



Early-life nutrition: ruolo della nutrizione della prima infanzia sulla salute futura

Elena Lionetti

Ricercatore Universitario - Dipartimento di Pediatria, Università Politecnica delle Marche

Segretario Società Italiana Di Gastroenterologia, Epatologia e Nutrizione Pediatrica (SIGENP)

....Febbre non è Malattia.....

La nutrizione infantile: come è cambiata



Infant nutrition research has historically focused on the prevention of malnutrition and deficiency states. With increasing economic prosperity, these concerns have receded. The emphasis has shifted toward achieving a balanced protein and energy intake and preventing the risk of long-term disease.

La nutrizione infantile: oggi



Infant nutrition research has historically focused on the prevention of malnutrition and deficiency states. With increasing economic prosperity, these concerns have receded. The emphasis has shifted toward achieving a balanced protein and energy intake and preventing the risk of long-term disease.

I primi 1000 giorni....



Early Nutritional Programming

“Complementary feeding”

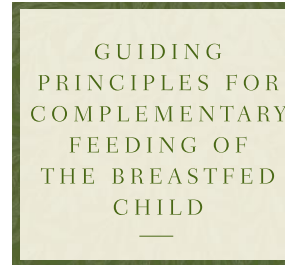
1. *D*efinizione

2. *Q*uando?

3. *C*osa?

4. *C*ome?

“Complementary feeding”: le linee guida



Journal of Pediatric Gastroenterology and Nutrition
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North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

Medical Position Paper

Complementary Feeding: A Commentary by the ESPGHAN Committee on Nutrition

Dietary prevention of allergic diseases in infants and small children

Part III: Critical review of published peer-reviewed observational and interventional
studies and final recommendations*

Effects of Early Nutritional Interventions on the Development of Atopic Disease in Infants and Children: The Role of Maternal Dietary Restriction, Breastfeeding, Timing of Introduction of Complementary Foods, and Hydrolyzed Formulas

WHO, GUIDING PRINCIPLES FOR COMPLEMENTARY FEEDING OF THE BREASTFED CHILD 2001

ESPGHAN committee on nutrition, JPGN 2008

EAACI guidelines, *Pediatr Allergy Immunol* 2004

AAP committee on nutrition 2008

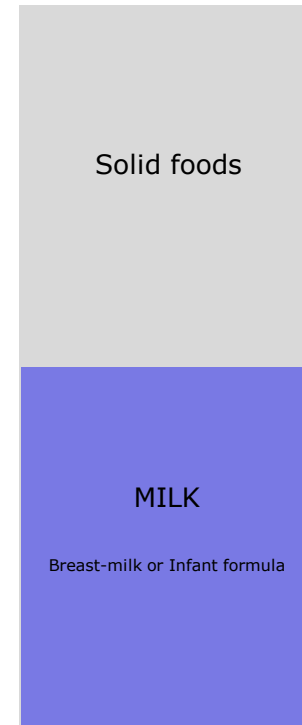
“Complementary feeding”

1. Definizione

Definizione



WHO



in pratica

WHO, GUIDING PRINCIPLES FOR COMPLEMENTARY FEEDING OF THE BREASTFED CHILD 2001

ESPGHAN committee on nutrition, JPGN 2008

EAACI guidelines, Pediatr Allergy Immunol 2004

AAP committee on nutrition 2008

“Complementary feeding”

2. *Quando?*

Quando?



WHO 2001

"Practice exclusive breastfeeding from birth to 6 months of age, and introduce complementary foods at 6 months of age while continuing to breastfeed".



"Exclusive or full breast-feeding for around 6 months is a desirable goal; the introduction of complementary foods should not be before 17 weeks but should not be delayed beyond 26 weeks"

WHO, GUIDING PRINCIPLES FOR COMPLEMENTARY FEEDING OF THE BREASTFED CHILD 2001

ESPGHAN committee on nutrition, JPGN 2008

EAACI guidelines, Pediatr Allergy Immunol 2004

AAP committee on nutrition 2008

Quando?



- ✓ *Acquisizione delle tappe fondamentali dello sviluppo neuromotorio*
 - ✓ *Sviluppo del senso del gusto*
 - ✓ *Maturazione funzionalità renale e gastrointestinale*
 - ✓ *Fabbisogno nutrizionale*
- ✓ *Fattori culturali, socioeconomici, tradizioni locali e familiari.*

WHO, GUIDING PRINCIPLES FOR COMPLEMENTARY FEEDING OF THE BREASTFED CHILD 2001

ESPGHAN committee on nutrition, JPGN 2008

EAACI guidelines, Pediatr Allergy Immunol 2004

AAP committee on nutrition 2008

Quando?



**Cochrane
Library**

Cochrane Database of Systematic Reviews

23 studi:

2 trial randomizzati

21 studi osservazionali

Optimal duration of exclusive breastfeeding (Review)

Kramer MS, Kakuma R

Vantaggi

- ✓ Nessun deficit di crescita
- ✓ Minore rischio di infezioni gastro-intestinali
- ✓ Minore rischio di infezioni delle alte vie respiratorie
- ✓ Minore rischio di infezioni polmonari
- ✓ Minore rischio di ospedalizzazione per infezione
- ✓ Minore rischio di obesità
- ✓ Maggiore perdita di peso della mamma

Limiti

- ✓ Maggiore rischio di sideropenia

“Complementary feeding”

3. *Cosa?*

Svezzamento e prevenzione

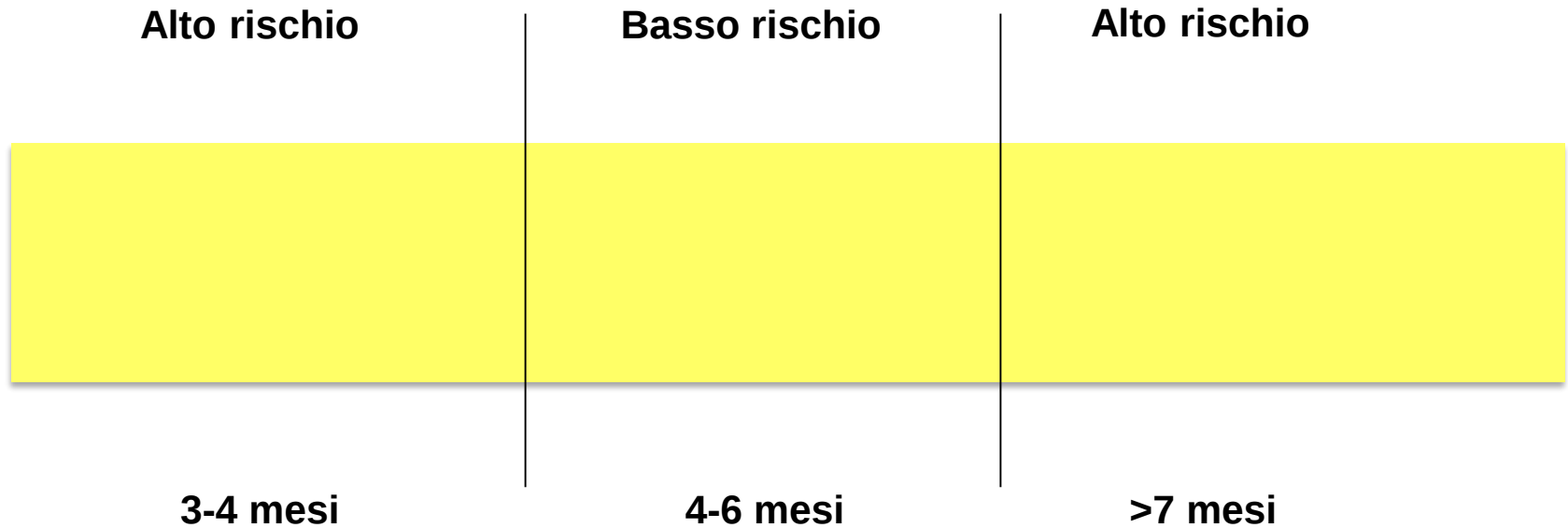


Epoca di introduzione del glutine nello svezzamento

- 1.** L'età di introduzione del glutine nella dieta influenza il rischio di malattia celiaca?



