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# Lack of long-term follow-up is common but does not associate with health outcomes in coeliac disease: Time for a more personalized approach?

**Short Title:** Long-term follow-up of coeliac disease

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**Keywords:** coeliac disease; compliance; personalized; transition; treatment

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**Abbreviations:** GSRS, Gastrointestinal Symptom Rating Scale; PGWB, Psychological General Well-Being questionnaire.

**Abstract**

**Background:** Follow-up of coeliac disease is recommended to prevent complications associated with unsuccessful treatment.

**Objective:** To evaluate the implementation and significance of long-term follow-up.

**Methods:** Medical data were collected of 585 and follow-up questionnaires sent to 559 currently adult coeliac disease patients diagnosed in childhood. Diagnostic features and adulthood health outcomes were compared between those with and without adulthood follow-up.

**Results:** Of paediatric patients, 92% were followed up 6–24 months after the diagnosis. 235 adults responded the questionnaires median of 18 years after the diagnosis and 25% of them reported regular follow-up. They were diagnosed more recently than those without follow-up (median year 2001 vs. 1995, p=0.001) being otherwise comparable at diagnosis. Those with follow-up were less often smokers (5% vs. 16%, p=0.042) and relatives of coeliac patients (48% vs. 66%, p=0.018), and more often students (48% vs. 28%, p=0.005) and type 1 diabetics (19% vs. 4%, p=0.001). Lack of follow-up was not associated with complications, ongoing symptoms, poorer general health or dietary adherence. All completely non-adherent patients were without follow-up.

**Conclusions:** Most coeliac disease patients diagnosed in childhood were not followed up according to recommendations in adulthood. The individual effect of this on long-term treatment outcomes varied markedly.

## Key Summary

### Established knowledge on this subject

- Current guidelines recommend regular follow-up of coeliac disease to support patients' dietary adherence and to detect possible complications associated with unsuccessful treatment.
- Implementation and significance of long-term follow-up are scarcely studied, especially in originally paediatric patients after the transition to adult care.

### New findings of this study

- Only 25% of patients diagnosed in childhood reported follow-up of coeliac disease in adulthood.
- Lack of follow-up was not associated with poorer long-term treatment outcomes in general, but all patients not adhering a gluten-free diet were without follow-up.
- The results support more personally tailored follow-up of coeliac disease.

## Introduction

With a prevalence of approximately 1–2%, coeliac disease is one of the most common chronic gastrointestinal diseases.[1,2] Achieving optimal treatment outcomes is therefore important both for the patients and for public health.[3] Inadequately treated coeliac disease predisposes to reduced quality of life and possibly severe long-term complications.[4,5] The only approved treatment, a strict gluten-free diet, may be demanding to maintain especially in food-related social situations and because of the expense and limited availability of appropriate products.[6–7] These challenges may lead to dietary lapses, highlighting the role of healthcare in supporting dietary adherence and preventing complications related to unsuccessful treatment.

In children, maintenance of a gluten-free diet is usually the responsibility of parents and other caregivers. The situation changes markedly in adolescence, when patients themselves should take responsibility for the treatment. Unfortunately, this change is realized in turbulent puberty, which increases the risk of poor adherence to an already challenging diet.[8-10] Hence, supporting young patients during the transfer to adult care would seem particularly important for strengthening their everyday coping with coeliac disease.[11] Although current guidelines recommend the regular monitoring of coeliac disease,[12-15] there is a lack of evidence about the actual implementation and significance of the follow-up of paediatric patients into adulthood.[16]

We investigated the prevalence and associated factors of regular follow-up in a large and well-defined cohort of adult coeliac disease patients diagnosed in childhood. Furthermore, the significance of follow-up for long-term treatment outcomes was evaluated.

