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Quantifying Lifetime Exposure to Ultraviolet Radiation in the Epidemiology of Cutaneous Malignant Melanoma: A Pilot Study

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ABSTRACT

This pilot study uses a unique method to calculate cumulative lifetime exposure to ultraviolet radiation-b to determine if this refined method would indicate differences in lifetime cumulative UVB exposure between age and sex matched controls. Forty-four age and sex matched cases and controls demonstrated no significant difference in mean cumulative lifetime UVB exposure based on the duration and location of residence. This pilot study suggests that further analysis of the dataset should be conducted to determine if the cumulative lifetime exposure hypothesis is of primary importance regarding the association between UVB exposure and development of cutaneous malignant melanoma.

KEY WORDS

epidemiology

cutaneous malignant melanoma

ultraviolet radiation

I. INTRODUCTION

Several case control studies have quantified lifetime exposure to ultraviolet radiation (UVR) as a risk factor in the etiology of cutaneous malignant melanoma (CMM). These studies have been categorized as measuring potential exposure or measuring actual exposure.[1] Because of differing ways of assessing exposure, measures of potential exposure tend to be more objective than measures of actual exposure, which depend on self-reports and individual recall. Relative risk estimates from existing case-control studies are not consistently elevated and lack statistical significance, suggesting that both measures lead to some misclassification (Table 1).[2,3,4,5]

To refine the measure of accumulated lifetime exposure, an alternative approach is proposed. Using the residential history from a case-control study of CMM, county-level UVB measurements obtained from groundbased instruments were applied to the duration and location of residence where respondents reported having lived throughout their lifetimes. The purpose of this pilot study is to determine if more accurate measures of lifetime potential UVB exposure may show that cases received more cumulative lifetime exposure than their age-sex matched controls. Analysis of the entire dataset (1,413 subjects) may show that this approach reduces the error that results when exposure misclassification occurs equally in cases and controls. If an association is present, reduced non-differential misclassification would enhance the relative risk estimate for lifetime UVB exposure and CMM.

II. METHODS

Case Selection

Cases and controls were obtained from a population-based case-control study of CMM conducted in Connecticut, USA.[6] Each case was histologically confirmed. All patients diagnosed between January 15, 1987 and May 15, 1989 with a primary cutaneous melanoma, who were 18 years of age or older at diagnosis and a resident of the State of Connecticut, were eligible for interview by trained, registered nurses. Controls were obtained through random digit dialing. One-hundred cases were randomly selected for the preliminary analysis presented here. Controls were matched with cases of the same sex and age (within five years, where possible) in a one to one ratio. The analysis was restricted to Caucasians who lived their entire lives in the contiguous United States. Forty-four matched pairs remained available for analysis.

Coding the Residential History

Residential histories of subjects were obtained during the structured in-person interview. Date of birth and location and duration of every residence of six months or more, including repeated stay at vacation homes, were coded. Attempts were made to identify specific towns within states.

The residential history was coded for state, county, and place (township, borough, precinct, city). Codes were obtained through a comprehensive archive of public data, the Socio-Economic Environmental Demographic Information System (SEEDIS), at Lawrence Berkeley Laboratory (LBL), Berkeley, CA.[7] Requisite geographic data files that contained state, county and place codes from the 1980 Census were extracted and stored in a file. The corresponding state and county codes were then assigned to each place of residence specified on the residential history.

The area code files in SEEDIS are updated to the 1980 Census, and do not include some locations which were not legally incorporated places. In these rare instances, the place and county of residence were ascertained by look-up in a recent publication.[8]

Latitude and Altitude

Latitude and altitude values were required for the estimation of potential lifetime UVB exposure. SEEDIS does not provide latitude and altitude for every place, but does contain latitude and altitude at the county level based on the 1970 Census.

Latitude values are provided at the county level as the population centroid of the county, which is the mean latitude of all county inhabitants.[9] Altitude is the elevation from sea level at that latitude in feet.[10] Place codes are necessary to obtain county codes, since the residential history requests place and state, but not county.

A second file was created by linking state and county codes with the corresponding latitude and altitude (Figure 1).

Exposure Calculation

The equation that calculates ln(UVB) was developed by Scotto and colleagues[11] at the National Cancer Institute (NCI) as follows:

$$\ln(UVB) = 15.5450 - (0.0389)(LAT) + (0.00010)(ALT)$$

where ln(UVB) is the natural log (ln) of the average annual amount of UVB for the county, LAT is the latitude, given in degrees north, and ALT is elevation from sea level, given in meters. This expression was used to calculate the ln(UVB) exposure for every location of residence.

