



How novel technologies improve the diagnosis of celiac disease

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Celiac disease - diagnosis

CME

ACG Clinical Guidelines: Diagnosis and Management of Celiac Disease

Alberto Rubio-Tapia, MD¹, Ivor D. Hill, MD², Claran P. I

Diagnosis and management of adult coeliac disease: guidelines from the British Society of Gastroenterology

Jonas F Ludvigsson,^{1,2} Julio C Bai,³ Federico Biagi,⁴ Timothy R Card,⁵ ⁶iclitira,⁷ Peter H R Green,⁸ Marios Hadjivassiliou,⁹ A van Heel,¹¹ Katri Kaukinen,^{12,13,14} Daniel A Leffler,¹⁵ nut E A Lundin,¹⁷ Norma McGough,¹⁸ Mike Davidson,¹⁹ n L Swift,²¹ Marjorie M Walker,²² Fabiana Zingone,²³ rs of the BSG Coeliac Disease Guidelines Development Group

European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders

Abdulbaki Al-Toma¹, Umberto Volta², Renata Auricchio^{3,*}, Gemma Castillejo^{4,*}, D Chris J Mulder⁷ and Kn

European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020

^{*}Steffen Husby, [†]Sibylle Koletzko, [‡]Ilma Korponay-Szabó, [§]Kalle Kurppa, ^{||}Maria Luisa Mearin, [¶]Carmen Ribes-Koninckx, ^{‡‡}Raanan Shamir, ^{***}Riccardo Troncone, ^{**}Renata Auricchio, ^{††}Gemma Castillejo, ^{‡‡}Robin Christensen, ^{§§}Jernej Dolinsek, ^{|||}Peter Gillett, [†]Mai Nielsen, ^{***}Alina Popp, ^{¶¶}ergreet Wessels

NASPGHAN Clinical Report on the Diagnosis and Treatment of Gluten-related Disorders

^{*}Ivor D. Hill, [†]Alessio Fasano, [‡]Stefano Guandalini, [§]Edward Hoffenberg, ^{||}Joseph Levy, [¶]Norelle Reilly, and ^{‡‡}Ritu Verma

Serology and laboratory test:

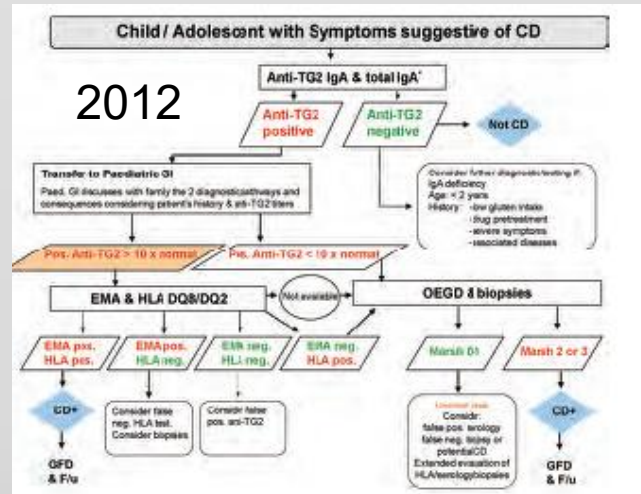
- **anti transglutaminase ab (tTG)**
- anti endomysial ab (EMA) → to confirm tTG positivity
- anti deamidated gliadine peptide (DGP)
- total IgA



Histology test

- Oesophageal-gastroduodenal endoscopy (EGDS)
- Duodenal biopsies

Celiac disease - diagnosis



1. Symptoms suggestive of CD (particularly malabsorption)
2. Serum levels of ≥ 10 times the upper limit of normal (ULN) of IgA antibodies against type-2 (tissue) transglutaminase (TGA-IgA)
3. Positive endomysial antibodies (EMA-IgA) in a second serum sample
4. Positive coeliac human leukocyte antigen (HLA) risk alleles DQ2 and/or DQ8
5. Omitting duodenal biopsies should only be considered in patients/parents who understand the diagnosis and are committed to a gluten-free diet. The diagnosis and follow-up of CD should be made by a paediatric gastroenterologist or paediatrician with extensive knowledge of CD.

European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020

*Steffen Husby, †Sibylle Koletzko, ‡Ilma Korponay-Szabó, §Kalle Kurppa, ||Maria Luisa Mearin, ¶Carmen Ribes-Koninckx, #Raanan Shamir, **Riccardo Troncone, ***Renata Auricchio, ††Gemma Castillejo, †††Robin Christensen, §§Jernej Dolinsek, ||||Peter Gillett, ¶¶Asbjørn Hróbjartsson, ##Tunde Koltai, §§Markku Maki, ††Sabrina Mai Nielsen, ***Alina Popp, ††††Ketil Størdal, †Katharina Werkstetter, and ††††Margreet Wessels

No biopsy

A no-biopsy approach is appropriate for children with TGA-IgA values ≥ 10 times the upper limit of normal with appropriate tests and positive endomysial antibodies (EMA-IgA) in a second serum sample.

Increased anti-tTG IgA titers can be especially important for children, where a titer 10 times the upper limit of normal ($>10\text{ULN}$) may eliminate invasive duodenal biopsies.

Celiac disease – diagnostic pitfalls



HISTOLOGY

- The histological features of the small intestinal enteropathy of CD may be patchy
- Duodenal damage may appear only in the duodenal bulb
- Biopsies' orientation may affect the result
- Needs skill pathologists, high inter-subject variability, subjective evaluation of damage



5-25% false negative results

(mild lesions are more difficult to diagnose than duodenal atrophy)

SEROLOGY

- Pre-analytical and post-analytical errors
- False Positive or False Negative results
- Newborn and children, patients with Down/Turner syndrome or T1D are at high risk of developing CD but may also experience temporary anti-tTG positive results: they may become negative or develop CD within 10 years.

CLINICAL—ALIMENTARY TRACT

Accuracy in Diagnosis of Celiac Disease Without Biopsies in Clinical Practice



Katharina Julia Werkstetter,¹ Ilma Rita Korponay-Szabó,^{2,3} Alina Popp,^{3,4} Vincenzo Villanacci,⁵ Marianna Saleme,⁵ Gabriele Heilig,¹ Søren Thue Lillevang,⁶ Maria Luisa Mearin,⁷ Carmen Ribes-Koninckx,⁸ Adrian Thomas,⁹ Riccardo Troncone,¹⁰ Birgit Filipiak,¹ Markku Mäki,³ Judit Gyimesi,² Mehri Najafi,¹¹ Jernej Dolinšek,¹² Stine Dydensborg Sander,¹³ Renata Auricchio,¹⁰ Alexandra Papadopoulou,¹⁴ Andreas Vécsei,¹⁵ Peter Sztanyi,¹⁶ Ester Donat,⁸ Rafaella Nenna,¹⁷ Philippe Alliet,¹⁸ Francesca Penagini,¹⁹ Hélène Garnier-Lengliné,²⁰ Gemma Castillejo,²¹ Kalle Kurppa,³ Raanan Shamir,²² Almuthe Christine Hauer,²³ Françoise Smets,²⁴ Susana Corujeira,²⁵ Myriam van Winckel,²⁶ Stefan Buderus,²⁷ Sonny Chong,²⁸ Steffen Husby,¹³ and Sibylle Koletzko,¹ on behalf of the ProCeDE study group

International multicenter study (33 centers in 21 countries) to verify the clinical performance of the ESPGHAN 2012 no-biopsy protocol

Table S21: Agreement between local and central histology summary

Table S21: Comparison between local and reference histopathology summarized into indicative for CD (Marsh 2 to 3A-C) or not (Marsh 0 and 1)

Local histopathology indicative for CD?	Reference histopathology indicative for CD?		
	No	Yes	Total
No	55	26	81
Yes	22	573	595
Total	77	599	676*

22 pos cases to neg

26 neg cases to pos

48 (7%) re-classified histology results

Table S23: Agreement between local histology statement and the final central diagnosis

Table S23: Comparison between local histopathology statement (biopsy specimen is considered to show normal villi or pathologic signs but not indicative for CD or signs of CD with villous atrophy) and the final central diagnosis; in contrast to tables S21, here are also patients included for whom the local pathologist did not give any Marsh staging but only an general judgement without staging.

