

Hospitalization outcomes and racial disparities in cervical cancer patients: An analysis of the national inpatient sample data from 2002 to 2014



Gurudatta Naik^{a,b}, Amrita Mukherjee^a, Tomi Akinyemiju^c, Sadeep Shrestha^{a,b,*}

^a Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham AL, United States

^b O'Neal Comprehensive Cancer Center at University of Alabama at Birmingham, Birmingham AL, United States

^c College of Public Health, University of Kentucky, Lexington KY, United States

ARTICLE INFO

Keywords:

Cervical cancer
Healthcare cost and utilization project national inpatient sample (HCUP-NIS)
Hospitalization outcomes
Racial difference

ABSTRACT

Background: Little is known about outcomes in patients after being hospitalized for care of cancer or comorbid conditions and the disparity between African-American and White cervical cancer patients.

Methods: Using the national inpatient sample (HCUP-NIS) database of the Healthcare Cost and Utilization Project between 2002–2014, we included 5217 African-American and 21,752 White patients hospitalized with a primary diagnosis of cervical cancer. We examined racial differences in hospitalization outcomes; length of stay (LOS) in hospital, mortality in hospital, post-operative complications in patients who underwent hysterectomy and discharge disposition. Patients were matched on age at primary diagnosis, insurance status, residential region, and median income of residential area, modified Deyo comorbidity index, stage of disease and treatment. Categorical outcomes were analyzed by conditional logistic regression accounting for matched study design and odds ratios (95%CI) were reported. LOS was analyzed using *t*-test and beta estimate for difference in means was reported.

Results: The LOS was significantly lower for Whites compared to African-American cervical cancer patients when matched on demographic only ($\beta = -0.41$, *p*-value < 0.0005, presentation + demographic ($\beta = -0.41$, *p*-value < 0.0006) and treatment + presentation + demographic variables ($\beta = -0.46$, *p*-value < 0.0001). White cervical cancer patients were commonly discharged to other intermediate nursing facility (OR = 1.30, 95%CI = 1.20–1.41, matched on demographic only; OR = 1.31, 95%CI = 1.21–1.43, matched on presentation + demographic; and OR = 1.32, 95%CI = 1.22–1.43), matched on treatment + presentation + demographic). Similar trends were seen in both older (≥ 65 years) and younger (< 65 years) patients, when stratified by age.

Conclusion: Disparities in hospitalization outcomes in cervical patients are not observed when different characteristics of African-American and White cervical patients are accounted for and matched.

1. Introduction

Cervical cancer is the third most commonly diagnosed gynecologic cancer among US women [1]. Although the introduction of Papanicolaou smear test in 1943 has led to decreased incidence and mortality rates of cervical cancer, 12,820 new cases and 4210 deaths were reported in 2017 in the US [2,3]. Epidemiologic and virologic data demonstrate that oncogenic HPVs are the primary (and necessary) causal agents of cervical cancer [4]. Cervical cancer is unique in that it is both preventable, with use of HPV vaccine and curable disease with various treatment modalities (laser therapy, cryotherapy, and surgery) to remove pre-cancerous and early cancerous lesions. However, despite these measures, there is wide disparity in access to care [5–8]. For

cervical cancer patients the incremental costs of care for over 4 years of follow up are 18,000 US dollars compared to non-cancer individuals accessing care [9–11]. There seems to be higher care of costs towards the end of life among cancer patients within the last 6 months of their life, predominantly due to inpatient hospitalization, hospice care, deaths in hospital more than outpatient care [12]. These costs significantly go higher up in the last month of their lives. There is growing interests in studying the overall cost of care in cancer survivors including cervical cancer patients; however, not much is known about disparities in costs between African-American and White cancer patients. Currently, US spends around 88 billion US dollars for management of cancer survivors [13]. More than 50% of these cervical cancer patients requiring hospitalization tend to be below 45 years of age,

* Corresponding author at: Department of Epidemiology, University of Alabama, RPHB 217L, Birmingham, United States.

E-mail address: sshrestha@uab.edu (S. Shrestha).

unlike other female-related cancers (ovarian and breast cancers) where older patients required more hospital stays [14]. Hence, age plays a role in response to cancer treatment in patients undergoing surgical resection (hysterectomy) and this needs to be evaluated more in the context of disparities in outcomes between African-American and White cervical cancer patients.

African-American women tend to have higher incidences and mortality due to cervical cancer as compared to White women [1,15–18]. Proffered reasons for the persistent disparity in cervical cancer outcomes include differential access to healthcare, differences in the prevalence of HPV infection and distribution of HPV subtypes, lack of routine screening, geographical region of residence, and insurance status [19–23]. Consequently, African-American women with cervical cancer tend to present at later stages, have delayed access to surgical treatment, and thus have a poorer prognosis [8,24–27]. When looking at high-volume and low-volume hospitals treating localized cervical cancer, there was a higher disparity in offering National Comprehensive Cancer Network (NCCN) guidelines concordant treatment between African-American and White cervical cancer patients in high-volume hospitals [28]. African-American cervical patients tend to receive less guidelines concordant treatment and this reflected in poorer survival outcomes compared to White patients. When corrected for hysterectomy, incidence of cervical cancer was higher in older black women compared to older white women [29]. Similarly, hysterectomy-corrected analysis of mortality rates in cervical cancer patients showed that mortality was underestimated in African-American women who were older (> 65 years of age) [17]. However, it remains unclear whether racial disparities in cervical cancer outcomes persist among African-American and White patients who are hospitalized.

The goal of the current study is to utilize the National Inpatient Sample (NIS) database to evaluate hospitalization outcomes; post-operative complications after hysterectomy, in-hospital mortality, LOS in hospital and discharge disposition, among African-American and White patients who have been hospitalized with a primary diagnosis of cervical cancer after matching on key demographic, clinical presentation and treatment characteristics. Further, we will evaluate disparities in outcomes overall as well as stratified by age (lower than or greater than 65 years).

