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HLA B*57 Does Not Fully Explain Hepatitis C Clearance in HIV Controllers

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A small percentage (1-5%) of people living with HIV are able to intrinsically control their HIV infection over long periods of time without the use of antiviral therapy (ART) [1]. Two groups of “HIV controllers” have been described: (1) Elite controllers, who have HIV antibodies (anti-HIV), but plasma HIV RNA levels below the detection limits of commercially available assays, and; (2) Viremic controllers, who have measurable, but very low levels of HIV RNA (< 2000 copies/mL). HIV controllers represent “outliers” in the clinical HIV spectrum, and are considered very important for studies of host immunological and genetic factors that control viral replication, with the expectation that they will inform vaccine and drug development, or perhaps identify strategies to achieve a “functional cure [1, 2].”

Interestingly, HIV controllers may also be more likely to spontaneously clear hepatitis C virus (HCV) infection. While not observed in all studies [3, 4], most studies suggest a significantly higher rate of spontaneous HCV clearance in HIV controllers (23-39%) [5, 6] than in monoinfected groups (25%) [7] and HIV non-controllers (6.6%-10%) [1, 5]. This has led several groups to examine host genetic factors that might contribute to the control of both virus infections. For example, HLA B*57, the major histocompatibility class I allele, is highly enriched in HIV controllers and is also associated with spontaneous HCV clearance [8-10]. In contrast, HLA Cw*04 has been associated with faster progression of both HIV disease and chronic HCV infection [11, 12]. The *IL28B* CC genotype has been shown to be significantly associated with spontaneous control of HCV [13-16], conferring as much as 3.1 higher odds of clearance compared to CT and TT genotypes [17, 18].

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Whether the CC genotype of *IL28B* is also enriched in HIV controllers remains controversial. A relatively small Spanish study found that the CC genotype of *IL28B* was enriched in Caucasian HIV controllers relative to non-controllers [4], while other studies in primarily African-American cohorts have not observed this [6, 19]. Furthermore, none of the much larger genome-wide association studies have found an association between the *IL28B* (CC) genotype and HIV control, at least at the genome-wide level of significance [20-23]. In one study the *IL28B* CC genotype has been associated with higher all-cause mortality among all people living with HIV [24].

In this study, we investigated the degree to which spontaneous clearance of HCV could be explained by HLA B*57 and/or *IL28B* CC genotype in a well characterized cohort of HIV controllers.

Methods

HIV-infected adults were sampled from the Study of the Consequences of the Protease Inhibitor Era (SCOPE), a clinic-based cohort of >1600 HIV-infected individuals at the University of California, San Francisco. This observational study has a large data and specimen bank of samples with carefully characterized clinical data, including HLA typing, and includes a large sample of HIV controllers [25]. For this study we included only anti-HCV positive participants, identified using a third generation enzyme immunoassay (EIA3) (Ortho Clinical Diagnostics®). Participants were classified as ‘HIV controllers’ if they were elite controllers or viremic-controllers. ‘Non-controllers’ had at least one HIV viral load > 10,000 copies/ml as measured by bDNA (Quantiplex HIV RNA, version 3.0; Chiron Corporation) prior to or during ART.

HCV RNA was measured using discriminatory HCV transcription-mediated amplification (dTMA) assay component of the Procleix HIV-1/HCV assay, developed and manufactured by Gen-Probe (San Diego, CA) and marketed by Novartis Vaccines and Diagnostics. The 50% limit of detection of this assay is 12.1 copies/mL (95% confidence interval [CI], 11.1–13.2) of HCV RNA when using the recommended 0.5-mL plasma input volume. Participants were classified as having spontaneously cleared HCV infection if they had detectable anti-HCV but no detectable HCV RNA and had no history of HCV treatment. To evaluate whether any of the known host genetic determinants of HCV clearance were enriched in HIV controllers, we compared the genetic polymorphisms known to be associated with control of HIV and HCV in the HIV controller group to the HIV non-controllers.

Genetic testing for *IL28B* SNP polymorphism was conducted using real-time PCR amplification. The methodology of determining *IL28B* SNP polymorphism has been previously reported [26].