La “finestra di tolleranza”



La “finestra di tolleranza”



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Medical Position Paper

Complementary Feeding: A Commentary by the ESPGHAN Committee on Nutrition

ESPGHAN Committee on Nutrition: *Carlo Agostoni, †Tamas Decsi, ‡³Mary Fewtrell, §Olivier Goulet, ¶Sanja Kolacek, ||¹Berthold Koletzko, **³Kim Fleischer Michaelsen, ††Luis Moreno, ‡‡John Puntis, §§Jacques Rigo, ¶¶Raanan Shamir, ||||²Hania Szajewska, ***Dominique Turck, and †††Johannes van Goudoever

“It is prudent to avoid both early (<4 months) and late (>7months) introduction of gluten and to introduce gluten gradually while the infant is still breast-fed because this may reduce the risk of CD, type 1 diabetes mellitus, and wheat allergy.”

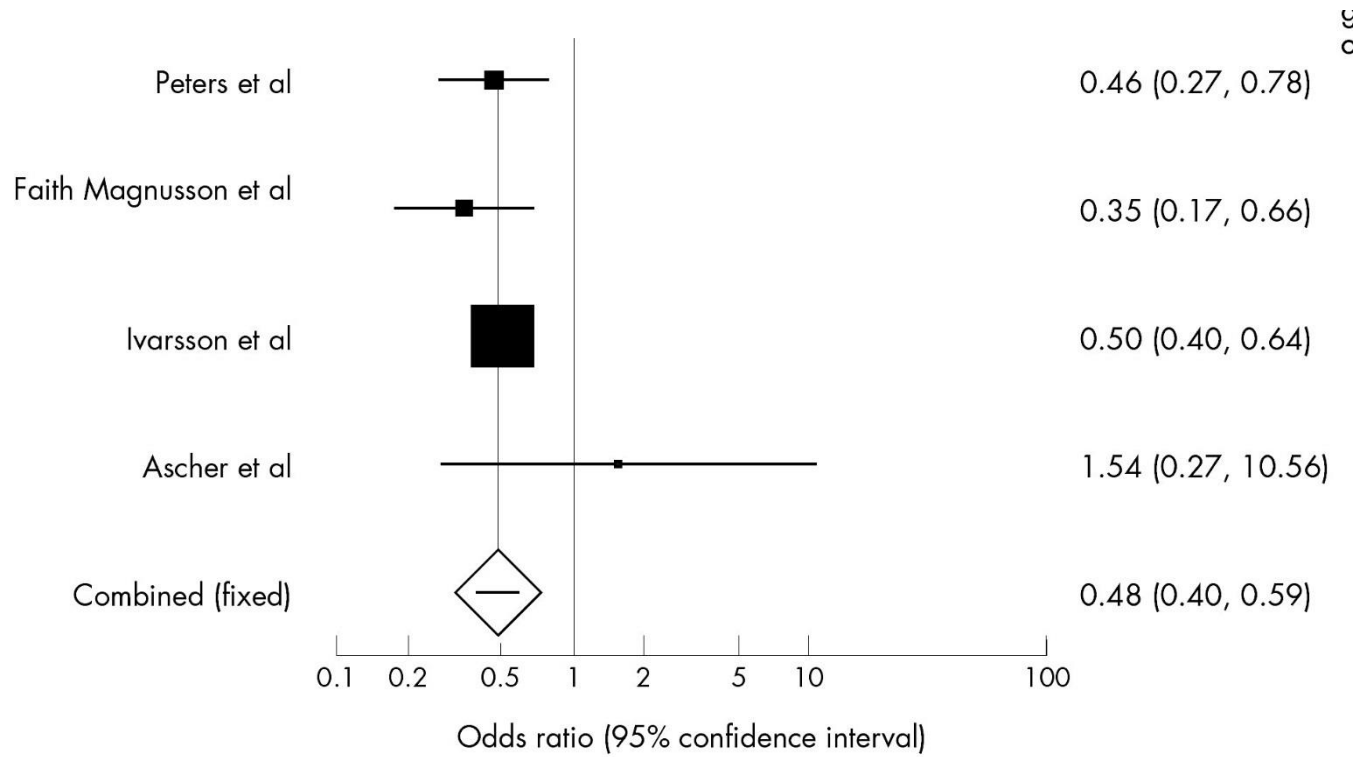
2. L'allattamento materno influenza il rischio di celiachia?



Effect of breast feeding on risk of coeliac disease: a systematic review and meta-analysis of observational studies

A K Akobeng, A V Ramanan, I Buchan, R F Heller

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Introduction of Gluten, HLA Status, and the Risk of Celiac Disease in Children

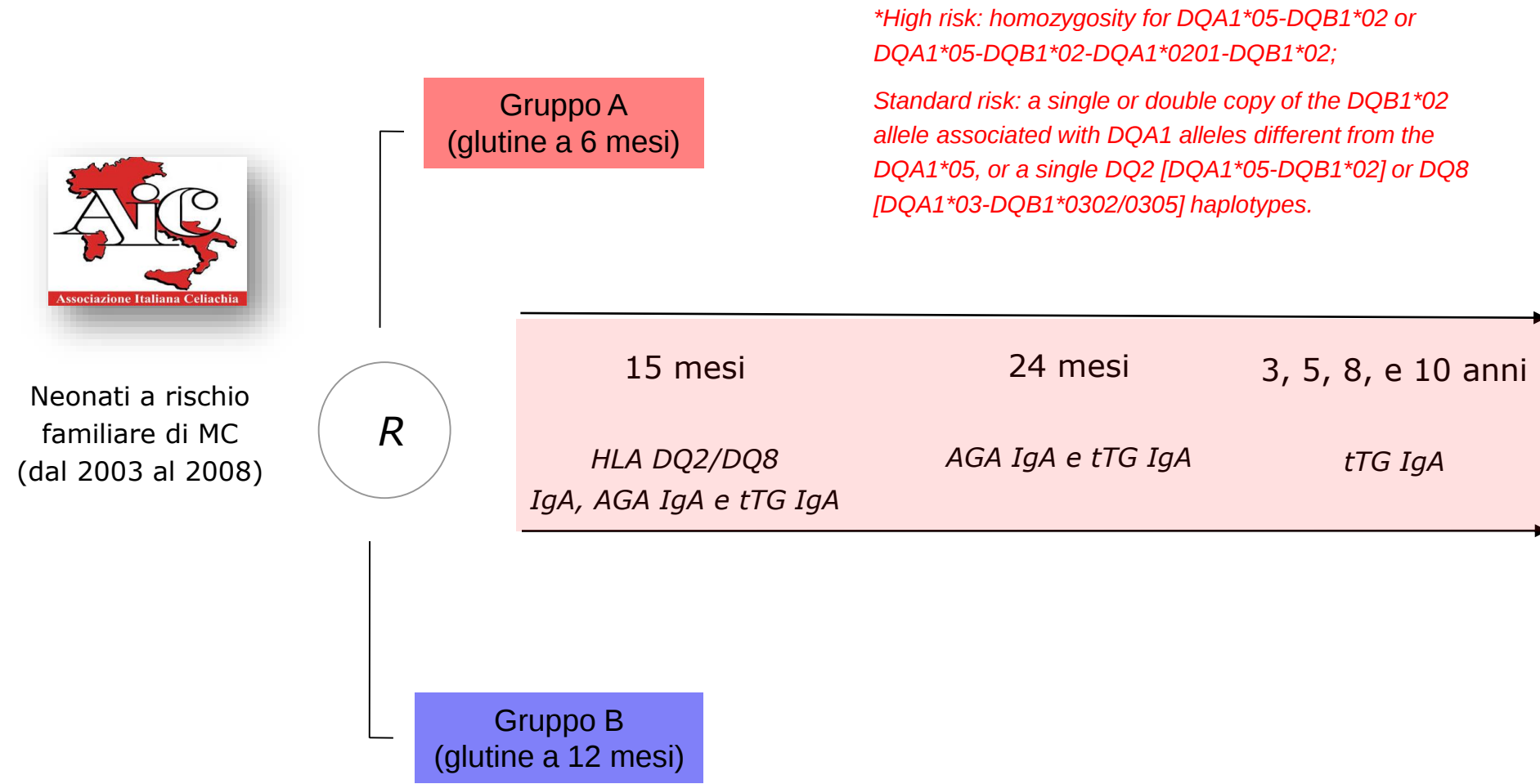
Elena Lionetti, M.D., Stefania Castellaneta, M.D., Ruggiero Francavilla, M.D., Ph.D.,
Alfredo Pulvirenti, Ph.D., Elio Tonutti, M.D., Sergio Amarri, M.D., Maria Barbato, M.D.,
Cristiana Barbera, M.D., Graziano Barera, M.D., Antonella Bellantoni, M.D.,
Emanuela Castellano, M.D., Graziella Guariso, M.D., Maria Giovanna Limongelli, M.D.,
Salvatore Pellegrino, M.D., Carlo Polloni, M.D., Claudio Ughi, M.D.,
Giovanna Zuin, M.D., Alessio Fasano, M.D., Ph.D., and Carlo Catassi, M.D., Ph.D.,
for the SIGENP (Italian Society of Pediatric Gastroenterology, Hepatology,
and Nutrition) Working Group on Weaning and CD Risk

