



Sensitization to lanolin in North-Eastern Italy, 1997–2021

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Conflict of Interests to disclose: None



Allergic Contact Dermatitis (ACD)

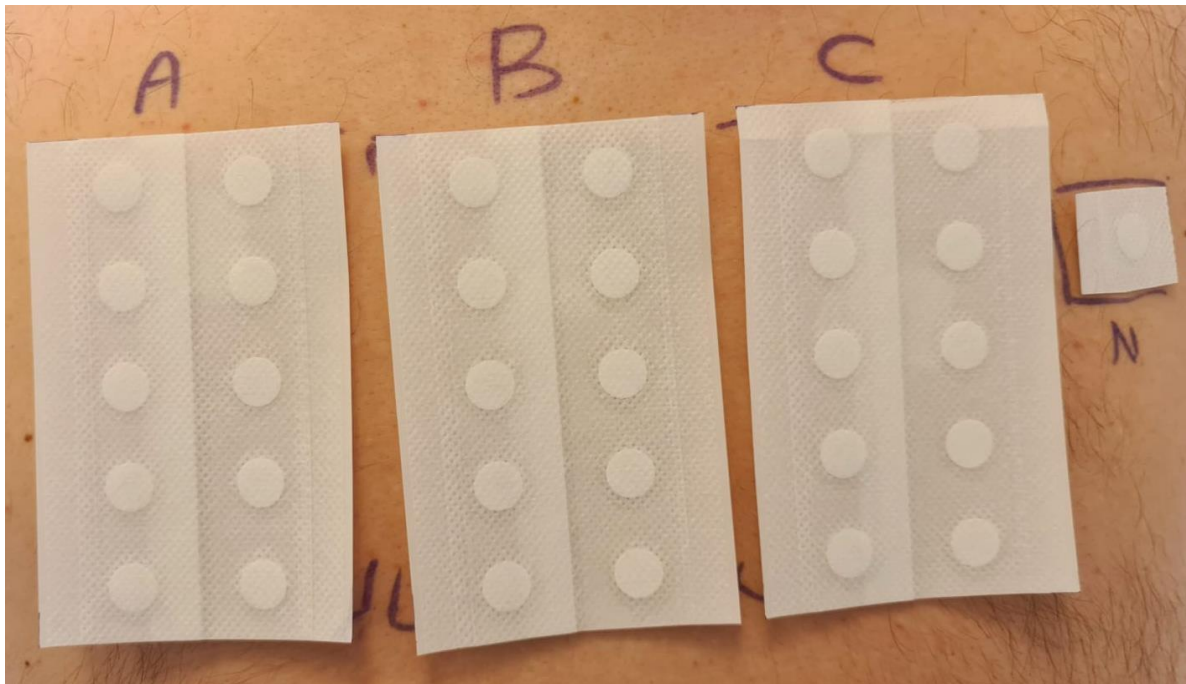
- **Type IV delayed hypersensitivity** reaction presenting with an itching eczematous rash developing after direct skin contact with a hapten.
- An **hapten** is an incomplete (low molecular weight) antigen, originally not immunogenic, which could induce sensitization if combined with a larger carrier, as a protein



- A previous sensitization event is necessary, at least 2 weeks before the onset of ACD
- A single exposure to an allergen - an event easily neglected at medical history taking - may be sufficient to induce sensitization.

Patch testing

- Necessary to confirm ACD in a patient presenting dermatitis
- However, debate still ongoing on the clinical relevance of positive patch test results.



Lanolin

- The term “lanolin” combines Latin words “*lana*” (wool) and “*oleum*” (oil)
- Crude lanolin (wool wax) is secreted by the sebaceous glands of sheep and can be extracted from wool with a complex chemo-physical procedure.
- In 1882, Otto Braun first patented a method to obtain pure lanolin by centrifuging the scouring liquid from wool washings.

Composition of Lanolin

Complex hydrophobic mixture including:

- high-molecular-weight esters, accounting for 87% crude lanolin
- 11% free elements (aliphatic alcohols, sterols, fatty acids and hydrocarbons)
- 2% unidentified components.