HLA typing was done using PCR-sequence-specific oligonucleotide probing [27]. Those positive for HBsAg or with a self-reported history of hepatitis treatment were excluded. The study was approved by the Committee for Human Subjects at the University of California San Francisco and all participants gave informed consent before undergoing any study-related procedures.

Statistical analyses

The main outcome variable of this study is spontaneous HCV clearance, as defined above. The principal exposure of interest was HIV controller status: controller vs. or non-controller. Other covariates of interest included IL28-B (CC vs. non-CC (CT or TT)), HLA B*57, and HLA Cw*04 status. Bivariate associations between groups were assessed using *chi-square* and median tests for categorical and continuous variables, respectively. A multivariable regression model was fitted to assess genetic and immunologic predictors of HCV clearance; adjusted prevalence ratios (APR) were estimated using Poisson regression models with robust standard errors. All analyses were conducted using STATA version 12.1 (StataCorp, College Station, TX).

Results

Of the 279 HIV/HCV-coinfected participants included in the analysis, 48 (17%) were HIV controllers. There was no difference in the sex, age or racial distribution between the HIV controller and non-controller groups (Table 1). HCV clearance did not appear to differ between HIV controllers and non-controllers in unadjusted analyses (35% vs. 27%, $p=0.23$).

HIV controllers were significantly enriched for HLA B*57 compared to HIV non-controllers (33% vs. 10%, $p<0.001$) (Table 2a). However, the HLA Cw*04 allele was similarly represented in controllers and non-controllers (26% vs. 17%, $p=0.19$), as was *IL28B* CC genotype (25% vs. 39% $p=0.49$). The only genetic factor significantly different by HCV clearance status, was *IL28B* CC: 59% of clearers were CC positive compared to 27% of non-clearers ($p<0.001$) (Table 2a). We next examined these associations stratified by sex (Table 2b). Male HIV controllers were significantly more likely to have HLA B*57 than male non-controllers (42% vs. 10%, $p<0.001$), but not female HIV controllers did not appear to be enriched for HLA B*57. Both females and males who cleared HCV were significantly more likely to be *IL28B* CC positive than non HCV clearers. The presence of HLA B*57 was not associated with HCV clearance among males or females.

To further evaluate whether HLA B*57 might explain the increased prevalence of HCV clearance on HIV controllers, we stratified our analysis by HLA B*57 status. Of the 24 HIV non-controllers positive for HLA B*57, 30% ($n=7$) spontaneously cleared their HCV infection compared to 27% ($n=55$) of the 207 HIV non-controllers without HLA B*57 ($p=0.79$). Similarly, among HIV controllers, 35% ($n=11$) of HIV controllers without HLA B*57 and 31% ($n=5$) of HIV controllers with HLA B*57 demonstrated HCV clearance ($p=0.83$).

The results of the multivariable analyses are shown in Table 3. After adjusting for HLA B*57, sex, age and race, two factors: HIV controller status (APR 1.78 (95% CI 1.06-3.00); $p=0.032$) and *IL28B* CC genotype (APR 2.76 (95% CI 1.85-4.11); $p<0.001$), were independently associated with spontaneous HCV clearance.

Discussion

In the current study, we confirm prior studies demonstrating higher rates of spontaneous HCV clearance in HIV controllers [5, 6, 28]. We did not observe crude differences in the proportions of HIV controllers and non-controllers who cleared HCV, however, in multivariable analyses, HIV controller status was independently predictive of HCV clearance. Results also suggest that HLA B*57, a factor known to be associated with HIV controller status, is not explanatory of this association between controller status and HCV clearance. A recent study has suggested that HLA B*57 might be associated with promoting a more robust HCV-specific T cell response [29], however, the combined findings that HLA B*57 was not associated with HCV clearance, and the equally high proportions of HIV controllers with (31%) and without (35%) HLAB*57 who cleared HCV suggests that other mechanism or host factors are at play. The HLA Cw*04 allele also failed to explain the increased proportion of HCV clearance in HIV controllers. Given the lack of association of *IL28B* genotype and HIV controller status, these results suggest that other factors associated with HIV controller status and as yet unmeasured in this group are associated with HCV clearance.

