

	RPL	Control	Total	P-value
	(N=4656)	(N=36019)	(N=40675)	
Age				
Mean (SD)	35.1 (4.86)	31.9 (5.46)	32.2 (5.49)	<0.001
Median [Min, Max]	35.4 [17.1, 44.0]	32.4 [15.0, 44.0]	32.8 [15.0, 44.0]	
Race				
American Indian or Alaska Native	16 (0.3%)	118 (0.3%)	134 (0.3%)	<0.001
Asian	1600 (34.4%)	11198 (31.1%)	12798 (31.5%)	
Black or African American	143 (3.1%)	1039 (2.9%)	1182 (2.9%)	
Native Hawaiian or Other Pacific Islander	75 (1.6%)	713 (2.0%)	788 (1.9%)	
No matching concept	982 (21.1%)	8779 (24.4%)	9761 (24.0%)	
White	1840 (39.5%)	14172 (39.3%)	16012 (39.4%)	
Ethnicity				
Hispanic or Latino	763 (16.4%)	10552 (29.3%)	11315 (27.8%)	<0.001
No matching concept	243 (5.2%)	757 (2.1%)	1000 (2.5%)	
Not Hispanic or Latino	3650 (78.4%)	24710 (68.6%)	28360 (69.7%)	
Number of visits (in study)				
Mean (SD)	44.3 (46.3)	23.6 (29.6)	26.0 (32.6)	<0.001
Median [Min, Max]	31.0 [0, 544]	14.0 [0, 1030]	16.0 [0, 1030]	
Years in EHR (in study)				
Mean (SD)	4.97 (4.65)	4.55 (4.84)	4.59 (4.82)	<0.001
Median [Min, Max]	3.14 [0, 23.4]	1.67 [0, 23.6]	1.83 [0, 23.6]	
Number of diagnoses (in study)				
Mean (SD)	15.8 (15.7)	12.2 (11.1)	12.6 (11.8)	<0.001
Median [Min, Max]	11.0 [1.00, 202]	9.00 [1.00, 216]	9.00 [1.00, 216]	

Supplementary Table 1: Patient demographics and healthcare utilization at Stanford. *P*-values were computed using chi-squared tests for categorical variables and t tests for numeric variables.

	RPL	Control	Total	P-value
	(N=1401)	(N=11012)	(N=12413)	
Age				
Mean (SD)	31.5 (3.24)	30.2 (4.06)	30.3 (4.00)	<0.001
Median [Min, Max]	32.4 [16.6, 35.0]	31.4 [15.1, 35.0]	31.5 [15.1, 35.0]	
Race				
American Indian or Alaska Native	17 (1.2%)	64 (0.6%)	81 (0.7%)	<0.001
Asian	259 (18.5%)	2386 (21.7%)	2645 (21.3%)	
Black or African American	97 (6.9%)	699 (6.3%)	796 (6.4%)	
Native Hawaiian or Other Pacific Islander	7 (0.5%)	82 (0.7%)	89 (0.7%)	
Other Race	243 (17.3%)	2414 (21.9%)	2657 (21.4%)	
Unknown	144 (10.3%)	679 (6.2%)	823 (6.6%)	
White	634 (45.3%)	4688 (42.6%)	5322 (42.9%)	
Ethnicity				
Hispanic or Latino	195 (13.9%)	2066 (18.8%)	2261 (18.2%)	<0.001
Not Hispanic or Latino	1073 (76.6%)	8200 (74.5%)	9273 (74.7%)	
Unknown	133 (9.5%)	746 (6.8%)	879 (7.1%)	
Number of visits (in study)				
Mean (SD)	58.2 (80.2)	47.4 (48.0)	48.6 (52.8)	<0.001
Median [Min, Max]	36.0 [1.00, 1700]	37.0 [1.00, 1230]	37.0 [1.00, 1700]	
Years in EHR (in study)				
Mean (SD)	5.16 (6.62)	4.59 (5.98)	4.65 (6.05)	0.00229
Median [Min, Max]	2.37 [0.225, 44.4]	1.69 [0.132, 38.9]	1.77 [0.132, 44.4]	
Number of diagnoses (in study)				
Mean (SD)	13.6 (16.0)	14.1 (11.3)	14.0 (11.9)	0.303
Median [Min, Max]	8.00 [1.00, 202]	12.0 [1.00, 186]	12.0 [1.00, 202]	

Supplementary Table 2: Patient demographics and healthcare utilization for the <35 stratum in the UCSF age-stratified analysis. P-values were computed using chi-squared tests for categorical variables and t tests for continuous variables.

	RPL (N=2439)	Control (N=6247)	Total (N=8686)	P-value
Age				
Mean (SD)	38.9 (2.41)	37.9 (2.15)	38.2 (2.28)	<0.001
Median [Min, Max]	38.9 [35.0, 44.0]	37.4 [35.0, 44.0]	37.7 [35.0, 44.0]	
Race				
American Indian or Alaska Native	16 (0.7%)	22 (0.4%)	38 (0.4%)	<0.001
Asian	566 (23.2%)	1486 (23.8%)	2052 (23.6%)	
Black or African American	83 (3.4%)	179 (2.9%)	262 (3.0%)	
Native Hawaiian or Other Pacific Islander	19 (0.8%)	63 (1.0%)	82 (0.9%)	
Other Race	327 (13.4%)	987 (15.8%)	1314 (15.1%)	
Unknown	222 (9.1%)	364 (5.8%)	586 (6.7%)	
White	1206 (49.4%)	3146 (50.4%)	4352 (50.1%)	
Ethnicity				
Hispanic or Latino	255 (10.5%)	803 (12.9%)	1058 (12.2%)	<0.001
Not Hispanic or Latino	1949 (79.9%)	5066 (81.1%)	7015 (80.8%)	
Unknown	235 (9.6%)	378 (6.1%)	613 (7.1%)	
Number of visits (in study)				
Mean (SD)	72.6 (79.0)	63.2 (57.6)	65.9 (64.5)	<0.001
Median [Min, Max]	48.0 [1.00, 1110]	50.0 [1.00, 635]	49.0 [1.00, 1110]	
Years in EHR (in study)				
Mean (SD)	6.47 (6.32)	5.37 (5.70)	5.68 (5.90)	<0.001
Median [Min, Max]	4.15 [0.137, 37.7]	2.74 [0.712, 41.4]	3.13 [0.137, 41.4]	
Number of diagnoses (in study)				
Mean (SD)	13.7 (14.8)	16.9 (12.0)	16.0 (12.9)	<0.001
Median [Min, Max]	9.00 [1.00, 162]	14.0 [1.00, 126]	13.0 [1.00, 162]	

Supplementary Table 3: Patient demographics and healthcare utilization for the 35+ stratum in the UCSF age-stratified analysis. P-values were computed using chi-squared tests for categorical variables and t tests for continuous variables.

