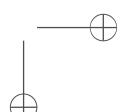
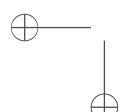


# Contents

Declaration of Authorship	iii
Abstract	v
Resumen	vii
Resum	ix
Acknowledgements	xi
Contents	xiii
<b>1 Introduction</b>	<b>1</b>
1.1 Motivation and Rationale . . . . .	1
1.2 Cardiac Anatomy and Electrophysiology . . . . .	3
1.2.1 The Heart . . . . .	3
1.2.2 Cardiac Tissue . . . . .	6
1.2.3 Cardiomyocytes . . . . .	8
1.3 Atrial Fibrillation . . . . .	11
1.3.1 Pathophysiology . . . . .	11
1.3.2 Treatment and Management of Atrial Fibrillation . . . . .	16
<b>2 State of the Art</b>	<b>21</b>
2.1 Clinical Stratification for Atrial Fibrillation . . . . .	21
2.1.1 Risk Scores for Stroke Prevention . . . . .	22
2.1.2 Risk Scores for Major Bleeding . . . . .	23

xiii



2.1.3	Risk Scores for AF Onset . . . . .	24
2.1.4	Risk Scores for AF Recurrence . . . . .	26
2.2	Machine Learning . . . . .	27
2.2.1	Supervised learning . . . . .	27
2.2.2	Unsupervised learning . . . . .	28
2.2.3	Semi-supervised learning . . . . .	30
2.3	Atrial Fibrillation Phenotypes . . . . .	31
2.4	Clinical Decision Support Systems . . . . .	33
2.4.1	Five Rights of CDSS . . . . .	33
2.4.2	CDSS Design Principles . . . . .	35
2.4.3	CDSS for the Management of Atrial Fibrillation . . . . .	37
<b>3</b>	<b>Hypotheses and Objectives</b>	<b>47</b>
3.1	Hypotheses . . . . .	47
3.2	Objectives . . . . .	48
<b>4</b>	<b>Materials and Methods</b>	<b>51</b>
4.1	Systematic Literature Review . . . . .	51
4.1.1	Search Strategy . . . . .	52
4.1.2	Inclusion and Exclusion Criteria . . . . .	52
4.1.3	Selection Process . . . . .	53
4.2	Semi-Supervised Clustering with Survival Data . . . . .	53
4.2.1	Background . . . . .	54
4.2.2	Survival Hierarchical Agglomerative Clustering (S-HAC) .	57
4.2.3	Locally Smoothed Survival KMeans . . . . .	60
4.2.4	Simulation Study . . . . .	61
4.2.5	Benchmark Study . . . . .	63
4.3	Procedure to Identify Atrial Fibrillation Phenotypes . . . . .	65
4.3.1	Study Data Base . . . . .	65
4.3.2	Knowledge Representation . . . . .	67
4.3.3	Study Design . . . . .	67
4.4	User Centered Evaluation . . . . .	72
4.4.1	Study Design . . . . .	72
4.4.2	Setting and Recruitment . . . . .	73
4.4.3	Data Collection . . . . .	73
4.4.4	Data Analysis . . . . .	83
<b>5</b>	<b>Results</b>	<b>85</b>
5.1	Systematic Literature Review . . . . .	85
5.1.1	Biomarkers . . . . .	88
5.1.2	Synthesis . . . . .	90

5.2	Semi-Supervised Clustering with Survival Data . . . . .	93
5.2.1	Simulation Study . . . . .	93
5.2.2	Benchmark Study . . . . .	96
5.3	Atrial Fibrillation Phenotypes . . . . .	98
5.3.1	Cohort Characteristics . . . . .	98
5.3.2	Patient Phenotypes . . . . .	100
5.3.3	Treatment Responses . . . . .	101
5.4	User Centered Evaluation . . . . .	105
5.4.1	Qualitative Analysis . . . . .	105
5.4.2	Quantitative Analysis . . . . .	115
<b>6</b>	<b>Discussion</b>	<b>119</b>
6.1	Systematic Literature Review . . . . .	119
6.2	Semi-Supervised Clustering with Survival Data . . . . .	120
6.2.1	Simulation Study . . . . .	120
6.2.2	Benchmark Study . . . . .	121
6.3	Atrial Fibrillation Phenotypes . . . . .	121
6.4	User Centered Evaluation . . . . .	123
6.4.1	Current Treatment Approaches . . . . .	123
6.4.2	Requirements for Treatment Selection . . . . .	124
6.4.3	CDSS Evaluation . . . . .	125
<b>7</b>	<b>Conclusion</b>	<b>129</b>
7.1	Revision of Study Objectives . . . . .	129
7.2	Limitations . . . . .	130
7.3	Future Work . . . . .	131
7.4	Scientific Contributions . . . . .	132
7.4.1	Journal Publications . . . . .	132
7.4.2	International Conferences . . . . .	132
<b>Bibliography</b>		<b>135</b>
<b>Index</b>		<b>167</b>
<b>Appendix</b>		<b>167</b>