2. Material and methods

2.1. Data resources

Data were analyzed from the Healthcare Cost and Utilization Project National Inpatient Sample (HCUP-NIS) database, which includes a 20% sample of inpatient visits between 2002–2014 from 10,000 US hospitals. Before the year 2012, this database included all inpatient admissions from 20% of the hospitals included from all states using a stratified probability sampling, whereas after 2012, 20% of inpatient visits from all hospitals were selected by systematic sampling design. The database is maintained by the Agency for Healthcare Resources and Quality (AHRQ) and includes detailed records on 83 million all-payer in-patient visits, including admissions, diagnoses and procedures (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] codes), patient demographic and socioeconomic information and hospital information. The database have detailed demographic characteristics like age, gender, race, income, residential region, and insurance status, which gives information on socio-economic markers for patients. It also collects information on primary and secondary diagnoses, procedures of all patients that are hospitalized which can enable us to identify patient population, and their comorbid conditions using ICD-9 codes since all visits occurred before 2015. Using procedure codes, we can identify which patients received surgical treatment. Data on chemotherapy and radiation therapy is not available for all cancer patients since most of these treatments are administered in outpatient setting. More detailed

information on this HCUP-NIS database can be obtained at <http://www.hcup-us.ahrq.gov/nisoverview.jsp>

The study population for this study included African-American and White women, 21 years and above, diagnosed with cervical cancer (ICD-9 code of 180.1) and who received treatment for cervical cancer [24]. A total of 45,549 cervical cancer patients were identified from the database between 2002 and 2014. Main study covariates included demographic, clinical presentation and treatment characteristics as outlined below. Since this database is publicly available and de-identified, the Institutional Review Board of University of Alabama at Birmingham considered this study exempt from human subjects' safety review.

2.2. Demographic variables

Information on all patients was collected from billing information that was submitted by hospitals to statewide data organizations, with the help of admission and discharge notes - age (in years) at the time of admission, residential region, insurance status, and median household income of their residential area. Residential region was derived from the population size of the patient's county of residence; 1) Large Metropolitan counties (> = 1 million population), 2) Small Metropolitan counties (between 50,000 and 999,999 population), 3) Micropolitan counties (between 10,000 and 49,999 population) and 4) Non-Metropolitan and Non-Micropolitan counties (under 10,000 population). Median household income was calculated by zip-code for the patient's area of residence and categorized as 1) Lowest Quartile (\leq \$25,000 per year), 2) Second Quartile (between \$25,001 and \$34,999 per year), 3) Third Quartile (between \$35,000 and \$44,999 per year) and 4) Highest Quartile (\geq \$45,000 per year). Insurance status of patients was categorized as Medicaid, Medicare, Private and others.

2.3. Clinical presentation variables

Two variables were created from clinical information available in the database. First, stage of the cancer was categorized as Non-Metastatic or Metastatic. In the absence of information on Tumor, Node and Metastasis (TNM) stage in the database, ICD-9 codes for metastatic disease were used and the rest of the cervical cancer patients were then included as Non-Metastatic disease [30]. Secondly, a modified Deyo Comorbidity Index was created as a composite index of individual burden of multiple comorbidities and included cerebrovascular diseases, congestive heart failure, diabetes mellitus, dementia, myocardial infarction, rheumatic diseases, peptic ulcer disease, liver disease, renal disease and HIV/AIDs [30,31]. Briefly, the index was created by identifying these diseases with their ICD-9 codes, assigning them each a value of 1, and then summing up the values based on the number of diseases in each patient.

2.4. Treatment variables

Cervical cancer is primarily treated by Hysterectomy (radical, open or laparoscopic), conization, Loop Electrosurgical Excision Procedure (LEEP), laser surgery and cryosurgery for localized disease, while radiation therapy and chemotherapy are administered to prevent, or control spread of disease or improve response to surgical treatment [32,33]. ICD-9 codes for hysterectomy, conization, LEEP, laser surgery, and cryosurgery (68.31, 68.41, 68.61, 68.51, 68.71, 68.39, 68.49, 68.69, 68.59, 68.79, V88.0, 68.1, 68.2, 68.3, 68.4, 68.5, 68.6, 68.7, 68.8, 68.9, 67.32, 67.33, 67.11, 67.12, 67.62, 67.2, 61.85, V67.01, V76.47, V88.01, V88.03, 752.43), radiation therapy (92.29, 92.27, 92.41) and chemotherapy (V58.11, 99.25, 54.97) were used [30,34]. Those patients who already had the above treatment codes at their first visit were excluded, to avoid including those procedures that may have been done for another indication besides cervical cancer.