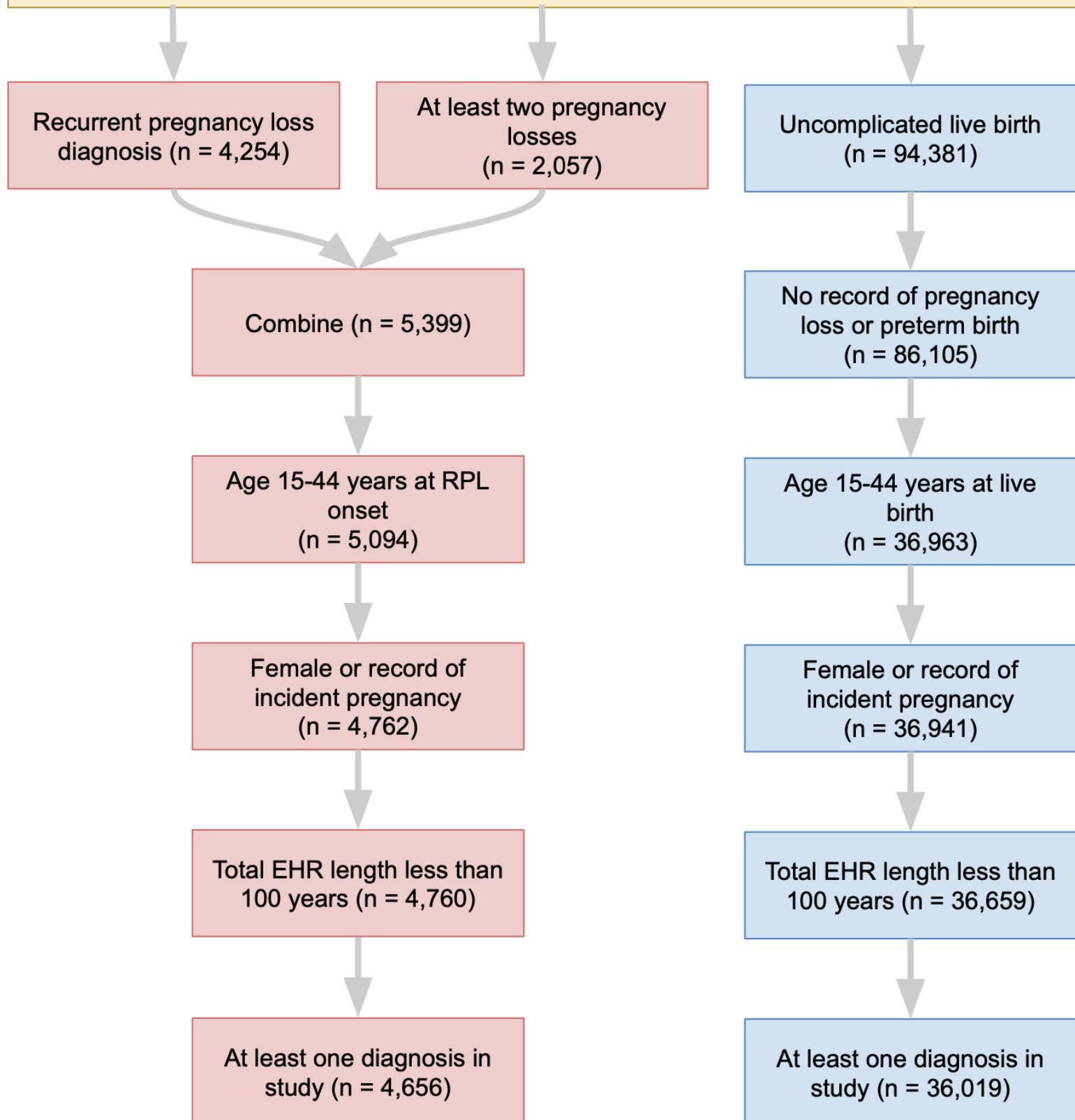
	RPL (N=2194)	Control (N=25343)	Total (N=27537)	P-value
Age				
Mean (SD)	31.0 (3.38)	29.4 (4.35)	29.5 (4.30)	<0.001
Median [Min, Max]	31.8 [17.1, 35.0]	30.5 [15.0, 35.0]	30.6 [15.0, 35.0]	
Race				
American Indian or Alaska Native	7 (0.3%)	91 (0.4%)	98 (0.4%)	<0.001
Asian	742 (33.8%)	7260 (28.6%)	8002 (29.1%)	
Black or African American	83 (3.8%)	826 (3.3%)	909 (3.3%)	
Native Hawaiian or Other Pacific Islander	37 (1.7%)	535 (2.1%)	572 (2.1%)	
No matching concept	503 (22.9%)	6894 (27.2%)	7397 (26.9%)	
White	822 (37.5%)	9737 (38.4%)	10559 (38.3%)	
Ethnicity				
Hispanic or Latino	439 (20.0%)	8364 (33.0%)	8803 (32.0%)	<0.001
No matching concept	106 (4.8%)	524 (2.1%)	630 (2.3%)	
Not Hispanic or Latino	1649 (75.2%)	16455 (64.9%)	18104 (65.7%)	
Number of visits (in study)				
Mean (SD)	39.1 (40.9)	21.9 (25.3)	23.2 (27.3)	<0.001
Median [Min, Max]	28.0 [0, 474]	14.0 [0, 466]	14.0 [0, 474]	
Years in EHR (in study)				
Mean (SD)	4.51 (4.55)	4.33 (4.75)	4.35 (4.73)	0.0746
Median [Min, Max]	2.51 [0, 23.4]	1.63 [0, 23.6]	1.64 [0, 23.6]	
Number of diagnoses (in study)				
Mean (SD)	15.6 (15.7)	11.8 (10.7)	12.1 (11.2)	<0.001
Median [Min, Max]	11.0 [1.00, 202]	9.00 [1.00, 188]	9.00 [1.00, 202]	

Supplementary Table 4: Patient demographics and healthcare utilization for the <35 stratum in the Stanford age-stratified analysis. P-values were computed using chi-squared tests for categorical variables and t tests for continuous variables.

	RPL (N=2462)	Control (N=10676)	Total (N=13138)	P-value
Age				
Mean (SD)	38.7 (2.44)	37.9 (2.15)	38.0 (2.24)	<0.001
Median [Min, Max]	38.5 [35.0, 44.0]	37.4 [35.0, 44.0]	37.6 [35.0, 44.0]	
Race				
American Indian or Alaska Native	9 (0.4%)	27 (0.3%)	36 (0.3%)	0.114
Asian	858 (34.8%)	3938 (36.9%)	4796 (36.5%)	
Black or African American	60 (2.4%)	213 (2.0%)	273 (2.1%)	
Native Hawaiian or Other Pacific Islander	38 (1.5%)	178 (1.7%)	216 (1.6%)	
No matching concept	479 (19.5%)	1885 (17.7%)	2364 (18.0%)	
White	1018 (41.3%)	4435 (41.5%)	5453 (41.5%)	
Ethnicity				
Hispanic or Latino	324 (13.2%)	2188 (20.5%)	2512 (19.1%)	<0.001
No matching concept	137 (5.6%)	233 (2.2%)	370 (2.8%)	
Not Hispanic or Latino	2001 (81.3%)	8255 (77.3%)	10256 (78.1%)	
Number of visits (in study)				
Mean (SD)	48.9 (50.1)	27.9 (37.5)	31.8 (41.0)	<0.001
Median [Min, Max]	34.0 [0, 544]	16.0 [0, 1030]	18.0 [0, 1030]	
Years in EHR (in study)				
Mean (SD)	5.37 (4.70)	5.06 (5.04)	5.12 (4.98)	0.00311
Median [Min, Max]	3.85 [0, 23.4]	2.32 [0, 23.5]	2.60 [0, 23.5]	
Number of diagnoses (in study)				
Mean (SD)	16.1 (15.7)	13.2 (12.0)	13.7 (12.8)	<0.001
Median [Min, Max]	11.0 [1.00, 169]	10.0 [1.00, 216]	10.0 [1.00, 216]	