This expression was developed using a generalized linear modelling procedure. Observed values of ground-based UVB were obtained from Robertson-Berger (RB) meter counts of UVB from 24 geographic areas (primarily Standard Metropolitan Statistical Areas (SMSAs)) from 1974 to 1990. The RB instrument records half-hourly UVB "counts" that measure solar ultraviolet radiation from 290 nm to 330 nm, weighted according to the erythema action spectrum (297 nm).[12] A description of the equation and its development has been described elsewhere.[11]

Once the ln(UVB) value was obtained for every location of residence specified on the residential history, the ln(UVB) was then exponentiated and multiplied by the years lived at that location to produce lifetime exposure. Lifetime potential exposure to UVB is recorded as the sum of all RB meter counts divided by 400. One minimal erythemal dose (MED) equals 400 RB meter counts for the average Caucasian skin. The quotient was then divided by 100,000.

A paired t-test (one-tailed, $p<0.05$)) was performed to determine whether differences exist between cases and controls.

III. RESULTS

For this pilot study there were 44 cases and 44 age and sex matched controls (N=88). Table 2 provides a few descriptive statistics. Cases and controls do not differ significantly comparing latitude, altitude or UVB exposure, although cases did receive a slightly higher mean lifetime exposure than controls. Figure 2 graphically displays exposure for cases and controls. The peak at approximately 0.50 shows the mean cumulative amount of UVB most subjects experienced.

Fourteen pairs were male and 30 pairs were female. Table 3 shows that twice as many females as males were selected in this random sample. Males were diagnosed younger than females and experienced less cumulative exposure than females cases. Male controls were older, but received less cumulative UVB than male cases. The female controls were older on average than the cases, because exact age matching could not be maintained in the oldest age categories (65 and over).

Figure 3 shows the state code by years lived in that state. It can be seen that most of the sample lived for some time in Connecticut (mean=25 years), as well as in New York and Massachusetts. The mean duration for cases in the states associated with high UVB exposure such as Florida, Texas, or Southern California was between 0 and 2.5 years. This sample was not highly mobile.

IV. DISCUSSION

The purpose of this study was to test if a refined method of summing potential lifetime exposure would show greater differences in exposure between cases and controls. The total amount of radiation delivered at a given location provides an upper bound of exposure, not the actual exposure. Actual exposures are modified by factors such as sunscreen use and clothing.

The major limitation of this pilot study was that only 44 pairs were included and that matching on age was not exact. Neverthless, it was surprising to find no significant mean difference between cases and controls. These findings lend support to the intermittent exposure hypothesis; that is, it is the short-term intense doses on unconditioned skin that damage melanocytes.

Subsequent analysis of the entire dataset (1,413 subjects) will examine the variables associated with assessing intermittent exposures, such as location, duration, and frequency of recreation and vacation, adjusting for use of sunscreens, skin type, or protective clothing. Analysis of cumulative exposure by age categories may suggest exposure during childhood or adolescence is more important than during other periods of life. Measures of intermittent exposure will be compared to the refined measures of lifetime exposure.

The approach here is a unique attempt to measure lifetime exposure quantitatively, an approach never before used in an analytic study on CMM. Because heavy reliance is placed on atmospheric and environmental databases, it is important to comment on these sources of potential bias. Latitude and altitude values from the 1970 Census do not exactly correspond to the state and county codes of the 1980 Census, since some census tracts were redrawn after 1970. The RB instrument used to measure observed values of groundbased UVB, slightly underestimates the amount of UVB that can cause sunburn (~297 nm). The meter itself is housed at airports and National Weather Service stations, where ambient air pollution reduces the number of counts being recorded and may attentuate true exposures in suburban and rural areas. However, these sources of bias are likely to equally affect cases and controls, and are, therefore, unlikely explanations for the lack of differences in observed UVB exposure.

In conclusion, although preliminary analysis of this sample indicates potential lifetime cumulative exposure is not significantly greater in cases than controls, this approach likely reduces non-differential measurement error. Further analysis of all case-control pairs should be more informative. The quantitative nature of exposure calculation may provide evidence to reject the cumulative exposure hypothesis.

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TABLE 1: MEASURES OF LIFETIME SUN EXPOSURE

Author	Measurement of Sun Exposure	Range of Relative Risk	95% CI
Potential Exposure			
Green et al. (1986)2	Average UVR levels at residence	No trend found	
Holman and Armstrong (1984)3	Mean annual hours of bright sunlight at place of residence	1.92-2.83	1.16-4.43
Graham et al. (1985)4	Ever resided below 40 degrees North latitude	1.2-1.5	0.64-2.45
Actual Exposure			
Graham et al. (1985)*	Cumulative hours of sun exposure for whole life	0.5-1.0	0.21-1.30
Green et al. (1986)+	Cumulative hours of sun exposure for whole life	1.0-2.3	0.40-5.1
Dubin et al. (1986)5	Lifetime sun exposure	0.63-1.22	0.41-1.68

