



***IMPACT OF REMINDER MODULE ON ADHERENCE AND TREATMENT
OUTCOMES AMONG HIV- POSITIVE PATIENTS ON ANTIRETROVIRAL
THERAPY IN HOSPITAL SUNGAI BULOH, MALAYSIA***

SURAJUDEEN ABIOLA ABDULRAHMAN



**IMPACT OF REMINDER MODULE ON ADHERENCE AND TREATMENT
OUTCOMES AMONG HIV- POSITIVE PATIENTS ON ANTIRETROVIRAL
THERAPY IN HOSPITAL SUNGAI BULOH, MALAYSIA**

By

SURAJUDEEN ABIOLA ABDULRAHMAN

**Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in
Fulfillment of the Requirements for the Degree of Doctor of Philosophy**

October 2015

All material contained within the thesis, including without limitation text, logos, icons, photographs and all other artwork, is copyright material of Universiti Putra Malaysia unless otherwise stated. Use may be made of any material contained within the thesis for non-commercial purposes from the copyright holder. Commercial use of material may only be made with the express, prior, written permission of Universiti Putra Malaysia.

Copyright © Universiti Putra Malaysia



DEDICATION

This work is dedicated to my beloved wife Maarufat Olaide Olaosebikan and daughters Haneefah Oyindamola Abdulrahman and Hannan Desola Abdulrahman.



Abstract of thesis presented to the senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy.

IMPACT OF REMINDER MODULE ON ADHERENCE AND TREATMENT OUTCOMES AMONG HIV- POSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY IN HOSPITAL SUNGAI BULOH, MALAYSIA

By

SURAJUDEEN ABIOLA ABDULRAHMAN

October 2015

Chairman : Professor Lekhraj Rampal MBBS, MPH, DrPH, FRSH, FAMM, FAMS, FPHMM

Faculty : Medicine and Health Sciences

Introduction: Adherence to treatment remains the cornerstone of long term viral suppression and successful treatment outcomes among patients receiving antiretroviral therapy (ART). According to WHO, minimum adherence levels of 95% are required for treatment success. Poor adherence to treatment (clinic visits and medication adherence) remains a stumbling block to the success of treatment programs and generates major concerns about possible resistance of the HIV virus to the currently available ARVs. The objective of this study was to evaluate the impact of a mobile phone reminder module on adherence and treatment outcomes among HIV positive patients on ART in Malaysia.

Methods: A single-blinded, parallel group randomized controlled trial conducted in Hospital Sungai Buloh, Malaysia in which 242 Malaysian patients were randomized to intervention or control groups was conducted between January and December, 2014. Intervention consisted of a reminder module delivered through SMS and telephone call reminders by trained research assistants for 24 consecutive weeks, in addition to adherence counseling at every clinic visit. Data on adherence behavior of patients was collected using specialized, pre-validated *Adult AIDS Clinical Trial Group* (AACTG) adherence questionnaires. Data on weight, clinical symptoms, CD4 count and viral load tests were also collected. Data was analyzed using SPSS version 21 and R software. A 5% level of statistical significance was considered for all analysis. Repeated measures ANOVA, Friedman's ANOVA and Multivariate regression models were used to evaluate efficacy of the intervention as well as to establish the relationship between the independent (predictors) and outcome variables.

Results: The response rate after 6 months follow up was 93%. There were no significant differences at baseline in gender, employment status, income distribution and residential location of respondents between the intervention and control group. After 6 months follow up, the mean adherence was significantly higher in the intervention group as compared to the control group. The proportion of respondents

who had good (>95%) adherence was significantly higher in the intervention group. A significantly lower frequency in missed appointments ($p=0.001$), lower viral load ($p=0.001$), higher rise in CD4 count ($p=0.017$), lower incidence of tuberculosis ($p=0.001$) and OIs ($p=0.001$) at 6 months follow up, was observed among patients in the intervention group. We found that both medication adherence and clinic attendance significantly predicts immunological and virological outcomes of antiretroviral therapy.

Conclusion: The findings of the current study indicates that mobile phone reminders are effective in improving adherence (clinic attendance and medication adherence) and treatment outcomes (immunological and virological) among HIV positive patients on ART. The ubiquitous nature of mobile phones even among HIV positive patients from low to middle income countries provides an excellent platform for targeted health interventions, irrespective of the nature of the epidemic, whether concentrated or generalized. Since the success of ART programs is largely measured by retention on treatment, the potential effects of this intervention in tracking patient's clinic attendance and ensuring that they are retained in care remains of immense value in HIV programming.

Keywords: Mobile phone reminders, HIV, adherence, antiretroviral therapy, treatment outcomes

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah.

**KESAN MODUL PERINGATAN BAGI MENINGKATKAN PEMATUHAN
DAN HASIL RAWATAN DI KALANGAN PESAKIT POSITIF HIV YANG
MENJALANI TERAPI ANTIRETROVIRAL DI HOSPITAL
SUNGAI BULOH, MALAYSIA**

Oleh

SURAJUDEEN ABIOLA ABDULRAHMAN

Oktober 2015

**Pengerusi : Profesor. Lekhraj Rampal MBBS, MPH, DrPH, FRSH,
FAMM, FAMS, FPHMM**

Fakulti : Perubatan dan Sains Kesihatan

Pengenalan: Kepatuhan kepada terapi adalah asas kepada supresi virus secara jangka panjang dan kejayaan terhadap terapi antiretroviral (ART). Menurut WHO, tahap pematuhan minimum sebanyak 95% diperlukan bagi kejayaan rawatan. Kepatuhan yang lemah terhadap rawatan (lawatan klinik dan pematuhan pengubatan) masih menjadi penghalang kepada kejayaan program rawatan serta melahirkan kebimbangan yang tinggi tentang kemungkinan kerintangan terhadap virus HIV dengan menggunakan ARV yang sedia ada. Objektif kajian ini bertujuan untuk menentukan keberkesanan telefon mudah alih (peringatan SMS dan panggilan telefon) dalam meningkatkan kepatuhan (kehadiran klinik dan pematuhan pengubatan) dan hasil rawatan di kalangan pesakit HIV yang menjalani ARV di Malaysia.

Kaedah: Satu percubaan klinikal terkawal secara rawak, kumpulan selari dan buta tunggal yang melibatkan 242 berwarganegara Malaysia, pesakit positif HIV yang menjalani terapi antiretroviral telah dijalankan di antara bulan Januari hingga Disember, 2014. Campur tangan terdiri daripada modul peringatan dihantar melalui SMS dan panggilan telefon peringatan pembantu penyelidik dilatih selama 24 minggu berturut-turut, selain menganut kaunseling di setiap lawatan klinik. Data tentang faktor sosiodemografi, gejala klinikal dan pematuhan tingkah laku responden dikumpulkan menggunakan borang soal selidik yang khusus iaitu *Adult AIDS Clinical Trial Group* (AACTG) yang diubah suai dan disahkan terlebih dahulu. Kiraan CD4, beban virus, berat badan, simptom klinikal juga dijalankan dan direkodkan. Data dianalisa dengan menggunakan SPSS versi 21 dan perisian R. Nilai-p < 0.05 dianggap signifikan dari segi statistik. Repeated measures ANOVA, Friedman's ANOVA dan model regresi multivariat digunakan untuk mengkaji keberkesanan intervensi serta menentukan perkaitan antara pemboleh ubah bebas dan pemboleh hasil.

Keputusan: Kadar tindak balas selepas 6 bulan susulan adalah 93%. Tiada perbezaan yang ketara di peringkat asas dari segi jantina, status pekerjaan, pendapatan, dan lokasi

kediaman dalam kumpulan campur tangan dan kumpulan kawalan. Selepas susulan daripada 6 bulan, pematuhan purata didapati meningkat di kalangan kumpulan campur tangan berbanding dengan kumpulan kawalan. Peratusan responden dalam kumpulan campur tangan juga didapati mempunyai kepatuhan yang baik ($> 95\%$) pada 6 bulan susulan. Terdapat kekerapan yang rendah dan kepentingan pembolehubah seperti pelantikan terlepas ($p = 0.001$), beban virus rendah ($p = 0.001$), tahap kiraan CD4 tinggi ($p = 0.004$), insiden yang lebih rendah daripada batuk kering ($p = 0.001$) dan OI ($p = 0.001$) pesakit dalam kumpulan campur tangan. Kami mendapati bahawa kedua-dua pematuhan kepada rawatan dan kehadiran klinik ketara boleh meramalkan hasil imunologi dan virologi terapi antiretroviral.

Kesimpulan: Dapatan kajian ini menunjukkan peringatan telefon mudah alih berkesan untuk meningkatkan kepatuhan (rawatan dan ubat) dan hasil rawatan (imunologi dan virologi) dalam kalangan pesakit HIV positif yang menjalani ART. Sifat sentiasa ada telefon mudah alih walaupun dalam kalangan pesakit HIV positif daripada negara berpendapatan rendah dan sederhana menyediakan platform terbaik untuk penambahbaikan kesihatan terarah tanpa mengira epidemik sama ada tertumpu mahu pun menyeluruh. Oleh sebab kejayaan program ART bergantung pada tempoh rawatan, potensi penambahbaikan ini dalam menjejak kehadiran pesakit menerima rawatan dan memastikan mereka terus dijaga adalah sesuatu yang bernilai dalam merawat HIV.

Kata kunci: Peringatan telefon bimbit, HIV, pematuhan, terapi antiretroviral, hasil rawatan

ACKNOWLEDGEMENTS

All praise are due to Allah, the Lord of the Universe, the benevolent, the merciful, by whose blessings, mercy and grace we are able to actualize our dreams. I bear witness that there is no God worthy of worship but Allah and that Muhammad is his messenger. May the peace and blessings of Allah be upon the noble prophet, the best of all creations, the exalted and of noble character, Muhammad (SAW), his pure progeny, his righteous companions and all those who follow their footsteps with sincerity and Monotheism up to the end of time? Most importantly, I want to give unreserved glory and praise to Almighty Allah, for giving me this noble opportunity to improve myself and achieve my dreams.

Let me begin by expressing my immeasurable, deep-seated feeling of gratitude and appreciation to my amiable supervisor and Chairman of my supervisory committee, Professor Dr. Lekhraj Rampal for providing me with his revered guidance, impeccable advice and invaluable assistance and encouragement throughout the period of my study in Malaysia. His continuous and unrelenting drive for excellence has rubbed off on me and set me in the path of greatness as I begin a new life as an independent researcher. For these and the opportunity he granted me to improve myself under his watch, I say a big THANK YOU!

I equally wish to thank my co-supervisors: Prof. Dr. Norlijah Othman, Assoc. Prof. Dr. Faisal bn. Haji Ibrahim, Dr. Hayati binti Kadir@Shahar and Dr. Anuradha P. Radhakrishnan, for their relentless guidance and support throughout my study. Without their support, I would have been unable to surmount some of the critical challenges that I faced during the course of my data collection and analysis. For these and every other assistance you provided to me, I remain grateful and may the good Lord continue to bless you all.