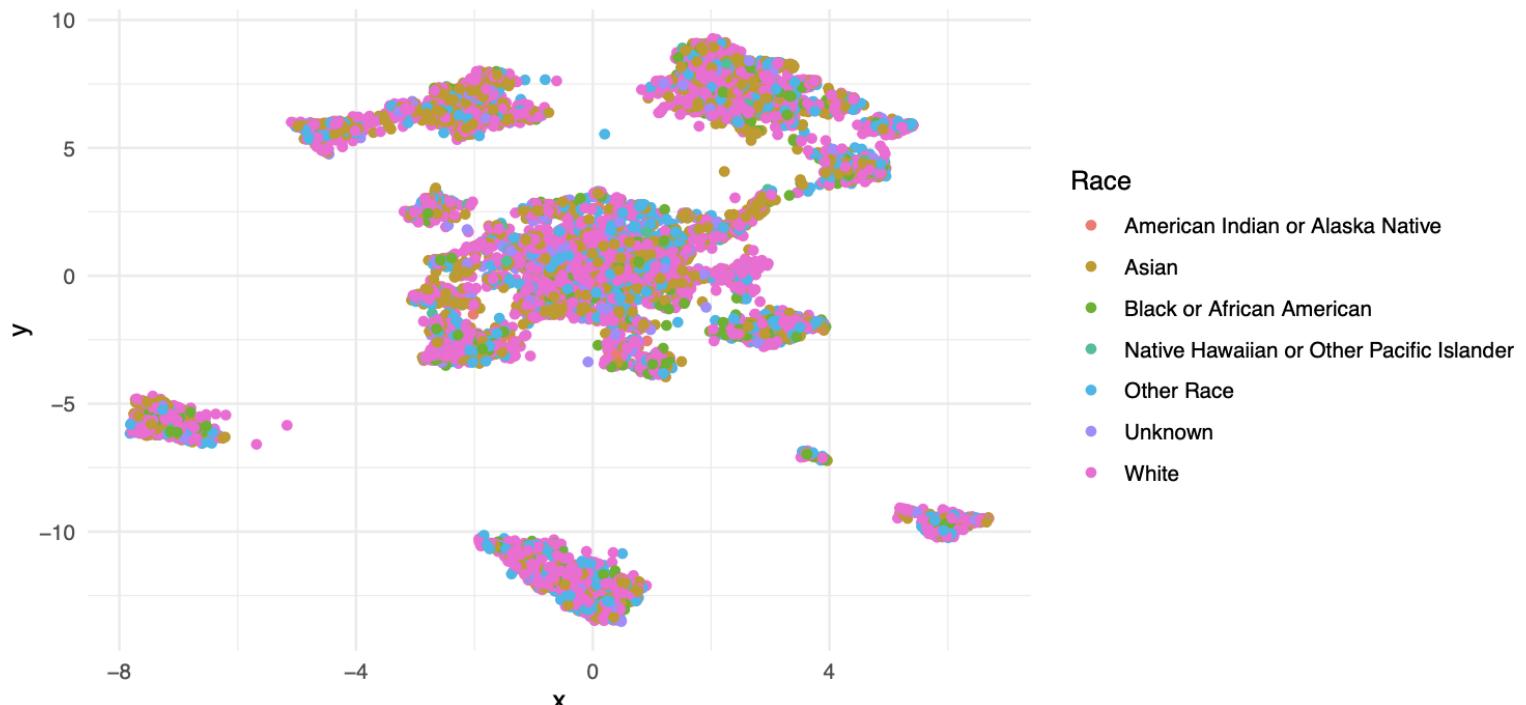
Supplementary Table 5: Patient demographics and healthcare utilization for the 35+ stratum in the Stanford age-stratified analysis. *P*-values were computed using chi-squared tests for categorical variables and t tests for continuous variables.

Stanford OMOP EHR database (n = 3,604,034)

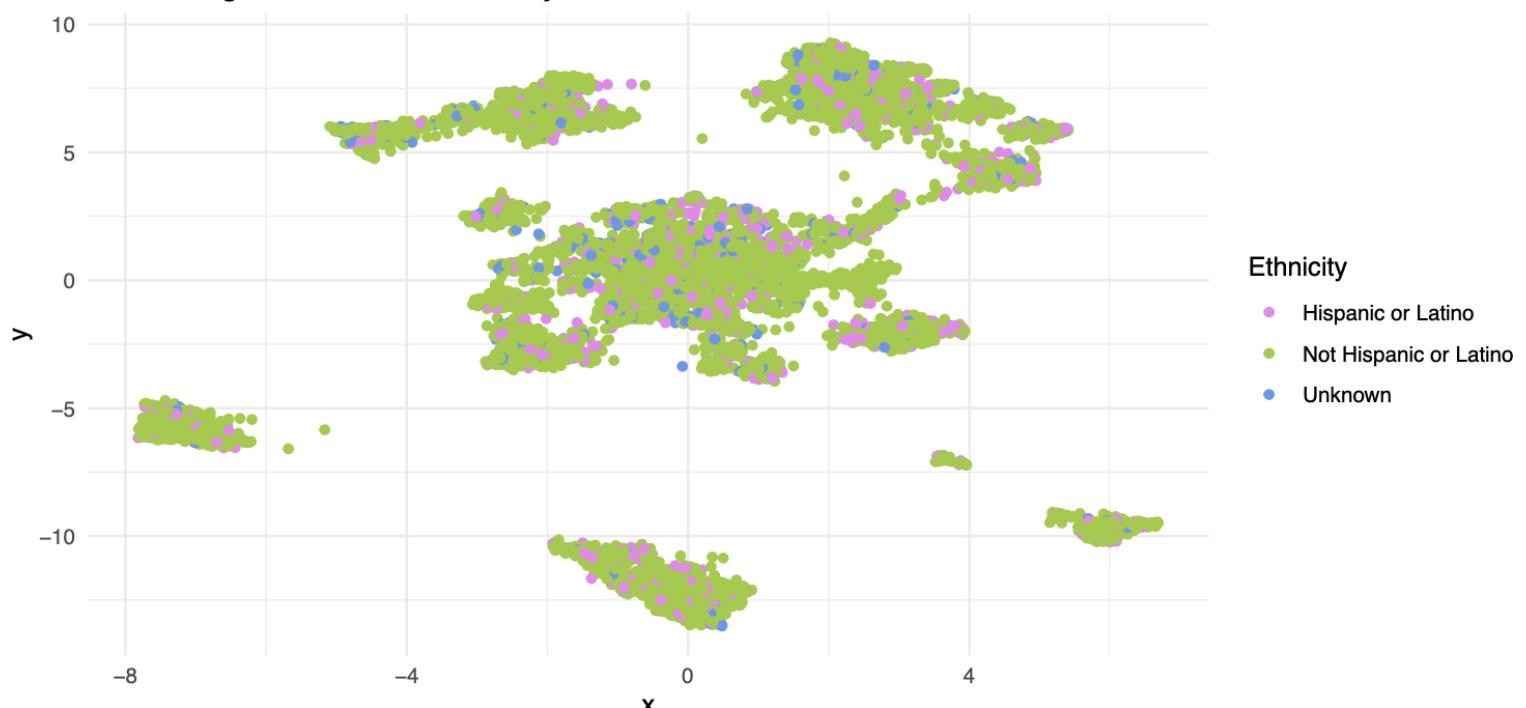


Supplementary Figure 1: Patient selection at Stanford. In total, 4,656 RPL patients were selected (red) and 36,019 Control patients were selected (blue).