CELIPREV – Scopo dello studio

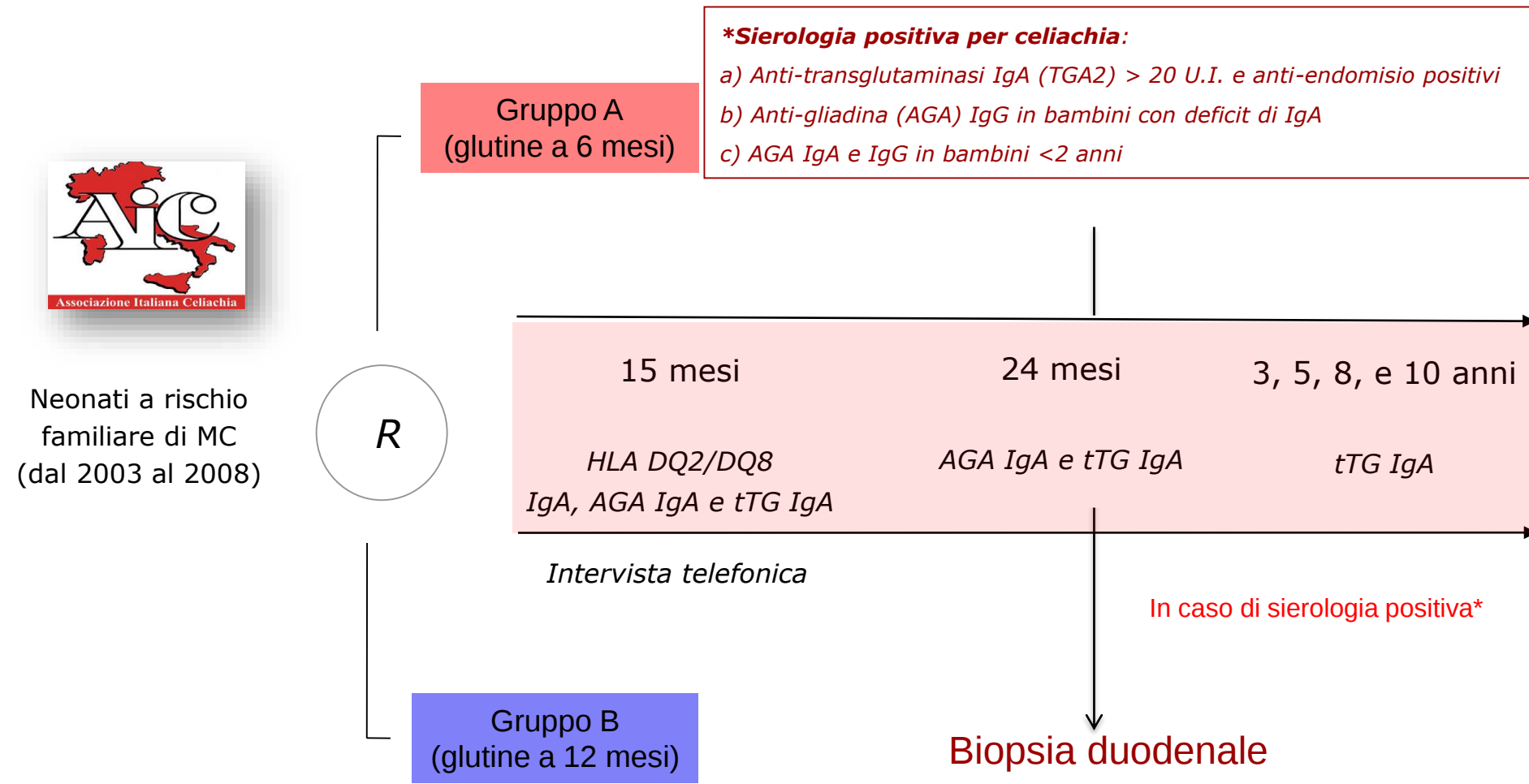
In un trial multicentrico prospettico di intervento nutrizionale in lattanti a rischio familiare di celiachia:

- 1) L'epoca di introduzione del glutine influenza il rischio di celiachia (*6 vs 12 mesi*)?
- 2) L'allattamento materno e introdurre il glutine durante l'allattamento materno influenzano il rischio di celiachia?
- 3) Qual è l'interplay tra tutte le variabili a disposizione nell'influenzare il rischio di celiachia?

Disegno dello studio



Disegno dello studio



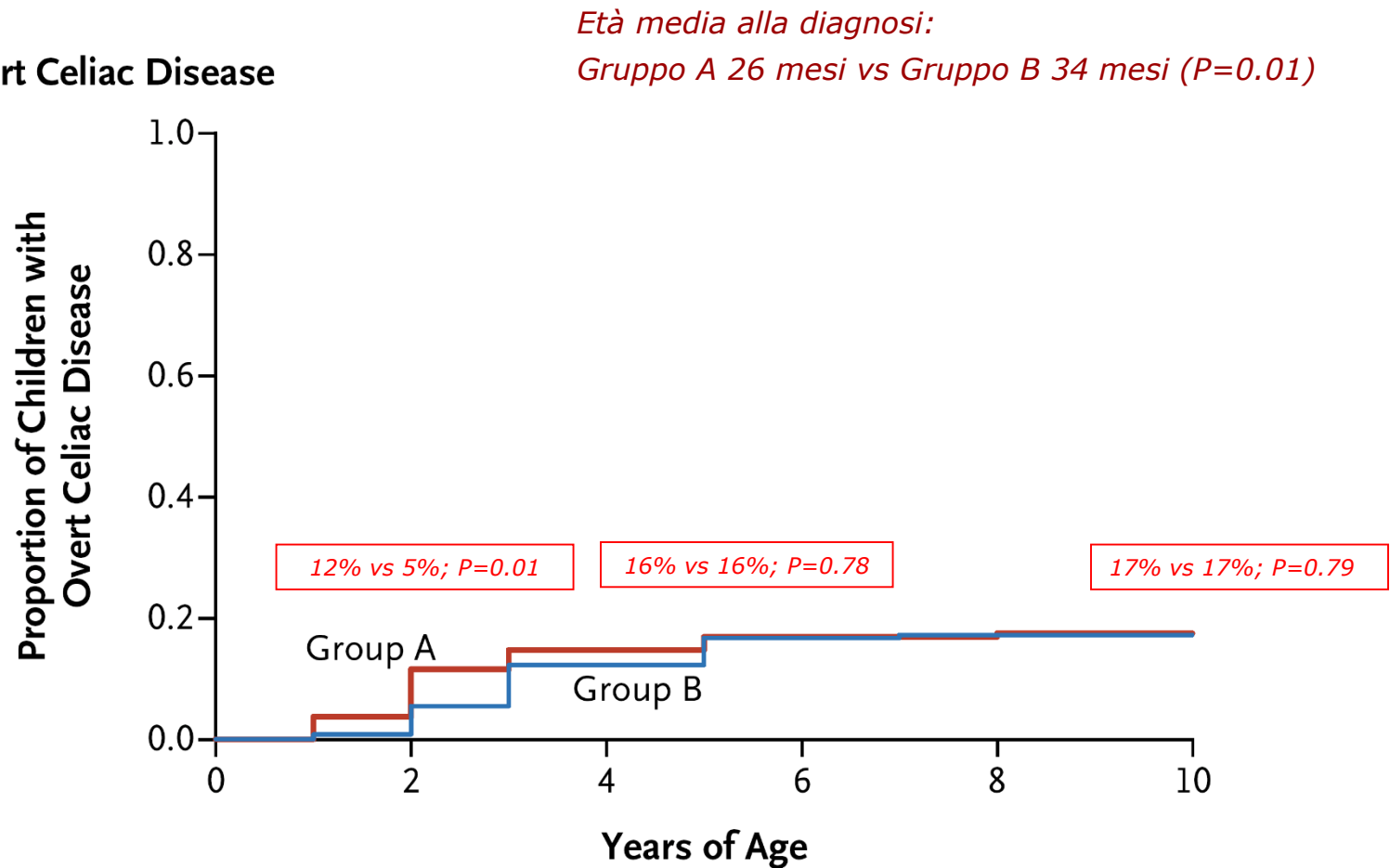
"Malattia celiaca conclamata": sierologia positiva* e Classificazione di Marsh 2 o 3