As noted, a high proportion of HIV infected controllers and non-controllers in this cohort demonstrated a spontaneous HCV clearance. The 27% rate of spontaneously cleared HCV infection among HIV non-controllers is much higher than normally seen in HIV-infected populations [30]. It is likely that most of these patients experienced their HCV infection and subsequent clearance before their HIV infection [31]. Few, if any, were infected with HCV after ART-mediated immune recovery, although HCV reinfection cannot be ruled out [32]

Females have been shown to be almost three times more likely to clear HCV infection than males [18, 33]. However, we found no differences in HCV clearance rates by sex overall, or stratified by HIV controller status. We also did not observe differences in HCV clearance by sex and *IL28B* genotype, as others have recently reported [15, 18] There is little evidence that HCV risk differed by HIV controller group; injection drug use was reported equally. One study has suggested an association between sexually acquired HCV and HCV clearance, [34], but this association has not been seen prospectively, nor has this been observed in HIV+ men who have sex with men, a group well-represented within the SCOPE cohort [35]. There is no clear explanation for why males were equally likely to clear their HCV infection as women in this cohort.

There are some limitations to this study. We excluded those with a history of prior HCV treatment based on self-report. It is possible that there was underreporting of HCV treatment history; Medical record review was undertaken at our institution and failed to identify prior HCV treatment among any patients reporting no history of treatment. However, if misclassification of treatment did occur, the proportion of those who demonstrated spontaneous clearance would be smaller and the role of the genetic markers in these patients overestimated.

Understanding the shared and separate mechanisms that contribute to the control of HIV and HCV may shed light on future directions for treatment, prevention and vaccine development

for both viruses. Because HIV controllers are more likely to clear HCV infection than HIV non-controllers, this unique group may provide new insights into the mechanisms underlying viral control. Our study suggests that HLAB*57 a factor highly associated with HIV controller status does not contribute to HCV clearance, and that *IL28B* CC genotype does. Identifying other factors that contribute to enhanced viral control may support the development of novel vaccine and treatment strategies for HIV and HCV, ultimately reducing the morbidity and mortality caused by these viruses.

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References

1. Deeks SG, Walker BD. Human immunodeficiency virus controllers: mechanisms of durable virus control in the absence of antiretroviral therapy. *Immunity*. 2007; 27:406–416. [PubMed: 17892849]
2. Walker BD, Burton DR. Toward an AIDS Vaccine. *Science*. 2008; 320:760–764. [PubMed: 18467582]
3. Ruiz-Mateos E, Machmach K, Romero-Sanchez M, Ferrando-Martinez S, Viciano P, Del Val M, et al. Hepatitis C virus replication in Caucasian HIV controllers. *J Viral Hepat*. 2011; 18:e350–357. [PubMed: 21692947]
4. Machmach K, Abad-Molina C, Romero-Sanchez MC, Abad MA, Ferrando-Martinez S, Genebat M. IL28B Single-Nucleotide Polymorphism rs12979860 Is Associated With Spontaneous HIV Control in White Subjects. *J Infect Dis*. 2012
5. Sadaji M, Shakeri N, Talwani R, Redfield R. Hepatitis C infection in HIV-1 natural viral suppressors. *AIDS*. 2010; 24:1689–1695. [PubMed: 20467290]
6. Salgado M, Kirk G, Cox A, Rutebemberwa A, Higgins Y, Astemborski J, et al. Protective interleukin-28B genotype affects hepatitis C virus clearance, but does not contribute to HIV-1 control in a cohort of African-American elite controllers/suppressors. *AIDS*. 2011; 25:385–387. [PubMed: 21099664]
7. Micallef JM, Kaldor JM, Dore GJ. Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. *J Viral Hepat*. 2006; 13:34–41. [PubMed: 16364080]
8. Kloverpris HN, Stryhn A, Harndahl M, van der Stok M, Payne RP, Matthews PC, et al. HLA-B*57 Micropolymorphism shapes HLA allele-specific epitope immunogenicity, selection pressure, and HIV immune control. *J Virol*. 2012; 86:919–929. [PubMed: 22090105]
9. Migueles SA, Sabbaghian MS, Shupert WL, Bettinotti MP, Marincola FM, Martino L, et al. HLA B*5701 is highly associated with restriction of virus replication in a subgroup of HIV-infected long term nonprogressors. *Proc Natl Acad Sci U S A*. 2000; 97:2709–2714. [PubMed: 10694578]
10. Miura T, Brockman MA, Schneidewind A, Lobritz M, Pereyra F, Rathod A, et al. HLA-B57/B*5801 human immunodeficiency virus type 1 elite controllers select for rare gag variants associated with reduced viral replication capacity and strong cytotoxic T-lymphocyte [corrected] recognition. *J Virol*. 2009; 83:2743–2755. [PubMed: 19116253]
11. Carrington M, Nelson GW, Martin MP, Kissner T, Vlahov D, Goedert JJ, et al. HLA and HIV-1: heterozygote advantage and B*35-Cw*04 disadvantage. *Science*. 1999; 283:1748–1752. [PubMed: 10073943]
12. Thio CL, Gao X, Goedert JJ, Vlahov D, Nelson KE, Hilgartner MW, et al. HLA-Cw*04 and hepatitis C virus persistence. *J Virol*. 2002; 76:4792–4797. [PubMed: 11967296]
13. Balagopal A, Thomas DL, Thio CL. IL28B and the control of hepatitis C virus infection. *Gastroenterology*. 2010; 139:1865–1876. [PubMed: 20950615]