UCSF diagnosis UMAP – race

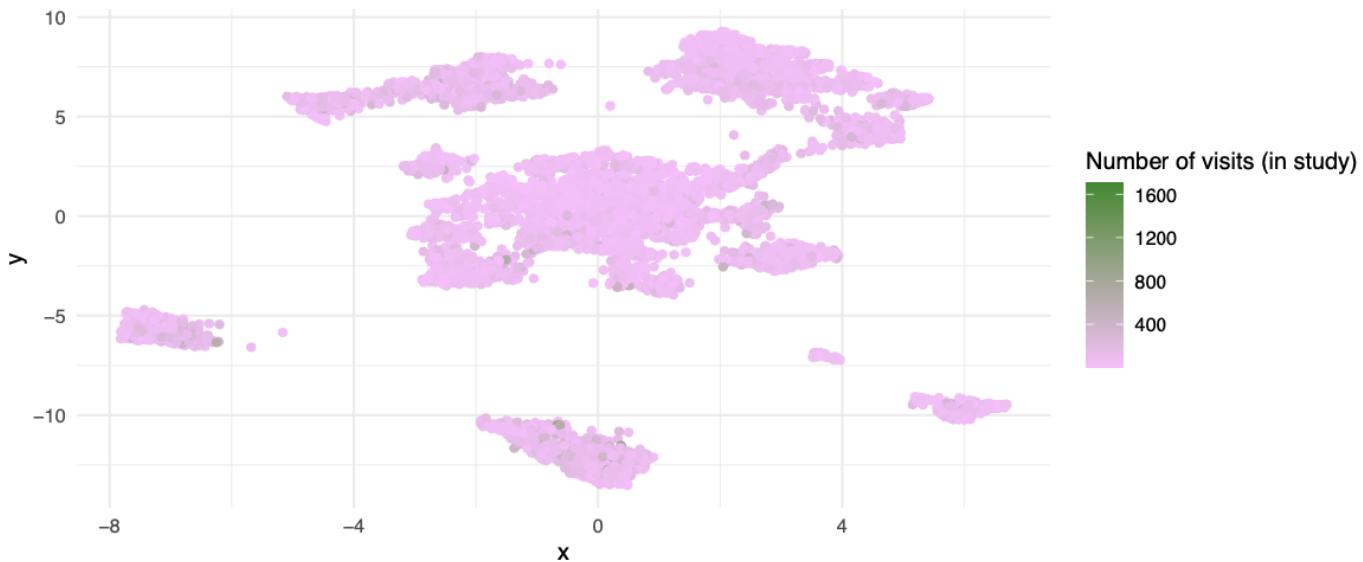


UCSF diagnosis UMAP – ethnicity

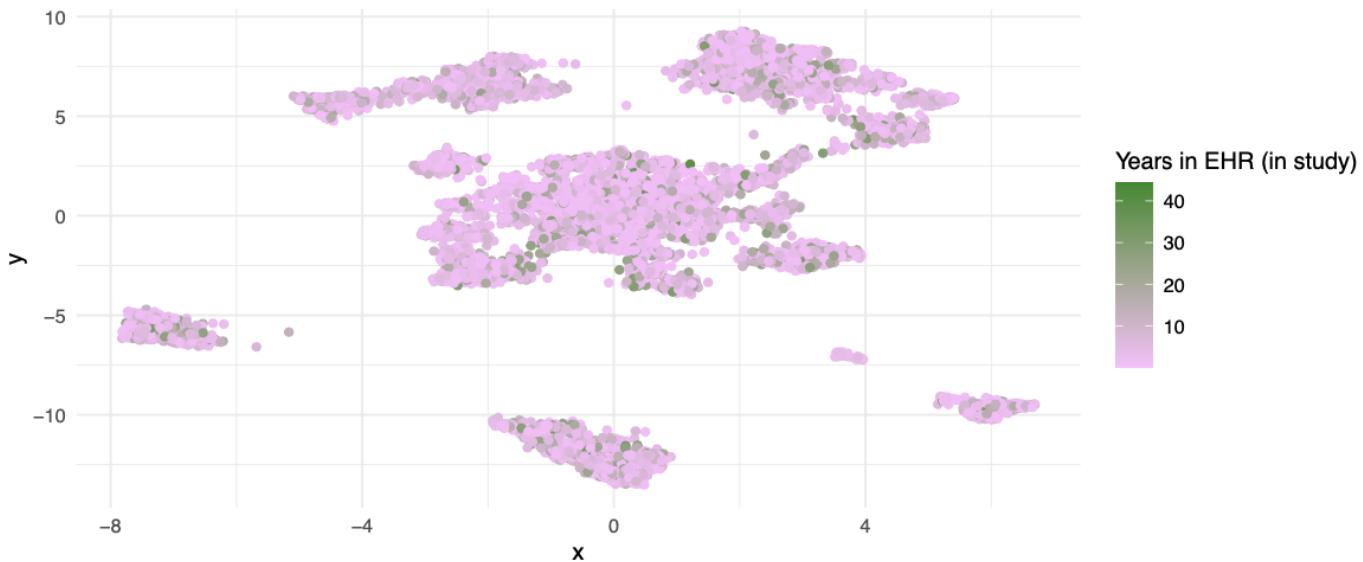


Supplementary Figure 2: UCSF diagnosis UMAPs colored by: (a) race and (b) ethnicity.

