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# Biologic, Clinical, and Sociodemographic Predictors of Multi-agent Systemic Therapy for Non-Hodgkin Lymphoma in People Living with HIV: A Population-based Investigation in the State of Georgia

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## Abstract

We conducted a population-based study of biologic, clinical, and sociodemographic factors associated with receipt of multi-agent systemic therapy (MAST) by people living with HIV (PLWH) who were diagnosed with non-Hodgkin lymphoma (NHL). Building on recent registry-based analyses, we linked records from the Georgia Cancer Registry, Georgia HIV/AIDS Surveillance Registry, and the Georgia Hospital Discharge Database to identify 328 PLWH adults (age≥18) diagnosed with NHL within 2004–2012. Through logistic regression modeling, we examined factors associated with patients receiving MAST for NHL. Robust predictors included CD4 count ≥200 cells/mm$^3$ around the time of cancer diagnosis, an advanced stage (III or IV) diagnosis of NHL, MSM HIV transmission, and having private health insurance. The strongest single predictor of MAST was CD4 count. Because there is now guideline-integrated evidence that PLWH receiving standard-of-care cancer therapy can achieve substantially improved outcomes, it is vital they have access to regimens routinely provided to HIV-negative cancer patients.

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**Keywords**

non-Hodgson lymphoma; HIV/AIDS; multi-agent systemic therapy; standard-of-care therapy

## Introduction

Non-Hodgkin lymphoma (NHL) diagnosed in people living with HIV (PLWH) is associated with poorer all-cause survival compared with NHL among individuals without HIV [1]. This points directly to the question: What is the influence of the individual's HIV status on the likelihood of receiving standard-of-care therapy for the cancer – that is, care consistent with the treatment typically recommended for NHL patients who are HIV-negative? A hallmark of such care is multi-agent systemic therapy (MAST), consisting of specific combinations of chemotherapy and monoclonal antibody-based agents. In response, this paper examines biologic, clinical, and sociodemographic determinants of receipt of MAST by PLWH who have been diagnosed with NHL.

Our investigation builds on two recent studies that have significantly advanced this line of inquiry:

Using data from 3 states (Connecticut, Michigan, and Texas) participating in the National Cancer Institute-supported HIV/AIDS Cancer Match Study [2], Suneja et al. [3] found that 21.7% (70/323) of HIV-infected diffuse large B-cell lymphoma (DLBCL) patients diagnosed within 2006–2010 did not receive any chemotherapy or radiation therapy as first course of treatment. In statistical analyses that pooled data across multiple cancer disease sites, including DLBCL, "lack of cancer treatment" for HIV-infected patients was associated with distant or unknown stage at diagnosis, being a male with injection drug use as the mode of HIV exposure, age 45–64 (compared with <45), black race, and a CD4 count below the sample median of 144 cells/$mm^3$. But the influence of viral load could not be examined owing to substantial missing data. Also not available were variables on comorbidity status, insurance coverage, sociodemographic status, and whether the patient's cancer center was accredited by the American College of Surgeons Commission on Cancer (CoC), which emphasizes multidisciplinary care.

Analyzing data from the National Cancer Database (NCDB) [4], Suneja et al. [5] reported that 17.8% (769/4,317) of HIV-infected DLBCL patients diagnosed within 2003–2011 did not receive any cancer therapy. In multivariable analyses that combined DLBCL and Hodgkin lymphoma patients, lack of treatment was positively associated with older age, being non-Hispanic black, and having ≥1 comorbidities (using the Modified Charlson-Deyo index). Receipt of some treatment (chemotherapy or radiation therapy) was positively associated with diagnosis at a later stage and having private health insurance. But the cancer registry-based NCDB does not have data on the HIV-infected person's CD4 count or viral load, as indicators of HIV control in this era of highly active antiretroviral therapy (ART). Also, because all cancer treatment facilities in the NCDB are CoC-approved, the influence of CoC status itself could not be examined.

In this paper, we report findings that expand upon this work in at least two ways.

First, our focus is not on whether the patient received *some* amount of cancer care, as opposed to none, but on whether treatment *consistent with* standard-of-care NHL therapy was received, with the administration of MAST (yes/no) serving as the line of demarcation, given the available data. Second, by taking full advantage of the patient-level data available in three distinct state-level databases, we constructed a predictor variable set that represents roughly the union of the explanatory variables available in the two papers above, and then some.