## Materials and methods

*Patients and study design*

The study was executed at Tampere University and Tampere University Hospital. The hospital is a tertiary referral centre serving a catchment area of approximately one million people, including 120,000 children. The comprehensive medical data of paediatric coeliac disease patients diagnosed in 1966–2014 were collected from medical records (n=1,070) (Figure 1). Patients now in adulthood (≥18 years) with a biopsy-proven diagnosis were recorded (n=585) and included in the study. After excluding subjects who were deceased (n=7) or had missing contact information (n=19), study questionnaires were sent to 559 patients (Figure 1).[17] The presence of follow-up in childhood 6–24 months, 5–10 years, and >10 years after the diagnosis was collected from the patient records. Furthermore, the responders were divided into two groups based on the self-reported follow-up of coeliac disease in adulthood as follows: 1) regular follow-up (at least every three years) and 2) no regular follow-up. All relevant information collected from medical records and by questionnaires were compared between these groups based on adulthood follow-up.

*Register-based data*

Clinical and histological presentation and haemoglobin and coeliac disease autoantibody values at diagnosis were collected along with the adherence and response to the gluten-free diet and follow-up visits to a physician and dietician after the diagnosis.

The main reason for suspicion of coeliac disease was classified as 1) gastrointestinal, such as diarrhoea and stomach pain; 2) extra-intestinal, including, e.g., rash, arthralgia, and poor growth, or 3) at-risk group screening. The presence and severity of symptoms were categorized retrospectively depending on their frequency and burden to daily life as 1) no symptoms, 2)

mild (minor/occasional symptoms), 3) moderate (more frequent/distracting symptoms), or 4) severe symptoms causing e.g. school absence or visits to an emergency room. Poor growth was defined based on Finnish nationwide recommendations.[18]

Serum anti-reticulin and endomysium antibodies, which resemble each other closely,[19] have been measured in our setting since the 1980s by indirect immunofluorescence. A titer of 1:5 is considered positive, and it is further diluted up to 1:4000.[20] Blood haemoglobin values (g/l) at diagnosis were collected when available. Anaemia was defined as a haemoglobin value lower than the age- and gender-dependent reference value.

Histology results at the time of coeliac disease diagnosis were collected from the pathology reports. In our clinical routine, at least four representative samples are taken from the duodenum in each esophagogastroduodenoscopy. Before the mid-1980s, the biopsies were taken by the Watson biopsy capsule. Morphological lesion in coeliac disease is classified as partial, subtotal, or total villous atrophy. In children, follow-up biopsies are rarely needed.[21]

Adherence to a gluten-free diet approximately 1–2 years after the diagnosis was categorized as 1) strict gluten-free diet, 2) only occasional lapses, and 3) non-adherence. Beneficial short-term response to the treatment was defined as clinical improvement and a decrease in coeliac disease autoantibodies.

*Questionnaires*

In addition to follow-up, a specific study questionnaire was used to collect information about the patients' current sociodemographic and lifestyle characteristics, such as employment, presence of children, family history of coeliac disease, membership of Finnish coeliac societies,

smoking, and physical activity. Furthermore, self-reported health and health concerns, ongoing coeliac disease-related symptoms, adherence to a gluten-free diet, and experience of daily life restrictions caused by the diet were surveyed along with the presence of coeliac disease-associated and other chronic comorbidities.

General health was categorized as 1) excellent/good or 2) moderate/poor, and health concerns as 1) none/minor or 2) moderate/severe concerns. Dietary adherence was classified as 1) strict diet, 2) occasional lapses (lapses less than once a month), or 3) frequent lapses or non-adherence (lapses monthly or more frequently). Experience of maintaining the diet was categorized as 1) easy, 2) somewhat difficult, or 3) difficult.

The Gastrointestinal Symptom Rating Scale (GSRS) was used to evaluate the presence and severity of gastrointestinal symptoms. Fifteen questions are scored on a Likert scale from 1 to 7, with higher scores indicating more severe symptoms. The total score is calculated as the mean of all answers in addition to five specific subgroup scores—including diarrhoea, indigestion, constipation, pain, and reflux—as means of 2–4 selected answers.[22]

The Psychological General Well-Being questionnaire (PGWB) was used to evaluate health-related quality of life. It contains 22 questions scored from 1 to 6, with a higher score indicating better well-being and quality of life. The total score is a sum of all questions, with the range being 22–132. More detailed subgroup scores are calculated as sums of 2–4 relevant questions for anxiety, depression, positive well-being, self-control, general health, and vitality.[23]

*Statistical Analysis*

Statistical analyses were performed with SPSS v25.0 (IBM Corp. Armonk, NY). Categorical variables are reported as percentages and numeric variables as medians with lower and upper quartiles. Chi-squared and Fisher's tests were used to assess significance in comparisons of ordinal or nominal variables, and the Mann–Whitney test was used in comparisons of numeric variables. Binary logistic regression was used to adjust the age difference between the study groups. A p-value <0.05 was considered significant.