14. Osburn WO, Fisher BE, Dowd KA, Urban G, Liu L, Ray SC, et al. Spontaneous control of primary hepatitis C virus infection and immunity against persistent reinfection. *Gastroenterology*. 2010; 138:315–324. [PubMed: 19782080]
15. van den Berg CH, Grady BP, Schinkel J, van de Laar T, Molenkamp R, van Houdt R, et al. Female Sex and IL28B, a Synergism for Spontaneous Viral Clearance in Hepatitis C Virus (HCV) Seroconverters from a Community-Based Cohort. *PLoS One*. 2011; 6:e27555. [PubMed: 22110669]
16. Thomas DL, Thio CL, Martin MP, Qi Y, Ge D, O'Huigin C, et al. Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. *Nature*. 2009; 461:798–801. [PubMed: 19759533]
17. Rauch A, Kutalik Z, Descombes P, Cai T, Di Iulio J, Mueller T, et al. Genetic variation in IL28B is associated with chronic hepatitis C and treatment failure: a genome-wide association study. *Gastroenterology*. 2010; 138:1338–1345. 1345 e1331–1337. [PubMed: 20060832]
18. Grebely J, Page K, Sacks-Davis R, Schim van der Loeff M, Rice TM, Bruneau J. The effects of female sex, viral genotype, and IL28B genotype on spontaneous clearance of acute hepatitis C Virus infection. *Hepatology*. 2013
19. Sajadi MM, Shakeri N, Talwani R, Howell CD, Pakyz R, Redfield RR, et al. IL28B genotype does not correlate with HIV control in African Americans. *Clin Transl Sci*. 2011; 4:282–284. [PubMed: 21884517]
20. Pereyra F, Jia X, McLaren PJ, Telenti A, de Bakker PI, Walker BD, et al. The major genetic determinants of HIV-1 control affect HLA class I peptide presentation. *Science*. 2010; 330:1551–1557. [PubMed: 21051598]
21. Fellay J, Shianna KV, Ge D, Colombo S, Ledergerber B, Weale M, et al. A whole-genome association study of major determinants for host control of HIV-1. *Science*. 2007; 317:944–947. [PubMed: 17641165]
22. Dalmasso C, Carpentier W, Meyer L, Rouzioux C, Goujard C, Chaix ML, et al. Distinct genetic loci control plasma HIV-RNA and cellular HIV-DNA levels in HIV-1 infection: the ANRS Genome Wide Association 01 study. *PLoS One*. 2008; 3:e3907. [PubMed: 19107206]
23. Catano G, Kulkarni H, He W, Marconi VC, Agan BK, Landrum M, et al. HIV-1 disease-influencing effects associated with ZNRD1, HCP5 and HLA-C alleles are attributable mainly to either HLA-A10 or HLA-B*57 alleles. *PLoS One*. 2008; 3:e3636. [PubMed: 18982067]
24. Parczewski M, Bander D, Leszczyszyn-Pynka M, Urbanska A, Socha L, Boron-Kaczmarek A. IL28B CC Genotype Is Associated with Higher All-Cause Mortality in Antiretroviral-Treated HIV-Infected Patients. *AIDS Res Hum Retroviruses*. 2012; 28:1640–1646. [PubMed: 22545770]
25. Hunt P, Hatano H, Sinclair E, Lee T, Busch M, Martin J, et al. HIV-specific CD4+ T cells may contribute to viral persistence in HIV controllers. *Clin Infect Dis*. 2011; 52:681–687. [PubMed: 21245154]
26. Gill RM, Lee TH, Utter GH, Reed WF, Wen L, Chafets D, et al. The TNF (-308A) polymorphism is associated with microchimerism in transfused trauma patients. *Blood*. 2008; 111:3880–3883. [PubMed: 18199828]
27. Martin MP, Qi Y, Gao X, Yamada E, Martin JN, Pereyra F, et al. Innate partnership of HLA-B and KIR3DL1 subtypes against HIV-1. *Nat Genet*. 2007; 39:733–740. [PubMed: 17496894]
28. Micallef JM, Macdonald V, Jauncey M, Amin J, Rawlinson W, van Beek I, et al. High incidence of hepatitis C virus reinfection within a cohort of injecting drug users. *J Viral Hepat*. 2007; 14:413–418. [PubMed: 17501762]
29. Kim AY, Schulze zur Wiesch J, Kuntzen T, Timm J, Kaufmann DE, Duncan JE, et al. Impaired hepatitis C virus-specific T cell responses and recurrent hepatitis C virus in HIV coinfection. *PLoS Med*. 2006; 3:e492. [PubMed: 17194190]
30. Matthews G, Dore G. HIV and hepatitis C coinfection. *J Gastroenterol Hepatol*. 2008; 23:1000–1008. [PubMed: 18707597]
31. Hahn JA, Page-Shafer K, Lum PJ, Ochoa K, Moss AR. Hepatitis C virus infection and needle exchange use among young injection drug users in San Francisco. *Hepatology*. 2001; 34:180–187. [PubMed: 11431749]