Included in the analyses are all individuals diagnosed with non-Hodgkin lymphoma (as their first primary cancer) in the state of Georgia within 2004–2012 who had become a PLWH by the time of their NHL diagnosis.

## Materials and Methods

### Data Sources and Linkages.

Through a process similar to that previously employed in the NCI HIV/AIDS Match Study, the Georgia Department of Public Health linked data from the Georgia Cancer Registry (GCR) and the Georgia HIV/AIDS Surveillance Registry to identify all adults (age≥18) diagnosed with cancer within 2004–2012 who also had a diagnosis of HIV and/or AIDS on record prior to or during any portion of this period.

Included in this cancer-HIV registry linkage was important biologic data: each individual's test-specific laboratory data (specifically, CD4 count and viral load) as recorded in the Enhanced HIV/AIDS Reporting System (eHARS) through 2012. This yielded a time series of CD4 counts (cells/$mm^3$) and viral load readings (copies/mL) with most, but not all, individuals having one or more readings on each test. While inherently continuous, CD4 count was deployed here as a 2-category variable, with severe immune suppression defined as CD4<200 cells/$mm^3$. This cutpoint is consistent with standard practice in HIV patient assessment, monitoring, and treatment planning [6]. Similarly, viral load readings were mapped into a 2-category variable, with viral load ≥ 400 copies/mL indicating active HIV.

Linkages were performed using a series of deterministic and "fuzzy" matching steps, including manual review when needed. Deterministic methods included blocking by various letter positions in the first and last names, year blocking for birth dates, and last-four-digit blocking for social security number. Fuzzy matching was performed using edit distance tools in SAS (SAS, Cary, NC) [7].

From the GCR we derived the following sociodemographic variables: age at NHL diagnosis, sex, race/ethnic status (Black and all Other), insurance status at NHL diagnosis (private, government, or not insured), residential status (Metro, Urban, Rural, as defined by the Rural-Urban Continuum Codes (RUCC) [8]), and the following clinical variables: subtype of NHL, as indicated by histological classification; primary/presenting disease site, either nodal (with disease involving the lymph nodes) or extranodal (with disease involving anatomic sites other than lymph nodes); the presence of B symptoms (Yes/No), which may include fever, night sweats, weight loss; Ann Arbor disease stage at diagnosis (dichotomized as I/II and III/IV); year of diagnosis (dichotomized as 2004–2008 and 2009–2012, to control for any

temporal trends in the immunocompromised status of PLWH at cancer diagnosis, NHL treatment patterns, or other factors); and whether NHL treatment included MAST (as discussed below). Also included was an indicator variable for whether the NHL patient was either diagnosed or treated at a CoC-approved facility.

From the GA HIV/AIDS Surveillance Registry, we used the 8-category Transmission Category variable (see Table 1) to construct a 2-category variable for whether the mode of HIV transmission was "Male sexual contact with other male (MSM)" (first category) *or* MSM and injection drug use (third category). About 44% of all patients fell into one of these two categories; hence, we used the following 2-level summary variable: MSM and All Other.

Finally, we linked these (linked) cancer-HIV records to the Georgia Hospital Discharge Database (GHDD) for all individuals with ≥1 hospitalizations prior to or following their NHL diagnosis (through 2012). For these individuals, we used the ICD-9 diagnosis codes from the hospital stay closest in time *and* within 1 year prior to the NHL diagnosis date to construct a modified Charlson-Deyo comorbidity index score. In doing so, we set the weights for cancer, metastatic carcinoma, and HIV/AIDS to 0, in line with Suneja et al. [5] (see their Table 1, note b for details). The GHDD was also used to identify the individual's insurance status when that could not be clearly determined from the cancer registry. The approach to linking to the GHDD was deterministic and stepwise, with last name, first name, date of birth, and sex (but not social security number) as the key matching variables.

### Patient HIV Status.

While receipt of MAST was consistent with standard of care for NHL over the 2004–2012 period (and remains so today) regardless of HIV status, we investigated whether the degree of immunosuppression in PLWH influenced the likelihood of actually receiving MAST. In our data, the median time gap between the date of NHL diagnosis and the most recent CD4 test score prior to diagnosis was 1.5 months, with 75% of NHL patients having had their final (pre-NHL) CD4 count reading within 6.5 months of NHL diagnosis; for viral load, the corresponding statistics were 1.2 months and 4.8 months. Consequently, we used the patient's *final pre-NHL* CD4 count and viral load readings as the predictor variables in our base-case models.

