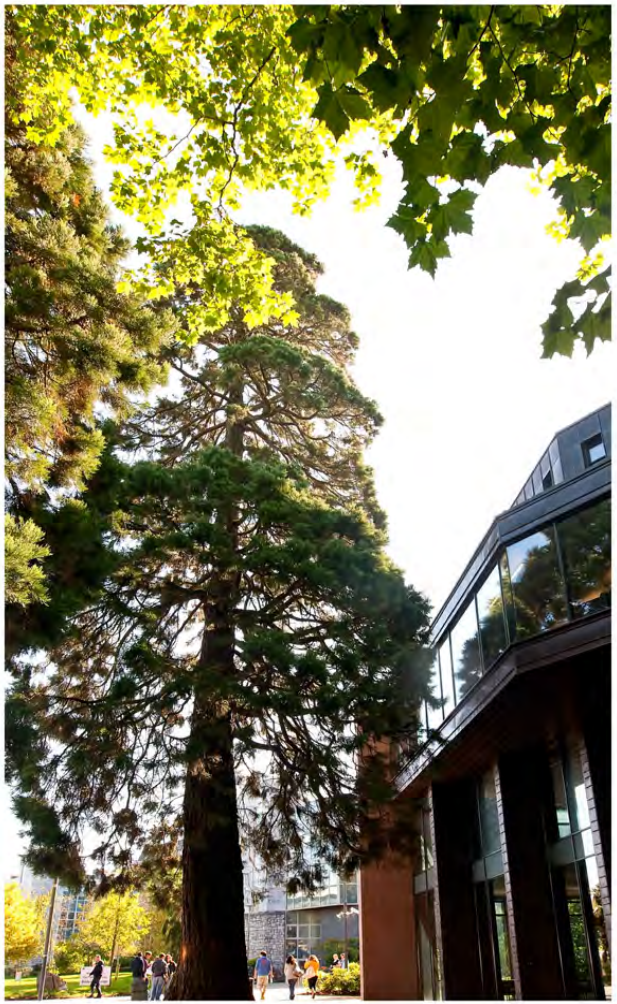

A TRADITION OF INDEPENDENT THINKING

UCC

University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Validating population thresholds

Jonathan Hourihane

Disclosures 2019

- **Employment**
  - UCC, HSE, Ireland
- **Research funding**
  - NCRC, Ireland
  - Dublin Skin and Cancer Hospital Charity
  - DBV Technologies
  - Aimmune Corporation
- **Stockholding / directorships**
  - None
- **Gifts**
  - None
- **Consultancies**
  - Aimmune Corporation
- **Patent**
  - Challenge outcome predictor
- **Societies**
  - IFAN, IAAI, EAACI, AAAAI, BSACI,
  - Clemens von Pirquet Foundation
- **Speaker fees**
  - Thermofisher
  - Danone


food allergy research
& resource program
farrp


FAAM


University College Cork
Coláiste na hOllscoile, Corcaigh


SaludMadrid
Comunidad de Madrid
Hospital Universitario
Clínico San Carlos


UniversitätsSpital
Zürich

CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

Abraham Lincoln knew his risk management "stuff"

POLITICS:

You can fool all of the people some of the time and some of the people all of the time, but you can't fool all of the people all of the time.

FOOD SAFETY:

You can protect all of the people some of the time and some of the people all of the time, but you can't protect all of the people all of the time.

Dose of Peanuts Causing Reactions in Peanut-Allergic Individuals

0.2mg (0.05 mg)	0.4mg (0.1 mg)	1.0mg (0.25 mg)	5.0mg (1.25 mg)	25mg (6.25 mg)	100mg (25 mg)	400mg (100 mg)
Lowest Eliciting Dose in mg whole peanut (mg peanut protein)						
Percent of Peanut-Allergic Population That Would React To Dose	0.3%	1%	4.25%	14%	30%	50%

Ballmer-Weber and Hourihane

Peanut 1 shot paper

Food, drug, insect sting allergy, and anaphylaxis

Peanut Allergen Threshold Study (PATS): Novel single-dose oral food challenge study to validate eliciting doses in children with peanut allergy

Jonathan O'B. Hourihane, MD, DM,[a] Katrina J. Allen, MD, PhD,[b,c] Wayne G. Shreffler, MD, PhD,[d] Gillian Dunngalvin, PhD,[a,e] Julie A. Nordlee, MS,[f] Giovanni A. Zurzolo, PhD,[b,g] Audrey Dunngalvin, PhD,[a,e] Lyle C. Gurrin, PhD,[h] Joseph L. Baumert, PhD,[f] and Steve L. Taylor, PhD[f]

