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| Bibliographic reference | <p>The American journal of gastroenterology 2000 95 (3) PAGES 712-714 Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery Dickey, W., Hughes, D. F. et al.</p> |
| Study type | Cohort |
| Study quality | <p>Could the selection of patients have introduced bias? UNCLEAR – not reported if a consecutive sample used Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? YES – 24 were excluded but explanation not given</p> |
| Number of patients | 53 |
| Patient characteristics | <p>Inclusion criteria: Presence of villous atrophy and positive IgA EMA</p> <p>Exclusion criteria: IgA deficiency, Non-compliance with diet or biopsy</p> <p>Age at diagnosis – mean (range): 51 years (16 – 81 years) Gender (M/F): 14/39 Immunoglobulin A (IgA) deficiency: None Time on gluten-free diet – mean (range) : 12 months Assessed by: Dietitian for adherence</p> |

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| Bibliographic reference | <p>The American journal of gastroenterology 2000 95 (3) PAGES 712-714 Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery Dickey, W., Hughes, D. F. et al.</p> |
| Intervention | <p>IgA EMA by indirect immunofluorescence using primate oesophagus (Biodiagnostics, Upto-upon-Severn, England) with a titer of ≥ 1.5 as cut-off Duodenal biopsy Dietitian assessment</p> |
| Comparison | NA |
| Length of follow up | 12 months |
| Location | Northern Ireland |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms 48/53 (90.6%)</p> <p>IgA EMA – number testing negative At 3 months = 13/53 (58%) At 6 months = 50/53 (75%) At 9 months = not reported At 12 months = 46/53 (87%)</p> <p>Duodenal biopsy TVA/STVA at baseline (n = 41) At 12 months = 13 were normal, 18 had PVA and 10 were non-responders (persistent TVA/STVA) PVA at baseline (n = 12): At 12 months = 7 were normal, 1 was Marsh grade 1 and 4 were non-responders (persistent PVA)</p> <p>Growth in children and young people Not reported</p> |

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| Bibliographic reference | <p>The American journal of gastroenterology 2000 95 (3) PAGES 712-714 Disappearance of endomysial antibodies in treated celiac disease does not indicate histological recovery Dickey, W., Hughes, D. F. et al.</p> |
| | <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence 5/53 (9.4%) reported as non-adherent</p> <p>Impact on carers Not reported</p> <p>Health-related quality of life Not reported</p> |
| Source of funding | None reported |
| Comments | <p>All responders were adherent to GFD, non-responders were non-adherent Of 79 candidates for inclusion, 2 were EMA negative at baseline due to IgA deficiency, and 62 test EMA positive at baseline, 9 did not have a full 12 months of GFD, only 53 EMA + at baseline were followed up Study did not report on agreement or correlation between serology and biopsy</p> |
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| Bibliographic reference | <p>Autoimmunity 2007 40 (2) PAGES 117-121 Two-year follow-up of anti-transglutaminase autoantibodies among celiac children on gluten-free diet: comparison of IgG and IgA Martin-Pagola, Ainhoa, Ortiz-Paranza, Lourdeset al.</p> |
| Study type | Cohort |
| Study quality | <p>Could the selection of patients have introduced bias? YES – unclear if a consecutive sample was used Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO</p> |
| Number of patients | 93 |
| Patient characteristics | <p>Inclusion criteria: ESPGHAN diagnosis of CD with HLA-DRB1 Typing and GFD adherent</p> <p>Exclusion criteria: Non-adherence to GFD</p> <p>Age at diagnosis – mean (range): 3.56 years (0.94 – 17.5) Gender (M/F): 35/58 (62.4% female) Immunoglobulin A (IgA) deficiency: Not reported</p> |

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|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bibliographic reference | <p>Autoimmunity 2007 40 (2) PAGES 117-121 Two-year follow-up of anti-transglutaminase autoantibodies among celiac children on gluten-free diet: comparison of IgG and IgA Martin-Pagola, Ainhoa, Ortiz-Paranza, Lourdeset al.</p> |
| | <p>Time on gluten-free diet – mean (range): 2 years Assessed by: Not reported</p> |
| Intervention | <p>IgA anti-tTG IgG anti-tTG Both determined by immunoprecipitation radioassays. S25 labeled human recombinant tTGase was incubated with 3µl of serum at 40C overnight and immune complexes were precipitated with a 25% (v/v) suspension of protein-A agarose (Amersham Biosciences, Barcelona, Spain) for IgG or a 20% (v/v) suspension of agarose-conjugated IgA specific antibodies (Sigma cat. No. A2691) St Louis, MO) for IgA. Cut-off values were set as the sum of the mean and 3/SD of the index values of 50 serum samples from the general population.</p> |
| Comparison | NA |
| Length of follow up | 24 months |
| Location | Spain |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms (reported as remission) Not reported</p> <p>Response – defined as number of people testing negative on serology</p> <p>At 6 months IgA: 46/93 (49%) IgG: 59/93 (63%)</p> <p>At 24 months IgA: 82/93 (88%) IgG: 90/93 (96%)</p> |

| Bibliographic reference | <p>Autoimmunity 2007 40 (2) PAGES 117-121 Two-year follow-up of anti-transglutaminase autoantibodies among celiac children on gluten-free diet: comparison of IgG and IgA Martin-Pagola, Ainhoa, Ortiz-Paranza, Lourdeset al.</p> |
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| | <p>Biopsy – response = normal biopsy N = 41*</p> <p>Of those with Marsh 3a or 3b at diagnosis</p> <p>4 (9%) were Marsh 2</p> <p>12 (30%) were Marsh 1</p> <p>25 (61%) were Marsh 0</p> <p>Growth in children and young people Not reported</p> <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence Not reported</p> <p>Impact on carers Not reported</p> <p>Health-related quality of life Not reported</p> |
| Source of funding | Funded by the Spanish Ministry of Health |
| Comments | <p>Only 41 consented to a second biopsy after 2 year GFD</p> <p>Only those with elevated serology titers at baseline followed up</p> |

