HHS Public Access

Author manuscript

Stroke. Author manuscript; available in PMC 2023 October 01.

Published in final edited form as:

Stroke. 2022 October ; 53(10): 3082–3090. doi:10.1161/STROKEAHA.121.038311.

Substance Use and Performance of Toxicology Screens in the Greater Cincinnati Northern Kentucky Stroke Study

Tracy E. Madsen, MD, PhD[*,1,2], **Olivia W. Cummings, BS**[*,1], **Felipe De Los Rios La Rosa, MD**[3,4], **Jane C. Khoury, PhD**[5], **Kathleen Alwell, BSN**[4], **Daniel Woo, MD, MS**[4,6], **Simona Ferioli, MD**[4,6], **Sharyl Martini, MD, PhD**[7], **Opeolu Adeoye, MD, MS**[8], **Pooja Khatri, MD, MSc**[4,6], **Matthew L. Flaherty, MD**[4,6], **Jason Mackey, MD, MS**[9], **Eva A. Mistry, MBBS, MSCI**[4,6], **Stacie L. Demel, DO, PhD**[4,6], **Elisheva Coleman, MD**[10], **Adam S. Jasne, MD**[11], **Sabreena J Slavin, MD**[12], **Kyle Walsh, MD**[4,6], **Michael Star, MD**[13], **Joseph P. Broderick, MD**[4,6], **Brett M. Kissela, MD, MS**[4,6], **Dawn O. Kleindorfer, MD**[4,6]

[1:]Department of Emergency Medicine, Alpert Medical School of Brown University, Providence, RI

[2:]Department of Epidemiology, Brown University School of Public Health, Providence, RI

[3:]Miami Neuroscience Institute, Baptist Health South Florida, Miami, FL

[4:]Department of Neurology and Rehabilitation Medicine, University of Cincinnati College of Medicine, Cincinnati, OH

[5:]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA

[6:]UC Gardner Neuroscience Institute, Cincinnati, OH

[7:]Neurology Program, Veterans Health Administration and Department of Neurology, Baylor College of Medicine, Houston, Texas

[8:]Department of Emergency Medicine, Washington University, St. Louis, MO

[9:]Department of Neurology, Indiana University School of Medicine, Indianapolis, IN

[10:]Department of Neurology, University of Chicago, Chicago, IL

[11:]Department of Neurology, Yale School of Medicine, New Haven, CT

[12:]University of Kansas Medical Center, Kansas City, KS

[13:]Soroka Medical Center, Beersheva, Israel

Abstract

Corresponding Author: Tracy E. Madsen, 55 Claverick Street, 2nd floor, Providence, RI 02903, Tracy_Madsen@brown.edu, Ph: 401-489-5275, Twitter: @tmadsenem.

*Dr. Madsen and Olivia Cummings contributed equally.

SUPPLMENTAL MATERIAL

Supplemental Table 1

Supplemental Table 2

Supplemental Table 3

Supplemental Table 3a

Supplemental Table 4

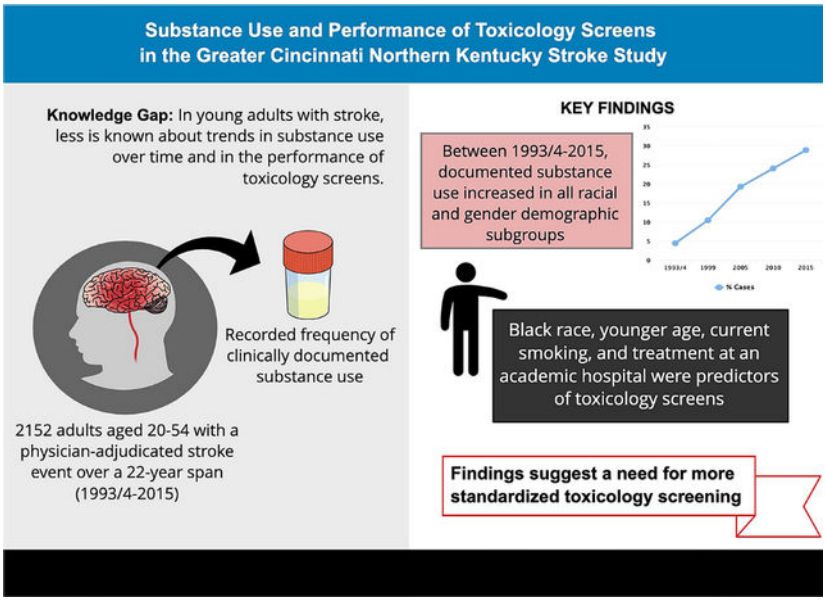
Background—Though stroke risk factors such as substance use may vary with age, less is known about trends in substance use over time or about performance of toxicology screens in young adults with stroke.

Methods—Using the Greater Cincinnati Northern Kentucky Stroke Study, a population-based study in a 5-county region comprising 1.3 million people, we reported the frequency of documented substance use (cocaine/marijuana/opiates/other) obtained from electronic medical record review, overall and by race/gender subgroups among physician-adjudicated stroke events (ischemic and hemorrhagic) in adults 20–54 years old. Secondary analyses included heavy alcohol use and cigarette smoking. Data were reported for 5 one-year periods spanning 22 years (1993/4–2015), and trends over time were tested. For 2015, to evaluate factors associated with performance of toxicology screens, multiple logistic regression was performed.