Given the predominance of high-molecular-weight esters, lanolin is classified as a wax rather than a fat

Applications of Lanolin

The **emollient and hydrophobic features** of lanolin and its derivatives—effective at repelling water from sheep—are used in skin care products to:

- soften/moisturize the epidermidis
- emulsify water/oil
- stimulate skin gas exchange
- facilitate wound healing
- prevent infections and
- lead cosmetics and pharmaceuticals inside the skin



Lanolin as allergen

- Lanolin first indicted as a potential allergen in 1922 in a patient with a “skin reaction” to a cream containing wool alcohols
- Several case reports of potential lanolin allergy to an ointment containing 6% wool were reported thereafter
- First positive patch test against lanolin performed in 1929

Clinical relevance of lanolin sensitization

Relevance of lanolin as a hapten and the significance of patch test result has been debated for decades, due to the risk of **false positive results** attributable to **different lanolin derivatives** employed in patch test formulations

Most used lanolin derivatives in patch testing:

- **Lanolin alcohol 30%** (included standard in European standard series since 1969)
- **Amerchol L-101** (mixture of lanolin alcohol 10% + mineral oils, included in North American standard series)

Amerchol (50% or 100%) more reactive than lanolin alcohol 30%, but suspected of false positive results



Allergen of year in 2023



- Although ACD induced by lanolin is relatively low in Western countries, certain conditions - as stasis dermatitis, leg ulcers, perianal/genital dermatitis, atopic dermatitis - enhance the risk (especially in older adults or children)
- Lanolin ACD seems more common in non-Hispanic Whites than in non-Hispanic Blacks.
- The **American Contact Dermatitis Society (ACDS)** elected lanolin «Allergen of the year» in 2023

The present study

- **4 centers from Triveneto (North-Eastern Italy):**
 - Trieste;
 - Padua;
 - Pordenone;
 - Trento/Bolzano/Rovigo;
- **Study period: 1997-2021 (25 years)**
- **Total patients patch - tested: 30,629**

Triveneto (North-Eastern Italy) comprises 3 regions: Veneto, Friuli-Venezia Giulia and Trentino Alto Adige.



Patch test procedure:

- Application on upper part of patient's back
- Removal after 48h
- Further reading at 72h and 96h.

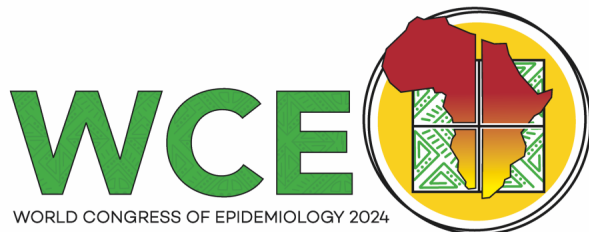
- Positive reactions: +, ++, +++
- Doubtful reactions?+ considered negative.

- Triveneto extended allergen series used



1	4-ter-Butylphenol- formaldehyde resin 1%
2	Carba mix 3%
3	Cobalt chloride hexahydrate 1%
4	Colophonium 20%
5	Disperse blu 35 1%
6	Disperse yellow 3 1%
7	Epoxy resin 1%
8	Formaldehyde 1% aq
9	Fragrance mix-I 8%
10	Methyl-chloro-isothiazolinon /methyl- isothiazolinon (Kathon) 0.02 aq.
11	Lanolin alcohol 30%,
12	Mercaptobenzothiazole 2%
13	Mercapto -benzothiazole mix
14	Neomycin sulfate 20%
15	Nickel sulphate 5%
16	N-Isopropy-N-phenyl-4-phenylendiamine 0.1%
17	Parabens mix
18	Peru balsam 25%
19	Potassium bichromate 0.5%
20	p-Phenylenediamine 1%
21	Quaternium-15 1%
22	Thiuram mix 1%