"Malattia celiaca potenziale": sierologia positiva* e Classificazione di Marsh 0 o 1

1. Epoca di introduzione del glutine e celiachia

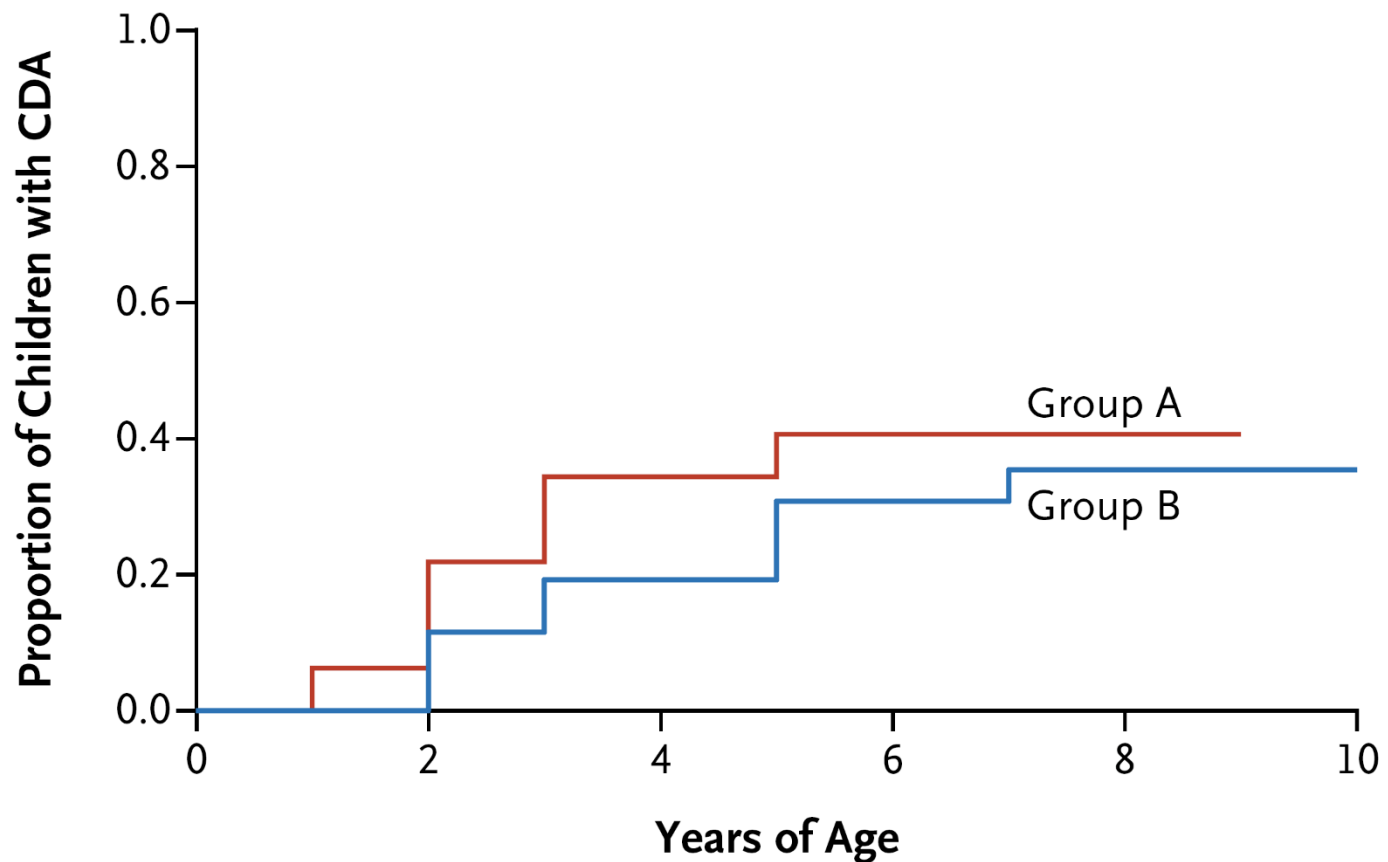
Kaplan-Meier dello sviluppo di celiachia in base al gruppo (A o B)

Overt Celiac Disease



1. Epoca di introduzione del glutine e celiachia

Kaplan-Meier dello sviluppo di celiachia in base al gruppo in bambini ad alto rischio HLA



Epoca di introduzione del glutine e celiachia - Prevent-CD

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Feeding Intervention in Infants at High Risk for Celiac Disease

S.L. Vriezinga, R. Auricchio, E. Bravi, G. Castillejo, A. Chmielewska, P. Crespo Escobar, S. Kolaček, S. Koletzko, I.R. Korponay-Szabo, E. Mummert, I. Polanco, H. Putter, C. Ribes-Koninckx, R. Shamir, H. Szajewska, K. Werkstetter, L. Greco, J. Gyimesi, C. Hartman, C. Hogen Esch, E. Hopman, A. Ivarsson, T. Koltai, F. Koning, E. Martinez-Ojinaga, C. te Marvelde, A. Mocic Pavic, J. Romanos, E. Stoopman, V. Villanacci, C. Wijmenga, R. Troncone, and M.L. Mearin

ABSTRACT

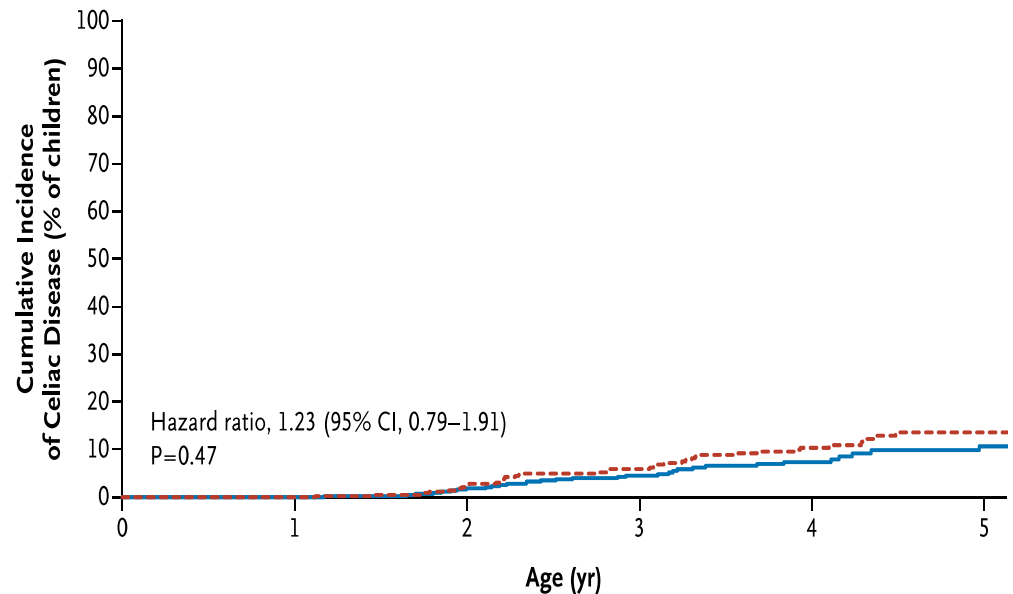
BACKGROUND

A window of opportunity has been suggested for reducing the risk of celiac disease by introducing gluten to infants at 4 to 6 months of age.