I would like to specially acknowledge the enormous support of Jayanthi Arumugam for the strategic role she played in the course of my data collection. Her selfless contribution to ensuring the successful completion of my research work will not be forgotten in a hurry. I am also grateful to the entire personnel of the ID clinic, Hospital Sungai Buloh for their support, encouragement and guidance throughout the period of my data collection in the clinic.

More importantly, I am grateful to my beloved parents, brothers, sisters, uncles and aunts for their unfailing love, prayers, care and empathy during these challenging years. Most of all, my deepest appreciation and gratitude goes to my beloved wife and daughters for their patience, endurance, unwavering support, love and thoughtfulness during these crucial years of my study. I am particularly humbled by their encouragement, sense of responsibility and motivation upon which I leveraged to achieve this feat. Indeed, you all made my study in Malaysia not only memorable but worthwhile. May the Almighty Allah continue to keep us together in love and good health.

It is noteworthy to also appreciate all those who were directly or indirectly involved in the realization of my fulfilled mission. Never will I forget some people like Engineer Abdulqayoom Tunji Lawal, his beloved wife Bisola and son AbdulAwwal for their support and encouragement that even led me to taking the first step towards this academic landmark achievement. Special thanks to Prof. Abdulkareem, Dr. Mukhtar Anka, Dr. Rufai Aliyu, Osman Abubakar Haji Mohamed and Dr. Chindo Ibrahim Bisallah for their support, friendliness and guidance during the course of my study. I remain grateful to you all.

It will remain evergreen in my mind the immeasurable knowledge and skills imparted in me by members of staff of the Department of Community Health, Faculty of Medicine and Health Sciences (FPSK) and Faculty of Education, Universiti Putra Malaysia. Indeed, you have all equipped me with the requisite capacity to excel in the challenging world of scientific research.

Finally, I would like to thank all my friends, colleagues and all those individuals who in one way or the other assisted me in life but their names do not appear in this text.

Surajudeen A. Abdulrahman

This thesis was submitted to the senate of the Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory committee were as follows:

Lekhraj Rampal, MBBS, MPH, DrPH, FRSH, FAMM, FAMS, FPHMM

Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Norlijah Othman, MBBS, MRCP (UK)

Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Faisal bin Hj. Ibrahim, MBBS, MPH, MPHMM

Associate Professor
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

**Hayati binti Kadir@Shahar, MBBChBAO, M.Community Health
(Epidemiology & Biostatistics)**

Senior Lecturer
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

Anuradha P. Radhakrishnan, MBBS, MRCP (UK)

Consultant Infectious Diseases
Hospital Sungai Buloh
Malaysia
(Member)

BUJANG KIM HUAT, PhD

Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature: _____
Name of
Chairman of
Supervisory
Committee: Professor Lekhraj Rampal,

Signature: _____
Name of
Member of
Supervisory
Committee: Professor Norlijah Othman

Signature: _____
Name of
Member of
Supervisory
Committee: Associate Professor Faisal bin Hj. Ibrahim

Signature: _____
Name of
Member of
Supervisory
Committee: Dr Hayati binti Kadir@Shahar,

Signature: _____
Name of
Member of
Supervisory
Committee: Anuradha P. Radhakrishnan

TABLE OF CONTENTS

ABSTRACT	Page
ABSTRAK	i
ACKNOWLEDGEMENTS	iii
APPROVAL SHEET	v
DECLARATION	vii
LIST OF TABLES	ix
LIST OF FIGURES	xv
LIST OF APPENDICES	xvii
LIST OF ABBREVIATIONS	xviii
	xx

CHAPTER

1	INTRODUCTION	1
	1.1 Background	1
	1.2 Problem statement	3
	1.3 Significance of the study	5
	1.4 Research questions	5
	1.5 Objectives of the study	5
	1.5.1 General objective	5
	1.5.2 Specific objectives	6
	1.6 Research Hypotheses	6
2	LITERATURE REVIEW	7
	2.1 Epidemiology of HIV/AIDS	7
	2.2 Modes of transmission	8
	2.3 Clinical history and features	8
	2.4 Immune response to HIV	9
	2.5 Antiretroviral therapy	10
	2.5.1 When to start ART	10
	2.5.2 What ART regimen to start with (first-line ART)	12
	2.5.3 What ART regimen to switch to (second-line ART)	12
	2.6 Monitoring response to ART and diagnosing treatment failure	13
	2.7 Adherence to ART	17
	2.8 Factors associated with non-adherence	18
	2.8.1 Patient-related factors	18
	2.8.1.1 Socio-demographic factors	18
	2.8.1.2 Psychosocial factors	19
	2.8.1.3 Adolescent transition factors	19
	2.8.1.4 Social support	19
	2.8.1.5 Patient's knowledge and beliefs about the disease and medications	19
	2.8.1.6 Confusion, forgetfulness, misunderstanding of the regimen and instructions	20
	2.8.2 Regimen-related factors	20
	2.8.2.1 Complexity of antiretroviral regimen	20
	2.8.2.2 Side effects	20
	2.8.3 Health system/health care team-related factors	21

2.8.4	Provider-patient relationship factors	21
2.9	Measuring and monitoring adherence to ART	22
2.9.1	Medication Event Monitoring System (MEMS) Caps	23
2.9.2	Pharmacy refill records	23
2.9.3	Pill counts	24
2.9.4	Self-report	24
2.9.5	Viral load monitoring	25
2.9.6	Biological markers	25
2.10	Interventions to improve adherence	26
2.10.1	Programme-level interventions	26
2.10.2	Individual-level interventions	27
2.10.2.1	Patient education and collaborative planning	28
2.10.2.2	Adherence case management	28
2.10.2.3	Directly observed therapy	29
2.10.2.4	Simplified treatment regimens	29
2.10.2.5	Adherence devices	29
2.10.2.5.1	Medication organizers	30
2.10.2.5.2	Visual medication schedules	30
2.10.2.5.3	Reminder devices	30
2.10.2.6	Substance use and mental health interventions	31
2.10.2.7	Nutritional support	31
2.10.2.8	Financial support	31
2.11	Systematic review of recent evidence supporting mobile phone interventions	32
2.12	Adherence behavioral change models	33
2.12.1	Social Cognition Models (SCM)	34
2.12.2	Azjen's Theory of Planned Behavior (TPB)	35
2.13	Conceptual Framework	38
3	METHODOLOGY	40
3.1	Study location	40
3.1.1	Background of study location	40
3.2	Study design	41
3.3	Study population	41
3.4	Sampling frame	41
3.5	Sampling unit	41
3.6	Sample size estimation	41
3.7	Sampling technique	43
3.8	Inclusion and exclusion criteria	43
3.8.1	Inclusion criteria	43
3.8.2	Exclusion criteria	44
3.9	Data collection	44
3.9.1	Study instruments	44
3.9.1.1	Baseline medication adherence questionnaire	44
3.9.1.2	Follow-up medication adherence questionnaire	47
3.9.2	Anthropometry and biomedical analysis	48
3.9.3	Data on scheduled clinic attendance for consultation and drug refill	49
3.10	Validity and reliability of the study instruments	49
3.10.1	Validity of questionnaire	49
3.10.1.1	Face validity	49

3.10.1.2	Content validity	49
3.10.2	Reliability	50
3.11	Intervention Protocol	51
3.11.1	Development of reminder module	51
3.11.2	Summary of the content of the reminder module	52
3.11.3	Quality control	55
3.11.3.1	Training of research assistants	55
3.11.3.2	Module validation and pretesting	56
3.11.4	Module implementation	57
3.12	Ethical approval and consent	59
3.13	Data processing and analysis	59
3.14	Study variables	60
3.15	Operational definition of terms	60
4	RESULTS	62
4.1	Response rate	62
4.2	Sociodemographic characteristics of respondents	63
4.3	Baseline medication adherence, understanding and preparedness for HIV medications, psychosocial support and other treatment-related factors	64
4.4	Baseline psychosocial symptoms/well-being	44
4.5	Baseline condition-related factors	69
4.6	Baseline therapy-related and patient-related factors	72
4.7	Baseline CD4 count, viral load, haematological, renal, liver, anthropometric and blood pressure profile	73
4.8	Sociodemographic predictors of adherence behavior	75
4.8.1	Univariate multinomial logistic regression analysis showing effect of sociodemographic factors on adherence	75
4.8.2	Multivariate multinomial logistic regression analysis showing effect of sociodemographic factors on adherence	76
4.9	Impact of mobile phone reminder module (delivered via SMS and telephone call reminders) on clinic attendance and medication adherence	77
4.9.1	Main effect of group, time and group x time interaction on adherence	77
4.9.2	Main effect of treatment group on hospital attendance (regularity of scheduled clinic visits)	82
4.10	Effect of intervention on clinical (weight) immunological (CD4 count) and virological (viral load) outcomes of treatment	83
4.10.1	Main effect of group, time and group x time interaction or CD4 count	83
4.10.2	Main effect of group, time and group x time interaction for Viral Load	86
4.10.3	Main effect of group, time and group x time interaction for weight	90
4.11	Effect of medication adherence on clinical (weight), immunological (CD4 count) and virological (viral load) outcomes of antiretroviral therapy	93
4.11.1	Simple linear regression analysis showing effect of adherence on weight, CD4 count, and viral load after 6 months follow up	93

4.11.2	Multiple linear regression analysis showing effect of adherence and hospital attendance on weight, CD4 count, and viral load after 6 months follow up	94
5	DISCUSSION	96
5.1	Baseline sociodemographic factors	96
5.1.1	Age	96
5.1.2	Gender	96
5.1.3	Ethnicity	97
5.1.4	Monthly family income	97
5.1.5	Education level	97
5.1.6	Employment status	98
5.1.7	Residential location	98
5.2	Baseline adherence	98
5.3	Baseline CD4 count	99
5.4	Baseline viral load	100
5.5	Baseline weight	101
5.6	Baseline TB status	101
5.7	Baseline opportunistic infection (OI) index	102
5.8	Sociodemographic predictors of adherence and hospital attendance	102
5.9	Effect of intervention on medication adherence	103
5.10	Effect of intervention on hospital attendance (regularity of scheduled clinic visits)	105
5.11	Effect of medication adherence on CD4 cell count	107
5.12	Effect of medication adherence on viral load	108
5.13	Effect of medication adherence on weight	109
5.14	Effect of hospital attendance (regular clinic visits) on CD4 count	110
5.15	Effect of hospital attendance (regular clinic visits) on viral load	111
5.16	Effect of hospital attendance (regular clinic visits) on weight	111
6	SUMMARY, CONCLUSION AND RECOMMENDATIONS	113
6.1	Strength of the study	113
6.2	Limitations	114
6.3	Conclusion	115
6.4	Recommendations	116
	REFERENCES	118
	APPENDICES	132
	BIODATA OF STUDENT	186
	LIST OF PUBLICATIONS	189