Local histopathology statement	Final central diagnosis			
	No CD	Inconclusive	Proven CD	Total
Normal	32	9	20	61
Pathologic but no CD	11	3	18	32
Compatible with active CD	3	4	607	614
Total	46	16	645	707

Table S24: Agreement between local and central diagnosis

Table S24: Comparison between the local diagnosis by the clinical center as reported in the database (no CD, unclear, proven CD) and the final central diagnosis (no CD, inconclusive case or proven CD)

Local diagnosis	Final central diagnosis			
	No CD	Inconclusive	Proven CD	Total
No CD	31	3	8	42
Unclear / Inconclusive	14	10	37	61
Proven CD	1	3	600	604
Total	46	16	645	707

Low agreement between histology e diagnosis !!!!

From the ideal world...to the real world!

CLINICIANS



LABORATORY

It is important that laboratory expert deeply know the performance of anti-tTG in order to support clinicians in the management, evaluation and follow up of patients with discrepancies between serology and duodenal biopsy

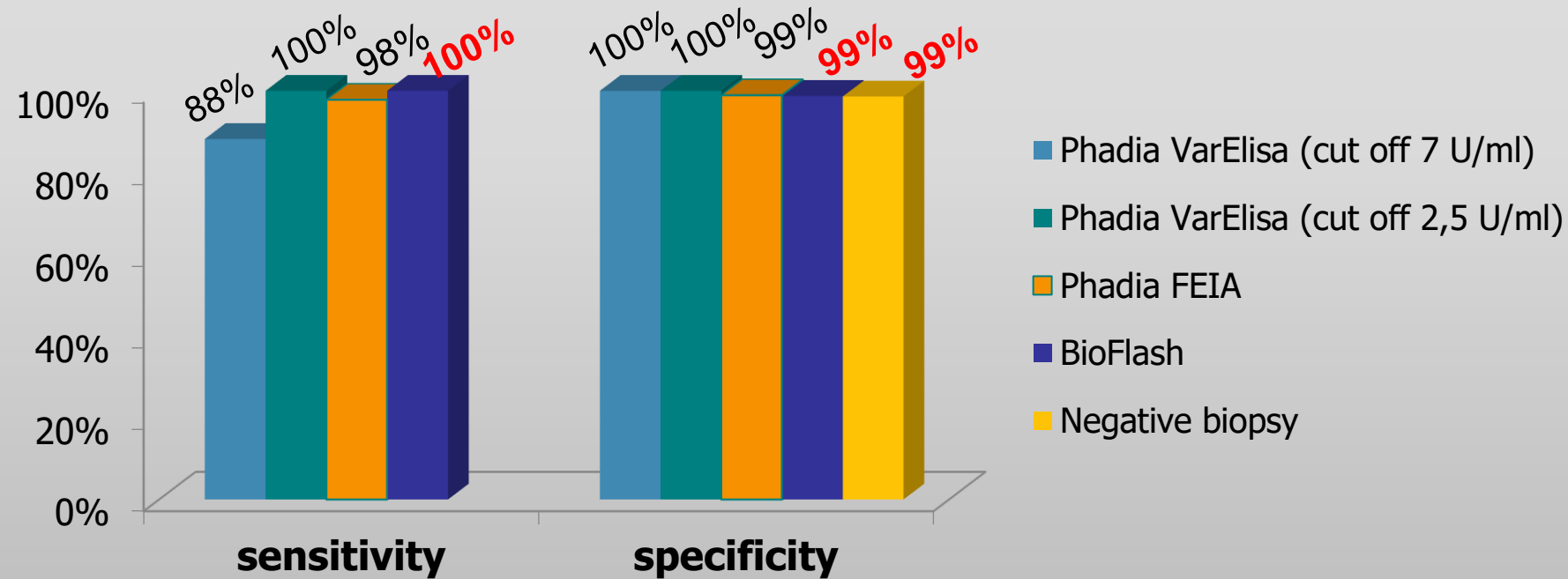


The laboratory added value

421 patients

100 CD patients biopsy-proven at diagnosis

321 control patients



High sensitivity and specificity

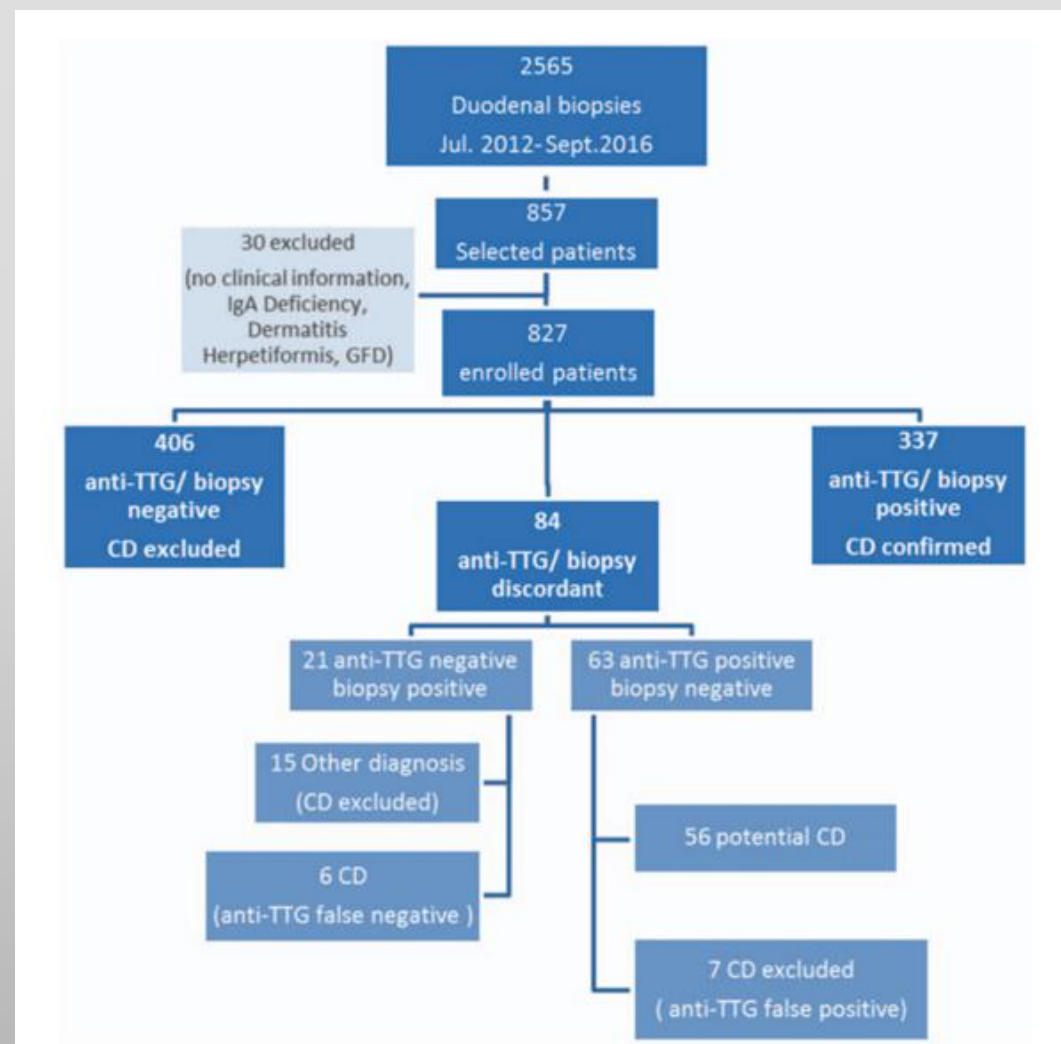


The laboratory added value

2116 consecutive patients on whom duodenal biopsy was performed at Papa Giovanni XXIII hospital from July 2012 to December 2015