*Ethics*

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The Department of Paediatrics and the Regional Ethics Committee of Tampere University Hospital approved the study design and questionnaire process (Ethical committee code R16091, 31 May 2016). All participants answering the questionnaires gave their written informed consent.

**Results**

*Follow-up in childhood*

At least one guidance visit after a coeliac disease diagnosis in childhood was arranged for all 585 now-adult patients, and 92% had another follow-up visit 6–24 months later. Thereafter, based on the patient record data, follow-up decreased gradually to 26% after >10 years. Correspondingly, 25% of the now-adult patients responding to the study questionnaires reported regular follow-up (Figure 2).

Dietary counselling at the time of diagnosis was given by a dietician in 63% and by another healthcare provider in 37% of cases. At 12–24 months after the diagnosis, 85% of the patients

reported a strict gluten-free diet, 12% had occasional lapses, and 3% did not adhere to the diet. Despite only partial adherence in some patients, 99% reported a beneficial dietary response.

*Follow-up in adulthood*

Altogether 235 (42%) of the now-adult patients answered the questionnaires. The responders were more often women (69% vs. 52%, $p<0.001$) and relatives of coeliac disease patients (56% vs. 44%, $p=0.035$), and they were less often co-existing type 1 diabetics (9% vs. 16%, $p=0.029$) when compared to the non-responders. Based on the medical records, the responders and non-responders did not differ in the age and year of diagnosis, clinical presentation, severity of histopathology or selected laboratory results (Table 1) or in presence of short-term follow-up, or in short-term dietary adherence and treatment response. Furthermore, the presence of follow-up 5–10 years after the diagnosis and current age were comparable (data not shown).

Among the 235 now-adults responding to the questionnaires, the childhood coeliac disease diagnosis had been established more recently in the 59 patients with regular adulthood follow-up, whereas the follow-up and no follow-up groups were comparable in gender, age, clinical presentation, severity of histological damage, and laboratory parameters as reported in the patient records (Table 1).

Based on the current evaluation, the patients who were followed up were younger and more often students, but they were less often smokers and relatives of coeliac disease patients. After adjustment for age, the differences in the presence of students, current smokers, and family history of coeliac disease were no longer significant. The groups were also comparable in employment status, presence of children, physical activity, and self-perceived health, as well as

in experiences of and adherence to a gluten-free diet (Table 2). However, all completely non-adherent patients (n=5) were without follow-up.

Lack of adulthood follow-up was not associated with a higher severity of persistent gastrointestinal symptoms or with a poorer quality of life as measured by the GSRS and PGWB (Table 3). Coexisting type 1 diabetes was more common among patients with regular follow-up, whereas there were no differences in the presence of other co-morbidities or coeliac disease-related complications (Table 4).

Regular follow-up comprised the evaluation of serology and contact with healthcare in all patients, but only 22 reported personal visits to a doctor or nurse. In a subgroup analysis, fractures were more common and a gluten-free diet was experienced as more difficult to adhere to among patients with personal visits compared to those with other healthcare contact, whereas the groups did not differ in other health-related outcomes or comorbidities (Table 5) or in the GSRS and PGWB scores (data not shown).

**Discussion**

We found that almost all paediatric patients received appropriate short-term monitoring of their coeliac disease, but after this early period the frequency of follow-up declined and was eventually reported only by one fourth of the sample in adulthood. To the best of our knowledge, there are only a few previous studies on this issue. In accord with us, O'Leary et al. found only 11 (22%) out of 50 coeliac disease patients attended follow-up after a median of 29 years from the childhood diagnosis.[24] More recently, Norsa et al. reported more positive results, as up to 83% of the patients had regular follow-up 30 years after the childhood diagnosis.[25] Studies focusing on patients diagnosed in adulthood have reported long-term

follow-up in 15–73% of their sample.[26-28] Taken together, the follow-up of paediatric and adult coeliac disease does not seem to meet the recommendations.[12-15]

Follow-up was even less frequent when only personal healthcare visits were counted, and a parallel finding was reported in an US study investigating short-term follow-up mainly in adults.[28] In the present study, the patients with personal contact reported more fractures and found the gluten-free diet more difficult, despite the comparability of their dietary adherence to those with other forms of healthcare contact. In the best-case scenario, follow-up is focused on those with health issues and challenges with the treatment. Notably, although caution is needed before drawing excessively strong conclusions, the lack of direct healthcare contact did not seem to affect the long-term treatment outcomes negatively.

