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Correspondence

Cost evaluation of mass screening of celiac disease in Italy: prediction is very difficult, especially if it is about the future

Dear Editor,

We read with great interest the article “Economic and organizational impact of a pediatric mass screening program for celiac disease in Italy” recently published on Digestive and Liver Disease. By analyzing the estimated costs of a region-wide celiac disease (CeD) pediatric screening, Gianiolo et al. conclude that the economic impact of mass CeD screening in Italy is hardly sustainable, while its benefits remain hypothetical [1].

Costs determination is an important step for evaluating the feasibility and the priority of any public health intervention. However, determining the cost of an articulated mass screening program that includes not only CeD but also the pre-symptomatic stage of Type 1 Diabetes (T1D) is complex and potentially misleading due to various limitations primarily related to model assumptions, evaluation methodology, and the difficulty of valuing intangible outcomes like quality of life or broader societal benefits.

First of all, authors based their calculations on the protocol of the D1Ce study, a pilot initiative aimed to evaluate the feasibility and the acceptability of the pediatric CeD and T1D screening [2]. However, the nationwide screening project will follow a different algorithm, that will be finalized soon after the results of the D1Ce screen will be fully analyzed. For instance, three different cohorts of children (aged 2, 6 and 10 yrs) underwent the CeD screening in the D1Ce study, while the nationwide CeD screening program will include only one or two age-groups, with a significantly lower economic impact, particularly during the first years of screening implementation. Furthermore, this cost analysis postulated that 100 % of children will participate to the CeD screening, while it is well known that a significant proportion of families refuse participation, with a consequent reduction of the economic load of the program. Other incorrect technical assumptions, that tend to inflate the costs of the CeD screening, are related to: (a) type of first-level screening test. This will not be the determination of total IgA and IgA class anti-transglutaminase (TTG) antibodies, but IgA- and IgG-TTG antibodies, that is less expensive and more suitable for large laboratory platforms; (b) the percentage of children requiring the small intestinal biopsy for diagnosis confirmation. Recent data show that in Italy this is currently much lower (18 %) [3] than that expressed in the cost analysis (45 %) [1]; (c) HLA genes determination. The D1Ce pilot-study included the search of HLA-permissive -DQ2 and -DQ8 genes, a test that is useful for excluding children with no genetic risk from repetition of CeD serology over time [2]. However, HLA testing will not be performed in the nationwide screening program, at least during the first years of screening implementation; (d) moreover, the cost of CeD-permissive HLA genes testing is overestimated (30–50 euros), since the determination of only HLA-DQB1*02 and DQB1*03:02 genes, which maximizes the negative predictive value of the test, costs <10 euros/sample if performed at scale [4].

It is important to note that nationwide CeD and T1D mass screening will most likely show a positive impact on several cost items, particularly in the long-term perspective, that may be difficult to forecast in advance (as the famous quote attributed to physicist Niels Bohr reminds us: “Prediction is very difficult, especially if it is about the future.”). For instance, (a) coupling of CeD and T1D, in addition to strengthen the screening for both diseases, will optimize some logistic costs, such as blood drawing and shipping of samples; (b) already today, the number of anti-TTG determinations that is covered by the National Health System is very high in Italy, since this test has become part of a routine hematological work-up in children. This cost load is expected to decrease as soon as the mass CeD screening will become effective countrywide. Furthermore, as Gianiolo and coworkers correctly noted, a significant economic implication of CeD screening is not related to screening itself, but to the follow up of identified cases, in relation with the reimbursement of gluten-free food by the Italian National Health System, one of the most generous worldwide. However, since the market of gluten-free food will raise significantly in parallel to the increasing prevalence of CeD generated by mass screening, the cost of gluten-free food is expected to decrease, as it happened in recent years particularly before the COVID epidemics [5].

Finally, and most importantly, it should be definitely recognized that screening-detected is not “silent” or asymptomatic” but rather “undiagnosed” CeD, a situation that may entail bad health for the child and costs for the caregivers and the society. The large majority of patients with screening-detected CeD do indeed benefit from a gluten-free diet with reduced gastrointestinal symptoms and improved health-related quality of life [6]. Although the possible negative effects of a strict dietary restriction on psychological well-being should receive special attention, early diagnosis and treatment may also protect against CeD-related long-term complications such as refractory CeD, infertility, impaired bone health, neurological symptoms and malignancies [7]. As recently pointed out by the Celiac Disease Screening and Autoimmunity Network (CD-SCAN) Group, there is no evidence suggesting that undiagnosed CeD without recognizable symptoms is biologically distinct from symptomatic CeD, particularly with respect to potential disease complications [8]. Despite some degree of uncertainty about the natural history of CeD, studies have shown that both pro-active CeD case-finding and mass screening, at a willingness to pay of €20,000 per QALY, are highly cost-effective compared with current care, but scenario analyses indicated that mass screening is likely

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the optimal strategy [9]. After all, individuals have the right to know their celiac status, and the decision to treat with the gluten-free diet should be guided by shared decision making with the child and the caretakers [8].

