDSS for SCD healthcare prediction modeling will be covered.

1.3.2 *Diabetes mellitus (DM)*

Every year, emergency departments in hospitals serve millions of patients. Although a sizable number of the patients are not emergencies, forcing hospitals to assign medical staff where it is not absolutely necessary, making inefficient use of personnel and handling genuine patient emergency situations [57,58]. In addition, there is an increasing shortage of doctors in rural areas, which results in underserved patients, in especially because of the changing demographics and an increase in the number of elderly patients [59,60]. Future application of AI-based models in healthcare as a proponent of systems medicine could be one way to solve these issues [61].

One of the most prevalent non-communicable diseases and a leading cause of morbidity and mortality worldwide is DM [62]. By 2030, diabetes is expected to overtake heart disease as the seventh biggest cause of death worldwide, affecting an estimated 422 million people [63,64]. In every nation, there are more persons with type 2 DM (T2DM), the most prevalent kind of the disease [62]. Between 1990 and 2010, the prevalence of diabetes nearly tripled in the United States [65], moreover, 1.7 million new adult cases were detected in 2012 [66]. There are 26% more Americans who have the condition than those who are 65 or older (4). For diabetic patients, hypoglycemia (HG) is known as the primary limiting factor in effective glycemic control [67,68]. Significantly detrimental consequences have been found on cardiovascular safety and quality of life [69,70]. Additionally, it raises the economic costs associated with managing HG and its effects through the use of healthcare resources, and additionally from patient disengagement and lost output [71].

Many diabetic patients are uninformed when HG begins, specifically those with recurrent bouts, notwithstanding the possibility of fatal and major adverse consequences. Finding patients who are particularly at risk for HG may offer the chance to take action and lower the frequency of occurrences [72]. It is difficult to identify HG using computer-based techniques and EMRs, due to the inconsistent use of HG diagnosis codes and the possibility of undercounting. Only an unstructured, narrative (text-based) style may be used to document the signs or symptoms of a given episode of HG, especially if they are not severe.

DM is diagnosed, treated, and monitored by physicians with relatively low rates of adherence to guidelines [73]. Alternative approaches to real-time patient monitoring are necessary due to time restraints, patient overcrowding, and complex requirements. MDSSs and monitoring systems, which are rapidly developing, offer an efficient answer to these issues. The goal of chronic illness means of combating is no longer to cure the patient, but to improve the patient's adherence to the treatment regimen, and to enhance the quality of life through collaboration. Because of this, the value of safeguarding, preserving, and enhancing health has been prioritized over the treatment of symptoms, fostering the idea of "self-care" [74].

Diabetes is a persistent medical condition. Patients with diabetes frequently experience difficulties during treatment, such as psychological issues and trouble adjusting to lifestyle modifications. In addition to the normal discomfort brought on by symptoms, consequences, and therapies. Future concerns for the patient have an impact on his social, cognitive, and emotional health [75]. In people with health issues like diabetes that require substantial treatment and support, self-efficacy beliefs are crucial, adjusting one's lifestyle and picking up new abilities to deal with the disease progression. Diabetics are required to possess considerable self to manage sophisticated diabetes treatment and management. By raising their levels of self-efficacy, diabetics can enhance their self-care habits [76].

Substantial proof studies carried out by professionals at the national and worldwide level serve as the foundation for the creation of DM standards and guidelines. The criteria for diagnosis are laid out in DM management guidelines, and the standards for diagnostic process are standardized [77]. The disease is then categorized based on the patient's medical history, physical assessment, and test results. The recommendations make recommendations for which tests should be run and which patient risk factors should be examined. Following diagnosis and differential diagnosis, the doctor is given various treatments based on the prescriptions provided by the evidence-based studies. These recommendations include a methodical approach to therapy and follow-up in accordance with the diagnosis and outlook [78].

Primary care physicians are crucial in the identification, management, and control of DM illness. According to the World Health Organization, primary healthcare is crucial in lowering chronic illness deaths and morbidity. All nations are working to improve primary care to ensure the management of chronic conditions. Therefore, adjusting the doctor's strategy to the most recent DM management recommendations and creating a consistent strategy will result in notable improvements in blood sugar control. The patient's life will be longer and of higher quality if their diabetes is under management. Patient applications to primary healthcare providers will decrease as a result of this. As a result, doctors will spend more time on each patient.

For the management of chronic diseases, a number of computerized MDSSs have been created [79]. The MDSS is used in primary care for a number of purposes, including depression, hypertension, and drug reviews [80–82]. Additionally, a number of AI-based and rule-based DSSs have been created for the diagnosis of diabetes [83,84].

According to research, measures started initially in pregnancy can lower the rate of DM in expectant mothers who are overweight or obese [85–87]. Applying remedies in every situation, meanwhile, can be expensive and time-consuming. A ML-based MDSS can be useful in supplying a strong and impartial computerized tool to support physicians in identifying women at risk of DM. By enabling focused intervention, it would significantly cut down on time and expense. Clinical settings offer significant promise for the MDSS, especially in light of the fact that many doctors have used telemedicine to keep a distance from patients during the COVID-19 pandemic [88].

Despite the literature on their effective deployment, MDSSs offer a potential to significantly improve healthcare delivery. There is a lack of MDSS data, particularly MDSSs that based on ML-based algorithms. In addition to system accuracy, authors in [89] noted that for a MDSS to be adopted and implemented into healthcare setting, efficiency and attractiveness are crucial. In order to easily get system outputs while juggling a heavy clinical workload, a MDSS should be time-saving, intuitive, and simple to operate. Additionally, they emphasized that black-boxes are unacceptable for MDSSs. This is consistent with the findings of authors in [90], who said that explainability is a crucial element for a MDSS to be successfully incorporated in practical application. A ML-based system can mirror the pattern in the training data, as demonstrated by a well-known example by authors in [91] but not transcend to clinical practice since it is at odds with medical understanding.

According to their computer model, people with a history of asthma were less likely than the general population to pass away from bronchitis. This is due to the vigorous treatment that patients who had asthma and had pneumonia typically received, which reduces their risk. Even if the system accurately recorded the training data, using it in clinical settings without knowing why the model performed this way would indeed be troublesome. AI-based model that is comprehensible and explainable can solve these issues and this is called XAI. The use of XAI in MDSS has been shown to offer numerous advantages, including boosting acceptability and credibility of the system, as well as raising the causality hypothesis and decisions assurance. However, the published literature as a whole clearly lacks the applicability and implementation of XAI in MDSSs [90].

1.3.3 Hypertensive retinopathy (HR)

Vision loss is a result of the retinal condition known as HR, which is brought on by persistently high blood pressure (hypertension). Millions of people around the world are afflicted with HR disease as a result of high blood pressure [92]. The irregularities, such as tortuous retinal arteries, abscess formation, cotton wool patches, hemorrhages, and enlargement of the optic disc (OD), are brought on by hypertension. Ophthalmologists can investigate these indicators of retinopathy brought on by HR by taking digital pictures with a fundus camera [93]. There are no early warning indications for this condition, and frequently, When the condition results in blindness or vision loss, HR is discovered at a later stage. As a result, hypertension people should often get their eyes examined. Figure 1.4 displays

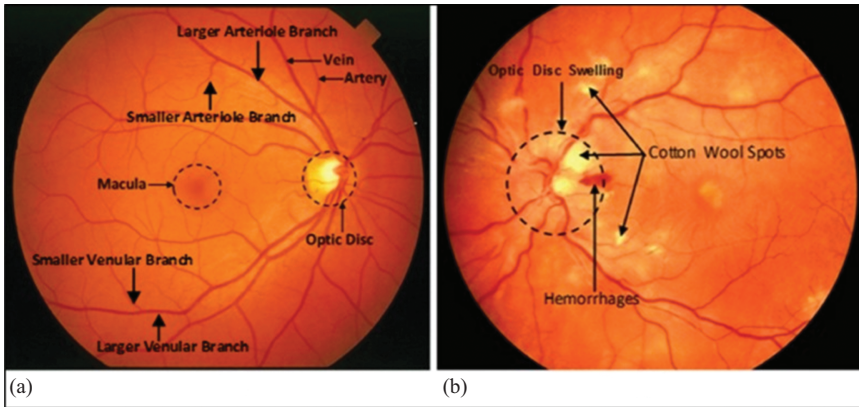


Figure 1.4 (a) A basic fundus retinal image, including the arteries, veins, OD, and macula. Additionally, smaller and larger venular branches and arteriole branches are visible; (b) fundus retinal picture was damaged by HR, and there were some hemorrhages, cotton wool spots, and OD edema

normal and HR pictures along with the fundamental fundus constituents and alterations, which are visible on the fundus because HR is present.