Results—Overall, 2152 strokes were included: 74.5% were ischemic, mean age was 45.7±7.6, 50.0% were women, and 35.9% were Black. Substance use was documented in 4.4%, 10.4%, 19.2%, 24.0% and 28.8% of cases in 1993/4, 1999, 2005, 2010 and 2015, respectively (p_{trend}<0.001). Between 1993/4 and 2015, documented substance use increased in all demographic subgroups. Adjusting for gender, comorbidities, and NIHSS, predictors of toxicology screens included Black race (aOR 1.58, 95%CI 1.02–2.45), younger age (aOR 0.70, 95%CI 0.53–0.91, per 10 years), current smoking (aOR 1.62, 95%CI 1.06–2.46) and treatment at an academic hospital (aOR 1.80, 95%CI 1.14–2.84). After adding chart reported substance use to the model, only chart reported substance abuse and age were significant.

Conclusions—In a population-based study of young adults with stroke, documented substance use increased over time, and documentation of substance use was higher among Black compared with White individuals. Further work is needed to confirm race-based disparities and trends in substance use given the potential for bias in screening and documentation. Findings suggest a need for more standardized toxicology screening.

Graphical Abstract



Keywords

stroke; stroke in young adults; substance use; stroke disparities; stroke; cerebrovascular disease/stroke; intracranial hemorrhage

Introduction

Each year, young adults between 18 and 50 years old experience 10% of all strokes in the United States,[1] and young adult patients experience a high burden of death and disability following stroke. Prospective data have demonstrated that the cumulative 20-year mortality for those 18 to 50 years old with stroke is four times higher than expected based on the general population.[2] The majority of young adult stroke survivors regain functional independence but are at risk of adverse outcomes such as an impaired quality of life, poststroke depression, and cognitive impairment.[3–5] In addition to these poor health outcomes, young adult patients may be burdened socially and financially by onset of disability during their peak productive years. Additional literature has reported racial, ethnic, geographic, and gender-based disparities in stroke hospitalization rates in young adults.[6–9]

There are also concerning temporal trends regarding an increasing incidence of strokes in young adults over time.[1,10] Contributors to the increasing incidence of stroke in young adults may include a growing prevalence of traditional stroke risk factors in that population, such as hypertension, diabetes, lipid disorders, and obesity,[6,11,12] but may also include more atypical risk factors such as substance use. Substance use, which has been shown to be associated with stroke, has also been increasing in the general population over the past decades.[13,14] In 2018, approximately 19.4% of the U.S. population age 12 and above reported substance use, most commonly marijuana and prescription pain relievers.[15] While sympathomimetic drugs of abuse such as cocaine and amphetamines have stronger associations with stroke than other substances, strokes associated with substances such as marijuana, heroin/opioids, synthetic cannabinoids, anabolic androgenic steroids, phenylcyclohexyl piperidine, and lysergic acid diethylamide have also been described in the literature.[11,16–21]

In a clinical setting, toxicology screening can be ordered when substance use is suspected to have contributed to a patient's stroke mechanism. However, disparities in toxicology screening have been reported for young adult patients with stroke. Young adult Black and male stroke patients have been found to be overrepresented in toxicology screening relative to the national prevalence of drug use in those populations.[22–24] Though positive results may contribute to knowledge of possible stroke etiology and allow for patient counseling regarding drug use, a focus on substance use as stroke etiology also has the potential to result in under testing for other important etiologies such as hypercoagulability, large vessel atherosclerosis, small vessel disease, or cardioembolic phenomena. Further, prior research has shown that there is low diagnostic yield for toxicology screening in stroke.[23,25]

Our study objectives were: 1) To describe patterns of documented substance use over the full study period of the Greater Cincinnati Northern Kentucky Stroke Study (GCNKSS) (22 years) and over the last 10 years of the study to capture more recent trends among stroke

patients in a large population-based stroke surveillance study; and 2) To investigate race and gender-based differences in toxicology screening of young adult patients (18 to 54 years old) with stroke. Our secondary objectives were to describe the breakdown of substance type used and/or reported by patients during the study periods and to evaluate rates of heavy alcohol use and cigarette smoking among young adults with stroke.

METHODS

Study Design/Study Population

The GCNKSS is a population-based study in which strokes occurring among residents of a 5-county region of southern Ohio and northern Kentucky are ascertained for a full year every 5 years. The GCNKSS population has been shown to be representative of the greater U.S. population in terms of Black race, sex, age, education, and income.[26] All physician-adjudicated cases of stroke among individuals age 18 to 54 presenting to one of the region's acute care hospitals in all study periods (7/1993–6/1994, 1999, 2005, 2010, 2015) were included along with a weighted sample of patients presenting to outpatient facilities. This study was approved by the IRB at each participating institution. We adhered to STROBE guidelines. Data are available to qualified investigators by request to the GCNKSS principal investigators.

Case Definitions/Data Abstraction

Potential stroke cases in each of the five study periods were identified by trained study nurses using International Classification of Diseases (ICD) stroke codes (ICD-9 codes 430–436 or ICD-10 160–169) followed by adjudication by trained study physicians. For consistency over the 5 study periods, imaging evidence of stroke was not required to meet the clinical case definition. Following adjudication of cases as stroke events, cases were then subtyped into ischemic (IS), intracerebral hemorrhage (ICH), or subarachnoid hemorrhage (SAH) as previously described.[26–28] Transient ischemic attacks were not included in this analysis.

