

Supplementary Materials: Hereditary Leiomyomatosis and Renal Cell Cancer Syndrome in Spain: Clinical and Genetic Characterization

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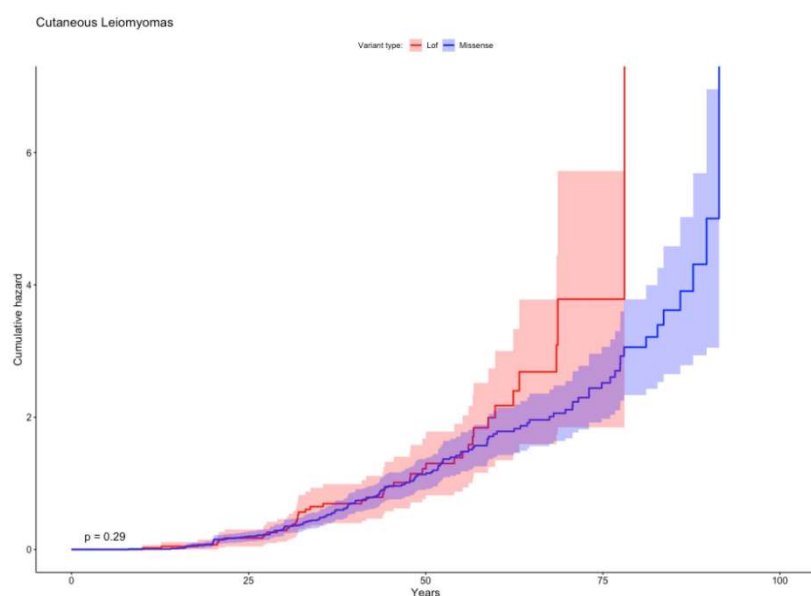


Figure S1. Cumulative incidence of cutaneous leiomyomas by variant type. Light-colored areas represent confidence intervals.

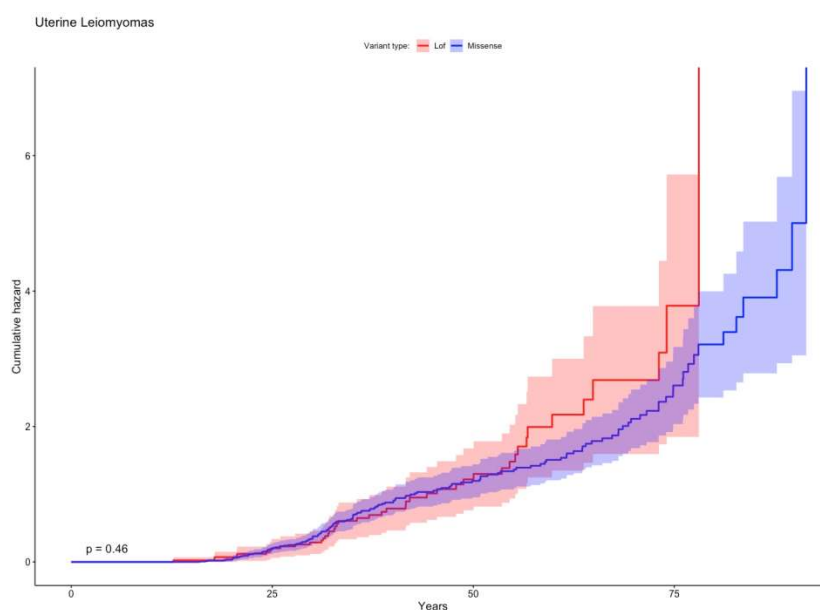


Figure S2. Cumulative incidence of uterine leiomyomas by variant type. Light-colored areas represent confidence intervals.

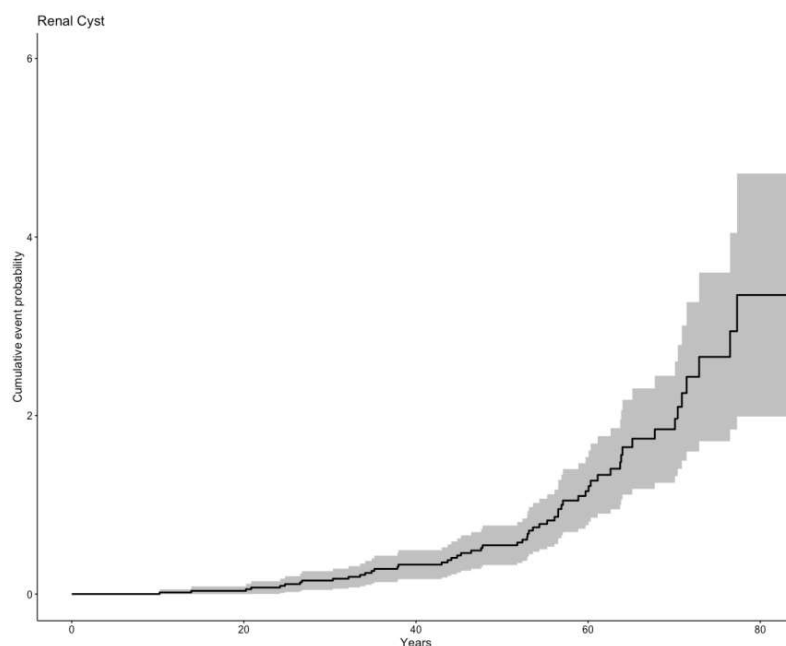


Figure S3. Cumulative incidence of renal cysts.