Systems for computer-aided diagnosis are frequently employed in the healthcare sector. Various retinal disorders are detected with computerized diagnostic techniques and are beneficial to both patients and ophthalmologists. These automated devices allow the ophthalmologists to adhere to the disease's treatment strategy. A form of computer-aided diagnostic system that can automatically detect and grade HR using retinal fundus images must therefore be developed. HR is also used as a marker for injury to certain target organs. Through HR indications, doctors can foresee the likelihood of heart illness, stroke, and even mortality [94]. The development of the HR signs and symptoms typically occurs in more established phases of the illness. These indicators support clinical therapy and rules for patients with hypertension [95,96]. There are various levels and grades in HR. Arteriovenous ratio (AVR) is the foundation for HR phases [97], which is regarded as a useful metric for the identification and evaluation of HR.

The evaluation of medical images is an essential tool for the computer-aided diagnosis of many diseases. Due to their dependability and adaptability, DL-based AL-based models are more prevalent in disease analysis than traditional image processing methods [98]. Computer vision has a promising possibility to evaluate these retinal disorders through image segmentation for early identification, diagnosis, and treatment of some retinal diseases that are linked to blindness or visual loss [99]. For quicker screening and computer-aided analysis of numerous retinal illnesses connected to retinal anatomy, DL-based technologies are widely acknowledged [100]. Due to their intricate structure, retinal blood vessels serve as crucial biomarkers for identifying and assessing various retinal dysregulation and

associated disorders [101]. Medical image categorization, one of many deep learning techniques, aids ophthalmologists and other medical professionals in making many challenging diagnoses. Segmentation techniques lessen the need for manual illness image recognition and DL-based semantic segmentation is a cutting-edge method for classifying medical images pixel-by-pixel, whether for diagnosis or symptom screening [102]. Due to the aberrant proliferation or deterioration of these capillaries, diabetes and hypertension cause changes in the retinal vessels, which can be found by precisely segmenting the retinal blood vessels [103].

There is a diagnostic load placed on medical specialists because to the laborious and time-consuming manual investigation and identification of this retinal vasculature; obviously, automated technologies could enable quicker diagnostics [104]. The thickness, surface roughness, formation, and removal of these retinal vessels can all be used as diagnostic cues [105]. A retinal condition known as HR is linked to hypertension and gets worse with elevated blood pressure. A retinal condition known as HR is linked to hypertension and gets worse with elevated blood pressure, specifically, localized and arteriolar shortening [106]. Vascular changes due to diabetes and hypertension can be subtle, necessitating a sharp eye for detail in retrospective analysis to detect the important changes brought on by the disease [107]. Deep learning has the ability to diagnose many illnesses and assist medical professionals in various medical applications [108,109].

Similar to this, resilient architecture and DL-based classification techniques can identify minute variations in the retinal blood vessels and can assist doctors in identifying the associated changes to make quicker and more accurate diagnosis. There are a number of deep feature-based techniques for detecting retinal blood vessels [110]. The creation of low-cost, reliable techniques that can precisely detect vasculature with slight alterations is nevertheless necessary. Additionally, current segmentation-based approaches [111] solely concentrate on segmentation rather than offering a comprehensive solution for the identification of HR.

1.3.4 *Carcinoma*

Non-melanoma skin cancers (NMSCs), which can afflict both sexes, are the fifth most prevalent type of cancer globally. According to estimates, there are more than a million new cases of NMSC each year, with squamous cell carcinoma (SCC) accounting for about 20% of all skin cancers [112]. Each year, more than 1.8 million new cases of NMSCs are recorded in the United States, and skin cancers are common, with cutaneous SCC being the most common type [113,114]. SCC is more common in Asian Indians and African Americans, and additionally, it is the second most common among Asians of Chinese/Japanese descent and Hispanic descent [115]. SCC has been identified as a keratinocyte-related cancer type. The skin condition carcinoma-in-situ, commonly known as actinic keratosis (AK), has been linked in multiple studies to the development of SCC. About 5–10% of all high-risk SCC cases are extremely challenging to identify and treat, with radiation or surgery being the preferred treatments in the majority of these situations.

Therapies for such high-risk metastatic skin cancer are less likely to be effective, especially in an elderly population [116], demonstrating the urgent need

for an effective but organized diagnosis and treatment plan for SCC [117]. The amount of microarray data is increasing, and the knowledge it provides about the genes that control for a point mutation is being employed for variation classification and investigation, in addition to other possibilities. Microarrays are a relatively new approach that analyzes gene expression in samples by placing hundreds of DNA probes on a small chip that are matched to target genes. Comparing cancer and healthy tissues was one of the approach's main applications, among other factors, diverse cancer subtypes, people with different prognostications [118]. In terms of recognizing microarray samples, support vector machines (SVMs) [119], ANNs [120], logistic regression, Naive Bayes [121], and other commonly used ML techniques performed wonderfully [122].

Many research use metabolomic data to understand the metabolites that characterize each organism state, and how those metabolites behave in different environments. Systems biology is incredibly dependent on the "omics" field. It has recently been widely adopted in a range of sectors due to its concentration on small molecules and relationships, such as the detection and acquisition of biomarkers, drug development, and personalized healthcare, among others [123]. Pioneering omics data investigations have produced tools for normalization like NOREVA [124–126], and ANPELA, a combined approach for data label-free quantification (LFQ) [126]. Various areas of scientific research have benefited greatly from these techniques.

Using ML-based techniques, previous studies have identified vital biomarkers in the search for genes with greater SCC risk prediction value, and this has helped scientists find compounds that have better predictive value [127]. Scientists are increasingly using AI-based and ML techniques to investigate the genetic diversity of cancer. It can be used to increase the accuracy of diagnoses, generate efficient biomarkers, as well as the success of cancer treatments [128]. AI refers to a robot's capacity to replicate human behavior, which is especially beneficial when working with enormous amounts of data. ML-based is one of the most significant applications of AI models, which enables computers to acquire knowledge through observation without explicit programming [129,130]. ML models can be viewed as a modeling technique that relies on gaining expertise together with performance improvement. These models are meant to assist in locating advantageous components and their relationships [131].

Over the past several years, AI has improved, transitioning from a mainly intellectual to a practical implementation condition. There are now strong prospects for the use of AI in many different industries, ML has already been used to analyze survival in cancer studies, in particular and predict models for advanced nasopharyngeal cancer, breast cancer, pancreatic cancer, and a number of other malignancies [132]. While ML algorithms in particular seem to be effective in producing results and predictions, and they suffer from opacity, which makes it difficult to understand their fundamental workings. It exacerbates the issue since it offers serious risks to entrusting crucial decisions to a system that is unable to adequately defend itself.

To solve this problem, XAI proposes a paradigm change toward more transparent and understandable AI. Its goal is to create a set of tactics that produce more

comprehensible models while maintaining high accuracy and achievement. The requirement to justify the model's judgments or forecasts to users and experts led to the creation of XA and it is attracting increasing amounts of interest in AI. Numerous XAI techniques have been established with diverse methodologies, and several classification schemes for XAI models have been presented by authors in [133], based on the size, length of the information extraction process, or model AI.

1.3.5 *COVID-19 pandemic*

Governments all over the world have adopted policies for social isolation, quarantine, and ultimately lockdowns due to COVID-19's extremely contagious existence [134]. Nigeria was not exempt from the significant health and economic problems brought on by these occurrences [135]. To aid in decision-making on the part of the federal and local governments, it is necessary to test the huge majority of the population. COVID-19 tests are only available to healthcare experts and patients with serious diseases due to a lack of resources. Consequently, it does not reach the vast majority of people. Since the pandemic started, the digital health landscape has captured everyone's interest to offer potential health solutions in this period of unprecedented medical crisis in order to lessen the effects of this epidemic [136].

Although AI techniques have previously been used to support clinical decisions, "Emergency AI" is currently in demand. There are chances for Automation decisions based on gathered vitals, test results, medication orders, and diagnoses throughout the patient care route [137]. There are still crucial factors to take into account while creating and verifying AI models in light of the continuously expanding datasets. AI techniques can be used to comprehend patient categories, direct clinical decision-making, and enhance both patient- and operation-centered results. This viewpoint emphasizes the advantages of these tools as seen in many therapeutic contexts and explains the importance of ML and AI techniques. When thoughtfully constructed, they might be enhanced during the COVID-19 pandemic.

ML models have been shown to predict the presence of clinical factors from medical imaging with remarkable accuracy. However, these complex models can be difficult to interpret and are often criticized as "black boxes". Prediction models that provide no insight into how their predictions are obtained are difficult to trust for making important clinical decisions, such as medical diagnoses or treatment. Explainable ML (XML) methods, such as Shapley values, have made it possible to explain the behavior of ML algorithms and to identify which predictors contribute most to a prediction. Incorporating XML methods into medical software tools has the potential to increase trust in ML-powered predictions and aid physicians in making medical decisions. Specifically, in the field of medical imaging analysis, the most used methods for explaining deep learning-based model predictions are saliency maps that highlight important areas of an image. However, they do not provide a straightforward interpretation of which qualities of an image area are important.