METHODS

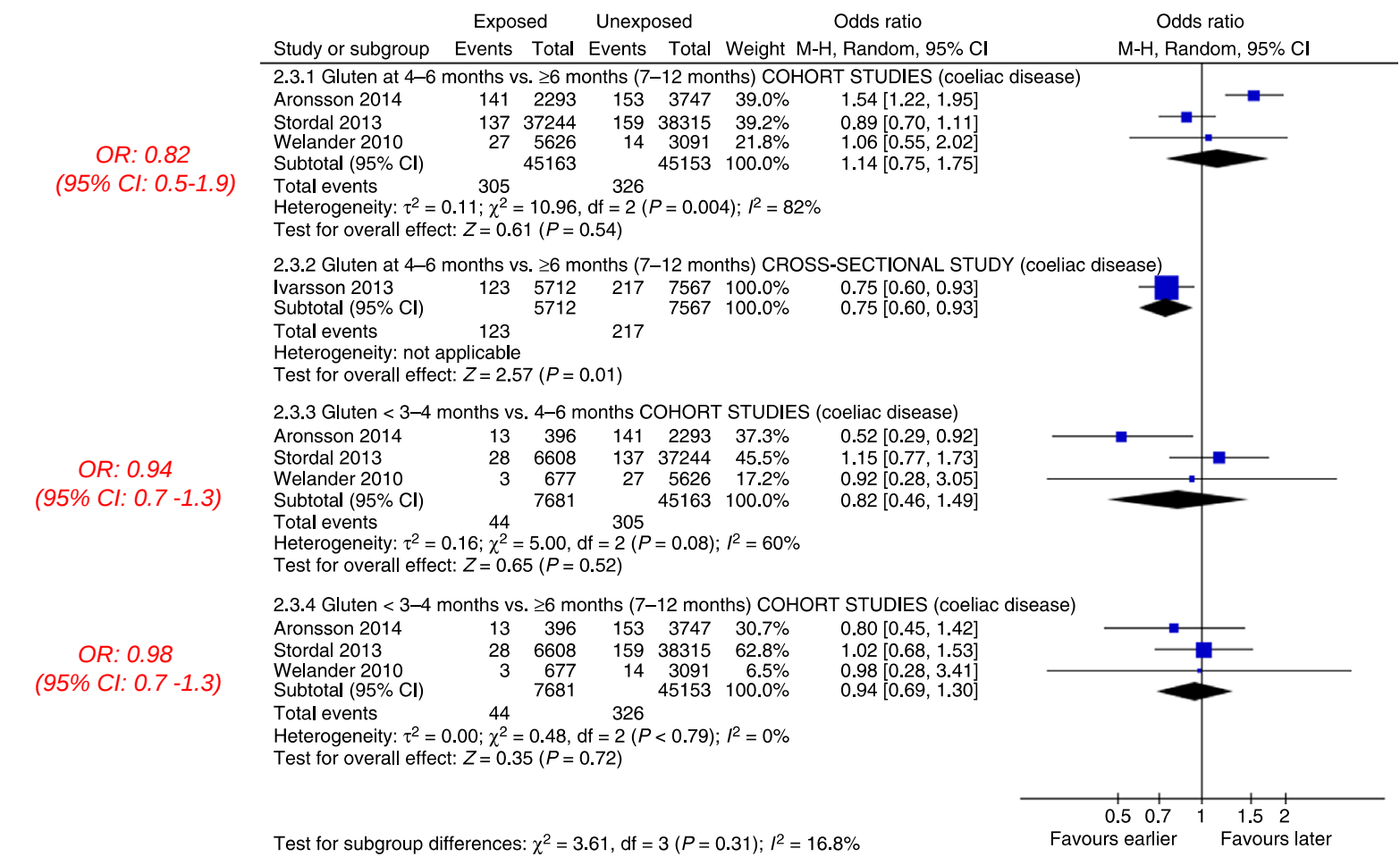
We performed a multicenter, randomized, double-blind, placebo-controlled dietary intervention study involving 944 children who were positive for HLA-DQ2 or HLA-DQ8 and had at least one first-degree relative with celiac disease. From 16 to 24 weeks of age, 475 participants received 100 mg of immunologically active gluten daily, and 469 received placebo. Anti-transglutaminase type 2 and antigliadin antibodies were periodically measured. The primary outcome was the frequency of biopsy-confirmed celiac disease at 3 years of age.

Incidenza cumulativa di celiachia in base al gruppo (glutine verso placebo)



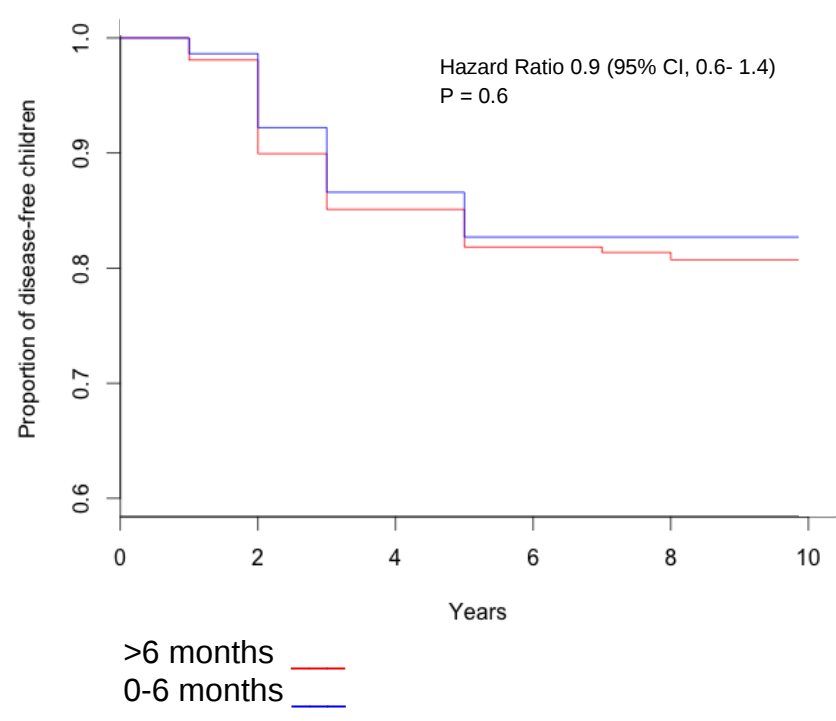
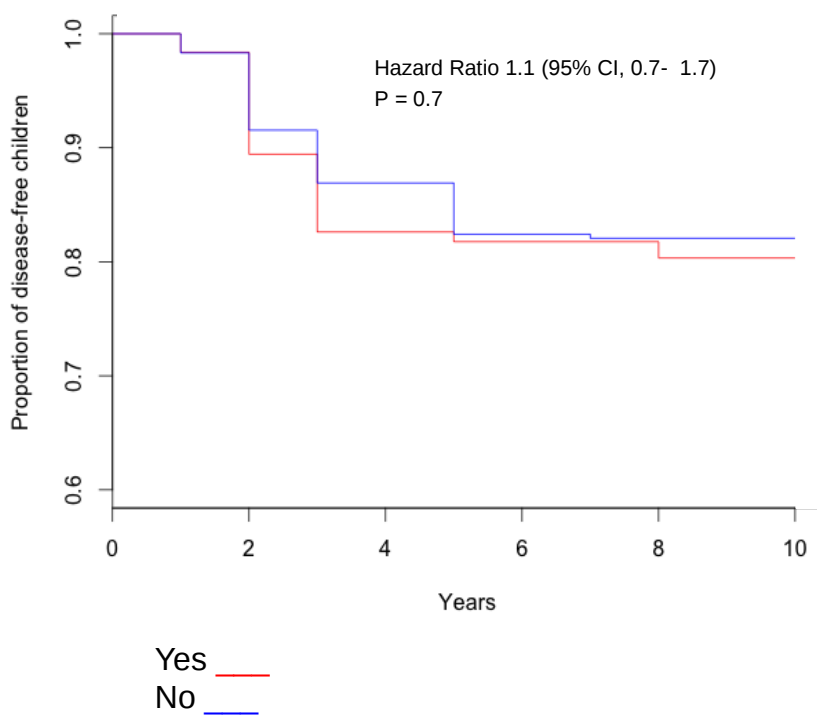
200 mg/day at 4-6 mo of age vs avoidance of gluten

Epoca di introduzione del glutine e rischio di malattia celiaca (studi osservazionali)



