Table S1. Published randomized controlled trial of milk OIT.

First Author, year	Sample size (n); age range (years)	Study Design; daily maintenance dose; duration (wk)	Safety	Quality of Life	Outcomes
Staden, U. *et al*., 2007 (1)	46 (OIT=25; A=20) Age: 6 mo-13 yrs	RCT; DMD: 3300; Duration: 84	All patients in the OIT group showed some ARs; 5/20 (25%) children in the A group had ARs after accidental ingestion	N/A	3.3 g of milk DBPCFC: 64% passed in the OIT group vs. 35% in the A group DBPCFC after 2 mo after OIT withdrawal: 36% passed in the OIT group vs. 12% in the P group
Morisset, M. *et al.*, 2007 (2)	57 (OIT=27; A=30) Age: 1-8	RCT; DMD: na; Duration: 24	ARs in 3 patients in the OIT group; no ARs in the A group.	N/A	200 ml of milk SBPCFC: 89% passed in the OIT group vs. 60% in the 1 group
Longo G. *et al.*, 2008 (3)	60 (OIT=30; A=30); Age: 5–17	RCT; DMD: 150 mL Duration: 1 yr	Almost all children presented with 1 or more ARs in the OIT group; 20% children in the A group had ARs after accidental ingestion	N/A	OIT group: 36% completely tolerant (≥ 150 mL) and 54% partially tolerant (5–150 mL)
Skripak JM. *et al.*, 2008;(4)	19 (OIT=12; P=7); Age: 6–17	RDBPCT; DMD: 500 mg Duration: 13	ARs in 45.4% (1107/2437) of doses in the OIT group; 11.2% (134/1193) of doses in the P group	N/A	Median threshold dose with DBPCFC was increased from 5 to 140 mg in OIT group; P group: no change in threshold dose
Pajno GB. *et al.*, 2010 (5)	30 (OIT=15; P=15); Age: 4–10	RPCT; DMD: 150- 200 mL; Duration: 48	ARs in 10/13 (76.9%) patients in the OIT group; no ARs in the P group	N/A	OIT group: 67% tolerant to 200 mL cow's milk vs. 0% in P group
Martorell A. *et al.*, 2011 (6)	60 (OIT=30; P=30); Age: 2–3	RPCT; DMD:200 mL Duration: 1 yrs	ARs in 24/30 (80%) patients in the OIT group	N/A	90% of patients in the OIT groupvs. 23% in the P group passed the final OFC
Salmivesi S. *et al*,. 2013 (7)	28 (OIT=18; P=10); Age: 6-14	RDBPCT; DMD:200 ml Duration:40	ARs in 100% patients in the OIT group; 63% in the P group.	N/A	SU: 79% in the OIT group

Yanagida N. *et al.*, 2015 (8)	37 (OIT=12;P=25); Age:>5	RCT, DMD:3 ml Duration: 48	ARs in 19.5% (729/3739) of doses in the OIT group	N/A	OIT group 58.3% vs P group 13.8% passed SU: OIT group 58.3%
Wood RA, *et al.*, 2016 (9)	57 (OIT+OMZ=28;C=29); Age:7-32	DBPCT; DMD:3800; Duration:30 (OMZ:16 wks pre-OIT)	ARs in 8.5% of doses in patients in the OIT + OMZ group; 26% doses in the control group of OIT + P	N/A	Desensitization: no significant difference between active (88.9%) and control group (71.4%) SU: no significant difference between active (48.1%) and control (35.7%) group
Takahashi M, *et al.*, 2017 (10)	16 (OIT+OMZ=10; P=6); Age:6-14	RCT; DMD: Duration:32 (OMZ:8 wk pre-OIT; OIT+OMZ 16 wk)	0.012 ARs per dose per child occurred in the escalation phase, 0.048 ARs per dose per child occurred in the maintenance phase	N/A	OFC at 32 wk: 100% passed in the OIT+OMZ group vs. 0% in P group SCD in the OMB-OIT treated group was significantly higher than that in the untreated

Legend:

A=avoidance; ARs= adverse reactions; C=control; DBPCFC=double blinded placebo controlled food challenge; DBPC=double blinded placebo controlled; DMD=daily maintenance dose; N/A= not available; n=number; mg=milligrams; ml= milligrams; mo=months; OMZ=omalizumab; OIT=oral immunotherapy; P=placebo; RCT=randomized-controlled trial; RDBPL=randomized double blinded placebo controlled; RPCT=randomized placebo-controlled trial; SBPCFC= single blinded placebo controlled food challenge; SCD=successfully consumed dose; SU=sustained unresponsiveness; vs= versus; wk=week; yr=year; yrs=years.