It has been demonstrated that ML-based models can accurately predict the existence of clinical variables from medical imaging [138]. ML models can deliver better predictions thanks to technologies that can capture intricate correlations between features, which may lead to "black box" models that are challenging to understand [138]. These techniques take patient MR images as inputs and output the

patient's projected likelihood of a particular result without revealing how the prognosis was made. As a result, even if these techniques can surpass conventional predictive models, a possible deterrent to using these predictions in clinical decision-making is the lack of openness in how they are made. Understanding what variables affect a model's prediction and gaining insight into these ML "black box" models is important. The application of XML techniques is receiving a lot of attention.

Numerous research focus on the diagnosis of COVID-19 by chest imaging, including radiography and computer tomography (CT). While precise in recognizing occurrences that are positive, most of these instruments are unable to distinguish COVID-19 from other lung illnesses [139]. Additionally, studies demonstrate implausible ideal outcomes, which are probably the result of issues with data leakage and a lack of transparency in the experimentation process, thus, making their work neither marketable nor replicable. By examining [140,141], it is obvious that the majority of methods rely on advanced DL and computer vision methods as well as image data. To assist doctors and field experts, model interpretability and prediction explanations are, however, given little to no importance.

A straightforward and incredibly effective ML method for identifying the COVID-19 utilizing basic features based on patient questionnaires was described by authors in [142]. Age, symptoms including fever and sore throat, and proven contact with an infected person were among the factors used. The test sets' results reveal an area under curve (AUC) measure of 0.9, which is regarded as a high standard result in the medical industry. The most important variables, such as cough, fever, and contact with an infected person, were discovered through Shapley additive explanations. This method has two important drawbacks: the first one cannot recognize patients without symptoms; additionally, the second is that it might be biased toward negative cases. Since the authors note that patients with negative test results may underestimate their symptoms, this tool can undoubtedly aid field agents on early trials in better managing COVID-19 tests in limited supply and guiding patient ward placement.

AI-based approaches should be encouraged and implemented as standard practice in the implementation of DL techniques for multimedia categorization, notably for issues with medical diagnosis. In actuality, when increasingly complex neural network topologies emerge, their inability to be debugged and inability to provide human-centered justification for their decisions continue to limit their utility. One of the key instruments in overcoming what continues to be a significant barrier for future AI is XAI, the "black-box technique," which involves creating easily interpretable models to deal with practical problems, to increase human comprehension of AI-based models [143].

In terms of clinical trials and medication repositioning, AI should be an addition to human procedures, to ensure that ML/DL tactics are adapted to particular contexts, it is carried out in multidisciplinary teams. Moreover, it is essential to research and intensify the challenges of building innovative approaches for molecular regeneration, recommended practices for data exchange are also mentioned [144]. Clinical trials and medication repurposing are two topics. Although there are commonalities between clinical research and computationally predicted drug repurposing, notwithstanding the promised applications of AI in this area, we were

unable to locate any specific proof that computational guidance was used to conduct clinical trials. As far as we are aware, the bulk of the research analyzed did not follow DL predictions with clinical proof. The collections of possibilities produced by computational approaches for possible pandemics should be encouraging, this can later be put to the test in studies or inspections. However, there is additional work to be done in this area of inquiry.

Regarding text modeling approaches, the majority of them integrated NLP approaches with a specially honed strategy for COVID-19-related data and after that displayed the conclusions drawn from such data. In our perspective, studies on string patterns did not provide anything fresh to test analysis or clinical testing. In terms of time series analysis, taking into account studies employing COVID-19 forecasts, the best model to utilize is not generally agreed upon. The anticipated mortality toll from COVID-19 is fluctuating, and a wide range of forecasting variances have been shown by all prediction models. Sadly, the paucity of information on COVID-19, particularly at the start of the pandemic, and additionally, policy changes have increased the significance of research that uses limited datasets or enhances the precision of mathematical model (such as the SIR model) [145], that anticipate smaller data. There is not an approach that consistently outperforms others, and it depends on preparation and fine-tuning. Utilizing data fusion approaches, as in [146,147], to combine time series from several data sources is a correct approach that we recommend. During the COVID-19 pandemic, Figure 1.5 depicted various areas where AI-based models could be applied.

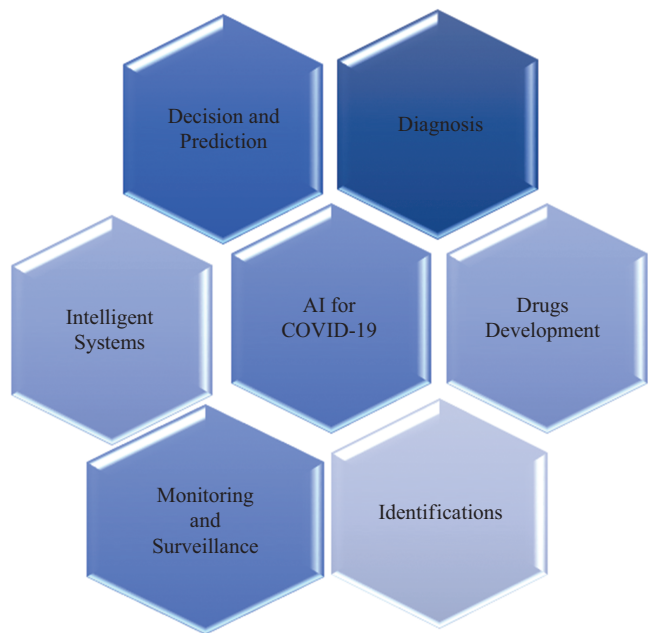


Figure 1.5 Some fundamental functions of AI in combating COVID-19 pandemic

Additionally, pattern identification, forecasting, describing, and classifying medical data are all areas where AI is particularly helpful. Infections with COVID-19 are projected, diagnosed, treated, be improved so that decision-making by government officials, medical professionals, and other policymakers can produce useful results. AI can assist in COVID-19 patient discovery, prediction, prevention, and monitoring of outbreaks, but it cannot replace scientific knowledge. The AI-based model can be used for cleaning up the environment, helping to make monoclonal antibodies and other treatments, managing health care, conducting business and trade, increasing transparency, and formulating policy, among other things.

1.4 XAI research trends and open issues

XAI intends to assist people in comprehending the reasoning behind a machine's choice and determining whether or not it is reliable. XAI is therefore unavoidably a paradigm for bridging AI and human intelligence, with the intention of facilitating and increasing human participants' acceptability of AI systems [148]. XAI can be thought of as "AI for citizens" in this context.

Although intelligent systems have a lot of potential, the concerns about providing such intelligent systems too much power without even being able to adequately explain the decision-making process underlying such complex systems to domain specialists are raised by the XAI research program (doctors, attorneys, financial specialists, etc.) a language and a format that they can understand. This not only clarifies the reasoning behind particular conclusions reached by such technologies but also inspires the study and urges academics to develop more humanistic (human-like) alternatives, and improved knowledge of the brain as natural phenomena for cognitive processing. Furthermore, user rights must be preserved because machines are increasingly replacing humans in making decisions in many aspects of daily life. Machine intelligence still struggle to process complex and deeper knowledge or abstract information unless it is first transformed into an algorithmic format. (attributes, results, and labels).

In several AI application fields, the aforementioned crucial issue has taken on a significant importance. For instance, a patient's intervention may be influenced by a decision made by a computerized diagnosis process; therefore, doctors must comprehend the rationale behind the decision and assess the associated risks. If we take autonomous drones for medical use, the reasons, circumstances, and locations of automated treatment, management, or monitoring by drones must be known to the doctors. Thus, a reliable XAI system becomes a crucial requirement before AI can be used to solve almost any real-world issue. Currently, a lot of study is being done on how to solve these kinds of issues.

Modern AI methods like DL have their origins in the simulation of the human brain. Finding a way to match human intellect is the fundamental objective in order to make DNNs understandable, to figure out a means to create a human-made "brain" that can comprehend, at least at a higher degree of functionality, the

neuronal activity in the human brain, connect the multilayered brain knowledge stream processors to the deep structures.

The properties of contemporary orthodox DL and the human brain differ significantly in two ways. First, the human brain lacks the ability to maintain very precise characteristics, more resembling an analog circuit. Second, unlike the meticulously “handcrafted” topologies of the contemporary standard DL, synapses in the human brain are densely linked. Therefore, it is odd that the mainstream DL literature has harsh criticism for supposedly “handcrafted” aspects [149], nevertheless is reluctant to acknowledge that the designs it is advancing are “hand-crafted,” very problem-specific as well as a variety of contextual, including stride, kernel sizes, the number of layers, and others.

