Skin lipids in the development of atopic dermatitis and food allergy

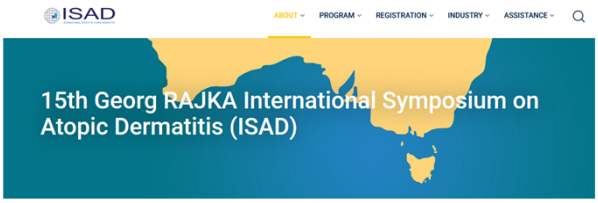
Adrian Lowe

Natalie (Chia-Lun) Chang

Allergy and Lung Health Unit
Melbourne School of Population and Global Health
University of Melbourne.

1

Declarations of interests



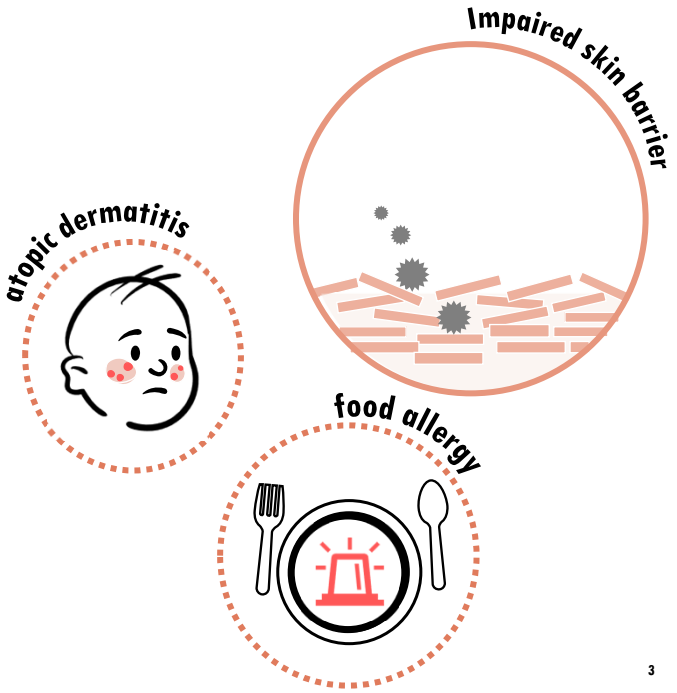
A. J. Lowe has

- received an investigator-initiated grant for unrelated research from
  - GlaxoSmithKline (GSK)
  - Sanofi Regeneron
- received an investigational product (EpiCeram) free of charge from Primus Pharmaceuticals

C-L Chang declares no conflicts of interest

2

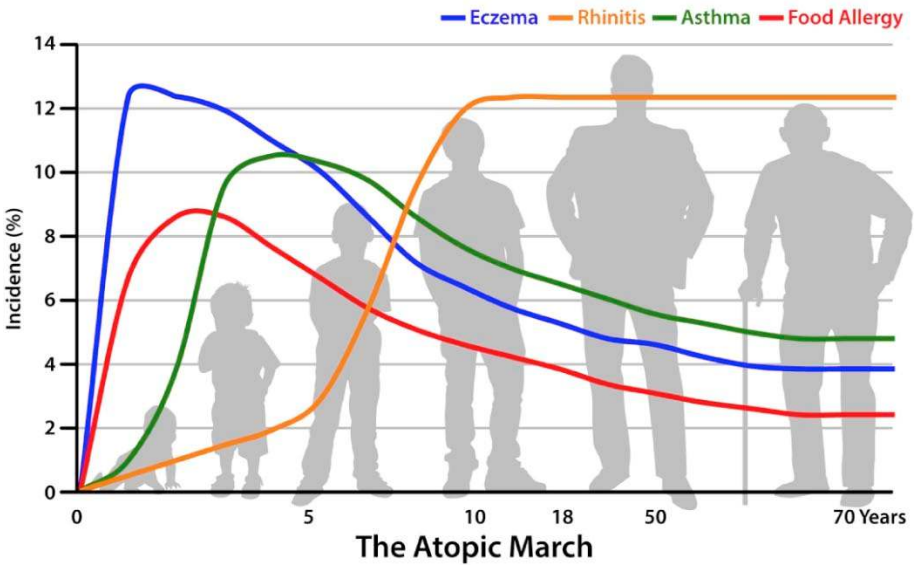
I. Background



3

3

The Atopic March



4

Understanding whether changes in skin lipids profile (a key component of the skin barrier) PRECEDES the development of atopic dermatitis (AD) / food allergy (FA) may be crucial, as this helps to identify predictive biomarkers that could inform

1.
Early life screening programs

2.
Targeted skincare interventions

5

5

AD (6 wks.)

Structure

- Background to skin lipids and role in the skin barrier & allergic disease
- Published work - associations between skin lipids @ 6 weeks & AD
- Ongoing work
  - associations between skin lipids @ 3 weeks & AD
  - associations between skin lipids @ 3 weeks & AD & FA
  - Establishment of skin lipid profiles & AD

6

6

From impaired skin barrier to atopic dermatitis and food allergy

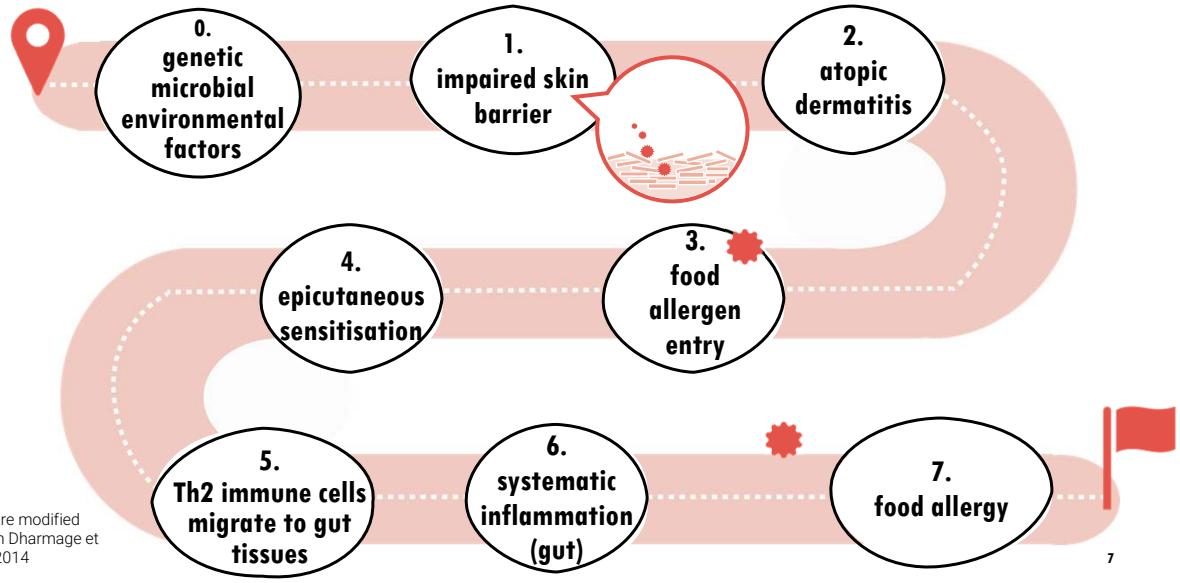
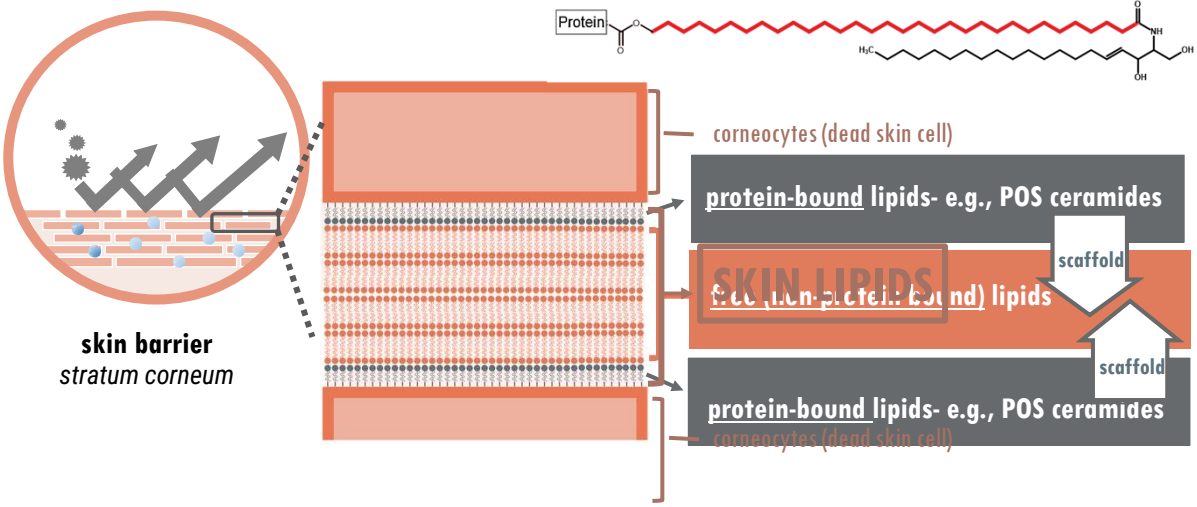