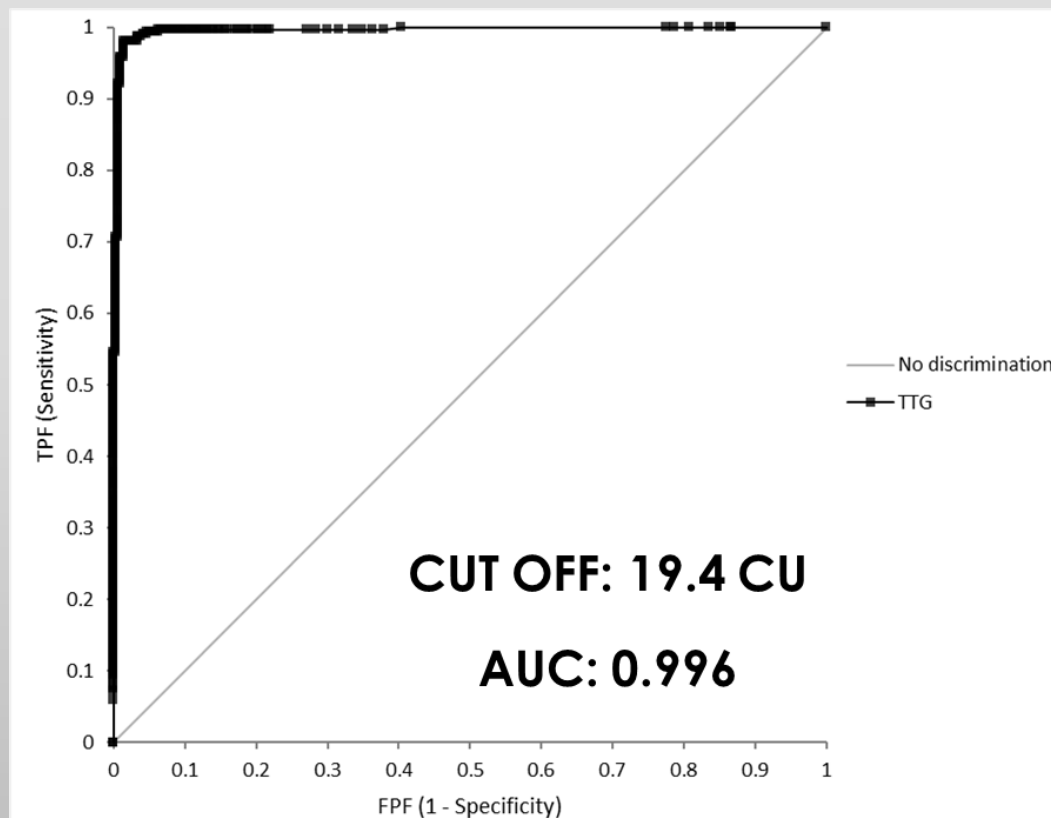
- **SEROLOGICAL TEST** (anti-tTG IgA) performed in our laboratory with BIO-FLASH®
- **DUODENAL BIOPSY** performed within + 3 months (from the serological test)
- **CLINICAL INFORMATION** available

827 enrolled patients

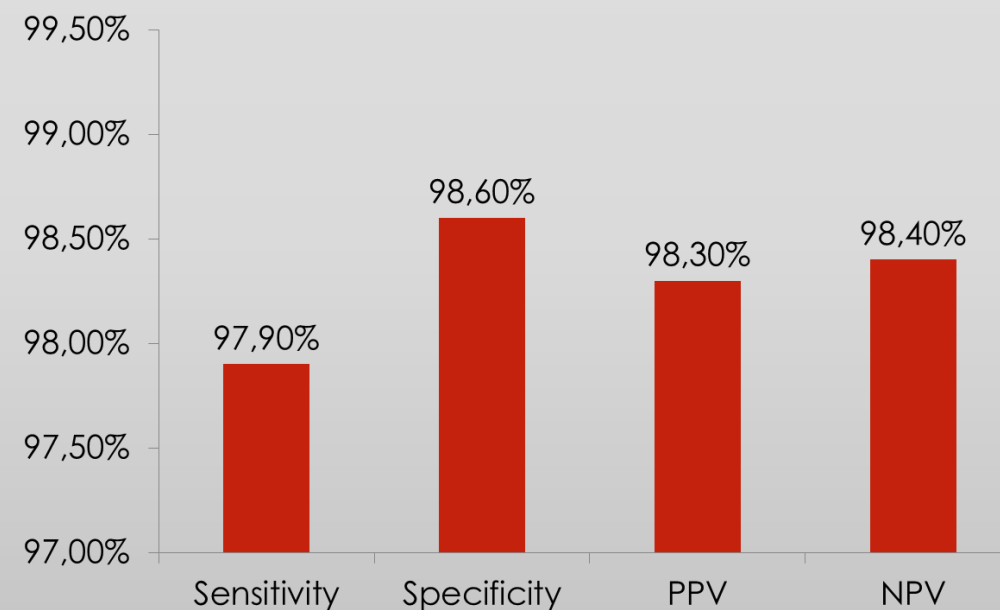




The laboratory added value



Confirmed cut-off



«Real» performance

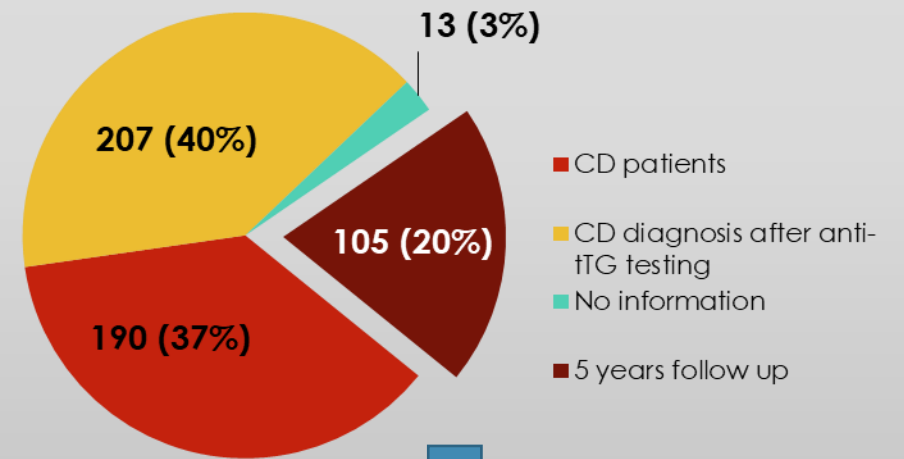
Predictive of serological test

We retrospectively collected the data of all patients who were tested for anti-tTG between June 2012 and December 2013

10914 patients

516 with anti-tTG >20 CU (4.7%)

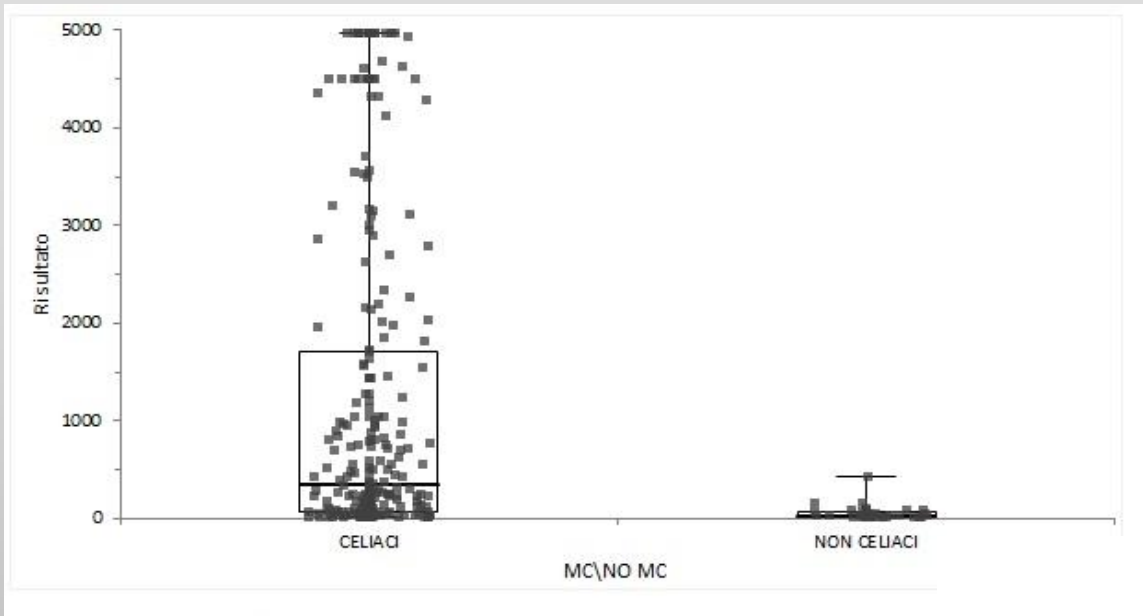
- ☐ 5 YEARS FOLLOW UP
- ☐ CLINICAL, SEROLOGICAL, GENETIC AND HISTOLOGICAL DATA COLLECTION