Other factors increasing the likelihood of long-term follow-up were being a student and having a more recent coeliac disease diagnosis. The Finnish Student Health Service offers low-threshold healthcare services at a reasonable price for those studying at higher education institutions.[29] This easier access to healthcare could play a significant role in the patients' motivation to attend follow-up. In our previous adult study, most coeliac disease patients wanted regular follow-up, but did not eagerly seek it if not prearranged by the healthcare.[26] In line with this, Hughey et al. reported the most common reason for neglecting the follow-up to be the patients' perception that there was no strong need for it.[27] The higher frequency of follow-up in more recently diagnosed patients could be due to better organization in recent years or because newer patients have not yet been lost to follow-up. Herman et al.[28] reported patients presenting with diarrhoea more often having short-term follow-up, although we did not observe a similar association. It is possible that the classical form of coeliac disease is considered to have a higher risk for complications and therefore the need for follow-up is more

intensive. However, evidence on this is lacking; in fact, adherence problems might be even more common among those with mild or atypical presentation.[30]

Remarkably, lack of long-term follow-up was associated neither with poor dietary adherence nor with major long-term health problems, such as complications. A similar lack of association between the strictness of the gluten-free diet and the presence of follow-up was observed in our previous studies with different designs.[9,26] However, studies from Israel[31] and Croatia[32] have reported poorer adherence among patients not followed up. It might be the case that depending on the local circumstances, other factors than the presence of regular follow-up play a more significant role in the long-term success of the treatment, including, e.g., the availability and prices of gluten-free products, individual knowledge about coeliac disease, and general attitudes toward the importance of a strict diet.[8,9,33] Educational training of professionals, membership of coeliac societies and information provided by physicians and dieticians for patients are another factors that may affect compliance with the diet.[34] These country- and patient-related differences are important to consider before implementing our results in clinical practice.

It must be emphasized that although here the lack of follow-up had no major influence on the long-term treatment outcomes, there might be a subgroup of patients who require special attention. In particular, all the subjects who reported complete non-adherence to a gluten-free diet were without follow-up, and smoking was more common among subjects not followed up, indicating a generally less healthy lifestyle. In fact, the proportion of such patients could be even higher, as these poorly motivated subjects might also have been more prone to refuse the study. These patients should be recognized and, if possible, receive special support with the dietary treatment, keeping in mind that long-term poor compliance predisposes to severe complications such as osteoporosis and even intestinal lymphoma.[4] Patients diagnosed in

adulthood may require particular attention, since they often have long diagnostic delay and gluten-free diet is likely less efficient to prevent the complications and co-morbidities.[5]

It is a challenge to predict who originally paediatric patient needs special support in adulthood and to determine how these patients can be monitored. The transition to adult care could be an opportunity to recognize those at risk for future challenges and to tailor the subsequent follow-up according to personal needs, as well as to ensure sufficient knowledge about coeliac disease before shifting the responsibility for treatment onto the adolescents themselves.[16] Thereafter, those without difficulties could be seen less frequently compared to the more problematic cases. Moreover, as monitoring methods improve, the follow-up could also be made easier, e.g., by using practical fingertip tests for antibodies[35] and urine tests for the detection of gluten immunogenic peptides – even at home.[36] Healthcare could then be contacted when there are compliance problems or other health concerns. As convenience seems to be an important factor affecting the motivation for follow-up,[26,27] such methods could encourage patients further to engage with their own treatment.

