

Age at gluten introduction and risk of celiac disease (CD): a prospective, multicentre, nutritional intervention study on infants at family risk

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Background (I)

- Celiac disease (CD) is an immune-mediated enteropathy caused by gluten ingestion in genetically predisposed individuals. CD is one of the commonest lifelong disorder showing a prevalence of 0.5 - 1 % in the general population of Europe and America. The disease prevalence is much higher among first-degree relatives of CD patients (8 - 15 %)
 - The complex interplay between genetic and environmental factors leading to the lack (or loss) of gluten tolerance is still poorly understood
 - Gluten is the external factor needed to trigger the disease. However the environmental component influencing CD development is complex and still unclear. Some aspects of gluten intake may influence the risk of CD occurrence, particularly (a) the amount of ingested gluten (the higher the amount the higher the risk); (b) the quality of ingested gluten (some grains contain more toxic epitopes than others), and (c) the pattern of infant feeding
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Background (II)

- ❑ The relationship between age at gluten introduction and the risk of CD is still controversial.
 - ❑ According to the recommendations of the European Society for Pediatric Gastroenterology and Nutrition (ESPGHAN), gluten-containing cereals must be introduced in the diet of European infants after the first 6 months of age. In infants who are at family risk of developing CD there is however the tendency of delaying gluten introduction even further. Primary prevention through food allergen avoidance may indeed reduce the prevalence of immune-mediated food intolerances.
 - ❑ The retrospective analysis of the so called “Swedish epidemics” of early-onset CD, suggested that
(a) prolonged breast feeding and (b) introduction of small amount of gluten while the infant was still breast fed between 4 and 6 months, reduced the risk of CD development.
 - ❑ Prospective studies on infants at genetic risk of T1D suggested that the risk of Type 1 Diabetes and CD is increased in infants started on gluten before 4 or after 7 months of age
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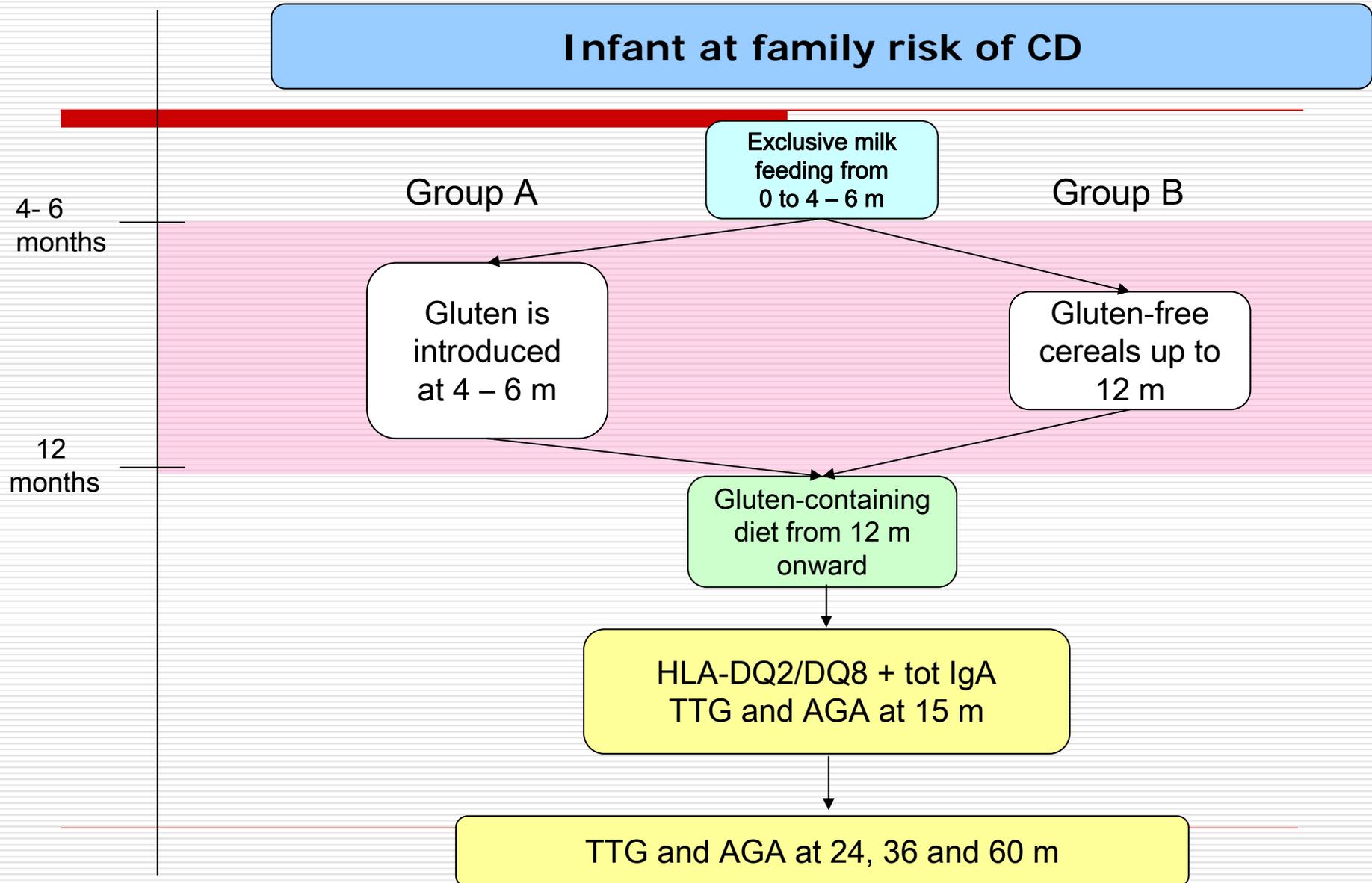
Aims of this study