63/105 (60%) CD diagnosis within 5 years

Predictive of serological test

342.7 vs 35.23



Anti-tTG median values are statistically different between CD and no-CD patients ($p < 0.0001$)

	EMA Positive	EMA pos 1:10	EMA pos >1:10
42/105 (40%) CD excluded/ Potential CD	18/42 (42.8%)	12/18 (66.6 %)	6/18 (33.3 %)
63/105 (60%) CD within 5 years	45/63 (71.4%)	19/45 (42.2%)	26/45 (47.3%)

Although EMA is more frequently positive (with higher title) in patients diagnosed within 5 years than patients with Potential CD/CD excluded, the difference is not statistical significative ($p < 0.007$)

Is it a common issue or is lack of specificity of the test???

- 130 samples anti-tTG IgA positive, EMA negative
- 5 methods: ELISA (Eurospital), 2 CLIA (Werfen, Menarini), 1 FEIA (Thermofisher), 1 MFI (Biorad)

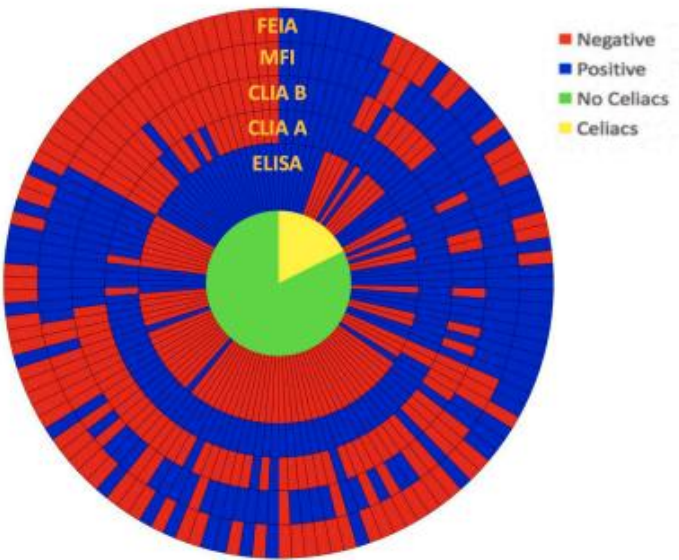


Fig. 1. Supervised cluster analysis, where the round angle of each circle is divided into 130 parts, and each circle sector corresponds to a sample. The most inner circle represents the diagnosis (green: no celiac – yellow: celiac), whereas the others represent the reactivity of each method. The positive tests are colored in blue, whereas the negative tests are colored in red. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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Research paper

Positive tissue transglutaminase antibodies with negative endomysial antibodies: Unresolved issues in diagnosing celiac disease

Maria Infantino^{a,*}, Mario Merone^{b,1}, Mariangela Manfredi^a, Valentina Grossi^a, Alessandra Landini^a, Maria Grazia Alessio^c, Giulia Previtali^c, Maria Teresa Trevisan^d, Brunetta Porcelli^e, Martina Fabris^f, Donatella Macchia^g, Danilo Villalta^h, Luigi Cinquantaⁱ, Federico D'Antoni^b, Giulio Iannello^b, Paolo Soda^b, Nicola Bizzaro^j

Table 2

Overall agreement (OA), positive agreement (PA) and negative agreement (NA) with 95% confidence interval (CI) among the five selection methods: tTG IgA EIA Eurospital (ELISA), tTG IgA CLIA Bioflash (CLIA A), tTG IgA CLIA Zenit RA (CLIA B), tTG IgA ALBIA BioRad (MFI), tTG IgA FEIA Thermofisher (FEIA).

	EIA [95%CI]			CLIA A [95%CI]			CLIA B [95%CI]			MFI [95%CI]		
	OA[%]	PA[%]	NA[%]	OA[%]	PA[%]	NA[%]	OA[%]	PA[%]	NA[%]	OA[%]	PA[%]	NA[%]
CLIA A	28.5 [20.7–36.2]	42.2 [32.7–51.8]	6.0 [12.6–0.0]									
CLIA B	64.5 [56.4–72.8]	54.0 [42.2–65.8]	71.2 [63.3–79.2]	50.0 [41.4–58.6]	58.0 [48.8–66.7]	38.1 [49.9–26.3]						
MFI	40.0 [31.6–48.4]	42.6 [32.2–53.1]	37.1 [26.3–47.9]	77.7 [70.5–84.9]	84.8 [79.35–90.3]	69.9 [44.1–71.9]	69.2 [61.3–76.2]	69.2 [78.3–60.2]	69.2 [60.1–78.3]			
FEIA	56.2 [47.6–64.7]	44.6 [32.7–56.6]	63.7 [59.1–72.5]	50.8 [42.18–59.4]	59.5 [50.4–68.5]	69.9 [25.3–49.2]	76.2 [68.9–83.5]	68.0 [57.4–78.7]	80.9 [87.5–74.4]	70.0 [62.1–77.9]	70.7 [61.9–79.5]	69.9 [60.1–78.5]

10x ULN the universal cut-off???

ORIGINAL ARTICLE: GASTROENTEROLOGY: CELIAC DISEASE

Celiac Disease Diagnosis Without Biopsy: Is a 10× ULN Antitransglutaminase Result Suitable for a Chemiluminescence Method?

*Giulia Previtali, †Lisa Licini, ‡Lorenzo D'Antiga, ‡Antonio Marseglia,
*Rudi Ravasio, *Francesca Nembrini, §Salvatore Greco, †Aurelio Sonzogni,
*Giovanna Azzarà, §Paolo Ravelli, and *Maria G. Alessio

01gen2017-31mar2023

51 pediatrics patients (<18y) with
anti-tTG between 200-560 CU

JPGN • Volume 66, Number 4, April 2018

Celiac Disease Diagnosis Without Biopsy

TABLE 2. Correlation between different antitissue transglutaminase immunoglobulin A cut offs and presence of duodenal mucosa damage suggestive for celiac disease (Marsh ≥ 2)

	Anti-tTG IgA cut off	Marsh ≥ 2	PPV %	NPV %	LR+	LR-
Children	200 CU (10× ULN*)	119/130	92	78	7.71	0.21
	560 CU (28× ULN)	85/86†	99	62	59.84	0.43
	1000 CU (50× ULN)	78/78	100	55	+∞	0.58
Adult	200 CU (10× ULN*)	134/143	94	82	28.84	0.38
	350 CU (17.5× ULN)	110/112	98	78	94.69	0.48
	400 CU (20× ULN)	106/106	100	77	+∞	0.5

CU = chemiluminescent units; LR = likelihood ratio; NPV = negative predictive value; PPV = positive predictive value; ULN = upper limit of normal.

*Cut off suggested by ESPGHAN 2012 to avoid duodenal biopsy.

†One patient with anti-tTG IgA 960 CU, EMA 1:320; Marsh 1 on a small biopsy fragment.

10x ULN the universal cut-off???

