Statistical Validation of Skindex Between Two Institutions

REINS

PARIS, 2018

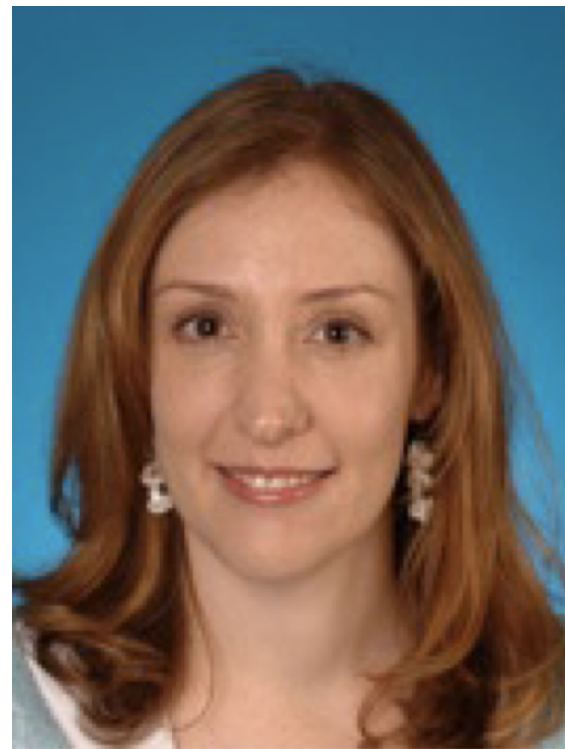# Sydney and Minneapolis Come Together to Help Solve NF1 Skin