Given the aforementioned issues, XAI can contribute to a mutually advantageous bridge between DL and neurology. On the one hand, neurology and cognitive science can assist in developing XAI models that are logical and easier for humans to comprehend [150,151]. The mechanisms of intelligence in the human brain can also be better understood using XAI models derived from DNNs, on the other hand [152,153]. The quest of fully comprehending how human intellect derives from neurons could be recast as the ultimate objective of XAI.

1.4.1 XAI perspective in healthcare

Putting more of an emphasis on prototype-based models is one possible avenue for future study [154,155] rather than on deeply engrained, abstract frameworks. Models based on prototypes are not new like the work of authors in [156] putting the simplest first (and very effective kNN example), by using ANNs of the RBF variety and IF...THEN criteria. Tibshiran recognized the potency of prototype-based models in the study of authors in [156], but, however, these have not yet been produced in the context of DL, where they can combine a more complex infrastructure with a manner of representation that is easily comprehensible. Despite being effective, the kNN method is not a learning method in the strictest sense because it needs all the data to be present and stored. A certain amount of sparsity is required, which might come from straightforward unsupervised learning methods like clustering or more intricate end-to-end auto-encoders.

There is a widespread misperception that the only type of learning is parameterized learning achieved through cost (or loss) function reduction. In reality, humans pick up prototypes from data samples utilizing resemblance to learn. According to this reasoning, the position becomes the central focus of the learning in prototype-based models, as opposed to the parameters/weights-centered approach that predominates in the mainstream, and the characteristics of the prototypes in the feature/data space. Additionally, there is a fundamental distinction between statistical learning and similarity (i.e., two different methods for analyzing the divergence and difference between two data items). While statistical measures require a large number of data points or samples, similarity can be defined over two (conceivably limitless) number of separate observations for the data.

The construction of Turing’s type-B random machines is another viable path (or chaotic machinery) [157,158], additionally random Boltzmann machines, which

might result in a generic AI. New cognitive neuroscience results will be included into XAI models, which will legitimize XAI investigation, likewise, such cross-disciplinary application will make XAI valuable for others outside of the field of AI. but potentially assist in resolving century-old problems on how to comprehend human intelligence. The following are open questions in this field: (a) how should the network/model architecture be determined?; (b) how should features be extracted and represented?; (c) what are the most accurate distance measurements, and what are the consequences?; (d) which way of optimization works the best?; and (e) how to select the group of prototypes that best capture the data (if an approach based on prototypes is employed)?

1.5 Conclusion and future directions

XAI is a recent research area that emphasizes ML interpretability and seeks to develop a more open AI. The main objective is to provide a set of interpretable methods and frameworks that produce representations that are easier to comprehend while retaining superior prediction accuracy. Unfortunately, there is not a standardized approach of what is explainable should accomplish. Although some scholars discriminate between the terms interpretability and explainability, others use them identically. The basic objective of XAI is to create a collection of approaches that offer models that are easier to understand while still having highly predicted accuracy. MDSS are computer programs created to influence physician decisions on a range of patients as soon as necessary and, most often, in real-time. The atmosphere for using XAI and MDSS innovation is rapidly changing, and most researchers have tried to see how these innovations is applicable in healthcare systems so as to make their adoptions in healthcare environments acceptable. Therefore, this chapter covers the current requirements and development issues for XAI and MDSS. The summary of potential areas for open issues, and further study comes towards the end of the chapter. The most recent statistics on the application of and effects of MDSSs and XAI in practice were given, and offered recommendations for users to take into account as these systems start to be integrated into commercialized products, and put into practice outside of research and development environments. Therefore, the chapter will provide wider knowledge for both academic researchers and healthcare policy makers and give access to a historical ready-made transcription of HMDSS in the healthcare sector, this can assist them in their future decision-making processes with respect to non-communicable diseases.

Acknowledgment

The work of Agbotiname Lucky Imoize is supported in part by the Nigerian Petroleum Technology Development Fund (PTDF) and in part by the German Academic Exchange Service (DAAD) through the Nigerian-German Postgraduate Program under grant 57473408.

References

- [1] M. Ghassemi, L. Oakden-Rayner, and A. L. Beam, “The false hope of current approaches to explainable artificial intelligence in health care,” *Lancet Digit. Heal.*, vol. 3, no. 11, pp. e745–e750, 2021, doi: 10.1016/S2589-7500(21)00208-9.
- [2] C. C. Yang, “Explainable artificial intelligence for predictive modeling in healthcare,” *J. Healthc. Informatics Res.*, vol. 6, no. 2, pp. 228–239, 2022, doi: 10.1007/s41666-022-00114-1.
- [3] J. Amann, A. Blasimme, E. Vayena, D. Frey, and V. I. Madai, “Explainability for artificial intelligence in healthcare: a multidisciplinary perspective,” *BMC Med. Inform. Decis. Mak.*, vol. 20, no. 1, pp. 1–9, 2020, doi: 10.1186/s12911-020-01332-6.
- [4] U. Pawar, D. O’Shea, S. Rea, and R. O’Reilly, “Explainable AI in healthcare,” In *2020 International Conference on Cyber Situational Awareness, Data Analytics and Assessment, Cyber SA 2020*, July, 2020, doi: 10.1109/CyberSA49311.2020.9139655.
- [5] O. Biran and C. Cotton, “Explanation and justification in machine learning: a survey,” In *IJCAI-17 Work. Explain. AI*, pp. 8–13, 2017.
- [6] D. Wang, Q. Yang, A. Abdul, B. Y. Lim, and U. States, “Designing theory-driven user-centric explainable AI,” In *CHI*, pp. 1–15, 2019.
- [7] J. A. Akrimi, A. R. Ahmad, L. E. George, and S. Aziz, “Review of artificial intelligence,” *Int. J. Sci. Res.*, India Online, vol. 2, no. 2, pp. 487–505, 2013, doi: 10.32628/ijrsrset1207625.
- [8] U. Pawar, D. O’Shea, S. Rea, and R. O’Reilly, “Incorporating explainable artificial intelligence (XAI) to aid the understanding of machine learning in the healthcare domain,” *CEUR Workshop Proc.*, vol. 2771, pp. 169–180, 2020.
- [9] N. H. Alharbi, R. O. Bameer, S. S. Geddan, and Hajar M. Alharbi, “Recent advances and machine learning techniques on sickle cell disease,” *Fut. Comput. Informat. J.*, vol. 5, no. 1, pp. 46–59, 2020, doi: 10.54623/fue.fcij.5.1.4.
- [10] M. J. Panaggio, D. M. Abrams, F. Yang, T. Banerjee, and N. R. Shah, “Can subjective pain be inferred from objective physiological data? Evidence from patients with sickle cell disease,” *PLoS Comput. Biol.*, vol. 17, no. 3, pp. 1–12, 2021, doi: 10.1371/journal.pcbi.1008542.
- [11] Y. Zhang, Y. Weng, and J. Lund, “Applications of explainable artificial intelligence in diagnosis and surgery,” *Diagnostics*, vol. 12, no. 237, pp. 1–18, 2022, doi: 10.3390/diagnostics12020237.
- [12] I. I. Kukhtevich, V. V. Goryunova, T. I. Goryunova, and P. S. Zhilyaev, “Medical decision support systems and semantic technologies in healthcare,” In *Advances in Economics, Business and Management Research*, 2020, vol. 148, pp. 370–375, doi: 10.2991/aebmr.k.200730.068.
- [13] R. T. Sutton, D. Pincock, D. C. Baumgart, D. C. Sadowski, R. N. Fedorak, and K. I. Kroeker, “An overview of clinical decision support systems: benefits, risks, and strategies for success,” *Digit. Med.*, vol. 3, no. 1, pp. 1–10, 2020, doi: 10.1038/s41746-020-0221-y.