Figure modified from Dharmage et al., 2014

7

7

Skin lipids



8

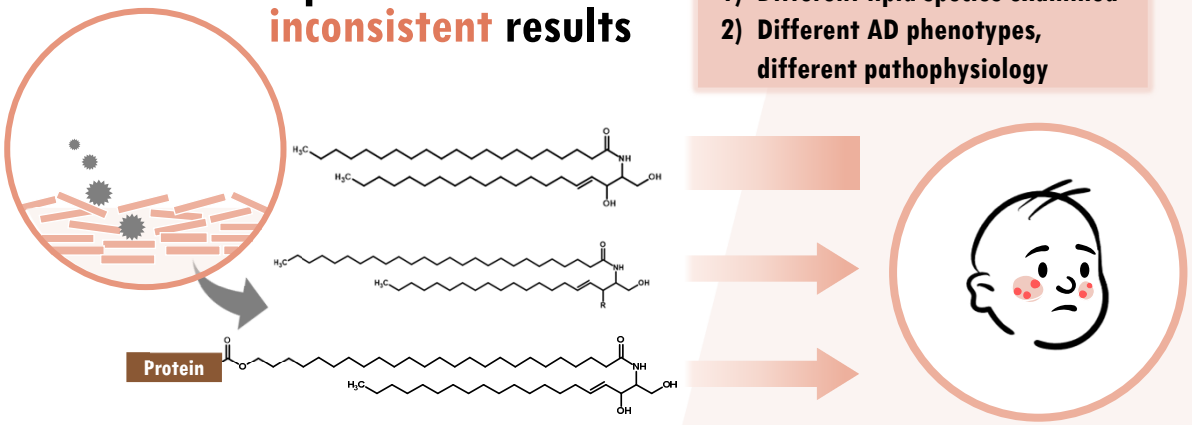
8

3 prospective cohort studies on skin lipids & AD

inconsistent results

WHY?

1) Different lipid species examined
2) Different AD phenotypes, different pathophysiology



skin lipid species

(Rinnov 2023, Berdyshev 2023, Zhang 2023)

subsequent AD

9

9

Aim

"To examine the relationship between skin lipids and subsequent risk of AD and AD phenotypes"

10

10

II. Methods

11

11

Study population- a subset cohort in the PEBBLES study

133 infants (Lowe 2019)
Melbourne Australia
Family history of allergic diseases
Different ethnicity background
(28% Asian 72% Non-Asian)

12

12

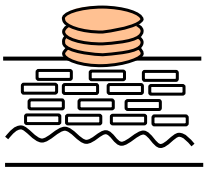
Data collection- prospective study design

Birth 3 wks. 6 wks. 1 yr.

skin lipids sample 1

skin lipids sample 2

AD & food allergy



13

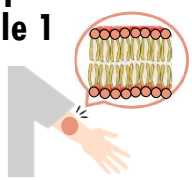
13

Lipid measurements

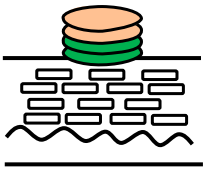
Birth 3 weeks. 6 weeks.

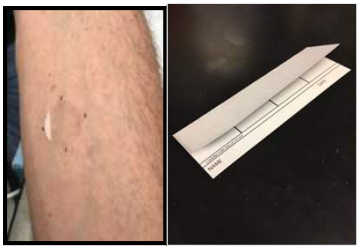
skin lipids sample 1

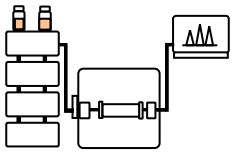
skin lipids sample 2



Non-invasive tape strips







liquid chromatography-tandem mass spectrometry (LC-MS/MS)

14

14

Outcome definitions

Birth 3 weeks. 6 weeks. 1 yr.

food allergy

Oral food challenges
Allergic sensitisation
Parent-reported food reaction history

AD

UK Working Party Criteria

15

15

AD phenotypes by 1 year of age

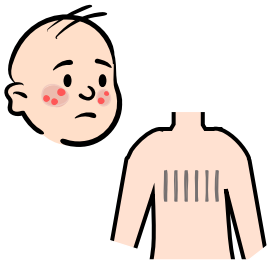
AD phenotypes

- AD with sensitization
- AD without sensitization
- Only sensitization
- No sensitization no AD

AD diagnosis & Skin Prick Test

3 food allergens
peanut, egg white, cow's milk

3 aero allergens
rye grass, house dust mite, cat dander



16

16

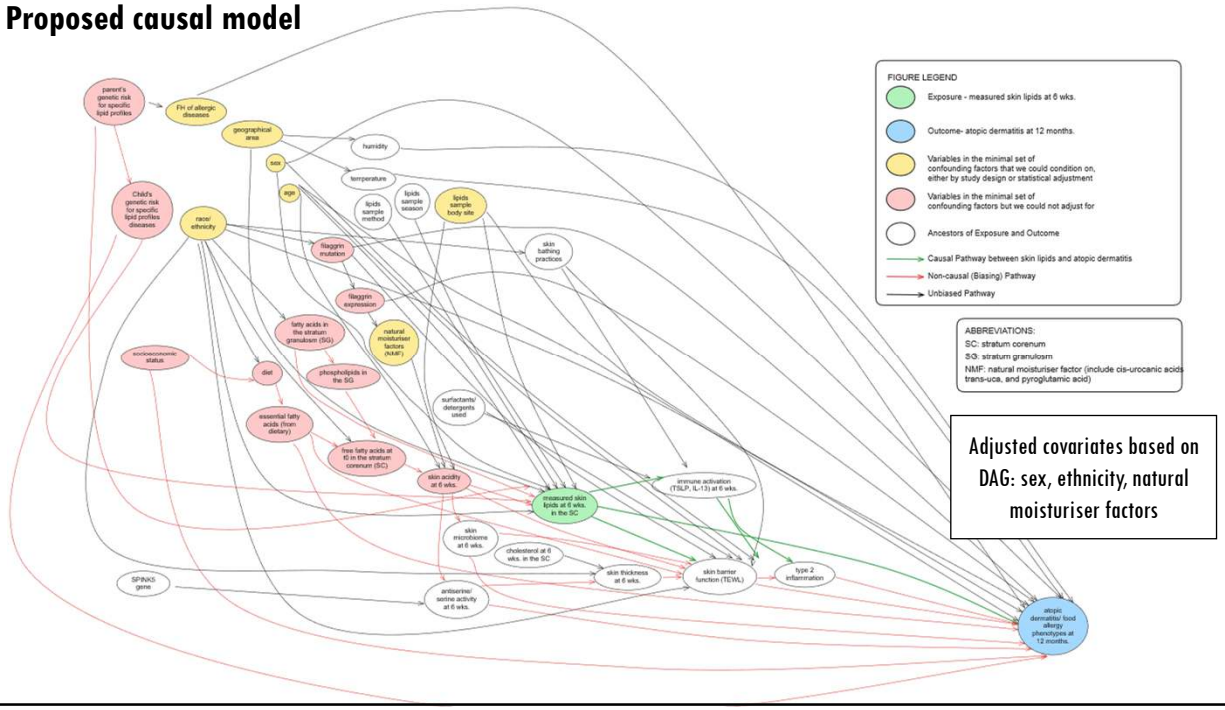
Statistical analysis

- All lipid species were first standardized into Z score → associations represent per 1 standard deviation increase
- Associations- multivariable logistic regression (adjusted for sex, ethnicity, natural moisturizer factors)
- R statistical package (version 4.3.1)