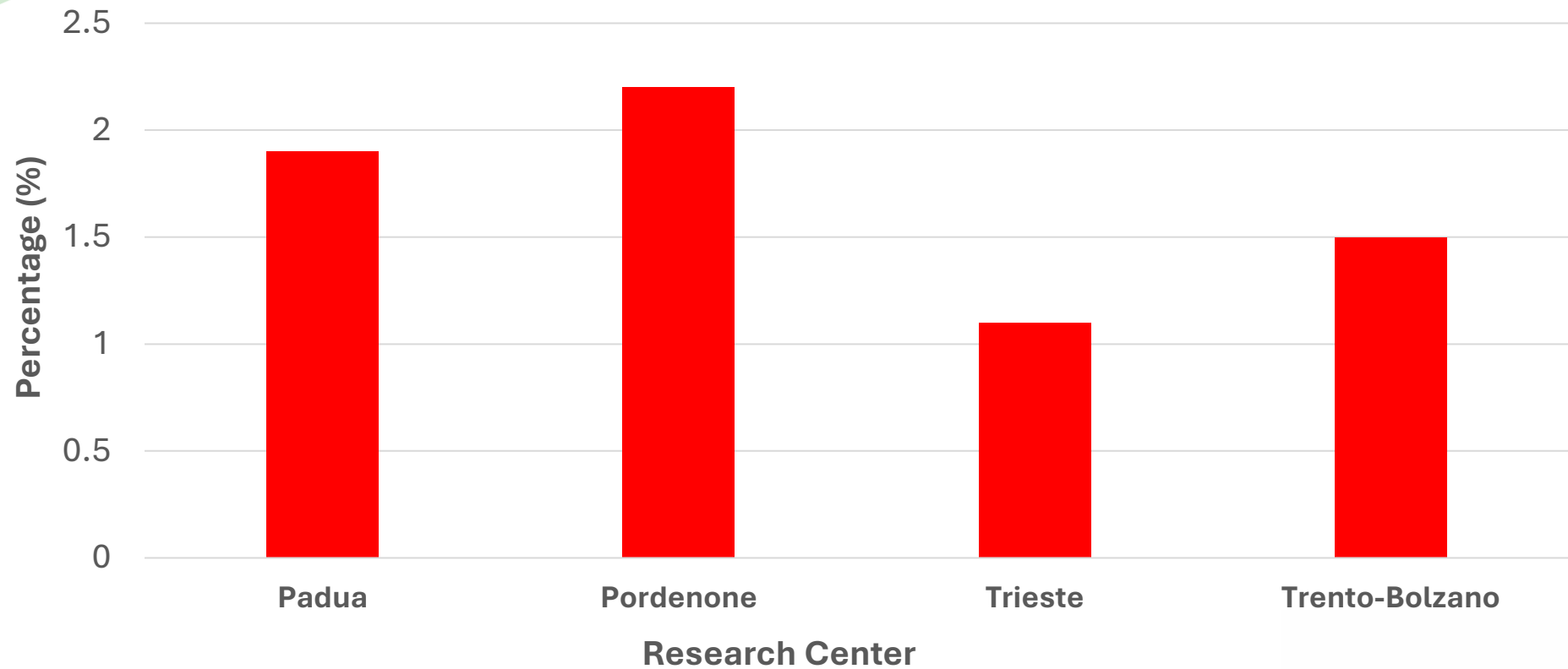
Triveneto patch test series (22 haptens) consistently tested in the entire study period (all in pet when not otherwise specified)