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| Bibliographic reference | Autoimmunity 2007 40 (2) PAGES 117-121 Two-year follow-up of anti-transglutaminase autoantibodies among celiac children on gluten-free diet: comparison of IgG and IgA Martin-Pagola, Ainhoa, Ortiz-Paranza, Lourdeset al. |
| | Study did not report on agreement or correlation between serology and biopsy |
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| Bibliographic reference | Journal of internal medicine 2004 256 (6) PAGES 519-524 Antibody levels in adult patients with coeliac disease during gluten-free diet: a rapid initial decrease of clinical importance Midhagen, G., Aberg, A. K.et al. |
| Study type | Cohort |
| Study quality | Could the selection of patients have introduced bias? NO Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. Yes – unclear of exact timing of tests Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO |
| Number of patients | 20 |
| Patient characteristics | Inclusion criteria: Diagnosed with CD with March 3 criteria Exclusion criteria: IgA deficiency |

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| Bibliographic reference | <p>Journal of internal medicine 2004 256 (6) PAGES 519-524 Antibody levels in adult patients with coeliac disease during gluten-free diet: a rapid initial decrease of clinical importance Midhagen, G., Aberg, A. K. et al.</p> |
| | <p>Age at diagnosis – median (range): 62 years (29 – 86 years) Gender (M/F): 10/12 (54.5% female) Immunoglobulin A (IgA) deficiency: NA Time on gluten-free diet – mean (range) : 12 months Assessed by: Dietitian for adherence</p> |
| Intervention | <p>AGA (AGA was tested using UniCAP Gliadin IgA (Pharmacia Diagnostics, Uppsala, Sweden) and was defined as positive with a result $>3 \text{ mg}_A \text{ L}^{-1}$.)</p> <p>tTGgrh (Celikey®, tTG_{rh}, IgA antibody assay (Pharmacia Diagnostics, Freiburg, Germany). It was defined by the producer as positive when $>8 \text{ U mL}^{-1}$, negative when $<5 \text{ U mL}^{-1}$, borderline between 5 and 8 U mL^{-1})</p> <p>tTGgp (Immulin®[®], tTGgp with guinea-pig-derived tTG (IMMCO, Buffalo, NY, USA). The result was defined by the producer as positive when $>25 \text{ U}$, negative when $<20 \text{ U}$, borderline when 20–25 U)</p> <p>IgA EMA (indirect immunofluorescence using monkey oesophageal tissue. Tissue sections from marmoset monkey oesophagus were mounted on microscopic slides. Undiluted sera and sera diluted 1 : 25 with phosphate-buffered saline (PBS) was applied to slides, which were incubated for 30 min at room temperature. After washing with PBS the sections were covered with fluorescein conjugated rabbit-antihuman IgA (Dako, Copenhagen, Denmark) for 30 min, washed with PBS and examined by fluorescence microscopy. Positive sera were further diluted (1 : 5, 1 : 10, 1 : 25, 1 : 100, 1 : 400 and 1 : 1600). Sera positive in dilution 1 : 10 or more were defined as positive</p> <p>Biopsy (Three to four biopsy specimens were obtained during upper endoscopic examination of each patient from the lower part of the duodenum descendens with standard forceps. All biopsies were fixed in a 4% buffered formaldehyde solution. Fixation, embedding and cutting were carried out according to routine methods)</p> |
| Comparison | NA |

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| Bibliographic reference | <p>Journal of internal medicine 2004 256 (6) PAGES 519-524 Antibody levels in adult patients with coeliac disease during gluten-free diet: a rapid initial decrease of clinical importance Midhagen, G., Aberg, A. K. et al.</p> |
| Length of follow up | 12 months |
| Location | Sweden |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms (reported as remission) 16/18 (88.9%)</p> <p>Response – defined as number of people testing negative on serology</p> <p><u>AGA IgA</u> at 3 months = 9/114 (74%) at 6 months = 14/15 (93%) at 9 months = not reported at 12 months = 15/15 (100%)</p> <p><u>IgA EMA</u> at 3 months = 7/17 (41%) at 6 months = 13/17 (65%) at 9 months = not reported at 12 months = 14/16 (87%)</p> <p><u>IgA tTG_r</u> at 3 months = 8/14 (57%) at 6 months = 10/14 (71%) at 9 months = not reported at 12 months = 14/14 (100%)</p> |

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| Bibliographic reference | <p>Journal of internal medicine 2004 256 (6) PAGES 519-524 Antibody levels in adult patients with coeliac disease during gluten-free diet: a rapid initial decrease of clinical importance Midhagen, G., Aberg, A. K. et al.</p> |
| | <p>Biopsy – response = normal biopsy At 12 months = 16/18 (88.9%)</p> <p>Growth in children and young people Not reported</p> <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence Not reported</p> <p>Impact on carers Not reported</p> <p>Health-related quality of life Not reported</p> |
| Source of funding | <p>Authors are research staff at Pharmacia Diagnostic manufactirers fo some of the testing kits but they state no financial support was received.</p> |
| Comments | <p>1 person excluded for IgA deficiency and 1 not included in results as they stopped the GFD 2 participants did not have a repeat biopsy at 12 months, Both non-responders at 12 months were in remission at follow-up biopsy but no timeframe reported Study did not report on agreement or correlation between serology and biopsy</p> |