References

1. Staden U, Rolinck-Werninghaus C, Brewe F, Wahn U, Niggemann B, Beyer K. Specific oral tolerance induction in food allergy in children: efficacy and clinical patterns of reaction. *Allergy* (2007) 62(11):1261-9. Epub 2007/10/09. doi: 10.1111/j.1398-9995.2007.01501.x. PubMed PMID: 17919140.
2. Morisset M, Moneret-Vautrin DA, Guenard L, Cuny JM, Frentz P, Hatahet R, et al. Oral desensitization in children with milk and egg allergies obtains recovery in a significant proportion of cases. A randomized study in 60 children with cow's milk allergy and 90 children with egg allergy. *Eur Ann Allergy Clin Immunol* (2007) 39(1):12-9. Epub 2007/03/23. PubMed PMID: 17375736.
3. Longo G, Barbi E, Berti I, Meneghetti R, Pittalis A, Ronfani L, et al. Specific oral tolerance induction in children with very severe cow's milk-induced reactions. *J Allergy Clin Immunol* (2008) 121(2):343-7. Epub 2007/12/26. doi: 10.1016/j.jaci.2007.10.029. PubMed PMID: 18158176.
4. Skripak JM, Nash SD, Rowley H, Brereton NH, Oh S, Hamilton RG, et al. A randomized, double-blind, placebo-controlled study of milk oral immunotherapy for cow's milk allergy. *J Allergy Clin Immunol* (2008) 122(6):1154-60. Epub 2008/10/28. doi: 10.1016/j.jaci.2008.09.030. PubMed PMID: 18951617; PubMed Central PMCID: PMCPMC3764488.
5. Pajno GB, Caminiti L, Ruggeri P, De Luca R, Vita D, La Rosa M, et al. Oral immunotherapy for cow's milk allergy with a weekly up-dosing regimen: a randomized single-blind controlled study. *Ann Allergy Asthma Immunol* (2010) 105(5):376-81. Epub 2010/11/09. doi: 10.1016/j.anai.2010.03.015. PubMed PMID: 21055664.
6. Martorell A, De la Hoz B, Ibáñez MD, Bone J, Terrados MS, Michavila A, et al. Oral desensitization as a useful treatment in 2-year-old children with cow's milk allergy. *Clinical & Experimental Allergy* (2011) 41(9):1297-304. doi: https://doi.org/10.1111/j.1365-2222.2011.03749.x.
7. Salmivesi S, Korppi M, Mäkelä MJ, Paassilta M. Milk oral immunotherapy is effective in school-aged children. *Acta Paediatr* (2013) 102(2):172-6. Epub 2012/08/18. doi: 10.1111/j.1651-2227.2012.02815.x. PubMed PMID: 22897785.
8. Yanagida N, Sato S, Asaumi T, Okada Y, Ogura K, Ebisawa M. A Single-Center, Case-Control Study of Low-Dose-Induction Oral Immunotherapy with Cow's Milk. *Int Arch Allergy Immunol* (2015) 168(2):131-7. Epub 2015/12/20. doi: 10.1159/000442157. PubMed PMID: 26683057.
9. Wood RA, Kim JS, Lindblad R, Nadeau K, Henning AK, Dawson P, et al. A randomized, double-blind, placebo-controlled study of omalizumab combined with oral immunotherapy for the treatment of cow's milk allergy. *J Allergy Clin Immunol* (2016) 137(4):1103-10 e11. Epub 2015/11/20. doi: 10.1016/j.jaci.2015.10.005. PubMed PMID: 26581915; PubMed Central PMCID: PMCPMC5395304.
10. Takahashi M, Taniuchi S, Soejima K, Hatano Y, Yamanouchi S, Kaneko K. Two-weeks-sustained unresponsiveness by oral immunotherapy using microwave heated cow's milk for children with cow's milk allergy. *Allergy Asthma Clin Immunol* (2016) 12(1):44. Epub 2016/08/30. doi: 10.1186/s13223-016-0150-0. PubMed PMID: 27570533; PubMed Central PMCID: PMCPMC5002153.

Table S2. Published randomized controlled trial of egg OIT.

First Autho, year	Sample size (n); age range (years)	Study Design; daily maintenance dose (mg); duration (wk)	Safety	QoL	Outcomes
Staden, U. *et al.*, 2007 (1)	46 (OIT=25; A=20) Age: 6 mo-13 yrs	RCT; DMD: 1600; Duration: 84	All patients in the OIT group showed some ARs; 5/20 (25%) children in the A group had ARs after accidental ingestion	N/A	4.6 g of egg DBPCFC: 64% passed in the OIT group vs. 35% in the A group DBPCFC 2 mo after OIT withdrawal: 36% passed in the OIT group vs. 12% in the P group
Morisset, M. *et al.*, 2007(2)	90 (OIT=49; A=35) Age: 1-8	RCT; DMD: na; Duration: 24	N/A	N/A	7 g of egg SBPCFC: 69% passed in the OIT group vs. 51% in the A group
Burks AW. *et al.*, 2012 (11)	55 (OIT=40; P= 15) Age: 5 -11	DBPCT; DMD: 2000; Duration:88	ARs in 25% of 11680 doses in the OIT group and 4% of 4018 doses in the P group	N/A	5 g of egg DBPCFC at 22 mo: 75% passed in the OIT group vs. 0% in the P group 10 g of DEP DBPCFC at 24 mo after 6-8 wk after OIT withdrawal: 28% passed in the OIT group
Dello Iacono I. *et al.*, 2013(12)	20 Age: 5-11	RCT; DMD: 40 ml of raw egg; Duration: 24	All patients in the OIT group had ARs; 30% of children in the A group had reactions after accidental ingestion	N/A	DBPCFC: 90% reached partial tolerance in the OIT group vs. 10% in the A group