17

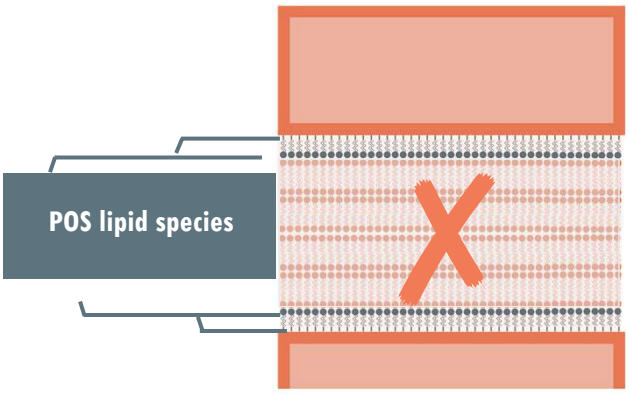
17

Proposed causal model



18

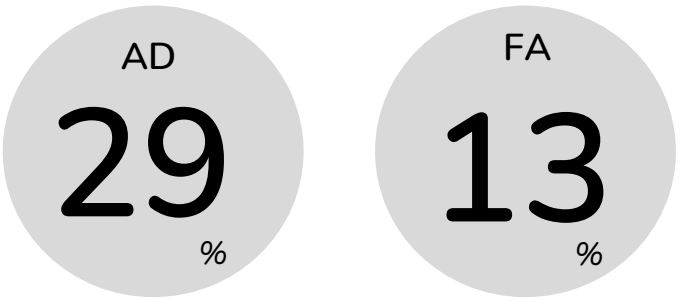
III. Key results



19

19

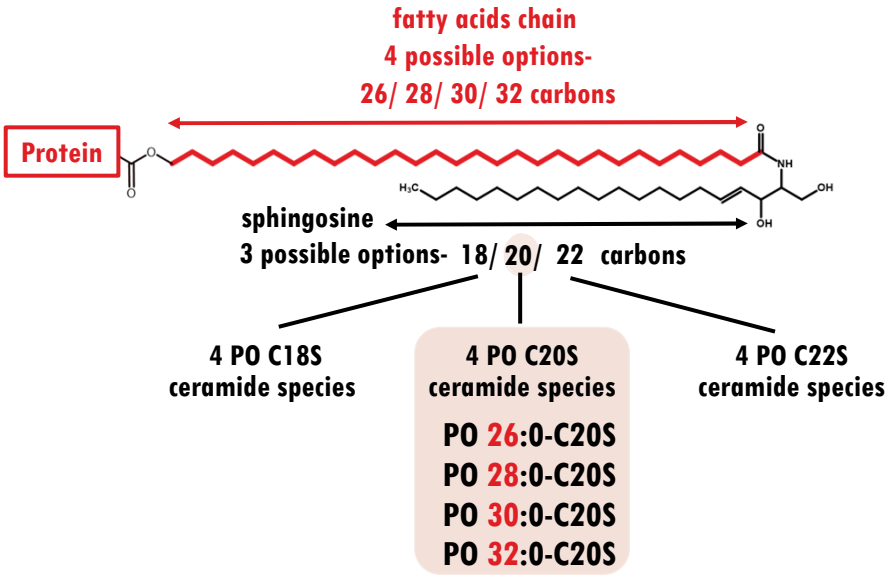
Prevalence of outcomes



20

20

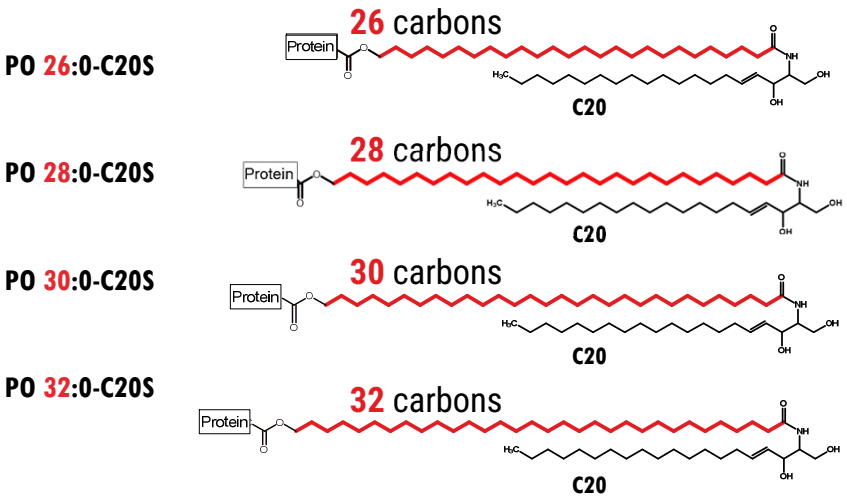
12 POS ceramide species



21

21

4 PO C20S ceramide species at 6 weeks

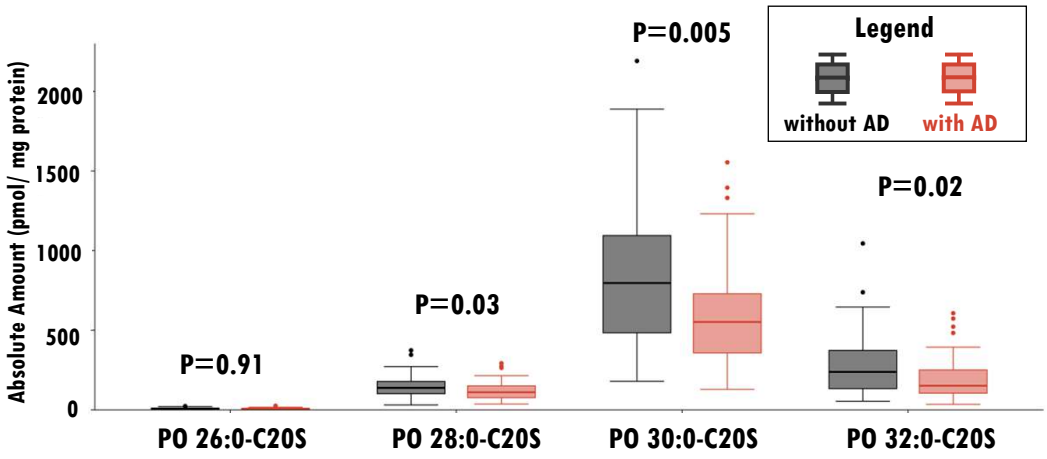


22

22

AD (6 wks.)

Absolute amount of 4 PO C20S species at 6 weeks & AD by 1 year



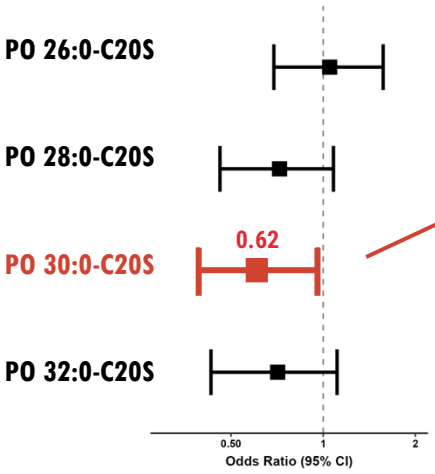
PO C20S ceramide species at 6 weeks were lower in children with AD by 1 year of age

23

23

AD (6 wks.)

Adjusted associations – 4 POS ceramide species at 6 weeks & AD by 1 yrs.



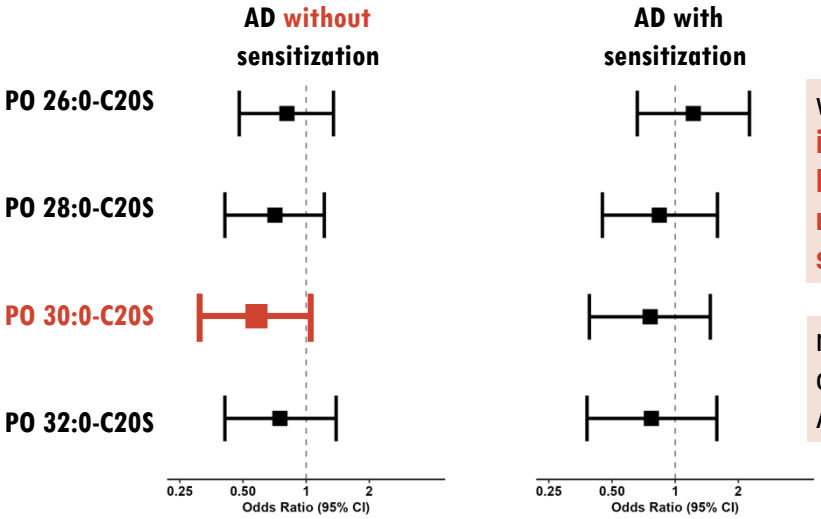
Increase levels in **PO30:0-C20S** (30-carbon fatty acid ceramides) was significantly associated (P=0.04) with a **reduced** risk of **developing AD**

The trend of association for PO28:0-C20S & PO32:0-C20S were similar to PO30:0-C20S, although not reaching statistically significant

24

AD (6 wks.)

4 PO C20S ceramide species at 6 weeks & AD phenotypes by 1 yrs.



weak association between **increased levels** of **PO30:0-C20S** and **reduced** risk of **AD without sensitization**

no association between any of the POS ceramides and AD with sensitization

25

25

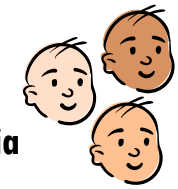
IV. Key takeaways

26

26

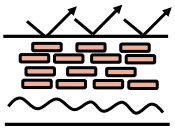
KEY TAKEAWAYS

Increased levels of most POS ceramide species were associated with a reduced risk of developing AD in an ethnically diverse (Asian & Non-Asian) cohort in Australia



These findings were consistent with a previous study conducted in an Asian cohort in South Korea

This suggests that POS ceramides are important for forming an effective skin barrier regardless of the ethnic background and the geographic region the child lives in



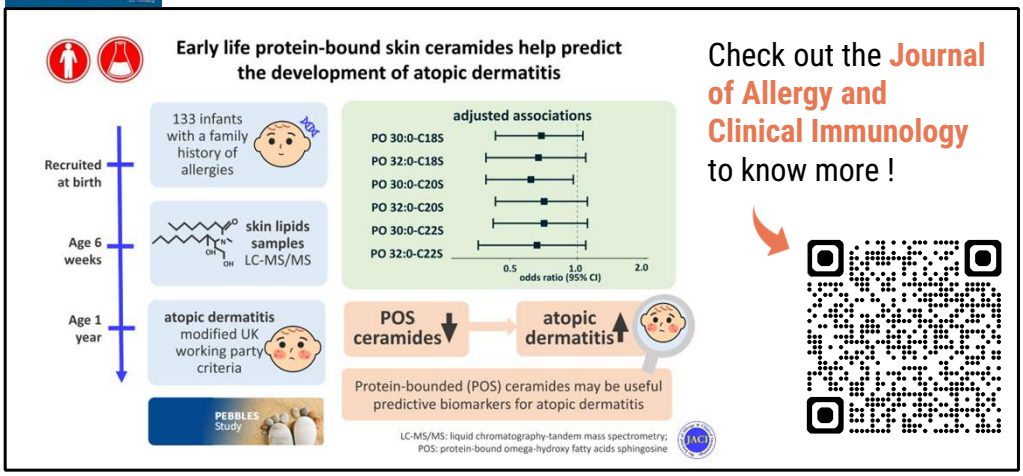
Results may inform strategies to increase POS to reduce incidence of AD

27

27

Chang et al. 2025. 155(3):856-864.