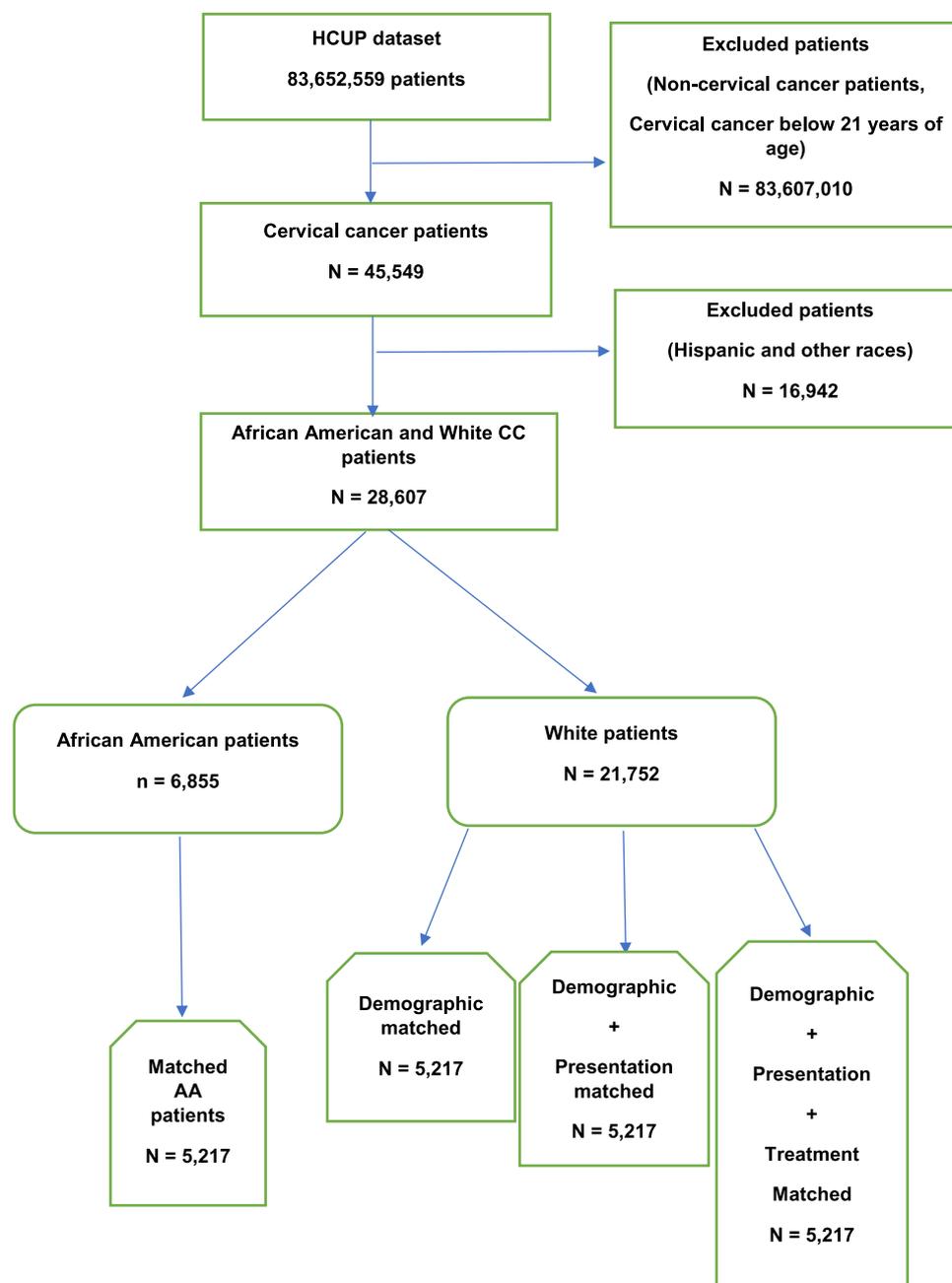


Fig. 1. Flowchart of sample-size nested within the Healthcare Cost and Utilization Project of the national inpatient sample (HCUP-NIS) database, following the study-design and inclusion/exclusion criteria.

2.5. Outcomes

To study disparities in hospitalization outcomes, four variables were created – 1) Length of Stay (LOS), 2) Post-operative complications, 3) Discharge Disposition and 4) In-hospital Mortality, as previously described [35]. LOS is cumulative number of days that a patient with cervical cancer was hospitalized for care of their cancer or for other comorbid conditions. Patients who were hospitalized and then discharged were included in the analysis for LOS and hence the minimum number of days of LOS was 1 day if they were discharged the next day after admission. Length of stay was recorded as a continuous variable. Presence of post-operative complications was coded as ‘Yes’, in patients undergoing hysterectomy, if any diagnoses included ICD-9 codes for mechanical and infectious complications. Mechanical complications included non-healing wound (989.83), hematoma at the site (998.12), seroma at the site (998.13), disruption of wound (998.31 and 998.32),

persistent fistula (998.6), while infectious complications included post-operative infection, infected post-operative seroma, intra-abdominal post-operative abscess, stitch post-operative abscess, and post-operative septicemia (998.5, 998.51, 998.59) using appropriate ICD-9 codes [36]. Those patients that did not undergo hysterectomy but had ICD-9 codes for post-operative complications, which could be due to other non-cancer relevant surgeries, were coded as ‘No’ for post-operative complications for this study. Patients who did not experience any post-operative complications listed above after hysterectomy were also coded ‘No’. In-hospital mortality was defined by death in these patients during stay in hospital [35]. It was coded as ‘Yes’ if patient died in hospital and ‘No’ if there was no code for death during hospital stay. Discharge disposition was derived from information in discharge summary if the patients were sent home (routine), to skilled or nursing facilities, or had other outcomes (short-term hospital, home health care, discharge against medical advice, intermediate care facility, or another type of

Table 1
Patient Characteristics comparing African-American and unmatched White Cervical Cancer patients, National Inpatient Sample, 2002–2014. * §.

	African-American (N = 6855)	White (N = 21,752)	p-value
Age at admission– year, Mean (SD)	52.23 (14.88)	51.46 (14.60)	0.0002
Residential Income, N (%)			
First Quartile-Lowest	3,544 (51.70)	5669 (26.06)	< 0.0001
Second Quartile	1,316 (19.20)	5487 (25.23)	
Third Quartile	923 (13.46)	4923 (22.63)	
Fourth Quartile-Highest	559 (8.15)	4342 (19.96)	
Missing	513 (7.49)	1331 (6.12)	
Number of co- morbidity, Mean (SD)	0.34 (0.62)	0.29 (0.57)	< 0.0001
Stage, N (%)			
Non-Metastatic	4,935 (71.99)	15,956 (73.35)	0.0266
Metastatic	1,920 (28.01)	5796 (26.65)	
Surgery, N (%)			
Yes	1,710 (24.95)	7757 (35.66)	< 0.0001
No	5,145 (75.05)	13,995 (64.34)	
Insurance Type, N (%)			
Medicaid	2,833 (41.33)	5318 (24.45)	< 0.0001
Medicare	1,560 (22.76)	4633 (21.30)	
Other	878 (12.81)	2201 (10.12)	
Private	1,584 (23.11)	9600 (44.13)	
Residential Region, N (%)			
Large Metro (> 1mil residents)	2921 (42.61)	6089 (27.99)	< 0.0001
Small Metro (< 1 mil residents)	624 (9.10)	3397 (15.62)	
Micropolitan (Adjacent to metro)	217 (3.17)	1550 (7.13)	
Non-metro and non- micropolitan	196 (2.86)	1136 (5.22)	
Missing	2,897 (42.26)	9580 (44.04)	
Post-operative complications N (%)			
Yes	116 (1.69)	498 (2.29)	0.0026
No	6739 (98.31)	21,254 (97.71)	
Died during Hospitalization N (%)			
Yes	192 (2.80)	469 (2.16)	0.0003
No	6,662 (97.20)	21,280 (97.84)	
Length of Stay – days, Mean (SD)	5.06 (6.17)	4.32 (5.23)	< 0.0001
Discharge Disposition, N (%)			
Routine Discharge	2,349 (34.27)	7087 (32.58)	0.0181
Skilled Nursing Facility	471 (6.87)	1459 (6.71)	
Other	4,035 (58.86)	13,206 (60.71)	

* Percentages may not add up to 100% due to rounding.

facility) including death.