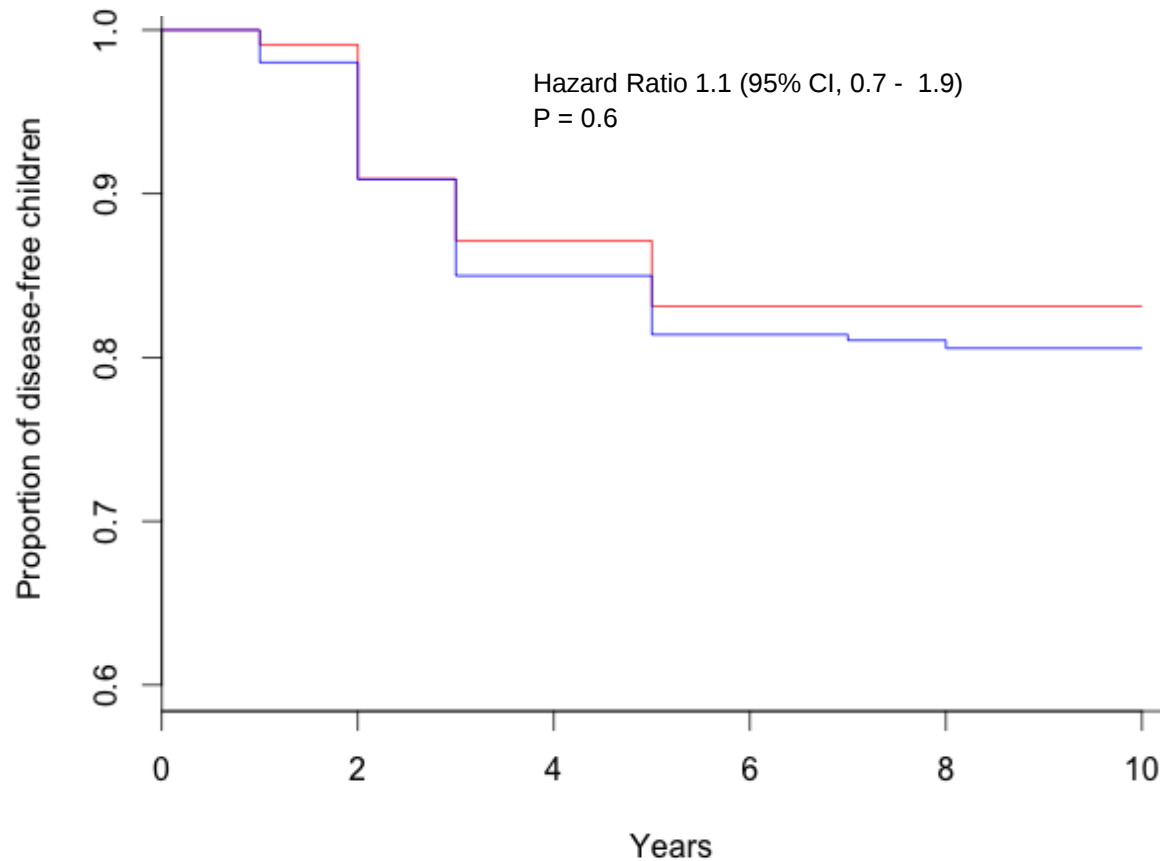
2. Allattamento e celiachia

Kaplan-Meier del rischio di MC in base all'allattamento



2. Allattamento e celiachia

Kaplan-Meier del rischio di MC in base all'allattamento durante l'introduzione del glutine

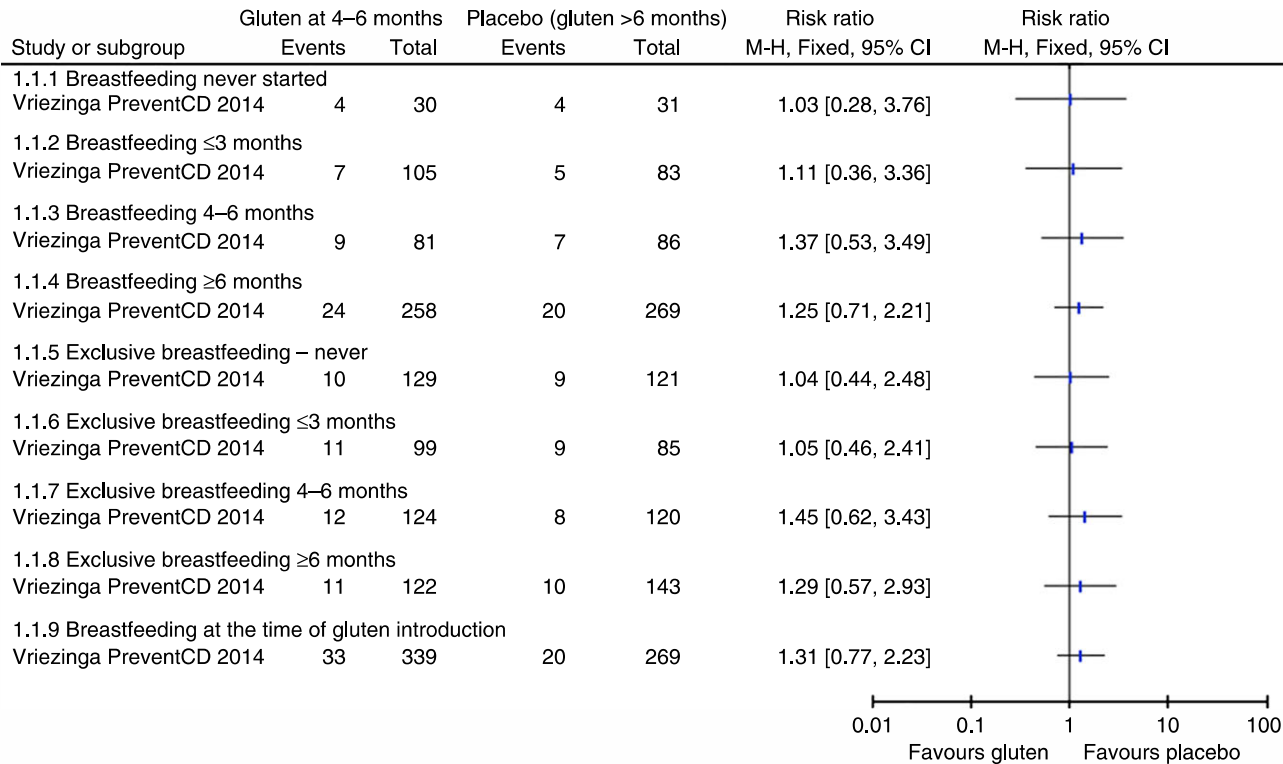


Breastfed during gluten introduction —

Not breastfed during gluten introduction —

Allattamento e rischio di celiachia - Prevent-CD

Effetto dell'allattamento sul rischio di celiachia

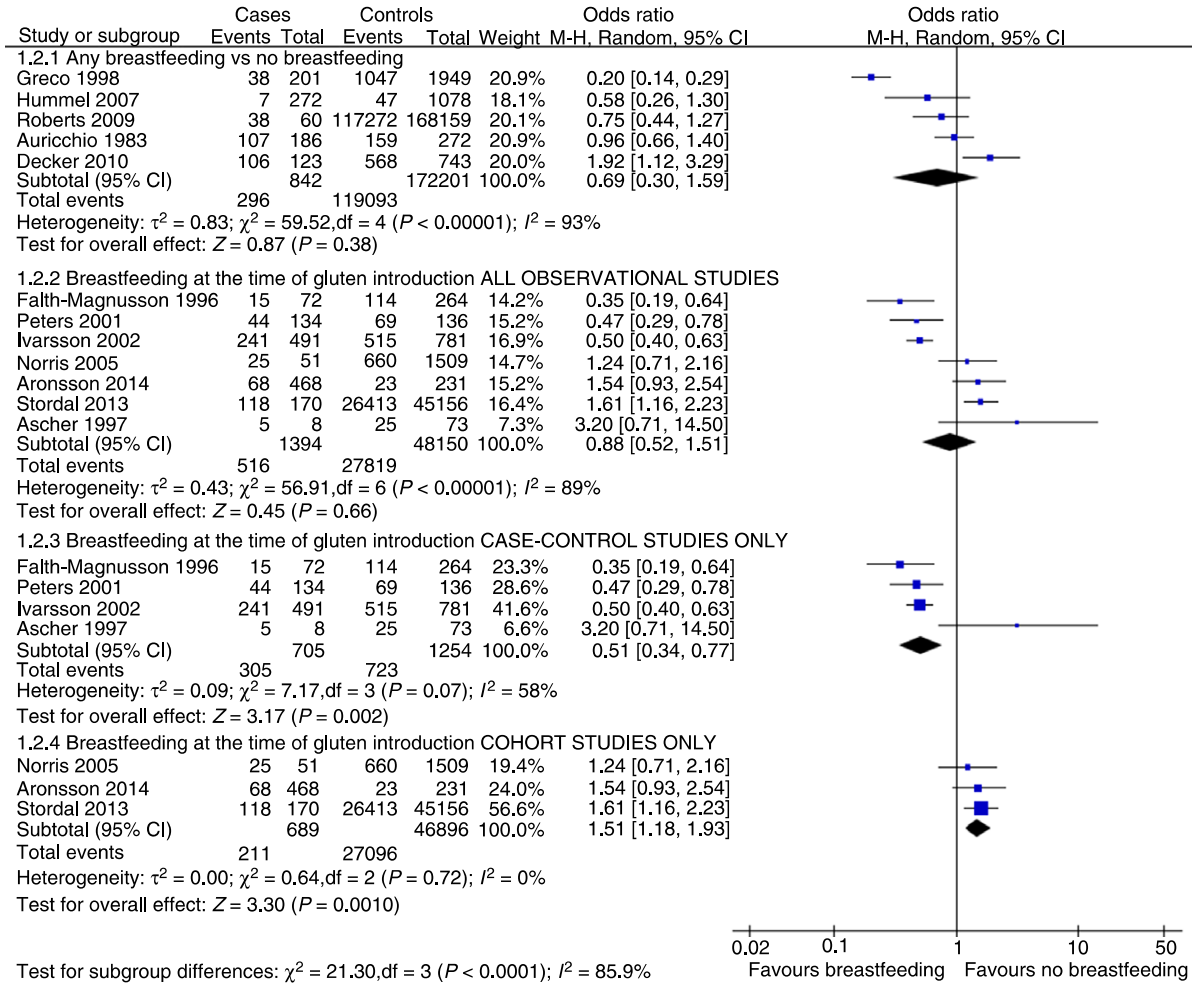


Allattamento e rischio di celiachia – dopo i trials....