Health
Northern Sydney
Local Health District
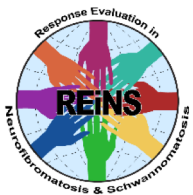
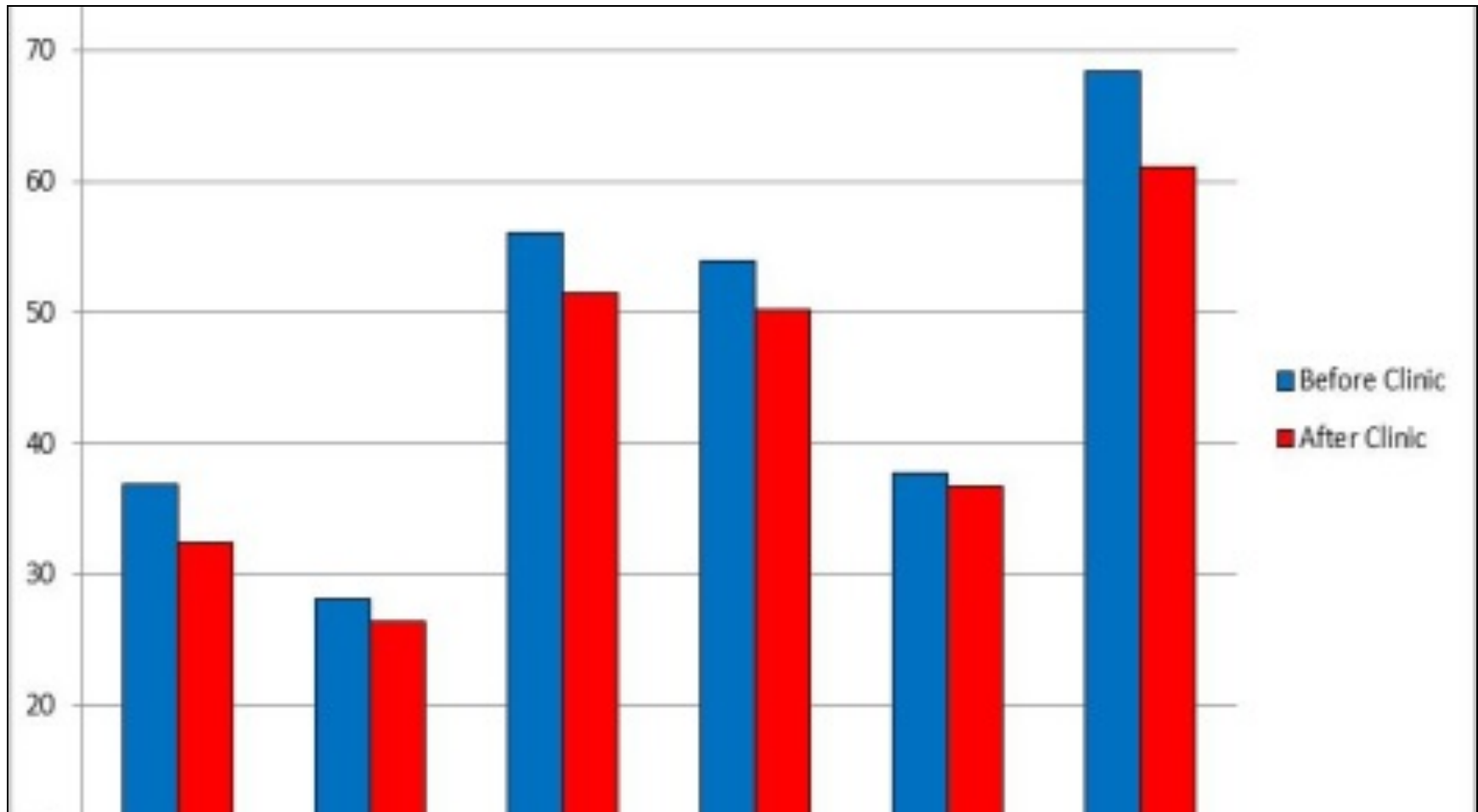University of Minnesota
Masonic Children's Hospital
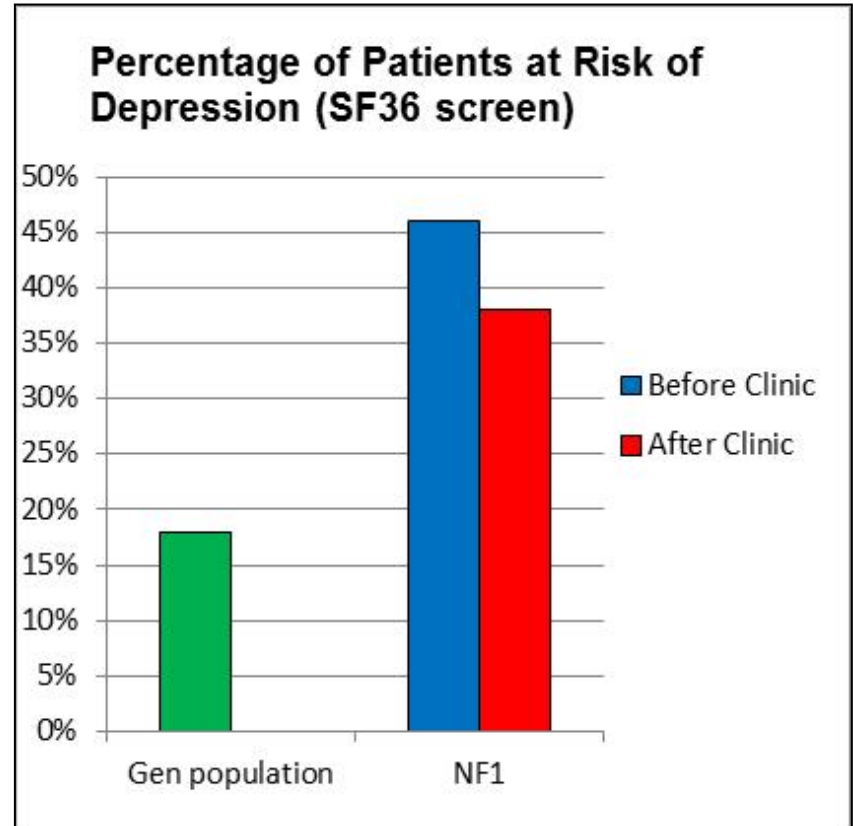
NF Skin Clinic 2015

- Temporary Funding Australian CTF
- Quality Improvement model
- Dermatology and Genetics
  - Excisions and shaving
  - RF ablation
  - LASER funded by CTF/donation- preferred treatment modality
  - Topical rapamycin/ ketotifen

Effect of Treatment on Skin and NF Related Symptoms (Skindex, NFQoL)

QoL Outcomes SF36

Social Functioning and Mental Health with treatment (SF36)

Population Norm

Before Clinic

After Clinic

Social Functioning | Mental Health

Percentage of Patients at Risk of Depression (SF36 screen)