Cork, Ireland, Melbourne, Australia, Boston, Mass, and Lincoln, Neb

Peanut allergen threshold study (PATS)

- Recruit 375 “unselected” consecutive patients in three centres (Cork, Boston, Melbourne)
- Anaphylaxis not an exclusion criterion
- Reaction or + challenge in last 2 yrs
  or “definitively high” SPT/spIgE
- Agreed stop criteria – objective only

Power

Table 1 Projected 95% confidence intervals for the prevalence of clinical reactivity in peanut allergic children and adults receiving the ED_{05} dose (6 mg of whole peanut = 1.5 mg of peanut protein) for sample sizes ranging from 70 to 200

Sample size (of peanut allergic individuals)	Value of target prevalence (5% for the ED_{05})	Projected 95% confidence interval
70	5%	0.9% - 12%
100	5%	1.6% - 11%
150	5%	2.3% - 10%
200	5%	2.4% - 9%
375	5%	3.1% - 7.8%

Zurzolo, 2013

PATS demographics

Table 1: Comparison of participants to non-participants

	Participants			Non-Participants		
	Cork	Melbourne	Boston	Cork	Melbourne	Boston
Number	124	126	128	63	24	53
Sex (%Male)	61%	56.3%	55.5%	60.3%	70.8%	71.7%
Age (Mean yrs)	6.36	7.63	6.55	6.78	11	6.65
Inclusion criterion met:						
Typical reaction<2years	68	60	74	38	12	8
Positive OFC<2years	43	16	2	8	1	1
SPT/SPIgE > 95% PPVs	13	50	52	17	11	4

More OFC proven cases in Ireland, higher SPT in Australia

Hourihane JACI 2017

PATS Results

- 8 subjects met pre-fixed criteria
- All reactions mild
- Only 4 received any meds
- None needed adrenaline /epinephrine

Hourihane JACI 2017

PATS

Table 2. Primary Outcomes (reaction to single dose) per centre.

	Total	Cork	Melbourne	Boston
		Participants		
Active Eligible Participants (completed OFC)	378	124	126	128
		Outcome Group		
Total	378	124	126	128
Non-reactors	245	94	65	86
Reactors	133	30	61	42
Subjective Reactors	67	19	30	18
Objective Reactors				
Total Objective	66	11	31	24
Not related	17	1	10	6
Possibly Related	22	4	10	8
Probably Related	25	5	11	9
Including	1	-	-	1
Highly Probable				
Including meeting predetermined criteria *	8	1	3	4

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All 8 reactors

Participant Number	Location	Age (yrs)	Gender	Diagnostic method	Peanut Wheal (mm)	Peanut SpIgE kUA/L	SpIgE rArah1	SpIgE Arah2	Criteria met*
35	Ireland	11	Female	History of typical exposure & reaction & positive SPT/ sIgE	15	69.10	11.20	59.20	Rhinoconjunctivitis
40	Australia	15	Male	History of typical exposure & reaction & positive SPT/ sIgE	13	2.06	0.53	1.74	Urticaria
43	Australia	9	Male	History of typical exposure & reaction & positive SPT/ sIgE	18	N/A	N/A	N/A	Vomiting
95	Australia	2	Female	Peanut never ingested but positive SPT/SpIgE> 95% PPVs	13	N/A	N/A	N/A	Vomiting
31	U.S.	9	Male	Peanut never ingested but positive SPT/SpIgE> 95% PPVs	11	0.36	0.10	0.14	Urticaria
97	U.S.	2	Male	History of typical exposure & reaction & positive SPT/ sIgE	N/A	100.00	14.80	100.00	Urticaria
109	U.S.	1	Male	History of typical exposure &reaction & positive SPT/ sIgE	N/A	57.70	0.10	49.60	Urticaria
124	U.S.	4	Male	History of typical exposure & reaction and positive SPT/ sIgE	N/A	46.70	14.70	16.20	Rhinorrhoea

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PATS

- No relation of reaction group to
  - any demographic
  - study centre
  - inclusion criteria
  - skin test
  - spIgE levels