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Review

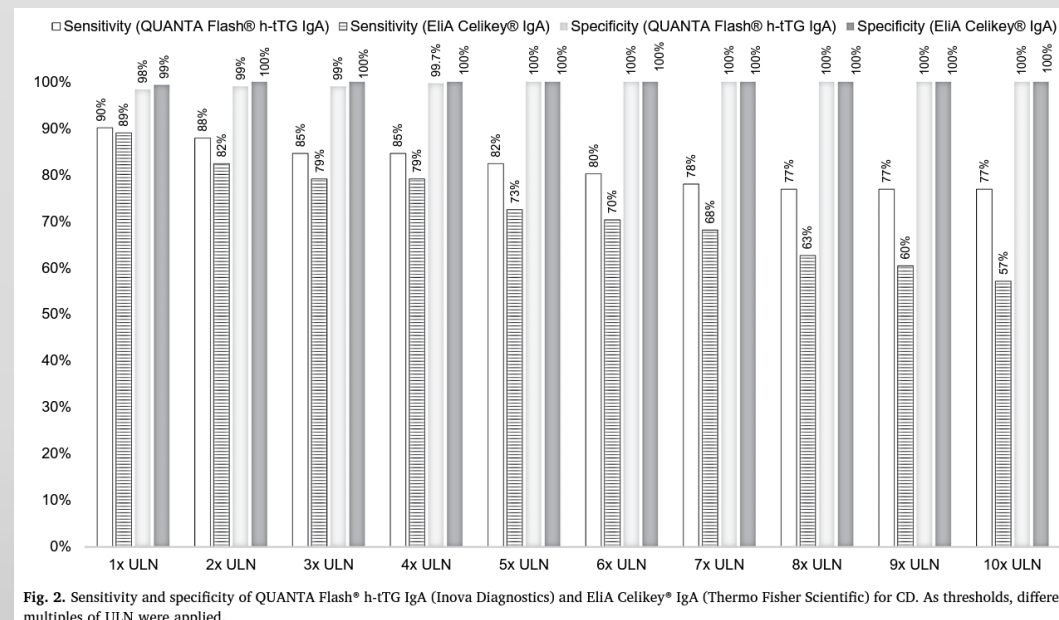
Optimization of serologic diagnosis of celiac disease in the pediatric setting

Laura Bogaert^{a,b,1}, Mathieu Cauchie^{c,1}, Lieve Van Hoovels^{a,g}, Pieter Vermeersch^b, Walter Fierz^d, Gert De Hertogh^e, Ilse Hoffman^f, Xavier Bossuyt^{b,g,*}

Table 4
Diagnostic performance of QUANTA Flash® h-tTG IgA (Inova Diagnostics) and EliA Celikey® IgA (Thermo Fisher Scientific).

	QUANTA Flash® h-tTG IgA		EliA Celikey® IgA	
	20 CU (1 × ULN)	200 CU (10 × ULN)	7 U/mL (1 × ULN)	70 U/mL (10 × ULN)
Sensitivity (%) (95%CI)	90 (84–96)	77 (68–86)	89 (83–95)	57 (47–67)
Specificity (%) (95%CI)	98 (97–99)	100	99 (98–100)	100
PPV (%) (95%CI)	89 (83–95)	100	95 (90–100)	100
NPV (%) (95%CI)	99 (98–100)	97 (96–98)	98 (97–99)	94 (92–96)

91 CD pediatric patients and 605 controls,
biopsy-proven



From this analysis, it can be concluded that the interpretation of IgA-tTG test results is not harmonized between the two companies (multiples of the cutoff are not aligned). Selecting thresholds based on a pre-defined specificity (e.g. 100% specificity) could be a better alternative to harmonize interpretation.

- Lack of international standard
- The number of patients eligible for no-biopsy protocol vary according to the method used for anti-tTG detection (77% vs 57%)

CLINICAL—ALIMENTARY TRACT

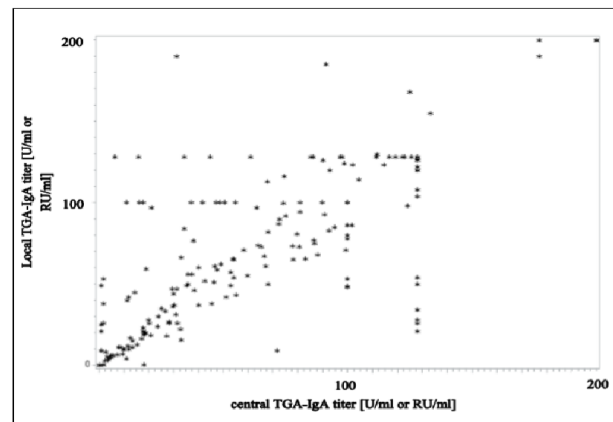
Accuracy in Diagnosis of Celiac Disease Without Biopsies in Clinical Practice

Katharina Julia Werkstetter,¹ Ilma Rita Korponay-Szabó,^{2,3} Alina Popp,^{3,4} Vincenzo Villanacci,⁵ Marianna Salemme,⁵ Gabriele Heilig,¹ Søren Thue Lillevang,⁶ Maria Luisa Mearin,⁷ Carmen Ribes-Koninckx,⁸ Adrian Thomas,⁹ Riccardo Troncone,¹⁰ Birgit Filiplak,¹ Markku Mäki,³ Judit Gyimesi,² Mehri Najafi,¹¹ Jernej Dolinšek,¹² Stine Dydensborg Sander,¹³ Renata Auricchio,¹⁰ Alexandra Papadopoulou,¹⁴ Andreas Vécsei,¹⁵ Peter Szitanyi,¹⁶ Ester Donat,⁸ Rafaella Nenna,¹⁷ Philippe Alliet,¹⁸ Francesca Penagini,¹⁹ Hélène Garnier-Lengliné,²⁰ Gemma Castillejo,²¹ Kalle Kurppa,³ Raanan Shamir,²² Almuthe Christine Hauer,²³ Françoise Smets,²⁴ Susana Corujeira,²⁵ Myriam van Winckel,²⁶ Stefan Buderus,²⁷ Sonny Chong,²⁸ Steffen Husby,¹³ and Sibylle Koletzko,¹ on behalf of the ProCeDE study group

International multicenter study (33 centers in 21 countries) to clinically verify the clinical performance of the ESPGHAN 2012 no-biopsy protocol

Figure S6: Comparison of central TGA-IgA and corresponding local TGA-IgA

Figure S6: Correlation between TGA-IgA-titers of the local laboratory and the titer of the corresponding TGA-IgA test in the central laboratory panel if included, and if both local and central test were analyzed from serum taken at the same day (N=334); as the local laboratories usually only measured up to the maximum measuring range for a certain test (100 U/ml, 128 U/ml or 200 U/ml), the central results were truncated to the same maximum titer level.



