OXFORD

JNCI J Natl Cancer Inst (2018) 0(0): pky007

doi: 10.1093/jncics/pky007
Article

ARTICLE

Racial Disparities in Time From Diagnosis to Treatment for Stage I Non–Small Cell Lung Cancer

Jordan A. Holmes, Ronald C. Chen

See the Notes section for the full list of authors' affiliations.
Correspondence to: Ronald C. Chen, MD, MPH, Department of Radiation Oncology, University of North Carolina Hospitals CB #7512, Chapel Hill, NC 27599 (e-mail: ronald_chen@med.unc.edu).

Abstract

Background: Delay in lung cancer treatment is associated with worse survival outcomes. We examined whether there are racial disparities in time from diagnosis to treatment initiation for stage I non–small cell lung cancer (NSCLC) using data from the National Cancer Data Base, which includes approximately 70% of incident cancer patients across the United States.
Methods: We analyzed 119 184 patients diagnosed with stage I NSCLC from 2008 to 2013. Median times (in days) from diagnosis to treatment initiation for external beam radiation (EBRT), stereotactic body radiotherapy (SBRT), and surgery (inclusive of wedge resection, lobectomy, and pneumonectomy) were calculated separately and compared among white vs African American (AA) patients using the Wilcoxon rank-sum test. Multivariable linear regression assessed racial differences in days to treatment while adjusting for sex, age, insurance status, regional income, Charlson-Deyo comorbidity score, region, facility type, and treatment. Statistical tests were two-sided.
Results: AA patients had a statistically significantly longer median time to treatment for all three treatment modalities: EBRT 54 days (AA) vs 48 days (white, $P < .001$); SBRT 66 days vs 55 days ($P < .001$); surgery 31 vs 26 days ($P < .001$). In addition, 34% AA vs 24% white patients ($P \leq .001$) had treatment initiation eight or more weeks after diagnosis. In multivariable analysis, AA patients experienced an average 8.2-day delay compared with white patients ($P < .001$).
Conclusions: These results shed light on one possible mechanism of the observed racial disparity in mortality outcomes in NSCLC. Future studies are needed to determine if interventions to reduce treatment delays can reduce racial disparities in this disease.

Lung cancer is the second most common cancer in both men and women and the leading cause of cancer death in both sexes in the United States (1). While most patients are diagnosed at an advanced stage, in 2016 an estimated 39 000 patients presented with localized disease that is potentially curable. With increased use of low-dose computed tomography (CT) screening for lung cancer in high-risk populations, the incidence of early, stage I lung cancer diagnosis is expected to rise.

Racial disparities in lung cancer incidence and survival are well documented ([2–4]). Potential explanations for this disparity in survival include possible delayed diagnosis/more advanced stage and less aggressive treatment received among African American patients ([5–8]). In addition, delay from diagnosis to treatment could also contribute to this survival disparity. A recent study by Sampson et al. found that nonwhite patients were more likely to have surgery eight or more weeks after diagnosis compared with whites (odds ratio [OR] = 1.45, 95% confidence interval [CI] = 1.39 to 1.52) (9). However, little remains known about the overall magnitude of racial disparity in time to treatment or whether there are delays in treatment for patients treated with primary radiotherapy.

Therefore, the purpose of this study is to describe racial differences in time to treatment in a contemporary nationwide cohort of patients. We specifically chose to study stage I patients because they represent the most curable non–small cell lung cancer (NSCLC) patient population, and therefore a patient group potentially most likely to benefit from timely treatment.

Received: September 6, 2017; **Revised:** February 6, 2018; **Accepted:** March 1, 2018

Methods

Data Source

Data for this study were obtained from the National Cancer Data Base (NCDB), the largest cancer registry in the United States, which captures approximately 70% of incident cancer patients in the country. The database is jointly maintained by the American College of Surgeons and the American Cancer Society. The NCDB contains medical information including disease-specific variables such as clinical and pathologic TNM staging and baseline Charlson-Deyo comorbidity score. The NCDB additionally contains patient-level demographic information including age at diagnosis, sex, race, and insurance status; and census tract demographic information including household income by quartile. The NCDB has details about the first course of treatment received and time from diagnosis to initiation of treatment. Treatment facility is classified as academic, comprehensive community (standalone center, >500 cancer cases per year), community (standalone center, 100–500 cancer cases per year), and integrated network (integrated multifacility cancer network). The use of NCDB data for this study was granted an institutional review board waiver.