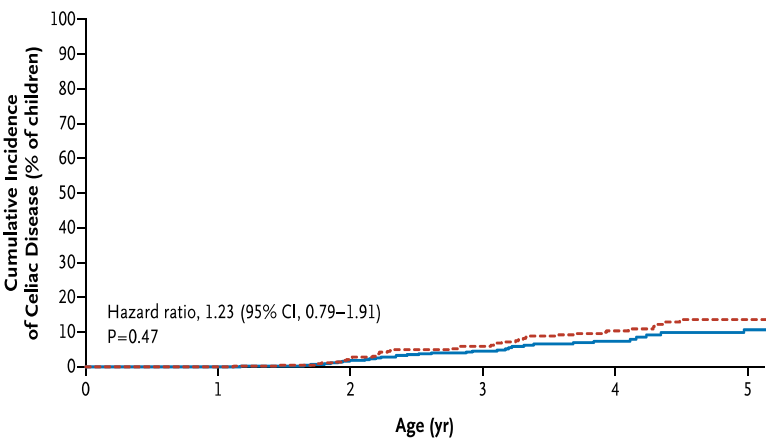
Durata di allattamento materno e rischio di malattia celiaca (studi osservazionali)

OR: 0.69
(95% CI: 0.3-1.5)

OR: 0.88
(95% CI: 0.5 -1.5)



3. La quantità e la qualità di glutine influenzano il rischio di celiachia?



200 mg/day at 4-6 mo of age vs avoidance of gluten

Dietary patterns during infancy and the risk of celiac disease before 2 y of age ¹					
Exposures	Bivariate analyses	Multivariate analyses			
		Model 1 ²	Model 2	Model 3 (final)	Model 4 ³
Breast-feeding status when flour was introduced					
Discontinued	1.0		1.0	1.0	1.0
Continued ⁴	0.55 (0.40, 0.77)		0.59 (0.42, 0.85)	0.59 (0.42, 0.83)	0.63 (0.46, 0.86)
Continued beyond ⁵	0.30 (0.22, 0.42)		0.35 (0.25, 0.50)	0.36 (0.26, 0.51)	0.35 (0.25, 0.48)
Age when flour was introduced					
1–4 mo	1.0	1.0	1.0	1.0	1.0
5–6 mo	1.8 (1.1, 2.9)	1.5 (0.93, 2.5)	1.5 (0.89, 2.5)	1.4 (0.87, 2.4)	1.2 (0.76, 1.9)
7–12 mo	0.86 (0.48, 1.6)	0.74 (0.40, 1.4)	0.79 (0.43, 1.5)	0.76 (0.41, 1.4)	0.71 (0.41, 1.3)
Daily average amount of flour consumed 2 wk after flour was introduced					
Small to medium	1.0	1.0	1.0	1.0	1.0
Large	2.0 (1.5, 2.7)	1.9 (1.4, 2.6)	1.6 (1.1, 2.3)	1.5 (1.1, 2.1)	1.4 (1.1, 1.9)
Type of food given when flour was introduced					
Solid foods	1.0	1.0	1.0		
Follow-up formula	1.4 (1.1, 1.9)	1.0 (0.75, 1.4)	0.89 (0.64, 1.2)		

Large vs small-medium gluten intake

Quando introdurre il glutine?

POSITION PAPER



Gluten Introduction and the Risk of Coeliac Disease: A Position Paper by the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition

^{*}Hania Szajewska, [†]Raanan Shamir, [‡]Luisa Mearin, [§]Carmen Ribes-Koninckx, ^{||}Carlo Catassi,
[¶]Magnus Domellöf, [#]Mary S. Fewtrell, ^{**}Steffen Husby, ^{††}Alexandra Papadopoulou,
^{‡‡}Yvan Vandenplas, ^{§§}Gemma Castillejo, ^{|||}Sanja Kolacek, ^{¶¶}Sibylle Koletzko,
^{###}Ilma R. Korponay-Szabó, ^{***}Elena Lionetti, ^{†††}Isabel Polanco, and ^{†††}Riccardo Troncone

1. *Neither any breast-feeding nor breast-feeding during gluten introduction has been shown to reduce the risk of CD.*
2. *Gluten may be introduced into the infant's diet anytime between 4 and 12 completed months of age.*
3. *In children at high risk for CD, earlier introduction of gluten (4 vs 6 months or 6 vs 12 months) is associated with earlier development of CD autoimmunity (defined as positive serology) and CD, but the cumulative incidence of each in later childhood is similar.*
4. *Consumption of large quantities of gluten should be avoided during the first weeks after gluten introduction and during infancy.*

Svezzamento e allergia



Prevenzione primaria: quale approccio?

Restrittivo



Promozionistico



Prevenzione primaria: approccio restrittivo



Prevenzione primaria: approccio restrittivo

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS



Hypoallergenic Infant Formulas
Committee on Nutrition
Pediatrics 2000;106;346-349



ACAAI
American College of Allergy, Asthma & Immunology

allergist

lattanti ad alto rischio



1 anno



2 anni



3 anni

American Academy of Pediatrics

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REVIEW ARTICLE

Primary prevention of food allergy in children and adults: systematic review

- ✓ In unselected populations one systematic review and two cohort studies found that introducing solid foods after 4 months did not protect against food allergy.
- ✓ In at risk infants two cohort studies found that delaying the introduction of solid foods longer than 4 months did not seem to confer any protective benefits.

Prevenzione primaria: approccio restrittivo



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††Luis Moreno, ‡‡John Puntis, §§Jacques Rigo, ¶¶Raanan Shamir, ||||²Hania Szajewska,
***Dominique Turck, and †††Johannes van Goudoever

“Avoidance or delayed introduction of potentially allergenic foods, such as fish and eggs, has not been convincingly shown to reduce allergies, either in infants considered at risk for the development of allergy or in those not considered to be at risk..”