LIST OF TABLES

Table	Page
2.1: Summary of when to initiate ART in adults and adolescents	11
2.2: Programme options for ART for PMTCT	11
2.3: Summary of recommendations on when to start ART in children	11
2.4: Summary of first-line ART regimens for adults, adolescents, pregnant and breastfeeding women and children	12
2.5: Summary of preferred second-line ART regimens for adults, adolescents, pregnant women and children	13
2.6: Laboratory monitoring before and after initiating ART	15
2.7: WHO definitions of clinical, immunological and virological failure for the decision to switch ART regimen	16
2.8: Results of rapid systematic review of mobile phone adherence interventions	33
3.1: Results of the test-retest reliability for baseline questionnaire	51
3.2: Result of the test-retest reliability for follow-up questionnaire	51
3.3: Sections of the reminder module which address the concepts of the TPB Model	54
4.1: Distribution of the study respondents by socio-demographic characteristics	63
4.2: Baseline medication adherence, understanding and preparedness for HIV medications, psychosocial support and other treatment-related factors	66
4.3: Baseline psychosocial symptoms/well-being	68
4.4: Baseline condition-related factors	71
4.5: Baseline therapy-related and patient-related factors	73
4.6: Baseline CD4 count, viral load, hematological, renal, liver, anthropometric and blood pressure profile	75
4.7: Univariate multinomial logistic regression of socio-demographic factors on adherence	76
4.8: Multivariate multinomial logistic regression showing significant predictors of adherence among socio-demographic factors	77
4.9: Main effect of treatment group on mean adherence	78
4.10: Main effect of treatment group on adherence level	78
4.11: Summary table of 2-way repeated measures ANOVA for adherence	78
4.12: Multiple pairwise comparison of adherence by time points in the intervention group	80
4.13: Multiple pairwise comparison of adherence by time points in the control group	80

4.14:	Change in adherence level following intervention in the intervention group	81
4.15:	Multiple pairwise comparison of adherence level by time points in the intervention group	81
4.16:	Multiple pairwise comparison of adherence level by time points in the control group	82
4.17:	Main effect of treatment group on Hospital attendance (regularity of scheduled clinic visits)	82
4.18:	Distribution of number of missed (scheduled) appointments by treatment group	83
4.19:	Main effect of treatment group on CD4 count	84
4.20:	Summary table of 2-way repeated measures ANOVA for CD4 count	84
4.21:	Pairwise comparison of CD4 count by time points in the intervention and control group	85
4.22:	Main effect of treatment group on Viral Load	86
4.23:	Summary table of 2-way repeated measures ANOVA for Viral Load	87
4.24:	Pairwise comparison of Viral Load by time points in the intervention and control group	88
4.25:	Main effect of treatment group on weight	91
4.26:	Summary table of 2-way repeated measures ANOVA for weight	91
4.27:	Multiple pairwise comparison of weight by time points in the intervention group	93
4.28:	Multiple pairwise comparison of weight by time points in the control group	93
4.29:	Simple linear regression analysis showing effect of adherence on weight, CD4 count, viral load and viral load log after 6 months follow up	94
4.30:	Multiple linear regression analysis showing effect of adherence and hospital attendance on weight, CD4 count and viral load after 6 months follow up	95

LIST OF FIGURES

Figure	Page
2.1: Azjen's Theory of Planned Behavior	36
2.2: Adherence behavioral control model (based on Azjen's TPB, 2006)	37
2.3: Conceptual framework of the study showing relationship between independent and outcome variables	69
3.1: Schematic diagram of the development of the reminder module	52
3.2: Study flow diagram showing recruitment procedure and key components of the intervention	58
4.1: Response rate	62
4.2: Interaction plot of treatment group x time on adherence	79
4.3: Interaction plot of treatment group x time on CD4 count	85
4.4: Interaction plot of treatment group x time for viral load log	89
4.5: Interaction plot of treatment group x time for viral load	90
4.6: Interaction plot of treatment group x time for weight	92

LIST OF APPENDICES

Appendix	Page
A: Respondents Information sheet (English)	132
B1: Consent form (English)	134
B2: Respondents Information sheet (Bahasa Malaysia)	135
B3: Consent form (Bahasa Malaysia)	135
B4: Baseline medication Adherence Questionnaire	138
B5: Part A: Understanding and level of preparedness to take HIV medications	138
B6: Part B: Level of psychosocial support	138
B7: Part C: Reasons for missing medications	139
B8: Part D: Period and number of missed medications	139
B9: Part E1: Assessment of psychosocial symptoms/well-being (past 1 week)	139
B10: Part E2: Assessment of psychosocial symptoms/well-being (past 1 month)	140
B11: Part F: History of drug and alcohol use	140
B12: Part G: Socio-demographic characteristics	142
B13: Part H: Source of HIV infection and disclosure status	143
B14: Part I: Review of symptoms	143
C1: Follow-up medication adherence Questionnaire	145
C2: Part A: Review of current medications	145
C3: Part B: Review of medication adherence in the past four days	147
C4: Part C: Review of medication schedule in the past four days	147
C5: Part D: Review of special instructions associated with medications	148
C6: Part E: Review of medication schedule on weekends	148
C7: Part F: When patient last missed medications	148
C8: Part G: Reasons for missing medications	148
C9: Part H: Review of symptoms	149
D: Intervention Module	151

E:	Ethical approval letter from UPM	179
F:	Approval letter from Ministry of Health	182
G:	Ethical approval letter from Hospital Sungai Buloh	186



LIST OF ABBREVIATIONS

ART	Antiretroviral Therapy
ARV	Antiretroviral
AACTG	Adults AIDS Clinical Trial Group
ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine Transaminase
ALP	Alkaline Phosphatase
ANOVA	Analysis of Variance
ATV/r	Atazanavir/ritonavir
AZT	Zidovudine
BP	Blood Pressure
CDC	Centers for Disease Control
CD4	Cluster of Differentiation 4
CD8	Cluster of Differentiation 8
CI	Confidence Interval
CONSORT	Consolidated Standards of Reporting Trials
DBP	Diastolic Blood Pressure
DNA	Deoxyribonucleic Acid
DOTS	Directly Observed Therapy Shortcourse
DRV	Drunavir
DRV/r	Drunavir/ritonavir
d4T	Stavudine
EDA	Exploratory Data Analysis
EFV	Efavirenz
FBC	Full Blood Count
FET	Fisher's Exact Test
FTC	Emtricitabine
HAART	Highly Active Antiretroviral Therapy

HAPA	Health Action Process Approach
HBM	Health Belief Model
HBV	Hepatitis B Virus
HBsAg	Hepatitis B surface Antigen
HIV	Human Immunodeficiency Virus
HIV-1	Human Immunodeficiency Virus – 1
HIV-2	Human Immunodeficiency Virus – 2
HTC	HIV Testing and Counselling
IDU	Injecting Drug Use/User
LFT	Liver Function Test
LTFU	Lost-to-follow-up
LPV/r	Lopinavir/ritonavir
MAC	Malaysia AIDS Council
MEMS	Medication Events Monitoring System
mmHg	Millimeter Mercury
MSM	Men who have sex with men
NIH	National Institute of Health
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NVP	Nevirapine
OI	Opportunistic Infection
OR	Odds Ratio
PCV	Packed Cell Volume
PCP	Pneumocystis Carinii Pneumonia
PI	Protease Inhibitor
PLHIV	People Living with HIV
PML	Progressive Multifocal Leukoencephalopathy
PMT	Protection Motivation Theory
PMTCT	Prevention of Mother to Child Transmission
RCT	Randomized Controlled Trial

RM	Ringgit Malaysia
RNA	Ribonucleic Acid
SBP	Systolic Blood Pressure
SD	Standard Deviation
SGPT	Serum Glutamic Pyruvic Transaminase
SMS	Short Message Service
SPSS	Statistical Package for Social Sciences
STI	Sexually Transmitted Infection
SQV/r	Saquinavir/ritonavir
TB	Tuberculosis
TDF	Tenofovir
TMC	Transtheoretical Model of Change
TPB	Theory of Planned Behaviour
UK	United Kingdom
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children Fund
UPM	Universiti Putra Malaysia
USA	United States of America
VAS	Visual Analogue Scale
VMS	Visual Medication Schedule
WHO	World Health Organization
ZDV	Zidivudine
3TC	Lamivudine

This chapter provides a brief overview on the background of the study, its objectives

CHAPTER 1

INTRODUCTION

This chapter provides a brief overview on the background of the study, its objectives, problem statement, research questions as well as the significance of the study. The research hypotheses and conceptual framework are also explicitly itemized.

1.1 Background

The first case of Acquired Immune Deficiency Syndrome (AIDS) was reported in 1981 among homosexual men in the United States. In 1983, its causative agent, the Human Immunodeficiency Virus (HIV), was identified. Shortly afterwards (mid-1980s), some evidence emerged to show how slowly over time the virus had spread unnoticed to several parts of the world. Several distinct epidemics characterize this globally devastating pandemic, each with their peculiar origin, with regards to geographical spread and population groups affected, and often consist of variations in frequencies and types of risk behaviours and practices, such as sharing drug injection equipment or engaging in unprotected, casual sex with multiple partners (United Nations/WHO, 2003). Since then, the epidemic has taken generalized, concentrated or low epidemic proportions within and between populations in different countries, with sub-Saharan Africa being worst hit.

Already, over 30 million deaths from AIDS-related diseases have been recorded globally (United Nations, 2011). 2.3 million new infections, and 1.6 million deaths from AIDS-related causes were reported among men, women and children in 2012 alone. As at 2012, the number of persons living with HIV globally stood at 35.3million (UNAIDS, 2013).

Greater diversity in the AIDS pandemic has been observed in Asia compared to Africa. Because Asia accounts for about 50% of the world's population, apparently minimal differences in the infection rates could translate to enormous increase in the absolute number of people infected. "The total number of people living with HIV (PLHIV) in Asia and the Pacific is thought to be about 4.9 million" (UNAIDS, 2013). About 50% (2.4 million) of these were in India, 15% (740,000) in China, 11% (530,000) in Thailand, 5% (240,000) in Myanmar and only about 1.9% (93,000) in Malaysia (UNAIDS, 2010). With the exception of Thailand, almost all other Asian countries have a national prevalence of less than 1% among their adult populations. However owing to very large population sizes in some of the countries in this region, infection rates and patterns in some smaller provinces and states may be masked by national averages. For example, more than 50% of people living with HIV in China are from five provinces (UNAIDS, 2011).

Men who have sex with men, injecting drug users, sex workers and their partners constitute the most-at-risk groups in many Asian countries. However, an evolution from a concentrated to a generalized epidemic has been witnessed in these areas lately. Thailand, among other Asian countries responded rapidly to the epidemic with extensive multi-sectoral campaigns to educate the public and prevent the spread of HIV through multiple simultaneous approaches to HIV prevention – and have succeeded in reducing the prevalence. “Other very populous regions, such as China, have only recently admitted that the spread of HIV threatens their populations, and as a result their prevention work is lagging behind the spread of the virus” (UNAIDS, 2011).