Patient Cohort

The primary objective of this study was to describe racial differences in time to treatment for stage I NSCLC. It is possible that with treatment delay, patients initially diagnosed as stage I may have progressed to more advanced disease by the time of treatment initiation. We used clinical staging consistently in this analysis because this is applicable to all patients who undergo surgery or radiotherapy. The analysis included non-Hispanic white and non-Hispanic African American patients with clinical stage I NSCLC (T1N0, T2aN0) diagnosed between 2008 and 2013 (n = 200 838). Patients were excluded if they received no treatment (n = 41 368), were missing information on clinical staging (n = 38 647), or had missing demographic information (n = 1639). This resulted in an analytic cohort of 119 184 patients (Supplementary Figure 1, available online).

Treatments were classified as surgery, stereotactic body radiotherapy (SBRT), and conventional external beam radiation therapy (RT) delivered within one year of diagnosis. Patients were classified as receiving SBRT if they received radiation as their first course of treatment, the radiation was targeted at the chest or lungs, fewer than 10 treatments were delivered, and the radiation modality was coded as stereotactic radiation. All patients who were treated with external beam radiation as the first course of treatment, for whom the radiation was targeted at the chest or lungs, and who did not meet the above criteria for SBRT were coded as receiving conventional external beam radiation.

Statistical Analysis

Descriptive statistics were used to report baseline patient characteristics, and the chi-square and *t* tests were used to report between-race group differences. The Wilcoxon rank-sum test was used to report differences in time to treatment by race overall and also further stratified by treatment type. The Fisher exact test was used to report differences in receipt of treatment by eight weeks. A multivariable linear regression model was created to examine the difference in time to treatment by race, adjusting for sex, age, insurance status, regional income, Charlson-Deyo comorbidity score, region, facility type, and treatment. Variables were selected for inclusion in the multivariable model based on significance in previous studies of survival or treatment disparity in lung cancer ([4–7]). All statistics were performed using Stata/IC 13.1 (StataCorp LP, College Station, TX). For all the statistical analyses, two-sided *P* values were used; a *P* value of less than .05 was considered statistically significant.

Of note, 27 509 patients included in the analytic cohort had a time to treatment of 0; that is, these patients were diagnosed with lung cancer at the time of surgical resection or initiation of radiation therapy. This could skew the results of the study, and to account for this, we constructed an additional multivariable regression model excluding these patients as a sensitivity analysis. Additional sensitivity analyses were conducted using a full multivariable model stratified by each quartile of income.

Results

Patient characteristics are outlined in Table 1 (Supplementary Table 1, available online, includes patients who did not receive treatment). African American patients were younger (median age = 67 vs 70 years), had higher Charlson-Deyo comorbidity scores, and were more likely to be on Medicaid or uninsured. African American (AA) patients were less likely to receive surgery (74.4% vs 76.2%) or SBRT (11.6% vs 12.4%) and more likely to receive conventional RT (14.0% vs 11.4%).

Median times to treatment for AA and white patients are reported in Table 2. In the overall comparison, AA patients had a longer time from diagnosis to treatment than white patients (39 vs 32 days, $P < .001$). AA patients had a statistically significantly longer median time to treatment for all three modalities: EBRT 54 days (AA) vs 48 days (white, $P < .001$); SBRT 66 days vs 55 days ($P < .001$); surgery 31 vs 26 days ($P < .001$). Figure 1 adds further details regarding distributions of time to treatment initiation for AA and white patients and shows that more AA patients experience a statistically significant delay in treatment. For example, 34% of AA vs 24% of white patients ($P < .001$) start treatment 56 or more days (eight weeks) after diagnosis. Table 2 shows that a delay was seen across all treatment types, with differences in median days to treatment of five days in patients who received surgery, 11 days for stereotactic body radiotherapy, and six days for conventional external beam radiotherapy.

Multivariable analysis, which adjusted for age, demographics, stage, and treatment type, showed that AA patients overall had an 8.2-day delay compared with CA patients (95% CI = 7.3 to 9.0, $P < .001$) (Table 3). In addition, patients were found to have a 0.4-day delay per five-year increase in age (95% CI = 0.2 to 0.5, $P < .001$); and patients with Medicare, Medicaid, or who were uninsured had delays compared with privately insured patients (2.3, 10.8, and 7.8 days respectively, $P < .001$ for all comparisons).