- [14] S. Aljarboa and S. J. Miah, “Acceptance of clinical decision support systems in Saudi healthcare organisations,” *Inf. Dev.*, pp. 1–21, 2021, doi: 10.1177/02666669211025076.
- [15] Vi. Bellotti and K. Edwards, “Intelligibility and accountability – human considerations in context-aware systems,” *Hum. Comput. Interact. – Taylor Fr.*, vol. 10, pp. 193–212, 2009, doi: 10.1207/S15327051HCI16234.
- [16] V. Petrauskas, G. Damuleviciene, A. Dobrovolskis, J. Dovydaitis, and A. Janaviciute, “XAI-based medical decision support system model,” *Int. J. Sci. Res. Publ.*, vol. 10, no. 12, pp. 598–607, 2020, doi: 10.29322/IJSRP.10.12.2020.p10869.
- [17] T. Jodie, S. Martins, M. Michel, *et al.*, “Evaluation of the acceptability and usability of a decision support system to encourage safe and effective use of opioid therapy for chronic, noncancer pain by primary care providers,” *Pain Med.*, vol. 11, no. 4, pp. 575–585, 2010, <http://0-ovidsp.ovid.com.lib.exeter.ac.uk/ovidweb.cgi?T=JS&PAGE=reference&D=emed12&NEWS=N&AN=358905180>
- [18] J. Kim, Y. M. Chae, S. Kim, S. H. Ho, H. H. Kim, and C. B. Park, “A study on user satisfaction regarding the clinical decision support system (MDSS) for medication,” *Healthc. Inform. Res.*, vol. 18, no. 1, pp. 35–43, 2012, doi: 10.4258/hir.2012.18.1.35.
- [19] J. Razmak, C. H. Bélanger, and W. Farhan, “Managing patients’ data with clinical decision support systems: a factual assessment,” *J. Decis. Syst. – Taylor Fr.*, vol. 27, no. 3, pp. 123–145, 2018, doi: 10.1080/12460125.2018.1533159.
- [20] D. Zikos and N. Delellis, “MDSS-RM: a clinical decision support system reference model,” *BMC Med. Res. Methodol.*, vol. 18, no. 1, pp. 1–14, 2018, doi: 10.1186/s12874-018-0587-6.
- [21] Y. Li, C. Bai, and C. K. Reddy, “A distributed ensemble approach for mining healthcare data under privacy constraints,” *Inf. Sci. (Ny).*, vol. 330, pp. 245–259, 2016, doi: 10.1016/j.ins.2015.10.011.
- [22] T.-Y. Leong, “Decision support systems in healthcare: emerging trends and success factors,” In *Appl. Decis. Support with Soft Comput.*, New York, NY: Springer, pp. 151–179, 2003, doi: 10.1007/978-3-540-37008-6_6.
- [23] A. X. Garg, N. K. J. Adhikari, H. McDonald, *et al.*, “Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review,” *J. Am. Med. Assoc.*, vol. 293, no. 10, pp. 1223–1238, 2005, doi: 10.1001/jama.293.10.1223.
- [24] M. Alther and C. K. Reddy, “Clinical decision support systems,” *OR Insight*, vol. 10, no. 2, pp. 18–32, 2007, doi: 10.1057/ori.1997.9.
- [25] D. Dinevski, U. Bele, and T. Sarenac, “Clinical decision support systems,” *Telemed. Tech. Appl.*, vol. 37, no. 6, pp. 491–498, 2021, doi: 10.1159/000519420.
- [26] M. A. Musen, Y. Shahar, and E. H. Shortliffe, “Clinical decision support systems,” In *Health Information System*, second ed., pp. 221–235, 2002, doi: 10.32628/cseit1952264.

- [27] K. Sadegh-Zadeh, "Clinical decision support systems: a virtual survey," *Philos. Med.*, vol. 119, pp. 705–722, 2015, doi: 10.1007/978-94-017-9579-1_20.
- [28] P. Status, U. Acceptance, and I. Diseases, "Health evaluation through logical programming (HELP)," *Clinfowiki*, pp. 1–4, 2015, [http://clinfowiki.org/wiki/index.php/Health_Evaluation_through_Logical_Programming_\(HELP\)](http://clinfowiki.org/wiki/index.php/Health_Evaluation_through_Logical_Programming_(HELP))
- [29] J. M. Kirigia, A. Seddoh, D. Gatwiri, L. H. K. Muthuri, and J. Seddoh, "E-health: determinants, opportunities, challenges and the way forward for countries in the WHO African Region," *BMC Public Health*, vol. 5, no. 137, pp. 1–11, 2005, doi: 10.1186/1471-2458-5-137.
- [30] C. Division, "Implementing e-health in developing countries: guidance and principles," In *International Telecommunication Union*, September, pp. 1–53, 2008.
- [31] WHO, "An assessment of e-health projects and initiatives in Africa," In *E-Health Telemed. Wolrd Heal. Organ.*, pp. 1–35, 2010.
- [32] WHO, "The Promise of eHealth in the African Region," Press Release, September, 2013, Available: <http://www.afro.who.int/en/media-centre/pressreleases/item/5816-the-promise-of-ehealth-in-the-african-region.html>
- [33] I. Sim and A. Berling, "A framework for classifying decision support systems," In *AMIA 2003 Symposium*, 2003, pp. 599–603.
- [34] E. H. Shortliffe and J. J. Cimino, *Biomedical Informatics – Computer Application in Healthcare and Biomedicine*, vol. 3. 2006.
- [35] C. Grosan and A. Abraham, *Machine Learning*, vol. 17, 2011, doi:10.1007/978-3-642-21004-4_10.
- [36] R. L. Kumar, In Wang Y, Poongodi T, Imoize AL, editors (eds.) , *Internet of Things, Artificial Intelligence and Blockchain Technology*, Cham: Springer; 2021.
- [37] G. Roth, "Machine learning with Python: an introduction," JavaWorld, pp. 1–5, 2019, <https://www.javaworld.com/article/3322898/application-development/machine-learning-with-python-an-introduction.html>
- [38] O. B. Ayoade, *Comparative Analysis of Selected Machine Learning Algorithms for Predicting Sickel Cell Disease*, Department Comput. Sci. Fac. Commun. Inf. Sci. Univ. Ilorin, Kwara State, Niger, December, pp. 1–270, 2021.
- [39] N. I. of H. NIH, *Health Information for the Public – Sickel Cell Disease (SCD)*, National Heart Lung and Blood Institute, 2016.
- [40] N. I. of H. NIH, *The Management of Sickel Cell Disease*, Natl. Hear. Lung Blood Inst., no. 02–2117, pp. 1–206, 2015, Available: <http://www.nhlbi.nih.gov>
- [41] L. M. Gunder and S. A. Martin, *Essentials of Medical Genetics for Health Professionals*, USA: Jones & Bartlett Learning, LLC, 2011.
- [42] S. E. Roger and H. R. Rodney, "Some medical and social aspects of the treatment for genetic-metabolic diseases," *Ann. Am. Acad. Polit. Soc. Sci.*, vol. 399, pp. 30–37, 2017.
- [43] M. Saad and Z. Salem, "Basic concepts of medical genetics, formal genetics," *Egypt. J. Med. Hum. Genet.*, vol. 15, no. 1, pp. 99–101, 2014, doi: 10.1016/j.ejmhg.2013.10.001.

- [44] World-Health-Organization, "Sickle-cell anemia," *World Heal. Organ.*, vol. 11, no. April, pp. 1–5, 2020.
- [45] P. L. Stephenson, M. V. Taylor, and C. Anglin, "Sickle cell disease," *J. Consum. Health Internet*, vol. 19, no. 2, pp. 122–131, 2015, doi: 10.1080/15398285.2015.1026706.
- [46] M. W. Darlison and B. Modell, "Sickle-cell disorders: limits of descriptive epidemiology," *Lancet (London, England)*, vol. 381, no. 9861, pp. 98–9, 2013, doi: 10.1016/S0140-6736(12)61817-0.
- [47] J. R. Frost, R. K. Cherry, S. O. Oyeku, *et al.*, "Improving sickle cell transitions of care through health information technology," *Am. J. Prev. Med.*, vol. 51, pp. 17–23, 2016, doi: 10.1016/j.amepre.2016.02.004.
- [48] C. P. Rivera, A. Veneziani, R. E. Ware, and M. O. Platt, "Sickle cell anemia and pediatric strokes: computational fluid dynamics analysis in the middle cerebral artery," *Exp. Biol. Med.*, vol. 241, pp. 755–765, 2016, doi: 10.1177/1535370216636722.
- [49] J. Kanter and R. Kruse-Jarres, "Management of sickle cell disease from childhood through adulthood," *Blood Rev.*, vol. 27, no. 6, pp. 279–87, 2013, doi: 10.1016/j.blre.2013.09.001.
- [50] S. D. Grosse, I. Odame, H. K. Atrash, D. D. Amendah, F. B. Piel, and T. N. Williams, "Sickle cell disease in Africa: a neglected cause of early childhood mortality," *Am. J. Prev. Med.*, vol. 41, no. 6 SUPPL.4, pp. S398–S405, 2011, doi: 10.1016/j.amepre.2011.09.013.
- [51] O. S. Platt, D. J. Brambilla, W. F. Rose, *et al.*, "Mortality in sickle cell disease-life expectancy & risk factors," *N. Engl. J. Med.*, vol. 330, no. 23, pp. 1639–1644, 2012.
- [52] D. Divya, K. N. Rao, Si. G. Ratnam, and D. Sowjanya, "Supervised machine learning algorithms for analysis on sickle cell anemia," *High Technol. Lett.*, vol. 26, no. 11, pp. 994–1004, 2020.
- [53] T. M. Sabu, "Bioinformatics," In *Fundam. Concepts Bioinforma.*, pp. 1–155, 2003.
- [54] A. D. Hardie, L. Ramos-Duran, and J. U. Schoepf, "Cardiac MR assessment of myocardial iron deposition in sickle cell disease: risk factors and association with cardiac function," *J. Cardiovasc. Magn. Reson.*, vol. 1, pp. 48–48, 2010, doi: 10.1186/1532-429X-12-S1-P274.
- [55] G. D. Magoulas and A. Prentza, *Machine Learning in Medical Applications*, New York, NY: Springer, vol. 204, no. 9, pp. 300–307, 2015, doi: 10.1007/3-540-44673-7.
- [56] R. V. Gardner, "Sickle cell disease: advances in treatment," *Ochsner J.*, vol. 18, no. 4, pp. 377–389, 2018, doi: 10.31486/toj.18.0076.
- [57] C. O'Keeffe, S. Mason, R. Jacques, and J. Nicholl, "Characterising non-urgent users of the emergency department (ED): a retrospective analysis of routine ED data," *PLoS One*, vol. 13, no. 2, p. e0192855, 2018.
- [58] K. Eastwood, K. Smith, A. Morgans, and J. Stoelwinder, "Appropriateness of cases presenting in the emergency department following ambulance