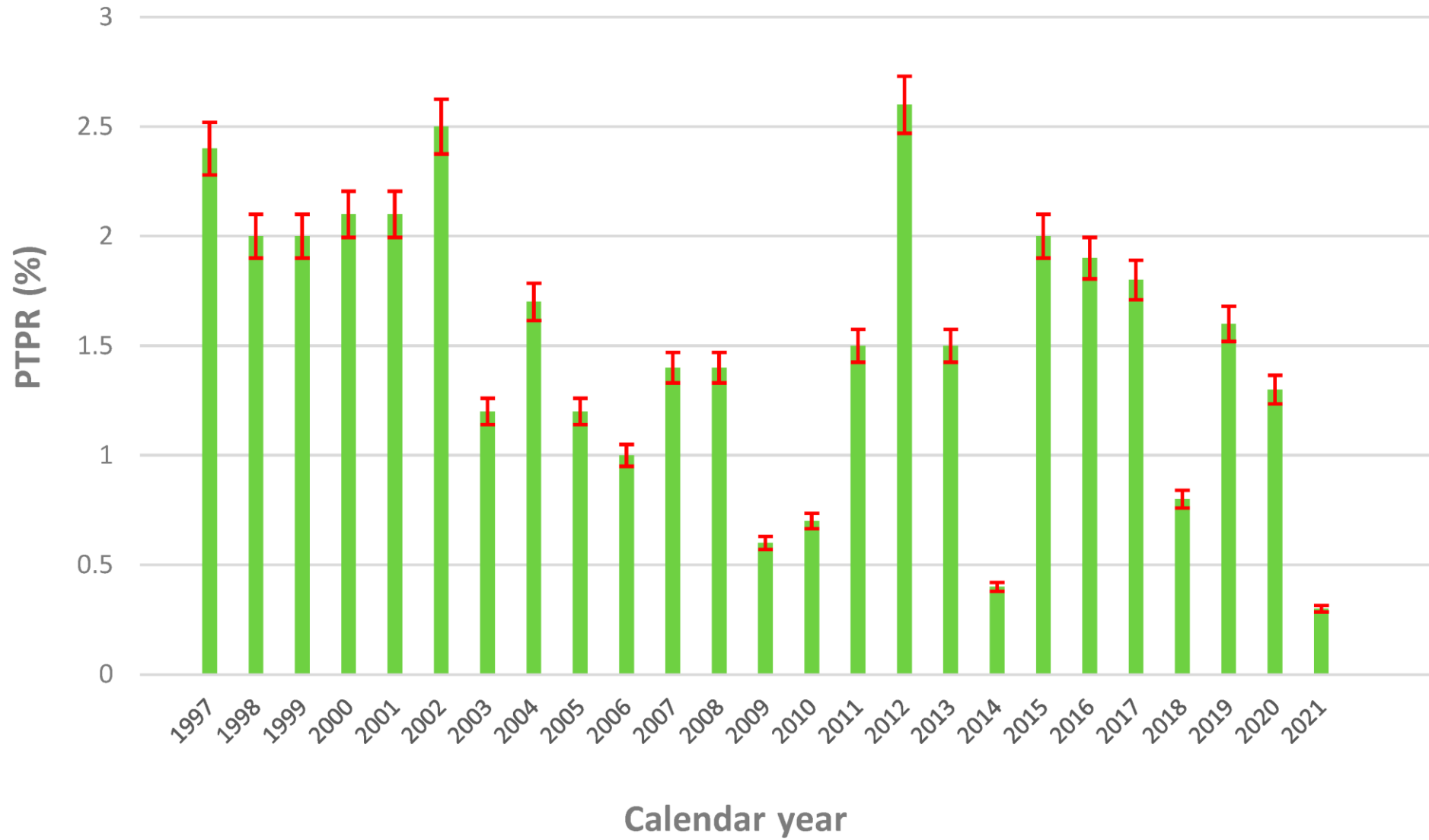
Calendar Year	Research Centre									
	All Patients		Padua		Pordenone		Trieste		Trento/Bolzano/Rovigo	
	N. Tests	PTPR	N. Tests	PTPR	N. Tests	PTPR	N. Tests	PTPR	N. Tests	PTPR
1997	1242	2.42	395	2.03	445	4.04	398	1.01	4	0
1998	2566	2.03	1083	2.95	325	2.15	418	0.24	740	1.62
1999	2868	1.95	1189	2.94	278	2.52	453	0.44	948	1.27
2000	2445	2.13	1042	2.69	208	2.88	817	1.96	378	0.53
2001	2412	2.07	677	1.92	226	5.31	703	1.42	806	1.86
2002	1460	2.47	1	0	353	4.25	701	1.28	405	2.96
2003	1472	1.22	412	1.70	314	2.55	485	0.62	261	0
2004	842	1.66	287	1.74	94	6.38	370	0.81	91	0
2005	1135	1.15	434	1.61	383	1.31	318	0.31	0	NA
2006	1032	0.97	409	1.47	336	0.89	287	0.35	0	NA
2007	1115	1.35	439	1.14	368	2.45	308	0.32	0	NA
2008	1257	1.43	528	1.70	355	1.41	374	1.07	0	NA
2009	1112	0.63	328	0.61	373	0.27	411	0.97	0	NA
2010	1046	0.67	354	0.56	366	0.55	326	0.92	0	NA
2011	1107	1.45	234	2.14	377	1.59	496	1.01	0	NA
2012	664	2.56	0	0	286	3.85	378	1.59	0	NA
2013	886	1.47	240	1.25	274	2.19	372	1.08	0	NA
2014	1011	0.40	322	1.24	288	0	401	0	0	NA
2015	958	1.98	246	0.81	327	2.14	385	2.60	0	NA
2016	749	1.87	230	1.30	239	1.67	280	2.50	0	NA
2017	501	1.80	102	0.98	241	2.90	158	0.63	0	NA
2018	836	0.40	135	2.22	451	0.67	250	0.40	0	NA
2019	1008	1.59	381	0.26	211	4.27	416	1.44	0	NA
2020	540	1.30	94	0	265	1.89	181	1.10	0	NA
2021	365	0.27	0	NA	88	0	277	0.36	0	NA
Total	501	1.64	3580	1.89	7471	2.17	9963	1.05	3633	1.46