2.6. Statistical analysis

Data on baseline characteristics and outcomes were compared between all African-American and all White patients with cervical cancer. In cases of categorical variables, data were compared by chi-square test while in the case of continuous variables, data were compared by *t*-test and their effect estimates and p-values are presented. Thereafter, a sequential multivariable matching was conducted in African-American and White patients with cervical cancer using baseline variables. All African-American cervical cancer patients were included in one group and then compared with three groups of White patients matched on selected sets of variables. These 3 sets of variables were as follows – 1) Demographic variables only = age, residential income, geographic region and insurance status; 2) Presentation plus demographic variables = stage, comorbidity index, in addition to age residential income, geographic region and insurance status; and 3) Treatment plus presentation plus demographic variables = surgery, in addition to stage, comorbidity index, age, residential income, geographic region and

insurance status [37–39]. To assess the impact of age in driving racial disparities within hospitalization outcomes, two subgroups were created = 1) < 65 years of age and 2) ≥ 65 years of age. The cut-off for age was selected since patients above 65 years of age can avail of Medicare coverage however; those below or equal to 65 years of age had different coverages including private and Medicaid. To compare outcomes in unmatched African-American and White patients that were categorical or continuous variables, logistic regression or *t*-test was conducted, and effect estimates were reported with 95% confidence intervals. A conditional logistic regression with 3 models was conducted, where each model included African-American cervical cancer patients matched with White cervical cancer patients based on Demographic variables, on Presentation plus demographic variables and finally on Treatment plus presentation plus demographic variables. Odds ratio were reported with 95% confidence interval for categorical variables like in-hospital mortality, and post-operative complications, while *t*-test were conducted to evaluate the differences in LOS between matched groups of patients. The beta estimate with negative number indicated shorter length of stay for White patients while positive number for beta estimate reflected longer LOS compared to African-American patients. All p-values were reported with a significance threshold of 0.05. In order to evaluate differences in discharge disposition, multinomial logistic regression was conducted with “discharge to home” as the reference category.

2.7. Sample size

In this retrospective study of patients hospitalized for various health conditions including cancer care, we identified 28,607 women (6855 (24%) African-Americans and 21,752 (76%) White), 21 years and older, that were diagnosed with cervical cancer and were then treated for it or other comorbidities (Fig. 1). Of these patients, those with racial background other than African-American and Caucasian were not included in this study. After matching was conducted, only 5217 pairs of African-American and White cervical cancer patients were included based on demographic only variables, presentation plus demographic variables and treatment plus presentation plus demographic variables (Fig. 1). Since there was no randomization, the balance between the two groups of patients was ensured by using propensity score matching with greedy matching technique [38,40]. In this method, each White patient who had the best match with an African-American patient based on propensity score, was selected for analysis without replacement. This technique previously described by Silber et al gives an unbiased estimation of effect when randomization is not possible [34,39].

3. Results

Table 1 describes the baseline demographic, clinical presentation and treatment variables for all patients included in the study stratified by race along with overall outcomes in both groups – post-operative complications, LOS in hospital, death in hospital and discharge disposition. Overall analysis showed that African-American patients were slightly older at the time of hospitalization compared to White patients (52.23 years vs 51.46 years respectively; $p = 0.0002$). African-American women were predominantly from regions with median residential income in the lowest quartile (52%) while only 26% of White patients were from regions with residential income in lowest quartile. African-American women had significantly higher ($p < 0.0001$) burden of comorbidities compared to that in White patients (mean modified Deyo score = 0.34 vs 0.29 respectively). The proportion of patients presenting with non-metastatic disease was similar in both races (72% vs 73%); however, the proportion of African-American patients undergoing surgery was considerably lower (25%) than that in White patients (36%). African-American patients were more likely to be covered with Medicaid (42%) whereas most White patients had private insurance coverage (44%). A greater proportion of African-American patients resided in large metropolitan areas (42%) compared to White patients

Table 2
Patient Characteristics comparing African-American and matched White Cervical Cancer patients, Nationwide Inpatient Sample, 2002–2014.*[§]

	African-Americans (N = 5217)	Whites- matched on Demographic (N = 5217)	Whites-matched on Presentation plus Demographic (N = 5217)	Whites- matched on Treatment plus presentation plus demographic (N = 5217)
Age at admission– year, Mean (SD)	51.88 (14.78)	52.56 (14.99)	52.30 (15.09)	52.41 (15.02)
p-value		0.0208	0.1531	0.0693
Residential Income, N (%)				
First Quartile-Lowest	2,693 (51.62)	2431 (46.60)	2442 (46.81)	2430 (46.58)
Second Quartile	988 (18.94)	1210 (23.19)	1,154 (22.12)	1166 (22.35)
Third Quartile	669 (12.82)	675 (12.94)	719 (13.78)	726 (13.92)
Fourth Quartile-Highest	415 (7.95)	393 (7.53)	403 (7.72)	394 (7.55)
p-value		0.1845	0.0910	0.0485
Number of Co-morbidities, Mean (SD)	0.31 (0.30)	0.28 (0.26)	0.29 (0.56)	0.29 (0.56)
p-value		0.0042	0.0514	0.0438
Stage, N (%)				
Non-Metastatic	3,791 (72.67)	3860 (73.99)	3793 (72.70)	3812 (73.07)
Metastatic	1,426 (27.33)	1357 (26.01)	1424 (27.30)	1405 (26.93)
p-value		0.1267	0.9650	0.6438
Surgery, N (%)				
Yes	1,260 (24.15)	1681 (32.22)	1658 (31.78)	1287 (24.67)
No	3,957 (75.85)	3536 (67.78)	3559 (68.22)	3930 (75.33)
p-value		0.0001	0.0001	0.5383
Insurance Type, N (%)				
Medicaid	2,125 (40.73)	1917 (36.75)	1964 (37.65)	2006 (38.45)
Medicare	1,137 (21.79)	1239 (23.75)	1221 (23.40)	1195 (22.91)
Other	710 (21.79)	765 (14.66)	740 (14.18)	720 (13.80)
Private	1,245 (23.86)	1296 (24.84)	1292 (24.77)	1296 (24.84)
p-value		0.0030	0.0205	0.0608
Residential Region, N (%)				
Large Metro	2510 (48.11)	2197 (42.11)	2203 (42.23)	2185 (41.88)
Small Metro	507 (9.72)	539 (10.33)	553 (10.60)	595 (11.41)
Micropolitan	187 (3.58)	178 (3.41)	168 (3.22)	167 (3.20)
Non-metro and non- micropolitan	165 (3.16)	163 (3.12)	160 (3.07)	156 (2.99)
p-value		0.0887	0.1531	0.7481

[§] The African-Americans column represents all African-American patients diagnosed with cervical cancer in the dataset; Whites matched on demographics represents Whites matched on Age, geographical region, residential income and insurance status; Whites matched on presentation plus demographic represent Whites matched on all demographic variables as well as disease stage and comorbidities; Whites matched on treatment plus presentation plus demographic represents Whites matched on all demographic and presentation variables as well as surgery.