6 weeks lipid samples



28

28

But …

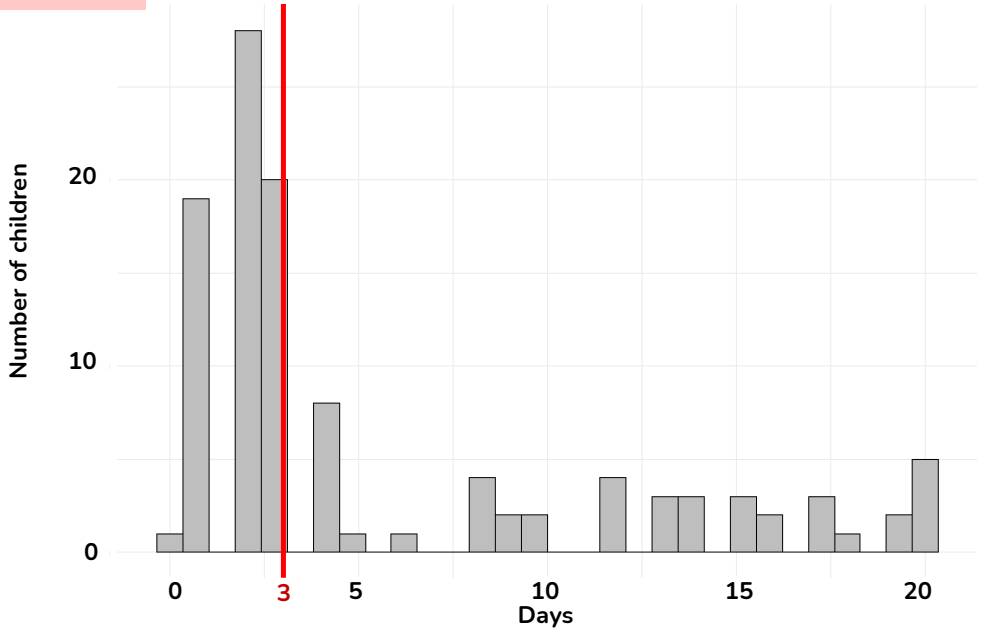
- Do samples collected close to birth predict outcomes?
- Do skin lipids predict the development of food allergy?
- Is it reasonable to look at each skin lipid species in isolation?

29

29

Study Characteristics (112 Children)

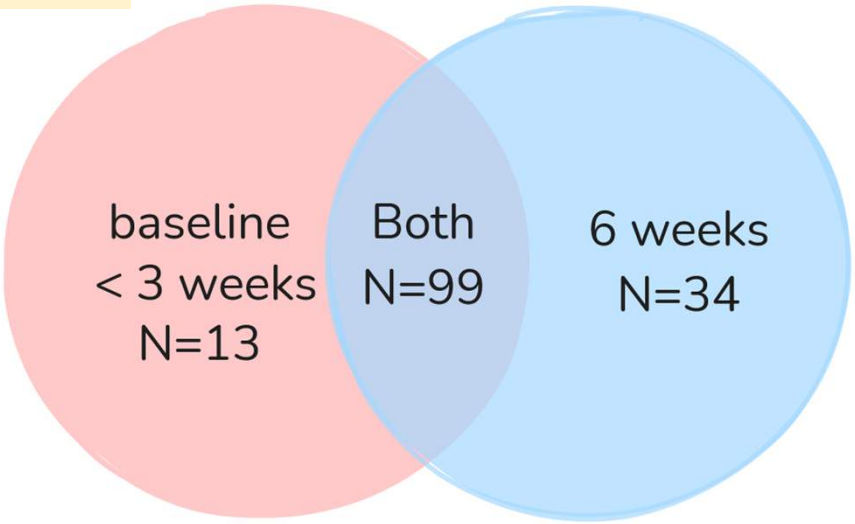
Median sampling time



30

30

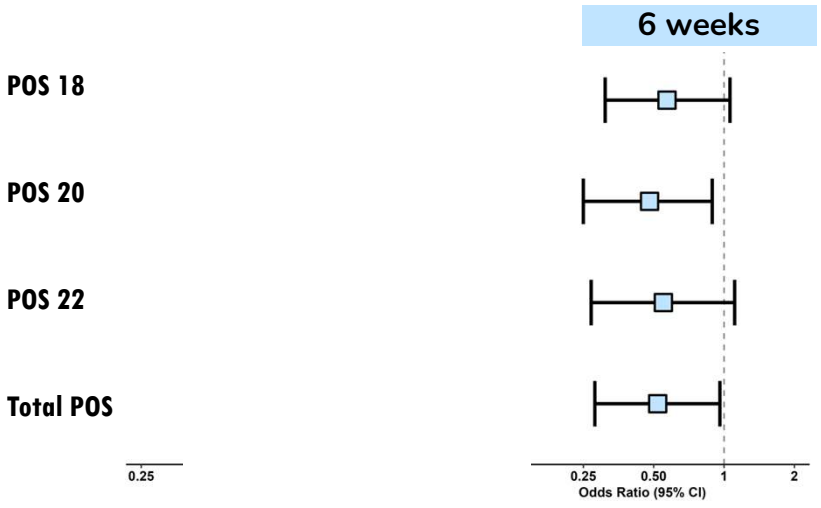
Children included in the analysis



31

31

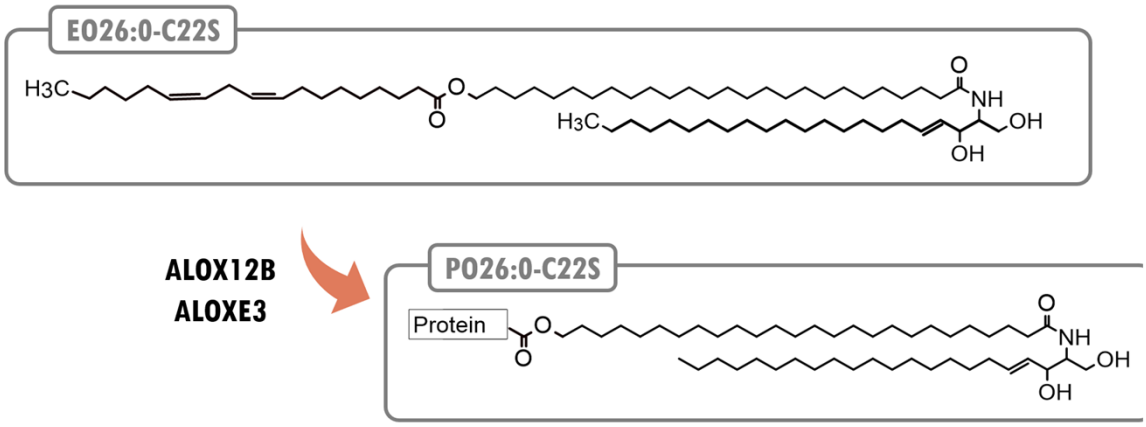
POS at baseline & 6 weeks & Atopic Dermatitis by 1 yrs



32

32

From EOS to POS ceramides

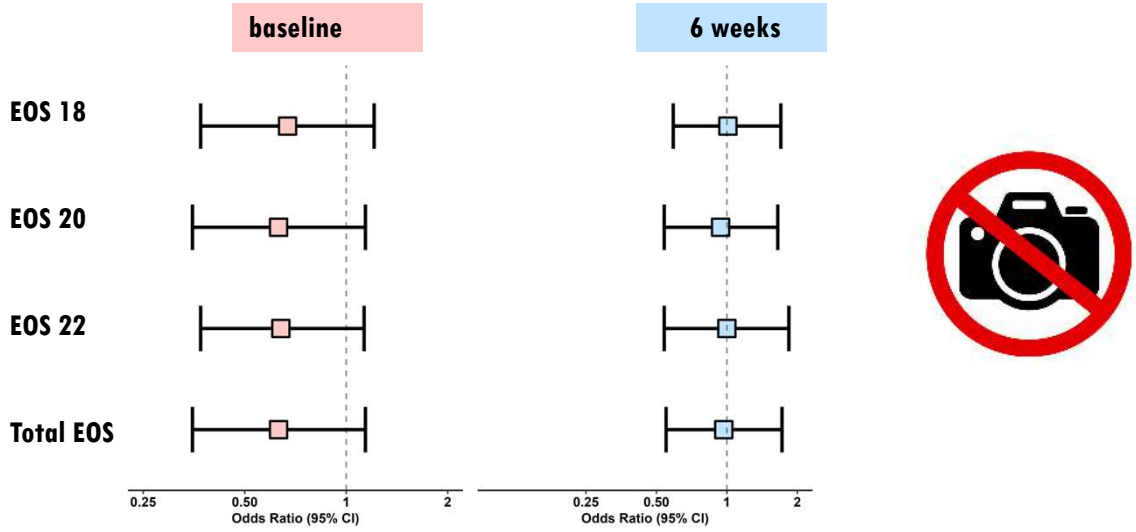


EOS - Esterified omega-hydroxy fatty acids sphingosine

33

33

EOS & Atopic Dermatitis by 1 yrs.