Results dispersion: lack of international standard reference

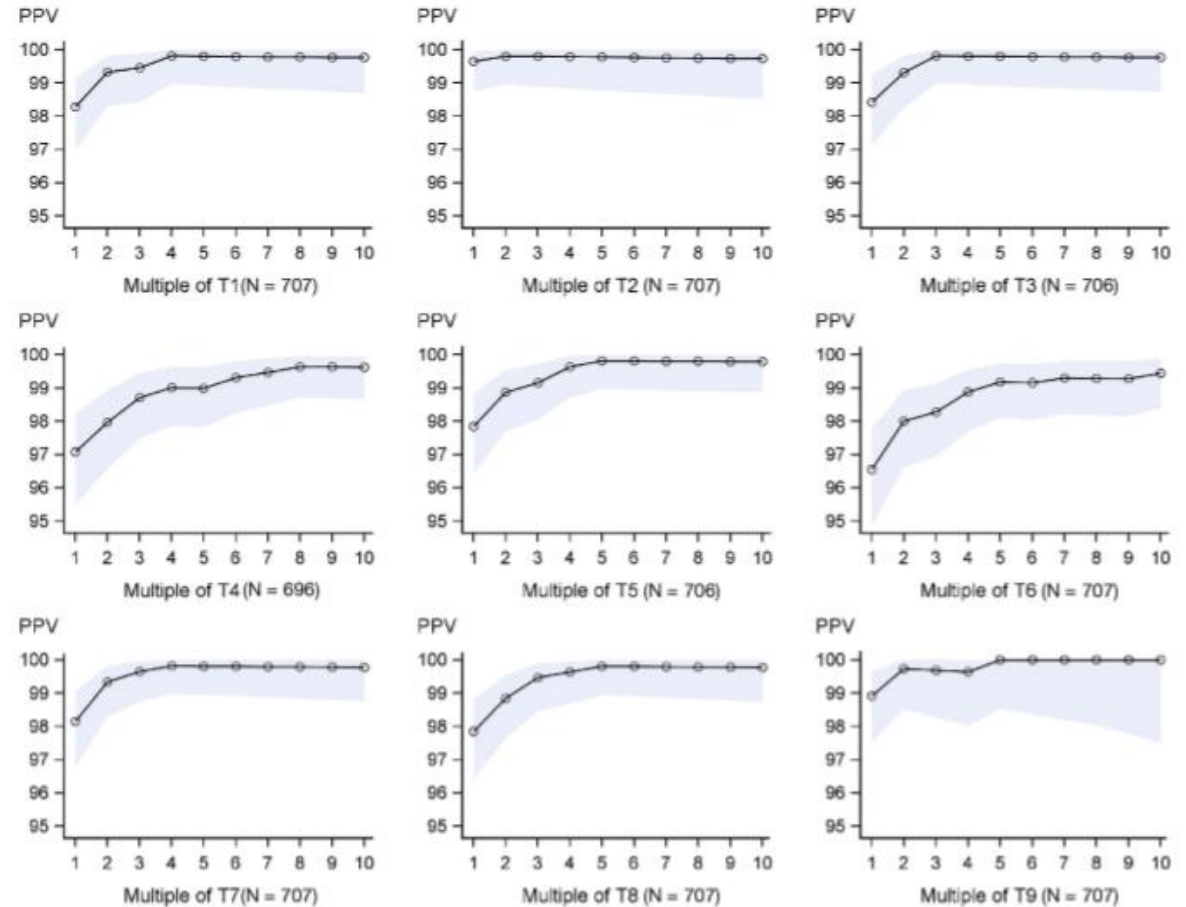


Figure 2. PPV with 95% CI (gray shaded) for CD diagnosis for each central TGA-serology, including 8 TGA-IgA tests (T1 to T8) and 1 TGA-IgG test (T9), all with calibration curve-based result calculations. The x-axis shows the multiple of the respective limit of normal according to the manufacturer's instructions (all truncated at 10xULN), the y-axis shows the PPV. Please see Table 3 for the names and manufacturers of each test.

PPV between 98.97 % and 100% for all the test for CD diagnosis

If patients has malabsorption or the indeterminate cases were excluded, no false positive results were detected (all method with 100% PPV)

Comments and note on the report

Pediatrici fino a 18 anni

La contemporanea positività di anticorpi anti endomisio e anti transglutaminasi è suggestiva della presenza di malattia celiaca. È consigliato rivolgersi ad un centro di gastroenterologia pediatrica per l'applicazione degli specifici protocolli diagnostici, **SENZA RIDURRE O ELIMINARE IL GLUTINE DALLA DIETA.**

Adulti

La contemporanea positività di anticorpi anti endomisio e anti transglutaminasi ha una specificità elevata per malattia celiaca. In questi casi è consigliata l'esecuzione della biopsia duodenale **PRIMA DI INTRAPRENDERE QUALSIASI REGIME DIETETICO**

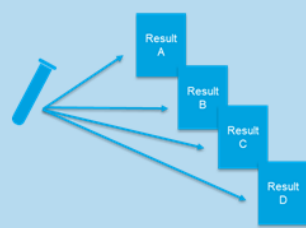
TTG TRA 20 E 100 EMA POS

Un valore tra 20 e 100 U/mL è da considerare come basso positivo; in presenza di positività EMA è necessaria la correlazione con i dati clinici e l'eventuale follow up a **DIETA LIBERA** e con carico di glutine, e ripetizione dei test tra 6-8 mesi.

TTG TRA 20 E 100 EMA NEG

Un valore tra 20 e 100 U/mL è da considerare come basso positivo; in assenza di EMA e di sintomi significativi si consiglia follow up a **dieta libera.**

Aptiva: Particle Based Multi-Analyte Technology



Holds **150**
primary patient
sample tubes



Holds **20**
reagent
cartridges



Time to
first set of
results



Time to
next set of
results



Time to
STAT
results

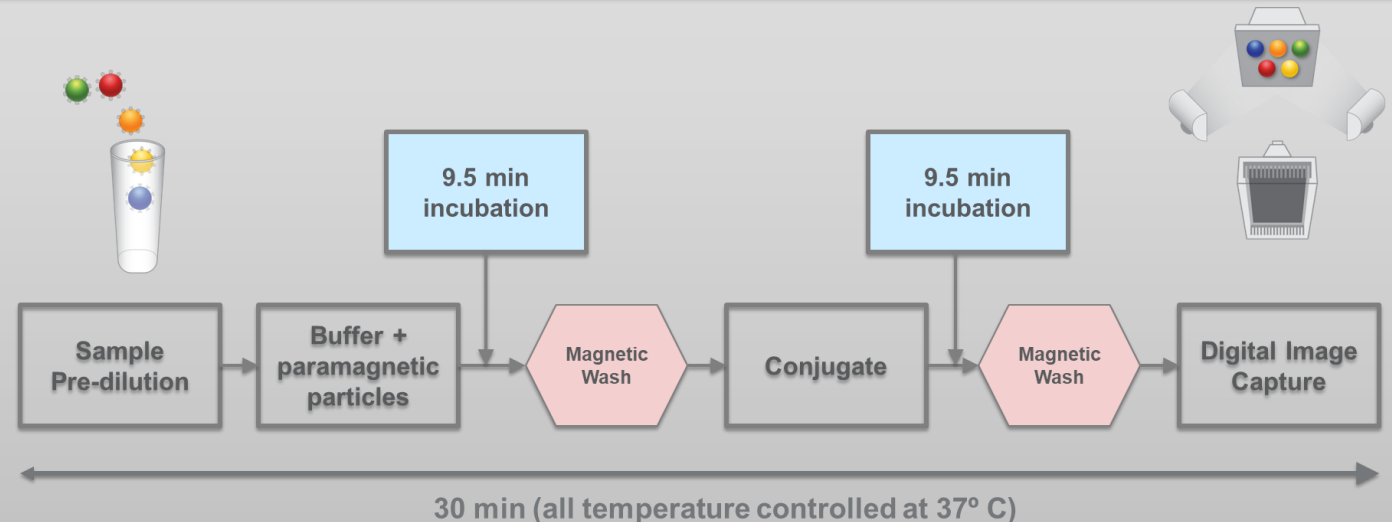


6.5 hour
consumable
walkaway time



LIS

- Automation of all steps
- High precision
- High reproducibility
- True Controls and Calibrators
- Pooled positive sera
- Human recombinant antibodies
- High throughput
- Up to 660 results per hour



Paramagnetic beads
specific for each analyte +
isotype bead controls

Two leds detect

- different beads
- Fluorescence intensity

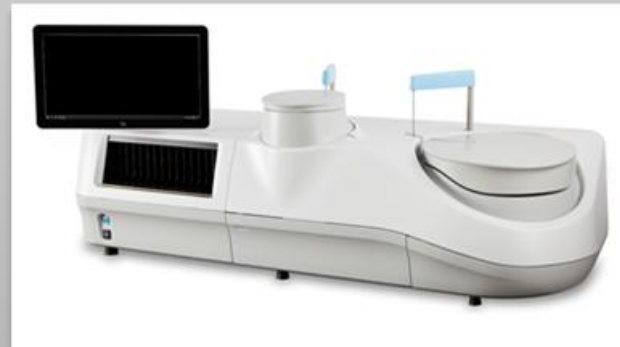
All raw data stored
for up to 90 days
Unveils additional
results without further
blood draws or retesting