(Adapted from Armstrong, 1988)
* Adjusted for age and presence of nevi on arms

TABLE 2: DESCRIPTIVE STATISTICS OF CASES AND CONTROLS

	MEAN		MINIMUM		MAXIMUM		PAIRED-T
	case	control	case	control	case	control	p-value
AGE	49	52	23	23	93	85	--
ALTITUDE*	292.80	366.32	5.0	7.0	3529	5283	0.772
LATITUDE#	40.8	41.0	25.8	29.4	46.9	45.0	0.411
UVB+	0.48	0.46	0.01	0.12	2.62	2.40	0.158

* feet
# degrees North
+Minimum erythemal dose by 100,000

TABLE 3: MEAN AGE AND EXPOSURE BY GENDER

	MALES(n=28)		FEMALES (n=60)		PAIRED-T
	case	control	case	control	p-value
AGE	46	47	50	55	--
UVB+	0.43	0.34	.0.51	0.56	0.31

+ Minimum erythemal dose divided by 100,000

Figure 1: Coding of Residential History and Linking with Latitude and Altitude

FILE 1

Sample Residential HX
New Haven, CT
New York, NY

SEEDIS Codes (1980 Census)

STATE	COUNTY	PLACE
09	009	1450
36	005	2505

Obtain State, County codes by Searching Place

FILE 2

SEEDIS Codes (1980 Census)

STATE	COUNTY	PLACE
09	009	1450
36	005	2505

SEEDIS Codes (1970 Census)