Definition of Documented Substance Use

For the purposes of examining patterns of documented substance use over time (excluding alcohol and smoking), substance use was defined as use of any of the following: crack/cocaine, marijuana, opiates, and several other recreational substances categorized as "other substances". Other substances included hallucinogenics, amphetamines, and non-prescribed benzodiazepines. Prescribed medications including prescribed opiates and benzodiazepines were not included in the analyses. A case was included as positive for substance use if there was documented history of the included substances (marijuana, crack/cocaine, opiates, or other) in the clinical record. For all study periods, documentation of substance use could have been due to patient report or positive toxicology screens, with consistent variables collected over time. In a sub-analysis, the frequencies of use of specific substances over time were reported using self-report data from the medical record. For 2015 two additional variables were added to the data collection; "Alcohol level ordered", and "Drug screen obtained". These variables were used only for a multivariable analysis of predictors of

performance of toxicology and alcohol screening in 2015, they were not used in the definition of substance use for comparisons over time.

Alcohol Use and Cigarette Smoking Definitions

Heavy alcohol use was defined as documentation of > 2 servings of alcohol per day present in the medical record. For cigarette smoking history (conventional cigarettes) (defined in the following categories: never, past, or current (defined as within 3 months)), data were abstracted from the medical records. For 2015 only, if use of electronic cigarettes were documented in the medical record, these data were recorded separately from conventional cigarettes.

Covariates relating to toxicology screening, and other variables

Data on demographic variables and clinical variables (history of diabetes, history of hypertension, history of coronary artery disease, or prior stroke), National Institutes of Health Stroke Scale (NIHSS) score, and treatment at an academic vs. community hospital were also abstracted from patient records.

For the purposes of investigating predictors of toxicology screening, data on whether urine or blood screens were ordered during the hospital admission were also abstracted by trained study nurses. These data (whether a toxicology screen was obtained) were only available during the 2015 study period. For alcohol, testing for alcohol levels was also abstracted from patient records, but again information regarding ordering of the screen was only available in 2015.

Statistical Analysis

Demographic and clinical characteristics of individuals in each study period (gender, race, stroke subtype (IS, ICH, or SAH), and age) were reported using descriptive statistics. As data collection of medical history variables involved medical record review, if the condition (e.g., diabetes) was not recorded as positive in the medical record, it was assumed as not present. Similarly, for documented substance use and use of specific drugs, no mention in the medical record was categorized as “no” for the purposes of analyses. All data were available for age, sex and race, though there were 5 individuals categorized as “other” race in which the “other” race was not specified. Missingness for heavy alcohol use and cigarette smoking status is shown in the appropriate tables. Missing data were not imputed.

For our first objective, to describe patterns of documented substance use over time among stroke patients, we reported the frequency and percentage of stroke cases that either self-reported or tested positive for non-prescribed substances excluding alcohol or cigarettes, both overall and in race/gender specific subgroups. To test for changes over time, we used the Cochran Armitage test for trend, first over all study periods and then over the last 3 study periods (from 2005 to 2015). We chose to also perform the trend test over the last 10 years of the study period in order to investigate trends over time in a more contemporary time frame. These analyses were repeated for heavy alcohol use and for cigarette use, as defined above.

For our second major objective, the frequency and proportion of patients in each demographic subgroup (Black women, White/Other women, Black men, White/Other men) in whom a toxicology screen was obtained for 2015 (the only study period when these data were available), and differences by groups were tested using chi-square tests. Because our study population is approximately 99% either Black or White (and <1% Other race), individuals categorized as "Other" were combined with White individuals for the purposes of these analyses. Sequential multivariable logistic regression models were then used to investigate factors associated with the performance of toxicology screening in 2015. In the model, we included factors hypothesized to affect the likelihood of toxicology screens. In the initial model, variables included age, co-morbidities including prior stroke, stroke severity as measured by the NIHSS, current smoking status, and treatment at an academic vs. non-academic treatment center. In a second model, we also included documentation of substance use in the medical record (either current or former). Odds ratios with 95% confidence intervals were reported.

Secondary analyses

As an exploratory objective, we described the breakdown of substances used and/or reported by patients during the study periods. First, for specific time periods, we examined the proportion of stroke cases in which patients self-reported use of marijuana, cocaine, opiates, or other substances. This was repeated by stroke subtype (IS, SAH, and ICH). For 2015, we specifically examined use within 24 hours given the possible contribution to stroke pathophysiology when used in this time frame.

Since prescription opiates were excluded from previous analyses, we reported use of prescription opioids as the frequency and proportion of cases (overall and stratified by subgroup) with prescribed opioids at time of admission. Trends over time were tested using the Cochran-Armitage test.

For 2015 only, we also reported the proportion of toxicology screens and blood alcohol tests with positive results, overall and by demographic subgroup. All analyses were performed using SAS® Version 9.4 (SAS Institute, Cary, NC). P-values < 0.05 were considered significant.

RESULTS

Baseline demographics

The present analysis included 2152 physician-confirmed strokes across all 5 study periods (Table 1). Overall, the mean age was 45.7 (SD 7.6). The percentages of women, Black, and White patients were 50.0%, 35.9%, and 63.2%, respectively. Overall, 20 of 2152, less than 1% of the sample was in the "Other" race category. Demographic characteristics by year are included in Table 1. Ischemic strokes were most common (74.9% of cases overall), followed by ICH (15.7%) and SAH (9.1%).