Sensitivity analysis excluding patients with time to treatment of zero days (Supplementary Table 2 and Supplementary Figure 2, available online) demonstrated similar results, with a difference between AA and white patients of 9.8 days in multivariable analysis (95% CI = 8.9 to 10.8, $P < .001$). An additional sensitivity analysis that was stratified by income quartile demonstrated a similar result (AA patients 8.5-, 5.8-, 8.2-, and 7.8-day delay for the first through fourth income quartiles,

Table 1. Patient characteristics

Characteristic	White (n = 109 233) No. (%)	African American (n = 9951) No. (%)	P
Age, median (range), y	70 (18–≥90)	67 (18–≥90)	<.001
Year			.10
2008	12 133 (11.1)	1027 (10.3)	
2009	13 910 (12.7)	1246 (12.5)	
2010	18 885 (17.3)	1702 (17.1)	
2011	20 155 (18.5)	1858 (18.7)	
2012	21 501 (19.7)	2021 (20.3)	
2013	22 649 (20.7)	2097 (21.0)	
Sex			.44
Male	49 008 (44.9)	4409 (44.3)	
Female	60 225 (55.1)	5542 (55.7)	
Charlson-Deyo Comorbidity Score			<.001
0	56 011 (51.3)	4894 (49.2)	
≥1	53 222 (48.7)	5057 (50.1)	
Insurance status			<.001
Private insurance	27 185 (24.9)	2480 (24.9)	
Medicare	74 543 (68.2)	5921 (59.5)	
Medicaid	3460 (3.2)	948 (9.5)	
Uninsured/unknown	4045 (3.7)	602 (6.1)	
Income (census tract)			<.001
Quartile 1 (0–25, lowest)	16 761 (15.3)	4659 (46.8)	
Quartile 2 (25–50)	27 021 (24.7)	2170 (21.8)	
Quartile 3 (50–75)	30 580 (28.0)	1754 (17.6)	
Quartile 4 (75–100, highest)	34 871 (31.9)	1368 (13.8)	
Region*			<.001
Northeast	24 208 (22.2)	1844 (18.5)	
South	40 347 (36.9)	5028 (50.5)	
Midwest	31 182 (28.6)	2644 (26.6)	
West	13 496 (12.4)	435 (4.4)	
Treatment facility type			<.001
Academic facility	38 400 (35.2)	4761 (47.8)	
Comprehensive community cancer program	54 671 (50.1)	3713 (37.3)	
Community cancer program	8268 (7.6)	638 (6.4)	
Integrated network cancer program	7894 (7.2)	839 (8.4)	
Treatment			<.001
Surgery	83 218 (76.2)	7405 (74.4)	
Stereotactic body radiotherapy	13 541 (12.4)	1153 (11.6)	
External beam radiotherapy	12 474 (11.4)	1393 (14.0)	
Clinical T stage			.07
T1	92 745 (84.9)	8380 (84.2)	
T2a	16 488 (15.1	1571 (15.8)	

*Regions: Northeast (CT, MA, ME, NH, RI, VT, NJ, NY, PA); South (DC, DE, FL, GA, MD, NC, SC, VA, WV, AL, KY, MS, TN, AR, LA, OK, TX); Midwest (IL, IN, MI, OH, WI, IA, KS, MN, MO, ND, NE, SD); West (AZ, CO, ID, MT, NM, NV, UT, WY, AK, CA, HI, OR, WA).

respectively, $P < .001$ for each model) (Supplementary Tables 3–6, available online).