Recent data clearly show that mass CeD screening is largely superior to either targeted screening or case-finding in detecting the large proportion of cases that remain currently undiagnosed [10]. Italy has been the homeland of CeD screening studies, and is the first country to offer the CeD and T1D screening free of charge to all children that are resident in the country [2]. This initiative is currently followed with great interest by many world experts who believe that mass screening is the way to go in order to improve the health and possibly prevent untreatable CeD complications in a large number of children. In many countries, such as the US, Sweden, Norway and the Netherlands, several pilot-projects are currently under way to investigate the feasibility of CeD mass screening, according to the local features of the Public Health System [8]. Although this procedure may need future adjustments to maximize benefits and reduce the associated costs, it should be recognized that the implementation of CeD and T1D mass screening in Italy is a milestone achievement of pediatric preventive medicine. Ignoring the burden of undiagnosed CeD is a cost that no modern health system should afford.

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References

[1] Gianolio L, Magnani L, Topa M, Poli A, Cocuccio C, Mantegazza C, Scaramella L, Marsilio M, Zuccotti G, Elli L, Norsa L. Economic and organizational impact of a paediatric mass screening program for coeliac disease in Italy. Dig. Liver Dis. 2025;57(12):2339–46.

[2] Vincentini O, Pricci F, Silano M, Agrimi U, Iacoponi F, Villa M, Porfilio C, Sedile AI, Ulivi F, Catassi C, Cherubini V, D'Avino A, Carrera P, Lampasona V, Bosi E. Study protocol of D1Ce Screen: a pilot project of the Italian national screening program for type 1 diabetes and coeliac disease in the paediatric population. PLoS One 2025;20:e0328624.

[3] Brusco M, Trivellini S, Cozzali R, Brusaferro A, Morelli O, Simonte R, Di Cara G, Valitutti F. The environmental impact of pediatric celiac disease diagnosis and follow-up. JPGN Rep. 2025;6:236–40.

[4] Pedersen FB, Hauge AW, Hansen JF, Andersen LS, Blomsterberg S, Bruunsgaard H. Cost-effective and highly scalable typing of HLA classes I and II genes of up to 96 individuals using nanopore sequencing. HLA 2025;105:e70164.

[5] Lee AR, Wolf RL, Lebwohl B, Ciaccio EJ, Green PHR. Persistent economic burden of the gluten free diet. Nutrients 2019;11:399.

[6] Kvamme JM, Sørbye S, Florholmen J, Halstensen TS. Population-based screening for celiac disease reveals that the majority of patients are undiagnosed and improve on a gluten-free diet. Sci. Rep. 2022;12:12647.

[7] Laurikka P, Kivelä L, Kurppa K, Kaukinen K. Review article: systemic consequences of coeliac disease. Aliment Pharmacol. Ther. 2022;56(Suppl 1 (Suppl 1)):S64–72.

[8] Stahl MG, Liu E, Catassi C. Celiac Disease Screening and Autoimmunity Network (CD-SCAN) Group. Screening the general population for celiac disease: lessons from the first international symposium held in Denver 2024. J. Pediatr. Gastroenterol. Nutr. 2025;81:153–7.

[9] Heijdra Suasnabar J, Meijer CR, Smit L, van Overveld F, Thom H, Keeney E, Mearin ML, van den Akker-van Marle ME. Long-term cost-effectiveness of case finding and mass screening for celiac disease in children. Gastroenterology 2024;167:1129–40.

[10] Catassi GN, Pjetraj D, Gatti S, Lionetti E, Catassi C. Celiac disease detection strategies: poor performance of the case-finding policy. Am. J. Gastroenterol. 2023;118:1702–3.

Carlo Catassi*, Elena Lionetti
Department of Pediatrics, Polytechnic University of Marche, Ancona, Italy

Giulia N. Catassi
Pediatric Gastroenterology, Hepatology and Cystic Fibrosis Unit, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico di Milano, Milan, Italy

Emanuele Bosi
Diabetes Research Institute, IRCCS San Raffaele Hospital, Milan, Italy

*Corresponding author at: Polytechnic University of Marche, via F. Corridoni 11, Ancona I-60123, Italy.
E-mail address: c.catassi@univpm.it (C. Catassi)