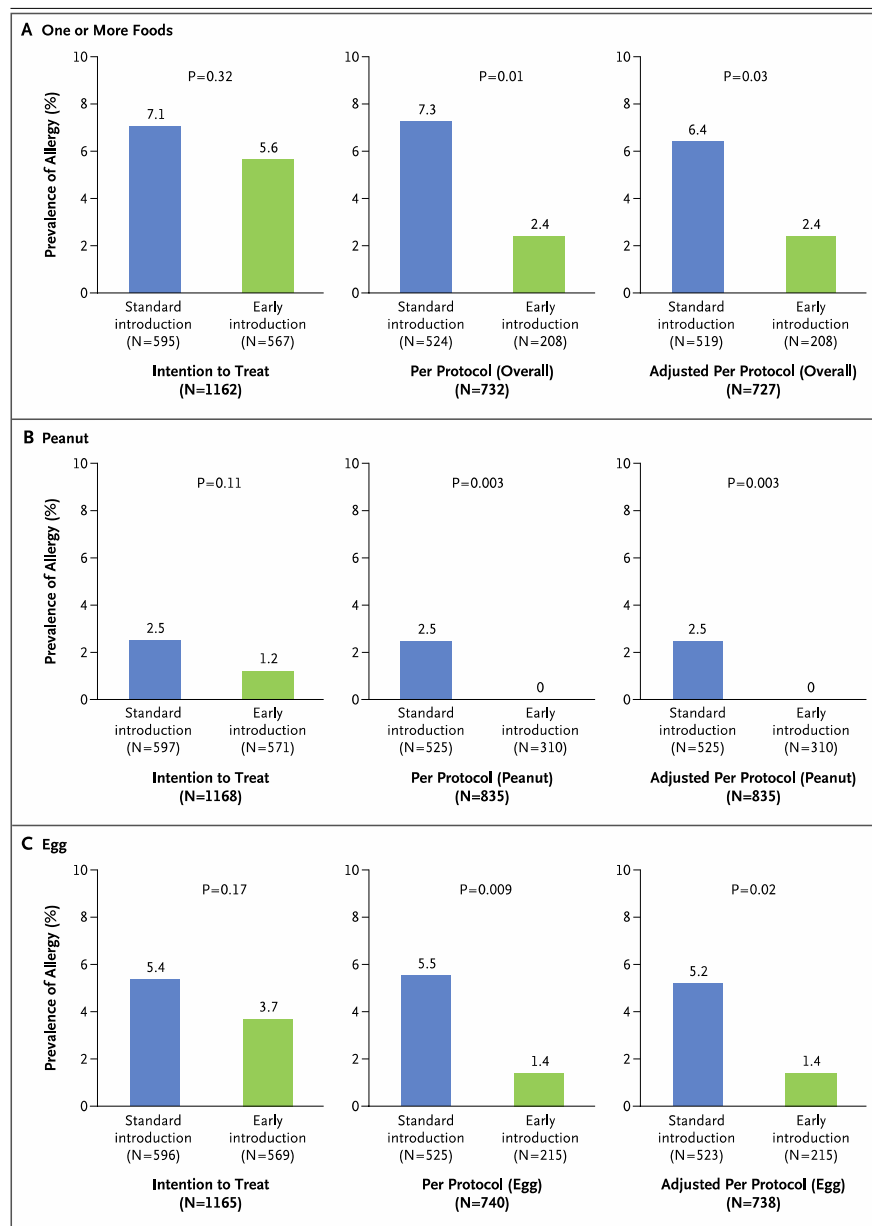
The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants

Michael R. Perkin, Ph.D., Kirsty Logan, Ph.D., Anna Tseng, R.D.,
Bunmi Raji, R.D., Salma Ayis, Ph.D., Janet Peacock, Ph.D., Helen Brough, Ph.D.,
Tom Marrs, B.M., B.S., Suzana Radulovic, M.D., Joanna Craven, M.P.H.,
Carsten Flohr, Ph.D., and Gideon Lack, M.B., B.Ch., for the EAT Study Team*

Prevenzione primaria: lo studio EAT



Prevenzione primaria: la metanalisi

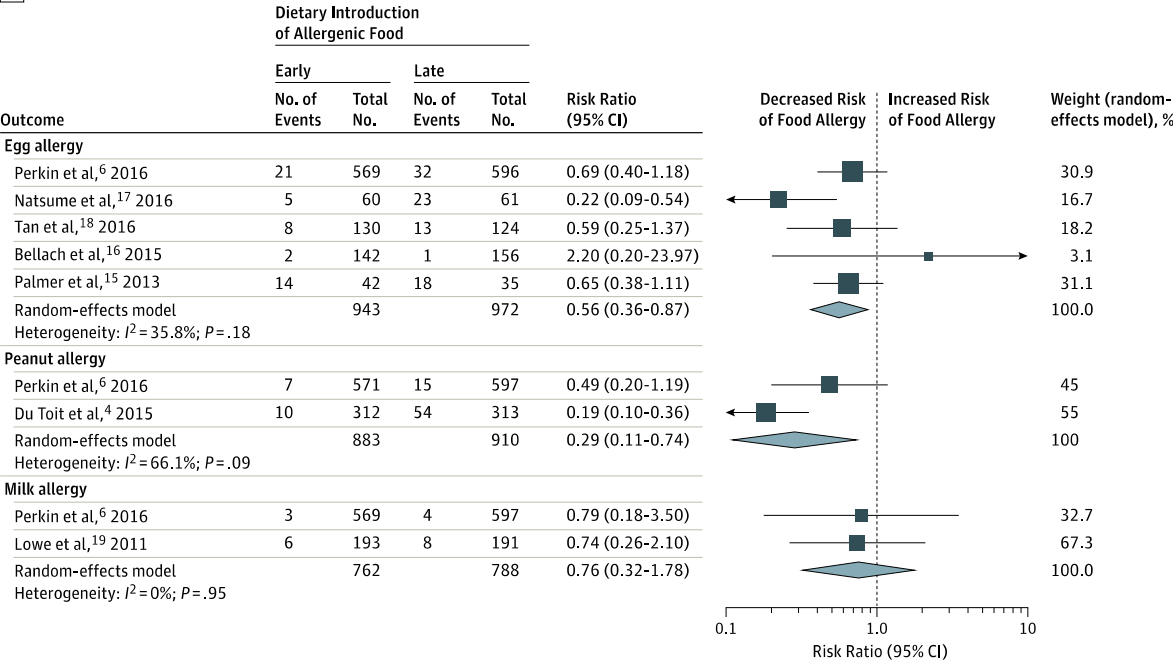
JAMA | Original Investigation

Timing of Allergenic Food Introduction to the Infant Diet and Risk of Allergic or Autoimmune Disease

A Systematic Review and Meta-analysis

Despo Ierodiakonou, MD, PhD; Vanessa Garcia-Larsen, PhD; Andrew Logan, PhD; Annabel Groome, BSc; Sergio Cunha, MD; Jennifer Chivinge, BSc; Zoe Robinson, BSc; Natalie Geoghegan, BSc; Katharine Jarrold, BSc; Tim Reeves, BSc; Nara Tagiyeva-Milne, PhD; Ulugbek Nurmatov, MD, PhD; Marialena Trivella, DPhil; Jo Leonardi-Bee, PhD; Robert J. Boyle, MD, PhD

A Risk of food allergy



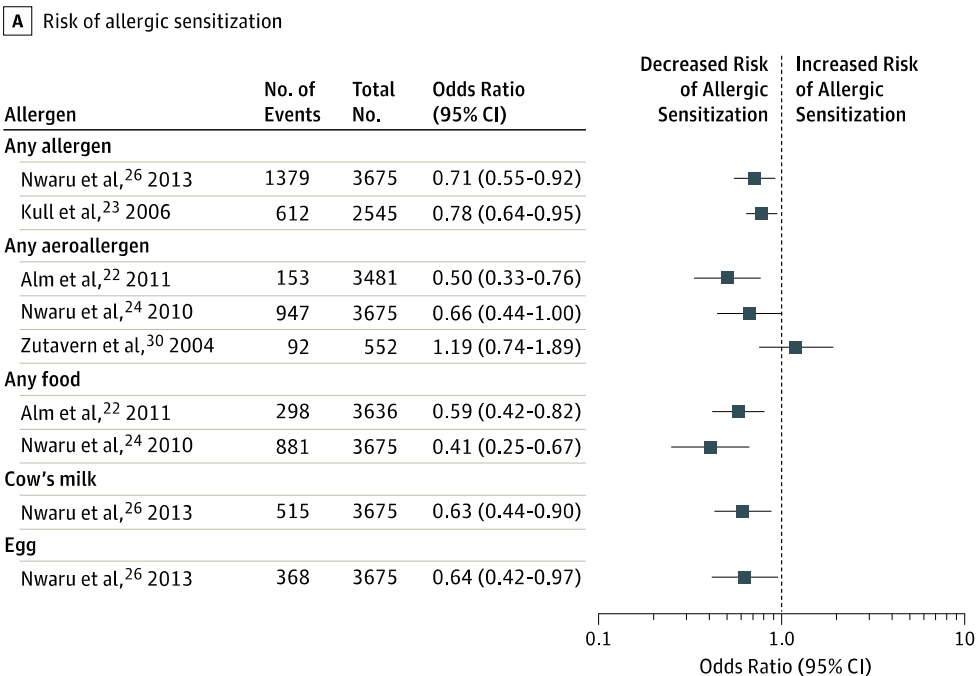
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Figure 2. Early Fish Introduction and Risk of Allergic Sensitization or Rhinitis



“Complementary feeding”

4. *Come?*

“Auto-svezzamento”



1. *Inadeguato intake di ferro?*
2. *Eccessivo apporto di sodio?*
3. *Apporto calorico insufficiente?*
4. *Rischio di aspirazione?*

Complementary feeding: conclusioni

1. *D*efinizione - *Introduzione di cibi solidi*

2. *Q*uando? - *Tra il 4° e il 6° mese*

3. *C*osa? - *Il glutine tra il 4° e il 12° mese;*

4. *C*ome? - *Responsive feeding*