### Non-Hodgkin Lymphoma Cases: Inclusion/Exclusion Criteria.

Included were all individuals age ≥18 whose first cancer diagnosis was within 2004–2012 and one of the following NHL subtypes (ICD-O-3 histology codes in parentheses): DLBCL (9680), Burkitt lymphoma (9687), plasmablastic lymphoma (9735), and peripheral T-cell lymphoma (9702, 9714, 9827). The first 3 subtypes are generally regarded as AIDS-defining, while peripheral T-cell is not [9]; but treatment for each subtype was chemotherapy-oriented during the study period, thus aligning with our general approach to defining therapy consistent with standard-of-care (see below).

Individuals were excluded if either the HIV diagnosis date or the cancer diagnosis date was missing. If the date for HIV diagnosis was after the date for AIDS diagnosis, the former was set equal to the latter.

Given the study's focus, we sought to include only those individuals whose HIV/AIDS diagnosis preceded their NHL diagnosis. Because some HIV/AIDS cases might have been reported to the state registry only in conjunction with the cancer diagnosis (when, typically, medical history is closely scrutinized), we included any NHL patient whose HIV/AIDS diagnosis was recorded to be ≤ 60 days following NHL diagnosis.

### Multi-agent Systemic Therapy for Non-Hodgkin Lymphoma.

Consistent with treatment recommendations from the National Comprehensive Cancer Network (NCCN) for NHL patients generally [10] over the 2004–2012 period, and based on the categorization of treatment choices as recorded in the GCR, patients were assigned to one of the following categories:

**MAST:** Multi-agent chemotherapy given; radiation therapy also may be delivered, but was regarded as neither necessary nor sufficient *alone* for treatment to be consistent with standard-of-care. Rituximab may have been a part of the multi-agent regimen, but such monoclonal antibody agents were not distinguished from chemotherapy in cancer registry treatment coding during 2004–2012.

**Not-MAST:** Received no chemotherapy or else single-agent chemotherapy only; or chemotherapy was not recommended or administered because of patient risk factors; or chemotherapy was recommended but refused by patient/family/guardian.

**Indeterminate:** Chemotherapy given, but number and type of agents not documented; patient died before planned therapy; chemotherapy was part of planned therapy, but not given and no reason indicated; or it was unknown if chemotherapy was recommended and/or given.

### Statistical Analyses.

Descriptive statistics for categorical variables are reported as frequencies and percentages; and for continuous variables, as counts with median and range. With the likelihood of an NHL patient receiving MAST as the outcome, we estimated univariate binary logistic regression models for each predictor variable. Guided by these results, we estimated a base-case multivariable binary logistic regression model for receipt of MAST. Patients with missing values on any variable included in the multivariable model were excluded in the estimation of that model. The influence of each predictor is reported as an odds ratio (OR), with statistical significance evaluated using $p = 0.05$ as the benchmark. The within-sample predictive validity of the multivariable model was assessed via the coefficient of concordance (c) statistic.

Analyses were performed in SAS 9.4 (SAS Institute, Inc., Cary, NC). The study was approved by the Institutional Review Boards at Emory University and the Georgia Department of Public Health.

## Results

From a total of 2,901 cancer cases in Georgia diagnosed within 2004–2012 in 2,486 individuals with an HIV/AIDS diagnosis, there were 328 non-Hodgkin lymphoma patients meeting inclusion/exclusion criteria (Table 1). Among these, 61.6% (202/328) received MAST, 30.2% (99/328) did not, and 8.2% (27/328) were classified as indeterminate. Of note across the multiple descriptive statistics in Table 1, about two-thirds of all NHL patients with CD4 readings available had a CD4 count <200 cells/mm$^3$ from the last test prior to their cancer diagnosis, while over 80% with available viral load results had a reading ≥ 400 copies/mL prior to NHL diagnosis. Thus, a substantial majority of individuals in this population-based sample were significantly immunocompromised around the time of their NHL diagnosis.

The univariate and base-case multivariable statistical analyses are reported in Table 2, focusing on the 184 patients who either did or did not receive MAST and were available for the multivariable model because they had no missing value for any included predictor. In this way, the odds ratios are pairwise comparable between univariate and multivariable analyses for each variable included in both.