Preliminary data- Aptiva Celiac Disease

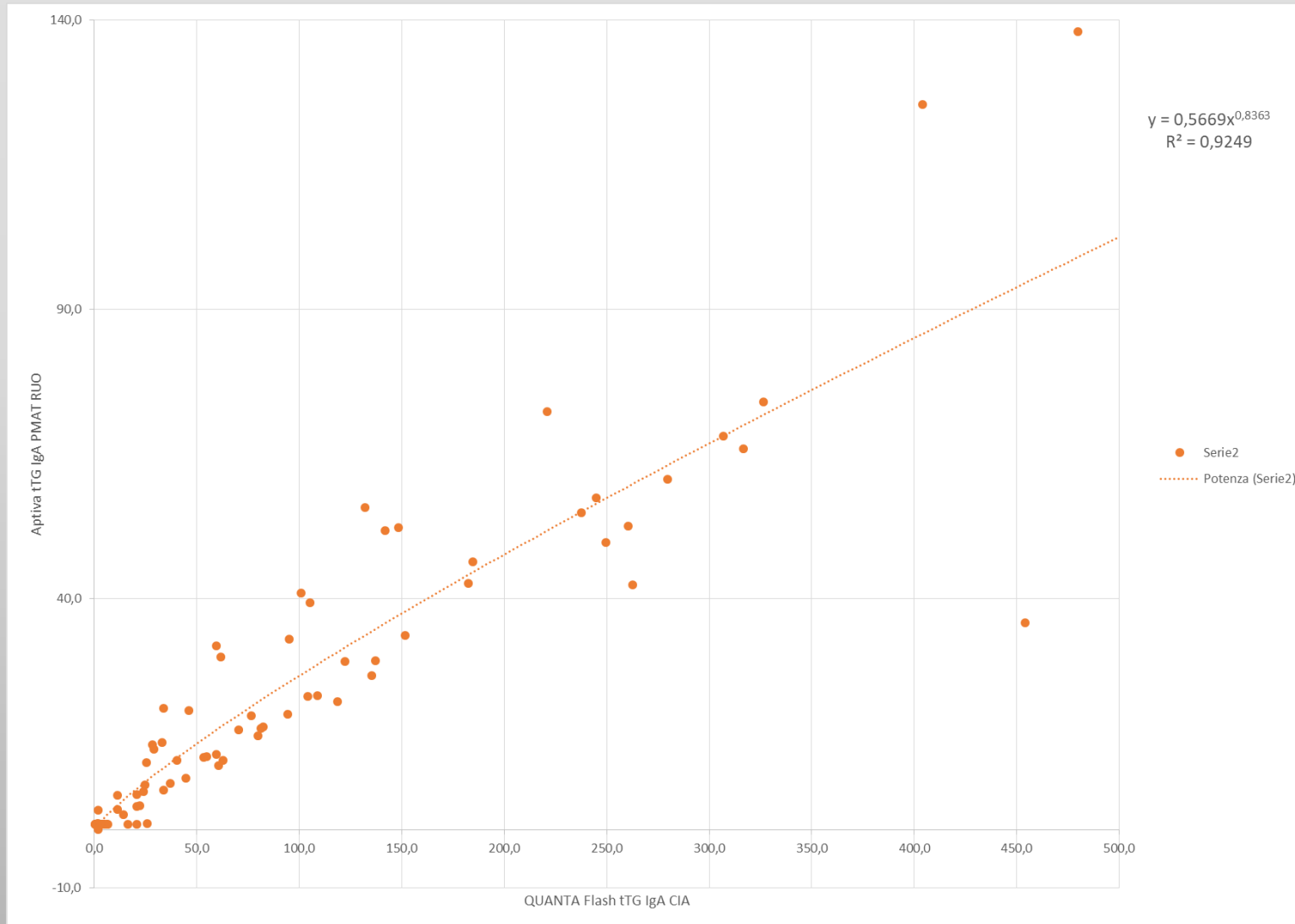
199 enrolled patients:

- 9 excluded patients (6 IgA deficiency and 3 GFD patients)
- **165** patients with **duodenal biopsy available** (not only for CD suspicious), were tested both on Aptiva and BIO-FLASH for anti-tTG IgA antibodies
- **25** pediatric patients tested both on Aptiva and BIO-FLASH for anti-tTG IgA antibodies that were diagnosed with the **ESPGHAN no-biopsy protocol**

190 patients



Preliminary data- Aptiva vs BIOFLASH



584 samples:

- 190 biopsy-tested samples
- 394 consecutive samples from daily routine

Dynamic Range:

APTIVA → 1,02-600 FTU

BIOFLASH → 1,9-4965,5 CU

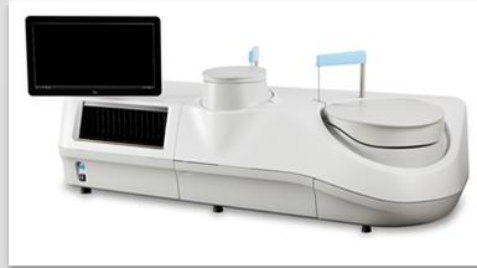
PMAT and CLIA vs CD diagnosis



	APTIVA (190 patients)	BIO-FLASH (190 patients)
SENSITIVITY	96,8%	100%
SPECIFICITY	91,4%	89,2%
LR-	0,035	0
LR+	11,2	9,3

Aptiva and BIOFLASH vs 10x ULN cut-off

87 pediatric patients
vs CD diagnosis



	APTIVA	BIO-FLASH
SENSITIVITY 10X	68,6%	68,6%
SPECIFICITY 10x	97,2%	97,2%
PPV 10x	97,2%	97,2%
PPV 100%	60 FLU (12x)	260 CU (13x)

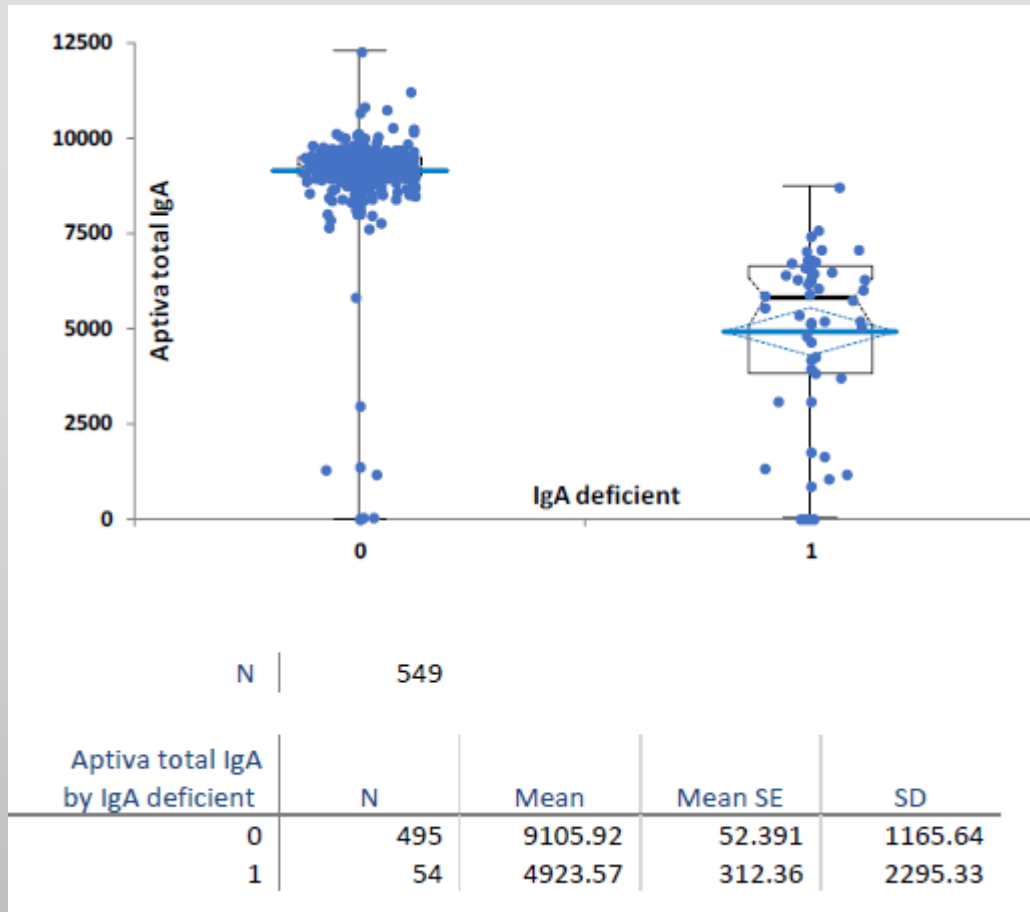


68,2% of positive
children can avoid
duodenal biopsy



ESPGHAN 2020
requires PPV 95%

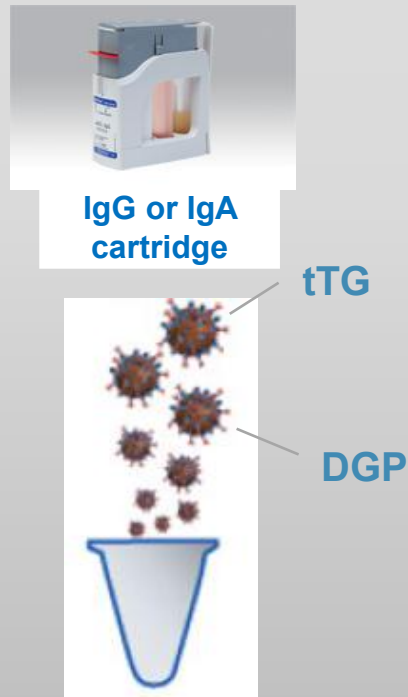
Results – IgA deficiency samples



- The IgA control bead is intended to be used to detect instrument error – no samples or no tracer added.
- However, correlation to this bead can be an indicator for IgA deficiency.
- As expected, IgA levels were significantly lower in samples defined as IgA deficient
- Of the 54 IgA deficient samples tested, none of the samples were positive on tTG IgA or DGP IgA.