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| Bibliographic reference | Journal of internal medicine 2004 256 (6) PAGES 519-524 Antibody levels in adult patients with coeliac disease during gluten-free diet: a rapid initial decrease of clinical importance Midhagen, G., Aberg, A. K. et al. |
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| Bibliographic reference | Journal of pediatric gastroenterology and nutrition 2011 53 (1) PAGES 55-60 Use of deamidated gliadin peptide antibodies to monitor diet compliance in childhood celiac disease Monzani, Alice, Rapa, Anna et al |
| Study type | Cohort (Prospective) |
| Study quality | <p>Could the selection of patients have introduced bias? YES – unclear of study numbers and how the sample were selected</p> <p>Is there concern that the included patients do not match the review question? NO</p> <p>Could the conduct or interpretation of the index test have introduced bias?. NO</p> <p>Is there concern that the index test, its conduct, or interpretation differ from the review question? NO</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? NO</p> <p>Is there concern that the target condition as defined by the reference standard does not match the review question? NO</p> <p>Could the patient flow have introduced bias? NO</p> |

Appendix D: Evidence tables

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| Bibliographic reference | <p>Journal of pediatric gastroenterology and nutrition 2011 53 (1) PAGES 55-60 Use of deamidated gliadin peptide antibodies to monitor diet compliance in childhood celiac disease Monzani, Alice, Rapa, Anna et al</p> |
| Number of patients | 28 |
| Patient characteristics | <p>Inclusion criteria: Newly diagnosed CD</p> <p>Exclusion criteria: None reported</p> <p>Age at diagnosis – median (range): 8.1 years (1 – 16.8 years) Gender (M/F): 11/17 (60.7% female) Immunoglobulin A (IgA) deficiency: Not reported Time on gluten-free diet – mean (range) : 12 months Assessed by: Dietitian for adherence</p> |
| Intervention | <p>a-DGP IgA (performed with Quanta Lite Gliadin IgA II with suggested cutoff of 20 arbitrary unites)</p> <p>a-DGP IgA+G (performed with Quanta Lite Celiac DGP screen with suggested cutoff of 20 arbitrary unites)</p> <p>anti-tTG gA (performed with EliA Celikey IgA with cutoff of 10U/ml)</p> <p>AGA IgA (performed with EliA Gliadin IgA with cut-off of 10U/ml)</p> |
| Comparison | NA |
| Length of follow up | 12 months |
| Location | Italy |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported</p> <p>Growth in children and young people Not reported</p> |

| Bibliographic reference | Journal of pediatric gastroenterology and nutrition 2011 53 (1) PAGES 55-60 Use of deamidated gliadin peptide antibodies to monitor diet compliance in childhood celiac disease Monzani, Alice, Rapa, Anna et al | |
|------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Complications of coeliac disease Not reported | | |
| Dietary adherence Accuracy of serology in detecting 'partially adherent' from 'strictly adherent' | | |
| | Partially adherent | Strictly adherent |
| a DGP IgA + at 2-4 months | 7 | 8 |
| a DGP IgA – at 2-4 months | 1 | 5 |
| a DGP IgA + at 6-8 months | 4 | 1 |
| a DGP IgA – at 6-8 months | 1 | 7 |
| a DGP IgA + at 9-12 months | 4 | 1 |
| a DGP IgA – at 9-12 months | 3 | 10 |
| | Partially adherent | Strictly adherent |
| a DGP IgA/G + at 2-4 months | 7 | 9 |
| a DGP IgA/G – at 2-4 months | 1 | 4 |
| a DGP IgA/G + at 6-8 months | 5 | 2 |
| a DGP IgA/G – at 6-8 months | 0 | 6 |
| a DGP IgA/G + at 9-12 months | 9 | 3 |
| a DGP IgA/G – at 9-12 months | 0 | 8 |

| Journal of pediatric gastroenterology and nutrition 2011 53 (1) PAGES 55-60 Use of deamidated gliadin peptide antibodies to monitor diet compliance in childhood celiac disease Monzani, Alice, Rapa, Anna et al | | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|--------------------|-------------------|
| Bibliographic reference | | Partially adherent | Strictly adherent |
| | Anti tTG IgA + at 2-4 months | 8 | 7 |
| | Anti tTG IgA – at 2-4 months | 0 | 6 |
| | Anti tTG IgA + at 6-8 months | 4 | 5 |
| | Anti tTG IgA – at 6-8 months | 1 | 3 |
| | Anti tTG IgA + at 9-12 months | 5 | 5 |
| | Anti tTG IgA – at 9-12 months | 4 | 6 |
| | | Partially adherent | Strictly adherent |
| | AGA IgA + at 2-4 months | 3 | 1 |
| | AGA IgA – at 2-4 months | 5 | 12 |
| | AGA IgA + at 6-8 months | 1 | 0 |
| | AGA IgA – at 6-8 months | 4 | 8 |
| | AGA IgA + at 9-12 months | 0 | 1 |
| | AGA IgA – at 9-12 months | 9 | 10 |
| | Impact on carers Not reported | | |
| | Health-related quality of life Not reported | | |
| Source of funding | 'Study was partially funded by a grant of the Regione Piemonte government' | | |

