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SUPPLEMENTAL DATA

Higher serum PFDA is associated with increased non- melanoma skin cancer odds in NHANES 2003–2018

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Full article is available at the following link: Higher serum PFDA is associated with increased non- melanoma skin cancer odds in NHANES 2003–2018

Table S1. Associations between serum PFAS levels and melanoma skin cancer: Analysis using the minimal adjustment set with variance adjusted for NHANES clustering and stratification

	Tertiles	aOR	95%UI	*p* value
PFDA *n*= 5873				
Level	1	1 (base)		
	2	0.85	0.32, 2.25	0.734
	3	1.65	0.87, 3.13	0.123
Continuous		1.30	0.85, 1.97	0.219
Binary#		0.91	0.43, 1.93	0.800
PFUnDA *n*= 5873				
Level	1	1 (base)		
	2	0.63	0.21, 1.88	0.405
	3	1.66	0.87, 3.17	0.123
Continuous		1.25	0.86, 1.82	0.233
Binary#		0.88	0.48, 1.63	0.690
2-(N-methyl-PFOSA) acetate *n*= 5873				
Level	1	1 (base)		
	2	1.86	1.06, 3.26	0.032
	3	0.68	0.28, 1.68	0.425
Continuous		0.98	0.72, 1.33	0.889
Binary#		1.01	0.52, 1.99	0.966

Models account for clustering at the primary sampling unit (PSU) level and stratification using survey design-based variance estimation.

Adjusted covariates include age, sex, race, smoke exposure, NHANES cycle and BMI

Detectable or Undetectable Serum PFAS (as a binary variable) and Melanoma Skin Cancer

PFDA tertiles: Wald F-test Prob > F = 0.000; goodness of link p= 0.350

PFDA continuous: Wald F-test Prob > F = 0.000; goodness of link p= 0.572

PFDA#: Wald F-test Prob > F = 0.000; goodness of link p= 0.813

PFUnDA tertiles: Wald F-test Prob > F = 0.000; goodness of link p= 0.513

PFUnDA continuous: Wald F-test Prob > F = 0.000; goodness of link p= 0.580
PFUnDA#: Wald F-test Prob > F = 0.000; goodness of link p= 0.862
2-(N-methyl-PFOSA) acetate tertiles: Wald F-test Prob > F = 0.000; goodness of link p= 0.838
2-(N-methyl-PFOSA) acetate continuous: Wald F-test Prob > F = 0.000; goodness of link p= 0.778
2-(N-methyl-PFOSA) acetate#: Wald F-test Prob > F = 0.000; goodness of link p= 0.811

Abbreviations: 2-(N-methyl-PFOSA) acetate, 2-(N-methyl-perfluorooctane sulfonamido) acetic acid; aOR, adjusted odds ratio; BMI, body mass index; NHANES, National Health and Nutrition Examination Survey; NMSC, non-melanoma skin cancer; PFAS, per- and polyfluoroalkyl substances; PFDA, perfluorodecanoic acid; PFUnDA, perfluoroundecanoic acid; PSU, primary sampling unit; UI, uncertainty interval.

Table S2. Associations between serum PFAS levels and melanoma skin cancer using the minimal adjustment set and prognostic variables (Firth penalized logistic regression)

	Tertiles	**aOR**	**95%UI**	***p* value**
PFDA *n*=1382				
Level	1	1 (base)		
	2	2.24	0.25, 20.1	0.471
	3	6.75	0.82, 55.6	0.076
Continuous		2.35	0.75, 7.43	0.144
Binary#		1.02	0.16, 6.74	0.981
PFUnDA *n*=1382				
Level	1	1 (base)		
	2	2.66	0.34, 21.2	0.354
	3	2.10	0.26, 17.0	0.486
Continuous		1.76	0.56, 5.53	0.332
Binary#		1.67	0.26, 10.6	0.584
2-(N-methyl-PFOSA) acetate *n*=1382				
Level	1	1 (base)		
	2	2.38	0.55, 29.2	0.171
	3	4.00	0.26, 21.6	0.441
Continuous		1.39	0.61, 3.18	0.437
Binary#		7.64	0.41, 140.1	0.172

Adjusted covariates include age, sex, race, smoke exposure, NHANES cycle, urine creatinine, BMI, diabetes, sunburn and urinary arsenic levels. # Detectable vs. Undetectable serum PFAS: A binary variable in relation to melanoma skin cancer

Abbreviations: 2-(N-methyl-PFOSA) acetate, 2-(N-methyl-perfluorooctane sulfonamido) acetic acid; aOR, adjusted odds ratio; BMI, body mass index; NHANES, National Health and Nutrition Examination Survey; PFAS, per- and polyfluoroalkyl substances; PFDA, perfluorodecanoic acid; PFUnDA, perfluoroundecanoic acid; UI, uncertainty interval.

