

	RPL	Control	Total	P-value
	(N=3840)	(N=17259)	(N=21099)	
Age				
Mean (SD)	36.2 (4.53)	33.0 (5.09)	33.6 (5.15)	<0.001
Median [Min, Max]	36.6 [16.6, 44.0]	33.4 [15.1, 44.0]	34.0 [15.1, 44.0]	
Race				
American Indian or Alaska Native	33 (0.9%)	86 (0.5%)	119 (0.6%)	<0.001
Asian	825 (21.5%)	3872 (22.4%)	4697 (22.3%)	
Black or African American	180 (4.7%)	878 (5.1%)	1058 (5.0%)	
Native Hawaiian or Other Pacific Islander	26 (0.7%)	145 (0.8%)	171 (0.8%)	
Other Race	570 (14.8%)	3401 (19.7%)	3971 (18.8%)	
Unknown	366 (9.5%)	1043 (6.0%)	1409 (6.7%)	
White	1840 (47.9%)	7834 (45.4%)	9674 (45.9%)	
Ethnicity				
Hispanic or Latino	450 (11.7%)	2869 (16.6%)	3319 (15.7%)	<0.001
Not Hispanic or Latino	3022 (78.7%)	13266 (76.9%)	16288 (77.2%)	
Unknown	368 (9.6%)	1124 (6.5%)	1492 (7.1%)	
Number of visits (in study)				
Mean (SD)	67.3 (79.8)	53.1 (52.3)	55.7 (58.5)	<0.001
Median [Min, Max]	42.5 [1.00, 1700]	41.0 [1.00, 1230]	41.0 [1.00, 1700]	
Years in EHR (in study)				
Mean (SD)	5.99 (6.46)	4.87 (5.89)	5.08 (6.01)	<0.001
Median [Min, Max]	3.44 [0.137, 44.4]	2.04 [0.132, 41.4]	2.23 [0.132, 44.4]	
Number of diagnoses (in study)				
Mean (SD)	13.7 (15.2)	15.1 (11.7)	14.8 (12.4)	<0.001
Median [Min, Max]	9.00 [1.00, 202]	13.0 [1.00, 186]	12.0 [1.00, 202]	

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

Diagnosis	UCSF odds ratio	UCSF p-value	Stanford odds ratio	Stanford p-value
(a) Known RPL associations				
Cervical incompetence	2.87	<0.001	4.68	<0.001
Chromosomal anomalies	3.14	<0.001	2.91	<0.001
Chronic lymphocytic thyroiditis	1.59	0.008	1.91	<0.001
Congenital anomalies of female genital organs	5.25	<0.001	4.46	<0.001
Early or threatened labor; hemorrhage in early pregnancy	1.44	<0.001	1.29	<0.001
Hemorrhage in early pregnancy	5.23	<0.001	6.49	<0.001
Hemorrhage NOS	3.35	<0.001	2.65	<0.001
Miscarriage; stillbirth	2977.4	<0.001	1975.63	<0.001
Multiple gestation	1.56	<0.001	2.21	<0.001
Pituitary hyperfunction	3.74	<0.001	4.14	<0.001
Polyp of corpus uteri	4.09	<0.001	5.76	<0.001
Primary hypercoagulable state	4.2	<0.001	4.83	<0.001
Threatened premature labor	1.55	0.047	2.09	<0.001
(b) Menstrual abnormalities				
Absent or infrequent menstruation	1.67	<0.001	2.74	<0.001
Disorders of menstruation and other abnormal bleeding from female genital tract	2.27	<0.001	4.48	<0.001
Dysmenorrhea	1.96	<0.001	2.94	<0.001
Excessive or frequent menstruation	1.94	<0.001	2.97	<0.001
Irregular menstrual bleeding	1.8	<0.001	3.53	<0.001
Irregular menstrual cycle	2.16	<0.001	4.95	<0.001
Irregular menstrual cycle/bleeding	2.67	<0.001	4.41	<0.001
(c) Infertility-associated diagnoses				
Endometriosis	3.13	<0.001	2.73	<0.001
Infertility, female	5.07	<0.001	9.69	<0.001
Infertility, female, associated with anovulation	2.88	<0.001	5.1	<0.001
Ovarian dysfunction	3.17	<0.001	5.05	<0.001
Polycystic ovaries	2.15	<0.001	3.76	<0.001
Premature menopause and other ovarian failure	3.75	<0.001	3.4	<0.001
(d) Infections & immunological conditions				
Acute pharyngitis	1.44	0.004	1.65	<0.001
Inflammatory diseases of uterus, except cervix	1.96	0.009	10.48	<0.001
Other immunological findings	3.63	<0.001	4.61	<0.001
Pelvic inflammatory disease, NOS	4.29	<0.001	5.65	<0.001
Unspecified diffuse connective tissue disease	7.32	<0.001	2.56	<0.001
Vaginitis and vulvovaginitis	1.48	<0.001	1.97	<0.001
(e) Other validated positive associations				
Complications following abortion or ectopic and molar pregnancies	>1	<0.05	24.55	<0.001
Disorders of uterus, NEC	2.26	<0.001	3.31	<0.001
Disorders secondary to childbirth, surgery, trauma	1.87	<0.001	2.26	<0.001
Disturbances of sulphur-bearing amino-acid metabolism	3.52	<0.001	7.61	<0.001
Dysmetabolic syndrome X	9.56	<0.001	9.83	<0.001
Gastroparesis	3.3	0.034	>1	<0.05
Noninflammatory female genital disorders	1.76	<0.001	3.34	<0.001
Other symptoms	1.57	0.029	1.65	0.002
Ovarian cyst	2.12	<0.001	3.07	<0.001
Poisoning by analgesics, antipyretics, and antirheumatics	>1	<0.05	>1	<0.05

Table 2: Inter-center validated positive associations. Odds ratios and p -values were computed from each diagnosis's covariate-adjusted GAM. All diagnoses in these tables had multiple-testing-corrected p -values<0.05 in both the UCSF and Stanford analyses. To maintain patient de-identification, exact odds ratios and p -values are redacted for diagnoses with counts <10.