In the univariate analyses, receipt of MAST was positively and significantly associated with CD4 count ≥ 200 cells/mm$^3$ ($p<0.001$), viral load count < 400 copies/mL ($p=0.030$), an advanced stage (III or IV) at diagnosis ($p=0.005$), and MSM transmission status ($p=0.005$); and negatively and significantly associated with NHL being DLBCL ($p=0.025$) and extranodal (0.009). Having private insurance was borderline significant ($p=0.097$) for receipt of MAST, as was being diagnosed or treated at a CoC facility ($p=0.089$).

These univariate analyses informed the selection of variables for the multivariable binary logistic regression model. Receipt of MAST for NHL was positively and significantly associated with CD4 ≥ 200 cells/mm$^3$ (OR=6.81, $p<0.001$); an advanced stage diagnosis (OR=2.92, $p=0.011$); MSM transmission (OR=2.82, $p=0.009$); and having private insurance (OR=3.50, $p=0.035$). The OR for viral load (1.49) aligned with expectations about direction of effect, but was not significant ($p=0.503$). The model's c statistic (0.811) indicates relatively strong internal predictive ability.

## Discussion

After linking data readily available from the GA Cancer Registry, GA HIV/AIDS Surveillance Registry, and GA Hospital Discharge Database, we investigated the determinants of receiving multi-agent systemic therapy for non-Hodgkin lymphoma among PLWH. In what follows, we appraise selected aspects of our findings.

### CD4 and Viral Load:

An impaired level of CD4 count, based on the last test result available prior to NHL diagnosis, was strongly associated with not receiving MAST, in both univariate and multivariable analyses, while viral load level was not significantly related to receipt of MAST after adjusting for other factors.

To examine further the possible interplay between CD4 and viral load, we re-specified the multivariable model in Table 2 to include a CD4-by-viral load interaction. In this expanded model, the interaction term was not significant (p=0.925); correspondingly, the resulting OR for CD4 ≥200 conditional on viral load <400 (namely, 6.42) was not statistically different than the OR for CD4 ≥200 conditional on viral load ≥400 (namely, 7.17). The implication is that CD4 count wields an independent influence on receipt of MAST, whatever the viral load level.

### A Closer Look at Intertemporal Effects.

The OR for receipt of MAST in the 2009–2012 window compared with 2004–2008 was >1 in both the univariate and multivariable analysis, but not significant in either. In separate calculations, we also found no significant time trends between 2004–2008 and 2009–2012 in the mean of ln[CD4] (t-test p=0.99) or in the mean of ln[viral load] (t-test p=0.14). The CD4 and viral load values here are those for the 328 PLWH in Table 1 and were log-transformed for t-tests because the measure distributions within each period were heavily right-skewed.

### Standard-of-Care Cancer Therapy for PLWH: Understanding the Performance Gap and Closing It.

In our full sample (N=328), over 30% of patients did not receive multi-agent systemic therapy for their NHL; among those in the base-case statistical analyses (Table 2), 33.2% (61/184) did not receive MAST.

Over the past two decades, there has been growing published evidence that PLWH who are diagnosed with lymphoma, including NHL, and receive multi-agent therapy can have substantially improved survival outcomes. This is consistent with findings reported by Gopal et al. [12] in a study of HIV-associated lymphoma patients in North Carolina diagnosed across 2000–2010. Based on their comprehensive review of the literature, Hunter, Vogt, and Ambinder [13] conclude that, “Lymphoma therapy is as effective in HIV-positive patients as in patients without HIV infection.” If this is indeed the case, how does one account for the fact that about a third of our NHL patients in Georgia, diagnosed within 2004–2012, did not receive MAST?

We believe there are multiple reasons, which might be usefully characterized as patient-related, provider-related, and health system-related. By health system-related, we mean the absence of major U.S.-based guidelines targeting the treatment of HIV/AIDS malignancies until, arguably, the publication of “Cancer in People Living with HIV” by the NCCN in early 2018 [14], followed by NCCN guidelines expressly for B-cell lymphomas in 2019 [15]. While the British HIV Association had published guidelines for HIV-associated malignancies as early as 2008 [16], their direct influence on U.S. clinical practice remains undocumented, to the best of our knowledge.