(28%).

Table 2 describes the population in detail after matching on 3 different sets of variables as mentioned in statistical analyses- Demographic, Presentation plus demographic and Treatment plus presentation plus demographic information. Each set of matching had 5217 pairs of African-American and White patients. When matched on all criteria (Demographic, Presentation and Treatment), there were no significant differences in the covariates between African-American and White patients except marginal statistical differences in comorbidities (p-value = 0.0438) and income status (p-value = 0.0485). This shows that for most part there was adequate matching of covariates in both groups.

Table 3 describes the outcomes in cervical cancer patients who are matched on demographic, presentation and treatment variables. The upper panel of Table 3 describes estimates for 4 outcomes in all individuals when matched on three sets of variables described in analyses, while the lower panel describes outcomes after stratification based on age < 65 years and ≥ 65 years.

Overall there were no differences in post-operative complications between African-American and White cervical cancer patients when matched on demographic, presentation and treatment variables. However, when stratified by age, compared with older African-American cancer patients (≥65 years) older White cancer patients experienced higher odds of post-operative complications (OR = 3.16 (95% CI = 1.54–6.48) when matched on demography only, OR = 3.16 (95% CI = 1.54–6.48) when matched on presentation plus demography variables and OR = 2.43 (95% CI = 1.16–5.11) when matched on

Treatment plus presentation plus demographic variables). These differences were not significant among younger cancer patients.

Overall, length of stay was significantly lower in White patients when matched on demographic only (beta estimate = -0.41, p-value = 0.0005), presentation plus demographic (beta estimate = -0.41, p-value = 0.0006) and treatment plus presentation plus demographic variables (beta estimate = -0.46, p-value = < 0.0001). However, when stratified by age, compared with younger African-American cancer patients (< 65 years) younger White cervical cancer patients experienced significantly shorter hospital stay (Table 3). This difference was not observed among older cancer patients.

In-hospital mortality was significantly lower in Whites compared to African-American cervical cancer patients when matched on demographic only (OR = 0.71, 95% CI = 0.55-0.92) but there was no statistically significant difference when matched on presentation plus demographic variables (OR = 0.80, 95% CI = 0.63–1.02) and treatment plus presentation plus demographic variables (OR = 0.87, 95% CI = 0.69–1.10). Similar trends in odds ratio were seen in younger patients while there was no statistically significant difference in odds ratio in older patients when matched on all three sets of variables. However, although not significant in-hospital mortality tended to be higher in Whites compared to African-American cancer patients when matched on all three variables Table 3).

On evaluating the trends in discharge disposition, Whites compared to African-American cervical cancer patients were commonly discharged to other intermediate nursing facility (OR = 1.30, 95%CI = 1.20–1.41 when matched on demographic only, OR = 1.31,

Table 3
Racial Differences in Cervical Cancer Outcomes following Hospitalization for Matched Groups – without stratification and stratified on basis of Age groups.

	African-Americans	White- matched on Demographic	White-matched on Presentation plus Demographic [§]	White- matched on Treatment plus Presentation plus Demographic ^Y
All				
Post-operative complications				
OR (95% CI)		1.28 (0.94, 1.64)	1.23 (0.93, 1.62)	1.00 (0.75, 1.34)
P-value		0.1368	0.1553	1.000
Length of Stay – days				
β-Estimate		– 0.41	– 0.41	– 0.46
P-value		0.0005	0.0006	< 0.0001
Died during Hospitalization N (%)				
OR (95% CI)		0.71 (0.55, 0.92)	0.80 (0.63, 1.02)	0.87 (0.69, 1.10)
P-value		0.0081	0.0749	0.2500
Discharge Disposition [OR (95% CI)]				
Skilled Facility		1.13 (0.98, 1.30)	1.11 (0.96, 1.28)	1.16 (1.01, 1.33)
Other		1.30 (1.20, 1.41)	1.31 (1.21, 1.43)	1.32 (1.22, 1.43)
Routine		Reference	Reference	Reference
< 65 years of age (N = 4134)				
Post-operative complications				
OR (95% CI)		1.20 (0.89, 1.63)	1.13 (0.83, 1.53)	0.92 (0.67, 1.27)
P-value		0.2247	0.4391	0.6258
Length of Stay – days				
β-Estimate		– 0.41	– 0.41	– 0.48
P-value		0.0022	0.0012	0.0001
Died during Hospitalization				
OR (95% CI)		0.73 (0.54, 0.98)	0.78 (0.59, 1.04)	0.80 (0.61, 1.07)
P-value		0.0334	0.0960	0.1316
Discharge Disposition [OR (95% CI)]				
Skilled Facility		1.16 (0.98, 1.38)	1.11 (0.94, 1.33)	1.11 (0.93, 1.32)
Other		1.22 (1.11, 1.33)	1.21 (1.11, 1.33)	1.21 (1.10, 1.32)
Routine		Reference	Reference	Reference
≥ 65 years of age (N = 1083)				
Post-operative complications				
OR (95% CI)		3.16 (1.54, 6.48)	3.16 (1.54, 6.48)	2.43 (1.16, 5.11)
P-value		0.0017	0.0017	0.0191
Length of Stay – days				
β-Estimate		– 0.31	– 0.31	– 0.37
P-value		0.2752	0.2752	0.1999
Died during Hospitalization				
OR (95% CI)		1.13 (0.73, 1.75)	1.13 (0.73, 1.74)	1.16 (0.75, 1.78)
P-value		0.5807	0.5807	0.5101
Discharge Disposition [OR (95% CI)]				
Skilled Facility		1.20 (0.92, 1.55)	1.20 (0.92, 1.55)	1.14 (0.88, 1.47)
Other		1.70 (1.41, 2.06)	1.70 (1.41, 2.06)	1.69 (1.40, 2.04)
Routine		Reference	Reference	Reference

Each outcome modeled separately comparing all African-American patients consecutively with White patients matched on demographic variables (age, residential income, Residential region and insurance status), presentation and treatment variables not matched.