Fuentes-Aparicio V, *et al.*, 2013 (13)	72 (OIT=40; A=32); Age:4-15	RCT; DMD: 10000; Duration: 4-28	ARs in 21/37 (56.8%) patients in the OIT group. One patient developed eosinophilic esophagitis	N/A	1 egg OFC: 92.5% passed in the OIT group vs. 21.8% in the A group
Meglio P, *et al.*, 2013 (14)	20 (OIT=10; A=10) Age: 4-14	RCT; DMD: 25 ml raw egg Duration: 24	ARs in 21/37 (56.8%) patients in the OIT group	N/A	OFC: 80% passed in the OIT group vs. 20% in the A group
Vazquez-Ortiz M. *et al.*, 2014 (15)	82 (OIT=50; A=32); Age: 5-18	DBPCT; DMD: 1 raw egg; Duration: 48-72	ARs in 45/50 (90%) patients in the OIT group	N/A	3.8 g of raw egg OFC at 12 mo: 54% passed in the OIT group vs. 15.6% in the A group
Caminiti L. *et al.*, 2015 (16)	31 (OIT=17; P=14) Age:4-11	RPCT; DMD: 4000 for 4 mo then 2-3 eggs per wk for 6 mo; Duration:40	Adverse ARs in OIT; no ARs in the P group.	N/A	94.11% of patients on OIT were desensitized 4 g of DBPCFC 3 mo after OIT withdrawal: 31% passed in the OIT group vs. 7% in the P group
Escudero C. *et al.*, 2015 (17)	61 (OIT=30;P= 31) Age: 5 - 17	RCT; DMD: 1 undercooked egg every 48 hours; Duration:12	145 ARs in patients in OIT	N/A	93% on OIT were desensitized 2808 mg of EWP DBPCFC 1 mo after OIT withdrawal: 37% passed in the OIT group vs. 3% in the A group
Giavi S. *et al.*, 2016 (18)	29; (OIT=15; P=14)	DBPCT; DMD: 9000; Duration:24	ARs in 7/15 (46.7%) patients in the OIT group; 2/14 (14.3%) in the P group.	N/A	DBPCFC at 24 wk: 36% passed in the OIT group vs. 21% in the P group

	Age: 1 - 5.5				
Jones SM. et al, 2016 (follow-up of Burks AW. *et al.*, 2012) (19)	55 (OIT=40;P=15); Age: 5 - 18	RPCT; DMD: 1600; Duration:88	Mild ARs in 12/22 (54.5%) patients during the 3rd and 4th year of OIT	N/A	DBPCFC at 4 years: 50% passed in the OIT group
Pérez-Rangel I. *et al.*, 2017 (20)	33 (OIT=15;A=14); Age: 5 - 18	RCT; DMD: 1 undercooked egg every 48 hours; Duration:20	ARs in 31% of doses administered during the build-up phase.	N/A	DBPCFC: 89% passed in the OIT group vs. 0% in the A group
Akaschi M. *et al.*, 2017 (21)	36 (OIT=18;A=18); Age: 3-15	RCT; DMD: 4000 DEP; Duration:24	ARs in 17/18 (94.4%) patients in the OIT group; no ARs in the A group.	N/A	4000 mg of EP DBPCFC: 57% passed in the OIT group vs. 0% in the A group
Itoh-Nagato N. *et al.*, 2018 (22)	45; Age: 5-15	RCT; DMD: 60 g of cooked egg and 1 g of EWP Duration: The early start group received rush OIT for 3 mo, while the late-start group continued the egg elimination diet (control). In the next stage, both groups received OIT until all participants had finished 12 mo of maintenance OIT	ARs in 19/23 (82.6%) patients in the OIT early-start group, none in the late-start group	QoL was evaluated by the FAQL-PB: The QOL in the early-start group showed a significant improvement of ≥10 points in comparison to the late-start group. QoL was significantly improved even after 3 mo of OIT (median 13 point improvement and the improvement was sustained after the maintenance phase.	The ratio of the participants with a significant increase in the TD was significantly higher in the early-start group (87.0%), than in the late-start group (22.7%).

Martín-Muñoz MF. *et al.*, 2019 (23)	101 (OIT=76; P=25); Age: 6-9	DBPCT; DMD: 3300 mg of PEW; Duration:36	ARs in 66/76 (86.8%) patients in the OIT group; 8/2 in the P group.	N/A	PEW DBPCFC at T12: 84.2% passed in the OIT group vs. 16% in the P group PEW DBPCFC at T18: 93.1% passed in the OIT group vs. 83.3% in the P group PEW DBPCFC at T24: 97.4% passed in the OIT group
Takaoka Y. *et al.*, 2019 (24)	33 (OIT=21; P=12); Mean age: 6	DBPCT; DMD: 7.9-11 EWP; Duration: 20	ARs in 99/1,938 (5.1%) intakes of OIT; 5/1,300 (0.4%) in the P group.	N/A	2 g of hard boiled EW OFC: 37% passed in the OIT group vs. 8% in the P group

Legend

A=avoidance; ARs=adverse reactions; DBPCFC=double blinded placebo controlled food challenge; DBPC=double blinded placebo controlled; DMD=daily maintenance dose; EWP= egg white protein; DEP=dry egg powder; N/A= not available; n=number; mg=milligrams; mo=months; OMZ=omalizumab; OIT=oral immunotherapy; P=placebo; PEW=pasteurized egg white; QoL= quality of life; RCT=randomized-controlled trial; RPCT=randomized placebo-controlled trial; RCT= randomized controlled trial; SBPCFC= single blinded placebo controlled food challenge; TD= threshold dose; vs= versus; wk=week; yrs=years.