- To evaluate the role of age at gluten introduction on the incidence of CD and related autoimmune serological changes in a large cohort of at-risk infants (first-degree relatives of patients with CD)
 - to investigate the role of other early environmental factors, particularly milk feeding, on the development of CD
 - to analyze the role of different HLA-DQ2/DQ8 molecules and genotypes (high risk versus low risk) on CD predisposition, and their interplay with infant nutrition patterns
 - to dissect the effect of different first-degree relationships on CD predisposition
 - to identify a cohort of infants at risk of developing CD that can be followed-up on a long-term basis for investigating the natural history of this common disorder, according to the pattern of infant nutrition
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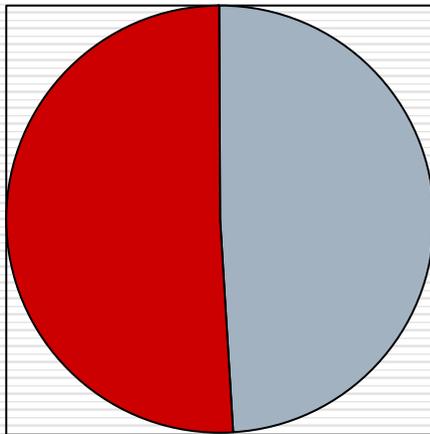
Inclusion criteria

- Newborns and infants aged less than 6 months still on exclusive milk feeding who were first-degree relatives of patients affected with biopsy-proven CD
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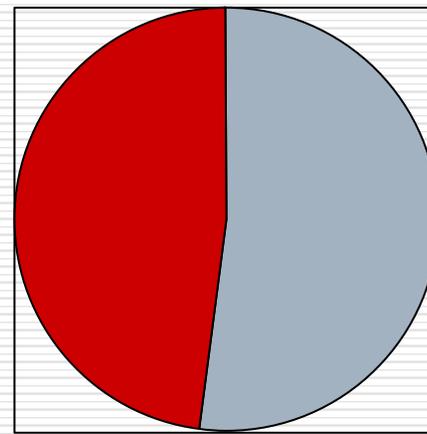
Study-design



Study group (n = 678)