In Malaysia, the first case of HIV was diagnosed in 1986. “By the end of 2013, there was a cumulative figure of 101, 672 HIV cases reported to the Ministry of Health, 20, 235 AIDS cases, and 16, 340 deaths, thus leaving the reported figure of 85, 332 as those living with HIV” (Malaysia 2014 Global AIDS Response Country Progress Report). In 2002, the epidemic peaked with a rate of 28.5 per 100,000 population. Subsequently, a steady decline achieved at a rate of 12.8 per 100,000 population was observed in 2010 (Malaysia National Strategic Plan, 2011-2015). By 2011, the number of persons living with HIV/AIDS increased to 81,000 with 3, 479 new infections in the same year, showing a gradual decline from the 2002 figure of 6, 978. In 2013, there were 3, 393 new infections reported to the Ministry of Health. Cumulative AIDS death in 2009 was estimated at 5,800 (4, 500 – 7,200). The country has an overall prevalence of 0.5% as at 2012.

Notwithstanding the concentrated nature of the HIV/AIDS epidemic in Malaysia among most-at-risk groups like IDUs, MSMs, female sex workers and transgender people, there is increasing evidence that overlapping of injecting drug use and risky sex behavior is occurring, with a resultant amplified HIV infection rates between the different populations. Against the background of IDU being the key driving factor earlier on, the implementation of harm reduction programmes since 2005 has resulted in a significant decline in the number of HIV infections through needle sharing. “In 2011, sexual transmission has superseded IDU as the key driving factor of the epidemic with a ratio of 6 sexual transmissions for every 4 IDU reported” (Malaysia 2012 Global AIDS Response Country Progress Report).

Males constitute majority (78.5%) of cumulative HIV cases in Malaysia. Amongst men, the major routes of infection reported in 2013 were injecting drug use (21.5%) and sexual transmission (73.6%). Likewise, most (51.4%) HIV infections in women occurred through heterosexual transmission (Malaysia 2014 Global AIDS Response Country Progress Report), with most of these being concentrated around Sabah and Sarawak States. Whereas the infection among males has shown a significant decline since 2003, infection in females has shown an opposite trend. Progressively, more infections amongst women and girls are being reported and constituted 21% of new infections countrywide in 2011, relative to about 5% in 2001. In reference to the 2012 UNAIDS Global Report, “the incidence rate of HIV infection among adults 15-49 years old has decreased from 49% to 26% between 2001 and 2011” (Malaysia National Strategic Plan, 2011-2015).

Worldwide, there have been significant and sustained efforts in ensuring universal access to HIV prevention, care and treatment services through collaborative efforts between the respective national Governments and International donor organizations, particularly in low and middle income countries, in line with the Millennium Development Goals. However, the gap between the number of those requiring ART and those who have access to it still leaves much to be desired, with most developing countries still having 50% – 60% unmet needs. The Malaysian Government, as at end of 2013, currently almost entirely provides all the funds for HIV treatment care and support for about 17,369 patients at no cost to the patients on first line medications and heavily subsidized for those on second line ARVs (Malaysia 2014 Global AIDS Response Country Progress Report). The current number of patient on ART in Malaysia represents only about 47% of the estimated number of PLHIV eligible for ART (37, 274). Despite these efforts, the globally recognized issues of injecting drug use, stigma and discrimination as well as poor adherence to treatment (clinic visits and medication adherence) remain a stumbling block to the success of treatment programs and generate major concerns about resistance of the HIV virus to the currently available ARVs.

1.2 Problem Statement

The primary goals of HIV treatment are to reduce morbidity, prolong survival, improve quality of life, sustain viral suppression and preserve or improve immunologic functions. Medication adherence remains the cornerstone of long-term HIV suppression. Medication adherence prevents disease progression, and the occurrence of resistant mutations, thereby reducing morbidity, and the necessity for more frequent, complicated regimens which are also relatively more expensive. According to WHO (2005), minimum adherence levels of 95% are required for treatment success (Fairly et al., 2005; Jani, 2004; Paterson et al., 2000; Saple, 2005). Other studies have demonstrated that ARV medication adherence levels of 54 – 95% is required to maintain prolonged viral load suppression depending on the allowable flexibility margins of each ART program. “It is however generally accepted that those patients who adhere strictly to their medication achieve viral suppression, while those who are not adherent may not” (Lee Preininger et al., 2011).

Adherence is a concept with social and emotional components, therefore a therapeutic alliance between the provider and the patient is required to stimulate positive behavioural change and optimize adherence to ART. Several studies to improve adherence have focused on re-enforcing the patient’s commitment and intention to adhere to their medications as a means to stimulate good adherence behaviour. These often include patient education and counselling, use of reminder devices including text messages, adherence case management, and directly observed therapy either as single interventions or in combination. Evidence from these studies have proven their relative effectiveness in improving adherence behaviour.

Several studies have identified stigma and discrimination, pill burden, disclosure issues, depression, medication side effects, drug and alcohol use, unemployment, health and religious beliefs, low family income, lack of community support and integration,

poor pre-initiation adherence counselling as some of the factors that contribute to poor medication adherence and the consequent rate of default and lost-to-follow-up.

Because of its strengths and evidence of wide applicability in the field of health behaviour research, the Theory of Planned Behaviour as described by Icek Azjen (1985) has gained international acceptability and recognition in its ability to enable researchers understand in details the determinants of current intentions and behaviour, predict future health intentions and behaviour and predict which health determinants should be targeted to change behaviour.

Recent innovations using mobile phone technologies such as text messaging to improve medication adherence among patients on ART have been examined and implemented across many countries of the world including Kenya, Peru, Brazil, Botswana, USA with high quality evidence proving the efficacy of weekly SMS reminders to patients in improving adherence to ART when compared to standard of care, particularly in three randomized controlled trials conducted in Kenya (Hovart T. et al., 2012; Lester R.T. et al., 2010; Pop-Eleches C. et al., 2011). Another study systematically reviewed the “scope and effectiveness of phone messaging for HIV/AIDS care” based on different study designs (RCTs, Intervention studies using other study designs, qualitative and cross-sectional surveys) across USA, UK, Kenya, Uganda, Botswana, South Africa, Peru, Pakistan among other countries and concluded that mobile phone messaging could play an important role in HIV/AIDS care and its use is acceptable (van Velthoven et al., 2013). However, further studies across low, middle and high income countries, scale-up of program evidence in hospitals, including cost-effectiveness analysis were recommended.

In Malaysia, like other parts of the world, poor or sub-optimal adherence to treatment (clinic visits and medication adherence) remains a stumbling block to the success of antiretroviral treatment programs and generates major concerns about possibility of growing resistance of the HIV virus to the currently available ARVs. Poor adherence is also a major cause of treatment failure, disease progression and death among HIV patients. Once treatment failure results from poor adherence, the preventive opportunity that antiretroviral treatment provides is lost. Poor adherence also has grave socioeconomic impact on program funding, as more patients who fail on first line regimens have to be provided with the more expensive and complex second line medications (Malaysia National Strategic Plan, 2011-2015; WHO, 2007). The effectiveness of routine adherence counselling (current standard of care) on treatment adherence among HIV patients on ART has not been studied in Malaysia. Factors affecting adherence to ART in HIV patients has also not been extensively studied in Malaysia. Previously, only one study on the factors affecting adherence to ART in HIV patients had been conducted in Malaysia (Yagoub et al., 2012). This is in addition to the seemingly high rate of IDUs, and other co-morbidities among HIV patients (Malaysia National Strategic Plan, 2011-2015). It has therefore become pertinent to identify innovative ways of improving clinic attendance, medication adherence and outcomes of HIV patients on ART.

1.3 Significance of the study

The findings of this study will contribute to the existing body of knowledge on factors associated with treatment default and lost-to-follow-up among ART patients. The results will also provide baseline information on the effectiveness of current standard of care (routine adherence counselling) on treatment adherence and clinical outcomes of HIV patients on ART, which has not been previously studied in Malaysia. As patient retention is the goal standard for measuring the success of any comprehensive HIV care and treatment program, this research will provide an opportunity to test the effectiveness of the introduction of mobile phone technology in improving patient retention (by reducing lost-to-follow-up) in the research location.

The outcome of this research will also inform policy decisions, new strategies and actions by Malaysian Government, care-givers and stakeholders at all levels in improving service delivery for HIV patients (especially with regards to treatment adherence and patient retention), reduce the cost of HIV treatment programs (by reducing the number of patients that will require second-line ARVs due to poor adherence) and also inform the scale-up of this intervention across Malaysia in the future.

This study is in line with key activity 6 of strategy 2 in the current drive by Malaysian Government to promote treatment adherence and enhance timely detection of treatment failure (Malaysia National Strategic Plan, 2011-2015). It is also consistent with current WHO recommendation of interventions to optimize adherence to ART (WHO, 2013).

1.4 Research Questions

1. What are the socio-demographic factors that affect treatment adherence and contribute to treatment default and Lost-to-follow-up among HIV patients on ART?
2. What is the impact of mobile phone reminder module (delivered via SMS and telephone call reminders) on clinic attendance and medication adherence among HIV patients on ART?
3. What is the effect of medication adherence on clinical (weight), immunological (CD4 count) and virological (viral load) outcomes of HIV patients on ART?

1.5 Objectives of the study

1.5.1 General objective

The general objective of this study was to determine the impact of mobile phone reminder module (delivered via SMS and phone call reminders) on adherence (clinic attendance and medication adherence) and treatment outcomes among human immunodeficiency virus positive patients on antiretroviral therapy in Malaysia.

1.5.2 Specific objectives

The specific objectives of the study were as follows:

1. To describe socio-demographic factors (such as age, ethnicity, gender, employment and education status, income) that affect treatment adherence and contribute to treatment default and lost-to-follow-up among HIV positive patients on ART.
2. To develop and implement a reminder module delivered through SMS and telephone calls to improve adherence (clinic attendance and medication adherence) among HIV positive patients on ART.
3. To determine the impact of mobile phone reminder module (delivered via SMS and telephone call reminders) on clinic attendance and medication adherence among HIV positive patients on ART.
4. To determine the effect of medication adherence on the clinical (weight), immunological (CD4 count) and virological outcome (viral load) of HIV positive patients on ART.

1.6 Research Hypotheses

- H₁:** There is no significant difference in the socio-demographic characteristics of HIV patients who adhere very well to their ART compared to those who do not.
- H₂:** The application of mobile phone reminder module (SMS and phone call reminders) will positively impact adherence and treatment outcomes of HIV patients on ART, when compared to routine adherence counselling and paper-based appointment scheduling alone.
- H₃:** There is a strong and direct relationship between good adherence to treatment (regular clinic visits and strict medication adherence) and clinical (weight), immunological (CD4 count) and virological (viral load) outcomes of antiretroviral treatment among HIV patients on ART.