32. Cotte L, Chevallier Queyron P, Schlienger I, Trabaud MA, Brochier C, Andre P, et al. Sexually transmitted HCV infection and reinfection in HIV-infected homosexual men. *Gastroenterol Clin Biol*. 2009; 33:977–980. [PubMed: 19765930]
33. Page K, Hahn JA, Evans J, Shiboski S, Lum P, Delwart E, et al. Acute hepatitis C virus infection in young adult injection drug users: a prospective study of incident infection, resolution, and reinfection. *J Infect Dis*. 2009; 200:1216–1226. [PubMed: 19764883]
34. Quinn PG, Jamal MM, Carey JD, Arora S, Harris T, Johnston DE, et al. A case-control study of the factors associated with spontaneous resolution of hepatitis C viremia. *Am J Gastroenterol*. 1999; 94:668–673. [PubMed: 10086649]
35. Shores NJ, Maida I, Soriano V, Nunez M. Sexual transmission is associated with spontaneous HCV clearance in HIV-infected patients. *J Hepatol*. 2008; 49:323–328. [PubMed: 18486266]

Table 1

Demographics by HIV controller status				
		Non-controllers N (col %) N=231	HIV controllers [†] N (col %) N=48	p-value
Gender				0.85
	Male	156 (68)	31 (65)	
	Female	66 (29)	14 (29)	
Age	Median (IQR)	40 (36-46)	41 (37-48)	0.69
Race/Ethnicity				0.57
	Caucasian	97 (42)	18 (38)	
	Non-Caucasian	134 (58)	30 (62)	
HIV risk:				0.16
	Injection drug use	109 (47)	28 (58)	
	No history of Injection drug use	122 (53)	20 (42)	
HCV clearance				0.23
	Yes	62 (27)	17 (35)	
	No	169 (73)	31 (65)	
Demographics by HCV clearance status				
		Did not clear N (col %) N=200	Cleared N (col %) N=79	
Gender				0.14
	Male	128 (64)	59 (75)	
	Female	62 (31)	18 (23)	
Age	Median (IQR)	40 (36-46)	40 (35-47)	0.78
Race/Ethnicity				0.08
	Caucasian	76 (38)	39 (49)	
	Non-Caucasian	124 (62)	40 (51)	
HIV risk:				0.20
	Injection drug use	103 (52)	34 (43)	
	No history of Injection drug use	97 (49)	45 (57)	
HIV controller status				0.23
	Non-controllers	169 (85)	62 (79)	
	HIV controllers	31 (16)	17 (22)	

Note:

[†] Elite controllers + HIV viremic controllers (<2000 copies/ML without ART for at least 12 months). Proportions may not add to 100% due to rounding and missing data.