References

1. Staden U, Rolinck-Werninghaus C, Brewe F, Wahn U, Niggemann B, Beyer K. Specific oral tolerance induction in food allergy in children: efficacy and clinical patterns of reaction. *Allergy* (2007) 62(11):1261-9. Epub 2007/10/09. doi: 10.1111/j.1398-9995.2007.01501.x. PubMed PMID: 17919140.
2. Morisset M, Moneret-Vautrin DA, Guenard L, Cuny JM, Frentz P, Hatahet R, et al. Oral desensitization in children with milk and egg allergies obtains recovery in a significant proportion of cases. A randomized study in 60 children with cow's milk allergy and 90 children with egg allergy. *Eur Ann Allergy Clin Immunol* (2007) 39(1):12-9. Epub 2007/03/23. PubMed PMID: 17375736.
3. Longo G, Barbi E, Berti I, Meneghetti R, Pittalis A, Ronfani L, et al. Specific oral tolerance induction in children with very severe cow's milk-induced reactions. *J Allergy Clin Immunol* (2008) 121(2):343-7. Epub 2007/12/26. doi: 10.1016/j.jaci.2007.10.029. PubMed PMID: 18158176.
4. Skripak JM, Nash SD, Rowley H, Brereton NH, Oh S, Hamilton RG, et al. A randomized, double-blind, placebo-controlled study of milk oral immunotherapy for cow's milk allergy. *J Allergy Clin Immunol* (2008) 122(6):1154-60. Epub 2008/10/28. doi: 10.1016/j.jaci.2008.09.030. PubMed PMID: 18951617; PubMed Central PMCID: PMCPMC3764488.

5. Pajno GB, Caminiti L, Ruggeri P, De Luca R, Vita D, La Rosa M, et al. Oral immunotherapy for cow's milk allergy with a weekly up-dosing regimen: a randomized single-blind controlled study. *Ann Allergy Asthma Immunol* (2010) 105(5):376-81. Epub 2010/11/09. doi: 10.1016/j.anai.2010.03.015. PubMed PMID: 21055664.
6. Martorell A, De la Hoz B, Ibáñez MD, Bone J, Terrados MS, Michavila A, et al. Oral desensitization as a useful treatment in 2-year-old children with cow's milk allergy. *Clinical & Experimental Allergy* (2011) 41(9):1297-304. doi: https://doi.org/10.1111/j.1365-2222.2011.03749.x.
7. Salmivesi S, Korppi M, Mäkelä MJ, Paassilta M. Milk oral immunotherapy is effective in school-aged children. *Acta Paediatr* (2013) 102(2):172-6. Epub 2012/08/18. doi: 10.1111/j.1651-2227.2012.02815.x. PubMed PMID: 22897785.
8. Yanagida N, Sato S, Asaumi T, Okada Y, Ogura K, Ebisawa M. A Single-Center, Case-Control Study of Low-Dose-Induction Oral Immunotherapy with Cow's Milk. *Int Arch Allergy Immunol* (2015) 168(2):131-7. Epub 2015/12/20. doi: 10.1159/000442157. PubMed PMID: 26683057.
9. Wood RA, Kim JS, Lindblad R, Nadeau K, Henning AK, Dawson P, et al. A randomized, double-blind, placebo-controlled study of omalizumab combined with oral immunotherapy for the treatment of cow's milk allergy. *J Allergy Clin Immunol* (2016) 137(4):1103-10 e11. Epub 2015/11/20. doi: 10.1016/j.jaci.2015.10.005. PubMed PMID: 26581915; PubMed Central PMCID: PMCPMC5395304.
10. Takahashi M, Taniuchi S, Soejima K, Hatano Y, Yamanouchi S, Kaneko K. Two-weeks-sustained unresponsiveness by oral immunotherapy using microwave heated cow's milk for children with cow's milk allergy. *Allergy Asthma Clin Immunol* (2016) 12(1):44. Epub 2016/08/30. doi: 10.1186/s13223-016-0150-0. PubMed PMID: 27570533; PubMed Central PMCID: PMCPMC5002153.
11. Burks AW, Jones SM, Wood RA, Fleischer DM, Sicherer SH, Lindblad RW, et al. Oral immunotherapy for treatment of egg allergy in children. *N Engl J Med* (2012) 367(3):233-43. Epub 2012/07/20. doi: 10.1056/NEJMoa1200435. PubMed PMID: 22808958; PubMed Central PMCID: PMCPMC3424505.
12. Dello Iacono I, Tripodi S, Calvani M, Panetta V, Verga MC, Miceli Sopo S. Specific oral tolerance induction with raw hen's egg in children with very severe egg allergy: a randomized controlled trial. *Pediatr Allergy Immunol* (2013) 24(1):66-74. Epub 2012/09/11. doi: 10.1111/j.1399-3038.2012.01349.x. PubMed PMID: 22957889.
13. Fuentes-Aparicio V, Alvarez-Perea A, Infante S, Zapatero L, D'Oleo A, Alonso-Lebrero E. Specific oral tolerance induction in paediatric patients with persistent egg allergy. *Allergol Immunopathol (Madr)* (2013) 41(3):143-50. Epub 2012/07/28. doi: 10.1016/j.aller.2012.02.007. PubMed PMID: 22835606.
14. Meglio P, Giampietro PG, Carello R, Gabriele I, Avitabile S, Galli E. Oral food desensitization in children with IgE-mediated hen's egg allergy: a new protocol with raw hen's egg. *Pediatric Allergy and Immunology* (2013) 24(1):75-83. doi: https://doi.org/10.1111/j.1399-3038.2012.01341.x.
15. Vazquez-Ortiz M, Alvaro M, Piquer M, Dominguez O, Machinena A, Martin-Mateos MA, et al. Baseline specific IgE levels are useful to predict safety of oral immunotherapy in egg-allergic children. *Clin Exp Allergy* (2014) 44(1):130-41. Epub 2013/12/21. doi: 10.1111/cea.12233. PubMed PMID: 24355019.
16. Caminiti L, Pajno GB, Crisafulli G, Chiera F, Collura M, Panasci G, et al. Oral Immunotherapy for Egg Allergy: A Double-Blind Placebo-Controlled Study, with Postdesensitization Follow-Up. *J Allergy Clin Immunol Pract* (2015) 3(4):532-9. Epub 2015/03/03. doi: 10.1016/j.jaip.2015.01.017. PubMed PMID: 25725940.
17. Escudero C, Rodriguez Del Rio P, Sanchez-Garcia S, Perez-Rangel I, Perez-Farinos N, Garcia-Fernandez C, et al. Early sustained unresponsiveness after short-course egg oral immunotherapy: a randomized controlled study in egg-allergic children. *Clin Exp Allergy* (2015) 45(12):1833-43. Epub 2015/08/04. doi: 10.1111/cea.12604. PubMed PMID: 26236997.
18. Giavi S, Vissers YM, Muraro A, Lauener R, Konstantinopoulos AP, Mercenier A, et al. Oral immunotherapy with low allergenic hydrolysed egg in egg allergic children. *Allergy* (2016) 71(11):1575-84. Epub 2016/04/10. doi: 10.1111/all.12905. PubMed PMID: 27059671.