REFERENCES

- Adherence to HIV Treatment Regimens. Recommendations for Best Practices. APHA – www.apha.org/ppp/hiv - June 2004 version. Accessed 13 May, 2013.
- Adherence to long-term therapies. Evidence for action. Geneva, World Health Organization, (2003). (www.who.int/entity/chp/knowledge/publications/adherence_full_report.pdf) accessed 18 April, 2014.
- Alasdair Breckenridge (2009). Pharmacology of Drugs for HIV, Medicine, Vol. 37, Issue 7, 374-377.
- Allen, C. F., Simon, Y., Edwards, J., Simeon, D. T., (2011). Adherence to antiretroviral therapy by people accessing services from Non-governmental HIV support organizations in Three Caribbean countries, West Indian Med. Journal, Vol. 60, Issue 3: 269-275
- Alexander, C. S., Asselin, J. J., Ting, L. S., Montaner, J. S., Hogg, R. S., Yip, B., O'Shaughnessy M. V., & Harrigan P. R. (2003). Antiretroviral concentrations in untimed plasma samples predict therapy outcome in a population with advanced disease. J Infect Dis 2003; 188:541-8.
- Altice, F. L., Mostashari, F., Friedland, G. H. (2001). Trust and the acceptance of and adherence to antiretroviral therapy. Journal of Acquired Immune Deficiency Syndromes, 2001, 28: 47-58.
- Altice, F. L., Bruce, R. D., Lucas, G. M., Lum, P. J., Todd Korthuis P., Flanagan, T. P., Cunningham C. O., et al. (2011). HIV treatment outcomes among HIV-infected, opioid-dependent patients receiving buprenorphine/naloxone treatment within HIV clinical settings: results from a multisite study. Journal of Acquired Immune Deficiency Syndromes, 2011, 56(Suppl. 1): S22-S32.
- Altice, F., Mezger, J., Bruce, R. D. (2003). Preliminary results of a randomized controlled trial of enhanced directly administered antiretroviral therapy (DAART) vs. self-administered therapy (SAT). In: Program and abstracts of the 41st Annual Meeting of the Infectious Diseases Society of America, October 9-12, 2003; San Diego. Abstract 652.
- Ammassari, A., Trotta, M. P., Shalev, N., Tettoni, M. C., Maschi, S., Di Sora, F., Orofino, G., et al. (2011). Timed short messaging service improves adherence and virologic outcomes in HIV-1 infected patients with sub-optimal adherence to antiretroviral therapy. Journal of Acquired Immune Deficiency Syndromes, 2011, 58:e113-e115.
- Andrew McMichael, Lucy Dorrell (2009). The Immune response to HIV, Medicine, Vol. 37, Issue 7, 321-325.
- Arnsten, J. H., Demas, P. A., Farzadegan, H., Grant, R. W., Gourevitch, M. N., Chang, C. J., Buono, D., et al. (2001). Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. Clin Infect Dis 2001; 33:1417-23.

- Baker, J. V., Peng, G., Rapkin, J., Abrams, D. I., Silverberg, M. J., MacArthur, R. D., Cavert, W. P., et al. (2008). CD4+ count and risk of non-AIDS diseases following initial treatment for HIV infection. *AIDS*, 2008, Apr 23; 22 (7):841-848.
- Bamberger, J. D., Unick, J., Klein, P., Fraser, M., Chesney, M., Katz, M. H., (2000). Helping the urban poor stay with antiretroviral HIV drug therapy. *Am J Public Health* 2000; 90:699-701.
- Bangsberg, D. R., Hecht, F. M., Charlebois, E. D., Zolopa, A. R., Holodniy, M., Sheiner, L., Bamberger, J. D., et al. (2000). Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. *Aids* 2000; 14:357-66.
- Bangsberg, D. R., Hecht, F. M., Clague, H., Charlebois, E. D., Ciccarone, D., Chesney, M., Moss, A. (2001). Provider assessment of adherence to HIV antiretroviral therapy. *J Acquir Immune Defic Syndr* 2001; 26:435-42.
- Bangsberg, D. R., (2005). Less than 95% adherence to non-nucleoside reverse transcriptase inhibitor therapy can lead to viral suppression. *Clin Infect Dis* 2006; 43: 939-41.
- Barnighausen, T., Chaiyachati, K., Chimbindi, N., Peoples, A., Haberer, J., Newell, M. (2011). Interventions to increase antiretroviral resistance in sub-Saharan Africa: a systematic review of evaluation studies. *Lancet Infectious Diseases*, 2011, 11:942-951.
- Bartlett, J. A., DeMasi, R., Quinn, J., Moxham, C., Rousseau, F. (2001). Overview of the effectiveness of triple combination therapy in antiretroviral-naïve HIV-1 infected adults. *Aids* 2001; 15:1369-77.
- Bisson, G. P., Gross, R., Bellamy, S., Chittams, J., Hislop, M., Regensberg, L., Frank, I., et al. (2008). Pharmacy refill adherence compared with CD4 count changes for monitoring HIV-infected adults on antiretroviral therapy. *PLoS Medicine*, 2008, 5:e109.
- Bottonari, K. A., Tripathi, S. P., Fortney, J. C., Curran, G., Rimland, D., Rodriguez-Barradas, M., Gifford, A. L., et al. (2012). Correlates of antiretroviral and antidepressant adherence among depressed HIV-infected patients. *AIDS Patient Care and STDs*, 2012, 26: 265-273.
- Bryant, A., Collingham, J., Till, M., et al. (2004). Virologic and clinical outcomes in HIV-infected pregnant women: directly observed therapy can overcome barriers to care. In: Program and abstracts of the 11th Conference on Retroviruses and Opportunistic Infections; February 4-8, 2004; San Francisco. Abstract 922.
- Bupamba, et al. (2010). Ambassadors for adherence: provision of highly effective defaulter tracing and re-engagement by peer educators in Tanzania. XVIII International AIDS Conference, Vienna Austria, 18-23 July 2010 (Abstract MOAE0303; www.iasociety.org/Abstracts/A200739059.aspx, accessed 21 April, 2014)

- Catz, S. L., Kelly, J. A., Bogart, L. M., Benotsch, E. G., and McAiliffe, T. L. (2000). Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychology*, 2000, 19:124–133.
- Chesney, M. A. (2000). Factors affecting adherence to antiretroviral therapy. *Clinical Infectious Diseases*, 2000, 30:S171–176.
- Chesney, M. A., Ickovics, J. R., Chambers, D. B., Gifford, A. L., Neidig, J., Zwickl, B., Wu, A.W. & Patient care committee & adherence working group of the outcomes committee of the Adults AIDS Clinical Trials Group (AACTG) (2000). Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: The AACTG Adherence Instruments, *AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV*, 12:3, 255-266.
- Chung, M. H., Richardson, B. A., Tapia, K., Benki-Nugent, S., Kiarie, J. N., Simoni, J. N., Overbaugh, J., et al. (2011). A randomized controlled trial comparing the effects of counselling and alarm device on HAART adherence and virologic outcomes. *PLoS Medicine*, 2011, 8:e1000422.
- Coffey, S. (2003). Options for Once-daily Dosing of Antiretrovirals: A review of studies published and presented at major conferences. *HIV InSite*, August 2003.
- Cohen, M. S., Chen, Y. Q., McCauley, M., Gamble, T., Hosseinipour, M.C., Kumarasamy, N., Hakim, J. G., et al. (2011). Prevention of HIV-1 infection with early antiretroviral therapy. *New England Journal of Medicine*, 2011, 365: 493-505.
- D'Arminio, M. A., Cozzi, L. A., Rezzac, G., Pezzottic, P., Antinorid, A., Phillips, A. N., Angaranoe, G., et al. (2000). Insights into the reasons for discontinuation of the first highly active antiretroviral therapy (HAART) regimen in a cohort of antiretroviral naïve patients. *AIDS*, 2000, 14:499–507.
- Da Costa, T. M., Barbosa, B. J. P., e Costa, D. A. G., Sigulem, D., Marin, H. D., Filho, A. C., Pisa, I. T. (2012). Results of a randomized controlled trial to assess the effects of mobile SMS-based intervention on treatment adherence in HIV/AIDS-infected Brazilian women and impressions and satisfaction with respect to incoming messages. *International Journal of Medical Informatics*, 2012, 81:257-269.
- Davis, M-A., Boule, A., Eley, B., Moultrie, H., Technau, K., Rabie, H., van Cutsem, G., et al. (2011). Accuracy of immunological criteria for identifying virologic failure in children on antiretroviral therapy – the IeDEA Southern Africa Collaboration. *Tropical Medicine and International Health*, 2011, 16: 1367-1371.
- Dewan, P. K., Gupta, D., Williams, B. G., Thakur, R., Bacahani, D., Khera, A., Wares, D., et al. (2010). National Estimate of HIV seroprevalence among tuberculosis patients in India. *The International Journal of Tuberculosis and Lung Disease*, Volume 14, Number 2, February 2010, pp. 247-249(3)

- Do, N.T., Phiri, K., Bussman, H., Gaolathe, T., Marlink, R.G., Wester, C.W. (2010). Psychosocial factors affecting medication adherence among HIV-infected adults receiving combination antiretroviral therapy (cART) in Botswana. *AIDS Res. Human Retroviruses*; 2010 June; 26(6): 685-691.
- Dowshen, N., Kuhns, L. M., Johnson, A., Holoyda, B. J., Garofalo, R. (2012). Improving adherence to antiretroviral therapy for youths living with HIV/AIDS: a pilot study using personalized, interactive, daily text message reminders. *Journal of Medical Internet Research*, 2012, 14:e51.
- Dowshen, N., D'Angelo, L. (2011). Health care transition for youth living with HIV/AIDS. *Paediatrics*, 2011, 128:762-771.
- Duncombe, C., Ball, A., Passarelli, C., Hirnschall, G. (2013). Treatment 2.0: catalysing the next phase of treatment, care and support. *Current Opinion in HIV and AIDS*, 2013, 8: 4-11.
- EngenderHealth Society (2006). Adherence to treatment for HIV, a training curriculum for counsellors.
- Fairly, C. K, Permana, A., Read, T. R. H. (2005). Long term utility of measuring adherence by self-report compared with pharmacy record in a routine clinic setting, *HIV Medicine* 6, 366-369.
- Family Health International 360 (FHI360) (2007). Adherence counselling participant manual. Community Counsellor training toolkit module 5.
- Fischl, M., Castro, J., Monroig, R., et al. (2001). Impact of directly observed therapy on long-term outcomes in HIV clinical trials. In: Program and abstracts of the 8th Conference on Retroviruses and Opportunistic Infections; February 4-8, 2001; Chicago. Abstract 528.
- Fogarty, L., Roter, D., Larson, S., Burke, J., Gillespie, J., Levy, R. (2002). Patient adherence to HIV medication regimens: a review of published and abstract reports. *Patient Educ Couns* 2002; 46:93-108.
- Free, C., Phillips, G., Galli, L., Watson, L., Felix, L., Edwards, P., Patel, V., & Haines, A. (2013). The effectiveness of Mobile-Health Technology-Based Health Behaviour Change or Disease Management Interventions for Health Care Consumers: A Systematic Review. *PLoS Med* 10(1): e1001 362. Doi: 10.1371/journal.p med.1001362.
- Gale, H. B., Gitterman, S. R., Hoffman, H. J., Gordin, F. M., Benator, D. A., Labriola, A. M., Kan, V. L. (2013). Is frequent CD4+ T-lymphocyte monitoring necessary for persons with counts ≥ 300 cells/ μ l and HIV-1 suppression? *Clinical Infectious Diseases*, 2013, 56: 1340-1343.
- Ganann, R., Ciliska, D., Thomas, H. (2010). Expediting systematic reviews: methods and implications of rapid reviews. *Implement Sci* 2010; 5:56.