Table S3. Characteristics of excluded and included participants

Variable	Excluded (*n* = 37,915)	Included (*n* = 5,934)	*p* value
Sex, *n* (%)	Male: 18,767 (49.5)	Male: 2,901 (48.9)	0.382
	Female: 19,148 (50.5)	Female: 3,033 (51.1)	
Race, *n* (%)	Hispanic: 3,888 (23.7)	Hispanic: 1,460 (24.6)	0.012
	White: 6,148 (37.4)	White: 2,091 (35.3)	
	Other: 6,400 (38.9)	Other: 2,383 (40.2)	
Age, mean (SD)	50.60 (18.21)	48.44 (17.32)	<0.001
BMI, mean (SD)	29.08 (6.90)	29.08 (6.90)	—

Statistical tests employed to evaluate group differences included independent samples t-tests and Mann–Whitney U tests, determined by the distribution of the data. Categorical variables were compared using chi-squared tests or Fisher's exact tests, as applicable. **Abbreviations**: BMI, body mass index; SD, standard deviation.

Table S4. Tertile cut-off values (ng/mL)

PFAS Compound	Minimum value	Tertile 1	Tertile 2	Maximum value
PFDA	0.07	0.20	0.30	51.3
PFUnDA	0.07	0.10	0.20	77.4
2-(N-methyl-PFOSA) acetate	0.06	0.10	0.30	6.3

Abbreviations: 2-(N-methyl-PFOSA) acetate, 2-(N-methyl-perfluorooctane sulfonamido) acetic acid; PFDA, perfluorodecanoic acid; PFUnDA, perfluoroundecanoic acid.

Table S5. *p* trend for trend analysis across PFAS tertiles

Exposure	aOR per tertile (trend)	95% UI	*p* trend
PFDA	1.13	0.88, 1.46	0.327
PFUnDA	1.07	0.81, 1.41	0.625
2-(N-methyl-PFOSA) acetate	0.94	0.73, 1.23	0.666

Abbreviations: 2-(N-methyl-PFOSA) acetate, 2-(N-methyl-perfluorooctane sulfonamido) acetic acid; aOR, adjusted odds ratio; PFDA, perfluorodecanoic acid; PFUnDA, perfluoroundecanoic acid; UI, uncertainty interval.

Table S6. Multiple imputation of associations between serum PFAS levels and NMSC using the minimal adjustment set

	Tertiles	aOR	95%UI	*p* value
PFDA *n*=11863				
Level	1	1 (base)		
	2	1.34	0.92, 1.93	0.123
	3	1.15	0.83, 1.59	0.417
Continuous		1.15	0.96, 1.37	0.128
Binary#		1.22	0.84, 1.76	0.301
PFUnDA *n*= 11863				
Level	1	1 (base)		
	2	1.08	0.73, 1.61	0.696
	3	1.06	0.71, 1.59	0.763
Continuous		0.99	0.82, 1.20	0.941
Binary#		1.23	0.91, 1.67	0.171
2-(N-methyl-PFOSA) acetate *n*=11863				
Level	1	1 (base)		
	2	1.03	0.70, 1.52	0.863
	3	1.07	0.71, 1.60	0.758
Continuous		0.99	0.85, 1.16	0.940
Binary#		0.96	0.71, 1.31	0.810

Abbreviations: 2-(N-methyl-PFOSA) acetate, 2-(N-methyl-perfluorooctane sulfonamido) acetic acid; aOR, adjusted odds ratio; PFDA, perfluorodecanoic acid; PFUnDA, perfluoroundecanoic acid; UI, uncertainty interval.

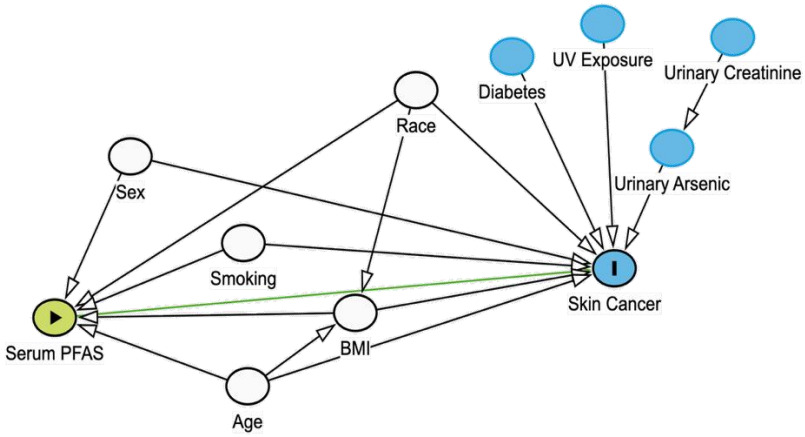


Figure S1. DAG of hypothesized relationships between serum PFAS and skin cancer. The DAG depicts the assumed causal structure linking serum PFAS (exposure) to skin cancer (outcome). White nodes indicate the covariates included in the minimal adjustment set used to control confounding (age, sex, race, BMI, and smoking), identified a priori from the literature and subject-matter expertise. Blue nodes denote prognostic variables additionally adjusted in expanded models to assess robustness (diabetes, UV exposure, urinary arsenic, and urinary creatinine). Directed edges represent hypothesized causal relationships. NHANES cycle was additionally controlled for in regression models but is not shown in the DAG. **Abbreviations**: BMI, body mass index; DAG, directed acyclic graph; NHANES, National Health and Nutrition Examination Survey; PFAS, per- and polyfluoroalkyl substances; UV, ultraviolet.