Given the absence of evidence-based, clearly defined guidelines for HIV/AIDS malignancies during 2004–2012, variation in clinical decision making about NHL treatment for PLWH would be anticipated. Underscoring the point that provider discretion may have been an important consideration in our study are findings reported by Suneja et al. [17]. From a multi-state survey of medical and radiation oncologists conducted in 2013, they concluded

that only about 77% of the medical oncologists queried would be expected to provide "standard" cancer therapy to PLWH who are assumed to have CD4>200 cells/$mm^3$ and diagnosed with a non-AIDS-defining cancer (based on self-reports about chemotherapy agents, dosing, and discontinuation of therapy). In addition, 69% of respondents indicated that current guidelines for HIV/AIDS malignancies were insufficient. Writing in 2014, Torres and Mulanovich [18] emphasized the absence of consensus about optimal ART regimens for PLWH diagnosed with cancer.

Another possible provider-related influence has been characterized by Geter et al. [19] as HIV-related stigma, based on a review of studies published over 2010–2017. The authors recommended developing "provider-centered stigma-reduction interventions" to promote more effective engagement with PLWH diagnosed with cancer.

Finally, there was in fact considerable patient-level variability in a host of factors that, on the margin, could influence the likelihood of receiving NHL treatment consistent with general standard of care (Table 1). The univariate and multivariable statistical results in Table 2 substantiate this contention. For example, a low CD4 count could well have been regarded as a "red light" for administration of MAST, especially in the absence (circa 2004–2012) of U.S.-based treatment guidelines for HIV/AIDS malignancies [20].

In addition, there was notable patient-level variability across the NHL subtypes. For example, among DLBCL patients in Table 2, 61.2% (74/121) received MAST, compared with 82.9% (34/41) of Burkitt lymphoma patients. Among DLBCL patients who were Not-MAST, 31.4% (38/121) were recorded as receiving either single-agent or no chemotherapy, while chemotherapy was either not recommended due to risk factors or else declined by patient/family for 7.3% (9/121) of DLBCL patients; for Not-MAST Burkitt lymphoma patients, the corresponding results were 14.6% (6/41) and 2.4% (1/41).

### Limitations.

Our analyses are subject to at least four notable limitations, all data related.

Missing values for available variables: Among the 301 NHL patients classified as MAST or Not-MAST, 107 were missing either CD4 or viral load (Table 1). To examine the potential for bias, we analyzed the bivariate relationship between an individual having no CD4 measurements and each of the other predictor variables in Table 2, and did likewise for viral load. (The idea was to see, for example, whether there was a difference in the distribution of patients by NHL stage at diagnosis between those with CD4 measures and those without.) For CD4, the only significant relationship ($p<0.001$) was with Insurance Status; for viral load, only the time period of NHL diagnosis was significant ($p=0.03$). The only other predictor with notable missingness, the Charlson-Deyo comorbidity score, was not significant in any MAST analysis.

Incomplete information about "standard of care" therapy: From the cancer registry data here we could ascertain whether multi-agent systemic therapy was administered – but not the specific agents involved, the dose density, or the timing of treatment cycles. To obtain the clinical detail required to ascertain whether the registry-observed MAST represents

guideline-consistent standard-of-care would require linkage to patient medical records; we are unaware of any *population-based* study of cancer treatment for PLWH in the U.S. that has attempted to link registry and EMR data. That said, we can be confident that *a patient who is Not-MAST did not receive standard-of-care therapy*.

Absence of data on the utilization of ART: With that acknowledged, we nonetheless have highly relevant "bottom-line" information – namely, the CD4 count and viral load recorded around the time when the cancer treatment decision was likely being made. Still, it would be very useful to have patient-level data on ART at the time of NHL diagnosis, especially since the new NCCN guidelines call for optimizing the compatibility of the patient's cancer and HIV/AIDS treatment regimens [14,15].

Limited ability to examine provider-related effects: Given the registry-oriented data here, we were only able to examine whether a facility's Commission-on-Cancer approval status influenced receipt of MAST; there was borderline evidence that it did (OR=2.21, p=0.117) in the multivariable analysis. Information about the professional characteristics of the patients' treating physicians could also be obtained, in principle, by linking cancer registry data to some combination of electronic health records, insurance claims files, and/or state medical licensure databases.

### Conclusion.

At least one-third of our Georgia-based sample of PLWH who were diagnosed with NHL within 2004–2012 did not receive cancer treatment that was consistent with standard-of-care therapy. The strongest single predictor was the patient's CD4 count, although multiple other variables were influential. Consequently, future analyses should attempt to sort out the direct and interactive effects of patient, provider, and health system factors on cancer care decision making for PLWH. Enhanced provider education with close attention to contemporary treatment guidelines that recommend multidisciplinary care, involving both oncology and infectious disease specialists, will be critically important.