PTPR= patch test positivity ratio

Lanolin patch test positive results, by research center



Lanolin patch test positivity ratio



Descriptive and logistic Regression analysis

(adjusted for age, sex, center, body area affected and occupation)

Terms	Total Patients with CD N (col %)	Lanolin + N (row %)	p-Value	OR (95%CI)	aOR (95%CI) (25,907 obs.)		
Total patients examined for CD	30,629 (100)	501 (1.64)					
Centre	Padua	9562 (31.22)	181 (1.89)		reference	reference	
	Pordenone	7471 (24.39)	162 (2.17)	<0.001	1.15 (0.93; 1.42)	1.38 (1.09; 1.75)	
	Trieste	9963 (32.53)	105 (1.05)		0.55 (0.43; 0.70)	0.67 (0.52; 0.88)	
	Trento/Bolzano/Rovigo	3633 (11.86)	53 (1.46)		0.77 (0.56; 1.04)	0.65 (0.45; 0.93)	
Sex	Females	20,694 (67.56)	304 (1.47)		reference	reference	
	Males	9935 (32.44)	197 (1.98)	0.001	1.36 (1.13; 1.63)	1.34 (1.09; 1.65)	
Age (years) (M: 3)	M ± SD	43.80 ± 17.24	49.13 ± 18.50				
	Median	42 (30; 57)	49 (34; 63.5)	<0.001 *			
	<28	6315 (20.62)	73 (1.16)		reference	reference	
	27–37	6411 (20.93)	74 (1.15)		1.00 (0.72; 1.38)	1.01 (0.71; 1.45)	
	38–48	6145 (20.06)	101 (1.64)	<0.001	1.43 (1.06; 1.93)	1.51 (1.08; 2.12)	
49–60	5687 (18.57)	99 (1.74)		1.51 (1.12; 2.05)	1.59 (1.12; 2.26)		
61+	6068 (19.81)	153 (2.52)		2.21 (1.67; 2.93)	1.94 (1.30; 2.91)		
Atopic dermatitis (M: 3143)	No	24,718 (89.93)	431 (1.74)		reference		
	Yes	2768 (10.07)	33 (1.19)	0.033	0.68 (0.48; 0.97)		
Occupational dermatitis (M: 31)	No	28,078 (91.76)	455 (1.62)		reference		
	Yes	2520 (8.24)	46 (1.83)	0.437	1.13 (0.83; 1.53)		
Body area affected by CD	Hand (M: 4432)	No	16,683 (63.68)	298 (1.79)		reference	
		Yes	9514 (36.32)	160 (1.68)	0.535	0.94 (0.77; 1.14)	
	Leg (M: 4430)	No	24,080 (91.1)	393 (1.63)		reference	reference
		Yes	2119 (8.09)	65 (3.07)	<0.001	1.91 (1.46; 2.49)	1.67 (1.27; 2.19)
Face (M: 4430)	No	21,084 (80.48)	388 (1.84)		reference		
	Yes	5115 (19.52)	70 (1.37)	0.021	0.74 (0.57; 0.96)		
Linear term (1997–2021)				<0.001	0.97 (0.96; 0.98)		