LATITUDE	ALTITUDE
40.72	12.0
40.72	132.0

Link Latitude and Altitude with County and State

Figure 2. Distribution of mean cumulative uvb for cases and controls

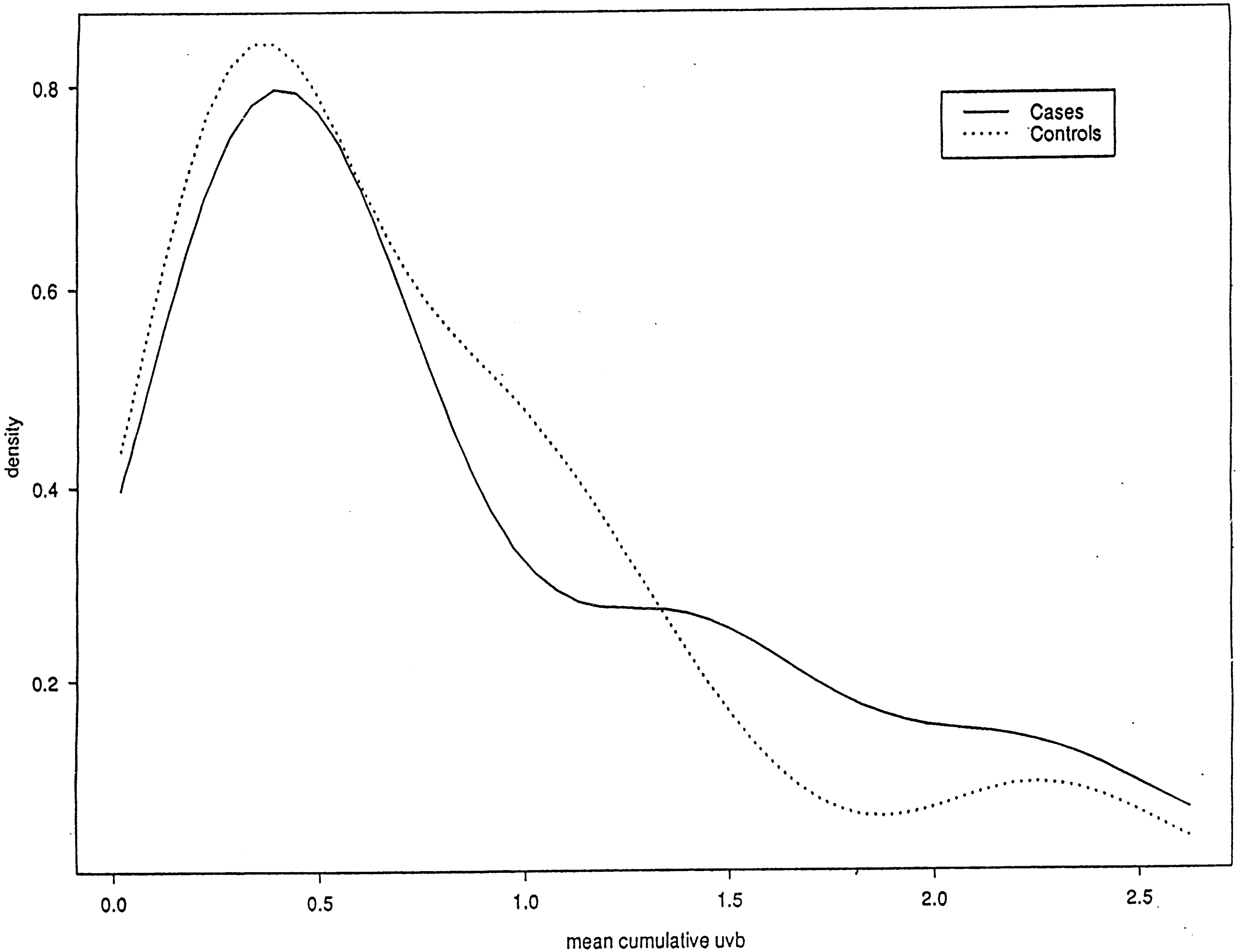
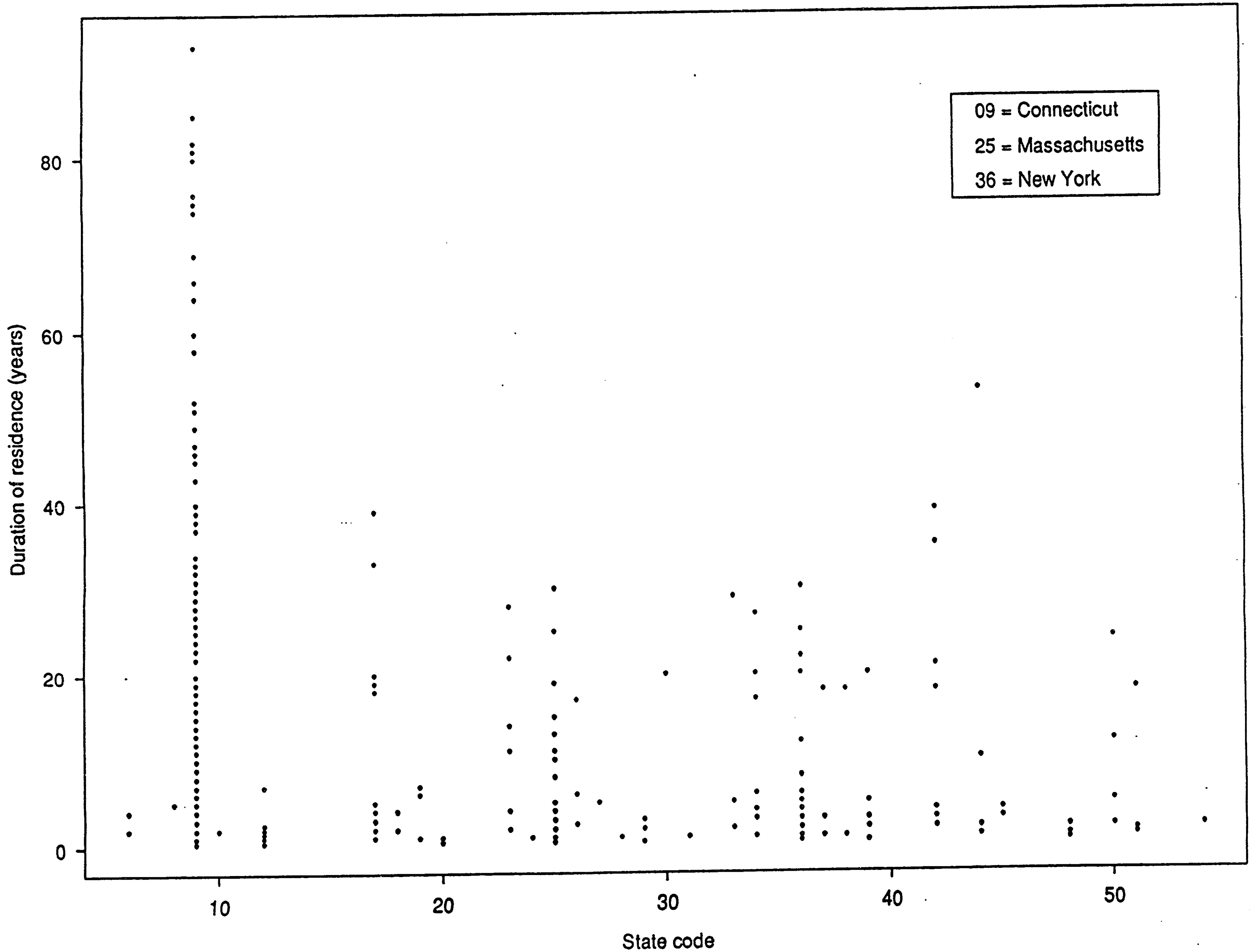


Figure 3. Duration of residence by state



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