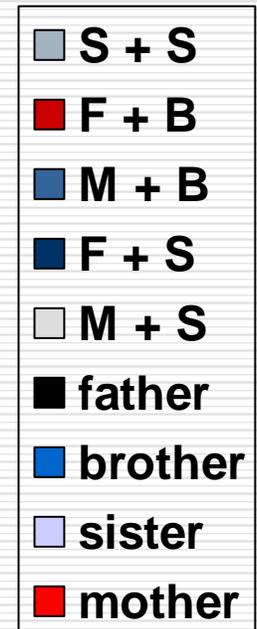
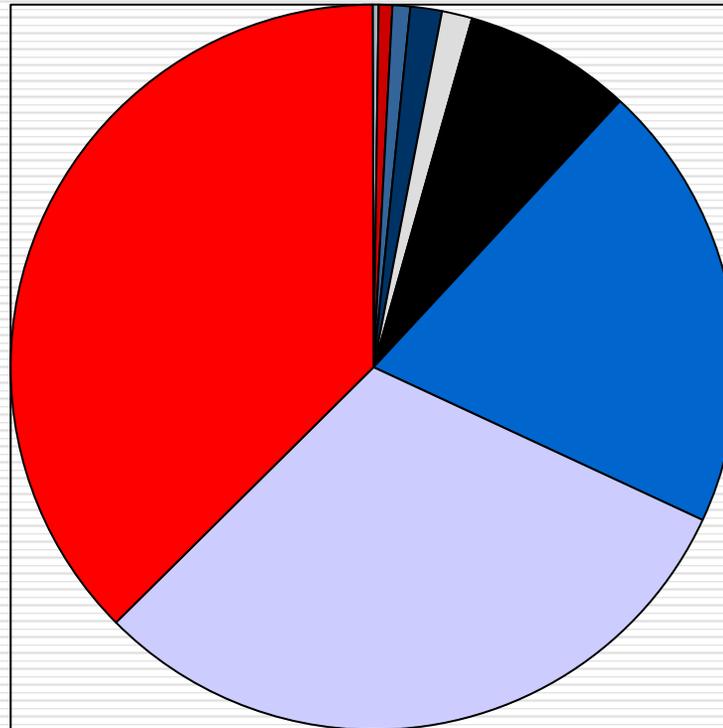