**Strengths and limitations**

The main strength of the present study is the large and well-defined cohort of paediatric coeliac disease patients. We also managed to collect comprehensive adulthood follow-up data, and the use of validated questionnaires for gastrointestinal symptoms and psychological well-being enhances the comparability of the results. Furthermore, the participants represented an unselected population as opposed to selected recruitment, e.g., via patient organizations. On the other hand, this probably explains the moderate response rate, which may predispose to selection bias. The risk for this was reduced by the similarity of the responders and non-responders as regards the register-based data. The fact that diagnostic and short-term follow-up

data were collected retrospectively and were partly incomplete, especially in classification of the severity of symptoms and some laboratory results, is another limitation. Short-term dietary adherence and treatment response were mainly reported by parents of the paediatric patients. Also, we did not have data about the causes of death in seven deceased patients.

## Conclusion

To conclude, we found the long-term follow-up of paediatric coeliac disease patients does not meet current recommendations.[12-15] Although in the majority of cases, this does not seem to affect dietary adherence or other long-term treatment outcomes, there might be a subgroup of patients who experience significant coping challenges, as all the non-adherent adult patients were without current follow-up. These individuals, as well as those experiencing persistent symptoms or with increased risk for complications and co-morbidities, should receive a particular attention. Together, these findings support a more personalized approach to the long-term monitoring of paediatric coeliac disease.

**Conflict of Interest**: Laura Kivelä, Katri Kaukinen, and Kalle Kurppa have received personal fees for lectures from the Finnish Coeliac Society outside the submitted work and act as members of the Finnish Coeliac Society' advisory committee. All other authors declare no conflict of interest.

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**Figure legends**

Figure 1. Flowchart of the study.

Figure 2. Presence of follow-up in children diagnosed with coeliac disease (n=585). *Self-reported, data from questionnaires (n=235).