Hourihane JACI 2017

Major Study Specific Inclusion criteria

- 1. Demonstrate strong clinical evidence of the specific food allergy as defined by history of unequivocal accidental exposure and typical acute allergic reaction within the preceding 2 years ***and*** positive allergen-specific SPT/sIgE,
  - Or
- Milk and egg as above **but within 2 months**

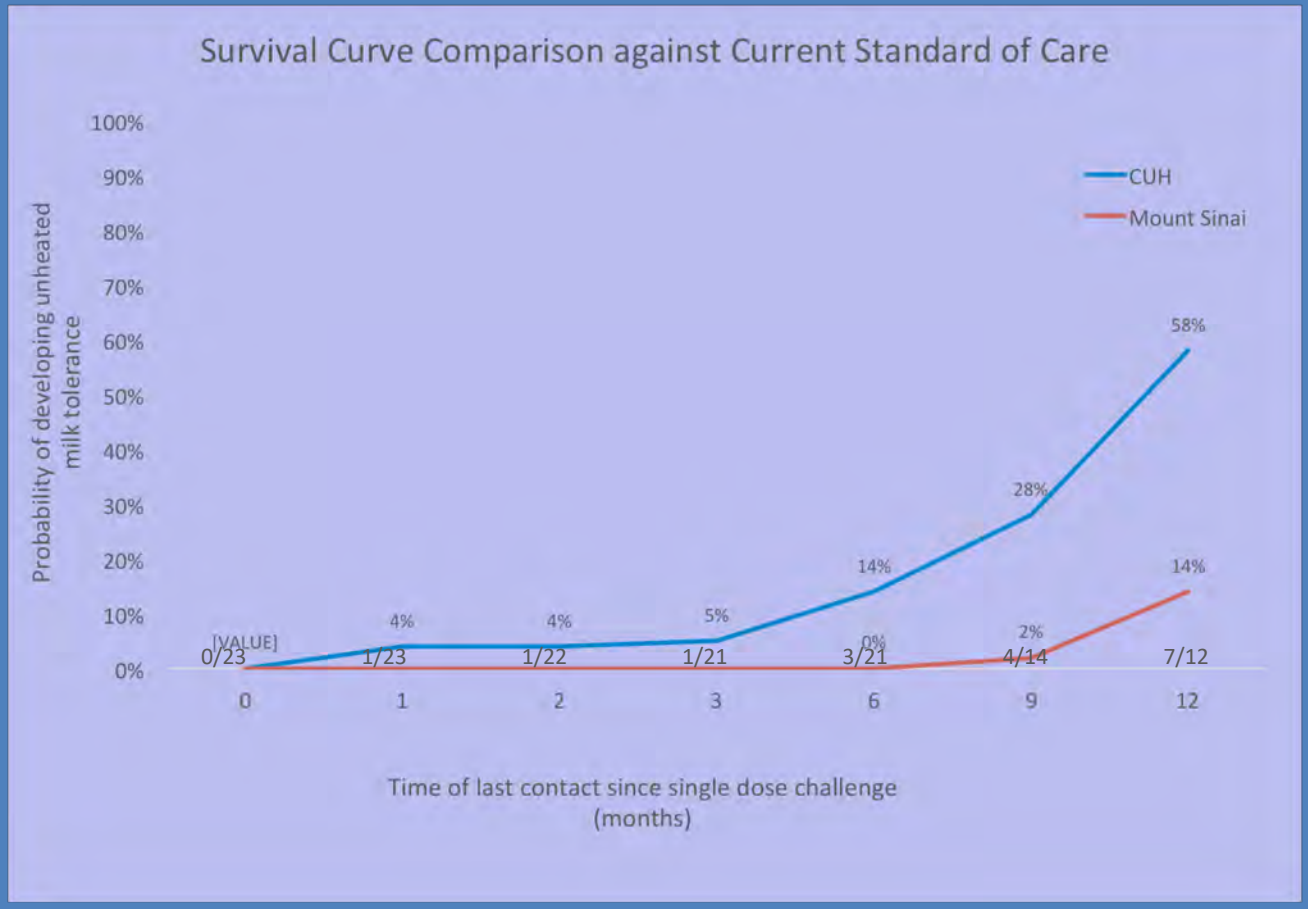
or

- 2. Recent positive oral food challenge **within previous 2 years** in children <16 years, but no time limit specified for adults,
- Or
- **Milk and egg within 2 months**.