- Gifford, A. L., Bormann, J. E., Shively, M. J., Wright, B. C., Richman, D. D., Bozzette, S. A. (2000). Predictors of self-reported adherence and plasma HIV concentrations in patients on multidrug antiretroviral regimens. *J Acquir Immune Defic Syndr* 2000; 23:386-95.
- Giordano, T. P., Guzman, D., Clark, R., Charlebois, E. D., Bangsberg, D. R. (2004). Measuring adherence to antiretroviral therapy in a diverse population using a visual analogue scale. *HIV Clin Trials* 2004; 5:74-9.
- Gonzalez, J. S., Batchelder, A. W., Psaros, C., and Safren S. A. (2011). Depression and HIV/AIDS treatment non-adherence: a review and meta-analysis. *Journal of Acquired Immune Deficiency Syndromes*, 2011, 58: 181-187.
- Gordillo, V., del Amo, J., Soriano, V., Gonzalez-Lahoz, J. (1999). Sociodemographic and psychological variables influencing adherence to antiretroviral therapy. *Aids* 1999; 13:1763-9.
- Haberer, J. E., Kiwanuka, J., Nansera, D., Wilson, I. B., Bangsberg, D. R. (2010). Challenges in using mobile phones for collection of antiretroviral therapy adherence data in a resource-limited setting. *AIDS and Behaviour*, 2010, 14:1294-1301.
- Hasanah, C. I., Zaliha, A. R., & Mahiran, M. (2011). Factors influencing the quality of life in patients with HIV in Malaysia. *Quality of Life Research*, 20(1), 91-100.
- Hardy, H., Kumar, V., Doros, G., Farmer, E., Drainoni, M.-L., Rybin, D., Skolnik, P. R. (2011). Randomized controlled trial of a personalized cellular phone reminder system to enhance adherence to antiretroviral therapy. *AIDS Patient Care STDS*, 25, 153-161
- Haubrich, R. H., Little, S. J., Currier, J. S., Forthal, D. N., Kemper, C. A., Beall, G. N., Johnson, D., et al. (1999). The value of patient-reported adherence to antiretroviral therapy in predicting virologic and immunologic response. California Collaborative Treatment Group. *Aids* 1999; 13:1099-107.
- HIV & AIDS: Society for General Microbiology, 2009.
- Hovart, T., Azman, H., Kennedy, G. E., Rutherford, G. W. (2012). Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection; Cochrane Database of Systematic Reviews, 2012, Issue 3, Art. No.: CD009756, DOI: 10.1002/14651858.CD009756.
- Hugen, P. W., Langebeek, N., Burger, D. M., Zomer, B., Van Leusen, R., Schuurman, R., Koopmans, P. P., & Hekster, Y. A. (2002). Assessment of adherence to HIV protease inhibitors: comparison and combination of various methods, including MEMS (electronic monitoring), patient and nurse report, and therapeutic drug monitoring. *J Acquir Immune Defic Syndr* 2002; 30:324-34.
- Hui-Chen Chu, Nai-Ying Ko (2013). Protocol for Using Mobile Phone Text Messaging to Improve Adherence to Highly Active Antiretroviral Therapy. *Canadian Social Science*, 9 (1), 92-96. Available from:<http://www.cscanada.net/index.php/css/article/view/j.css.1923669720130901.1993> DOI: <http://dx.doi.org/10.3968/j.css.1923669720130901.1993>.

- Icek Azjen (2006). Constructing a TpB Questionnaire: Conceptual and Methodological Considerations. September, 2002 (Revised January, 2006).
- Ikeda, J. M., et al. (2012). SMS messaging improves treatment outcome among the HIV-positive Mayan population in rural Guatemala. XIX International AIDS Conference, Washington, DC, USA, 22-27 July, 2012 (Abstract TUPE673; www.iasociety.org/Abstracts/A200745374.aspx, accessed 28 April, 2014).
- Jani, A. A., (2004). Adherence to HIV treatment regimens: recommendations for best practices, pp. 3-72. Available from <http://www.alpha.org/ppp/hiv>
- Joan M. Duggan, Ann Locher, Brian Fink, Chrystal Okonta and Joana Chakraborty (2009). Adherence to antiretroviral therapy: A survey of factors associated with medication usage, *AIDS Care*, Vol. 21, No. 9, September 2009, 1141-1147.
- Kantor, R., Diero, L., DeLong, A., Kamle, L., Muyonga, S., Mambo, F., Walumbe, E., et al. (2009). Misclassification of first-line antiretroviral treatment failure based on immunological monitoring of HIV infection in resource-limited settings. *Clinical Infectious Diseases*, 2009, 49: 454-462.
- Kimmerling Mina, Wagner Glenn, Ghosh-Dastider Bonnie (2003). Factors associated with accurate self-reported adherence to HIV antiretrovirals. *International Journal of STD & AIDS*; Apr 2003; 14, 4; ProQuest Central pg. 281.
- King, M. S., Brun, S. C., Kempf, D. J. (2005). Relationship between adherence and the development of resistance in antiretroviral-naïve, HIV-1-infected patients receiving lopinavir/ritonavir nelfinavir. *J Infect Dis* 2005; 191: 2046-52.
- Kowalska, J. D., Mocroft, A., Ledergerber, B., Florence, E., Ristola, M., et al. (2011). A standardized algorithm for determining the underlying cause of death in HIV infection as AIDS or non-AIDS related: results from the EuroSIDA study. *HIV Clinical Trials*, 2011, 12:109-117.
- Kunutsor, S., Walley, J., Katabira, E., Muchuro, S., Balidawa, H., Namagala, E., & Ikoona, E. (2010). Using mobile phones to improve clinic attendance amongst an antiretroviral treatment cohort in rural Uganda: A cross-sectional and prospective study. *AIDS & Behaviour*, 14(6), 1347-1353.
- Kunutsor, S., Evans, M., Thoullass, J., Walley, J., Katabira, E., Newell, J. N., & Ikoona, E. (2010). Ascertaining baseline levels of antiretroviral therapy adherence in Uganda: a multimethod approach. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 55(2), 221-224.
- Kunutsor, S., Walley, J., Katabira, E., Muchuro, S., Balidawa, H., Namagala, E., & Ikoona, E. (2010). Clinic attendance for medication refills and medication adherence amongst an antiretroviral treatment cohort in Uganda: a prospective study. *AIDS research and treatment*, 2010.
- Laurent, C., Kouanfack, C., Laborde-Balen, G., Aghokeng, A. f., Mbougua, J. B. T., Boyer, S., Carrieri, M. P., et al. (2011). Monitoring of HIV viral loads, CD4 cell counts, and clinical assessments versus clinical monitoring alone for antiretroviral therapy in rural district hospitals in Cameroon (Stratall ANRS 12110/ESTHER): a randomized non-inferiority trial. *Lancet Infectious Diseases*, 2011, 11:825-833.

- Lester, R. T., Ritvo, P., Mills, E. J., Kariri, A., Karanja, S., Chung, M. H., Jack, W., et al. (2010). Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya 1): a randomized trial. *Lancet* 2010, Nov. 27; 376 (9755): 1838-45.
- Levine, A. M., Richardson, J. L., Marks, G., et al. (1987). Compliance with oral drug therapy in patients with haematologic malignancy. *J Clin Oncol.* 1987; 5:1469-76.
- Liechty, C. A., Alexander, C. S., Harrigan, P. R., Guzman, J. D., Charlebois, E. D., Moss, A. R., & Bangsberg, D. R. (2004). Are untimed antiretroviral drug levels useful predictors of adherence behavior? *Aids* 2004; 18:127-9.
- Liu, H., Golin, C. E., Miller, L. G., Hays, R. D., Beck, C. K., Sanandaji, S., Christian, J., et al. (2001). A comparison study of multiple measures of adherence to HIV protease inhibitors. *Ann Intern Med* 2001; 134:968-77.
- Loutfy, M. R., Wu, W., Letchumanan, M., Bondy, L., Antoniou, T., Margolese, S., Zhang, Y., et al. (2013). Systematic review of HIV transmission between heterosexual serodiscordant couples where the HIV-positive partner is fully suppressed on antiretroviral therapy. *PLoS One*, 2013, 8:e55747.
- Lucas, G., Weidle, P., Hader, S., et al (2004). Comparison of directly administered antiretroviral therapy in a methadone clinic and self-administered therapy in HIV-infected patients. In: Program and abstracts of the 11th Conference on Retroviruses and Opportunistic Infections; February 4-8, 2004; San Francisco. Abstract 563.
- Lucas, G. M., Mullen, B. A., Weidle, P. J., Hader, S., McCaul, M. E., and Moore, R. D. (2006). Directly administered antiretroviral therapy in methadone clinics is associated with improved HIV treatment outcomes, compared with outcomes among concurrent comparison groups. *Clinical Infectious Diseases*, 2006, 42: 1628-1635.
- Machtinger, E.L., Bangsberg, D.R., (2005). Adherence to HIV Antiretroviral Therapy. Available at <http://hivinsite.ucsf.edu/Insite?page=kb-03-02-09#S1X> (accessed 09/03/13).
- Mohamed, H., Bachmann, M. O. (1998). Block appointments in an overloaded South African health centre: quantitative and qualitative evaluation. *International Journal of Health Care Quality Assurance*, 1998, 11:123-126.
- Malaysia AIDS Council Annual Report 2013.
- Malaysia National Strategic Plan 2011 – 2015.
- Malaysia 2012 Global AIDS Response Country Progress Report.
- Malaysia 2014 Global AIDS Response Country Progress Report.
- Malta, M., Magnanini, M. M., Strathdee, S. A., & Bastos, F. I. (2010). Adherence to antiretroviral therapy among HIV-infected drug-users: a meta-analysis. *AIDS and Behaviour*, 2010, 14: 731-747.