19. Jones SM, Burks AW, Keet C, Vickery BP, Scurlock AM, Wood RA, et al. Long-term treatment with egg oral immunotherapy enhances sustained unresponsiveness that persists after cessation of therapy. *J Allergy Clin Immunol* (2016) 137(4):1117-27.e10. Epub 2016/03/01. doi: 10.1016/j.jaci.2015.12.1316. PubMed PMID: 26924470; PubMed Central PMCID: PMCPMC4826859.
20. Pérez-Rangel I, Rodríguez del Río P, Escudero C, Sánchez-García S, Sánchez-Hernández JJ, Ibáñez MD. Efficacy and safety of high-dose rush oral immunotherapy in persistent egg allergic children: A randomized clinical trial. *Annals of Allergy, Asthma & Immunology* (2017) 118(3):356-64.e3. doi: 10.1016/j.anai.2016.11.023.
21. Akashi M, Yasudo H, Narita M, Nomura I, Akasawa A, Ebisawa M, et al. Randomized controlled trial of oral immunotherapy for egg allergy in Japanese patients. *Pediatr Int* (2017) 59(5):534-9. Epub 2016/12/04. doi: 10.1111/ped.13210. PubMed PMID: 27914210.
22. Itoh-Nagato N, Inoue Y, Nagao M, Fujisawa T, Shimojo N, Iwata T, et al. Desensitization to a whole egg by rush oral immunotherapy improves the quality of life of guardians: A multicenter, randomized, parallel-group, delayed-start design study. *Allergol Int* (2018) 67(2):209-16. Epub 2017/08/06. doi: 10.1016/j.alit.2017.07.007. PubMed PMID: 28778455.
23. Martín-Muñoz MF, Alonso Lebrero E, Zapatero L, Fuentes Aparicio V, Piquer Gibert M, Plaza Martín AM, et al. Egg OIT in clinical practice (SEICAP II): Maintenance patterns and desensitization state after normalizing the diet. *Pediatr Allergy Immunol* (2019) 30(2):214-24. Epub 2018/11/11. doi: 10.1111/pai.13002. PubMed PMID: 30414284.
24. Takaoka Y, Maeta A, Takahashi K, Y MI, Takahashi S, Muroya T, et al. Effectiveness and Safety of Double-Blind, Placebo-Controlled, Low-Dose Oral Immunotherapy with Low Allergen Egg-Containing Cookies for Severe Hen's Egg Allergy: A Single-Center Analysis. *Int Arch Allergy Immunol* (2019) 180(4):244-9. Epub 2019/10/03. doi: 10.1159/000502956. PubMed PMID: 31578023.
25. Varshney P, Jones SM, Scurlock AM, Perry TT, Kemper A, Steele P, et al. A randomized controlled study of peanut oral immunotherapy: clinical desensitization and modulation of the allergic response. *J Allergy Clin Immunol* (2011) 127(3):654-60. Epub 2011/03/08. doi: 10.1016/j.jaci.2010.12.1111. PubMed PMID: 21377034; PubMed Central PMCID: PMCPMC3060783.
26. Anagnostou K, Islam S, King Y, Foley L, Pasea L, Bond S, et al. Assessing the efficacy of oral immunotherapy for the desensitisation of peanut allergy in children (STOP II): a phase 2 randomised controlled trial. *Lancet* (2014) 383(9925):1297-304. Epub 2014/02/04. doi: 10.1016/S0140-6736(13)62301-6. PubMed PMID: 24485709; PubMed Central PMCID: PMCPMC4255069.
27. Syed A, Garcia MA, Lyu SC, Bucayu R, Kohli A, Ishida S, et al. Peanut oral immunotherapy results in increased antigen-induced regulatory T-cell function and hypomethylation of forkhead box protein 3 (FOXP3). *J Allergy Clin Immunol* (2014) 133(2):500-10. doi: 10.1016/j.jaci.2013.12.1037. PubMed PMID: 24636474; PubMed Central PMCID: PMCPMC4121175.
28. MacGinnitie AJ, Rachid R, Gragg H, Little SV, Lakin P, Cianferoni A, et al. Omalizumab facilitates rapid oral desensitization for peanut allergy. *J Allergy Clin Immunol* (2017) 139(3):873-81 e8. Epub 2016/10/19. doi: 10.1016/j.jaci.2016.08.010. PubMed PMID: 27609658; PubMed Central PMCID: PMCPMC5369605.
29. Kukkonen AK, Uotila R, Malmberg LP, Pelkonen AS, Makela MJ. Double-blind placebo-controlled challenge showed that peanut oral immunotherapy was effective for severe allergy without negative effects on airway inflammation. *Acta Paediatr* (2017) 106(2):274-81. Epub 2016/11/20. doi: 10.1111/apa.13668. PubMed PMID: 27859599.
30. Vickery BP, Berglund JP, Burk CM, Fine JP, Kim EH, Kim JI, et al. Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective. *J Allergy Clin Immunol* (2017) 139(1):173-81 e8. Epub 2016/08/16. doi: 10.1016/j.jaci.2016.05.027. PubMed PMID: 27522159; PubMed Central PMCID: PMCPMC5222765.