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**Table 1.**

Characteristics of PLWH Diagnosed with Non-Hodgkin Lymphoma in Georgia, 2004–2012

| Variable | Level | MAST (N=202) | Not-MAST (N=99) | Indeterminate (N=27) | Total [a] (N=328) |
|---|---|---|---|---|---|
| Age | Median (Range) | 42 (18 – 69) | 44 (14 – 66) | 42 (27 – 76) | 43 (14 – 76) |
| NHL subtype | DLBCL | 119 (58.9%) | 76 (76.8%) | 22 (81.5%) | 217 (66.2%) |
| | Burkitt lymphoma | 65 (32.2%) | 12 (12.1%) | 3 (11.1%) | 80 (24.4%) |
| | Plasmablastic lymphoma | 11 (5.4%) | 2 (2.0%) | 0 (0.0%) | 13 (4.0%) |
| | T-cell lymphoma | 7 (3.5%) | 9 (9.1%) | 2 (7.4%) | 18 (5.5%) |
| Sex | Male | 166 (82.2%) | 84 (84.8%) | 20 (74.1%) | 270 (82.3%) |
| | Female | 36 (17.8%) | 15 (15.2%) | 7 (25.9%) | 58 (17.7%) |
| Race [b] | Black | 119 (58.9%) | 69 (69.7%) | 22 (81.5%) | 210 (64.0%) |
| | Other (White/American Indian/Alaska Native/Asian) | 83 (41.1%) | 30 (30.3%) | 5 (18.5%) | 118 (36.0%) |
| Insurance status [c] | Private insurance | 71 (37.2%) | 21 (22.8%) | 10 (38.5%) | 102 (33.0%) |
| | Government - Medicaid, Medicare, TRICARE, Military, etc. | 89 (46.6%) | 51 (55.4%) | 15 (57.7%) | 155 (50.2%) |
| | Not Insured | 31 (16.2%) | 20 (21.7%) | 1 (3.8%) | 52 (16.8%) |
| | Missing | 11 | 7 | 1 | 19 |
| Nodal type [d] | Nodal | 146 (72.3%) | 48 (48.5%) | 16 (59.3%) | 210 (64.0%) |
| | Extranodal | 56 (27.7%) | 51 (51.5%) | 11 (40.7%) | 118 (36.0%) |
| Ann Arbor stage | I/II | 61 (30.5%) | 50 (51.0%) | 12 (46.2%) | 123 (38.0%) |
| | III | 42 (21.0%) | 12 (12.2%) | 2 (7.7%) | 56 (17.3%) |
| | IV | 97 (48.5%) | 36 (36.7%) | 12 (46,2%) | 145 (44.8%) |
| | Missing | 2 | 1 | 1 | 4 |
| B symptoms | No | 85 (47.2%) | 35 (45.5%) | 16 (72.7%) | 136 (48.7%) |
| | Yes | 95 (52.8%) | 42 (54.5%) | 6 (27.3%) | 143 (51.3%) |

