

Patient and Health System Factors Associated with First Line Tuberculosis Treatment Adherence, 2009-2014

Gifty Adu, Bernice N. Harris, Andy Beke

School of Health Systems and Public Health, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa

Email: mynanaama@yahoo.com

How to cite this paper: Adu, G., Harris, B.N. and Beke, A. (2022) Patient and Health System Factors Associated with First Line Tuberculosis Treatment Adherence, 2009-2014. *Journal of Tuberculosis Research*, 10, 220-229.

<https://doi.org/10.4236/jtr.2022.104017>

Received: October 12, 2022

Accepted: December 25, 2022

Published: December 28, 2022

Copyright © 2022 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: The prevalence and incidence rate of tuberculosis remains high although the disease is known to be almost always curable provided the patient adheres to the treatment regimen. This study assessed the strength of association between known patient and health system factors associated with first line tuberculosis treatment adherence. **Methods:** A quantitative cross sectional study. Retrospective chart reviews were conducted among 570 persons who had primary tuberculosis and received first line treatment at a health facility within the Nkangala district, Mpumalanga province and who had a treatment outcome recorded between 1st January 2009 and 31st December 2014. Adherence to first line tuberculosis treatment was defined as taking $\geq 80\%$ of tuberculosis prescribed drugs within a period of 6 to 8 months. Stata software (logistic regressions model) was used to analyze results and find the strength of association between known factors and treatment adherence. **Results:** Out of the 570 study participants, 473 were adherent and 96 were not adherent. There was a statistically significant association between age 18 years and above (OR: 1.02, P-value: 0.027), sex (lower in males OR: 0.44, P-value: 0.001) and support (OR: 3.04, P-value: 0.05) and HIV (OR: 1, P-value: 0.634) and first line TB treatment adherence. **Conclusion and Recommendation:** $>80\%$ adherence to first line tuberculosis outcome is possible. The support given to people with tuberculosis will further enhance adherence to first line tuberculosis treatment.

Keywords

Adherence, First-Line, Tuberculosis, Treatment, Non-Adherence, Health System Factors, Patient

1. Introduction

Non-adherence to medical treatment remains a challenge for medical professionals and social scientists [1]. This is particularly so for infective and communicable infections such as *Mycobacterium tuberculosis* the causative agent for tuberculosis (TB) with serious public health consequences [1] [2]. Efforts to improve TB care and control have been intensified since the mid-1990s and TB was declared a global public health emergency by the World Health Organization (WHO) [2]. The WHO adopted, directly observed treatment short course (DOTS) and the Stop TB strategy [1] [3], an inexpensive strategy that could prevent millions of TB cases and death [4]. Dots consist of five key elements: government commitment to sustained TB control; detection of active TB cases through sputum smear microscopy among people with symptoms; regular and uninterrupted supply of high-quality anti-TB drugs; six to eight months of regularly supervised treatment (including direct observation of drug taking for at least the first 2 months), and reporting systems to monitor treatment progress and program performance [2] [3] [4] [5]. Despite the adoption of the DOTS by almost all countries, it is estimated that up to 2.3 billion of the world population is infected with TB [5]; 8 million people get infected with *Mycobacterium tuberculosis* every year and up to 3 million people die from the resultant disease [2] [4] [6] [7]. South Africa has the third highest TB incidence rate in the world after India and China [3] [6] with estimated 405,982 persons diagnosed with TB each year (incidence rate 971 per 1,000,000), 8 approximately 1% of South Africa's population. Current TB control efforts are based on early detection of the disease and institution of the appropriate drug therapy on the basis of case definition as well as the implementation of appropriate infection control strategies [4] [5]. New patients who have never had treatment for TB, or have taken anti-TB drugs for less than one month with positive or negative bacteriology and pulmonary or extrapulmonary TB, are assigned the standard first line TB treatment. First line anti-TB drugs consist of a four drug combination of isoniazid, rifampicin, pyrazinamide and ethambutol, for the treatment of drug susceptible TB [3]. The South Africa National TB program (NTP) adopted the DOTS strategy nationwide for the treatment of TB patients in 1996 but compliance among TB patients at a success rate of 74% - 76%, remains well below WHO's targets of 85% cured or completing treatment necessary to mitigate the spread of TB [8] [9] [10] [11]. Tuberculosis (TB) is nearly always curable if patients are treated with effective uninterrupted anti-tuberculosis therapy. Adherence to treatment is critical for cure of individual patients, controlling the spread of infection and minimizing the development of drug resistance [12] [13]. Re treatment of TB or treatment of multi-drug resistant TB is far more complicated and expensive. Thus with first line TB treatment, there is a window of opportunity to cure the patient from TB which should not be missed [3] [4]. This study outlined the strength of association between patients and health system factors influencing patient adherence to first line TB treatment [14] [15]. The aim is to contribute to