34

34

Association between skin lipids and FA

Only one study has examined AD & FA phenotypes (Berdyshev 2024)

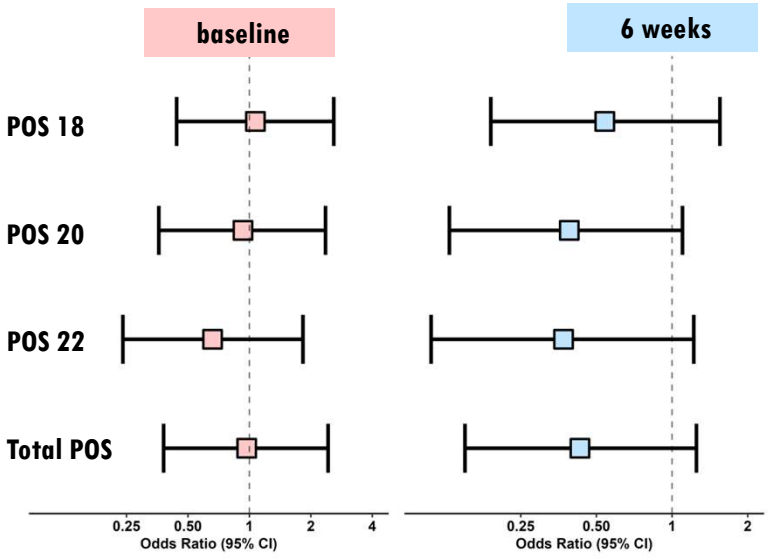
Food Allergy

35

35

CC1

POS & Food Allergy by 1 yrs.



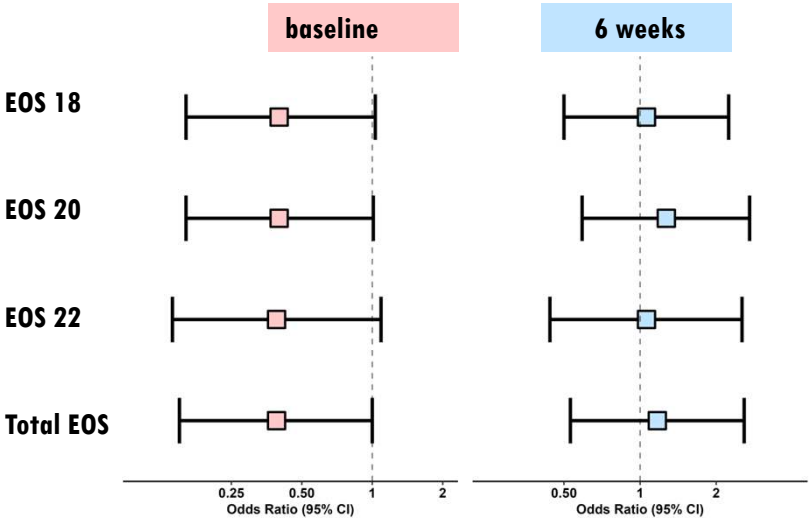
36

36

Slide 36

CC1 Total POS 6 weeeks problem
Chia-Lun Chang, 2025-10-13T02:34:52.306

EOS & Food Allergy by 1 yrs.



37

37

IV. Conclusion

38

38

Summary – POS & EOS and AD & food allergy

Associations between EOS and POS and AD and FA appear vary according to when the skin sample was collected

POS

@baseline - no clear associations
@6 weeks - higher levels appear protective of FA and AD

EOS

@baseline – higher levels associated with reduced risk of FA, and possibly AD
@6 weeks- no clear associations

39

39

KEY TAKEAWAYS

Novel age dependant association with EOS

- Early life environment impairing the transformation of EOS to POS?
- May indicate a brief window of opportunity to intervene to promote conversion from EOS to POS
- Currently unclear what factors drive this conversion

40

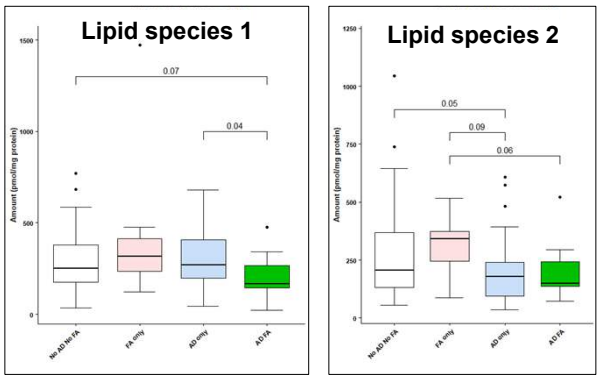
40

V. Future directions

41

41

We could analyse each lipid species individually



… 176 lipid species, 176 analyses

42

42

But…

- Examine each lipid species separately

→ assumes each skin lipid species works individually in the skin barrier

- In reality, different skin lipid species
  - Are associated with the same skin barrier
  - may work together (synergistic interactions) to influence the skin barrier function, and the development of atopic dermatitis & food allergy
  - may share similar biological pathways, enzymes, precursors

43

43

Identification of "skin lipid profiles"

Applied statistical methods to identify possible skin lipid profiles (profiles that include a combination of different species)

44

44

Statistical analysis

R statistical package (4.3.1)

176 skin lipid species (standarised levels – mean = 0; SD = 1)

133 individuals

	cer_n14_0_s18	cer_n16_0_s18	cer_n17_0_s18	cer_n18_0_s18	cer_n20_0_s18	cer_n22_0_s18	cer_n22_
1	-0.57976776	-0.480731591	-0.756618290	-0.56895257	-0.45448012	-0.626873409	-0.4
2	0.43966151	-0.432003672	-0.391300809	-0.65811838	-0.56047594	-0.877095050	-0.7
3	1.38310329	-0.044486202	0.657916022	0.77165167	0.04827530	0.934184963	-0.3
4	0.26782892	-0.635569924	-0.324143964	-0.59616219	-0.74874449	-0.718793130	-1.1
5	-0.69866675	-0.740612891	-0.649447298	-0.48096249	-0.71213230	-0.856927096	-0.9
6	-1.27204788	-0.581453321	-0.910594786	-0.03398906	-0.63112247	-0.379058050	-0.8
7	-0.26902212	-0.739142232	-0.703107583	-0.60248187	-0.30124368	-0.417774944	-0.3
8	-0.11764569	0.021553743	0.391401796	-0.15885716	-0.14910922	0.237286251	-0.1
9	-0.59015376	-0.582178138	-0.235611330	-0.58878353	-0.23693632	-0.252238422	-0.9

.....