Diagnosis	UCSF odds ratio	UCSF p-value	Stanford odds ratio	Stanford p-value
Abnormality in fetal heart rate or rhythm	0.19	<0.001	0.25	<0.001
Abnormality of organs and soft tissues of pelvis complicating pregnancy, childbirth, or the puerperium	0.43	<0.001	0.44	<0.001
Acute posthemorrhagic anemia	0.41	<0.001	0.64	<0.001
Anemia during pregnancy	0.29	<0.001	0.51	<0.001
Carbuncle and furuncle	0.55	0.034	0.57	<0.001
Coagulation defects complicating pregnancy or postpartum	0.56	<0.001	0.65	<0.001
Complications of labor and delivery NEC	0.31	<0.001	0.47	<0.001
Diabetes or abnormal glucose tolerance complicating pregnancy	0.37	<0.001	0.43	<0.001
Fetal distress and abnormal forces of labor	0.26	<0.001	0.32	<0.001
Hypertension complicating pregnancy, childbirth, and the puerperium	0.28	<0.001	0.46	<0.001
Infectious and parasitic complications affecting pregnancy	0.34	<0.001	0.52	<0.001
Known or suspected fetal abnormality affecting management of mother	0.51	<0.001	0.67	<0.001
Late pregnancy and failed induction	0.22	<0.001	0.19	<0.001
Malposition and malpresentation of fetus or obstruction	0.37	<0.001	0.49	<0.001
Maternal complication of pregnancy affecting fetus or newborn	0.59	0.036	0.61	<0.001
Mental disorders during/after pregnancy	0.38	<0.001	0.63	<0.001
Normal delivery	0.14	<0.001	0.17	<0.001
Obstetrical/birth trauma	0.12	<0.001	0.12	<0.001
Other and unspecified complications of birth; puerperium affecting management of mother	0.38	<0.001	0.29	<0.001
Other anemias	0.42	<0.001	0.8	0.003
Other complications of pregnancy NEC	0.44	<0.001	0.75	<0.001
Other complications of the puerperium NEC	0.31	<0.001	0.55	<0.001
Other conditions or status of the mother complicating pregnancy, childbirth, or the puerperium	0.31	<0.001	0.44	<0.001
Other disorders of the breast associated with childbirth and disorders of lactation	0.38	<0.001	0.52	<0.001
Other perinatal conditions of fetus or newborn	0.85	0.008	0.76	<0.001
Other tests	0.38	<0.001	0.59	<0.001
Placenta previa and abruptio placenta	0.32	<0.001	0.51	<0.001
Preeclampsia and eclampsia	0.25	<0.001	0.39	<0.001
Problems associated with amniotic cavity and membranes	0.34	<0.001	0.44	<0.001
Retention of urine	0.44	<0.001	0.4	<0.001
Secondary thrombocytopenia	0.32	<0.001	0.39	<0.001
Thrombocytopenia	0.42	<0.001	0.61	<0.001
Umbilical cord complications during labor and delivery	0.26	<0.001	0.23	<0.001
Venous/cerebrovascular complications embolism in pregnancy and the puerperium	0.41	<0.001	0.54	<0.001

Table 3: Inter-center validated negative associations. Odds ratios and p -values were computed from each diagnosis's covariate-adjusted GAM. All diagnoses in these tables had multiple-testing-corrected p -values<0.05 in both the UCSF and Stanford analyses.

Diagnosis	UCSF odds ratio	UCSF p-value	Stanford odds ratio	Stanford p-value
Anxiety disorder	0.74	<0.001	1.4	<0.001
Constipation	0.76	0.025	1.29	0.004
Depression	0.7	0.034	1.78	<0.001
Generalized anxiety disorder	0.63	0.007	1.72	<0.001
Impaired fasting glucose	0.59	0.001	1.5	<0.001
Infections of genitourinary tract during pregnancy	0.66	<0.001	1.26	0.016
Iron deficiency anemias, unspecified or not due to blood loss	0.6	<0.001	1.32	0.003
Major depressive disorder	0.7	<0.001	1.57	<0.001
Other abnormal glucose	0.61	0.002	2.25	<0.001
Other high-risk pregnancy	0.7	<0.001	1.18	<0.001
Pruritus and related conditions	0.7	0.003	1.27	0.012
Rhesus isoimmunization in pregnancy	0.59	<0.001	1.51	0.003

Table 4: Discordant association results. Odds ratios and p -values were computed from each diagnosis's covariate-adjusted GAM. All diagnoses in these tables had multiple-testing-corrected p -values<0.05 in both the UCSF and Stanford analyses.