- Mannheimer, S., Friedland, G., Matts, J., Child, C., Chesney, M. (2002). The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. *Clin Infect Dis* 2002; 34:1115-21.
- Martin, S., Elliott-DeSorbo, D. K., Wolters, P. L., Toledo- Tamula, M. A., Roby, G., Zeichner, S., et al. (2007). Patient, caregiver and regimen characteristics associated with adherence to highly active antiretroviral therapy among HIV-infected children and adolescents. *Paediatric Infectious Diseases Journal*, 2007, 26: 61-67.
- Mbuagbaw, L., van der Kop, M. L., Lester, R. T., Thirumurthy, H., Pop-Eleches, C., Ye, C., Smieja, M., et al. (2012). The Cameroon Mobile Phone SMS (CAMPS) trial: a randomized trial of text messaging versus usual care for adherence to antiretroviral therapy. *PLoS One*, 2012, 7:e46909.
- Mc Mahon, J. H., Jordan, M. R., Kelley, K., Bertagnolio, S., Hong, S. Y., Wanke, C. A., Lewin, S. R., and Elliott, J. H. (2011). Pharmacy adherence measures to assess adherence to antiretroviral therapy: review of the literature and implications for treatment monitoring. *Clinical Infectious Diseases*, 2011, 52:493-506.
- mHealth: new horizons for health through mobile technologies, based on the findings of the second global survey on eHealth. Geneva, World Health Organization, 2011 (www.who.int/goe/publications/goe_mhealth_web.pdf, accessed 28 April, 2014).
- Michael M. Lederman, Benigno Rodriguez, Scott Sieg (2006). Immunopathogenesis of HIV infection. HIV In site Knowledge Base Chapter October 2004, Content reviewed January 2006. Available at <http://hivinsite.ucsf.edu/InSite?page=kb-02-01-04#S7X> (accessed 18/04/2014).
- Miller, N. H. (1997). Compliance with treatment regimens in chronic asymptomatic diseases. *American Journal of Medicine*, 1997, 102:43–49.
- Mills, E. J., Nachega, J. B., Bangsberg, D. R., Singh, S., Rachlis, B., Wu, P., Wilson, K., et al. (2006). Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators. *PLoS Medicine*, 2006, 3: 2039.
- Mocroft, A., Youle, M., Moore, A., Sabin, C. A., Madge, S., Lepri, C. A., Tyrer, M., et al. (2001). Reasons for modification and discontinuation of antiretrovirals: results from a single treatment centre. *AIDS*, 2001, 15:185–194.
- Mocroft, A., Reiss, P., Kirk, O., Mussini, C., Girardi, E., Morlat, P., Stephan, C., et al. (2010). Is it safe to discontinue primary *Pneumocystis jirovecii* pneumonia prophylaxis in patients with virologically suppressed HIV infection and a CD4 cell count <200 cells/μl? *Clinical Infectious Diseases*, 2010, 51: 611-619.
- Molina, J. M., Ferchal, F., Rancinan, C., et al. (2003). Once-daily combination of emtricitabine, didanosine, and efavirenz vs continued PI-based HAART in HIV-infected adults with undetectable plasma HIV-RNA: 48-week results of a prospective randomized multicenter trial (ALIZE-ANRS 99). In: Program and

abstracts of the 10th Conference on Retroviruses and Opportunistic Infections; February 10-14, 2003; Boston. Abstract 551.

- Montaner, J. S., Lima, V. D., Barrios, R., Yip, B., Wood, E., Kerr, T., Shannon, K., et al. (2010). Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. *Lancet*, 2010, 376: 532-539.
- Moore, R. D., Gebo, K. A., Lucas, G. M., Keruly, J. C. (2008). Rate of comorbidities not related to HIV infection or AIDS among HIV infected patients, by CD4 cell count and HAART use status. *Clinical Infectious Diseases*, 2008, 47:1102-1104.
- Mugusi, F., Mugusi, S., Bakari, M., Hejdemann, B., Josiah, R., Janabi, M., Aboud, S., et al. (2009). Enhancing adherence to antiretroviral therapy at the HIV clinic in resource constrained countries; the Tanzanian experience. *Tropical Medicine and International Health*, 2009, 14: 1226-1232.
- Munoz, M., Finnegan, K., Zeladita, J., Caldas, A., Sanchez, E., Callacna, M., Rojas, C., et al. (2010). Community-based DOT-HAART accompaniment in an urban resource-poor setting. *AIDS and Behaviour*, 2010, 14:721-730.
- Murphy, D. A., Wilson, C. M., Durako, S. J., Muenz, L. R., Belzer, M. E. (2001). Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA. *AIDS Care*, 2001, 13:27-40.
- Murphy, D. A., Sarr, M., Durako, S. J., Moscicki, A., Wilson, C. M., Muenz, L. R. (2003). Barriers to HAART adherence among human immunodeficiency virus-infected adolescents. *Archives of Paediatrics and Adolescent Medicine*, 2003, 157: 249-255.
- Murri, R., Ammassari, A., Gallicano, K., De Luca, A., Cingolani, A., Jacobson, D., Wu, A. W., & Antinori, A. (2000). Patient-reported nonadherence to HAART is related to protease inhibitor levels. *J Acquir Immune Defic Syndr* 2000; 24:123-8.
- Nakimuli-Mpungu, E., Bass, J. K., Alexandre, P., Mills, E. J., Musisi, S., Ram, M., Katabira, E. and Nachega, J. B. (2012). Depression, alcohol use and adherence to antiretroviral therapy in sub-saharan Africa: a systematic review. *AIDS and Behaviour*, 2012, 16: 2101-2118.
- Ndubuka, N. O., Ehlers, V. J. (2011). Adult patients' adherence to antiretroviral treatment: a survey correlating pharmacy refill records and pill counts with immunological and virological indices. *International Journal of Nursing Studies*, 2011, 48: 1323-1329.
- Ng, J. J., Rosen, R. K., Malcolm, S. E., Stein, M. D., & Stone, V. E. (2000). Adherence to highly active antiretroviral therapy in substance abusers with HIV/AIDS. *Journal of General Internal Medicine*, 2000, 15:165.
- Nyamogoba, H. D. N., Muthia, G., Mining, S., Kikui, G., Kikui, R., Mpoke, S., & Waiyaki, P. G. (2013). HIV co-infection with tuberculous and non-tuberculous mycobacteria in western Kenya: challenges in the diagnosis and management. *African health sciences*, 12(3), 305-311.

- Orrell, C., Harling, G., Lawn, S. D., Kaplan, R., McNally, M., Bekker, L. G., & Wood, R. (2007). Conservation of first-line antiretroviral treatment regimen where therapeutic options are limited. *Antiviral Therapy*, 2007, 12(1), 83-88.
- Ostrop, N. J., Hallett, K. A., Gill, M. J. (2000). Long-term patient adherence to antiretroviral therapy. *Annals of Pharmacotherapy*, 2000, 34:703–709.
- Panel on Clinical Practices for Treatment of HIV (2002). Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents (NIH 2002). Morbidity and Mortality Weekly Report. Atlanta, GA, Centers for Diseases Control and Prevention, 2002, Vol. 51, No. RR07.
- Park, W. B., Choe, P. G., Kim, S. H., Jo, J. H., Bang, J. H., Kim, H. B., Kim, N. H., et al. (2007). One year adherence to clinic visits after highly active antiretroviral therapy: a predictor of clinical progress in HIV patients. *J Intern Med*. 2007; 261:268-75.
- Paterson, D. L., Swindells, S., Mohr, J., Brester, M., Vergis, E. N., Squire, C., Wagener, M.M., & Singh, N., (2000). Adherence to protease inhibitor therapy and outcomes of patients with HIV infection, *Annals of Internal Medicine* 133 (1), 21-30.
- Penny Lewthwaite, Ed Wilkins (2009). *Natural History of HIV/AIDS, Medicine*, Vol. 37, Issue 7, 333-337.
- Pop-Eleches, C., Thirumurthy, H., Habyarimana, J. P., Zivin, J. G., Goldstein, M. P., de Walque, D., et al. (2011). Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. *AIDS* 2011; 26(6): 825-34.
- Preininger, L., Cantwell-McNelis, K., James, C., Sullivan, M. C., Szabo, S. and Bincsik, A. (2011). Long term Medication adherence in patients receiving antiretroviral therapy, *Current HIV Research*, 2011, 9, 253-255.
- Pyne, J. M., Fortney, J. C., Curran, G. M., Tripathi, S., Atkinson, J. H., Kilbourne, A. M., Hildi, J., et al. (2011). Effectiveness of collaborative care for depression in human immunodeficiency virus clinics. *Archives of internal medicine*, 2011, 171(1), 23-31.
- Raffi, F., Saag, M., Cahn, P., et al. (2003). A randomized, double-blind multicentre comparison of emtricitabine QD to stavudine BID in treatment-naïve HIV-infected patients. In: Program and abstracts of the 2nd International AIDS Society Conference on HIV Pathogenesis and Treatment; July 13-16, 2003; Paris. Abstract 38.
- Rastegar, D. A., Fingerhoo, M. I., Jasinski, D. R. (2003). Highly active antiretroviral therapy outcomes in a primary care clinic. *AIDS Care*. 2003; 15:231-7.
- Rawizza, H., et al. (2011). Immunologic criteria are poor predictors of virologic outcome: implications for HIV treatment monitoring in resource-limited settings. *Clinical Infectious Diseases*, 2011, 53: 1282-1290.