A total of 549 samples were tested
(54 of them defined as IgA deficient).

Possible future application for the profile approach



Pediatric guidelines for diagnosis of celiac disease suggest to test patients only for tTG, DGP testing is no more recommended even in children under 2 years old

Is it possible to evaluate new applications for DGP in selected cases??

- Patients with persistent **low positive/borderline tTG**: can DGP identify those patients who are at higher risk of developing clinical CD?
- Patients on **gluten free diet** with long-lasting positive tTG: can DGP differentiate compliant and non-compliant patients?

Celiac disease in Lithuania



Article

Population-Based Screening for Coeliac Disease in Lithuanian Children from 2009 to 2014

Vaidotas Urbonas , Jolita Sadauskaite and Dominykas Varnas *

- Random sample of **1,458** children aged 11–13 from several Lithuanian schools.
- Used a point-of-care fingertip test for IgA class TG2 antibodies; positives confirmed by duodenal biopsy.
- **Prevalence** found: **~0.14%** (1 case in 729 children).
- Some children had IgA deficiency; in those cases, IgG-based testing was used. IgA-deficiency was ~4/1458 in this cohort.

Celiac disease in Italy

In Europe, USA, Canada, and New Zealand, the number of newly diagnosed cases has exploded:

Cases per 100 000 population



This rise is mostly due to...



Increased awareness



Increased availability of simple, accurate tests

CD is still largely underdiagnosed



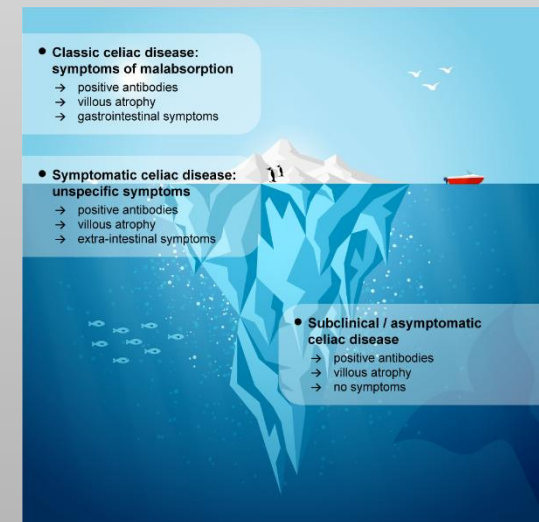
Catassi C, Lancet 2022

Italian Ministry of Health
Annual report on Celiac Disease 2023

265102 celiac patients

Mean new diagnosis from 2020 to 2023:
9921/year

About 400.000 patients not diagnosed



Is it time for mass screening??



Up to now, **case finding** in high risk groups is the suggested strategy



First degree relatives: 7,5%
Iron deficiency anemia: 10-20%
Autoimmune thyroiditis: 3-10%
Type I diabetes: 4-6 %
Genetic disorders (Down or Turner syndrome, IgA deficiency): 4-6 %



High throughput, easy to use, reliable analysers are now available. Compared to oncological programs, CD mass screening will be less expensive and invasive





Nn. 727, 524 e 801-A

Relazione orale
Relatore Russo

**TESTO DEGLI ARTICOLI FORMULATO IN SEDE REDIGENTE
DALLA 10ª COMMISSIONE PERMANENTE**

(AFFARI SOCIALI, SANITÀ, LAVORO PUBBLICO E PRIVATO,
PREVIDENZA SOCIALE)

nella seduta del 1º agosto 2023

Comunicato alla Presidenza il 3 agosto 2023

PER IL

DISEGNO DI LEGGE

Disposizioni concernenti la definizione di un programma diagnostico per l'individuazione del diabete di tipo 1 e della celiachia nella popolazione pediatrica (n. 727)

d'Iniziativa dei deputati MULÈ e CAVANDOLI

(V. Stampato Camera n. 622)

approvato dalla Camera dei deputati il 23 maggio 2023

*Trasmesso dal Presidente della Camera dei deputati alla Presidenza
il 24 maggio 2023*

CON ANNESSO TESTO DEI

DISEGNI DI LEGGE

Modifiche alla legge 4 luglio 2005, n. 123, concernenti lo svolgimento di indagini diagnostiche per l'accertamento della celiachia nei bambini di età compresa tra sei e dieci anni (n. 524)

d'Iniziativa del senatore DE POLI

13th Sempember 2023:

- Mass screening for T1D e CD in pediatric patients (1-17 yo)
- The screening will last three years starting from 2024 (about 3 million €/year)
- Aims: prevent chetoacidosis in T1D patients and slow the progression of the disease; early diagnosis of CD
- 4 regions (Lombardia, Marche, Campania, Sardegna) will start the screening in 2024 as a study pilot to evaluate the participation, costs and efficacy of a mass screening

D1Ce Screening



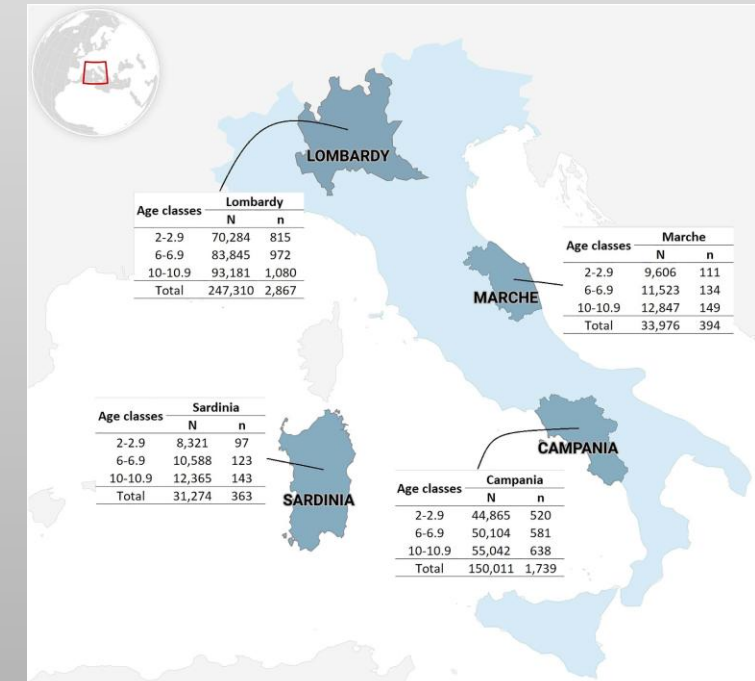
STUDY PROTOCOL

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

- Healthy children tested at the ages of 2-3, 6-7, and 10-11 years using capillary blood
- To assess the feasibility, adherence, organizational challenges, and cost–benefit ratio of implementing the program on a national scale.
- Pilot screening program was conducted in four Italian regions: Lombardy, Marche, Campania, and Sardinia.

About **5363** (1.6% italian pediatric population) children were screened:

- 0.97% positive children for T1D tests (GAD65, IA-2, ZnT8)
- **2.8%** positive children for tTG IgA
- 26% decrease in the incidence of diabetic ketoacidosis and a 49% decrease in the incidence of severe ketoacidosis were observed among children in the pilot regions compared with those in regions not participating in the screening program.





THANK YOU FOR YOUR ATTENTION