Single dose/1 shot

- Hazelnut: 1.5 mg hazelnut protein
- Milk: 0.5 mg milk protein
- Egg: 0.5 mg egg protein.

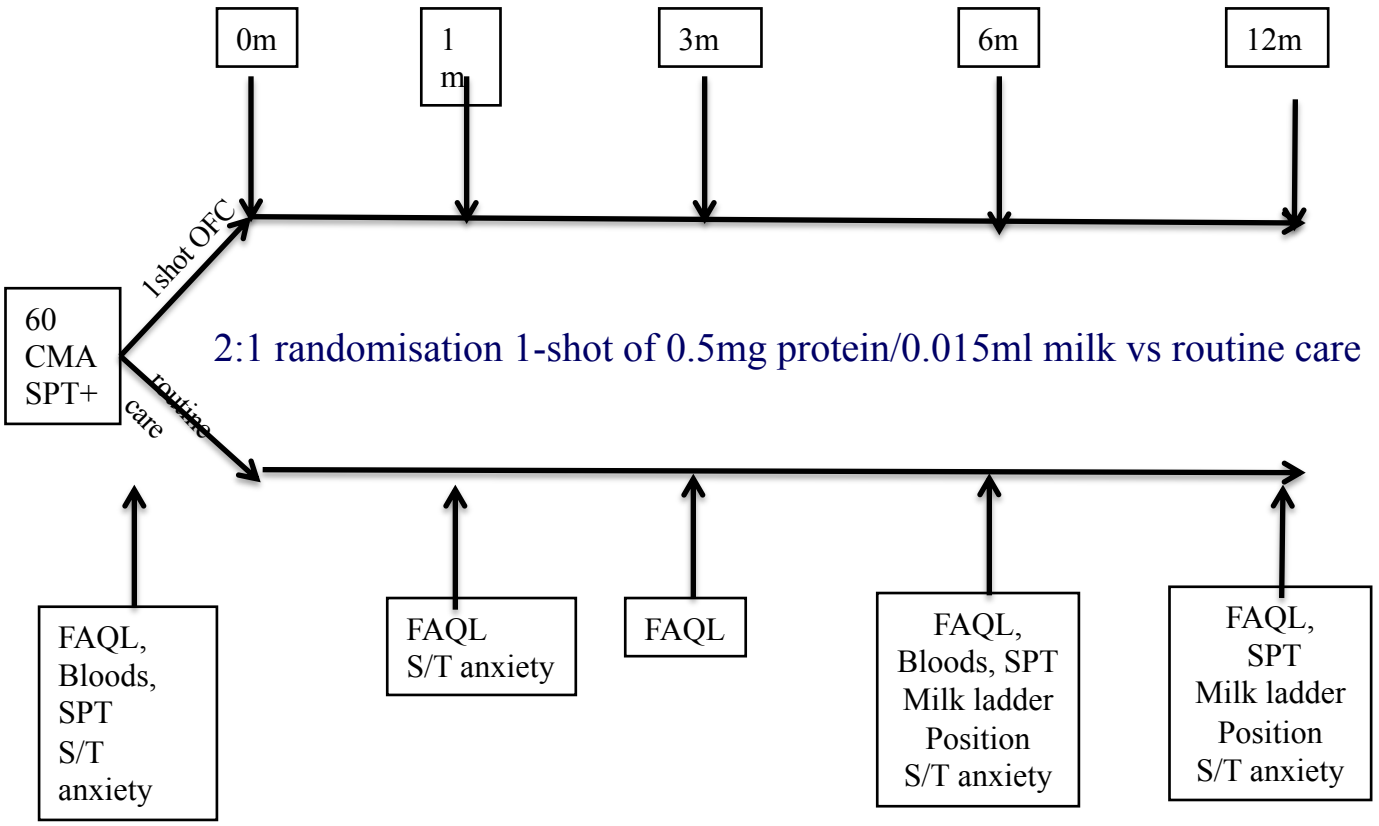
Fast resolution of milk allergy noted in Cork after 1-IFAAM shot study



Buckley, d'Art, Hourihane

NATIONAL CHILDREN'S RESEARCH CENTRE

NCRC funded project 2017-2020



CMA = cows milk allergy; SPT = skin prick test; FAQL= Food allergy related QoL(parent form)