[§] presentation plus demographic (disease stage and number of comorbidities in addition to age, residential income, Residential region and insurance status), treatment variable not matched.

^Y treatment plus presentation plus demographic (surgery, in addition to stage, comorbidity index, age, residential income, Residential region and insurance status).

95% CI = 1.21–1.43 when matched on presentation plus demographic and OR = 1.32, 95% CI = 1.22–1.43) when matched on treatment plus presentation plus demographic matched patients). Similar trends were seen in both older and younger patients, when stratified by age (Table 3).

4. Discussion

Overall, disparities among African-American and White cervical cancer patients were observed in LOS in hospital, in-hospital mortality, and post-operative complications. African-American patients had longer LOS, and higher in-hospital mortality but fewer post-operative complications. There were no apparent differences in discharge disposition between White and African-American cervical cancer patients. This study used a three-tiered method of propensity-based matching where we intended to study outcomes of hospital-based care in White cervical patients who presented like African-American patients or African-American patients who had characteristics similar to White patients.

The length of stay in hospital for African-American patients was significantly higher even when matched on all covariates (treatment plus presentation plus demographic). One possible explanation shown from our analysis is that comorbidities have been significantly higher in African-American patients compared to White patients. The other reasons could be due to African-American patients being treated at low volume hospitals, they are more likely to have a protracted course of treatment, refuse surgical treatment or have contra-indicated treatment options due to comorbid conditions compared to White patients with cervical cancer [41–43]. Similarly, the differences in hospital mortality narrowed between African-American and White patients as they were matched on most covariates, thus indicating that differences in outcomes could be driven by delay in initiating treatment for their cancer or higher comorbidities [44,45]. Cervical cancer patients who are treated at high volume hospitals tend to have higher overall survival by 13 months compared to overall survival after being treated in low volume hospitals [46]. This combined with African-American patients accessing care in low volume hospital could lead to higher mortality in African-American cervical cancer patients when they are unmatched or

matched only on demographics. Post-operative complications were higher in White patients compared to African-American patients when matched on Demographics only and Presentation plus demographic variables but it was similar when matched on Treatment plus presentation plus demographic variables. This was expected because when unmatched on treatment variables, White patients had a higher proportion of patients who opted for surgical resection than African-American patients. When the two races were not matched on treatment, the proportion of white patients undergoing surgery was around 32%, which was near the peak National rates of surgical intervention for cervical cancer [47]. In general, African-American women undergo higher hysterectomies compared to White women, however, this may be due to aggressive treatment of benign gynecologic indications [48–53]. In our population, we noticed that when unmatched on presentation variables, higher number of African-American women with cervical cancer presented with metastatic disease. Hence this leads to lower proportion of African-American women with cervical cancer undergoing surgical resections. The differences in these proportions between African-American and White patients could be due to poor treatment options offered, patients' attitude towards definitive therapy like radiation, refusal of treatment and higher comorbidity [54]. Interestingly, White patients were more frequently transferred to skilled nursing facilities or intermediate care institutions after discharge or were discharged against medical advice compared to African-American when matched on Demographics only, Presentation plus demographic variables and Treatment plus presentation plus demographic variables. However, since these patients were matched on insurance status that could otherwise drive patient care decisions post-discharge, the trend could be influenced by social and family support and patient preferences in the two populations. Care of cancer survivors post discharge from hospitals is vital to their improved overall survival. Since White patients who are often discharged to skilled nursing home or other institutional facilities from hospital could be available for sustained care for their disease. The possibility of higher re-admission in African-American cervical cancer patients need to be explored after being initially discharged, specifically to home. Although, we could not study re-admission rates in these population due to the nature of dataset, our finding of higher length of stay in hospital complements our findings of discharge trends.

Within each race, there were some noticeable disparities among younger (< 65 years) and older (\geq 65 years) populations. Specifically, younger African-American patients had significantly higher LOS even when matched on all three sets of variables, however, there was no significant differences in mortality when they were matched on presentation and treatment variables. The possibility that cervical cancer could be aggressive when detected in younger African-American female could not be studied in detail from this dataset. The findings show us that once the patients are older than 65 years at diagnosis, age does not play any role in disparity in outcomes like mortality, length of stay and discharge patterns after hospitalization. The post-operative complications were much higher in older patients even on matching on demographic, presentation and treatment variables while there was no statistical difference in younger patients. Thus, there is a need to examine factors beyond insurance coverage, income status, age, and treatment choices that could drive some of these differences. In order to reduce disparities in cervical cancer patients, more efforts are needed and must be invested to identify women in younger age with pre-cancerous lesions through screening and then controlling the progression to full blown cancer.

This study had some limitations. First, this database was not focused on collecting information relevant to cancer and hence details on staging were not available and we created a surrogate stage variable using the ICD-code for metastatic disease. Second, this cancer is driven primarily by HPV, and the role of screening, out-patient treatment and vaccination could not be evaluated, since this database contained only in-patient procedures. As a result, many young patients who could have

been screened with pre-cancerous lesion by PAP testing and this could have resulted in better outcomes. However, most of the individuals in this study, with a median age of cervical cancer presentation over 50, were from an era before HPV vaccination were available. Third, we relied on using ICD-9 coding to confirm all diagnoses and procedures and hence, there is a possibility that they were not recorded properly, which could lead to missing or uncaptured data. Lastly, there is a possibility of residual confounding due to risk factors that may not have been accounted for in our analyses.

The unique approach to examining the data in this study has several important strengths, which address most limitations discussed above. First, the matching process by propensity scores ensures that any two groups are adequately matched such that for any given African-American patient there is a White patient with similar characteristics. While conducting matching we had 5217 African-American cervical cancer patients and access to 21,752 White cervical cancer patients to match from. This provided ample pool of patients to ensure that matching was close in both groups based on variables selected. Second, this database covers 96% of population in U.S., hence the findings from this study could be generalizable. Thus, we have shown that disparities in outcomes in cervical patients, such as LOS in hospital and mortality in hospital can be negated as different characteristics of African-American and White cervical patients are made as similar as possible based on various demographic, clinical presentation and treatment variables, leaving only their biological and histological differences. Matching also showed that outcomes like discharge disposition and post-operative complications are similar in African-American patients as compared to White cervical cancer patients. These findings need to be confirmed by prospective studies in patients who are offered similar treatment options irrespective of race, insurance status, socioeconomic status and biological factors, and evaluating their outcomes.