31. Bird JA, Spergel JM, Jones SM, Rachid R, Assa'ad AH, Wang J, et al. Efficacy and Safety of AR101 in Oral Immunotherapy for Peanut Allergy: Results of ARC001, a Randomized, Double-Blind, Placebo-Controlled Phase 2 Clinical Trial. *J Allergy Clin Immunol Pract* (2018) 6(2):476-85 e3. Epub 2017/11/03. doi: 10.1016/j.jaip.2017.09.016. PubMed PMID: 29092786.
32. Investigators PGoC, Vickery BP, Vereda A, Casale TB, Beyer K, du Toit G, et al. AR101 Oral Immunotherapy for Peanut Allergy. *N Engl J Med* (2018) 379(21):1991-2001. Epub 2018/11/20. doi: 10.1056/NEJMoa1812856. PubMed PMID: 30449234.
33. Nagakura KI, Sato S, Yanagida N, Nishino M, Asaumi T, Ogura K, et al. Oral Immunotherapy in Japanese Children with Anaphylactic Peanut Allergy. *Int Arch Allergy Immunol* (2018) 175(3):181-8. Epub 2018/01/18. doi: 10.1159/000486310. PubMed PMID: 29339650.
34. Fauquert JL, Michaud E, Pereira B, Bernard L, Gourdon-Dubois N, Rouzaire PO, et al. Peanut gastrointestinal delivery oral immunotherapy in adolescents: Results of the build-up phase of a randomized, double-blind, placebo-controlled trial (PITA study). *Clin Exp Allergy* (2018) 48(7):862-74. Epub 2018/04/18. doi: 10.1111/cea.13148. PubMed PMID: 29665158.
35. Reier-Nilsen T, Carlsen KCL, Michelsen MM, Drottning S, Carlsen KH, Zhang C, et al. Parent and child perception of quality of life in a randomized controlled peanut oral immunotherapy trial. *Pediatr Allergy Immunol* (2019) 30(6):638-45. Epub 2019/04/24. doi: 10.1111/pai.13066. PubMed PMID: 31013372.
36. Blumchen K, Trendelenburg V, Ahrens F, Gruebl A, Hamelmann E, Hansen G, et al. Efficacy, Safety, and Quality of Life in a Multicenter, Randomized, Placebo-Controlled Trial of Low-Dose Peanut Oral Immunotherapy in Children with Peanut Allergy. *J Allergy Clin Immunol Pract* (2019) 7(2):479-91 e10. Epub 2018/11/14. doi: 10.1016/j.jaip.2018.10.048. PubMed PMID: 30423449.
37. Chinthrajah RS, Purington N, Andorf S, Long A, O'Laughlin KL, Lyu SC, et al. Sustained outcomes in oral immunotherapy for peanut allergy (POISED study): a large, randomised, double-blind, placebo-controlled, phase 2 study. *Lancet* (2019) 394(10207):1437-49. Epub 2019/09/17. doi: 10.1016/S0140-6736(19)31793-3. PubMed PMID: 31522849; PubMed Central PMCID: PMCPMC6903389.

Table S3. Published randomized controlled trial of peanut OIT.

First Author, year	Sample size (n); age range (years)	Study Design; daily maintenance dose (mg); duration (wk)	Safety	QoL	Outcomes
Varshney P. *et al.*, 2011 (25)	19 Age: 3-11	RPCT; DMD:2000; Duration:48	ARs in 9/19 (47%) patients in the OIT group; no ARs in the P group.	N/A	5000 mg peanut protein DBPCFC: 84% passed in the OIT group vs. 0% in the P group
Anagnostou K. *et al.*, 2014 (26)	99 (OIT=49; A=50) Age:7-16	RPCT; DMD:800; Duration:26	ARs in 6.3% of doses in the OIT group	FAQLQ-PF score was similar in OIT and A groups at baseline. Both groups showed a similar and clinically meaningful improvement (decrease) in QoL after OIT: -1.61 and – 1.41, respectively.	1400 mg peanut protein DBPCFC: 62% passed in the OIT group vs. 0% in the A group
Syed A, *et al.*, 2014 (27)	43 (OIT=23;P=20) Age 4-45	RPCT; DMD:4000; Duration: 96	N/A	N/A	DBPCFC 3 mo after withdrawal OIT: 30% passed in the OIT group vs. 0% in the P group DBPCFC 6 mo after withdrawal: 43,8% passed in the OIT group vs. 0% in the P group