Discussion

The overall prognosis for patients with lung cancer is poor, and racial disparities are well described, with African American vs white patients having worse overall survival, partially due to more advanced stage at diagnosis ([2–4]). However, patients with stage I disease have the most curable form of NSCLC. For this group, in patients fortunate enough to have an early diagnosis, the patterns of care of AA vs white patients are not well described. This is the first contemporary study to describe racial disparities in time from diagnosis to treatment initiation for stage I NSCLC. Using the NCDB, which includes approximately 70% of all incident cancers in the United States, we found an

Table 2. Time to treatment in days overall and by treatment category*

Treatment	Time to treatment, median (IQR)	Bivariate P
Overall	33 (7–56)	<.001
White	32 (7–56)	
African American	39 (11–69)	
Surgery	27 (0–48)	<.001
White	26 (0–48)	
African American	31 (0–60)	
Stereotactic body RT	56 (37–83)	<.001
White	55 (37–82)	
African American	66 (42–98)	
External beam RT	48 (31–74)	<.001
White	48 (31–72)	
African American	54 (33–89)	

*IQR = interquartile range; RT = radiation therapy.

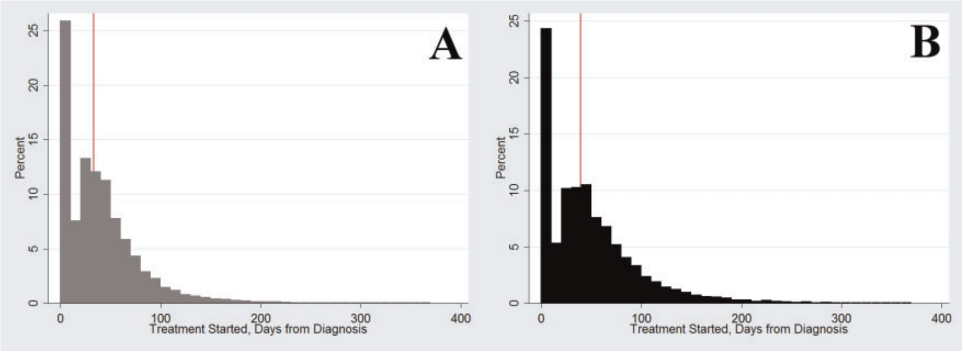

Figure 1. Distribution of time from diagnosis to treatment in days for white **(A)** and African American **(B)** patients. **Vertical lines** represent median time to treatment.

Table 3. Multivariable linear regression model of time to treatment in days*

Variable	Beta coefficient (95% CI)	*P*
Race		
White	Referent	–
African American	8.2 (7.3 to 9.0)	<.001
Age (per 5-y increase), y	0.4 (0.2 to 0.5)	<.001
Sex		
Male	Referent	–
Female	−0.7 (−1.1 to −0.2)	.004
Charlson Comorbidity Score		
0	Referent	–
1–2	1.0 (0.2 to 1.3)	<.001
Insurance		
Private insurance	Referent	–
Medicare	2.3 (1.7 to 2.9)	<.001
Medicaid	10.8 (9.6 to 12.1)	<.001
Uninsured/unknown	7.8 (6.6 to 9.0)	<.001
Income (census tract)		
Quartile 1 (0–25, lowest)	Referent	–
Quartile 2 (25–50)	−1.4 (−2.1 to −0.7)	<.001
Quartile 3 (50–75)	−1.9 (−2.6 to −1.2)	<.001
Quartile 4 (75–100, highest)	−4.8 (−5.5 to −4.1)	<.001
Region		
Northeast	Referent	–
South	−3.0 (−3.6 to −2.4)	<.001
Midwest	−1.2 (−1.8 to −0.6)	<.001
West	4.6 (3.8 to 5.5)	<.001
Facility type		
Comprehensive community cancer program	Referent	–
Academic facility	3.1 (2.6 to 3.6)	<.001
Community cancer program	1.4 (0.6 to 2.3)	.001
Integrated network cancer program	0.8 (−0.1 to 1.7)	.068
Treatment		
Surgery	Referent	–
Stereotactic body radiotherapy	32.2 (31.5 to 32.9)	<.001
External beam radiotherapy	25.1 (24.3 to 25.8)	<.001
Clinical T stage		
T1	Referent	
T2a	2.4 (1.8 to 3.0)	<.001

*The intercept for the time to treatment model is 25.7 days. Example calculation for a man age 60 years, Medicare patient, census tract highest quartile income, South region, treated at an academic facility with surgery: white: 25.7 + 0 + (60 years/5)*0.4 + 0 + 2.3 – 4.8 – 3.0 + 3.1 + 0 = 28.1 days; African American: 25.7 + 8.2 + (60 years/5)*0.4 + 0 + 2.3 – 4.8 – 3.0 + 3.1 + 0 = 36.3 days. CI = confidence interval.