	Administrative clerks	6692 (21.985)	87 (1.30)		reference	reference
	Health care workers	3087 (10.08)	40 (1.30)		1.00 (0.68; 1.45)	0.89 (0.59; 1.33)
	Teachers	364 (1.19)	5 (1.37)		1.06 (0.43; 2.62)	1.31 (0.52; 3.30)
	Cashiers	26 (0.08)	0		-	-
	Sellers	353 (1.15)	2 (0.57)		0.43 (0.11; 1.76)	0.58 (0.14; 2.37)
	Restaurant workers	1297 (4.23)	23 (1.77)		1.37 (0.86; 2.18)	1.31 (0.80; 2.16)
	Hairdressers	388 (1.27)	1 (0.26)		0.20 (0.03; 1.41)	0.29 (0.04; 2.11)
	Farmers	257 (0.84)	6 (2.33)		1.81 (0.79; 4.19)	1.27 (0.50; 3.18)
	Construction workers	1178 (3.85)	20 (1.70)		1.31 (0.80; 2.14)	0.81 (0.47; 1.41)
	House painters	26 (0.08)	3 (11.54)		9.90 (2.92; 33.59)	7.56 (1.73; 33.15)
	Painters, other	76 (0.25)	1 (1.32)		1.01 (0.14; 7.36)	0.90 (0.12; 6.59)
	Construction cleaners	17 (0.06)	0		-	-
Occupation	Mechanics	1485 (4.85)	24 (1.62)	<0.001	1.25 (0.79; 1.97)	1.03 (0.64; 1.66)
	Workers of wood industry	440 (1.44)	3 (0.68)		0.52 (0.16; 1.65)	0.38 (0.12; 1.22)
	Artisan general	454 (1.48)	9 (1.98)		1.54 (0.77; 3.07)	1.28 (0.61; 2.69)
	Leather artisans	114 (0.37)	0		-	-
	Chemistry Industry workers	229 (0.75)	4 (1.75)		1.35 (0.49; 3.71)	0.72 (0.22; 2.30)
	Drivers	280 (0.91)	5 (1.79)		1.38 (0.56; 3.43)	1.00 (0.40; 2.53)
	Cleaners	411 (1.34)	9 (2.19)		1.70 (0.85; 3.40)	1.89 (0.93; 3.83)
	Housewives	3564 (11.64)	69 (1.94)		1.50 (1.09; 2.06)	1.09 (0.75; 1.58)
	Students	830 (2.71)	11 (1.33)		1.02 (0.54; 1.92)	1.50 (0.75; 2.98)
	Pensionants	4394 (14.35)	119 (2.71)		2.11 (1.60; 2.79)	1.23 (0.83; 1.23)
	Unemployed	661 (2.16)	11 (1.66)		1.28 (0.68; 2.42)	1.26 (0.65; 2.46)
	Other	3847 (12.56)	49 (1.27)		0.98 (0.69; 1.39)	1.09 (0.74; 1.62)
		Military	159 (0.52)		0	--

The impact of Occupation

(Logistic model adjusted for age, sex, center, body area affected and occupation)

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Descriptive findings

- 501 (**1.64%**) patients patch tested positive to lanolin (1.47% in females vs. 1.98% in males)
- **Variability by research center**, with higher prevalence in Pordenone (2.07%) and lower in Trieste (1.05%)
- Median age of patients testing positive to lanolin: **49 years**
- Body area most frequently affected by dermatitis were the hands (36.32%), but lanolin sensitization was higher in **legs** (3.07%)
- 10.07% of patients had atopic dermatitis, and 1.19% of them were positive to lanolin.
- 8.24% patients had occupational dermatitis and 1.83% of them were positive to lanolin.

Study	Design	N of patients	Years	Patch test formulation	Prevalence	
European Surveillance System on Contact Dermatitis	Multi-center (12 countries)	58,833	2009–12	Lanolin alcohol 30%	1.65%	
					1.7%	
London (UK)	Single Center	24,449	1982-86	Lanolin alcohol 30%	1.7%	
NACDG	Multicenter	26,479	1994–2006	Lanolin alcohol 30%	2.5% ←	
NACDG	Multicenter	43,691	2001-2018	Both	3.27%	
			2001-2011	Lanolin alcohol 30%	2.16% ←	
			2011-2018	Amerchol 50%.	4.63%	
IVDK	Multicenter	82,251	2006-2016	lanolin alcohol 30%	2.38% ←	
		115,885	2006-2016	Amerchol 50%	3.48%	
	Multicenter	79,969	2006-2016	Both	Both	2.05%
					Lanolin alcohol 30%	1.19%
Amerchol 50%					1.43%	
				At least one	4.67%	

Prevalence

- Prevalence of sensitization in the present study (1.64%) overlapped with other studies using the same patch test formulation
- Decreasing sensitization over time, consistently with a NACDG study on 26,479 patients patch-tested with lanolin alcohol 30% during 1994–2006 – mean prevalence of 2.5% (decreasing from 3.7% in 1996–1998 to 1.8% to 2005–2006)
- Variable prevalence of sensitization in the open literature, likely reflecting different patch test formulations employed
- Suspected higher prevalence of false positives to Amerchol® L-101, due to irritative effects on human skin
- Variability by research center and over time in the present study endorsed the ongoing debate of the clinical relevance of lanolin as a allergen