Appendix D: Evidence tables

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| Bibliographic reference | Journal of pediatric gastroenterology and nutrition 2011 53 (1) PAGES 55-60 Use of deamidated gliadin peptide antibodies to monitor diet compliance in childhood celiac disease Monzani, Alice, Rapa, Anna et al |
| Comments | Study did not report on agreement or correlation between serology and biopsy |
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| Bibliographic reference | Digestive diseases and sciences 1999 44 (10) PAGES 2133-2138 Clinical application of immunological markers as monitoring tests in celiac disease Fotoulaki, M., Nousia-Arvanitakis, S. et al |
| Study type | Cohort (Prospective) |
| Study quality | Could the selection of patients have introduced bias? UNCLEAR – not reported if consecutive sample used Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO |

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|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bibliographic reference | Digestive diseases and sciences 1999 44 (10) PAGES 2133-2138 Clinical application of immunological markers as monitoring tests in celiac disease Fotoulaki, M., Nousia-Arvanitakis, S. et al |
| | Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO |
| Number of patients | 30 |
| Patient characteristics | Inclusion criteria: Diagnosis of CD according to EPSGHAN criteria Exclusion criteria: None reported Age at diagnosis – mean (range): 6 (1 – 24 years) Gender (M/F): 13/17 (56.7% female) Immunoglobulin A (IgA) deficiency: 3/30 (10%) Time on gluten-free diet – mean (range) : 12 months Assessed by: Not reported |
| Intervention | IgA EMA Ig ARA |
| Comparison | NA |
| Length of follow up | 12 months |
| Location | Greece |
| Outcomes measures and effect size | Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported Response – defined as the number of people testing negative on serology <u>IgA EMA</u> At 3 months = 17/30 (57%) At 6 months = 25/30 (83%) At 9 months = 17/30 (90%) |

| Bibliographic reference | Digestive diseases and sciences 1999 44 (10) PAGES 2133-2138 Clinical application of immunological markers as monitoring tests in celiac disease Fotoulaki, M., Nousia-Arvanitakis, S.et al |
|-------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | <p>At 12 months = 30/30 (100%)</p> <p><u>Ig ARA</u></p> <p>At 3 months = 23/30 (77%)</p> <p>At 6 months = 26/30 (87%)</p> <p>At 9 months = 30/30 (100%)</p> <p>At 12 months = 30/30 (100%)</p> <p>Growth in children and young people Not reported</p> <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence Not reported</p> <p>Impact on carers</p> <p>Health-related quality of life Not reported</p> |
| Source of funding | None reported |
| Comments | <p>This study reports that ‘as the half-life of IgA is shorter than that of IgG, the IgA antibodies respond more rapidly to gluten changes in the diet and, therefore, are more appropriate for the follow-up of CD patients”</p> <p>IgA AGA and IgG AGA examined with home-made kits also studied so data were not used in this review</p> |

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| Bibliographic reference | Digestive diseases and sciences 1999 44 (10) PAGES 2133-2138 Clinical application of immunological markers as monitoring tests in celiac disease Fotoulaki, M., Nousia-Arvanitakis, S.et al |
| | Study did not report on agreement or correlation between serology and biopsy |
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| Bibliographic reference | Scandinavian journal of gastroenterology 2013 48 (6) PAGES 764-766 Rapid anti-transglutaminase assay and patient interview for monitoring dietary compliance in celiac disease Zanchi, Chiara, Ventura, Alessandro et al. |
| Study type | Cohort (Prospective) |
| Study quality | Could the selection of patients have introduced bias? UNCLEAR – not reported if a consecutive sample used Is there concern that the included patients do not match the review question? NO Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO |

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| Bibliographic reference | <p>Scandinavian journal of gastroenterology 2013 48 (6) PAGES 764-766 Rapid anti-transglutaminase assay and patient interview for monitoring dietary compliance in celiac disease Zanchi, Chiara, Ventura, Alessandro et al.</p> |
| | <p>Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? YES – 35 (10%) of the study population did not report on dietary adherence</p> |
| Number of patients | 350 |
| Patient characteristics | <p>Inclusion criteria: ESPGHAN diagnosed CD</p> <p>Exclusion criteria: None reported</p> <p>Age at diagnosis – median (range): 14 (6 – 45) Gender (M/F): 123/227 (65% female) Immunoglobulin A (IgA) deficiency: Not reported Time on gluten-free diet – mean (range) : 24 months Assessed by: Not reported</p> |
| Intervention | <p>IgA -anti-tTG using ELISA methods (Eu-tTG, Eurospital, Trieste, IT) using manufacturers cut-offs (IgA <9 U/ml) Rapid test (Eu-tTG Quick, Eurospital, Trieste, IT) using manufacturers cut-off</p> |
| Comparison | NA |
| Length of follow up | 24 months |
| Location | Italy |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported</p> <p>Growth in children and young people Not reported</p> <p>Response Not reported</p> |