the generation of knowledge which can assist in enhancing first line TB treatment adherence in South Africa, enhancing disease control and reducing the disease burden in the public health community. From the various articles reviewed, adherence to TB is influenced by: health system factors, individual health-seeking behaviours, age and gender, perceived cause of TB, co-infection with HIV, family support, social and economic resources, poverty, and the use of African indigenous healing system [16] [17] [18] [19].

2. Methods

2.1. Setting and Study Population

This study was conducted at a health facility within the DR J Moroka municipality (Nkangala District, Mpumalanga province). During the study period, this district had the highest incidence of TB cases within the province with most cases seeking treatment at the particular health facility. The facility had an average annual TB incidence of 90 - 100 cases. Mpumalanga province rates seventh highest for TB incidence in the country (South Africa) with TB incidence of “467 per 100,000” [20] [21]. The prevalence of multi-drug resistant TB among newly diagnosed patients in the province is 2.7% and this is imminent to the WHO “hot spot” level of three percent.²³ Nkangala district has an incidence of 336.7 per 100,000. It had a new pulmonary smear positive increase of 185.2% in 2013/2014.²² The district had a TB treatment success rate was 75.1% in 2013/2014 which was the highest the district had achieved, however it fell lower than the national target rate of 85% [20] [21] [22]. A clinic known to have the highest case load of tuberculosis was selected for the study due to financial and logistic constraints. The study population included all persons with smear positive TB (new/primary TB) identified through the hospital records to have been put on first line tuberculosis treatment. Patients were excluded if they died or transferred outside of the study facility or had no record of TB treatment outcome.

2.2. Study Design and Data Collection

A quantitative cross sectional study design was chosen. Patients’ files for the specified study period were retrieved from the health facility and demographic data was abstracted and recorded for study inclusion participants.

2.3. Study Definitions

Adherence to first line tuberculosis treatment was defined as taking $\geq 80\%$ of firstline tuberculosis prescribed drugs within a period of 6 to 8 months under direct supervision at the health facility or mutually agreed upon location. Patients were defined as non-adherent if they did not meet the criteria for adherence mentioned above.

2.4. Analysis

The statistical software STATA 12 was used to analyze data. Descriptive statistics

were used to describe demographic characteristics of all participants included in the study. The logistic regression model was used to examine factors associated with adherence. Each variable was examined independently and univariate odds ratios calculated. A multivariate model was developed using variables with P value P value < 0.05 were considered statistically significant [23] [24] [25] [26] [27].

2.5. Ethical Approval

The study protocol was reviewed and approved by the research and ethics committee of the University of Pretoria. Ethical approval was also obtained from the Mpumalanga province prior to the study. The study did not involve any informed consent as data was based on existing patient hospital records. Patient information and records were handled under anonymity.

3. Results

We assessed a total of five hundred and ninety four (594) patient files. Of these, twenty four (4.04%) were excluded due to; death 9 (1.51%) transfer out 10 (1.68%) unknown treatment outcome 5 (0.84%). We were left with a sample size of five hundred and seventy (570). Generally 476 (83.5%) were adherent and 94 (16.5%) were non adherent. Of those who adhered to treatment 47.8% were male and 52.2% were females, 56% were HIV serous positive and 44% were HIV serous negative, 80.4% had support and 19.6% had no support, 62% were unemployed, 24% were employed (Figure 1 and Table 1).