Table 2a
Overall (percent)

Overall Polymorphisms column percent			
Genetic polymorphisms by HIV controller status			
	Non-controllers N (col %) N=231	HIV controllers [†] N (col %) N=48	p-value
HLA B*57 status			<0.001
No	207 (90)	32 (67)	
Yes	24 (10)	16 (33)	
HLA Cw*04			0.19
No	172 (74)	40 (83)	
Yes	59 (26)	8 (17)	
<i>IL28B</i> genotype [§]			0.49
Non-CC	137 (59)	24 (50)	
CC	89 (39)	12 (25)	
Genetic polymorphisms by HCV clearance status			
	Did not clear N (col %) N=200	Cleared N (col %) N=79	p-value
HLA B*57 status			0.53
No	173 (86)	66 (84)	
Yes	27 (14)	13 (16)	
HLA Cw*04			0.12
No	147 (73)	65 (82)	
Yes	53 (27)	14 (17)	
<i>IL28B</i> genotype [§]			<0.001
Non-CC	133 (67)	28 (35)	
CC	54 (27)	47 (59)	

Note:

[†] Elite controllers + HIV viremic controllers (<2000 copies/ML without ART for at least 12 months). Proportions may not add to 100% due to rounding and missing data.

[§] *IL28B* genotype missing for 17 participants.

Table 2b

Stratified by gender:

Females:			
Genetic polymorphisms by HIV controller status			
	HIV Non-controllers N (col %) N=66	HIV controllers [†] N (col %) N=14	p-value
HLA B*57	8 (12)	3 (21)	0.36
HLA Cw*04	25 (38)	4 (29)	0.51
<i>IL28B</i> (CC)	25 (38)	3 (21)	0.932
Genetic polymorphisms by HCV clearance status			
	Did not clear N (col %) N=62	Cleared N (col %) N=18	p-value
HLA B*57	8 (13)	3 (17)	0.68
HLA Cw*04	27 (44)	2 (11)	0.012
<i>IL28B</i> (CC)	17 (27)	11 (61)	0.002

Male:			
Genetic polymorphisms by HIV controller status			
	HIV Non-controllers N (col %) N=156	HIV controllers [†] N (col %) N=31	p-value
HLA B*57	16 (10)	13 (42)	<0.001
HLA Cw*04	33 (21)	3 (10)	0.14
<i>IL28B</i> (CC)	62 (40)	8 (26)	0.346
Genetic polymorphisms by HCV clearance status			
	Did not clear N (col %) N=129	Cleared N (col %) N=58	p-value
HLA B*57	19 (15)	10 (17)	0.71
HLA Cw*04	25 (19)	11 (19)	0.89
<i>IL28B</i> (CC)	35 (27)	35 (60)	<0.001

Note:

[†] Elite controllers + HIV viremic controllers (<2000 copies/ML without ART for at least 12 months). Proportions may not add to 100% due to rounding and missing data.

[§] *IL28B* genotype missing for 17 participants.

Table 3
Multivariable Analysis on Spontaneous HCV Clearance

	Adjusted Prevalence Ratio [*]	95% CI	P-value
HIV elite/viremic controller status			
Non-controller	ref	-	-
Controller	1.78	1.06-3.00	0.030
HLA B [*] 57			
No	ref	-	-
Yes	1.36	0.71-2.60	0.349
Gender			
Female	ref	-	-
Male	1.57	0.98-2.51	0.062
IL28B			
Non-CC	ref	-	-
CC	2.76	1.85-4.11	<0.001
HIV elite/viremic controller with HLA B [*] 57			
No	ref	-	-
Yes	0.52	0.18-1.45	0.210

* models adjusted for age and race/ethnicity