| Bibliographic reference | Scandinavian journal of gastroenterology 2013 48 (6) PAGES 764-766 Rapid anti-transglutaminase assay and patient interview for monitoring dietary compliance in celiac disease Zanchi, Chiara, Ventura, Alessandro et al. | | | | | | | | | | | | | | | | | | | | |
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| | <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence Reported as diagnostic accuracy of detecting 'self-reported' partially adherent to GFD at 24 months</p> <table border="1" data-bbox="539 635 1131 786"> <thead> <tr> <th></th> <th>Partially adherent</th> <th>Strictly adherent</th> </tr> </thead> <tbody> <tr> <td>IgA anti-tTG ELISA +</td> <td>19</td> <td>8</td> </tr> <tr> <td>IgA anti-tTG ELISA -</td> <td>24</td> <td>264</td> </tr> </tbody> </table> <table border="1" data-bbox="539 826 1131 978"> <thead> <tr> <th></th> <th>Partially adherent</th> <th>Strictly adherent</th> </tr> </thead> <tbody> <tr> <td>Rapid test +</td> <td>19</td> <td>5</td> </tr> <tr> <td>Rapid test -</td> <td>24</td> <td>267</td> </tr> </tbody> </table> <p>Impact on carers Not reported</p> <p>Health-related quality of life Not reported</p> | | | | Partially adherent | Strictly adherent | IgA anti-tTG ELISA + | 19 | 8 | IgA anti-tTG ELISA - | 24 | 264 | | Partially adherent | Strictly adherent | Rapid test + | 19 | 5 | Rapid test - | 24 | 267 |
| | Partially adherent | Strictly adherent | | | | | | | | | | | | | | | | | | | |
| IgA anti-tTG ELISA + | 19 | 8 | | | | | | | | | | | | | | | | | | | |
| IgA anti-tTG ELISA - | 24 | 264 | | | | | | | | | | | | | | | | | | | |
| | Partially adherent | Strictly adherent | | | | | | | | | | | | | | | | | | | |
| Rapid test + | 19 | 5 | | | | | | | | | | | | | | | | | | | |
| Rapid test - | 24 | 267 | | | | | | | | | | | | | | | | | | | |
| Source of funding | Authors report no conflict of interests | | | | | | | | | | | | | | | | | | | | |
| Comments | Unclear if all data reported for rapid test Participants were questioned about the number of dietary transgressions in previous six months but no further details given | | | | | | | | | | | | | | | | | | | | |

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| | Study did not report on agreement or correlation between serology and biopsy |
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| Bibliographic reference | <p>Laboratory Medicine 2011 42 (8) PAGES 497-501 Importance of the educational environment in the evolution of celiac disease Samasca, G., Iancu, M. et al.</p> |
| Study type | Cohort (prospective) |
| Study quality | <p>Could the selection of patients have introduced bias? UNCLEAR – not reported if a consecutive sample used Is there concern that the included patients do not match the review question? UNCLEAR – age group not reported Could the conduct or interpretation of the index test have introduced bias?. NO Is there concern that the index test, its conduct, or interpretation differ from the review question? NO Could the reference standard, its conduct, or its interpretation have introduced bias? NO</p> |

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| Bibliographic reference | Laboratory Medicine 2011 42 (8) PAGES 497-501 Importance of the educational environment in the evolution of celiac disease Samasca, G., Iancu, M. et al. |
| | Is there concern that the target condition as defined by the reference standard does not match the review question? NO Could the patient flow have introduced bias? NO |
| Number of patients | 50 |
| Patient characteristics | Inclusion criteria: Diagnosis of CD based on the presence of flattened intestinal villi on duodenal biopsy. Exclusion criteria: None reported Age at diagnosis – mean (sd): mean not reported range 6 – 11 years Gender (M/F): 17/33 (67% female) Immunoglobulin A (IgA) deficiency: Not reported Time on gluten-free diet – 24 months |
| Intervention | .IgA tTG |
| Comparison | NA |
| Length of follow up | 24 months |
| Location | Romania |
| Outcomes measures and effect size | Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported number of people with negative test results <u>IgA tTG</u> at 3 months = 34/50 (68%) at 6 months = 34/50 (68%) at 9 months – not reported at 12 months = 41/50 (82%) at 24 months = 40/50 (80%) |

| Bibliographic reference | Laboratory Medicine 2011 42 (8) PAGES 497-501 Importance of the educational environment in the evolution of celiac disease Samasca, G., Iancu, M. et al. |
|-------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | <p>Growth in children and young people Not reported</p> <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence Not reported</p> <p>Impact on carers Not reported</p> <p>Health-related quality of life Not reported</p> |
| Source of funding | The authors report no conflicts of interest. |
| Comments | Study did not report on agreement or correlation between serology and biopsy |
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|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bibliographic reference | Autoimmune Diseases 2014, Article ID 623514, 7 pages, 2014 Celiac disease in adult patients: specific autoantibodies in the diagnosis, monitoring, and screening, Trigoni, E., Tsirogianni, A et al |
| Study type | Cohort (Retrospective) |
| Study quality | <p>Could the selection of patients have introduced bias? UNCLEAR not reported if a consecutive sample used</p> <p>Is there concern that the included patients do not match the review question? NO</p> <p>Could the conduct or interpretation of the index test have introduced bias?. NO</p> <p>Is there concern that the index test, its conduct, or interpretation differ from the review question? NO</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? NO</p> <p>Is there concern that the target condition as defined by the reference standard does not match the review question? NO</p> <p>Could the patient flow have introduced bias? NO</p> |
| Number of patients | 70 |
| Patient characteristics | <p>Inclusion criteria: Newly diagnosed with CD</p> <p>Exclusion criteria: None reported</p> <p>Age at diagnosis – mean (sd): 39 years (11.1)</p> <p>Gender (M/F): 20/50 (71.4% female)</p> <p>Immunoglobulin A (IgA) deficiency: 0/70 (0%)</p> <p>Time on gluten-free diet – 36 months</p> <p>Assessed by: Not reported</p> |