Documented Substance Use Over Time

Data describing rates of documented substance use in the overall study population and stratified by demographic subgroups are included in Figure 1 and Supplemental Table 1. Between the first and last study periods and between 2005 and 2015, there was a significant increase in documented substance use overall ($P_{trend} < 0.0001$ and $P_{trend} = 0.0004$, respectively). Over the same 10-year time period, among all stroke cases by race/gender subgroup, there was a significant increase in substance use among White/Other women (6.8% in 2005 to 17.6% in 2015, $P_{trend} = 0.006$) and White/Other men (17.1% in 2005 to 28.1% in 2015, $P_{trend} = 0.02$). In contrast, rates of documented substance use were relatively stable among Black women (31.0% in 2005 to 34.6% in 2015, $P_{trend} = 0.54$) and Black men (33.7% in 2005 to 41.0% in 2015, $P_{trend} = 0.33$). For heavy alcohol use (Table 2), there was no significant linear trend overall or in specific demographic subgroups between 2005 and 2015. There was a decrease in heavy alcohol use for Black men between 1993/4 and 2015.

Cigarette smoking rates over time and by subgroup are displayed in Supplemental Table 2. There was no significant temporal trend overall in the proportion of cases who reported current smoking, either overall or in specific subgroups. Current smoking rates ranged from 43.4% in 1993/4 to 46.7% in 2015 (p=0.56). Regarding electronic cigarette use, only 0.7% of the 457 cases in 2015 reported electronic cigarette use. These data were not collected in prior years.

Documented use of specific substances over time is displayed in Supplemental Table 3 and by stroke subtype in Supplemental Table 3a (by stroke subtype). Over time, there was a significant increase in reported rates of documented substance use for all substances (Supplemental Table 2, p<0.0001). Reported use of marijuana, cocaine, and other substances increased over the observed study periods. Overall, 4% of study participants reported use of a specific substance in 1993/4 compared with 28.8% in 2015. Rates of marijuana use had the largest increase in reported use over time, from 0.7% in 1993/4 to 9.8% in 2005 to 19.0% in 2015. Cocaine was the second most frequently reported substance used in every study period after 1999. The rate of documented cocaine use increased from 2.4% in 1993/4 to 9.4% in 2015 (p=0.0002). Documented use of opiates and other substances (including benzodiazepines and non-cocaine sympathomimetics) occurred less frequently than marijuana and cocaine in all study periods. Finally, in 2015, for documented substance use within 24 hours of stroke, 3.3% reported marijuana use, 2.0% reported crack/cocaine use, 1.3% reported opiate use (excluding prescriptions), and 2.6% reported other substances. Other substances included non-prescribed drugs that did not fit into the categories of marijuana, cocaine, or opiates. These included hallucinogenics (phenylcyclohexyl piperidine, 3, 4-methylenedioxy-N-methamphetamine, lysergic acid diethylamide), amphetamines, benzodiazepines, and barbiturates.

Prescription opioids were excluded from the main analysis, but we understand that prescriptions are likely the source of opioids for some individuals. In 1993/4 there were no reported prescription opioids compared with 18.8% of the stroke cases (n=458) in 2015. Linear trends over time between 2005 and 2015 were not significant in any of the demographic subgroups (data not shown).

Screening Rates

Urine or blood toxicology screening was ordered on 32.0% of young adults with stroke in 2015 (Supplemental Table 3). Black men had the highest proportion (42.3%) of toxicology screens ordered, followed by Black women (35.6%). The proportions White/Other men and White/Other women who were tested were lower (28.1% and 27.2%, respectively). In the same year, 15.5% of patients had blood alcohol levels tested, with frequencies of about 17% for all race/sex subgroups except for White/Other women (12.0%). Data on the yield of toxicology screens was limited (data on specific substances were not available), but overall positivity rates by group are similar (Supplemental Table 4).

In multivariable analysis, Black patients had 58% higher odds (aOR 1.58 95%CI 1.02–2.45) of being screened for substances compared with White/Other patients, adjusting for age, gender, history of diabetes, hypertension, coronary artery disease, prior stroke, NIHSS score, smoking status, treatment at an academic center, and stroke type (p=0.04) (Table 3). Current smoking, younger age, and treatment at an academic medical center were also significant predictors of toxicology screening, and there was no significant effect of gender in this model (Table 3). After adding current or former substance use as documented in the medical record to the model, however, Black race was no longer significant (aOR 1.30, 95%CI 0.82–2.07, p=0.26). In the model with blood alcohol testing as the outcome (data not shown), only NIHSS score at presentation (aOR 1.06, 95% CI 1.02–1.08) and current smoking (aOR 1.82, 95%CI 1.05–3.14) were significant as predictors of testing, though current smoking was no longer significant after including chart documented substance use in the model.

DISCUSSION

In this population-based study of young adults with stroke, we sought to investigate the trends in documented substance use over a 22-year period as well as the performance of toxicology and alcohol screens in the 2015 study period. Our major findings were that documented substance use increased over time, particularly marijuana and cocaine. Overall, documented substance use seemed to increase most substantially among White women and White men, while rates in Black women and men have gone up since 1993/4 but not since 2005. Rates of heavy alcohol use and smoking were stable over time with the exception of a decrease in heavy alcohol use among Black men from 1993/4 to 2015. In addition, substance use was documented more frequently among Black individuals. Overall, our findings of increasing documented substance over time parallels trends in the U.S. population during a similar time frame.[13,29] This has been found to be true across many race/ethnicity and gender subgroups in the overall U.S. population, although there is limited published longitudinal data analyzing trends in substance use by race/ethnicity and gender.