Before Clinic

After Clinic

Gen population | NF1
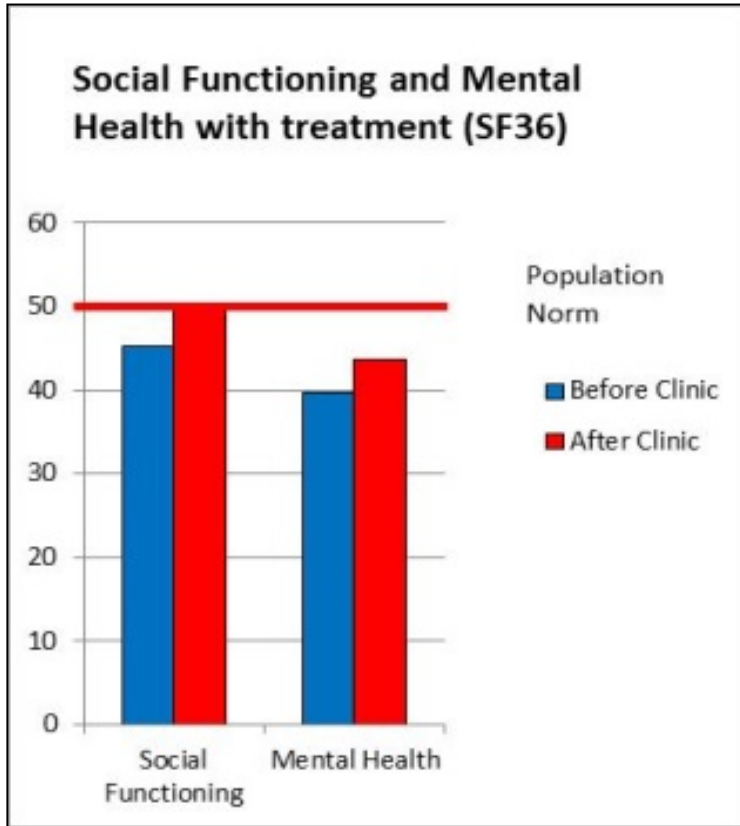
Power: need 100 patients - aim for end 2019 and more definitive treatments in 2019

Management of Itch in Neurofibromatosis Type 1 (NF1): A Single-centre Experience

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Children's Tumour Foundation
CONQUERING NF

Background

- Previous studies have reported a high frequency of itch (19-70%) amongst individuals with Neurofibromatosis Type 1 (NF1)[1,2,3].
- Chronic itch can be an independent factor for altered QoL, disrupting sleep and daily living[2].
- NF1-associated itch has been postulated to be of neuropathic origin, resulting from neuronal or glial damage[4].
- We selected a tricyclic antidepressant as our preferred treatment option based on its effectiveness on neuropathic itch[5].
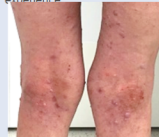- Here we report on the characteristics and management of itch in NF1 from a single-centre experience.

Figure 1. Skin lacerations from chronic itch in NF1.

- This study aims to characterise chronic itch in NF1 and evaluate the effectiveness of a tricyclic antidepressant for the management of NF1-associated itch.

Method

- Adults (N=32) attending an NF1 clinical genetics dermatological service (skin clinic) in Sydney, Australia (Table 1).
- Median age 39y, range 26-69y.

Table 1. Patient characteristics (N=32)

Gender	Female	19
	Male	13
Age	25-34	9
	35-44	12
	45-54	5
	55-64	2
	>65	4

- As part of routine clinical care since 2017, patients attending the skin clinic are questioned regarding their experience of itch and previous treatments.
- Patients who reported itch were offered treatment, and outcomes were recorded and analysed.

Results

Clinical Characteristics

- 78% (25/32) of patients described itchiness of the skin (Figure 1).
- 76% (16/21) moderate to severe.
- Half of patients (7/13) reported daily or almost daily symptoms.
- A further two patients reported severe and daily itch during the warmer months only.
- Distribution was reported to be generalised (7/16) or localised at particular regions of the body (8/16) or to cutaneous neurofibromas (1/16).
- Most patients (12/16) reported trialling treatments with little to no effect.

Figure 2. Frequency bar charts summarising clinical characteristics of itch in NF1.

Treatment

- Of the 16 patients offered, 7 commenced treatment with a low dose tricyclic antidepressant (Table 2).
- Barriers for uptake include minimal concerns, unacceptable side effects, medication stigma and non-compliance.
- Six patients reported improvements and one ceased treatment due to unrelated health complications.
- Adverse effects included weight gain, sedation and a wearing-off effect.
- Two patients with weight gain reported a significant improvement to itch and daily living, preferring to continue treatment despite adverse effects.

Table 2. Patient characteristics and outcomes of treatment of itch with tricyclic antidepressant.