| Bibliographic reference | Autoimmune Diseases 2014, Article ID 623514, 7 pages, 2014 Celiac disease in adult patients: specific autoantibodies in the diagnosis, monitoring, and screening, Trigoni, E., Tsirogianni, A et al |
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| Intervention | <p>Anti-endomysium (EmA) which were determined semiquantitative by the technique of indirect immunofluorescence (IIF) using a commercial kit INOVA (NOVA Lite Monkey Oesophagus IFA Kit/Slides, USA) on a 5-μm-thin cryostat section of distal monkey oesophagus as antigen substrate. Patient samples were tested in dilutions ranging from 1 : 5 to 1 : 2560. The antibody titre was defined as the highest sample dilution yielding fluorescence. Titre below 1 : 5 was considered negative.</p> <p>Anti-tissue transglutaminase class IgA (tTG-A) which were assayed using a commercial anti-tTG type IgA ELISA test kit (QUANTA LiteTM, INOVA Diagnostics, USA). The cut-off value provided was 25U. ELISA was performed in duplicate according to the manufacturer's instruction.</p> |
| Comparison | NA |
| Length of follow up | 36 months |
| Location | Greece |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported</p> <p>Growth in children and young people Not reported</p> <p>Response reported as number of people testing negative serology among those who were strictly compliant</p> <p><u>IgA EMA</u> At 6 months = 20/51 (39.2%) At 12 months = 37/51 (72.5%) At 36 months = 48/51 (94.1%)</p> <p><u>IgA tTG</u> At 6 months = 10/51 (19.6%) At 12 months = 25/51 (49.0%)</p> |

| Bibliographic reference | Autoimmune Diseases 2014, Article ID 623514, 7 pages, 2014 Celiac disease in adult patients: specific autoantibodies in the diagnosis, monitoring, and screening, Trigoni, E., Tsirogianni, A et al |
|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | <p>At 36 months = 41/51 (80.4%)</p> <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence 19 were considered partially adherent while 51 were considered strictly adherent</p> <p>Impact on carers Not reported</p> <p>Health-related quality of life Not reported</p> |
| Source of funding | No funding reported but conflicts of interest listed |
| Comments | <p>Unable to calculate data for accuracy of detecting non-adherence</p> <p>Study did not report on agreement or correlation between serology and biopsy</p> |
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| Bibliographic reference | Clinical chemistry 2002 48 (6 Pt 1) PAGES 960-963 Comparative evaluation of serologic tests for celiac disease diagnosis and follow-up Martini, Silvia, Mengozzi, Giulio et al |
| Study type | Cohort (prospective) |
| Study quality | <p>Could the selection of patients have introduced bias? NO</p> <p>Is there concern that the included patients do not match the review question? NO</p> <p>Could the conduct or interpretation of the index test have introduced bias?. NO</p> <p>Is there concern that the index test, its conduct, or interpretation differ from the review question? NO</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? NO</p> <p>Is there concern that the target condition as defined by the reference standard does not match the review question? NO</p> <p>Could the patient flow have introduced bias? NO</p> |
| Number of patients | 101 |
| Patient characteristics | <p>Inclusion criteria: CD confirmed buy biopsy (Marsh 2 or March 3) and positive clinical response to GFD</p> <p>Exclusion criteria: None reported</p> <p>Age at diagnosis – median (range): 37 years (21 – 72)</p> <p>Gender (M/F): 22/79 (78.1% female)</p> <p>Immunoglobulin A (IgA) deficiency: (%)</p> <p>Time on gluten-free diet – 12 months</p> <p>Assessed by: Not reported</p> |
| Intervention | <p>Serum EmAs were detected by immunofluorescence, using commercial slides of monkey esophagus (The Binding Site Ltd., distributed by Alfa Biotech). Sera were tested, as indicated by the manufacturer, at a 1:10 initial dilution, with the inclusion of positive and negative controls in every batch of tests. CD EmA-negative sera were further tested at a 1:5 dilution, and no false-negative results were obtained.</p> |

| Bibliographic reference | Clinical chemistry 2002 48 (6 Pt 1) PAGES 960-963 Comparative evaluation of serologic tests for celiac disease diagnosis and follow-up Martini, Silvia, Mengozzi, Giulio et al |
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| | <p>Used four commercially available sandwich ELISAs that use human recombinant antigen (h-tTG): h-tTG 1 (DRG Diagnostics, distributed by Pantec S.r.l.); h-tTG 2 (EU-tTG® IgA; Eurospital S.p.A); h-tTG 3 (Immunodiagnostik, distributed by Li StarFISH); and h-tTG 4 (CELIKEYTM; Pharmacia & Upjohn, which uses human recombinant antigen extracted from eukaryotic cells. The same evaluation was also carried out with a sandwich ELISA that uses guinea pig tTG antigen (gp-tTG; GENESIS Diagnostics, distributed by Pantec S.r.l)</p> <p>Duodenal biopsy</p> |
| Comparison | NA |
| Length of follow up | 12 months |
| Location | Italy |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported</p> <p>Growth in children and young people Not reported</p> <p>Response reported as number of people normal duodenal biopsy at 12 months Normal (mucosal recovery) = 12/101 (12%) Improvement (Marsh grade I) = 51/101 (50%) no change (Marsh grade II or III) = 38/101 (38%)</p> <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence NA</p> |