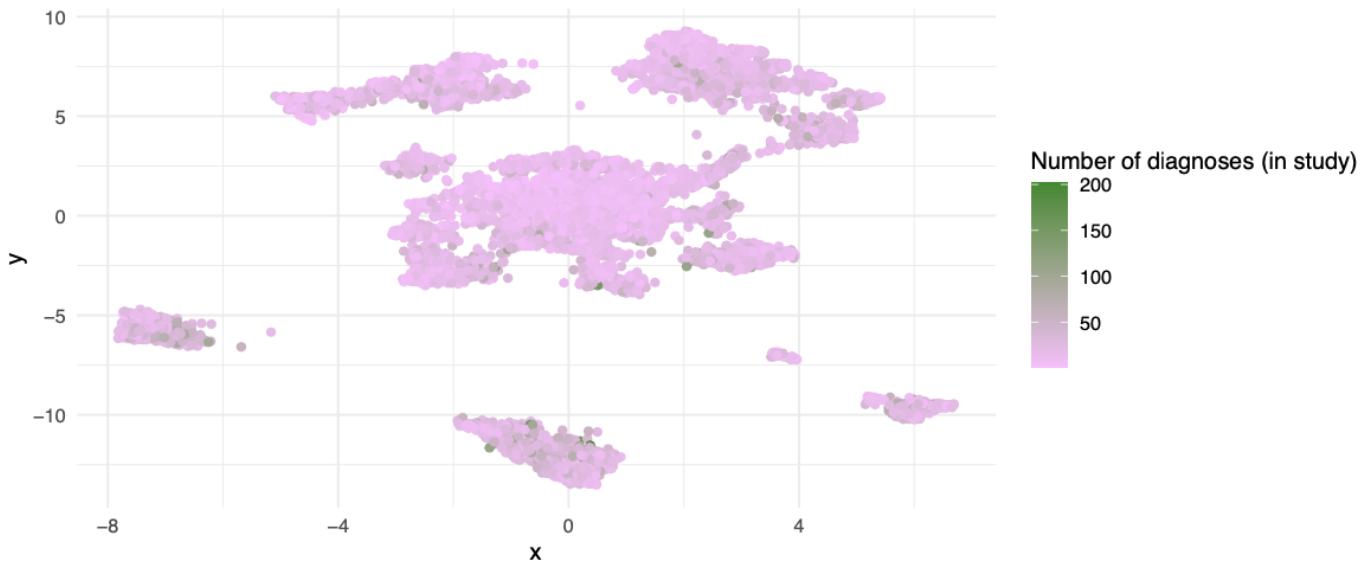
UCSF diagnosis UMAP – number of visits



UCSF diagnosis UMAP – years in EHR

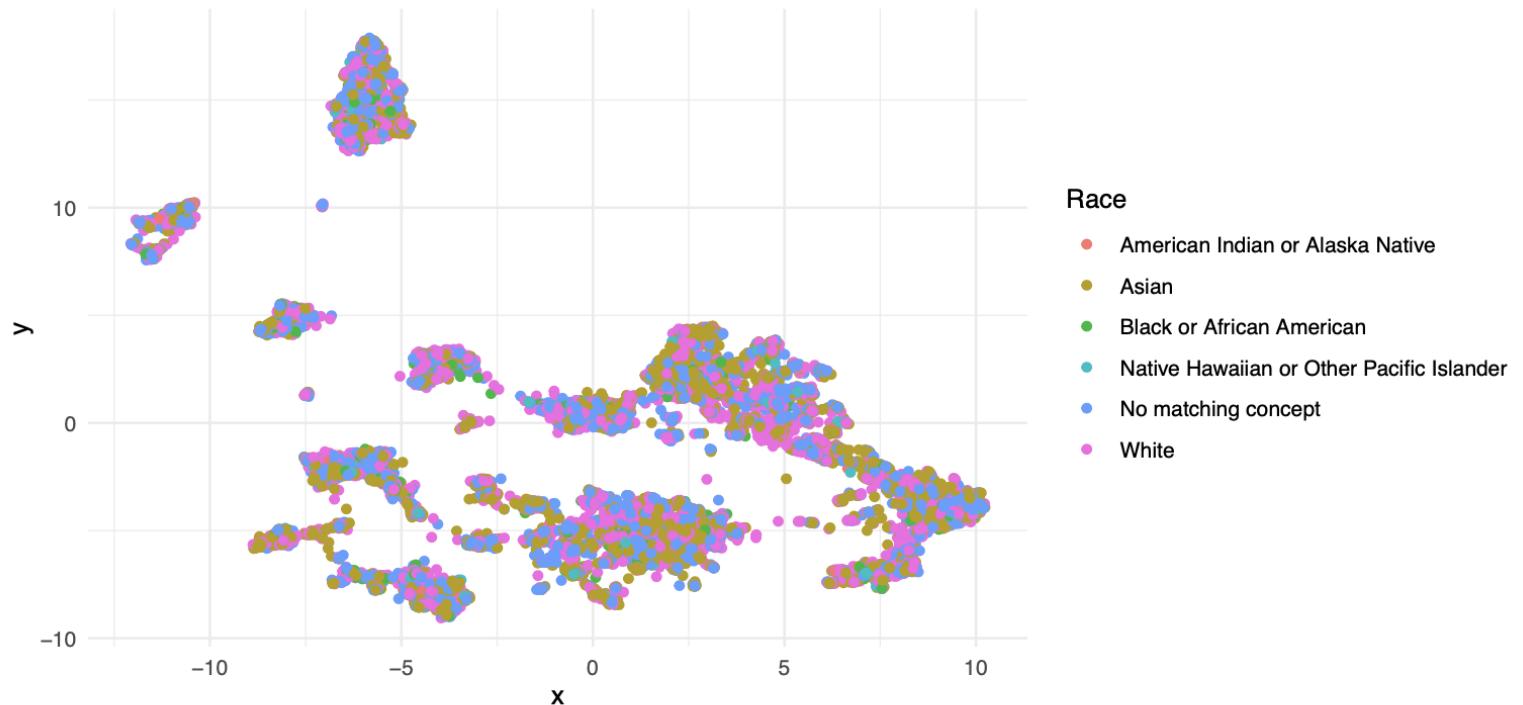


UCSF diagnosis UMAP – number of diagnoses

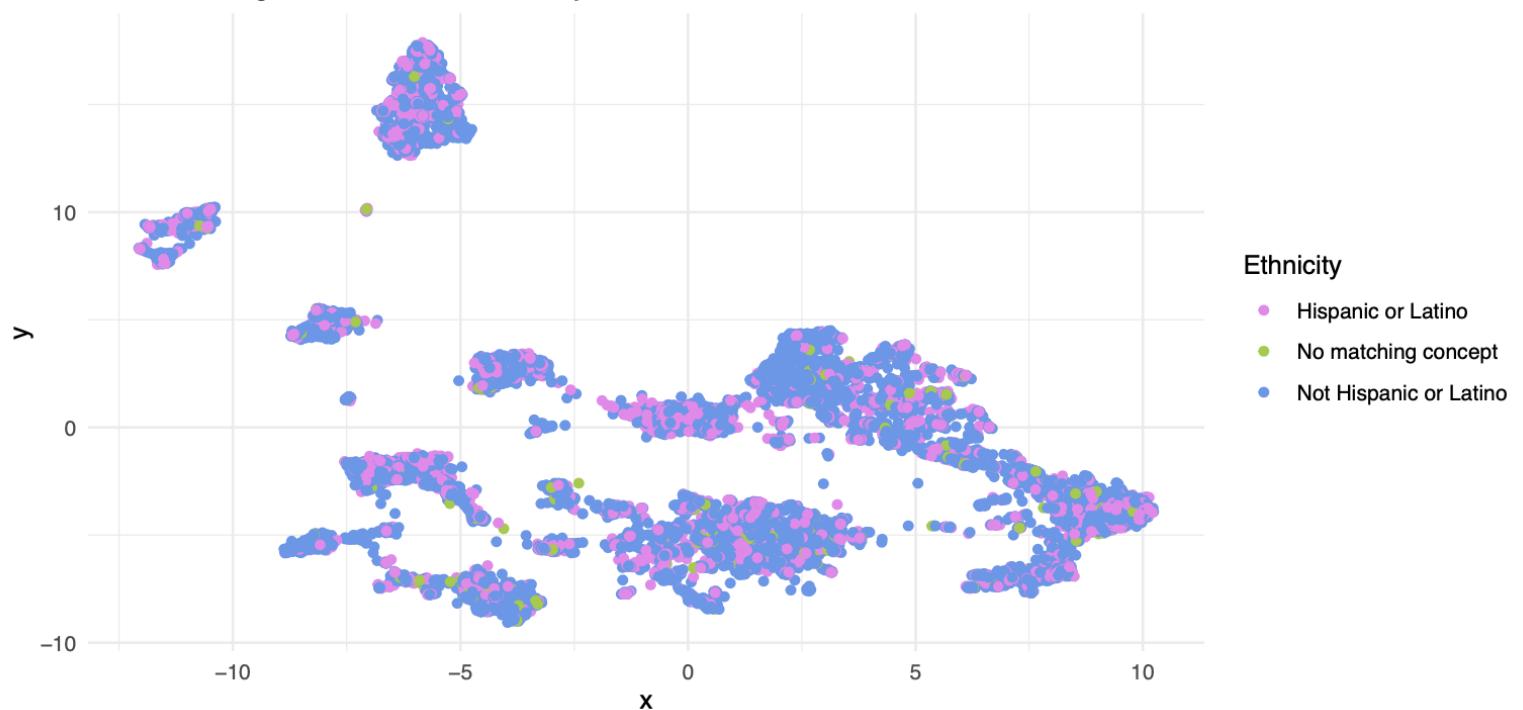


Supplementary Figure 3: UCSF diagnosis UMAPs colored by: (a) years in EHR, (b) number of visits, and (c) number of diagnoses.

Stanford diagnosis UMAP – race

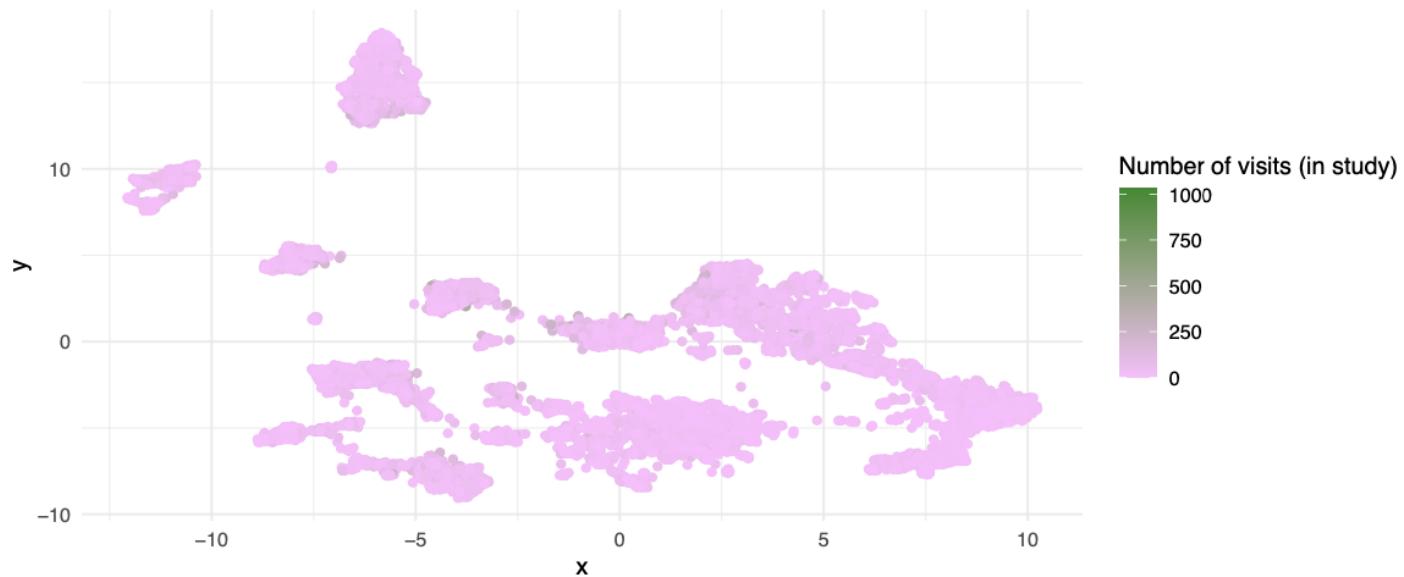


Stanford diagnosis UMAP – ethnicity

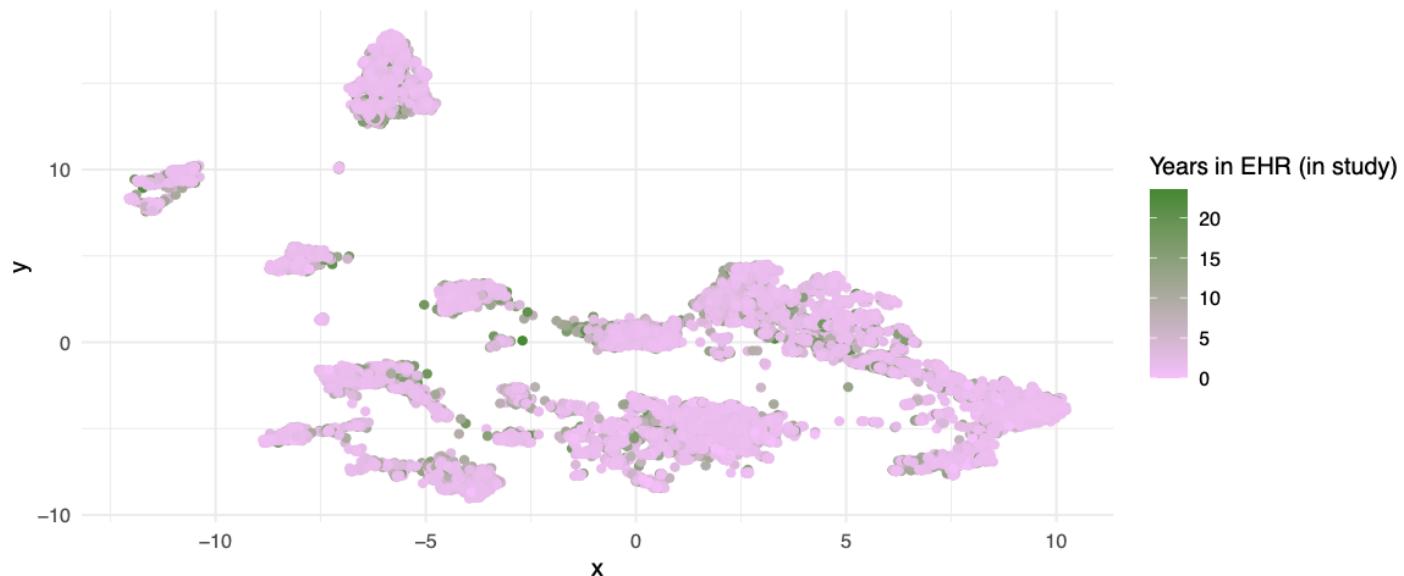


Supplementary Figure 4: Stanford diagnosis UMAPs colored by: (a) race and (b) ethnicity.