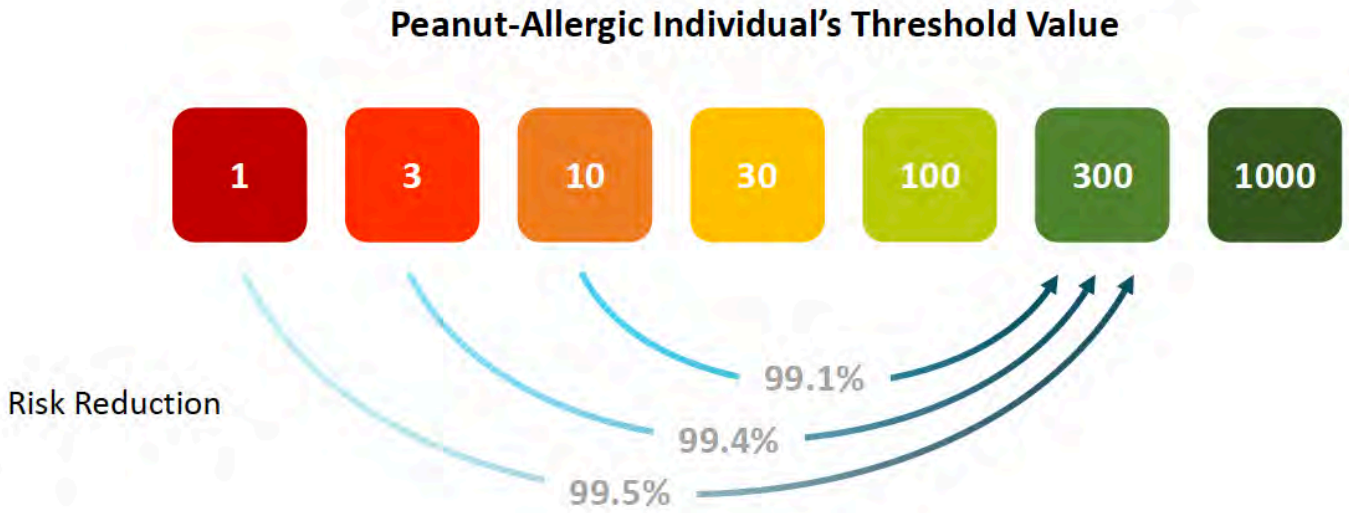
Milk ladder

(NCRC study Cork)

NATIONAL CHILDREN'S RESEARCH CENTRE

Increasing Threshold Doses Could Reduce the Risk of an Allergic Reaction After Accidental Exposure to Peanut

- Increases in individual dose thresholds result in a significant reduction in risk of allergic reaction due to peanut residue in ice cream



1. Baumert JL, et al. *J Allergy Clin Immunol Pract*. 2017. doi: 10.1016/j.jaip.2017.05.006. [Epub ahead of print].

Single dose and PAL

Original Article

The Health and Economic Outcomes of Peanut Allergy Management Practices

Marcus Shaker, MD, MS[a,b]**, and Matthew Greenhawt, MD, MBA, MSc**[c] *Lebanon and Hanover, NH; and Aurora, Colo*

What is already known on this subject? The health and economic benefits of 2 peanut allergy management strategies, strict avoidance of items with precautionary allergen labeling and administering epinephrine for known allergen ingestion even in the absence of symptoms, are unknown.

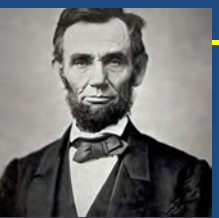
What this article adds to our knowledge? Assuming a 10- to 1000-fold risk increase associated with the alternative, routine precautionary allergen labeling (PAL) avoidance and pre-emptive epinephrine use for peanut ingestion without symptoms were not cost-effective. A low-dose supervised peanut threshold challenge was cost-effective to facilitate PAL consumption.

How does this study impact current management guidelines? Single low-dose peanut threshold challenges should be considered to facilitate PAL consumption. Patients should wait for symptom development to administer epinephrine after peanut consumption.

JACI-IP 2018

Single dose challenge a new risk assessment paradigm

- ED_{05}validated for peanut, milk and hazel
- Safe (safer than routine OFC)
- Precision of dose possible to achieve
- Most reactions mild, but a single severe reaction has happened
  - (but that's a good thing, it's a live biosystem)



- Very easy to perform
  - could get data from non-expert centres
- Could use single dose in other ways
  - For very anxious patients
  - Or even *every* new patient.

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- Wayne Shreffler