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| Bibliographic reference | Clinical chemistry 2002 48 (6 Pt 1) PAGES 960-963 Comparative evaluation of serologic tests for celiac disease diagnosis and follow-up Martini, Silvia, Mengozzi, Giulio et al |
| | <p>Impact on carers Not reported</p> <p>Health-related quality of life Not reported</p> |
| Source of funding | None reported |
| Comments | <p>Mean percentage changes in anti-tTG values were 81% (range, 75–86%) for h-tTG 1, 51% (range, 43–60%) for h-tTG 2, 51% (range, 42–61%) for h-tTG 3, 77% (range, 69–85%) for h-tTG 4, and 75% (range, 67–82%) for gp-tTG.</p> <p>The concordances of the different assays in both positive (persistent histologic impairment and positive serologic markers) and negative (reconstituted mucosa and negative serologic markers) individuals vs histologic score were 29% for h-tTG 1, 65% for h-tTG 2, 14% for h-tTG 3, 16% for h-tTG 4, and 19% for gp-tTG, compared with 48% for EmA testing.</p> |
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| Bibliographic reference | Journal of human nutrition and dietetics : the official journal of the British Dietetic Association 2013 26 (4) PAGES 349-358 Nutritional inadequacies of the gluten-free diet in both recently-diagnosed and long-term patients with coeliac disease Shepherd, S. J. and Gibson, P. R |
| Study type | Cohort (prospective) |
| Study quality | <p>Could the selection of patients have introduced bias? NO</p> <p>Is there concern that the included patients do not match the review question? NO</p> <p>Could the conduct or interpretation of the index test have introduced bias?. NO</p> <p>Is there concern that the index test, its conduct, or interpretation differ from the review question? NO</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? NO</p> <p>Is there concern that the target condition as defined by the reference standard does not match the review question?</p> <p>Could the patient flow have introduced bias? YES not all recruited were assessed 7/57 (12%) not assessed</p> |
| Number of patients | 50 |
| Patient characteristics | <p>Inclusion criteria: newly diagnosed CD using EPSGHAN criteria</p> <p>Exclusion criteria: None reported</p> <p>Age at diagnosis – median (range): 44 years (18 – 71)</p> <p>Gender (M/F): 17/33 (71% female)</p> <p>Immunoglobulin A (IgA) deficiency: 0/50 (0%)</p> <p>Time on gluten-free diet – 12 months</p> <p>Assessed by: Dietitian for adherence</p> |
| Intervention | Biochemical and haematological indices were measured in peripheral blood samples taken from all patients at entry to the studies and, additionally, at 3, 6 and 12 months for the newly-diagnosed cohort. These included a complete blood count, electrolytes, renal function, liver function tests and iron studies, as well as serum folate, vitamin B12, zinc, vitamin D, magnesium, calcium and phosphate, using routine methodologies. Patients also had a repeat and histopathological |

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| Bibliographic reference | <p>Journal of human nutrition and dietetics : the official journal of the British Dietetic Association 2013 26 (4) PAGES 349-358 Nutritional inadequacies of the gluten-free diet in both recently-diagnosed and long-term patients with coeliac disease Shepherd, S. J. and Gibson, P. R</p> |
| | <p>examination of duodenal biopsies or close to 12 months after the initial assessment.</p> <p>Patients were then educated in a nutritionally adequate 'no detectable gluten' diet, which was recommended to be followed for life. Education included description of the five-food-group healthy-eating model, including recommended servings and attention to fibre and variety in the diet. At the first interview, all patients were asked to keep a 7- day food record. Patients were provided with a recording diary card and instructions for its completion. They were asked to record the type and brand of food and how much was eaten or drunk using household measures on each day for the 7-day period before the review appointment. Measuring cups, spoons and reference diagrams were provided. Recorded information was checked at the consultation</p> <p>Adherence to the GFD diet was evaluated in detail at every interview by direct questions about any gluten consumed, either accidentally or intentionally in the time since their last review, by specific questioning and, if available, by the 7-day food diary entries.</p> |
| Comparison | NA |
| Length of follow up | 12 months |
| Location | Australia |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported</p> <p>Growth in children and young people Not reported</p> <p>Complications of coeliac disease Not reported</p> <p>Dietary adherence</p> |

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| <p>Bibliographic reference</p> | <p>Journal of human nutrition and dietetics : the official journal of the British Dietetic Association 2013 26 (4) PAGES 349-358 Nutritional inadequacies of the gluten-free diet in both recently-diagnosed and long-term patients with coeliac disease Shepherd, S. J. and Gibson, P. R</p> |
| | <p>50/50 (100%) 5/50 (10%) did not meet target nutrient density*</p> <p>Impact on carers Not reported</p> <p>Health-related quality of life Not reported</p> |
| <p>Source of funding</p> | <p>Supported by a Dora Lush Scholarship from the NHMRC of Australia and a Grant in Aid from the Australian and New Zealand Coeliac Research Fund.</p> |
| <p>Comments</p> | <p>7 participants excluded from analysis due to incomplete follow-up</p> <p>This applied to four nutrients (fibre, vitamin A, calcium, zinc; and fibre, folate, calcium, iron) in two patients, two nutrients (fibre, folate; and thiamin, folate) in two patients, and one nutrient (fibre) in one.</p> <p>Inadequate nutrient intake was associated with inadequate overall food intake (in relation to EER) for fibre, thiamin, calcium, magnesium and folate ($P < 0.05$ Fisher's exact test). Only for iron ($P = 0.23$) and vitamin A ($P = 1.0$) was inadequate intake independent of volume of food eaten.</p> |
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| Bibliographic reference | Gastroenterology Today 2005 Issue 1 PAGES 11-12 Dietitian-led Coeliac Clinic:A successful change in working practice in modern healthcare Wylie, c., Geldart., S., et al |
| Study type | Before and after study |
| Study quality | <p>Could the selection of patients have introduced bias? YES – Convenience sample used</p> <p>Is there concern that the included patients do not match the review question? NO</p> <p>Could the conduct or interpretation of the index test have introduced bias?. NO</p> <p>Is there concern that the index test, its conduct, or interpretation differ from the review question? NO</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? NO</p> <p>Is there concern that the target condition as defined by the reference standard does not match the review question? NO</p> <p>Could the patient flow have introduced bias? YES – unclear of numbers in 'before' phase of study Study reports on 99 patients, 78 of whom were not previously under hospital review</p> |
| Number of patients | 99 |
| Patient characteristics | <p>Inclusion criteria: Adults with histology present CD</p> <p>Exclusion criteria: Not reported</p> <p>Age at diagnosis – Range: 23 – 86 (Mean or median not reported)</p> <p>Gender (M/F): 30/69 (69.7% female)</p> <p>Immunoglobulin A (IgA) deficiency: Not reported</p> <p>Time on gluten-free diet – mean (range) : Not reported</p> <p>Assessed by: Dietitian for adherence</p> |
| Intervention | Introduction of a dietitian into a Coeliac clinic |