Patient	Gender	Itch Severity	Improvement to Itch	Other Outcomes	Dose Changes
1	Female	Moderate	Some	Sedation	Reduced
2	Male	Moderate	Some	Sedation	Treatment ceased
3	Male	Moderate	Some	Improved sleep	Unchanged
4	Female	Moderate	Great	Weight gain	Unchanged
5	Female	Moderate	N/A	Unrelated health complications	Treatment ceased
6	Male	Severe	Great	None	Unchanged
7	Female	Severe	Great	Improved sleep, Wearing-off effect, Weight gain	Increased

Conclusions

- Consistent with other reports, chronic itch in NF1 is common in our skin clinic cohort and can impact on quality of life.
- NF1-associated itch is amenable to effective treatment with low dose tricyclic antidepressant.
- When seeking treatment outside of a specialist NF service, many patients received treatment that was ineffective and potentially harmful.
- We hope these findings will increase awareness of itch as a manifestation of NF1 and facilitate development of best practices for clinical management of this potentially debilitating symptom.
- Findings were used to guide the development of patient-reported outcome measures for standardised long-term evaluation of treatment efficacy.

References

1. Khosrotherani K, et al. Am J Med Gen, 2005, 132(1), 49-53.
2. Brenaut E, et al. Acta Derm Venereol, 2015, 96(3), 398-399.
3. Fjermestad KW, et al. J Genet Couns, 2018, 27(5), 1102-1110.
4. Misery L, et al. Nat Rev Neurol, 2014, 10, 408-416.
5. Weisshaar E, et al. Acta Derm Venereol, 2012, 92(5), 563-586

## Acknowledgement

NSW GOVERNMENT | **Health** Northern Sydney Local Health District

Now added 5d itch survey to screening PROMs

Question 1: Do the RNS and UMN patient populations differ for the various clinical factors?

Variable	Overall (n = 79)	RNS (n = 40)	UMN (n = 39)	p-value
Skindex (total avg)	30.7 (25.9)	38.8 (25.6)	22.4 (23.9)	0.004
Skindex (physical avg)	31.1 (24.0)	37.1 (24.6)	24.9 (21.9)	0.022
Skindex (emotions avg)	39.7 (32.6)	51.6 (32.2)	27.4 (28.4)	<0.001
Skindex (fuctional avg)	21.5 (25.0)	26.7 (25.0)	16.2 (24.1)	0.060
Skindex (Itch Q)	53.2 (32.9)	57.5 (33.6)	48.7 (31.9)	0.237
Age	38.7 (12.7)	40.7 (12.4)	36.7 (12.8)	0.159
Gender, M (%)	32 (40.5%)	15 (37.5%)	17 (43.6%)	0.650
# of cut. NFS				
0	6 (7.6%)	0 (0%)	6 (15.4%)	
1-19	15 (19.0%)	6 (15%)	9 (23.1%)	
20-99	17 (21.5%)	11 (27.5%)	6 (15.4%)	0.012
100-500	11 (13.9%)	2 (5.0%)	9 (23.1%)	
>500	29 (36.7%)	20 (50.0%)	9 (23.1%)	
Missing	1 (1.3%)	1 (2.5%)	0 (0%)	
Face, Yes (%)	41 (52%)	18 (45%)	23 (59%)	0.365
Riccardi				
Minimal	2 (2.5%)	1 (2.5%)	1 (2.6%)	
Mild	16 (20.3%)	14 (35%)	1 (5.1%)	
Moderate	41 (52%)	18 (45%)	23 (59.0%)	0.010
Severe	18 (22.8%)	7 (17.5%)	11 (28.2%)	
Missing	2 (2.5%)	0 (0%)	2 (5.1%)	
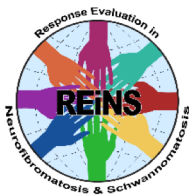
Question 2: What is the relationship between each of the factors, both overall, and within each site?
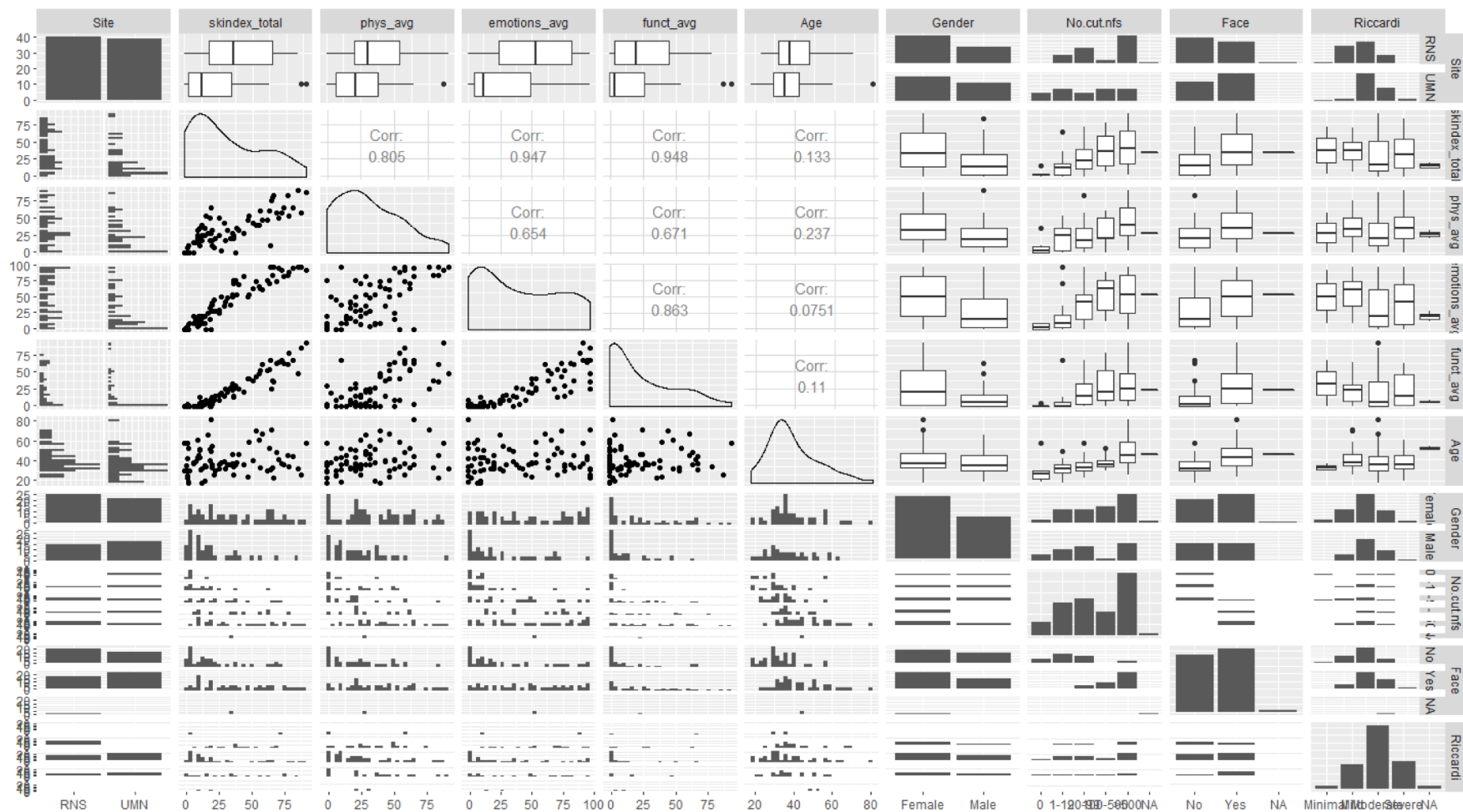
Question 2: What is the relationship between each of the factors, both overall, and within each site?