- Reynolds, N. R., Testa, M. A., Su, M., Chesney, M. A., Neidig, J. L., Frank, I., Smith, S., et al. (2008). Telephone Support to Improve Antiretroviral Medication Adherence – A Multisite Randomized Controlled Trial. *Journal of Acquired Immune Deficiency Syndrome*, Vol. 47, 62-68.
- Rich, M. L., Miller, A. C., Niyigena, P., Franke, M. F., Niyonzima, J. B., Socci, A., Drobac, P. C., et al. (2012). Excellent Clinical Outcomes and High Retention in Care Among Adults in a Community-Based HIV Treatment Program in Rural Rwanda. *JAIDS Journal of Acquired Immune Deficiency Syndromes*; 2012, 59(3): e35-e42 doi: 10.1097/QAI.0b013e31824476c4
- Rodrigues, R., Shet, A., Antony, J., Sidney, K., Arumugam, K., Krishnamurthy, S., D'Souza, G., DeCosta, A. (2012). Supporting adherence to antiretroviral therapy with mobile phone reminders: results from a cohort in South India. *PLoS One*. 2012;7(8):e40723. doi: 10.1371/journal.pone.0040723.
- Roux, P., Carrieri, M. P., Villes, V., Dellamonica, P., Poizot-Martin, I., Ravaux, I., & Spire, B. (2008). The impact of methadone or buprenorphine treatment and ongoing injection on highly active antiretroviral therapy (HAART) adherence: evidence from the MANIF2000 cohort study. *Addiction*, 103(11), 1828-1836.
- Rueda, S., Park-Wyllie, L. Y., Bayoumi, A., Tynan, A. M., Antoniou, T., Rourke, S., & Glazier, R. (2006). Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS. *The Cochrane Library*. *Cochrane Database of Systematic Reviews*, 2006, (3):CD001442.
- Sabin, L. L., DeSilva, M. B., Hamer, D. H., Xu, K., Zhang, J., Li, Tao., Wilson, I. B., & Gill, C. J. (2010). Using Electronic Drug Monitor Feedback to Improve Adherence to Antiretroviral Therapy among HIV-Positive Patients in China. *AIDS Behav*. 2010 Jun; 14(3): 580-589. PMID: PMC2865631
- Sabin, L. L., Bachman, D. M., Gill, C. J., Zhong, L., Vian, T., Xie, W., Cheng, F. et al. (2015). Improving Adherence to Antiretroviral Therapy With Triggered Real-time Text Message Reminders: The China Adherence Through Technology Study. *J Acquir Immune Defic Syndr*. 2015 Aug 15; 69(5):551-9. doi: 10.1097/QAI.0000000000000651.
- Saple, D. (2005). Improving adherence to anti-retroviral therapy (Review articles). *India Journal of Dermatology, Venereology and Leprology*. Available from: <http://www.highbeam.com/librarydoc3.asp?DOCID=1G1:136743728&num=1&ao=&Fr> (accessed 21.04.14).
- Sarna, A., Luchters, S., Geibel, S., Chersich, M. F., Munyao, P., Kaai, S., & Rutenberg, N. (2008). Short-and long-term efficacy of modified directly observed antiretroviral treatment in Mombasa, Kenya: a randomized trial. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 48(5), 611-619.
- Schillinger, D., Machtiger, E., & Win, K. (2004). Are pictures worth a thousand words? Communication regarding medications in a public hospital anticoagulation clinic In: Henriksen K, Battles J, Lewin DI, Marks E, editors. *Advances in Patient Safety: From Research to Implementation*. Rockville, MD: Agency for Healthcare Research and Quality; 2004.

- Shuter, J. (2008). Forgiveness of Non-adherence to HIV-1 antiretroviral therapy. *J Antimicrob Chemother* 2008; 61: 769-73.
- Sidney K, Antony J, Rodrigues R, Arumugam K, Krishnamurthy S, D'souza G, De Costa A, Shet A. Supporting patient adherence to antiretrovirals using mobile phone reminders: patient responses from South India. *AIDS Care*. 2012; 24(5):612–7. doi: 10.1080/09540121.2011.63035
- Siegel, K., Karus, D., Schrimshaw, E. W. (2000). Racial differences in attitudes toward protease inhibitors among older HIV-infected men. *AIDS Care*, 2000, 12:423–434.
- Smith, V., Devane, D., Begley, C. M., Clarke, M. (2011). Methodology in conducting a systematic review of systematic reviews of healthcare interventions. *BMC Med Res Methodol* 2011; 11:15.
- Springer, S. A., Dushaj, A., Azar, M. M. (2012). The impact of DSM-IV mental disorders on adherence to combination antiretroviral therapy among adult persons living with HIV/AIDS: a systematic review. *AIDS and Behaviour*, 2012, 16: 2119-2143.
- Stacey M. Lavsa, Ashley Holzworth, Nicole T. Ansani (2011). Selection of a validated scale for measuring medication adherence; *Journal of American Pharmacists Association*, 2011; 51(1): 90-94.
- Stone, V. E., Hogan, J. W., Schuman, P., Rompalo, A. M., Howard, A. A., Korkontzelou, C., Smith, D. K. (2001). Antiretroviral regimen complexity, self-reported adherence, and HIV patients' understanding of their regimens: survey of women in the study. *J Acquir Immune Defic Syndr* 2001; 28:124-31.
- Talam, N. C., Gatongi, P., Rotich, J., Kimaiyo, S. (2008). Factors affecting antiretroviral drug resistance among HIV/AIDS adult patients attending HIV/AIDS clinic at Moi Teaching and Referral Hospital, Eldoret, Kenya, *East African Journal of Public Health*, Vol. 5, No. 2, 74-78.
- The treatment 2.0 framework for action: catalysing the next phase of treatment, care and support. Geneva, World Health Organization, 2011 (http://whqlibdoc.who.int/publications/2011/9789241501934_eng.pdf, accessed 21 April, 2014)
- Tuldra, A., Fumaz, C. R., Ferrer, M. J., Bayes, R., Arno, A., Balague, M., Bonjoch, A., et al. (2000). Prospective randomized two-Arm controlled study to determine the efficacy of a specific intervention to improve long-term adherence to highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* 2000; 25:221-8.
- UNAIDS (2010). 'Global report - UNAIDS report on the global AIDS epidemic'.
- UNAIDS (2011, November). 'World AIDS Day Report 2011'.
- UNAIDS (2013). 'Global Report – UNAIDS report on the global AIDS epidemic'.
- UNAIDS (2013). 'HIV in Asia and the Pacific'.

- United Nations (2011). 'Political Declaration of HIV/AIDS: Intensifying our Efforts to Eliminate HIV/AIDS'.
- United Nations/WHO (2003). 'Workshop on HIV/AIDS and Adult Mortality in Developing Countries' New York, 8-13 September 2003.
- Uzma, Q., Emmanuel, F., Ather, U., Zaman, S. (2011). Efficacy of interventions for interventions for improving antiretroviral therapy adherence in HIV/AIDS cases at PIMS, Islamabad. *Journal of International Association of Physicians in AIDS Care* (Chicago), 2011, 10:373-383.
- van Velthoven, M.H.M.M.T., Brusamento, S., Majeed, A., & Car, J. (2013). Scope and effectiveness phone messaging for HIV/AIDS care: A systematic review, *Psychology, Health & Medicine*, 18:2, 182-202.
- Wagner, G. J. (2002). Predictors of antiretroviral adherence as measured by self-report, electronic monitoring, and medication diaries. *AIDS Patient Care STDS* 2002; 16:599-608.
- Walsh, J. C. M. S., Gazzard, B. G. (2002). Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. *AIDS*. 2002 Jan 25; 16(2):269-77.
- Wamalwa, D. C., Farquhar, C., Obimbo, E. M., Selig, S., Mbori-Ngacha, D. A., Richardson, B. A., Overbaugh, J., et al. (2009). Medication diaries do not improve outcomes with highly active antiretroviral therapy in Kenyan children: a randomized controlled trial. *Journal of the International AIDS Society*, 2009: 12:8.
- Wanyenze, R. K., Wagner, G., Alamo, S., Amanyire, G., Ouma, J., Kwarisima, D., Sunday, P., et al. (2010). Evaluation of the efficiency of patient flow at three HIV clinics in Uganda. *AIDS Patient Care and STDs*, 2010, 24: 441-446.
- Were, M. C., Sutherland, J. M., Bwana, M., Ssali, J., Emenyonu, N., & Tierney, W. M. (2008). Patterns of care in two HIV continuity clinics in Uganda, Africa: a time-motion study. *AIDS care*, 20(6), 677-682.
- Westley, B. P., DeLong, A. K., Tray, C. S., Sophearin, D., Dufort, E. M., Nerrienet, E., Schreier, L., et al. (2012). Prediction of treatment failures using 2010 World Health Organization guidelines is associated with high misclassification rate and drug resistance among HIV-infected Cambodian children, *Clinical Infectious Diseases*, 2012, 55: 432-440.
- Whitlock, E. P., Lin, J. S., Chou, R., Shekelle, P., Robinson, K. A. (2008). Using existing systematic reviews in complex systematic reviews. *Ann Intern Med* 2008; 148:776-782.
- WHO (2007). 'Prioritizing Second-Line Anti-retroviral Drugs for Adults and Adolescents: a Public Health Approach'. Report of a WHO Working Group Meeting, 21-22 May, 2007.
- WHO (2013). 'Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, recommendations for a public health approach'.

- Wood, E., Hogg, R. S., Yip, B., Harrigan, P. R., O'Shaughnessy, M. V., Montaner, J. S. (2003). Effect of medication adherence on survival of HIV-infected adults who start highly active antiretroviral therapy when the CD4⁺ cell count is 0.200 to 0.350 x 10⁹ cells/L. *Ann Intern Med* 2003; 139:810-6.
- Yagoub, U., Bulgiba, A. M., Peramalah, D., Didi, E., Mustafa, A., Lee, C., Chik, Z. (2012). Factors affecting adherence level to HAART (adherence predictors) in Kuala Lumpur, Malaysia. *Life Science Journal* 2012; 9(4): 3600-3603.



LIST OF PUBLICATIONS

Abdulrahman, S. A., Rampal, L., Othman, N., Ibrahim, F., Kadir@Shahar, H., Radhakrishnan, A. P. (2015). Baseline adherence, socio-demographic, clinical, immunological, virological and anthropometric characteristics of 242 HIV positive patients on ART in Malaysia. *Malaysian Journal of Medicine and Health Sciences*, 11 (2), June 2015: 45-58.

Abdulrahman, S. A., Rampal, L., Othman, N., Ibrahim, F., Kadir@Shahar, H., Radhakrishnan, A. P. (2016). Mobile phone reminders improve adherence and treatment outcomes of patients on ART in Malaysia: a randomized clinical trial. *PLoS One*, 2016 (Under review).





UNIVERSITI PUTRA MALAYSIA

STATUS CONFIRMATION FOR THESIS / PROJECT REPORT AND COPYRIGHT

ACADEMIC SESSION : _____

TITLE OF THESIS / PROJECT REPORT :

IMPACT OF REMINDER MODULE ON ADHERENCE AND TREATMENT OUTCOMES
AMONG HIV- POSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY IN HOSPITAL
SUNGAI BULOH, MALAYSIA

NAME OF STUDENT : SURAJUDEEN ABIOLA ABDULRAHMAN

I acknowledge that the copyright and other intellectual property in the thesis/project report belonged to Universiti Putra Malaysia and I agree to allow this thesis/project report to be placed at the library under the following terms:

1. This thesis/project report is the property of Universiti Putra Malaysia.
2. The library of Universiti Putra Malaysia has the right to make copies for educational purposes only.
3. The library of Universiti Putra Malaysia is allowed to make copies of this thesis for academic exchange.

I declare that this thesis is classified as :

*Please tick (✓)

☐

CONFIDENTIAL

(Contain confidential information under Official Secret Act 1972).

☐

RESTRICTED

(Contains restricted information as specified by the organization/institution where research was done).

☐

OPEN ACCESS

I agree that my thesis/project report to be published as hard copy or online open access.

This thesis is submitted for :

☐

PATENT

Embargo from _____ until _____
(date) (date)

Approved by:

(Signature of Student)
New IC No/ Passport No.:

Date :

(Signature of Chairman of Supervisory Committee)
Name:

Date :

[Note : If the thesis is **CONFIDENTIAL** or **RESTRICTED**, please attach with the letter from the organization/institution with period and reasons for confidentiality or restricted.]