| Bibliographic reference | Gastroenterology Today 2005 Issue 1 PAGES 11-12 Dietitian-led Coeliac Clinic: A successful change in working practice in modern healthcare Wylie, c., Geldart., S., et al | | | | | | | | | | | | | |
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| Comparison | 12 months before introduction of dietitian | | | | | | | | | | | | | |
| Length of follow up | 12 months | | | | | | | | | | | | | |
| Location | United Kingdom | | | | | | | | | | | | | |
| Outcomes measures and effect size | <p>Resolution of gastrointestinal and non-gastrointestinal symptoms Not reported</p> <p>Growth in children and young people Not reported</p> <p>Complications of coeliac disease – reported at 1 year <u>DEXA scan</u> Normal = 41 (42%) Ostopenia = 37 (39%) Osteoporosis = 18 (19%)</p> <p>19 were referred for gastroenterology review due to abnormal findings on serology or symptoms. Further investigation lead to 1 case of caecal carcinoma, hypo-thyroidism, iron deficiency anaemia in pregnancy and adjustment of B12 therapy</p> <p>Dietary adherence</p> <table border="1"> <thead> <tr> <th></th> <th>12 months pre-dietitian</th> <th>12 months With Dietitian</th> </tr> </thead> <tbody> <tr> <td>Perceived dietary adherence</td> <td>71 (72%)</td> <td>76 (77%)</td> </tr> <tr> <td>Actual dietary adherence</td> <td>54 (54%)</td> <td>65 (66%)</td> </tr> <tr> <td>Satisfaction</td> <td>42 (42%)</td> <td>80 (100%)</td> </tr> </tbody> </table> <p>Impact on carers</p> | | | 12 months pre-dietitian | 12 months With Dietitian | Perceived dietary adherence | 71 (72%) | 76 (77%) | Actual dietary adherence | 54 (54%) | 65 (66%) | Satisfaction | 42 (42%) | 80 (100%) |
| | 12 months pre-dietitian | 12 months With Dietitian | | | | | | | | | | | | |
| Perceived dietary adherence | 71 (72%) | 76 (77%) | | | | | | | | | | | | |
| Actual dietary adherence | 54 (54%) | 65 (66%) | | | | | | | | | | | | |
| Satisfaction | 42 (42%) | 80 (100%) | | | | | | | | | | | | |

Appendix D: Evidence tables

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| Bibliographic reference | Gastroenterology Today 2005 Issue 1 PAGES 11-12 Dietitian-led Coeliac Clinic:A successful change in working practice in modern healthcare Wylie, c., Geldart., S., et al |
| | Not reported |
| | Health-related quality of life Not reported |
| Source of funding | None reported |
| Comments | |

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| Bibliographic reference | Galli (2014) Histological recovery and gluten-free diet adherence: a prospective 1 year follow-up study of adult patients with coeliac disease. |
| Study type | Prospective cohort study |
| Study quality | Moderate |
| Number of patients | N = 65 |
| Patient characteristics | 65 consecutive patients newly diagnosed with CD were included 72.3% female Median age = 38 years, range 18 - 70 |
| Intervention | One year prospective follow up using: <ul style="list-style-type: none"> • A questionnaire of dietary adherence • serological testing to measure seroconversion • histological recovery investigated through intestinal biopsy |

| Bibliographic reference | Galli (2014) Histological recovery and gluten-free diet adherence: a prospective 1 year follow-up study of adult patients with coeliac disease. |
|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | serology for Iga EMA, adherence, and histology assessed at baseline and post one year after instructed to follow a GFD. |
| Comparison | Not applicable. |
| Length of follow up | 1 year |
| Location | Italy |
| Outcomes measures and effect size | <ul style="list-style-type: none"> • Overall, 81.5% of all patients were assessed to have adequate dietary adherence (ADA) • 18.5% had inadequate dietary adherence (IADA) • ADA group n = 53; IADA n = 12 • 66% ADA and 0% IADA patients achieved complete histological recovery (p=0.0001) • In ADA patients, antibody seroconversion and symptoms were not significantly different between patients who had achieved complete histological recovery and those with partial recovery • Multivariate analysis revealed Marsh 3 C (complete villous atrophy) was a risk factor for incomplete histological recovery in ADA patients - OR = 8.74, 95% CI: 1.87, 40.83 |
| Source of funding | Supported by grants from University Sapienza |
| Comments | <p>Data for serological recovery from IgA tTG and/or IgA EMA are presented in patients with complete and partial histological recovery respectively, meaning that it is impossible to assess serological recovery as a unique entity from histology recovery. Due to the fact that IgA tTG and/or IgA EMA was conducted on each patient and presented as a unitary 'serology' entity, and that this information is presented only as a proportion of those who showed histological recovery or not, the data on serological recovery in patients with CD 1 year post diagnosis is unable to be pooled with other contributing studies in this chapter.</p> |