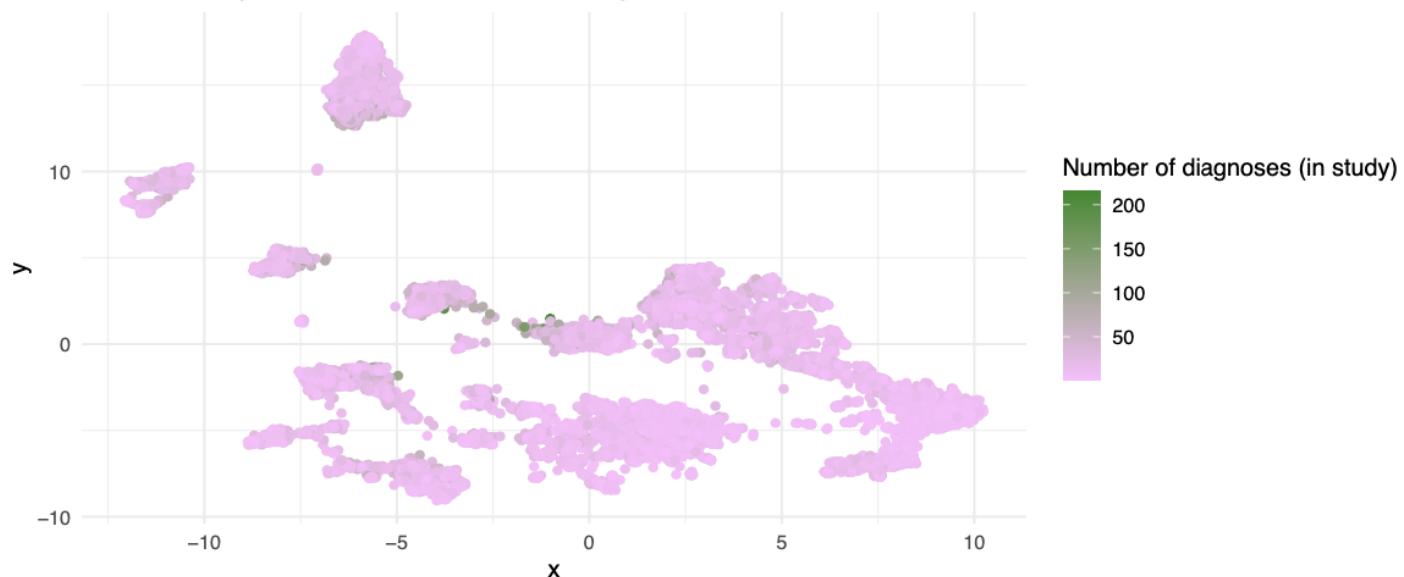
Stanford diagnosis UMAP – number of visits