- service secondary telephone triage: a retrospective cohort study,” *BMJ Open*, vol. 7, no. 10, p. e016845, 2017.
- [59] K. E. Deligiannidis, “Primary care issues in rural populations,” *Phys. Assist. Clin.* vol. 4, no. 1, pp. 11–19, 2019.
 - [60] W. S. Eidson-Ton, J. Rainwater, D. Hilty, *et al.*, “Training medical students for rural, underserved areas: a rural medical education program in California,” *J. Health Care Poor Underserved*, vol. 27, no. 4, pp. 1674–1688, 2016.
 - [61] J. Baumbach and H. H. Schmidt, “The end of medicine as we know it: introduction to the new journal, systems medicine,” *Syst. Med.* vol. 1, no. 1, pp. 1–2, 2018.
 - [62] I. D. Federation and I. D. Atlas, *International Diabetes Federation. IDF Diabetes Atlas*, 6th ed, Brussels: International Diabetes Federation, 2013.
 - [63] I. D. Oladipo, A. O. Babatunde, J. B. Awotunde, and M. Abdullaheem, “An improved hybridization in the diagnosis of diabetes mellitus using selected computational intelligence,” In *International Conference on Information and Communication Technology and Applications 2020* Nov 24, Cham: Springer, pp. 272–285.
 - [64] World Health Organization. World Health Organization Diabetes Fact Sheet. 2018 [Updated 2018 October 30].
 - [65] Centers for Disease Control and Prevention. National Diabetes Fact Sheet: National Estimates and General Information on Diabetes and Prediabetes in the United States, 2011. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, 2011; vol. 201, no. 1, pp. 2568–2569.
 - [66] Centers for Disease Control and Prevention (CDC). National Diabetes Statistics Report, 2014. Centers for Disease Control and Prevention. US Department of Health and Human Services, Atlanta, GA, 2014.
 - [67] V. J. Briscoe and S. N. Davis, “Hypoglycemia in type 1 and type 2 diabetes: physiology, pathophysiology, and management,” *Clin. Diabetes*, vol. 24, no. 3, pp. 115–121, 2006.
 - [68] N. N. Zammit and B. M. Frier, “Hypoglycemia in type 2 diabetes: pathophysiology, frequency, and effects of different treatment modalities,” *Diabetes Care*, vol. 28, no.12, pp. 2948–2961, 2005.
 - [69] P. F. Hsu, S. H. Sung, H. M. Cheng, *et al.*, “Association of clinical symptomatic hypoglycemia with cardiovascular events and total mortality in type 2 diabetes: a nationwide population-based study,” *Diabetes Care*, vol. 36, no. 4, pp. 894–900, 2013.
 - [70] P. Vexiau, P. Mavros, G. Krishnarajah, R. Lyu, and D. Yin, “Hypoglycaemia in patients with type 2 diabetes treated with a combination of metformin and sulphonylurea therapy in France,” *Diabetes Obesity Metabol.* vol. 10, pp. 16–24, 2008.
 - [71] L. Jönsson, B. Bolinder, and J. Lundkvist, “Cost of hypoglycemia in patients with Type 2 diabetes in Sweden,” *Value Health*, vol. 9, no. 3, pp. 193–198, 2006.

- [72] X. Li, S. Yu, Z. Zhang, *et al.*, “Predictive modeling of hypoglycemia for clinical decision support in evaluating outpatients with diabetes mellitus,” *Curr. Med. Res. Opin.*, vol. 35, no. 11, pp. 1885–1891, 2019.
- [73] Ö. Kart, V. Mevsim, A. Kut, İ. Yürek, A. Ö. Altın, and O. Yılmaz, “A mobile and web-based clinical decision support and monitoring system for diabetes mellitus patients in primary care: a study protocol for a randomized controlled trial,” *BMC Med. Inform. Dec. Mak.* vol. 17, no. 1, pp. 1-0, 2017.
- [74] P. Aggleton and H. Chalmers, “Models and theories. Five. Orem’s self-care model,” *Nursing Times*, vol. 81, no. 1, pp. 36–39, 1985.
- [75] M. J. Pearce, K. Pereira, and E. Davis, “The psychological impact of diabetes: a practical guide for the nurse practitioner,” *J. Am. Assoc. Nurse Practition.* vol. 25, no. 11, pp. 578–583, 2013.
- [76] K. A. Weinger, J. O. Yi, F. R. Pouwer, H. E. Ad, and F. J. Snoek, “The confidence in diabetes selfcare scale,” *Diabetes Care*, vol. 26, no. 3, pp. 713–718, 2003.
- [77] İ. Satman, Ş. İmamoğlu, C. Yılmaz, S. Akalın, S. Salman, and N. Dinççağ, “Diabetes Mellitus ve komplikasyonlarının tanı, tedavi ve izlem kılavuzu,” Miki Matbacılık: Türkiye Endokrinoloji ve Metabolizma Derneği, Ankara, Mayıs, 2014, pp. 15–25.
- [78] American Diabetes Association, “Standards of medical care in diabetes—2015 abridged for primary care providers,” *Clin. Diabetes: Publ. Am. Diabetes Assoc.*, vol. 33, no. 2, p. 97, 2015.
- [79] P. S. Roshanov, S. Misra, H. C. Gerstein, *et al.*, “Computerized clinical decision support systems for chronic disease management: a decision-maker-researcher partnership systematic review,” *Implement. Sci.*, vol. 6, no. 1, pp. 1–6, 2011.
- [80] R. Anchala, E. Di Angelantonio, D. Prabhakaran, and O. H. Franco, “Development and validation of a clinical and computerised decision support system for management of hypertension (DSS-HTN) at a primary health care (PHC) setting,” *PLoS One*, vol. 8, no. 11, p. e79638, 2013.
- [81] B. T. Kurian, M. H. Trivedi, B. D. Grannemann, C. A. Claassen, E. J. Daly, and P. Sunderajan, “A computerized decision support system for depression in primary care,” *Primary Care Companion J. Clin. Psychiatry*, vol. 11, no. 4, 140, 2009.
- [82] M. C. Meulendijk, M. R. Spruit, P. A. Jansen, M. E. Numans, and S. Brinkkemper, “STRIPA: A rule-based decision support system for medication reviews in primary care,” *ECIS 2015 Research-in-Progress Papers*, 2015, pp. 1–13.
- [83] S. Rahaman, “Diabetes diagnosis decision support system based on symptoms, signs and risk factor using special computational algorithm by rule base,” In *2012 15th International Conference on Computer and Information Technology (ICCIT)*, 2012 Dec 22. New York, NY: IEEE, pp. 65–71.
- [84] S. F. Jaafar and D. M. Ali, “Diabetes mellitus forecast using artificial neural network (ANN),” In *2005 Asian Conference on Sensors and the*