It is unknown the extent to which our findings of race-based differences in use or temporal changes in use are truly reflective of substance use rates among stroke patients, as it is also possible that differences in rates of documented substance use reflect biases in screening and documentation. In our study, race-based differences in documented substance use were substantially larger than previously documented race differences in the prevalence of substance use in the population,[30] though our race-based differences in prevalence of documented substance use are consistent with prior GCNKSS data.[31] There are data to

support the possibility of race-based biases in medical record documentation[32] as well as race and age-based biases in drug testing of stroke patients,[24] but it is unknown whether biases in documentation contributed to our findings. Data from other population-based studies on cocaine use among young adults with stroke did not demonstrate differences between Black women and White women but did demonstrate higher rates of cocaine use among Black men compared with White men,[33] though this difference was not as pronounced as in our findings. It is also interesting to note that in the current study, the positivity rate of toxicology screens was similar across the demographic subgroups, though this analysis is limited by small numbers of positive results. With regard to temporal changes in how physicians screen for and document substance use, it is possible that documented rates of substance use increased over time in our study partially because of changes in physician awareness of substance use or due to changes in medical practice that have resulted in increased screening rates. Unfortunately, potential biases in screening for and documentation of substance use is a construct that is not easily measured but should be considered in future studies on this topic. Further, future prospective study designs could be used to attempt to better capture substance use among patients with stroke in an unbiased manner.

Especially concerning in our study were the rates of current smoking in this young adult population with stroke. Rates in this population have not decreased over time despite public health efforts to decrease the prevalence of smoking nationwide, though stable smoking rates among adults with stroke may not be representative of the population estimates, where smoking rates have decreased.[34] Smoking, however, remains an important modifiable stroke risk factor in young adults.

There are numerous other potential implications of our findings of increasing rates of documented substance use over time, the most obvious being the possible link to either stagnant or increasing stroke incidence among young adults when compared to decreasing stroke rates among older adults. Even if increased rates of documented substance use are not causally linked to increasing rates of stroke at the population level, other negative physical and mental health effects of substance use cannot be ignored.

With regards to performance of lab based toxicology screens, patients that were younger, Black, or treated at an academic center were more likely to have toxicology screens performed, consistent with prior single center studies.[24] One potential implication here is that patient race affects physicians' medical decision making for stroke patients. It is important to note, however, that race became non-significant in the model when documented substance use was added as a variable, though this should be interpreted with caution given the retrospective nature of data collection and potential biases in documentation of substance use in the chart. Specifically, because data were collected retrospectively, it is possible that substance use was documented in the medical record after the return of the drug screen results.

It remains concerning that there is a difference in rates of screening for substances between racial groups given the potential for related biases in care and outcomes. The intended value of toxicology and alcohol screening in the context of an acute stroke is to assess risk factors

that may have led to the illness. If a screen is positive, patient counseling and referral to appropriate services can aid in rehabilitation and future stroke prevention. As such, protocols should be designed to incorporate appropriate toxicology screening into acute stroke care while minimizing potential biases by race or other factors such as age.

Our findings of selective toxicology screening point to the need for further, thoughtful consideration of the importance of urine toxicology screening when patients present with stroke. Recent guidelines on the secondary prevention of stroke from the American Heart Association[35] recommend that patients with cryptogenic stroke should be screened for substances (Level 2a recommendation), as there is a particularly increased risk of stroke associated with use of cocaine and/or amphetamines.[33,35] The same guidelines recommend (Level 1) that counselling services be provided to those patients with stroke or TIA with known substance use disorders, those who test positive for simulants, or those who meet criteria for heavy alcohol use (> 2 drinks per day for men or > 1 drink per day for women).[35] Further, in the guidelines for care of the acute ischemic stroke patient, it is noted that "illicit drug use may be a contributing factor to incident stroke" and that substance use is not a contraindication to intravenous alteplase.[36] To avoid biases in screening for and detecting substance use and to ensure opportunities for counselling for patients regardless of demographic subgroup, we would advocate for the inclusion of toxicology screens as part of established protocols with the nuance that detection of substances does not necessarily imply causation of the stroke and that other etiologies should be investigated and other risk factors addressed. It is unknown whether the detection of substances on the toxicology screens of stroke patients affects whether a full diagnostic work-up is completed (e.g., performance of vessel imaging, cardiac testing/echocardiogram), but this could be a topic of future research.

Limitations

There are several additional limitations of this study. First, as discussed above, there are likely biases in the screening for and documentation of substance use which may have affected the rates of documented substance use in our study. Cultural trends in the practice of screening stroke patients for substances (either by asking patients to self-report substance use or sending laboratory screens) may also have affected our results. On a population-level, it is impossible to interpret true substance use rates from this dataset due to surveillance bias. Further, our study is based largely on Black and White participants and may not be generalizable to patients who identify with other race or ethnic groups.

Conclusions

In summary, rates of documented substance use among young adult patients with stroke increased significantly over a 22-year period, which is concerning given the known negative impact of substance use on overall health and on stroke risk in some cases. Though race-based differences in screening and documented substance use were identified, more work is needed to understand the contribution of potential biases in screening and documentation. Clinical practice may be improved by standardizing stroke protocols to reduce population-based disparities in screening while ensuring that suspected substance use in stroke patients does not preclude the consideration of other important stroke etiologies and risk factor management strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

FUNDING SOURCES

The GCNKSS was funded by a grant from the National Institutes of Neurological Disorders and Stroke (R01 NS 30678). TEM is funded by the NHLBI (K23 HL140081).

DISCLOSURES: JCK, KA, HS, DW, SF, PK, MLF, JM, EM, SJS, BMK, and DOK are supported by a research grant (NINDS R01NS30678). FR reports employment by Baptist Health South Florida and compensation from AstraZeneca for other services. OA reports service as Chief Medical Officer for sense diagnostics and compensation from NICO Corporation for data and safety monitoring services. MLF reports compensation from CSL Behring for other services and compensation from Alexion Pharmaceuticals for other services. SLD reports compensation from Genentech for other services. KW reports grants from Jan Medical Inc.; grants from Sense Diagnostics LLC; and grants from American Heart Association. BMK reports service as Board of Directors, Member for American Academy of Neurology, and employment by University of Cincinnati.

