

CONTENTS

Topic	Page
DEDICATION	II
ACKNOWLEDGEMENTS	III
ABSTRACT	IV
CONTENTS	VI
CHAPTER ONE	
INTRODUCTION	
1.1 Introduction	1
1.2 Research Problem	2
1.3 Research Significance	3
1.4 Research Objectives	3
1.5 Research Hypotheses	4
1.6 Research Methodology	5
1.7 Research Plan	5
1.8 Research Terminology	6

CHAPTER TWO	
LITERATURE REVIEW	
2.1 Introduction	8
2.2 Adaptive Design Definition	12
2.3 Adaptive Design Types	15
1. Adaptive randomization	15
2. Adaptive treatment switching	16
3. Adaptive dose escalation	16
4. Drop the loser design	17
5. Adaptive sample size re-estimation	17
6. Group sequential design	18
7. Adaptive biomarker	19
8. Adaptive hypotheses	19
9. Adaptive seamless phase <i>II/III</i> trial	19
10. Multiple adaptive design	20
2.4 Covariate Adaptive Randomization Methods	20
1. Zelen's method	21
2. Pocock-Simon's method	22

3. Atkinson Optimal Method	25
4. Imbalance Minimization Method	27
5. Marginal Urn Method	29
CHAPTER THREE	
CRITICAL PERCENTAGE METHOD	
3.1 Introduction	31
3.2 Description of Method	31
3.3 Comparison of CPM, MIN and RM Methods	35
CHAPTER FOUR	
A SIMULATION EXPERIMENT	37
CHAPTER FIVE	
PERFORMANCE OF METHODS IN SMALL SAMPLES	
5.1 Introduction	40
5.2 Sample of Size 10	40
5.3 Sample of Size 20	49

CHAPTER SIX	
PERFORMANCE OF METHODS IN MEDIUM SAMPLES	
6.1 Introduction	56
6.2 Sample of Size 40	56
6.3 Sample of Size 60	64
6.4 Sample of Size 80	71
6.5 Sample of Size 100	79
CHAPTER SEVEN	
PERFORMANCE OF METHODS IN LARGE SAMPLES	
7.1 Sample of Size 200	88
7.2 Sample of Size 400	97
7.3 Sample of Size 600	106
7.4 Sample of Size 800	114
7.5 Sample of Size 1000	124
CHAPTER EIGHT	
CONCLUSION	
8.1 Research results	136

8.2 Research recommendations	137
References	138
Appendix A	146
Appendix B	178
Appendix C	192