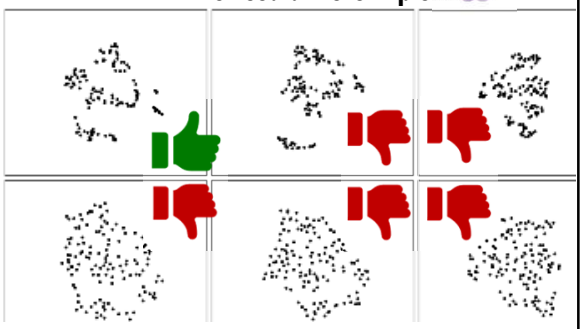
high dimensionality data

UMAP

2D dimension (2D) plot

Influence by the parameters given

Tried different parameters, Browsed different plots 👀



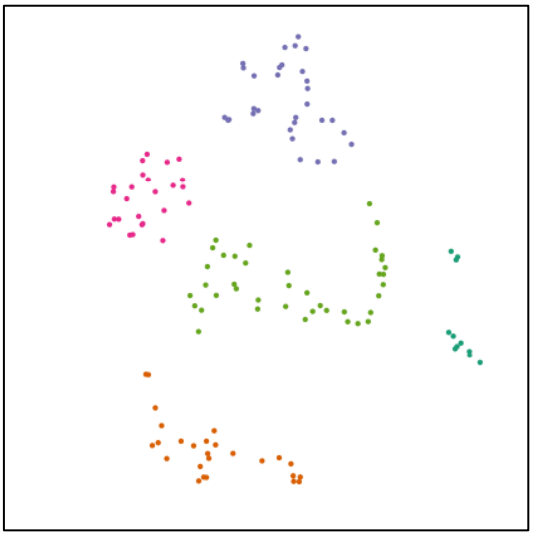
45

III. Key results

46

46

UMAP Plot – 6-week lipids



Profiles

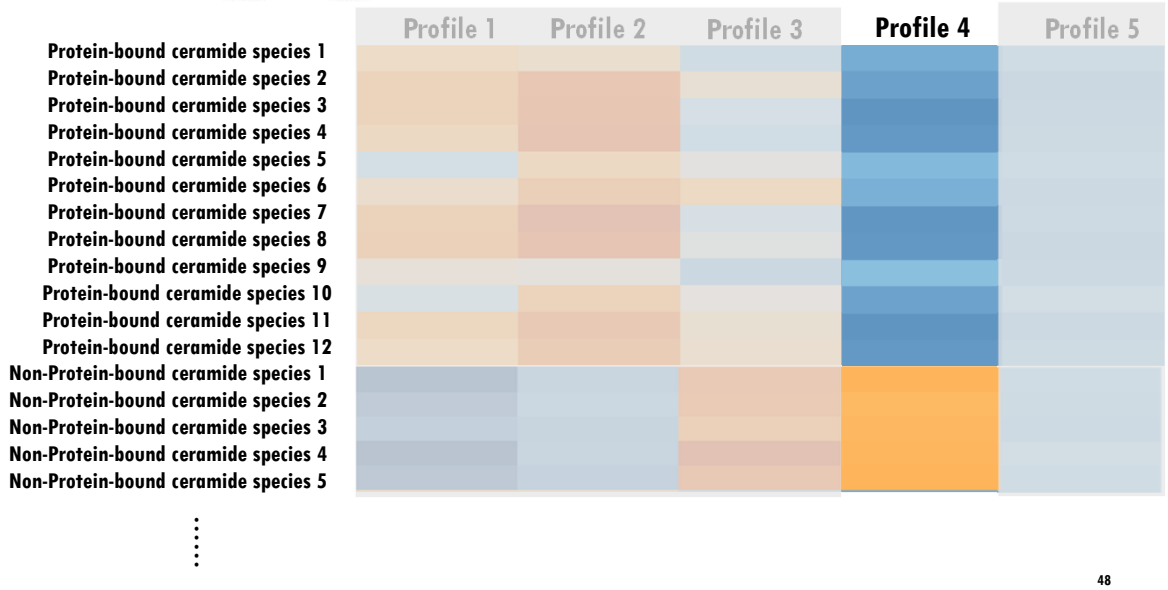
- 1 (n=11)
- 2 (n=26)
- 3 (n=31)
- 4 (n=25)
- 5 (n=40)

47

47

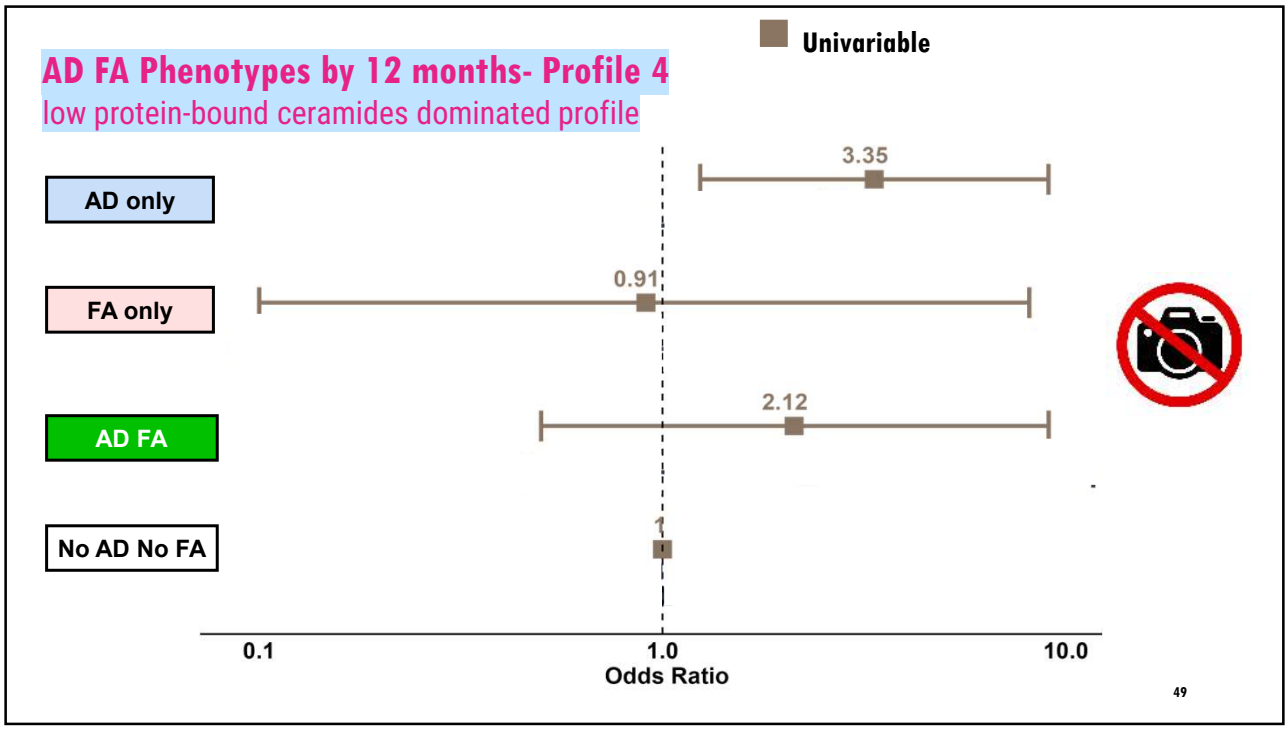
Heatmap

Lower levels — Median Z-Amount — Higher levels

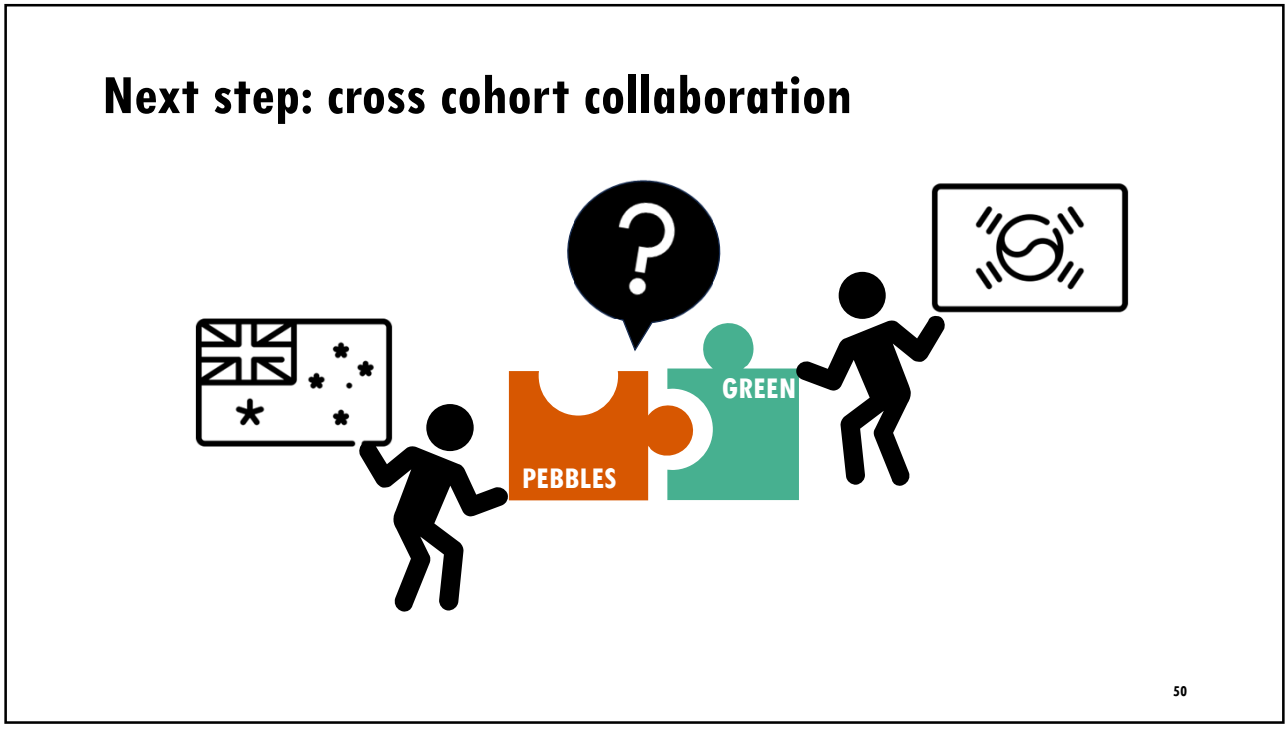


48

48


Univariable
AD FA Phenotypes by 12 months- Profile 4
low protein-bound ceramides dominated profile
AD only
FA only
AD FA
No AD No FA
3.35
0.91
2.12
1
0.1
1.0
10.0
Odds Ratio
49

49


Next step: cross cohort collaboration
PEBBLES
GREEN
50

50

Acknowledgements

Centre for Food Allergy Research
Funded by the NHMRC since 2013
Australian Government
National Health and Medical Research Council
NHMRC
NIH National Institutes of Health
Turning Discovery Into Health
NIH National Institute of Allergy and Infectious Diseases
The University of Melbourne
125 Years National Jewish Health
National Jewish Health
Breathing Science is Life.
ALHU
ALLERGY & LUNG HEALTH UNIT
PEBBLES Study