Risk factors

- **Male sex** (aOR=1.34; 95%CI; 1.09; 1.35%)
- **Age 38+ years** (especially 61+ years)
- **Leg dermatitis** (aOR=1.67; 95%CI: 1.27; 2,19)
- **House painting occupation** (aOR=7.56; 1.73; 33;15)

		Terms		ALL PATIENTS		MALES		FEMALES	
				Lanolin + N (row %)	aOR (95%CI) (25,907 obs.)	Lanolin + N (row %)	aOR (95%CI) (8127 obs.)	Lanolin + N (row %)	aOR (95%CI) (17,513 obs.)
Sex		Females		304 (1.47)	reference				
		Males		197 (1.98)	1.34 (1.08; 1.65)				
Leg CD (Interaction term)	No	Age (years)	<28	73 (1.16)	Reference	31 (1.58)	reference	42 (0.97)	reference
			27-37	74 (1.15)	1.02 (0.71; 1.47)	27 (1.27)	1.02 (0.57; 1.83)	47 (1.10)	1.00 (0.63; 1.59)
			38-48	101 (1.64)	1.50 (1.06; 2.12)	30 (1.55)	1.02 (0.56; 1.88)	71 (1.69)	1.70 (1.11; 2.60)
			49-60	99 (1.74)	1.53 (1.07; 2.19)	45 (2.41)	1.77 (1.01; 3.07)	54 (1.41)	1.32 (0.82; 2.12)
			61+	73 (1.16)	1.67 (1.10; 2.53)	64 (3.15)	1.71 (0.87; 3.36)	89 (2.21)	1.54 (0.90; 2.64)
	Yes	Age (years)	<28	3 (0.98)	0.78(0.24; 2.50)	2 (1.71)	1.03 (0.24; 4.47)	1 (0.53)	0.50 (0.07; 3.68)
			27-37	2 (0.66)	0.57(0.14; 2.36)	0	1.05 (0.20; 5.51)	2 (1.03)	0.99 (0.24; 4.19)
			38-48	7 (1.79)	1.63 (0.73; 3.62)	3 (2.00)	1.48 (0.43; 5.07)	4 (1.66)	1.66 (0.58; 4.77)
			49-60	11 (2.82)	2.34 (1.20; 4.57)	6 (3.17)	2.14 (0.84; 5.48)	5 (2.49)	2.35 (0.89; 6.20)
			61+	42 (5.75)	4.21 (2.59; 6.85)	16 (4.94)	2.92 (1.34; 6.39)	26 (6.40)	5.33 (2.87; 9.89)
Occupation		Administrative		87 (1.30)	Reference	38 (1.84)	Reference	49 (1.06)	Reference
		House painters		3 (11.54)	7.69 (1.75; 33.76)	0	NA	3 (14.29)	10.92 (2.39; 49.90)
Calendar year		1997-2002		190 (2.08)	Reference	80 (2.71)	Reference	110 (1.78)	Reference
		2003-2007		131 (1.79)	0.49 (0.36; 0.66)	46 (1.90)	0.49 (0.30; 0.81)	85 (1.73)	0.48 (0.32; 0.72)
		2008-2012		57 (1.02)	0.43 (0.32; 0.59)	23 (1.30)	0.48 (0.30; 0.78)	34 (0.90)	0.41 (0.27; 0.61)
		2013-2017		69 (1.49)	0.47 (0.34; 0.64)	31 (215)	0.47 (0.29; 0.79)	38 (1.19)	0.48 (0.32; 0.71)
		2018-2021		54 (1.35)	0.34 (0.22; 0.51)	17 (1.26)	0.30 (0.16; 0.59)	37 (1.40)	0.37 (0.22; 0.61)

Model adjusted for age, sex, center, body area affected and occupation

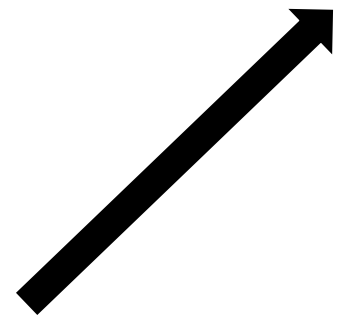
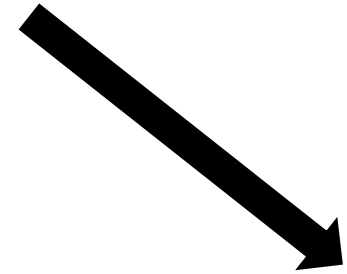