MacGinnitie AJ *et al.*, 2016 (28)	37 (OIT=29;P=8); Open label: 8 Age:6-19	RPCT + open label DMD: 2000; Duration: 7 OMZ untill wk 19 (12 wk pre-OIT)	ARs in 7.8% of OIT doses given in the OMZ arm versus 16.8% in P group	N/A	2000 mg peanut protein DBPCFC 6 wk after withdrawal of OMZ: 73.9% passed in the OIT group vs .12.5% in the P group 4000 mg peanut protein DBPCFC 12 wk after withdrawal of OMZ: 75.9% passed in the OIT group vs. 12.5% in the P group
Kukkonen K. *et al.*, 2017 (29)	60 (OIT=39; P= 21) Age:6 -18	DBPCT; DMD:100-2000; Duration:32	ARs in 30/39 (77%) patients in the OIT group	FAQLQ-CF and FAQLQ-TF in the OIT group showed an improvement of QoL after OIT (p= 0.03). The same did not occur for the caregivers. No further improvement was shown in the longer term.	1255 mg peanut protein DBPCFC: 67% passed in the OIT group vs. 0% in the A group
Vickery B. *et al.*, 2017 (30)	194 (OIT=40; P=154) Age:9 mo-3 yrs	DBPCT; DMD:300 LD-OIT - 3000 HD-OIT; Duration:116	ARs in 95% of patients in the OIT group, most mild	N/A	5000 mg peanut protein DBPCFC: 85 % passed in the LD-OIT group vs. 76% in the HD-OIT group 5000 mg peanut protein DBPCFC after 4 wk elimination: 85% passed in the LD-OIT group vs. 71% in the HD-OIT group
Bird JA. *et al.*, 2018 (31)	55 (OIT=29;P= 26) Age:4-26	DBPCT; DMD:300; Duration:20-24	ARs in 28/29 (96.6%) patients in the OIT group; 22/26 (84.6%) ARs in the P group.	N/A	≥443 mg peanut protein DBPCFC: 79% passed in the OIT group vs. 19% in the P group 1043 mg peanut protein DBPCFC: 62% passed in the OIT group vs. 0% in the P group

PALISADE group, 2018 (32)	496 (OIT= 372; P=124) Age:4-17	DBPCT; DMD:300; Duration:24	ARs in 367/372 (98.7%) patients in the OIT group; 118/124 (95.2%) reactions in the P group.	N/A	≥600 mg peanut protein DBPCFC: 67.2% passed in the OIT group vs. 4% in the P group
Nagakura K. *et al.*, 2018 (33)	22 (OIT=22;P=11) Age:5-18	DBPCT; DMD:795; Duration:96	ARs in 45.4% of OIT doses given in the rush phase, 5.6% in the home dosing phase	N/A	3000 mg peanut protein DBPCFC after 2 wk elimination: 68.1% passed in the OIT group vs. 18.1% in the P group
Fauquert JL. *et al.*, 2018 (34)	30 (OIT=21; P=9) Age:12-18	DBPCT; DMD:400 Duration:24	ARs in 19/21 (90.5%) patients in the OIT group; 8/9 (88.9%) reactions in the P group.	N/A	400 mg of peanut protein DBPCFC: 81.0 % passed in the OIT group vs. 11.1% in the P group passed
Reier-Nilsen et al, 2019 (35)	77; (OIT=57;A=20) Age: 5-15	RCT DMD:250-5000 Duration: 96	11/57 (19.3%) patients in the OIT group withdrew because of ARs; no patients in the A group	PedsQL 4.0 in children showed a significant improvement of QoL in the OIT group ($P < 0.0001$), whereas in the A group did not change significantly. The mean QoL change in the OIT group was not significantly different from the change in A group (p-value = 0.12). The PedsQL 4.0 proxy report improved significantly in the OIT group (p-value < 0.0001), which was significantly higher than the improvement in QoL among the A group. The mean change in PedsQL 4.0 proxy report in the OIT group was significantly different from the A group (p-value = 0.02).	7500 peanut protein OFC: 61% passed in the OIT group

				Parents' QoL reported by the FAQL-PB improved significantly among both the OIT and A groups.	
Blumchen K. *et al.*, 2019 (36)	62 (OIT=31; P=31) Age:3-17	DBPCT; DMD:125-250; Duration:64	ARs in 4.3% of doses in the OIT group, 1.2% of doses in the P group.	QoL improved for all domains in children (FAQLQ-CF) and for the domain of "social and dietary limitations" in mothers' proxy reports of the active group (FAQLQ-PF), considering an improvement of > 0.5 MCID as significant. FAQLQ-PF and FAQLQ-CF not exceeded MCID of 0.5 in the P group. Comparing the placebo and active group there was no significant group difference in median change in QoL for all domains of the FAQLQ-PF reported by mothers post OIT. Children of the peanut-OIT group reported a statistically significant improvement in QoL within the two domains of "risk of accidental exposure" and "emotional impact" when compared to the placebo group.	≥300 mg peanut protein OFC: 74.2% passed in the OIT group vs. 16.1% in the P group
Chinthrajah RS., *et al.*, 2019 (37)	120 (OIT=95;P=25) Age:7-55	RCT; DMD:4000 Duration:208	ARs in 32/35 (91%) patients in the OIT group; 16/25 (64%) ARs in the P group at year 1. ARs in 20/31 (65%) patients in the OIT group;	N/A	4 g of peanut protein OFC at 104 and 117 wk: 35% passed in the OIT group vs. 4% in the A group

			6/23 (26%) ARs in the P group at year 2. ARs in 6/30 (20%) patients in the OIT group; 1/20 (5%) reactions in the P group at year 3.		

Legend

A=avoidance; ARs=adverse reactions; DBPCFC= double blinded placebo controlled food challenge; DBPC=double blinded placebo controlled; DMD=daily maintenance dose; FAQLQ-PF= Food Allergy Quality of Life- Parent Form; FAQLQ-CF= Food Allergy Quality of Life Questionnaire – Child Form; FAQLQ-TF= Food Allergy Quality of Life Questionnaire-Teenager Form; HD-OIT= high dose oral immunotherapy; LD-OIT= low dose oral immunotherapy; MCID: minimum clinically important difference; N/A= not available; n=number; mg=milligrams; mo=months; OMZ=omalizumab; OIT=oral immunotherapy; P=placebo; RC=randomized-controlled; RPC=randomized placebo-controlled; SLIT=sublingual immunotherapy; SU: sustained unresponsiveness; vs= versus; wk=week.