8.2-day delay in median time to treatment initiation for AA vs CA patients, and this difference was even larger for patients who received radiation treatment.

Racial disparities in time to initiation of treatment have been documented in other disease sites ([10–14]). Using Surveillance, Epidemiology, and End Results (SEER)–Medicare data that included patients age 65 years and older, studies have shown a longer time from diagnosis to treatment for AA compared with CA patients in breast cancer (difference = 9.1 days, $P < .001$) (10) and prostate cancer (difference = 7.6 days, $P = .004$) (11). Disparities in treatment initiation have not been well studied in NSCLC. A prior study by Gomez et al. using SEER-Medicare data of patients diagnosed from 2004 through 2007 (15) showed that AA vs Caucasian patients had 1.18 times the odds of starting treatment more than 35 days after diagnosis. A recent study conducted by Samson et al. using a contemporary cohort of stage I NSCLC patients from the NCDB corroborated this finding; AA patients were more likely than whites to undergo surgery more than eight weeks after diagnosis (OR = 1.45, 95% CI = 1.39 to 1.52) (9). However, the magnitude of the difference in time to initiation of treatment and whether these disparities exist among patients not treated with primary surgery are unknown. The current study fills this knowledge gap. With increased awareness of and efforts to address racial disparities in cancer over the past decade (16), our study shows that a disparity in delay to treatment continues to exist. Of note, the 8.2-day median delay found in this study for lung cancer is of similar magnitude to those found prior studies in breast and prostate cancers.

We also noted a larger delay in treatment for AA vs CA patients who received radiation (instead of surgical) treatment. This may be related to the additional coordination of care necessary for these patients. Most patients with stage I NSCLC consult with a surgeon first, but for a patient to receive radiation therapy, he/she needs to be subsequently referred to a radiation oncologist for consultation and simulation. Further, stereotactic body radiation patients may require the most complicated coordination of care because these patients might additionally need fiducial marker placement before radiation simulation. Each additional step in the care pathway could contribute to a delay in AA vs white patients.

Treatment delay in lung cancer is associated with worse outcomes, specifically in patients with early-stage and potentially curable disease. In an NCDB analysis, Samson et al. reported outcomes from a propensity score–matched cohort of 13 511 patients who underwent surgical resection fewer than eight weeks or eight or more weeks from diagnosis. They found more pathologic upstaging (16.6% vs 18.3%) and worse survival (median survival = 69.2 vs 57.7 months) for patients in the latter group (17). Another study published by Bott et al. of patients with stage I or II lung cancer similarly showed that time to surgery of more than eight weeks was statistically significantly associated with pathologic upstaging in multivariable analysis (18). Multiple other studies using SEER-Medicare and institutional data have shown an association between treatment delay and worse overall survival (15,19).

This study has potential limitations. The first limitation is that the study did not fully capture the complex patient, provider, and health care system variations that contribute to the process of moving from diagnosis to treatment. While the NCDB captures approximately 70% of incident cancer cases in the United States, patients from nonaccredited centers are not captured. This can lead to geographic and socioeconomic groups that are underrepresented in the database, and the effect this might have on the measured racial disparities is unknown (20). In addition, the clinical significance of an 8.2-day average delay in AA vs white patients is unclear. However, our study showed an overall difference in the distribution of time from diagnosis to treatment start between AA and white patients; it is possible that the higher proportion of AA patients who experience delays may be more clinically important in driving patient outcomes. Further research is needed in this area.

In conclusion, this is the first contemporary study to describe racial disparities in time from diagnosis to treatment initiation for stage I NSCLC patients treated with surgery, SBRT, or external beam radiation. We found that AA patients on average have an 8.2-day delay in treatment initiation compared with CA patients, and more AA patients (34% vs 24%) start treatment eight weeks or more after diagnosis. This study contributes to an overall understanding of mechanisms that can lead to racial disparities in mortality among NSCLC patients and provides a potential target for intervention to reduce these disparities.

Funding

None.

Notes

Affiliations of authors: Department of Radiation Oncology (JAH, RCC) and Sheps Center for Health Services Research (RCC), University of North Carolina at Chapel Hill, Chapel Hill, NC; University of North Carolina-Lineberger Comprehensive Cancer Center, Chapel Hill, NC (RCC).