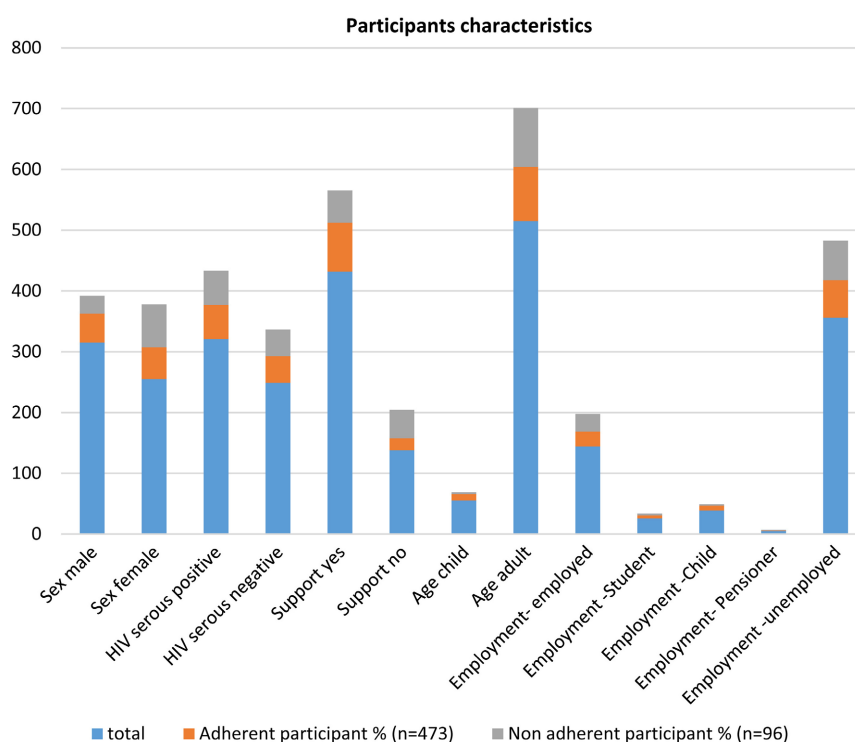


Figure 1. Characteristics of participants.

Table 1. Characteristics of participants.

Variable	Total	Adherent participant % (n = 474)	Non adherent participant % (n = 96)
Sex male	315	47.780	29.2
Sex female	255	52.22	70.8
HIV serous positive	321	56.236	56.25
HIV serous negative	249	43.763	43.75
Support yes	432	80.338	53.125
Support no	138	19.661	46.875
Age child	55	10.78	3.125
Age adult	515	89.2	96.875
Employment-employed	144	24.524	29.166
Employment-Student	26	4.862	3.125
Employment-Child	39	7.822	2.0833
Employment-Pensioner	5	0.845	1.04
Employment-unemployed	356	61.945	64.5833

4. Discussion

Our study revealed that majority of patients with primary tuberculosis adhered to firstline tuberculosis treatment. Patients aged 18 years and above had an increase probability of adhering to treatment. People 18 years and above are believed to be matured enough to understand the disease process and implications for non-adherence to treatment regimen. This might explain the likelihood of adherence with increasing age. Pre-counselling and education geared towards adherence to treatment regimen must be tailored to suit patients understanding before the commencement of treatment (**Figure 2** and **Table 2**).

One study showed adherence in females or women to be higher than that of men [16]. This study proved same. Men in most cases are the bread winners for the family, and hence get busy with work than their health. Most men are likely to adhere when they are very weak and incapacitated. Efforts must be put into thorough education of men before the commencement of the treatment regimen and if possible, treatment modalities must be tailored to suit their work schedules. Peer groups consisting of male patients with similar characteristics can be formed to provide support system for each other as this could serve as a source of encouragement for patients and improve adherence rate amongst male patients.

Our study further revealed that support was increasingly associated with patients' adherence to treatment. We found out that the clinics does allocate support in the form of a family member, hospital staff, life partner or spouse if

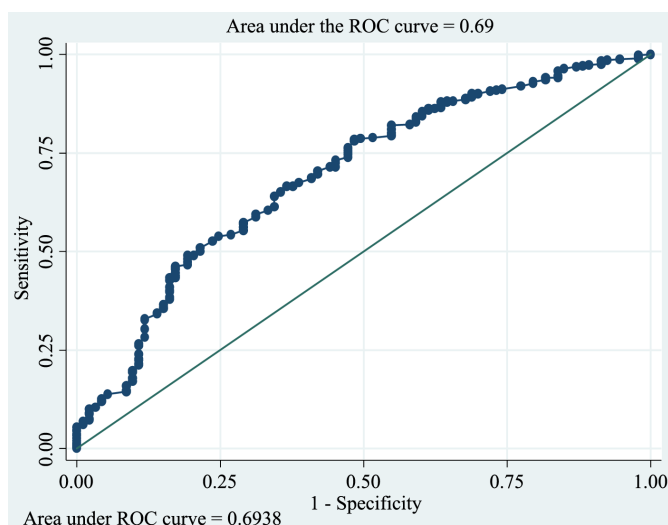


Figure 2. Post-regression analyses for the adult model.

