Longitudinal Patterns of Adherence for Oral Endocrine Therapy Among US Women with Breast Cancer: A Group-based Trajectory Modeling Study

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BACKGROUND

- Breast cancer (BC) is the most common cancer among US women, accounting for about 30% of all new cancer cases annually
- Over 70% of BC cases in US women are hormone receptor-positive (HR+), making it the most common subtype of BC
- HR+ BC patients can benefit from oral endocrine therapy (OET), such as tamoxifen and aromatase inhibitors (AIs), which reduce the risk of recurrence and improve overall survival
- Despite the well-documented benefits of OET, non-adherence continues to be a major clinical challenge for HR+ BC patients resulting in recurrences, progression, and increased health care utilization, and cost of care
- OET adherence is particularly low among minority and underserved patients due to several factors, including lack of support, uncertainty about medication efficacy, and adverse drug reactions

Group-Based Trajectory Modeling

- Unlike traditional methods, group-based trajectory modeling (GBTM) describes longitudinal patters of adherence by incorporating both quantity and timing of medication availability
- GBTM identifies clusters of patients sharing common characteristics which could inform development of tailored interventions for nonadherent individuals
- GBTM utilizes monthly indicators of adherence (PDC≥0.80) and generates models to determine longitudinal patterns
- The final trajectory model is selected based on Bayesian criteria, clinical significance, and minimum 5% membership requirement

OBJECTIVE

- This study aimed to develop group-based trajectory models to identify longitudinal patterns of adherence to OET among HR+ breast cancer patients

METHODS

- **Study Design:** Retrospective cohort
- **Data Source:** Epic Health Electronic Health Record (EHR)
- **Study Population:** HR+ BC patients who were seen and followed at Harris Health System from June 2019-Dec 2020 with at least one outpatient dispense record of OET
- **Exclusion Criteria:** Patients who were not taking appropriate doses of OET, discontinued OET due to severe side effects, or were on OET for reasons other than BC prevention or treatment
- **Adherence measurement:**
  - ✓Monthly adherence to OET measured by PDC and modeled by GBTM from Oct 2019-Dec 2020
  - ✓Four trajectory models were generated using 2-5 adherence groups and the second order polynomial function of time
- **Statistical Analysis:**
  - ✓Descriptive statistics: Chi-square and ANOVA tests

Figure 1. Results of 2-5 Group Trajectory Modeling

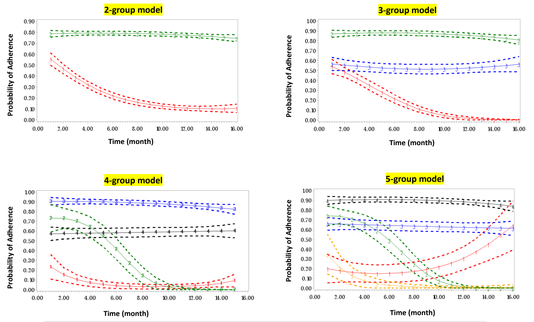
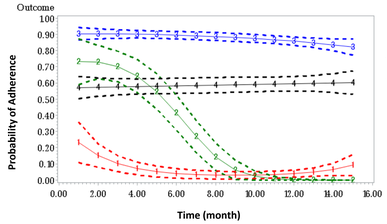


Table 1. Bayesian Criteria Calculation

Number of groups	BIC (All data points)	BIC (Number of subjects)	AIC	Log (2ΔBIC)
2	-4392.5	-4382.88	-4368.13	
3	-4282.90	-4267.65	-4244.47	2.36
4	-4212.95	-4192.16	-4160.55	2.18
5	-4201.80	-4175.46	-4135.42	1.52

RESULTS

Figure 2. Final Trajectory Model



Trajectory groups	Percent
1-Low adherence with gradual decline	14.6
2- Rapid decline	11.5
3- Constant high adherence	41.4
4- Constant PDC at ~0.6	32.6

Table 2. Patient Demographics and Clinical Characteristics (N=496)