| Variable | Level | MAST (N=202) | Not-MAST (N=99) | Indeterminate (N=27) | Total [a] (N=328) |
|---|---|---|---|---|---|
| | Missing | 22 | 22 | 5 | 49 |
| Charlson-Deyo comorbidity score | 0 | 71 (64.0%) | 51 (60.0%) | 11 (57.9%) | 133 (61.9%) |
| | 1+ | 40 (36.0%) | 34 (40.0%) | 8 ((42.1%) | 82 (38.1%) |
| | Missing | 91 | 14 | 8 | 113 |
| Year of diagnosis | 2004–08 | 99 (49.0%) | 61 (61.6%) | 18 (66.7%) | 178 (54.3%) |
| | 2009–12 | 103 (51.0%) | 38 (38.4%) | 9 (33.3%) | 150 (45.7%) |
| Transmission category | Male sexual contact with other male (MSM) | 95 (47.0%) | 29 (29.3%) | 6 (22.2%) | 130 (39.6%) |
| | Injection drug use (nonprescription) (IDU) | 5 (2.5%) | 12 (12.1%) | 1 (3.7%) | 18 (5.5%) |
| | Male sexual contact with other male and injection drug use (MSM+IDU) | 12 (5.9%) | 2 (2.0%) | 1 (3.7%) | 15 (4.6%) |
| | Adult received clotting factor for hemophilia/coagulation disorder | 1 (0.5%) | 1 (1.0%) | 0 (0.0%) | 2 (0.6%) |
| | Heterosexual contact | 22 (10.9%) | 14 (14.1%) | 5 (18.5%) | 41 (12.5%) |
| | Adult with No Identified Risk (NIR) | 46 (22.8%) | 32 (32.3%) | 14 (51.9%) | 92 (28.0%) |
| | Adult with No Reported Risk (NRR) | 19 (9.4%) | 8 (8.1%) | 0 (0.0%) | 27 (8.2%) |
| | Perinatal exposure | 2 (1.0%) | 1 (1.0%) | 0 (0.0%) | 3 (0.9%) |
| Transmission Mode | MSM | 107 (53.0%) | 31 (31.3%) | 7 (25.9%) | 145 (44.2%) |
| | All Other | 95 (47.0%) | 68 (68.7%) | 20 (74.1%) | 183 (55.8%) |
| CD4 count | <200 | 88 (55.3%) | 77 (87.5%) | 3 (21.4%) | 179 (66.5%) |
| | >=200 | 71 (44.7%) | 11 (12.5%) | 11 (78.6%) | 90 (33.5%) |
| | Missing | 43 | 11 | 13 | 59 |
| Viral load | <400 | 31 (23.1%) | 7 (10.6%) | 3 (21.4%) | 41 (19.2%) |
| | >=400 | 103 (76.9%) | 59 (89.4%) | 11 (78.6%) | 173 (80.8%) |
| | Missing | 68 | 33 | 13 | 114 |
| Diagnosed or treated at CoC facility | No | 36 (17.8%) | 20 (20.2%) | 6 (22.2%) | 62 (18.9%) |
| | Yes | 166 (82.2%) | 79 (79.8%) | 21 (77.8%) | 266 (81.1%) |

*Leuk Lymphoma*. Author manuscript; available in PMC 2021 April 01.

| Variable | Level | MAST (N=202) | Not-MAST (N=99) | Indeterminate (N=27) | Total [a] (N=328) |
|---|---|---|---|---|---|
| Rural-urban status [e] | Metro | 182 (90.1%) | 90 (90.9%) | 27 (100.0%) | 299 (91.2%) |
| | Non-Metro | 20 (9.9%) | 9 (9.1%) | 0 (0.0%) | 29 (8.8%) |

[a]Among these 328 NHL patients, only 17 had their recorded date of diagnosis of HIV/AIDS in the 60-day window starting from the date of the NHL diagnosis; of these, 11 were MAST, 3 were Not-MAST, and 3 were Indeterminate. The remaining 311 NHL patients all had a recorded date of diagnosis for HIV/AIDS that was prior to the NHL diagnosis date.

[b]There are two specific points to note about the two-level categorization (Black and Other) adopted here. First, because Hispanics comprise under 5% of the total NHL sample here, Whites include both non-Hispanic and Hispanic whites, and likewise for the category Black. Second, because of very small cell sizes for the cancer registry-defined categories American Indian/Alaska Native (AI/AN) and Asian, we followed standard registry reporting practice in consolidating those categories with one or more larger categories – here, they are combined with Whites. In fact, the total number of AI/AN and Asian individuals in the sample is < 5.

[c]In light of sample size limitations, we worked from the GCR's 16-category Primary Payer variable to create this 3-category summary variable, wherein Private insurance also includes "private, not otherwise specified"; Government includes coverage by any of these public sector sources listed; and Uninsured includes self-pay as well as "uninsured, not otherwise specified."

[d]Among these 118 extra-nodal cases, 23 were primary central nervous system (CNS) lymphomas; of these, 23 were histologically classified as DLBCL, 2 as T-Cell lymphoma, and 1 as Burkitt lymphoma. Among our 328 NHL cases, none were classified as having primary effusion lymphoma.

[e]Based on the Rural-Urban Continuum Code (RUCC) classification system, the county of residence for each NHL patient at the time of cancer diagnosis was either Metro (meaning the county lay within a defined Metropolitan Statistical Area whose total population was at least 250,000) or Non-Metro. The RUCC classification of Georgia's 159 counties in 2013, based on data from the 2010 Census, showed that 74 counties were Metro (and collectively containing a high percentage of the state's total population) and 85 were Non-Metro [8]. It is not surprising, therefore, that over 90% of these patients resided in Metro counties at the time of their NHL diagnosis.