■ Females
■ Males

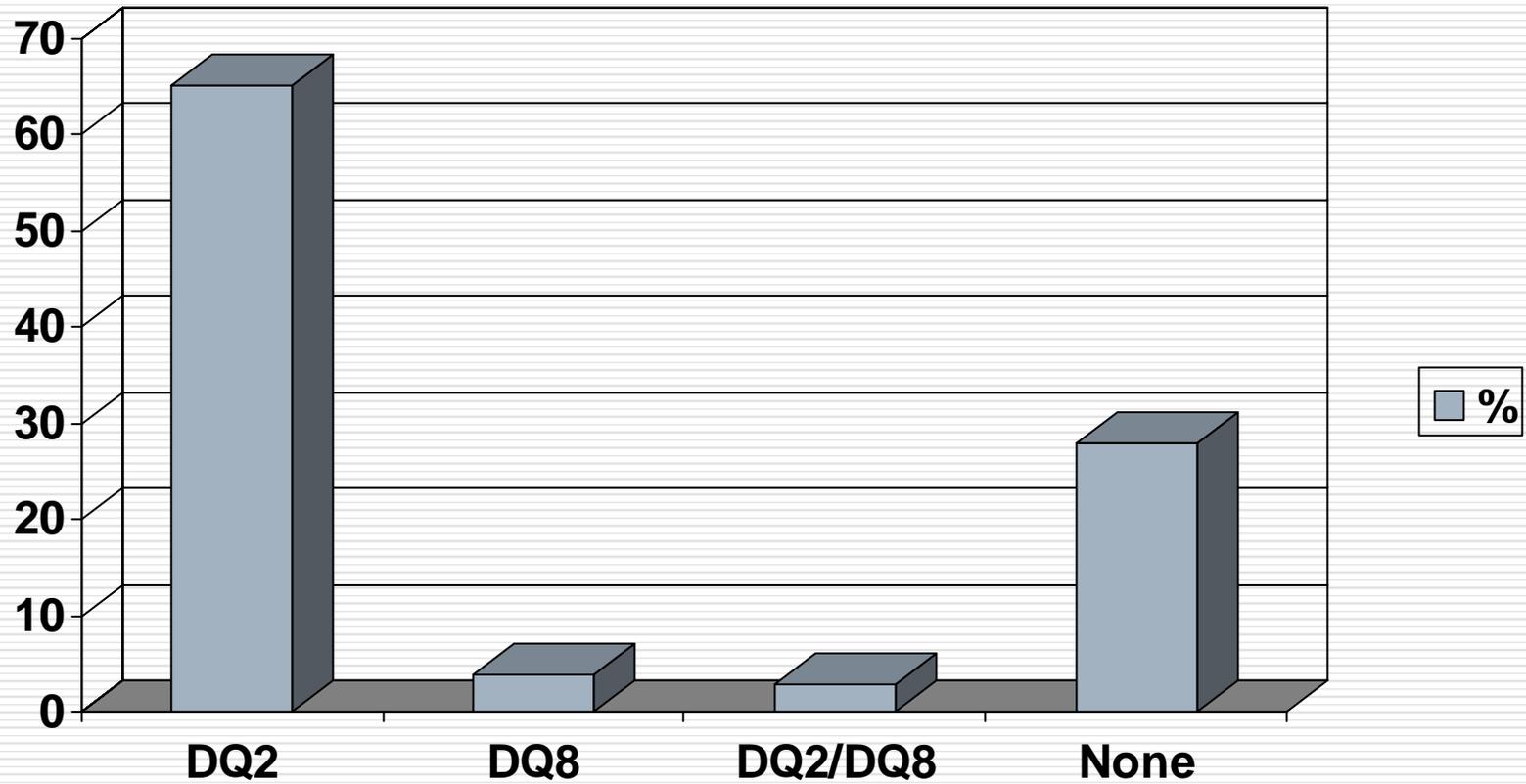


■ Group A
■ Group B

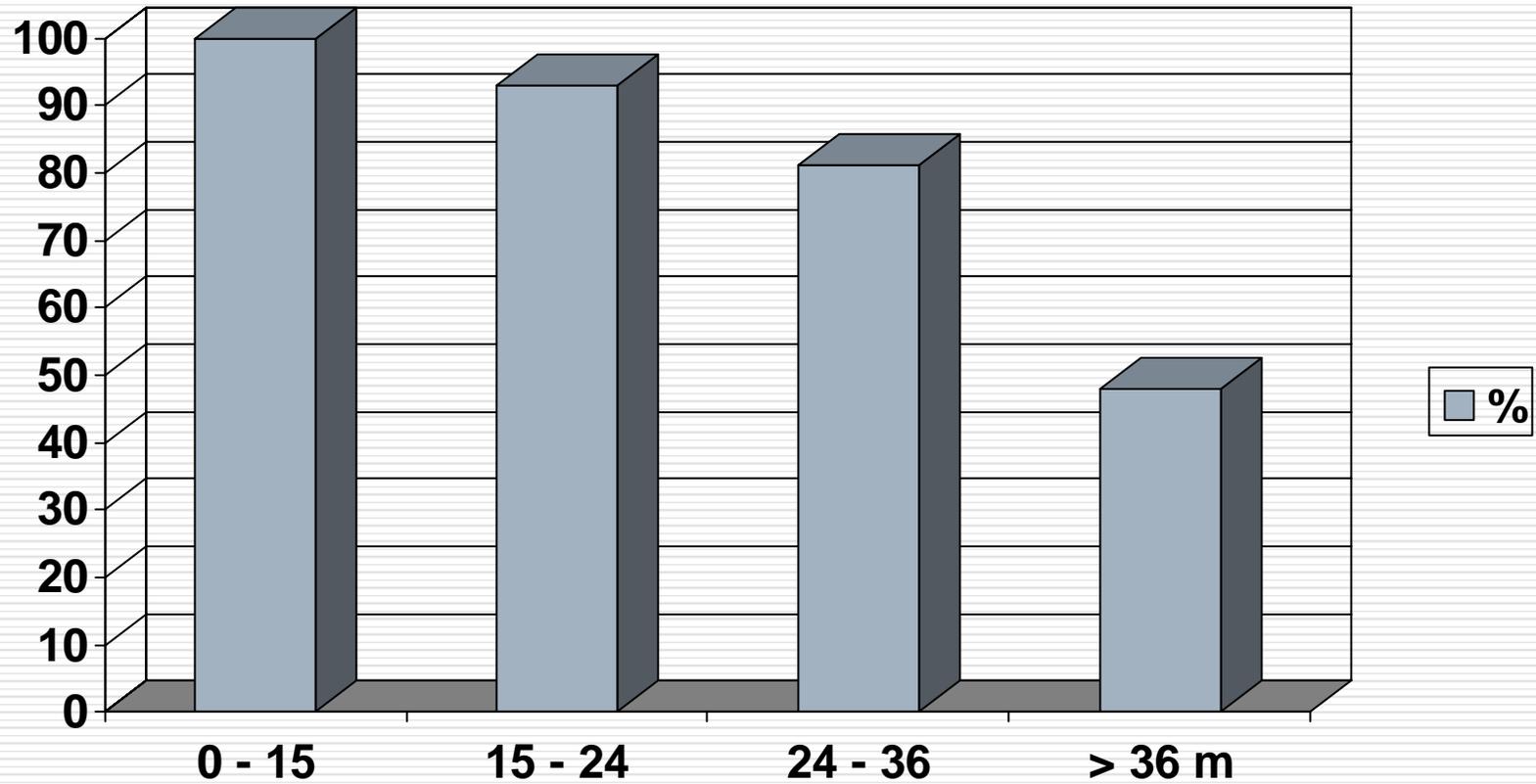
CD affected relative



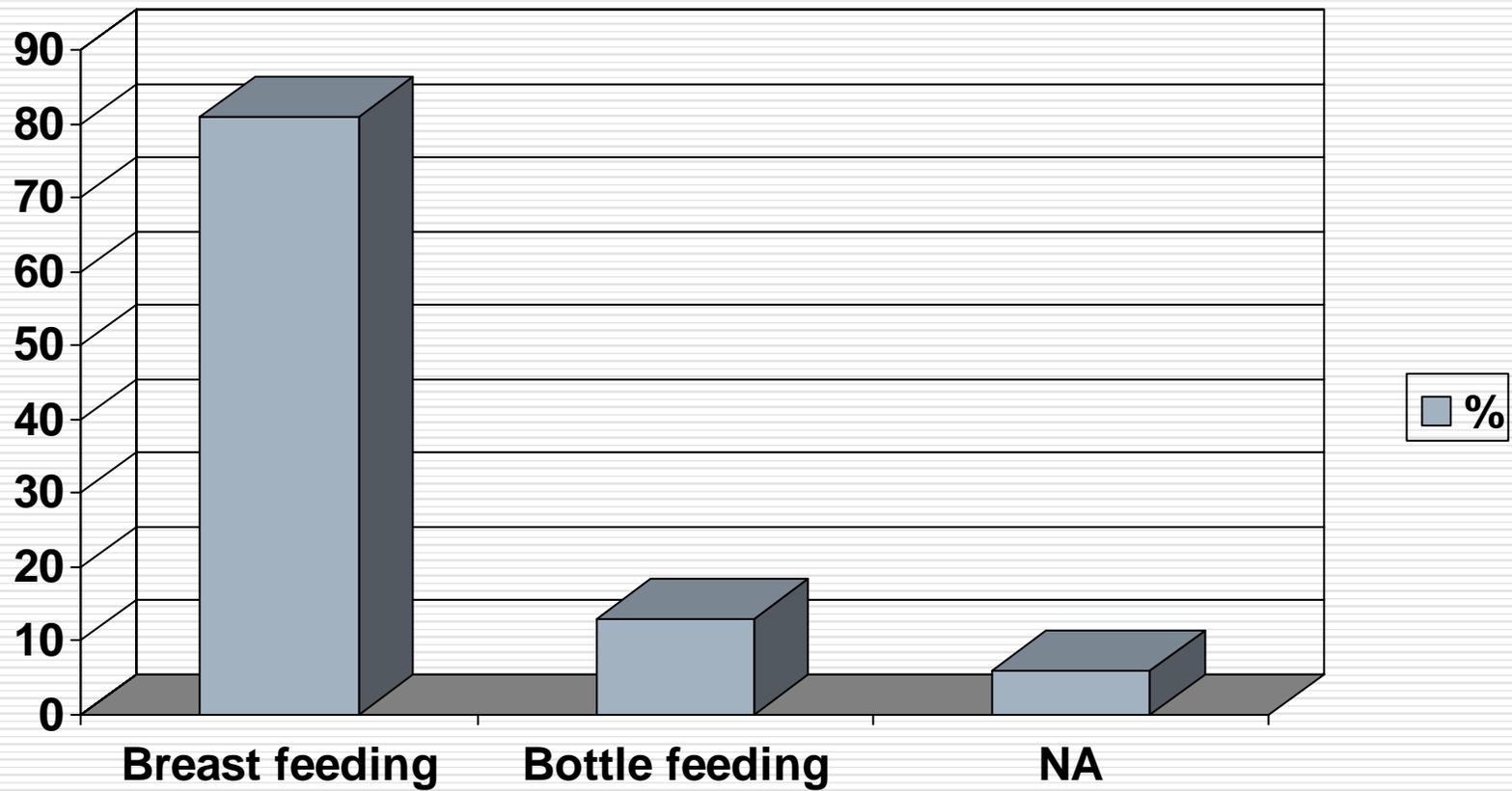
HLA-DQ status



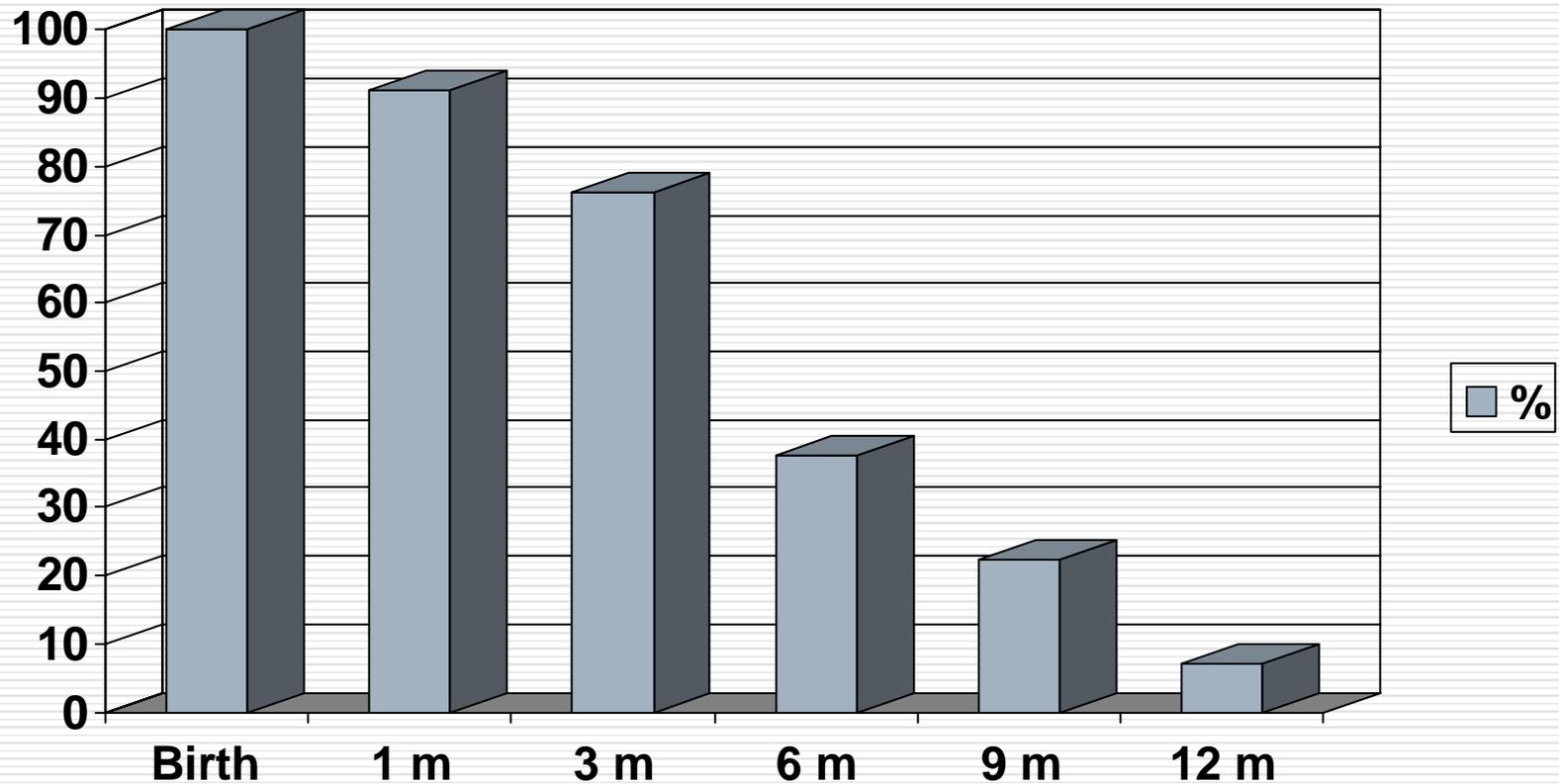
Duration of follow up