The authors have no conflicts of interest to report.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin*. 2016;66(1):7–30.
2. Williams CD, Salama JK, Moghanaki D, Karas TZ, Kelley MJ. Impact of race on treatment and survival among U.S. veterans with early-stage lung cancer. *J Thorac Oncol*. 2016;11(10):1672–1681.
3. Hunt B, Balachandran B. Black:white disparities in lung cancer mortality in the 50 largest cities in the United States. *Cancer Epidemiol*. 2015;39(6):908–916.
4. DeSantis CE, Siegel RL, Sauer AG, et al. Cancer statistics for African Americans, 2016: Progress and opportunities in reducing racial disparities. *CA Cancer J Clin*. 2016;66(4):290–308.
5. Corso CD, Park HS, Kim AW, Yu JB, Husain Z, Decker RH. Racial disparities in the use of SBRT for treating early-stage lung cancer. *Lung Cancer (Amsterdam, Netherlands)*. 2015;89(2):133–138.
6. Harrison MA, Hegarty SE, Keith SW, Cowan SW, Evans NR 3rd. Racial disparity in in-hospital mortality after lobectomy for lung cancer. *Am J Surg*. 2015;209(4):652–658.
7. Williams CD, Stechuchak KM, Zullig LL, Provenzale D, Kelley MJ. Influence of comorbidity on racial differences in receipt of surgery among US veterans with early-stage non-small-cell lung cancer. *J Clin Oncol*. 2013;31(4):475–481.
8. Yang R, Cheung MC, Byrne MM, et al. Do racial or socioeconomic disparities exist in lung cancer treatment? *Cancer*. 2010;116(10):2437–2447.
9. Samson P, Crabtree T, Broderick S, et al. Quality measures in clinical stage I non-small cell lung cancer: Improved performance is associated with improved survival. *Ann Thorac Surg*. 2017;103(1):303–311.
10. Bleicher RJ, Ruth K, Sigurdson ER, et al. Preoperative delays in the US Medicare population with breast cancer. *J Clin Oncol*. 2012;30(36):4485–4492.
11. Stokes WA, Hendrix LH, Royce TJ, et al. Racial differences in time from prostate cancer diagnosis to treatment initiation: A population-based study. *Cancer*. 2013;119(13):2486–2493.
12. Fedewa SA, Ward EM, Stewart AK, Edge SB. Delays in adjuvant chemotherapy treatment among patients with breast cancer are more likely in African American and Hispanic populations: A national cohort study 2004-2006. *J Clin Oncol*. 2010;28(27):4135–4141.
13. Smith EC, Ziogas A, Anton-Culver H. Delay in surgical treatment and survival after breast cancer diagnosis in young women by race/ethnicity. *JAMA Surg*. 2013;148(6):516–523.
14. Bustami RT, Shulkin DB, O'Donnell N, Whitman ED. Variations in time to receiving first surgical treatment for breast cancer as a function of racial/ethnic background: A cohort study. *JRSM Open*. 2014;5(7):2042533313515863.
15. Gomez DR, Liao KP, Swisher SG, et al. Time to treatment as a quality metric in lung cancer: Staging studies, time to treatment, and patient survival. *Radiother Oncol*. 2015;115(2):257–263.
16. Medicine I, Policy BHS, Care CUEREDH, Nelson AR, Stith AY, Smedley BD. *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*. Washington, DC: National Academies Press; 2002.
17. Samson P, Patel A, Garrett T, et al. Effects of delayed surgical resection on short-term and long-term outcomes in clinical stage I non-small cell lung cancer. *Ann Thorac Surg*. 2015;99(6):1906–1912; discussion 1913.
18. Bott MJ, Patel AP, Crabtree TD, et al. Pathologic upstaging in patients undergoing resection for stage I non-small cell lung cancer: Are there modifiable predictors? *Ann Thorac Surg*. 2015;100(6):2048–2053.
19. Bryant AS, Cerfolio RJ. Impact of race on outcomes of patients with non-small cell lung cancer. *J Thorac Oncol*. 2008;3(7):711–715.
20. Boffa DJ, Rosen JE, Mallin K, et al. Using the National Cancer Database for outcomes research: A review. *JAMA Oncol*. 2017;3(12):1722–1728.