**Table 2.**

Determinants of Receipt of Multi-agent Systemic Therapy for PLWH Diagnosed with NHL [a]

| | | | Univariate | | Multivariable [b] | |
|---|---|---|---|---|---|---|
| **Variable** | **Level** | **N** | **OR (95% CI)** | **p-value** | **OR (95% CI)** | **p-value** |
| Age | | 184 | 0.98 (0.95–1.02) | 0.279 | | |
| NHL subtype [c] | Non-DLBCL | 63 | 2.22 (1.11–4.47) | **0.025** | 1.88 (0.81–4.36) | 0.142 |
| | DLBCL | 121 | Ref | | Ref | |
| Sex | Male | 154 | 0.69 (0.29–1.66) | 0.411 | | |
| | Female | 30 | Ref | | | |
| Race [d] | Black | 119 | 0.76 (0.39–1.46) | 0.404 | 1.56 (0.67–3.62) | 0.305 |
| | Other | 65 | Ref | | Ref | |
| Insurance status | Government | 94 | 1.15 (0.53–2.50) | 0.722 | 1.47 (0.58–3.68) | 0.482 |
| | Private/Other | 52 | 2.17 (0.87–5.43) | 0.097 | 3.50 (1.09–11.24) | **0.035** |
| | Not Insured | 38 | Ref | | Ref | |
| Nodal type [e] | Extranodal | 66 | 0.43 (0.23–0.81) | **0.009** | 0.83 (0.36–1.88) | 0.652 |
| | Nodal | 118 | Ref | | Ref | |
| Ann Arbor stage | III/IV | 117 | 2.50 (1.32–4.71) | **0.005** | 2.92 (1.28–6.70) | **0.011** |
| | I/II | 67 | Ref | | Ref | |
| B symptoms | Yes | 89 | 1.02 (0.52–1.98) | 0.964 | | |
| | No | 75 | Ref | | | |
| Charlson-Deyo | 1+ | 45 | 1.04 (0.49–2.18) | 0.925 | | |

| | | | Univariate | | Multivariable [b] | |
|---|---|---|---|---|---|---|
| **Variable** | **Level** | **N** | **OR (95% CI)** | **p-value** | **OR (95% CI)** | **p-value** |
| comorbidity index | 0 | 75 | Ref | | | |
| Year of diagnosis | 2009–12 | 110 | 1.42 (0.76–2.65) | 0.269 | 1.21 (0.55–2.70) | 0.635 |
| | 2004–08 | 74 | Ref | | Ref | |
| Transmission Mode [f] | Male-MSM | 88 | 2.53 (1.33–4.82) | **0.005** | 2.82 (1.30–6.13) | **0.009** |
| | All Other | 96 | Ref | | Ref | |
| CD4 count | ≥200 | 69 | 7.84 (3.31–18.59) | **<.001** | 6.81 (2.59–17.89) | **<.001** |
| | <200 | 115 | Ref | | Ref | |
| Viral load | <400 | 35 | 2.83 (1.10–7.24) | **0.030** | 1.49 (0.46–4.81) | 0.503 |
| | ≥400 | 149 | Ref | | Ref | |
| Diagnosed or treated at CoC facility | Yes | 154 | 1.99 (0.90–4.41) | 0.089 | 2.21 (0.82–5.98) | 0.117 |
| | No | 30 | Ref | | Ref | |
| Rural-urban status | Non-Metro | 16 | 0.61 (0.22–1.72) | 0.350 | | |
| | Metro | 168 | Ref | | | |

[a] N = 184. All of these patients had a date of diagnosis for HIV/AIDS that was prior to the date of diagnosis for NHL.

[b] To guard against overfitting any binary logistic regression model, we were guided by a variant of "Harrell's Rule" [11]: the number of included predictor variable levels should not (much) exceed m/10, where m = min (# MAST cases, # Not-MAST cases). For the estimated multivariable model here, c = 0.811.

[c] Non-DLBCL includes those patients with Burkitt lymphoma, plasmablastic lymphoma, and T-cell lymphoma.

[d] Other includes patients who are White, American Indian, Alaskan Native, or Asian; as noted also in Table 1, the categories Black and White together include those (few) patients who were Hispanic.

[e] Among these 66 extra-nodal cases, there were 15 primary CNS lymphomas; of these, 13 were DLBCL, 1 was T-cell lymphoma, and 1 was Burkitt lymphoma.

[f] All Other thus includes Male-Non-MSM and Female, as discussed in the text.