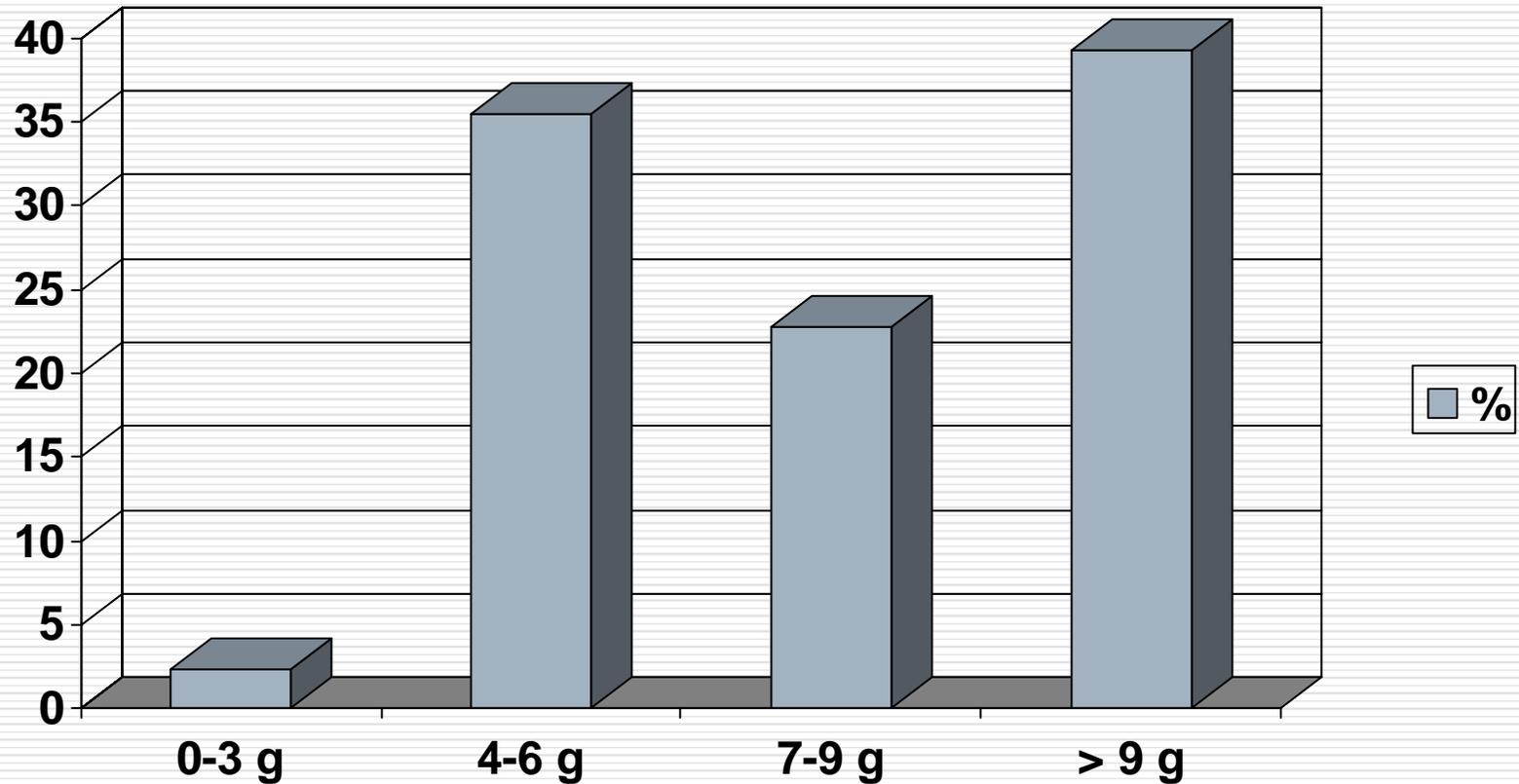
Milk feeding



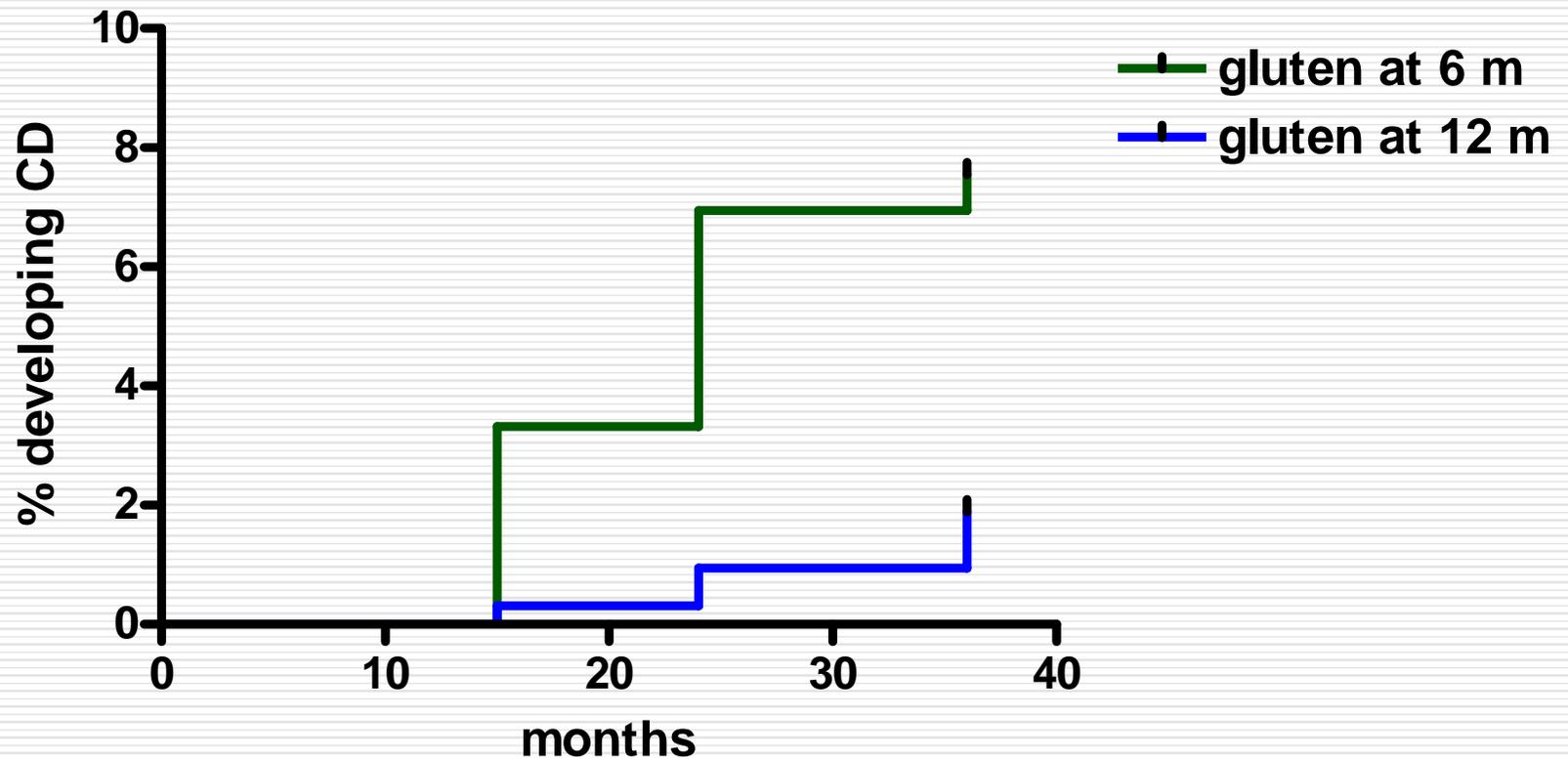
Duration of breast feeding



Daily gluten intake at 15 m



Age at gluten introduction and risk of CD development



Conclusive remarks (1)

- The recruitment phase of this prospective, nutritional intervention study has been completed between October 2004 and June 2007
 - 678 infants at family risk of CD have been enrolled in Italy and USA
 - In this selected group of infants (a) the duration of breast feeding was long, and (b) gluten intake after 12 months of age was high, compared with national standards
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Conclusive remarks (2)

- A significant proportion of newborns at family risk of CD show a HLA status at low risk of disease development
 - At 3 years of age the proportion of infants developing biopsy-proven CD was significantly higher among those weaned with gluten at 6 than at 12 months of age
 - A prolonged follow-up is required to clarify whether age at gluten introduction influences the risk of CD development or merely delays gluten sensitization
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