The correlation between each of the Skindex domains are very strong (all correlations (r) are above 0.67).

Age doesn't correlate very strongly with the Skindex scores (all r < 0.25).

It seems that females have higher Skindex scores on all domains.

As # of cutaneous NFs increase, the Skindex scores also increase. The # of cNFs also increases with age, and females and those with facial cNFs also tend to have more # cNFs.

Those with facial cNFs have higher Skindex scores.

Riccardi severity doesn't seem to change much for the total skindex or the physical average. The more severe Riccardi categories may have small emotional and functional averages.

Question 3: Does the relationship between the total avg skindex score and each of the factors differ by site?

Clinical Factor	Interaction size	p-value
Age	0.35	0.435
Gender (M)	7.5	0.490
# of cut NFs	3.2	0.426
Face	11.4	0.281
Riccardi	5.2	0.530

None of the interactions were significant, so we cannot say that the relationship between the total avg Skindex score different on any of the clinical factors differed by site. This provides some evidence that the data can be combined.

Questions 4: Do the Skindex scores differ between sites, after adjusting for the differences in the various clinical factors?

Response variable	Unadjusted diff (UMN – RNS)	Unadjusted p-value	Adjusted diff (UMN – RNS)	Adjusted p-value
Skindex avg total	-16.4	0.004	-11.6	0.081
Physical avg	-12.2	0.022	-8.0	0.230
Emotions avg	-24.2	<0.001	-16.8	0.036
Functional avg	-10.5	0.060	-7.2	0.292
Itch question	-8.8	0.237	-2.8	0.776

Conclusion

- Overall, the Skindex domain scores at the RNS site were higher than the UMN site. However, the sites also differed among many clinical factors. After adjusting for these differences, the Skindex differences were now smaller, and mostly non-significant.

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