Table 2. Logistic regression results for the adult patients (n = 515).

Variable	Univariate ORs		Full model		Final model	
	OR	P-value*	OR	P-value**	OR	P-value**
Age	1.02	0.096	1.03	0.021	1.02	0.027
Sex	0.42	<0.001	0.43	0.001	0.44	0.001
Support	3.27	<0.001	3.02	<0.001	3.04	<0.001
Employment 1***	-	-	Reference group		-	-
Employment 2	-	-	1.22	0.818	-	-
Employment 4	-	-	0.54	0.608	-	-
Employment 5	-	-	0.91	0.714	-	-
HIV	1.00	0.634	-	-	-	-

ORs = Odds Ratios; *Chi square test; **z-test; ***Employment category 3 was omitted due to perfect prediction.

married to assist patients and provide them with the needed support to complete the treatment regimen. Some patients refuse support due to the fear of stigmatization. 80% of patients who had support adhered to the treatment regimen and only 19% of patients without support adhered to the treatment regimen. This goes to show that support, if given as per the individuals need will enhance patient's adherence to the treatment regimen. The national department of health must institute a policy on the allocation of individualized based support for all TB patients as part of the treatment regimen.

Similar to the study done by Mazinyo *et al.* [19], our study revealed no significant association between HIV coinfection and first line TB treatment adherence. There was also, no significant association between employment and first-line tuberculosis treatment adherence. This could be due to the financial as-

sistance given to unemployed patients in the form of grant, thus relieving the burden of poverty found to be associated with non-adherence to first line TB treatment. The mass campaign on the curability of the infection irrespective of HIV status could probably explain the insignificant association between HIV coinfection and first line TB treatment adherence. Patient education on TB curability must be strengthened at all levels of care before commencement and during the treatment period. “Educate before you medicate” to ensure treatment adherence sustainability.

Some other health system factors that were thought to also influence first line adherence to TB treatment were; the geographical location of the clinic made it easily accessible to its clients. Public transports were within reach to convey patients to and from the hospital. This could also explain the increasing rate of adherence amongst study participants. Drug availability: from the hospital records, drugs were always available throughout the period of study. The facility was never short of TB drugs and always had adequate stock for its clients. Affordability: treatment regimen is free of charge and no patient was denied treatment. Patients who were unemployed were given a grant to assist them financially. These factors did influence the positive treatment outcomes. Adequacy: the clinic did not run a 24 hour service. It operated from half past 7 in the morning to 16 h00 in the afternoon from Monday to Friday. This might not be favorable for all the patients especially those working. The department of health must expand the operating hours of the clinic to make it more user friendly and responsive to the community’s needs.

There were some limitations to our study. First, data used was from one municipality (Siyabuswa clinic) and it is possible that this clinic performed differently compared to other TB clinics, however, we randomly selected and captured patient’s files. Secondly, we relied on routinely collected data for this evaluation, which might not have been initially intended for research purposes; however, data completeness and accuracy was almost perfect. Lastly, factors identified in previous literature including: use of African indigenous healing system [17], social resources and stigmatization [4] [13] [17], perceived cause of tuberculosis [4] [8] [15] [16] [18] and some health system barriers such as staff attitudes [10] [14] could not be evaluated from the data captured.

Although the results from the study apply to Siyabuswa tuberculosis clinic and should be applied to other clinics with caution, the study offers insight to factors that may affect first line tuberculosis treatment adherence in similar high-burden settings.

5. Conclusion

In conclusion, our study revealed an association between some patient and health system factors and adherence to first line tuberculosis treatment. There were significant associations between age, sex and support. Efforts to improve first line tuberculosis treatment adherence must be geared at strengthening pa-

tient support and tailoring patient education to suit individual age. Furthermore, this study goes to show that first line tuberculosis treatment outcomes can be improved.