Stanford diagnosis UMAP – years in EHR

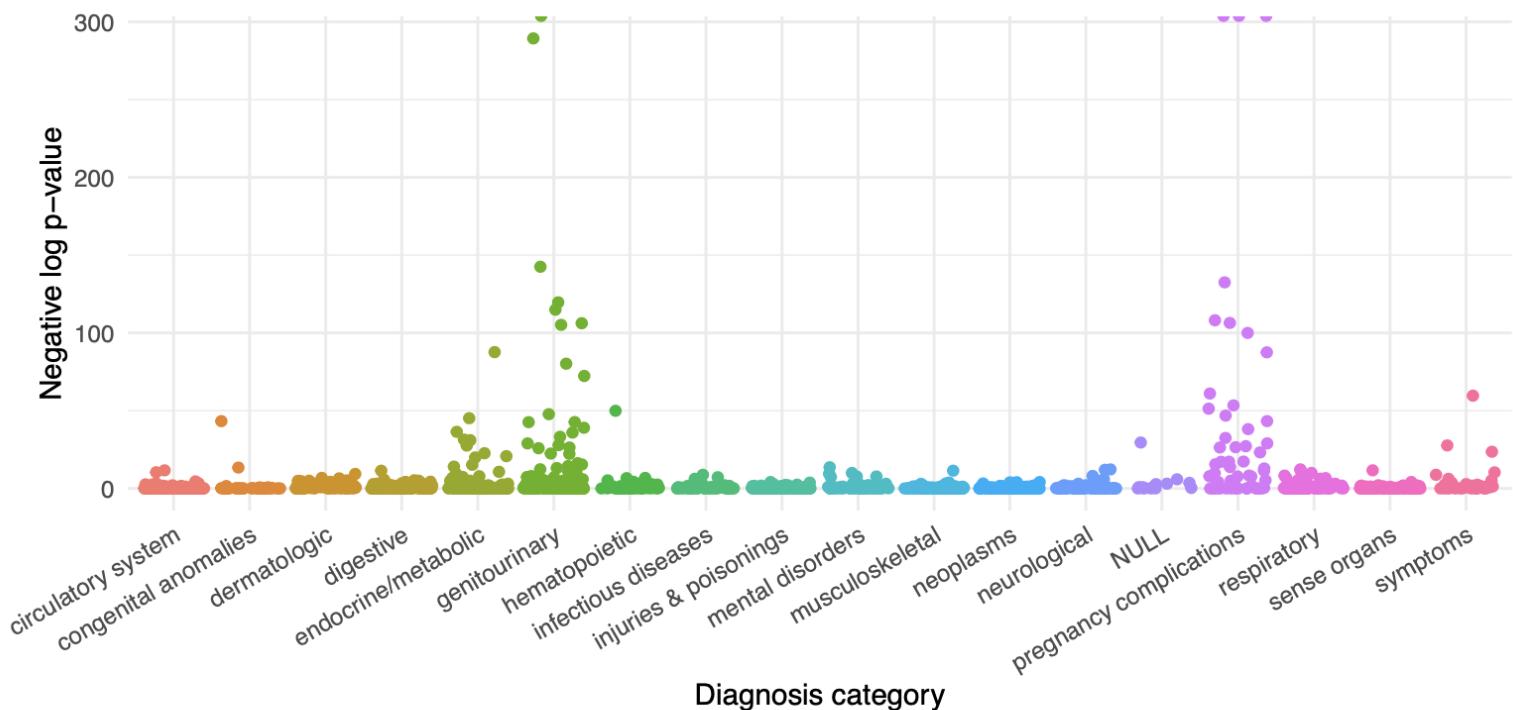


Stanford diagnosis UMAP – number of diagnoses

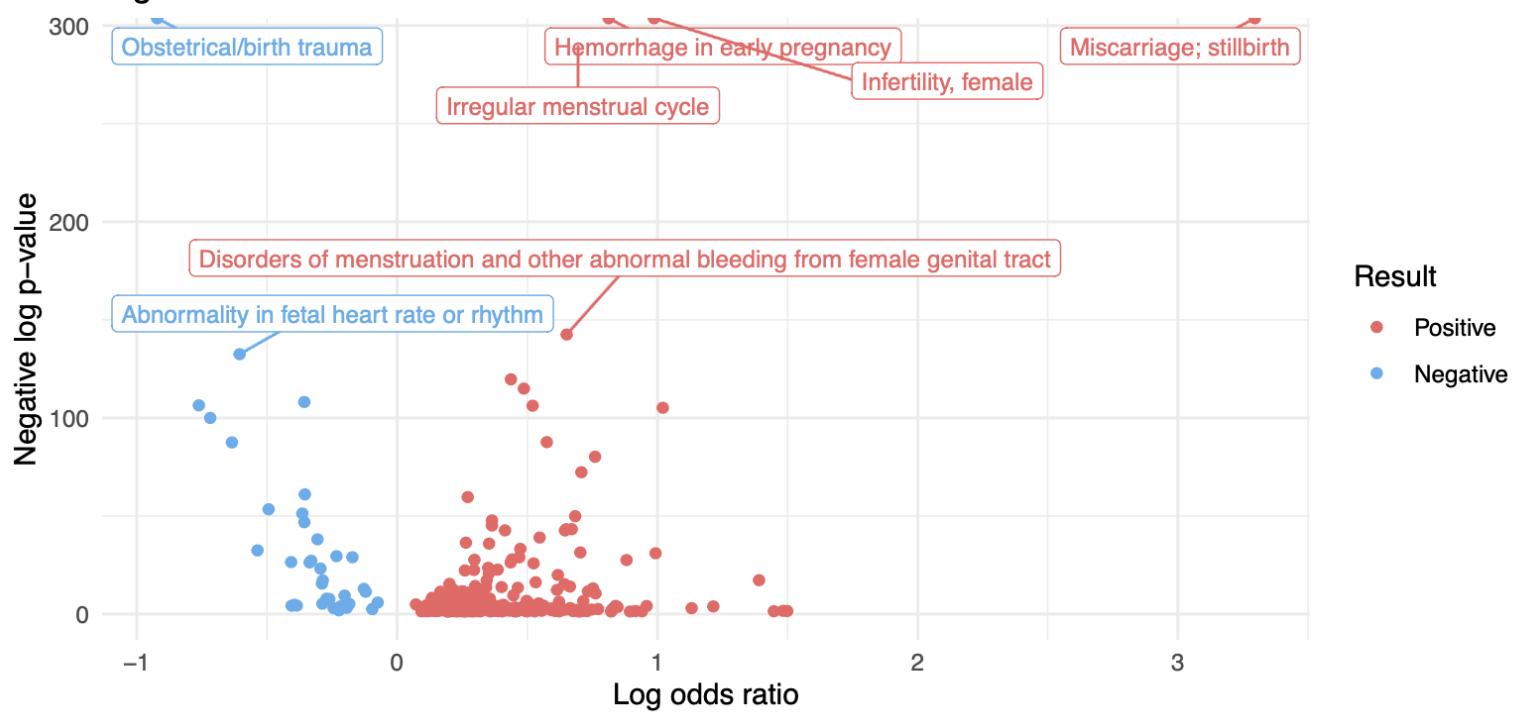


Supplementary Figure 5: Stanford diagnosis UMAPs colored by: **(a)** years in EHR, **(b)** number of visits, and **(c)** number of diagnoses.

a All associations tested at Stanford

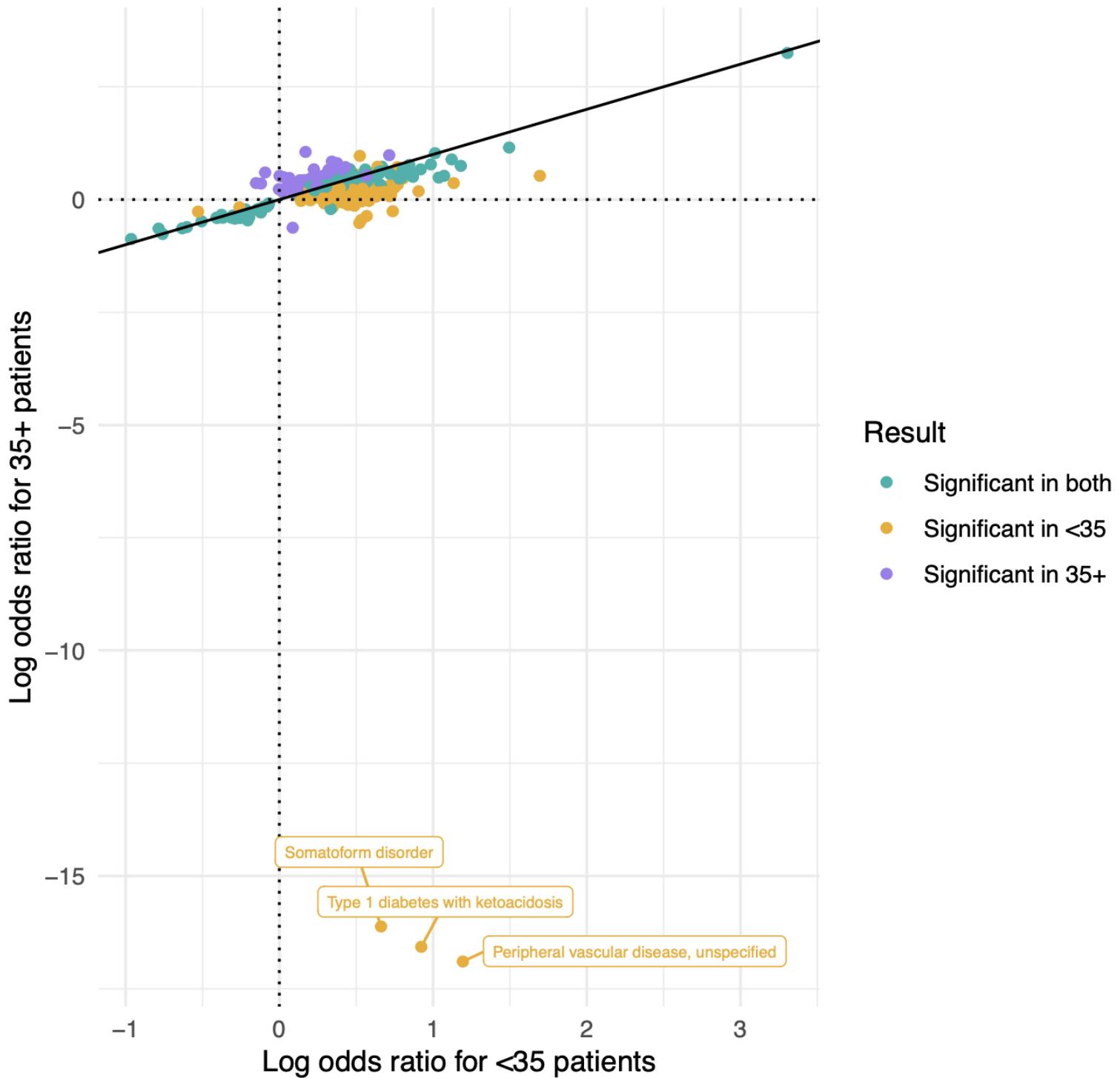


b Significant associations at Stanford



Supplementary Figure 6: Stanford association analysis results. (a) Manhattan plot of all diagnoses tested in the UCSF analysis. Diagnosis categories are listed on the x-axis. The y-axis is the negative log of each associations' p-value, from each diagnosis's GAM. (b) Volcano plot of significant ($p\text{-value} < 0.05$) associations. In the Manhattan and Volcano plots, a few diagnoses have negative log p-values that are approaching infinity, so their corresponding points are located on the top border of the plot. All log transformations in these plots are in base 10.

Significant associations by age strata at Stanford (zoomed out)



Supplementary Figure 7: Full Log-Log plot from age-stratified analysis at Stanford. The zoomed-in version of this plot is in Figure 5b. All points in the Log-Log plot were filtered to include diagnoses where ≥ 10 patients in either the RPL or Control group have a record of that diagnosis. All log transformations in these plots are in base 10.