Variable	Low adherence with gradual decline (N=73)	Rapid decline (N=57)	Constant high adherence (N=203)	Constant PDC at ~0.6 (N=163)
Age				
< 65 years	61 (83.56)	44 (77.19)	166 (81.77)	139 (85.28)
≥ 65 years	12 (16.44)	13 (22.81)	37 (18.23)	24 (14.72)
Race/ethnicity				
Black/African American	17 (23.29)	9 (15.79)	26 (12.81)	23 (14.11)
Hispanic	39 (53.42)	32 (56.14)	128 (63.05)	111 (68.10)
White/Not Hispanic/Others	17 (23.29)	16 (28.07)	49 (24.14)	29 (17.79)
Hyperlipidemia*				
Yes	46 (63.01)	30 (52.63)	100 (49.26)	66 (40.49)
No	27 (36.99)	27 (47.37)	103 (50.74)	97 (59.51)
Hypertension*				
Yes	46 (63.01)	30 (52.63)	128 (63.05)	77 (47.24)
No	27 (36.99)	27 (47.37)	75 (36.95)	86 (52.76)
Diabetes				
Yes	37 (50.68)	22 (38.60)	73 (35.96)	65 (39.88)
No	36 (49.32)	35 (61.40)	130 (64.04)	98 (60.12)
Depression				
Yes	13 (17.81)	13 (22.81)	37 (18.23)	39 (23.93)
No	60 (82.19)	44 (77.19)	166 (81.77)	124 (76.07)
Body Mass Index				
≤ 24.9	10 (13.70)	7 (12.28)	30 (14.78)	18 (11.04)
25.0 - 29.9	18 (24.66)	20 (35.09)	57 (28.08)	44 (26.99)
≥ 30.0	45 (61.64)	30 (52.63)	116 (57.14)	101 (61.96)
BC Stages				
0	14 (19.18)	14 (24.56)	31 (15.27)	29 (17.79)
I	22 (30.14)	22 (38.60)	67 (33.00)	37 (22.70)
II	19 (26.03)	14 (24.56)	62 (30.54)	47 (28.83)
III	13 (17.81)	6 (10.53)	38 (18.72)	41 (25.15)
IV	5 (6.85)	1 (1.75)	5 (2.46)	9 (5.52)
Type of OET				
Aromatase Inhibitor	54 (73.97)	36 (63.16)	131 (64.53)	97 (59.51)
Tamoxifen	19 (26.03)	21 (36.84)	72 (35.47)	66 (40.49)
Years on Therapy				
≤ 1 year	27 (36.99)	24 (42.11)	93 (45.81)	61 (37.42)
2-3 years	17 (23.29)	19 (33.33)	68 (33.50)	52 (31.90)
≥ 4 years	29 (39.73)	14 (24.56)	42 (20.69)	50 (30.67)

* Statistically significant difference

- A total of 496 patients were included in the study, with majority under the age of 65 (82.6%) and White/Hispanic (62.5%)
- The most common diagnosis was stage I (29.8%) and stage II (28.6%), followed by stage III (19.7%), stage 0 (17.7%), and stage IV (4.0%)
- Aromatase inhibitors (anastrozole, exemestane, and letrozole) were the more common OET (64.1%), compared to tamoxifen (35.8%)
- More patients were receiving OET for one year or less (41.3%) or for 2-3 years (31.4%), compared to four years or more (27.2%)
- Patients in the "low adherence with gradual decline" group had a higher mean duration of therapy compared to "constant high adherence" group (3.1 vs 2.17 years, p-value=0.01)
- A greater proportion of patients in "constant high adherence" group had hypertension (45.5%, p-value=0.01) and hyperlipidemia (41.3%, p-value=0.01) compared to the other groups

CONCLUSION

- This study demonstrated the use of GBTM to identify longitudinal patterns of OET adherence and selected the four-group trajectory as final model to describe medication taking behavior in this population
- Despite the significant benefits of OET in BC survival, ~60% of patients in our study showed non-adherent trajectories which indicates a need for adherence improvement interventions in underserved populations
- Identifying factors associated with non-adherent trajectories can guide the development of tailored interventions and enhance adherence to OET

References

- Franklin JM, Shrank WH, Pakes J, et al. Group-based trajectory models: a new approach to classifying and predicting long-term medication adherence. Med Care. 2013;51(9):789e796.
- Nagin DS. Group-based trajectory modeling: an overview. Ann Nutr Metab. 2014;65(2e3):205e210.