Non-standard Abbreviations and Acronyms

GCNKSS	Greater Cincinnati Northern Kentucky Stroke Study
IS	Ischemic Stroke
ICH	Intracerebral hemorrhage
SAH	Subarachnoid hemorrhage
NIHSS	National Institutes of Health Stroke Scale

REFERENCES

1. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, et al. Heart Disease and Stroke Statistics—2021 Update: A Report From the American Heart Association. Circulation. 2021;43:e254–e743.
2. Rutten-Jacobs LA Arntz R, Maaijwee N, Schoonderwaldt H, Dorresteijn L, Van Dijk E, De Leeuw F. Long-term Mortality After Stroke. JAMA. 2013;309:1136–1144. [PubMed: 23512060]
3. Singhal AB, Biller J, Elkind MS, Fullerton HJ, Jauch EC, Kittner SJ, Levine DA, Levine SR. Recognition and management of stroke in young adults and adolescents. Neurology. 2013;81:1089–1097. [PubMed: 23946297]
4. Edwards JD, Kapral MK, Lindsay MP, Fang J, Swartz RH. Young stroke survivors with no early recurrence at high long-term risk of adverse outcomes. J Am Heart Assoc. 2019;8:8–12.
5. Kapoor A, Scott C, Lanctot KL, Herrmann N, Murray BJ, Thorpe KE, Lien K, Sicard M, Swartz RH. Symptoms of depression and cognitive impairment in young adults after stroke/transient ischemic attack. Psychiatry Res. 2019;279:361–363. [PubMed: 31272664]
6. George MG, Tong X, Bowman BA. Prevalence of cardiovascular risk factors and strokes in younger adults. JAMA Neurol. 2017;74:695–703. [PubMed: 28395017]
7. Pathak EB, Sloan MA. Recent racial/ethnic disparities in stroke hospitalizations and outcomes for young adults in Florida, 2001–2006. Neuroepidemiology. 2009;32:302–311. [PubMed: 19287184]
8. Ramirez L, Kim-Tenser MA, Sanossian N, Cen S, Wen G, He S, Mack WJ, Towfighi A. Trends in Acute Ischemic Stroke Hospitalizations in the United States. J Am Heart Assoc. 2016;5:1–8.
9. Boan AD, Feng WW, Ovbiagele B, Bachman DL, Ellis C, Adams RJ, Kautz SA, Lackland DT. Persistent racial disparity in stroke hospitalization and economic impact in young adults in the buckle of stroke belt. Stroke. 2014;45:1932–1938. [PubMed: 24947293]

10. Kissela BM, Khoury JC, Alwell K, Moomaw CJ, Woo D, Adeoye O, Flaherty ML, Khatri P, Ferioli S, De Los Rios La Rosa F, et al. Age at stroke: Temporal trends in stroke incidence in a large, biracial population. Neurology. 2012;79:1781–1787. [PubMed: 23054237]
11. Westover AN, McBride S, Haley RW. Stroke in young adults who abuse amphetamines or cocaine: A population-based study of hospitalized patients. Arch Gen Psychiatry. 2007;64:495–502. [PubMed: 17404126]
12. Ekker MS, Boot EM, Singhal AB, Tan KS, Debette S, Tuladhar AM, de Leeuw FE. Epidemiology, aetiology, and management of ischaemic stroke in young adults. Lancet Neurol. 2018;17:790–801. [PubMed: 30129475]
13. Moeller SJ, Fink DS, Gbedemah M, Hasin DS, Galea S, Zvolensky MJ, Goodwin RD. Trends in illicit drug use among smokers and non-smokers in the United States, 2002–2014. J Clin Psychiatry. 2018;79:17m11718.
14. Fehnel CR, Ayres AM, Rost NS. Socioeconomic status does not predict cocaine use among ischemic stroke patients: A nested case-control study. JRSM Cardiovasc Dis. 2014;3:204800401453966.
15. Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health. HHS Publ No PEP19–5068, NSDUH Ser H-54. 2019;170:51–58.
16. Kaku DA, Lowenstein DH. Emergence of recreational drug abuse as a major risk factor for stroke in young adults. Ann Intern Med. 1990;113:821–827. [PubMed: 2240897]
17. Zhu Z, Osman S, Stradling D, Shafie M, Yu W. Clinical characteristics and outcomes of methamphetamine-associated versus non-methamphetamine intracerebral hemorrhage. Sci Rep. 2020;10:1–8. [PubMed: 31913322]
18. Martin-Schild S, Albright KC, Hallevi H, Barreto AD, Philip M, Misra V, Grotta JC, Savitz SI. Intracerebral hemorrhage in cocaine users. Stroke. 2010;41:680–684. [PubMed: 20185779]
19. Esse K, Fossati-Bellani M, Traylor A, Martin-Schild S. Epidemic of illicit drug use, mechanisms of action/addiction and stroke as a health hazard. Brain Behav. 2011;1:44–54. [PubMed: 22398980]
20. Tsatsakis A, Docea A, Calina D, Tsarouhas K, Zamfira L, Mitrut R, Sharifi-Rad J, Kovatsi L, Siokas V, Dardiotis E, et al. A Mechanistic and Pathophysiological Approach for Stroke Associated with Drugs of Abuse. J Clin Med. 2019;8:1295.
21. Freeman WD, Louh IK. Ischemic stroke after use of the synthetic marijuana spice. Neurology. 2014;83:772–773.
22. Perloff MD, Blattner MR, Spengler DC, Kase CS. Urgent neurological symptoms and urine toxicology, an outcomes study. J Subst Use. 2018;23:211–213.
23. Kalani R, Liotta EM, Prabhakaran S. Diagnostic yield of universal urine toxicology screening in an unselected cohort of stroke patients. PLoS One. 2015;10:1–7.
24. Silver B, Miller D, Jankowski M, Murshed N, Garcia P, Penstone P, Straub M, Logan SP, Sinha A, Morris DC, et al. Urine toxicology screening in an urban stroke and TIA population. Neurology. 2013;80:1702–1709. [PubMed: 23596074]
25. Ji R, Schwamm LH, Pervez MA, Singhal AB. Ischemic stroke and transient ischemic attack in young adults: Risk factors, diagnostic yield, neuroimaging, and thrombolysis. Arch Neurol. 2013;70:51–57.
26. Broderick J, Brott T, Kothari R, Miller R, Khoury J, Pancioli A, Gebel J, Mills D, Minneci L, Shukla R. The Greater Cincinnati Northern Kentucky Stroke Study: preliminary first-ever and total incidence rates of stroke among blacks. Stroke. 1998;29:415–421. [PubMed: 9472883]
27. Kleindorfer DO, Khoury J, Moomaw CJ, Alwell K, Woo D, Flaherty ML, Khatri P, Adeoye O, Ferioli S, Broderick JP, et al. Stroke Incidence Is Decreasing in Whites But Not in Blacks. Stroke. 2010;54:1326–1331.
28. Woo D, Sauerbeck LR, Kissela BM, Khoury JC, Szaflarski JP, Gebel J, Shukla R, Pancioli AM, Jauch EC, Menon AG, et al. Genetic and environmental risk factors for intracerebral hemorrhage: Preliminary results of a population-based study. Stroke. 2002;33:1190–1195. [PubMed: 11988589]
29. Key substance use and mental health indicators in the United States: Results from the 2020 National Survey on Drug Use and Health (HHS Publication No. PEP21-07-01-003, NSDUH Series H-56). Rockville, MD: 2021.