With growing interest in studying racial disparities in pathophysiologic progression of cervical cancer, it is important to study racial disparities in cancer care and outcomes due to healthcare services available to these patients to reduce economic and human costs. Such studies can help guide public policies to identify and reduce factors that drive disparities and create an imbalance in money spent in healthcare and their value to American society.

Ethics

Since this database is publicly available and de-identified, the Institutional Review Board of University of Alabama at Birmingham considered this study exempt from human subjects' safety review.

Author statement

All authors have seen and approved the content of the manuscript and have contributed significantly to the work. There has been no outside writing assistance other than from the co-authors. The manuscript has not been submitted to any other journals and have not been accepted as a manuscript in other journals.

Author contribution

Study conception and design: GN, SS

Acquisition of data: GN, SS

Analysis of data: GN

Interpretation of data: GN, AM, TA, SS

Manuscript writing: GN, SS

Critical review of the manuscript and final approval of the results and manuscript: GN, AM, TA, SS

Transparency document

The [Transparency document](#) associated with this article can be

found in the online version.

Declaration of Competing Interest

None

Acknowledgment

We are grateful to Dr. Mansoor Saleh, MD for insights into the clinical implications of this study. The work was also supported by the Quetelet Endowed Professor Research Fund (SS).

References

- American Cancer Society, Cancer Facts & Figures 2017, [cited 2018 November 6]; Available from: (2018) <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2017/cancer-facts-and-figures-2017.pdf>.
- National Cancer Institute Surveillance, E., and End Results Program., Cancer Stat Facts: Cervical Cancer. [cited 2018 March 8]; Available from: <https://seer.cancer.gov/statfacts/html/cervix.html>.
- UpToDate. Screening for Cervical Cancer, (2018) June 11 [cited 2018 March 26]; Available from: https://www.uptodate.com.ezproxy3.lhl.uab.edu/contents/screening-for-cervical-cancer?search=cervical%20cancer&source=search_result&selectedTitle=4~150&usage_type=default&display_rank=4.
- F.X. Bosch, et al., The causal relation between human papillomavirus and cervical cancer, *J. Clin. Pathol.* 55 (4) (2002) 244–265.
- R.A. Hiatt, et al., Cancer screening practices from National Health Interview Surveys: past, present, and future, *J. Natl. Cancer Inst.* 94 (24) (2002) 1837–1846.
- J. Nolan, et al., Barriers to cervical cancer screening and follow-up care among Black Women in Massachusetts, *J. Obstet. Gynecol. Neonatal Nurs.* 43 (5) (2014) 580–588.
- R.P. Harris, T.J. Wilt, A. Qaseem, A value framework for cancer screening: advice for high-value care from the American College of Physicians, *Ann. Intern. Med.* 162 (10) (2015) 712–717.
- C. Arvizo, H. Mahdi, Disparities in cervical cancer in African American women: what primary care physicians can do, *Cleve. Clin. J. Med.* 84 (10) (2017) 788–794.
- R.P. Insinga, et al., Healthcare Resource Use and Costs Associated With Cervical, Vaginal and Vulvar Cancers in a Large U.S. Health Plan, (2008), pp. 1095–6859 (Electronic).
- G.P. Guy Jret al., Economic Burden of Chronic Conditions Among Survivors of Cancer in the United States, (2017), pp. 1527–7755 (Electronic).
- C. Nwankwo, R. Shah, Y. Kwon, S. Corman, 981PEconomic and humanistic burden of cervical cancer in the United States, *Ann. Oncol.* 29 (suppl.8) (2018).
- B. Chastek, et al., Health Care Costs for Patients With Cancer at the End of Life, 1935–469X (Electronic) (2012).
- The Costs of Cancer - Addressing Patient Costs*, (2017) April 2017 [cited 2019 25 January]; Available from: <https://www.fightcancer.org/sites/default/files/Costs%20of%20Cancer%20-%20Final%20Web.pdf>.
- M. Milenkovic, C.A. Fau - Russo, A. Russo, Ca Fau - Elixhauser, A. Elixhauser, Hospital Stays for Cervical Cancer, Statistical Brief #22 BTI - Healthcare Cost and Utilization Project (HCUP) Statistical Briefs, (2004).
- Henry J Kaiser Family Foundation, The HPV Vaccine: Access and Use in the U.S. October 9 [cited 2018 October 20]; Available from: (2018) <https://www.kff.org/womens-health-policy/fact-sheet/the-hpv-vaccine-access-and-use-in-the-u-s/>.
- U.S. Department of Health and Human Services, C.f.D.C.a.P.a.N.C.I. *Rate of New Cancers. Cervix, United States*, U.S. Cancer Statistics Data Visualizations Tool, based on November 2017 submission data (1999–2015). [cited 2018, March 10; Available from: (2015) <https://gis.cdc.gov/cancer/USCS/DataViz.html>.
- A.L. Beavis, P.E. Gravitt, A.F. Rositch, Hysterectomy-corrected cervical cancer mortality rates reveal a larger racial disparity in the United States, *Cancer* 123 (6) (2017) 1044–1050.
- W. Yoo, et al., Recent trends in racial and regional disparities in cervical cancer incidence and mortality in United States, *PLoS One* 12 (2) (2017) e0172548.
- H.J. Dalton, J.H. Farley, Racial disparities in cervical cancer: worse than we thought, *Cancer* 123 (6) (2017) 915–916.
- S. Fleming, et al., Black and white women in Maryland receive different treatment for cervical cancer, *PLoS One* 9 (8) (2014) e104344.
- A.R. Karuri, et al., Disparity in rates of HPV infection and cervical cancer in underserved US populations, *Front. Biosci. Schol. Ed. (Schol Ed)* 9 (2017) 254–269.