- International Conference on New Techniques in Pharmaceutical and Biomedical Research*, 2005 Sep 5. New York, NY: IEEE, pp. 135–139.
- [85] J. A. Quinlivan, L. T. Lam, and J. Fisher, “A randomised trial of a four-step multidisciplinary approach to the antenatal care of obese pregnant women,” *Austral. New Zealand J. Obst. Gynaecol.* vol. 51, no. 2, pp. 141–146, 2011.
 - [86] Y. Sun and H. Zhao, “The effectiveness of lifestyle intervention in early pregnancy to prevent gestational diabetes mellitus in Chinese overweight and obese women: a quasi-experimental study,” *Appl. Nurs. Res.*, vol. 30, pp. 125–130, 2016.
 - [87] C. Wang, Y. Wei, X. Zhang, *et al.*, “A randomized clinical trial of exercise during pregnancy to prevent gestational diabetes mellitus and improve pregnancy outcome in overweight and obese pregnant women,” *Am. J. Obst. Gynecol.*, vol. 216, no. 4, pp. 340–351, 2017.
 - [88] D. M. , S. Nikpay, and R. S. Huckman, “The business of medicine in the era of COVID-19,” *Jama*, vol. 323, no. 20, pp. 2003–2004, 2020.
 - [89] E. H. Shortliffe and M. J. Sepúlveda, “Clinical decision support in the era of artificial intelligence,” *Jama*, vol. 320, no. 21, pp. 2199–2200, 2018.
 - [90] A. M. Antoniadi, Y. Du, Y. Guendouz, *et al.*, “Current challenges and future opportunities for XAI in machine learning-based clinical decision support systems: a systematic review,” *Appl. Sci.*, vol. 11, no. 11, p. 5088, 2021.
 - [91] R. Caruana, Y. Lou, J. Gehrke, P. Koch, M. Sturm, and N. Elhadad, “Intelligible models for healthcare: predicting pneumonia risk and hospital 30-day readmission,” In *Proceedings of the 21th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, 2015, pp. 1721–1730.
 - [92] World Health Organization, *A Global Brief on Hypertension: Silent Killer, Global Public Health Crisis: World Health Day 2013*, Geneva: World Health Organization, 2013..
 - [93] S. Akbar, M. U. Akram, M. Sharif, A. Tariq, and U. ullah Yasin, “Arteriovenous ratio and papilledema based hybrid decision support system for detection and grading of hypertensive retinopathy,” *Comput. Methods Prog. Biomed.*, vol. 154, pp. 123–141, 2018.
 - [94] T. Y. Wong and P. Mitchell, “Hypertensive retinopathy,” *N. Eng. J. Med.* vol. 351, no. 22, pp. 2310–2317, 2004.
 - [95] G. Mancia, R. Fagard, K. Narkiewicz, *et al.*, “Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC): ESH/ESC Task Force for the Management of Arterial Hypertension,” *J. Hypertens*, vol. 31, no. 10, pp. 1925–1938, 2013.
 - [96] C. Guerrero-García and A. F. Rubio-Guerra, “Combination therapy in the treatment of hypertension,” *Drugs Context*, vol. 7, pp. 212531, 2018.
 - [97] J. C. Parr and G. F. Spears, “Mathematic relationships between the width of a retinal artery and the widths of its branches,” *Am. J. Ophthalmol.*, vol. 77, no. 4, pp. 478–483, 1974.

- [98] S. Kazeminia, C. Baur, A. Kuijper, *et al.*, “GANs for medical image analysis,” *Artif. Intell. Med.*, vol. 109, pp. 101938, 2020.
- [99] K. Mittal and V. Rajam, “Computerized retinal image analysis-a survey,” *Multimed. Tools Appl.*, vol. 79, no. 31, pp. 22389–22421, 2020.
- [100] M. Badar, M. Haris, and A. Fatima, “Application of deep learning for retinal image analysis: a review,” *Comput. Sci. Rev.*, vol. 35, pp. 100203, 2020.
- [101] D. L. Castro, D. Tegolo, and C. Valenti, “A visual framework to create photorealistic retinal vessels for diagnosis purposes,” *J. Biomed. Inform.*, vol. 108, pp. 103490, 2020.
- [102] N. Tajbakhsh, L. Jeyaseelan, Q. Li, J. N. Chiang, Z. Wu, and X. Ding, “Embracing imperfect datasets: a review of deep learning solutions for medical image segmentation,” *Med. Image Anal.*, vol. 63, pp. 101693, 2020.
- [103] Q. Fu, S. Li, and X. Wang, “Mscnn-am: a multi-scale convolutional neural network with attention mechanisms for retinal vessel segmentation,” *IEEE Access*, vol. 8, pp. 163926–163936.
- [104] Y. Guo and Y. Peng, “BSCN: bidirectional symmetric cascade network for retinal vessel segmentation,” *BMC Med. Imaging*, vol. 20, no. 1, pp. 1–22, 2020.
- [105] M. Miri, Z. Amini, H. Rabbani, and R. Kafieh, “A comprehensive study of retinal vessel classification methods in fundus images,” *J. Med. Signals Sens.*, vol. 7, no. 2, pp. 59, 2017.
- [106] W. Dai, N. Dong, Z. Wang, X. Liang, H. Zhang, and E. P. Xing, “Scan: structure correcting adversarial network for organ segmentation in chest x-rays,” In *Deep Learning in Medical Image Analysis and Multimodal Learning for Clinical Decision Support*, Cham: Springer, pp. 263–273, 2018.
- [107] Y. D. Kim, K. J. Noh, S. L. Byun, *et al.*, “Effects of hypertension, diabetes, and smoking on age and sex prediction from retinal fundus images,” *Sci. Rep.*, vol. 10, no. 1, pp. 1–4, 2020.
- [108] M. Arsalan, M. Owais, T. Mahmood, J. Choi, and K. R. Park, “Artificial intelligence-based diagnosis of cardiac and related diseases,” *J. Clin. Med.*, vol. 9, no. 3, pp. 871, 2020.
- [109] M. Owais, M. Arsalan, T. Mahmood, J. K. Kang, and K. R. Park, “Automated diagnosis of various gastrointestinal lesions using a deep learning-based classification and retrieval framework with a large endoscopic database: model development and validation,” *J. Med. Internet Res.*, vol. 22, no. 11, pp. e18563, 2020.
- [110] N. Tsiknakis, D. Theodoropoulos, G. Manikis, *et al.*, “Deep learning for diabetic retinopathy detection and classification based on fundus images: a review,” *Comput. Biol. Med.*, vol. 135, pp. 104599, 2021.
- [111] W. L. Alyoubi, W. M. Shalash, and M. F. Abulkhair, “Diabetic retinopathy detection through deep learning techniques: a review,” *Inform. Med. Unlocked*, vol. 20, pp. 100377, 2020.

- [112] M. Cives, F. Mannavola, L. Lospalluti, *et al.*, “Non-melanoma skin cancers: biological and clinical features,” *Int. J. Mol. Sci.*, vol. 21, no. 15, pp. 5394, 2020.
- [113] U. Leiter and C. Garbe, “Epidemiology of melanoma and nonmelanoma skin cancer—the role of sunlight,” In *Sunlight, Vitamin D and Skin Cancer*, New York, NY: Springer, 2008, pp. 89–103.
- [114] A. Esteva, B. Kuprel, R. A. Novoa, *et al.*, “Dermatologist-level classification of skin cancer with deep neural networks,” *Nature*, vol. 542, no. 7639, pp. 115–118, 2017.
- [115] H. M. Gloster Jr and K. Neal, “Skin cancer in skin of color,” *J. Am. Acad. Dermatol.*, vol. 55, no. 5, pp. 741–760, 2006.
- [116] D. Melzer, L.C. Pilling, and L. Ferrucci, “The genetics of human ageing,” *Nat. Rev. Genet.*, vol. 21, no. 2, pp. 88–101, 2020.
- [117] V. R. Yanofsky, S. E. Mercer, and R. G. Phelps, “Histopathological variants of cutaneous squamous cell carcinoma: a review,” *J. Skin Cancer*, vol. 2011, 210813, 2011.
- [118] A. Gluba, J. Rysz, and T. Pietrucha, “Microarray technology in the study of genetic determinants of cardiovascular diseases,” *Central Eur. J. Med.*, vol. 4, no. 1, pp. 1–10, 2009.
- [119] Q. X. Yang, Y. X. Wang, F. C. Li, *et al.*, “Identification of the gene signature reflecting schizophrenia’s etiology by constructing artificial intelligence-based method of enhanced reproducibility,” *CNS Neurosci. Ther.*, vol. 25, no. 9, pp. 1054–1063, 2019.
- [120] S. Cui, Q. Wu, J. West, and J. Bai J, “Machine learning-based microarray analyses indicate low-expression genes might collectively influence PAH disease,” *PLoS Comp. Biol.*, vol. 15, no. 8, pp. e1007264, 2019.
- [121] S. O. Folorunso, J. B. Awotunde, N. O. Adeboye, and O. E. Matiluko, “Data classification model for COVID-19 pandemic,” In *Advances in Data Science and Intelligent Data Communication Technologies for COVID-19 2022*, Cham: Springer, pp. 93–118, 2022.
- [122] S. O. Folorunso, J. B. Awotunde, F. E. Ayo, and K. K. Abdullah, “RADIOt: the unifying framework for iot, radiomics and deep learning modeling,” In *Hybrid Artificial Intelligence and IoT in Healthcare*, Singapore: Springer, pp. 109–128, 2021.
- [123] A. Cambiaghi, M. Ferrario, and M. Masseroli, “Analysis of metabolomic data: tools, current strategies and future challenges for omics data integration,” *Brief. Bioinform.*, vol. 18, no. 3, pp. 498–510, 2017.
- [124] J. Fu, Y. Zhang, Y. Wang, *et al.*, “Optimization of metabolomic data processing using NOREVA,” *Nat. Protocols*, vol. 17, no. 1, pp. 129–151, 2022.
- [125] B. Li, J. Tang, Q. Yang, *et al.*, NOREVA: normalization and evaluation of MS-based metabolomics data,” *Nucleic Acids Res.*, vol. 45, no. W1, pp. W162–W170, 2017.