51

51

Thank you

Adrian Lowe
lowea@unimelb.edu.au

Natalie (Chia-Lun) Chang
natalie.chang@student.unimelb.edu.au

52

52

References

- Berdyshev, E., Kim, J., Kim, B. E., Goleva, E., Lyubchenko, T., Bronova, I., . . . Leung, D. Y. M. (2023). Stratum corneum lipid and cytokine biomarkers at age 2 months predict the future onset of atopic dermatitis. Journal of Allergy and Clinical Immunology 151(5), 1307-1316. doi:10.1016/j.jaci.2023.02.013
- Chang, C. L., Berdyshev, E., Milanzi, E., Lodge, C. J., Lopez, D. J., Bronova, I., ... & Lowe, A. J. (2025). Early-life protein-bound skin ceramides help predict the development of atopic dermatitis. Journal of Allergy and Clinical Immunology.
- Lowe, A., Su, J., Tang, M., Lodge, C. J., Matheson, M., Allen, K. J., . . . Dharmage, S. (2019). PEBBLES study protocol: a randomised controlled trial to prevent atopic dermatitis, food allergy and sensitisation in infants with a family history of allergic disease using a skin barrier improvement strategy. BMJ Open, 9(3), e024594. doi:10.1136/bmjopen-2018-024594
- Rinnov, M. R., Halling, A. S., Gerner, T., Ravn, N. H., Knudgaard, M. H., Trautner, S., . . . Thyssen, J. P. (2023). Skin biomarkers predict development of atopic dermatitis in infancy. Allergy, 78(3), 791-802. doi:10.1111/all.15518
- Zhang, Y., Gu, H., Ye, Y., Li, Y., Gao, X., Ken, K., . . . Yan, W. (2023). Trajectory of stratum corneum lipid subclasses in the first year of life and associations with atopic dermatitis: A prospective cohort study. Pediatric Allergy and Immunology, 34(11), e14045. doi:https://doi.org/10.1111/pai.14045

53

53

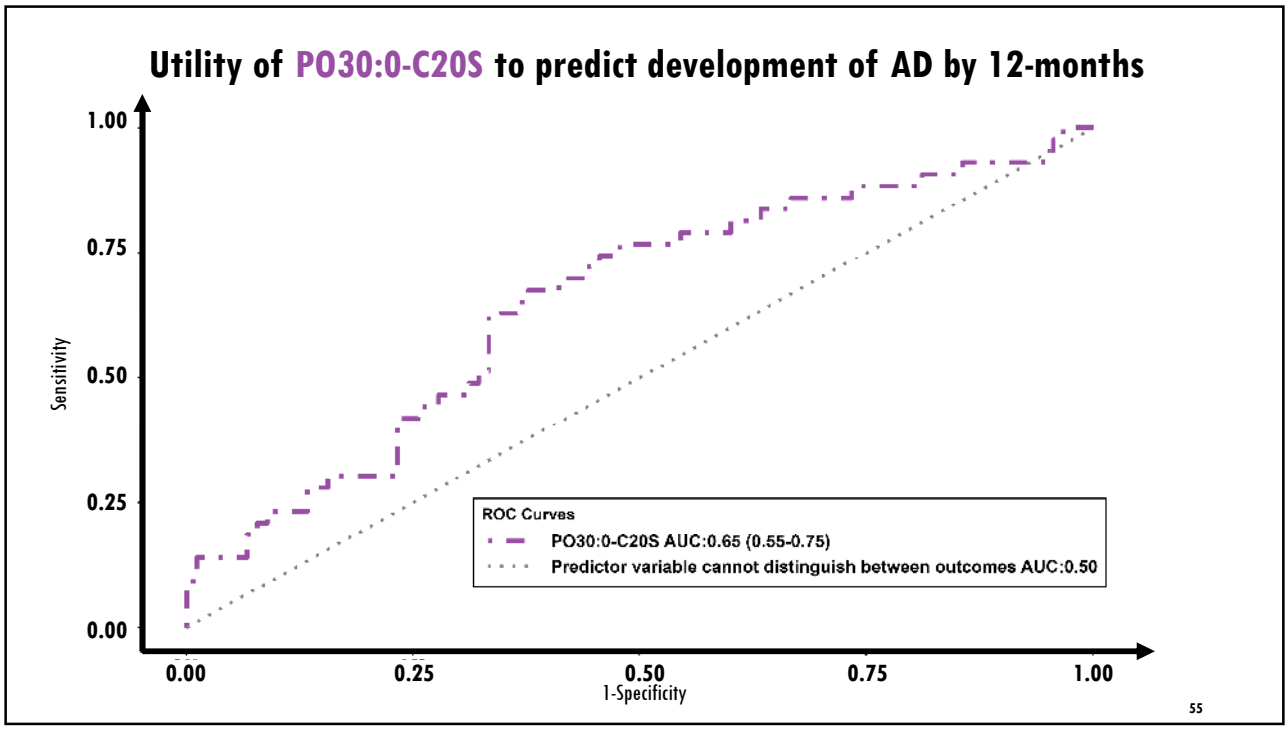
Are skin lipids useful for:

1.