Acknowledgements

The authors would like to thank the staff of Siyabuswa clinic for their support with respect to the retrieval of patients' files especially Joyce Ntuli (data capturer Dr. J Moroka municipality), Sr Cecilia Ntuli (operations manager Siyabuswa clinic) and also Sr Rose N Nxumalo (TB Sr in charge). We also acknowledge the Mpumalanga provincial department of health especially Bella Sekgabi (data capturer for the Mpumalanga province). We appreciate the work of colleagues who proof checked the data entry.

Conflicts of Interest

The authors declare that they have no financial or personal relationships that may inappropriately influence them in writing this article.

Author's Contribution

The authors contributed differently to this work. The first author Gifty Adu was responsible for conceptualization, data analysis, first and second drafts, finalization of the manuscript. The second and third authors were the supervisors of the study and reviewed the article.

Data Availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Disclaimer

The findings and conclusions in this manuscript are those of the authors and do not certainly denote the authorized position of the University of Pretoria.

References

- [1] World Health Organisation (2003) Adherence to Long Term Therapies: Evidence for Action. WHO, Geneva. <https://apps.who.int/iris/handle/10665/42682>
- [2] Kunnath-Velayudhan, S., Salamon, H., Wang, H.-Y., Davidow, A.L., Molina, D.M., Huynh, V.T., *et al.* (2010) Dynamic Antibody Responses to the Mycobacterium Tuberculosis Proteome. *Proceedings of the National Academy of Sciences*, **107**, 14703-14708. <https://doi.org/10.1073/pnas.1009080107>
- [3] Naidoo, P., Dick, J. and Cooper, D. (2009) Exploring Tuberculosis Patients' Adherence to Treatment Regimen and Prevention Programs at a Public Health Site. *Qualitative Health Research*, **19**, 55-70. <https://doi.org/10.1177/1049732308327893>
- [4] Jassal, M.S. and Bishai, W.R. (2010) Epidemiology and Challenges to the Elimination of Global Tuberculosis. *Clinical Infectious Diseases*, **50**, 156-164.