- A.M. McCarthy, et al., Racial/ethnic and socioeconomic disparities in mortality among women diagnosed with cervical cancer in New York City, 1995–2006, *Cancer Causes Control* 21 (10) (2010) 1645–1655.
- S.S. Wang, et al., Cervical adenocarcinoma and squamous cell carcinoma incidence trends among white women and black women in the United States for 1976–2000, *Cancer* 100 (5) (2004) 1035–1044.
- Y. Collins, et al., Gynecologic cancer disparities: a report from the Health Disparities Taskforce of the Society of Gynecologic Oncology, *Gynecol. Oncol.* 133 (2) (2014) 353–361.
- W.J. Koh, et al., Cervical Cancer, version 2.2015, *J. Compr. Canc. Netw.* 13 (4) (2015) 395–404 quiz 404.
- D.A. Patel, et al., A population-based study of racial and ethnic differences in survival among women with invasive cervical cancer: analysis of surveillance, epidemiology, and end results data, *Gynecol. Oncol.* 97 (2) (2005) 550–558.
- J.A. Rauh-Hain, et al., Racial disparities in cervical cancer survival over time, *Cancer* 119 (20) (2013) 3644–3652.
- S. Uppal, et al., Association of Hospital Volume With Racial and Ethnic Disparities in Locally Advanced Cervical Cancer Treatment (1873–233X (Electronic)), (2017).
- A.F. Rositch, R.G. Nowak, P.E. Gravitt, Increased age and race-specific incidence of cervical cancer after correction for hysterectomy prevalence in the United States from 2000 to 2009, *Cancer* 120 (13) (2014) 2032–2038.
- ICD-9-CM Diagnosis and Procedure Codes: Abbreviated and Full Code Titles - Centers for Medicare & Medicaid Services, (2014) [cited 2019 25 January]; Available from: <https://www.cms.gov/medicare/coding/icd9providerdiagnosticcodes/codes.html>.
- R.A. Deyo, D.C. Cherkin, M.A. Ciol, Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases, *J. Clin. Epidemiol.* 45 (6) (1992) 613–619.
- A. Gadducci, et al., Treatment options in recurrent cervical cancer (Review), *Oncol. Lett.* 1 (1) (2010) 3–11.
- D.R. Roque, W.Z. Wysham, J.T. Soper, The surgical management of cervical cancer: an overview and literature review, *Obstet. Gynecol. Surv.* 69 (7) (2014) 426–441.
- J.H. Silber, et al., Racial disparities in colon cancer survival: a matched cohort study, *Ann. Intern. Med.* 161 (12) (2014) 845–854.
- C.M. Bhamidipati, et al., Transcatheter arterial revascularization outcomes at vascular and general surgery teaching hospitals and nonteaching hospitals are comparable, *J. Vasc. Surg.* 56 (1) (2012) p. 247–55.e2.
- G.W. Poorman, et al., Rates of mortality in cervical spine surgical procedures and factors associated with its occurrence over a 10-Year period: a study of 342 477 patients on the nationwide inpatient sample, *Int. J. Spine Surg.* 12 (2) (2018) 276–284.
- H.J.K.F. Foundation, States Getting a Jump Start on Health Reform's Medicaid Expansion, June 2 [cited 2018 March 10]; Available from: (2012) <https://www.kff.org/health-reform/issue-brief/states-getting-a-jump-start-on-health/>.
- G. Naik, T. Akinyemiju, Disparities in hospitalization outcomes among African-American and White prostate cancer patients, *Cancer Epidemiol.* 46 (2017) 73–79.
- J.H. Silber, et al., Characteristics associated with differences in survival among black and white women with breast cancer, *Jama* 310 (4) (2013) 389–397.
- L.S. Parsons, Reducing Bias in a Propensity Score Matched-Pair Sample Using Greedy Matching Techniques, Available from: (2019) <https://support.sas.com/resources/papers/proceedings/proceedings/sugi26/p214-26.pdf>.
- R.M. Merrill, A.V. Merrill, L.S. Mayer, Factors associated with no surgery or radiation therapy for invasive cervical cancer in Black and White women, *Ethn. Dis.* 10 (2) (2000) 248–256.
- A.J. Mundt, et al., Race and clinical outcome in patients with carcinoma of the uterine cervix treated with radiation therapy, *Gynecol. Oncol.* 71 (2) (1998) 151–158.
- F.L. Lucas, et al., Race and Surgical Mortality in the United States, (2006) (0003-4932 (Print)).
- W.W. Thoms, et al., Clinical determinants of survival from stage Ib cervical cancer in an inner-city hospital, *J. Med. Assoc.* 90 (5) (1998) 303–308.
- B.A. Virnig, et al., A matter of race: early-versus late-stage cancer diagnosis, *Health Aff. (Millwood)* 28 (1) (2009) 160–168.
- B.L. Seagle, et al., Survival Disparities by Hospital Volume Among American Women With Gynecologic Cancers, (2017) (2473-4276 (Electronic)).
- R. Pokras, V.G. Hufnagel, Hysterectomy in the United States, 1965–84, *Am. J. Public Health* 78 (7) (1988) 852–853.
- A.L. Alexander, et al., Examining Disparities in Route of Surgery and Postoperative Complications in Black Race and Hysterectomy, (2019) (1873-233X (Electronic)).
- M.L. Barrett, et al., Procedures to treat benign uterine fibroids in hospital inpatient and hospital-based ambulatory surgery settings, 2013: statistical brief #200, Healthcare Cost and Utilization Project (HCUP) Statistical Briefs, (2006) Rockville (MD).
- J.K. Bower, et al., Black-White Differences in Hysterectomy Prevalence: the CARDIA Study (1541-0048 (Electronic)), (2009).
- V.L. Jacoby, et al., Racial and ethnic disparities in benign gynecologic conditions and associated surgeries, *Am. J. Obstet. Gynecol.* 202 (6) (2010) 514–521.
- W.R. Robinson, et al., For U.S. Black Women, Shift of Hysterectomy to Outpatient Settings May Have Lagged Behind White Women: a Claims-based Analysis, (2011) 2011–2013. (1472-6963 (Electronic)).
- G. Weiss, et al., Racial Differences in Women Who Have a Hysterectomy for Benign Conditions (1049-3867 (Print)), (2009).
- V.L. Shavers, M.L. Brown, Racial and ethnic disparities in the receipt of cancer treatment, *J. Natl. Cancer Inst.* 94 (5) (2002) 334–357.