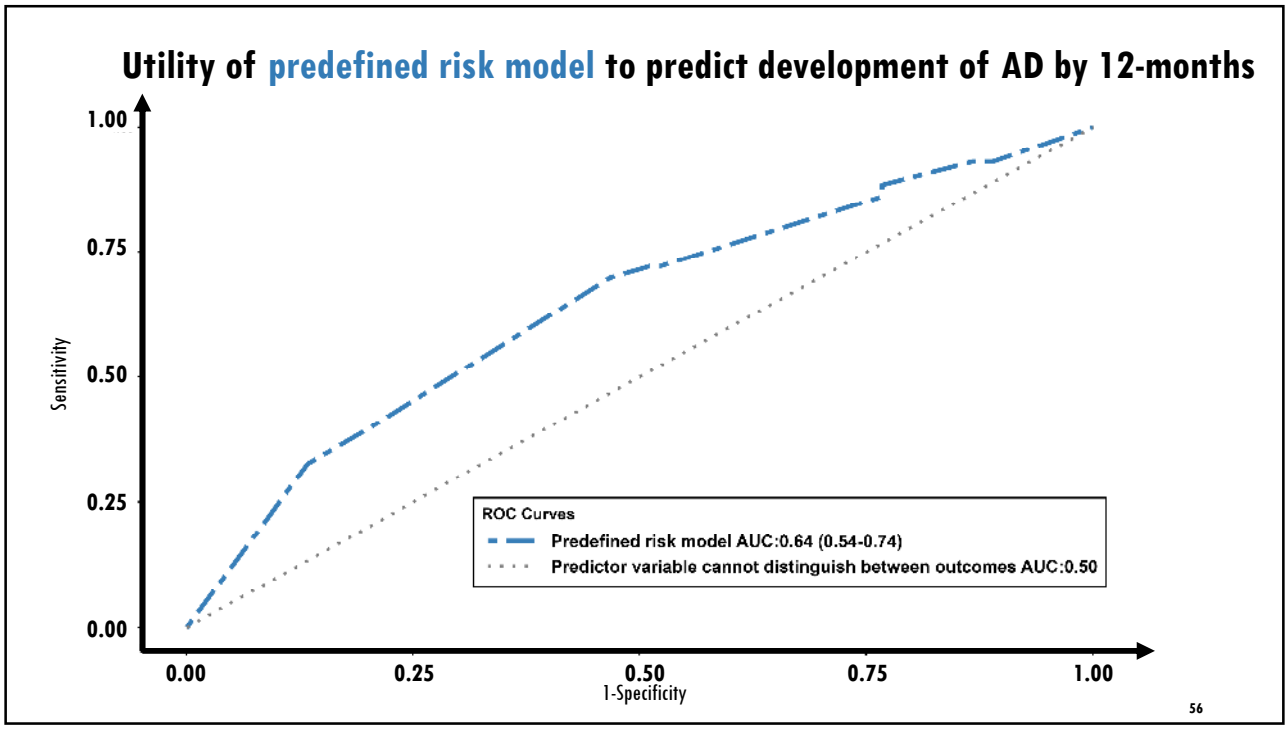
Early life screening program

54

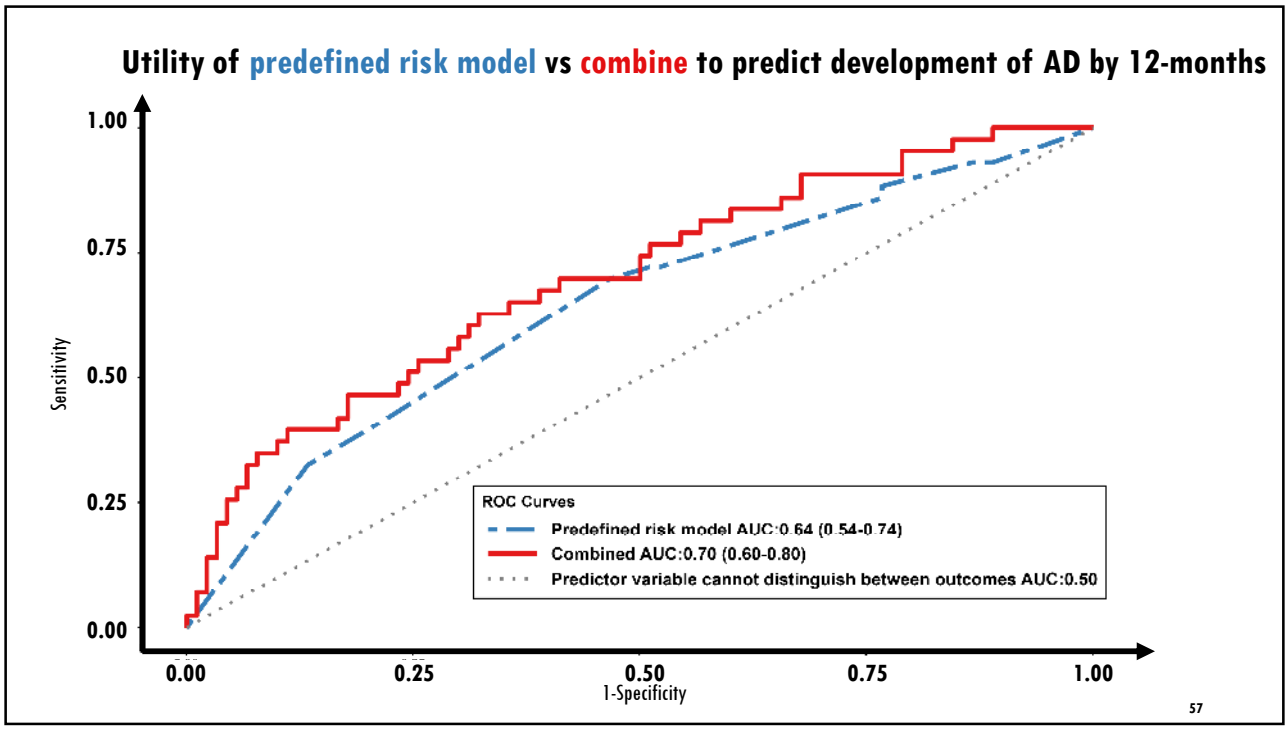
54


Utility of PO30:0-C20S to predict development of AD by 12-months
1.00
0.75
0.50
0.25
0.00
Sensitivity
0.00
0.25
0.50
0.75
1.00
1-Specificity
ROC Curves
PO30:0-C20S AUC:0.65 (0.55-0.75)
Predictor variable cannot distinguish between outcomes AUC:0.50
55

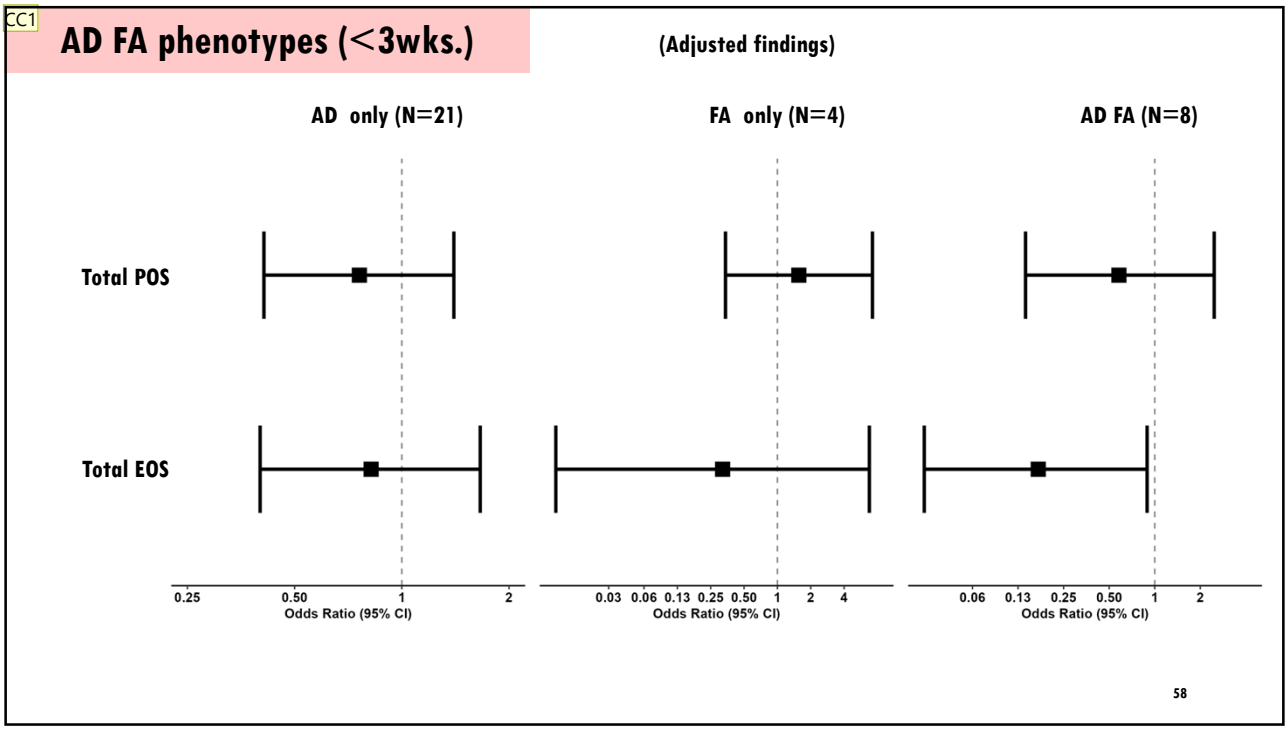
55


Utility of predefined risk model to predict development of AD by 12-months
1.00
0.75
0.50
0.25
0.00
Sensitivity
0.00
0.25
0.50
0.75
1.00
1-Specificity
ROC Curves
Predefined risk model AUC:0.64 (0.54-0.74)
Predictor variable cannot distinguish between outcomes AUC:0.50
56

56


Utility of predefined risk model vs combine to predict development of AD by 12-months
1.00
0.75
0.50
0.25
0.00
Sensitivity
0.00
0.25
0.50
0.75
1.00
1-Specificity
ROC Curves
Predefined risk model AUC:0.64 (0.54-0.74)
Combined AUC:0.70 (0.60-0.80)
Predictor variable cannot distinguish between outcomes AUC:0.50
57

57


CC1
AD FA phenotypes (<3wks.)
(Adjusted findings)
AD only (N=21)
FA only (N=4)
AD FA (N=8)
Total POS
Total EOS
0.25
0.50
1
2
Odds Ratio (95% CI)
0.03
0.06
0.13
0.25
0.50
1
2
4
Odds Ratio (95% CI)
0.06
0.13
0.25
0.50
1
2
Odds Ratio (95% CI)
58

58

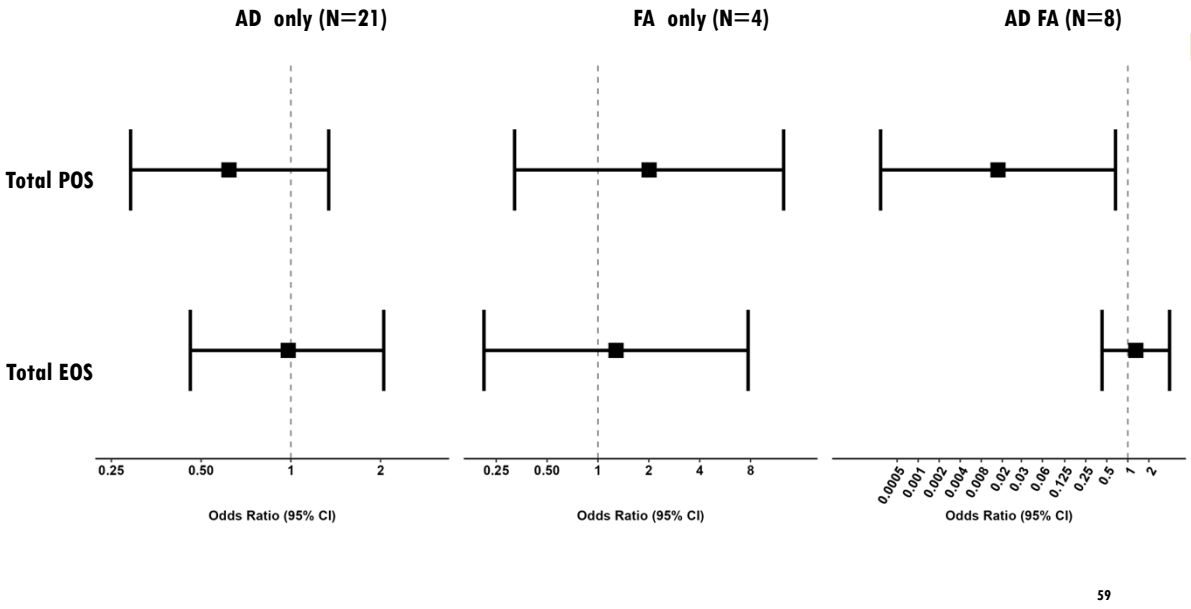
Slide 58

CC1 Among 99 children,
No ad no fa = 63 children;
Only FA= 4 children
Only AD= 21 children
AD fA=8 children
3 children were excluded because they did not have FA data
Chia-Lun Chang, 2025-10-06T10:19:07.124

CC1 0 Very few fa cases
Chia-Lun Chang, 2025-10-06T10:20:29.466

AD FA phenotypes (6 wks.)

(Adjusted findings)



CC1

59

Slide 59

CC1 The total pos and adfa ci is very wide pos (95% ci)- 0.0139 (0.00029, 0.666); with the small lower 95% ci end, the x axis numbers are tilted
Chia-Lun Chang, 2025-10-06T11:00:41.844

CC1 0 Although wide ci, it is interesting that at baseline, it was eos that was associated with adfa, but then at 6 weeks it was pos, and that eos is the precursor of eos, something happening to the skin in the first week of life?
Do you think it is a better if we have eos on top row then pos in next row?
Chia-Lun Chang, 2025-10-06T21:44:19.343