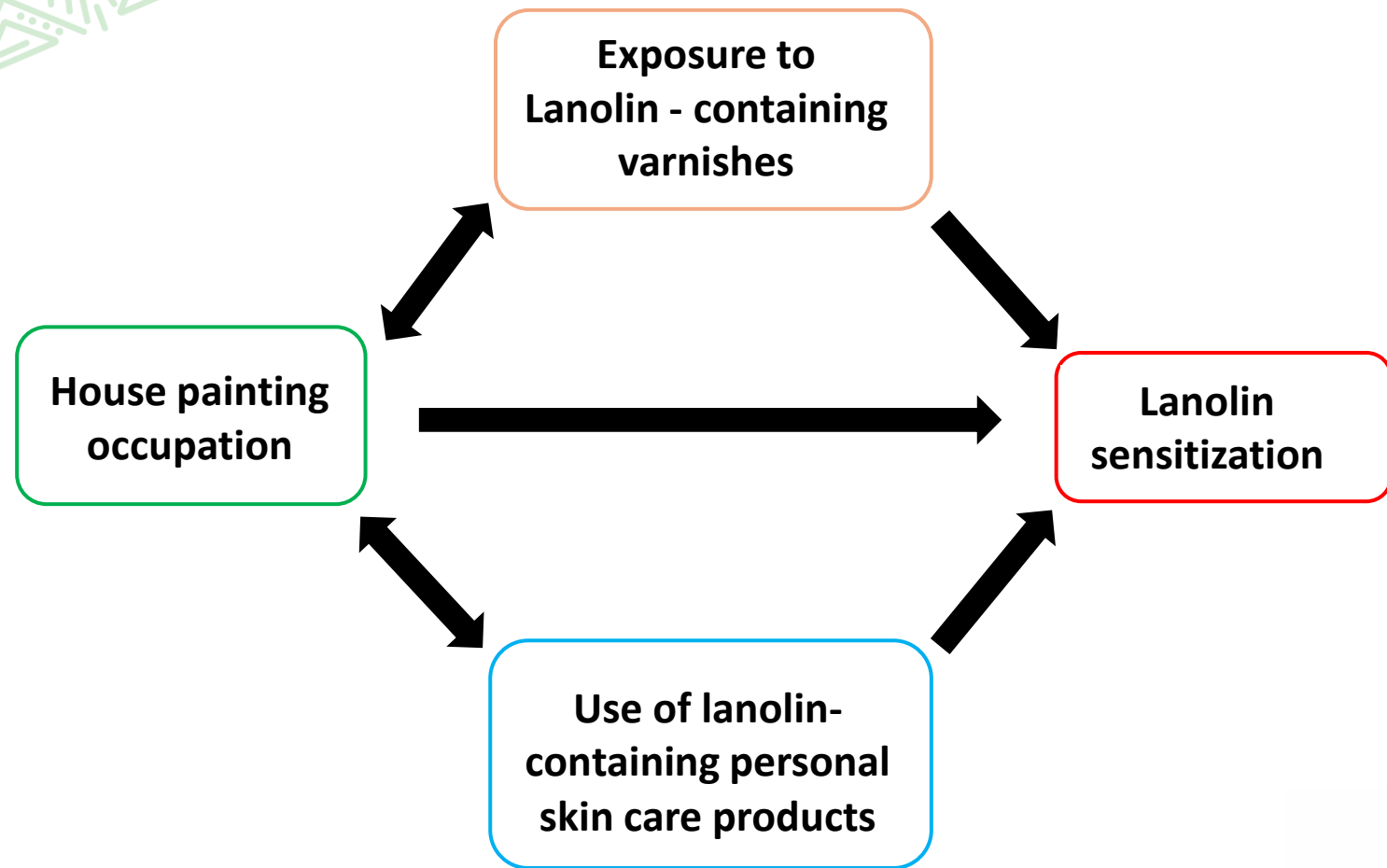
**Leg CD in patients
>48 years**

**Leg ulcer/stasis
dermatitis**

**Use of lanolin-
containing personal
skin care products**

**Lanolin
sensitization**









Article

Sensitization to Lanolin in North-Eastern Italy, 1997–2021: Prevalence, Risk Factors and the Impact of Occupation

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Thank you



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