30. Substance Abuse and Mental Health Services Administration, Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-48, HHS Publication No. (SMA) 14–4863. Rockville, MD: Substance Abuse and Mental Health S.

31. De Los Ríos F, Kleindorfer DO, Khoury J, Broderick JP, Moomaw CJ, Adeoye O, Flaherty ML, Khatri P, Woo D, Alwell K, et al. Trends in substance abuse preceding stroke among young adults: A population-based study. Stroke. 2012;43:3179–3183. [PubMed: 23160887]

32. Park J, Saha S, Chee B, Taylor J, Beach MC. Physician Use of Stigmatizing Language in Patient Medical Records. JAMA Netw Open. 2021;4:1–11.

33. Cheng YC, Ryan KA, Qadwai SA, Shah J, Sparks MJ, Wozniak MA, Stern BJ, Phipps MS, Cronin CA, et al. Cocaine use and risk of ischemic stroke in young adults. Stroke. 2016;47:918–922. [PubMed: 26965853]

34. United States Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress A Report of the Surgeon General. A Rep Surg Gen. 2014;1081.

35. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2021;52:e364–e467. [PubMed: 34024117]

36. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2019;50:e344–e418. [PubMed: 31662037]

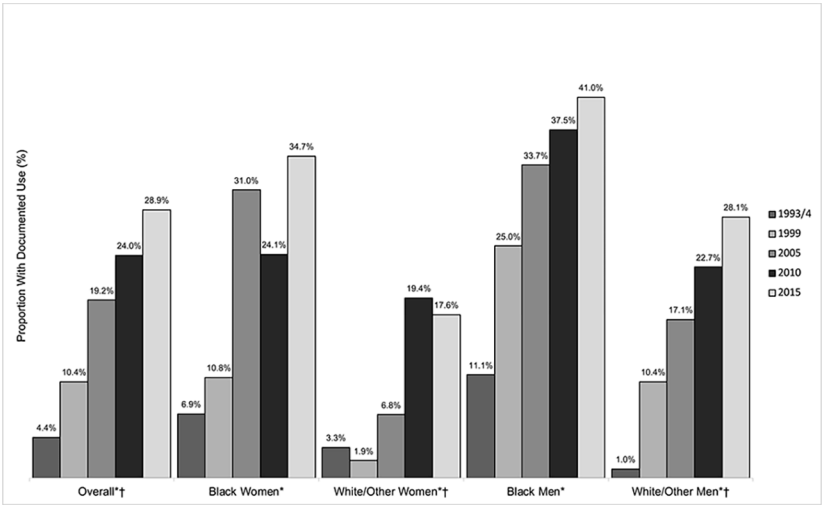


Figure 1.

Documented Substance Use Over Time by Demographic Subgroup Among Young Adults (18–54 years of age) with Stroke in the GCNKSS

Data presented as the proportion (%) of stroke cases in a given year and subgroup (or overall) that either self-reported or tested positive for non-prescribed substances, excluding alcohol or cigarettes.

*P-value <0.05 for trend, 1993/4–2015, †P-value <0.05 for trend, 2005–2015.