- <https://doi.org/10.1086/651486>
- [5] Zumla, A., Nahid, P. and Cole, S.T. (2013) Advances in the Development of New Tuberculosis Drugs and Treatment Regimens. *Nature Reviews Drug Discovery*, **12**, 388-404. <https://doi.org/10.1038/nrd4001>
- [6] National Department of Health (South Africa) (2007) National TB Infection Control Guidelines. <https://www.health.gov.za/tuberculosis>
- [7] Naidoo, P., Peltzer, K., Louw, J., Matseke, G., Mchunu, G. and Tutshana, B. (2013) Predictors of Tuberculosis (TB) and Antiretroviral (ARV) Medication Non-Adherence in Public Primary Care Patients in South Africa: A Cross Sectional Study. *BMC Public Health*, **13**, Article No. 396. <https://doi.org/10.1186/1471-2458-13-396>
- [8] Bronner, L.E., Podewills, L.J., Peters, A., Somnath, P., Nshuti, L., Van der Walt, M. and Mametja, L.D. (2012) Impact of Community Tracer Teams on Treatment Outcomes among Tuberculosis Patients in South Africa. *BMC Public Health*, **12**, Article No. 621. <https://doi.org/10.1186/1471-2458-12-621>
- [9] Atkins, S., Lewin, S., Ringsberg, K. and Thorson, A. (2012) Towards an Empowerment Approach in Tuberculosis Treatment in Cape Town, South Africa: A Qualitative Analysis of Programmatic Change. *Global Health Action*, **5**, Article 14385. <https://doi.org/10.3402/gha.v5i0.14385>
- [10] Calver, A.D., Falmer, A.A., Murray, M., Strauss, O.J., Streicher, E.M., Hanekom, M., et al. (2010) Emergence of Increased Resistance and Extensively Drug-Resistant Tuberculosis Despite Treatment Adherence, South Africa. *Emerging Infectious Diseases*, **16**, 264-271. <https://doi.org/10.3201/eid1602.090968>
- [11] World Health Organization (2013) Global Tuberculosis Control: Surveillance, Planning, Financing. WHO, Geneva. http://www.who.int/tb/publications/global_report/en
- [12] Brust, J.C., Shah, N.S., Scott, M., Chaiyachati, K., Lygizos, M., Van der Merwe, T.L., et al. (2012) Integrated, Home-Based Treatment for MDR-TB and HIV in Rural South Africa: An Alternate Model of Care. *The International Journal of Tuberculosis and Lung Disease*, **16**, 998-1004. <https://doi.org/10.5588/ijtld.11.0713>
- [13] Lutge, E., Lewin, S., Volmink, J., Friedman, I. and Lombard, C. (2013) Economic Support to Improve Tuberculosis Treatment Outcomes in South Africa: A Pragmatic Cluster-Randomized Controlled Trial. *Trials*, **14**, Article No. 154. <https://doi.org/10.1186/1745-6215-14-154>
- [14] Uwimana, J., Jackson, D., Hausler, H. and Zarowsky, C. (2012) Health System Barriers to Implementation of Collaborative Tuberculosis and HIV Activities Including Prevention of Mother to Child transmission in South Africa. *Tropical Medicine & International Health*, **17**, 658-665. <https://doi.org/10.1111/j.1365-3156.2012.02956.x>
- [15] Brust, J.C.M., Gandhi, N.R., Carrara, H., Osburn, G. and Padayatchi, N. (2011) High Treatment Failure and Default Rates for Patients with MDR TB in KwaZulu-Natal, South Africa, 2000-2003. *The International Journal of Tuberculosis and Lung Disease*, **14**, 413-419.
- [16] Cramm, J.M., Van Exel, J., Møller, V. and Finkenflügel, H. (2010) Participants View on Determinants of Compliance with Tuberculosis Treatment in the Eastern Cape, South Africa: An Application of Q-Methodology. *The Patient: Patient-Centered Outcomes Research*, **3**, 159-172. <https://doi.org/10.2165/11531900-000000000-00000>
- [17] Cramm, J.M., Finkenflügel, H.J.M., Moller, V. and Neiboer, A.P. (2010) TB Treatment Initiation and Adherence in a South African Community Influenced more by Perception than By Knowledge of Tuberculosis. *BMC Public Health*, **10**, Article No.

72. <https://doi.org/10.1186/1471-2458-10-72>
- [18] Gebremariam, M.K., Bjune, G.A. and Frich, J.C. (2010) Barriers and Facilitators of Adherence to Tuberculosis Treatment in Patients on Concomitant TB and HIV Treatment: A Qualitative Study. *BMC Public Health*, **10**, Article No. 651. <https://doi.org/10.1186/1471-2458-10-651>
- [19] Mazinyo, E.W., Kim, L., Masuku, S., Lancaster, J.L., Odendaal, R., Uys, M., Podewils, L.J. and Van der Walt, M.L. (2016) Adherence to Concurrent Tuberculosis Treatment and Antiretroviral Treatment among Co-Infected Persons in South Africa, 2008-2010. *PLOS ONE*, **11**, e0159317. <https://doi.org/10.1371/journal.pone.0159317>
- [20] Nkangala District Municipality (2015) Nkangala District Municipality. <https://www.nkangaladm.gov.za/>
- [21] Republic of South Africa, Department of Health (2015) Nkangala Clinic Directory (Health services). <http://www.mpuhealth.gov.za/>
- [22] Mpumalanga Province of AIDS Council (2016) Annual Progress Report 2014/15. Provincial Strategic Plan 2012-2016. <https://sanac.org.za/>
- [23] G*Power 3. Statistical Power Analyses for Mac and Windows. <https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower>
- [24] Vittinghoff, E., Glidden, D.V., Shiboski, S.C. and McCulloch, C.E. (2012) Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models. 2nd Edition, Springer, New York.
- [25] Hosmer, D.W., Lemeshow, S. and Sturdivant, R.X. (2013) Applied Logistics Regression. 3rd Edition, Wiley, Hoboken. <https://doi.org/10.1002/9781118548387>
- [26] Klein, D.G. and Klein, M. (2010) Logistic Regression: A Self-Learning Text. 3rd Edition, Springer, New York.
- [27] Hilbe, J.M. (2009) Logistic Regression Models. Chapman and Hall/CRC, New York. <https://doi.org/10.1201/9781420075779>