References:

1. Varshney P, Jones SM, Scurlock AM, Perry TT, Kemper A, Steele P, et al. A randomized controlled study of peanut oral immunotherapy: clinical desensitization and modulation of the allergic response. *J Allergy Clin Immunol* (2011) 127(3):654-60. Epub 2011/03/08. doi: 10.1016/j.jaci.2010.12.1111. PubMed PMID: 21377034; PubMed Central PMCID: PMCPMC3060783.

2. Anagnostou K, Islam S, King Y, Foley L, Pasea L, Bond S, et al. Assessing the efficacy of oral immunotherapy for the desensitisation of peanut allergy in children (STOP II): a phase 2 randomised controlled trial. *Lancet* (2014) 383(9925):1297-304. Epub 2014/02/04. doi: 10.1016/S0140-6736(13)62301-6. PubMed PMID: 24485709; PubMed Central PMCID: PMCPMC4255069.

3. Syed A, Garcia MA, Lyu SC, Bucayu R, Kohli A, Ishida S, et al. Peanut oral immunotherapy results in increased antigen-induced regulatory T-cell function and hypomethylation of forkhead box protein 3 (FOXP3). *J Allergy Clin Immunol* (2014) 133(2):500-10. doi: 10.1016/j.jaci.2013.12.1037. PubMed PMID: 24636474; PubMed Central PMCID: PMCPMC4121175.

4. MacGinnitie AJ, Rachid R, Gragg H, Little SV, Lakin P, Cianferoni A, et al. Omalizumab facilitates rapid oral desensitization for peanut allergy. *J Allergy Clin Immunol* (2017) 139(3):873-81 e8. Epub 2016/10/19. doi: 10.1016/j.jaci.2016.08.010. PubMed PMID: 27609658; PubMed Central PMCID: PMCPMC5369605.

5. Kukkonen AK, Uotila R, Malmberg LP, Pelkonen AS, Makela MJ. Double-blind placebo-controlled challenge showed that peanut oral immunotherapy was effective for severe allergy without negative effects on airway inflammation. *Acta Paediatr* (2017) 106(2):274-81. Epub 2016/11/20. doi: 10.1111/apa.13668. PubMed PMID: 27859599.

6. Vickery BP, Berglund JP, Burk CM, Fine JP, Kim EH, Kim JI, et al. Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective. *J Allergy Clin Immunol* (2017) 139(1):173-81 e8. Epub 2016/08/16. doi: 10.1016/j.jaci.2016.05.027. PubMed PMID: 27522159; PubMed Central PMCID: PMCPMC5222765.

7. Bird JA, Spergel JM, Jones SM, Rachid R, Assa'ad AH, Wang J, et al. Efficacy and Safety of AR101 in Oral Immunotherapy for Peanut Allergy: Results of ARC001, a Randomized, Double-Blind, Placebo-Controlled Phase 2 Clinical Trial. *J Allergy Clin Immunol Pract* (2018) 6(2):476-85 e3. Epub 2017/11/03. doi: 10.1016/j.jaip.2017.09.016. PubMed PMID: 29092786.

8. Investigators PGoC, Vickery BP, Vereda A, Casale TB, Beyer K, du Toit G, et al. AR101 Oral Immunotherapy for Peanut Allergy. *N Engl J Med* (2018) 379(21):1991-2001. Epub 2018/11/20. doi: 10.1056/NEJMoa1812856. PubMed PMID: 30449234.

9. Nagakura KI, Sato S, Yanagida N, Nishino M, Asaumi T, Ogura K, et al. Oral Immunotherapy in Japanese Children with Anaphylactic Peanut Allergy. *Int Arch Allergy Immunol* (2018) 175(3):181-8. Epub 2018/01/18. doi: 10.1159/000486310. PubMed PMID: 29339650.

10. Fauquert JL, Michaud E, Pereira B, Bernard L, Gourdon-Dubois N, Rouzaire PO, et al. Peanut gastrointestinal delivery oral immunotherapy in adolescents: Results of the build-up phase of a randomized, double-blind, placebo-controlled trial (PITA study). *Clin Exp Allergy* (2018) 48(7):862-74. Epub 2018/04/18. doi: 10.1111/cea.13148. PubMed PMID: 29665158.

11. Reier-Nilsen T, Carlsen KCL, Michelsen MM, Drottning S, Carlsen KH, Zhang C, et al. Parent and child perception of quality of life in a randomized controlled peanut oral immunotherapy trial. *Pediatr Allergy Immunol* (2019) 30(6):638-45. Epub 2019/04/24. doi: 10.1111/pai.13066. PubMed PMID: 31013372.

12. Blumchen K, Trendelenburg V, Ahrens F, Gruebl A, Hamelmann E, Hansen G, et al. Efficacy, Safety, and Quality of Life in a Multicenter, Randomized, Placebo-Controlled Trial of Low-Dose Peanut Oral Immunotherapy in Children with Peanut Allergy. *J Allergy Clin Immunol Pract* (2019) 7(2):479-91 e10. Epub 2018/11/14. doi: 10.1016/j.jaip.2018.10.048. PubMed PMID: 30423449.

13. Chinthrajah RS, Purington N, Andorf S, Long A, O'Laughlin KL, Lyu SC, et al. Sustained outcomes in oral immunotherapy for peanut allergy (POISED study): a large, randomised, double-blind, placebo-controlled, phase 2 study. *Lancet* (2019) 394(10207):1437-49. Epub 2019/09/17. doi: 10.1016/S0140-6736(19)31793-3. PubMed PMID: 31522849; PubMed Central PMCID: PMCPMC6903389.