Table 1

Demographics of Stroke Cases Among Patients 18 to 54 Years Old in the Greater Cincinnati Northern Kentucky Stroke Study

	1993/4 N=297	1999 N=376	2005 N=501	2010 N=521	2015 N=457	Overall p-value
Age	45.3 (8.0)	45.3 (7.5)	45.6 (7.4)	46.6 (7.0)	45.5 (8.1)	0.16
Sex	149 (50.2)	181 (48.1)	248 (49.5)	273 (52.4)	226 (49.4)	0.76
Women						
Race						0.51 *
Black	103 (34.7)	134 (35.6)	176 (35.1)	180 (34.6)	179 (39.2)	
White	190 (64.0)	239 (63.6)	321 (64.1)	339 (65.1)	271 (59.3)	
Other	4 (1.3)	3 (0.8)	4 (0.8)	2 (0.4)	7 (1.5)	
Stroke Subtype						0.01 **
Ischemic	219 (73.7)	260 (69.2)	374 (74.6)	404 (77.5)	355 (77.7)	
ICH	46 (15.5)	61 (16.2)	80 (16.0)	79 (15.2)	71 (15.5)	
SAH	32 (10.8)	53 (14.1)	41 (8.2)	38 (7.3)	31 (6.8)	
Unknown	0	2 (0.5)	6 (1.2)	0	0	
Age group (years)						0.11
18–34	40 (13.5)	39 (10.4)	47 (9.4)	39 (7.5)	51 (11.2)	
35–44	64 (21.6)	94 (25.0)	120 (24.0)	106 (20.4)	106 (23.2)	
45–54	193 (65.0)	243 (64.6)	334 (66.7)	376 (72.2)	300 (65.6)	

Data presented as mean (standard deviation), or n (%); ICH: Intracerebral hemorrhage; SAH: Subarachnoid hemorrhage

* p-value does not include “Other” race

** p-value does not include “Unknown” stroke type

Over all 5 study periods, 20 individuals were included in the “Other” race category: 11 Asian, 5 Not specified, 2 multiple races, 2 Arab/Middle Eastern and North African descent.

Table 2:

Documented Heavy Alcohol Use Over Time (by subgroup) Among Young Adults (18–54 years of age) with Stroke

	1993/4 N=297	**1999 N=376**	**2005 N=501**	**2010 N=521**	**2015 N=457**	**p-value for trend† 1993/4–2015**	**p-value for trend† 2005–2015**
Overall Unknown	28 (9.4) 43	48 (12.8) 19	52 (10.4) 9	53 (10.2) 3	42 (9.2) 2	0.73	0.54
Black Women Unknown	0/58 12	6/74 (8.1) 3	6/87 (6.9) 2	6/108 (5.6) 0	6/101 (5.9) 0	0.38	0.43
White/Other Women Unknown	1/91 (1.1) 10	5/107 (4.7) 5	3/161 (1.9) 1	2/165 (1.2) 0	1/125 (0.8) 0	0.25	0.54
Black Men Unknown	12/45 (26.7) 8	17/60 (28.3) 5	13/89 (14.6) 5	9/72 (12.5) 0	10/78 (12.8) 2	0.005	0.73
White / Other Men Unknown	15/103 (14.6) 13	20/135 (14.8) 6	30/164 (18.3) 1	36/176 (20.4) 3	25/153 (16.3) 0	0.37	0.67

Data presented as n (%) and represent the frequency (%) of stroke cases in a given subgroup (or overall) with documentation of > 2 servings of alcohol per day.

†Cochran-Armitage test for trend, over all study periods and then over last 3 study periods from 2005 to 2015. Complete case analysis was performed; missing observations are noted in the table.

Table 3:

Multivariable Analysis of Predictors of Performance of Toxicology and Alcohol Screening in the GCNKSS, 2015 only, Ages 18–54

GCNKSS 2015	Toxicology Screen Obtained			
	Model 1		Model 2	
	aOR (95%CI)	p-value	aOR (95%CI)	p-value
Women	0.86 (0.57, 1.31)	0.47	1.00 (0.65, 1.5)	0.99
Black race (vs. White/Other race)	1.58 (1.02, 2.45)	0.04	1.30 (0.82, 2.07)	0.26
Age (per 10 years)	0.70 (0.53, 0.91)	0.01	0.71 (0.54, 0.94)	0.02
History of diabetes	0.72 (0.44, 1.20)	0.21	0.73 (0.43, 1.25)	0.25
History of hypertension	0.93 (0.56, 1.54)	0.78	0.88 (0.52, 1.49)	0.64
History of CAD	0.97 (0.49, 1.92)	0.93	0.93 (0.46, 1.90)	0.85
History of prior Stroke	0.95 (0.55, 1.65)	0.86	0.86 (0.48, 1.54)	0.62
NIHSS (each point)	1.02 (0.99, 1.04)	0.18	1.10 (0.96, 1.25)	0.17
Current Smoker vs past or never	1.62 (1.06, 2.46)	0.02	1.08 (0.68, 1.72)	0.74
Treated at an academic center (vs. community)	1.80 (1.14, 2.84)	0.01	1.63 (1.01, 2.62)	0.046
Hemorrhagic stroke (vs. Ischemic)	0.70 (0.40, 1.22)	0.21	0.68 (0.38, 1.21)	0.19
Documented substance use			4.10 (2.51, 6.71)	<.0001

Effect estimates obtained from multivariable logistic regression models adjusted for all variables listed in table. CAD: coronary artery disease; NIHSS: National Institutes of Health Stroke Scale.

Toxicology screen information not available on two subjects (Total n=455).

Sex, race, and age available on all subjects. If past medical history was not checked as present in the medical record it was assumed not present. The 3 missing smoking history were assumed non-smokers for this analysis. Retrospective NIHSS was available on all subjects, as was institution of treatment, stroke type and documented substance use.