- [126] J. Tang, J. Fu, Y. Wang, *et al.*, “ANPELA: analysis and performance assessment of the label-free quantification workflow for metaproteomic studies,” *Brief. Bioinform.*, vol. 21, no. 2, pp. 621–636, 2020.
- [127] M. X. Li, X. M. Sun, W. G. Cheng, *et al.*, “Using a machine learning approach to identify key prognostic molecules for esophageal squamous cell carcinoma,” *BMC Cancer*, vol. 21, no. 1, pp. 1–1, 2021.
- [128] Z. Dlamini, F. Z. Francies, R. Hull, and R. Marima, “Artificial intelligence (AI) and big data in cancer and precision oncology,” *Comput. Struct. Biotechnol. J.*, vol. 18, pp. 2300–2311, 2020.
- [129] T. Davenport, A. Guha, D. Grewal, and T. Bressgott, “How artificial intelligence will change the future of marketing,” *J. Acad. Market. Sci.*, vol. 48, no. 1, pp. 24–42, 2020.
- [130] Y. Dong, J. Hou, N. Zhang, and M. Zhang, “Research on how human intelligence, consciousness, and cognitive computing affect the development of artificial intelligence,” *Complexity*, vol. 2020, pp. 1–10, 2020.
- [131] A. Bohr and K. Memarzadeh, “The rise of artificial intelligence in healthcare applications,” In *Artificial Intelligence in Healthcare*, Academic Press, pp. 25–60, 2020.
- [132] I. H. Sarker, “Machine learning: algorithms, real-world applications and research directions,” *SN Comput. Sci.*, vol. 2, no. 3, pp. 1–21, 2021.
- [133] A. Adadi and M. Berrada, “Peeking inside the black-box: a survey on explainable artificial intelligence (XAI),” *IEEE Access*, vol. 6, pp. 52138–52160, 2018.
- [134] J. B. Awotunde, S. Oluwabukonla, C. Chakraborty, A. K. Bhoi, and G. J. Ajamu, “Application of artificial intelligence and big data for fighting COVID-19 pandemic,” *Decis. Sci. COVID-19*, pp. 3–26, 2022.
- [135] S. O. Folorunso, J. B. Awotunde, O. O. Banjo, E. A. Ogundepo, and N. O. Adeboye, “Comparison of active COVID-19 cases per population using time-series models,” *Int. J. E-Health Med. Commun. (IJEHMC)*, vol. 13, no. 2, pp. 1–21, 2021.
- [136] J. B. Awotunde, R. G. Jimoh, M. AbdulRaheem, I. D. Oladipo, S. O. Folorunso, and G. J. Ajamu, IoT-based wearable body sensor network for COVID-19 pandemic. In *Advances in Data Science and Intelligent Data Communication Technologies for COVID-19*, 2022, pp. 253–275.
- [137] S. Debnath, D. P. Barnaby, K. Coppa, *et al.*, “Machine learning to assist clinical decision-making during the COVID-19 pandemic,” *Bioelectron. Med.*, vol. 6, no. 1, pp. 1–8, 2020.
- [138] M. M. Banoei, R. Dinparastisaleh, A. V. Zadeh, and M. Mirsaeidi, “Machine-learning-based COVID-19 mortality prediction model and identification of patients at low and high risk of dying,” *Critical Care*, vol. 25, no. 1, pp. 1–4, 2021.
- [139] M. Ghaderzadeh and F. Asadi, “Deep learning in the detection and diagnosis of COVID-19 using radiology modalities: a systematic review,” *J. Healthc. Eng.*, vol. 2021, pp. 1–10, 2021.

- [140] H. Mohammad-Rahimi, M. Nadimi, A. Ghalyanchi-Langeroudi, M. Taheri, and S. Ghafouri-Fard, "Application of machine learning in diagnosis of COVID-19 through X-ray and CT images: a scoping review," *Front. Cardiovasc. Med.*, vol. 8, pp. 638011, 2021.
- [141] M. Roberts, D. Driggs, M. Thorpe, *et al.*, "Common pitfalls and recommendations for using machine learning to detect and prognosticate for COVID-19 using chest radiographs and CT scans," *Nat. Mach. Intell.*, vol. 3, no. 3, pp. 199–217, 2021.
- [142] Y. Zoabi, S. Deri-Rozov, and N. Shomron, "Machine learning-based prediction of COVID-19 diagnosis based on symptoms," *NPJ Digital Med.*, vol. 4, no. 1, pp. 1–5, 2021.
- [143] L. Longo, R. Goebel, F. Lecue, P. Kieseberg, and A. Holzinger, "Explainable artificial intelligence: concepts, applications, research challenges and visions," In *International Cross-Domain Conference for Machine Learning and Knowledge Extraction 2020 Aug 25*, Cham: Springer, pp. 1–16.
- [144] J. B. Awotunde, S. A. Ajagbe, M. A. Oladipupo, *et al.*, "An improved machine learnings diagnosis technique for COVID-19 pandemic using chest X-ray images," In *International Conference on Applied Informatics 2021 Oct 28*, Cham: Springer, pp. 319–330, 2021.
- [145] J. B. Awotunde, R. O. Ogundokun, A. E. Adeniyi, K. M. Abiodun, and G. J. Ajamu, "Application of mathematical modelling approach in COVID-19 transmission and interventions strategies," In *Modeling, Control and Drug Development for COVID-19 Outbreak Prevention*, Cham: Springer, pp. 283–314, 2022.
- [146] K. M. Abiodun, J. B. Awotunde, D. R. Aremu, and E. A. Adeniyi, "Explainable AI for fighting COVID-19 pandemic: opportunities, challenges, and future prospects," In *Computational Intelligence for COVID-19 and Future Pandemics*, 2022, pp. 315–32.
- [147] Y. Kim, P. C. Kyriakidis, and N. W. Park, "A cross-resolution, spatio-temporal geostatistical fusion model for combining satellite image time-series of different spatial and temporal resolutions," *Remote Sensing*, vol. 12, no. 10, pp. 1553, 2020.
- [148] P. P. Angelov, E. A. Soares, R. Jiang, N. I. Arnold, and P.M. Atkinson, "Explainable artificial intelligence: an analytical review," *Wiley Interdiscip. Rev. Data Mining Knowl. Discov.*, vol. 11, no. 5, pp. e1424, 2021.
- [149] I. J. Goodfellow, J. Pouget-Abadie, M. Mirza, *et al.*, *Generative Adversarial Nets (Advances in Neural Information Processing Systems)*, Red Hook, NY: Curran, pp. 2672–2680, 2014.
- [150] R. M. Byrne, "Counterfactuals in Explainable Artificial Intelligence (XAI): evidence from human reasoning." In *IJCAI 2019 Aug 10*, pp. 6276–6282.
- [151] J. E. Taylor and G. W. Taylor, "Artificial cognition: how experimental psychology can help generate explainable artificial intelligence," *Psychono. Bull. Rev.*, vol. 28, no. 2, pp. 454–475, 2021.

- [152] M. A. Vu, T. Adalı, D. Ba, *et al.*, “A shared vision for machine learning in neuroscience,” *J. Neurosci.*, vol. 38, no. 7, pp. 1601–1607, 2018.
- [153] J. M. Fellous, G. Sapiro, A. Rossi, H. Mayberg, and M. Ferrante, “Explainable artificial intelligence for neuroscience: behavioral neurostimulation,” *Front. Neurosci.*, vol. 13, pp. 1346, 2019.
- [154] P. Angelov and E. Soares, “Towards explainable deep neural networks (xDNN),” *Neural Netw.*, vol. 130, pp. 185–194, 2020.
- [155] P.P. Angelov and X. Gu, “Toward anthropomorphic machine learning,” *Computer*, vol. 51, no. 9, pp. 18–27, 2018.
- [156] J. Bien and R. Tibshirani, “Prototype selection for interpretable classification,” *Ann. Appl. Stat.*, vol. 5, no. 4, pp. 2403–2424, 2011.
- [157] R. Jiang and D. Crookes, “Shallow unorganized neural networks using smart neuron model for visual perception,” *IEEE Access*, vol. 7, pp. 152701–152714, 2019.
- [158] C. S. Webster, “Alan Turing’s unorganized machines and artificial neural networks: his remarkable early work and future possibilities,” *Evol. Intell.*, vol. 5, no. 1, pp. 35–43, 2012.

