

TABLE OF CONTENTS

AKNOWLEDGEMENTS	13
1.0 INTRODUCTION.....	13
1.1 GENERAL FRAMEWORK.....	15
1.2 LITERATURE REVIEW	17
1.2.1 Radiation dose-response models	18
1.2.2 Radiation effects at chromosomal and cellular level	22
1.2.3 Radiosensitivity of the hematopoietic system	23
1.2.4 Mayak Product Association	27
1.2.5 Previous studies of long term occupational radiation exposure	30
1.2.6 Sex related differences in radiosensitivity	35
1.2.7 Review of repeated measures analysis techniques	36
1.2.7.1 Univariate analysis of variance (ANOVA)	37
1.2.7.2 Generalized Linear Models (GLM)	37
1.2.7.3 Linear mixed models	38
1.2.7.4 Marginal model and GEE (generalized estimating equations).....	39
1.2.7.5 Spline functions.....	43
1.2.7.6 Missing data	45
1.2.7.7 Methodological overview - summary	46

1.3	OBJECTIVES AND SPECIFIC AIMS	47
2.0	METHODOLOGY.....	49
2.1	BACKGROUND	49
2.2	MAYAK PA WORKERS' EARLY CLINICAL EFFECT DATABASE....	50
2.2.1	Sampling procedures for MWECE database implementation	51
2.2.2	MWECE database format.....	51
2.2.3	Study cohort	53
2.3	STUDY DESIGN	55
2.3.1.1	Definition of study variables.....	56
2.3.1.2	Descriptive analysis	58
2.3.1.3	Statistical methods	59
2.3.1.4	Missing Data.....	67
3.0	RESULTS	70
3.1	DESCRIPTIVE ANALYSIS RESULTS.....	70
3.1.1	Study Cohort Structure.....	70
3.2	MISSING DATA ASSESSMENT RESULTS.....	99
3.2.1	Background	99
3.2.2	Descriptive analysis of the missing data patterns	101
3.2.3	Missing data patterns and mechanisms assessment	102
3.2.3.1	Drop-outs description.....	102
3.2.3.2	Drop-outs mechanism assessment.....	104
3.2.3.3	Mixed patterns missing data description.....	107
3.2.3.4	Mixed patterns missing data assessment.....	109

3.2.3.5	Missing data analysis conclusion.....	113
3.3	STATISTICAL MODELING RESULTS.....	114
3.3.1	Assessment of the coefficients in the models.....	119
3.3.2	Assessment of goodness of fit of the models.....	126
3.3.3	Numerical assessment of goodness of fit of the models	156
3.3.4	Predicting the lymphocyte counts using the five models	159
4.0	DISCUSSION	166
4.1	STRENGTHS OF THE ANALYSIS.....	180
4.2	LIMITATION OF THE ANALYSIS.....	181
5.0	CONCLUSIONS	184
5.1	PUBLIC HEALTH SIGNIFICANCE.....	185
	APPENDIX A - RADIATION PHYSICS.....	186
	APPENDIX B - MWECE DATABASE FORMAT	190
	APPENDIX C - MISSING DATA ASSESSMENT (STATA OUTPUT).....	193
	APPENDIX D - LYMPHOCYTE COUNTS RANGE IN HUMANS	198
	BIBLIOGRAPHY	199