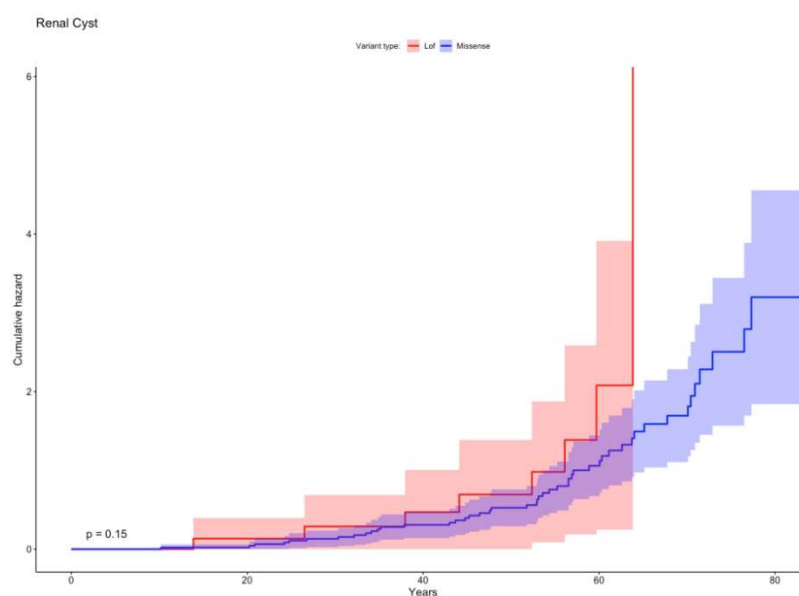


Figure S4. Cumulative incidence of renal cysts by variant type. Light-colored areas represent confidence intervals.

Table S2. Univariate analysis for Cutaneous Leiomyomas, Uterine Leiomyomas, Renal Cysts, Renal Cell Cancer and risk factors.

Clinical Manifestations	CLM		ULM		RCy		RCC	
	N af / T (%)	p-Value	N af T / (%)	p-Value	N af / T (%)	p-Value	N af / T (%)	p-Value
Variant type								
Missense	97/141 (68.8)	0.038*	75/78 (96.1)	0.001*	49/115 (42.6)	0.017*	13/133 (9.8)	0.412*
Lof	21/41 (51.2)		18/25 (72)		8/38 (21)		6/42 (14.3)	
Gender		0.272*		-		0.566*		0.236*

Male	49/81 (60.5)	-	24/69 (34.8)	11/79 (14)		
Female	69/101 (68.3)	-	33/84 (39.3)	8/96 (8.3)		
Obesity						
No	92/149 (61.7)	0.669*	71/80 (88.7)	47/136 (34.5)	14/148 (9.5)	1 [†]
Yes	10/14 (71.4)		8/8 (100)	8/12 (66.6)	1/13 (7.7)	
HBP						
No	84/132 (63.6)	0.848*	67/76 (88.1)	40/119 (33.6)	11/129 (8.5)	1 [†]
Yes	19/29 (65.5)		10/10 (100)	13/27 (48.1)	3/30 (10)	
Phy.activity						
No	82/136 (60.3)	0.378*	67/75 (89.3)	44/123 (35.7)	9/134 (6.7)	0.126 [†]
Yes	10/13 (76.9)		5/5 (100)	3/11 (27.3)	3/13 (23.1)	
Tobacco						
No	59/102 (57.8)	0.196*	55/62 (88.7)	29/93 (31.2)	9/102 (8.8)	0.510*
Yes	35/51 (68.6)		18/20 (90)	21/45 (46.6)	6/49 (12.2)	

CLM: cutaneous leiomyomas; ULM: uterine leiomyomas; RCy: renal cyst; RCC: renal cell carcinoma; N af, no. affected; T, total; LoF: Loss of Function; HBP: high blood pressure; Phy.activity: vigorous physical activity; *X² test; [†]Fisher's exact test.

Table S3. Multivariate logistic regression model for Cutaneous Leiomyomas, Uterine Leiomyomas, Renal Cysts, Renal Cell Cancer and risk factors.

Clinical Manifestations	CLM		ULM		RCy		RCC	
	OR (95% CI)	p-Value*	OR (95% CI)	p-Value*	OR (95% CI)	p-Value*	OR (95% CI)	p-Value*
Variant type								
Missense	Ref. 0,27	-	Ref. 0,07	-	Ref. 0,23	-	Ref. 0,98	-
LoF	(0,11- 0,64)	0,003	(0,01- 0,43)	0,004	(0,07- 0,64)	0,013	(0,23- 4,12)	0,978
Obesity								
No	Ref. 1,18	-	Ref. Inf (0, inf)	-	Ref. 2,51	-	Ref. 1,16	-
Yes	(0,32- 4,29)	0,801		0,996	(0,66- 9,56)	0,177	(0,12- 11,45)	0,896
HBP								
No	Ref. 1,11	-	Ref. Inf (0, inf)	-	Ref. 1,44	-	Ref. 0,97	-
Yes	(0,43- 2,86)	0,836		0,996	(0,54- 3,86)	0,468	(0,18- 5,19)	0,968
Phy.activity								
No	Ref. 2,81	-	Ref. Inf (0, inf)	-	Ref. 0,83	-	Ref. 4,21 (0,9- 19,55)	-
Yes	(0,67- 11,71)	0,156		0,997	(0,19- 3,59)	0,804		0,067
Tobacco								
No	Ref.	-	Ref.	-	Ref.	-	Ref.	-

Yes	1,55 (0,71- 3,40)	0,272	1,43 (0,13- 15,96)	0,77	2,43 (1,07- 5,509)	0,033	0,93 (0,25-3,5)	0,916
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CLM: cutaneous leiomyomas; ULM: uterine leiomyomas; RCy: renal cyst; RCC: renal cell carcinoma; LoF: Loss of Function; OR: Odd Ratio; HBP: high blood pressure; Phy.activity: vigorous physical activity; * Wald's test.



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