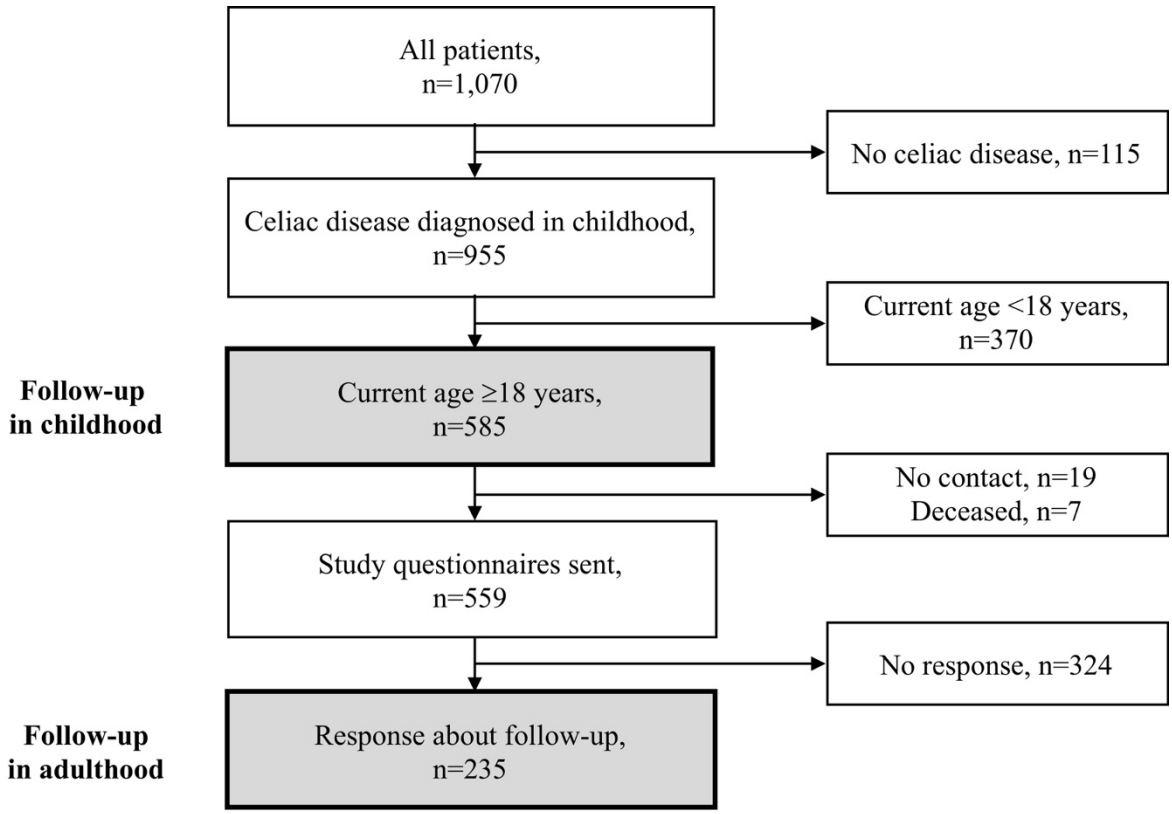


**Figure 1.** Flowchart of the study.

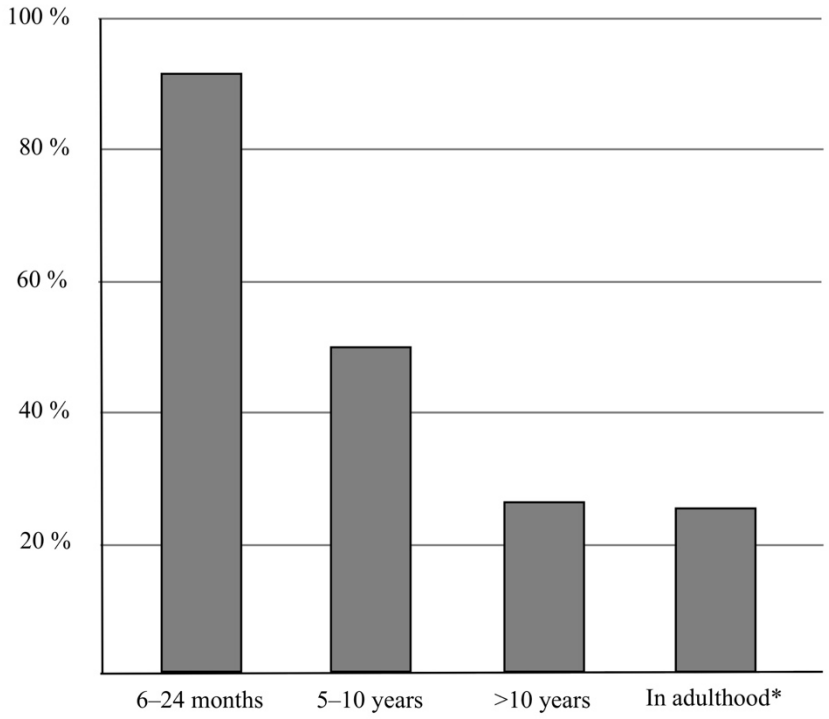


**Figure 2.** Presence of follow-up in children diagnosed with celiac disease (n=585). *Self-reported, data from questionnaires (n=235).

**Table 1.** Characteristics at the time of childhood coeliac disease diagnosis in 235 responders with and without regular follow-up in adulthood and in 324 non-responders.

| | **Regular adulthood follow-up** | | | |
|---|---|---|---|---|
| | **Yes, n=59** | **No, n=176** | **P-value[1]** | **Non-responders, n=324** |
| Girls, % | 68 | 71 | 0.700 | 52 |
| Age, median ($Q_1$, $Q_3$), yr | 8.8 (5.6, 13.6) | 9.7 (5.0, 13.7) | 0.975 | 10.1 (6.3, 13.6) |
| Year of diagnosis, median ($Q_1$, $Q_3$) | 2001 (1996, 2006) | 1995 (1984, 2002) | **0.001** | 1999 (1990, 2005) |
| Main clinical presentation, % | | | 0.667 | |
| *Gastrointestinal* | 53 | 53 | | 45 |
| *Extra-intestinal* | 24 | 28 | | 30 |
| *Screen-detected* | 24 | 19 | | 25 |
| Diarrhoea, % | 39 | 50 | 0.161 | 40 |
| Abdominal pain, % | 49 | 42 | 0.411 | 48 |
| Anaemia, % | 27 | 29 | 0.796 | 23 |
| Poor growth, % | 37 | 47 | 0.177 | 39 |
| Severity of symptoms[2], % | | | 0.506 | |
| *None* | 34 | 29 | | 30 |
| *Mild* | 38 | 38 | | 40 |
| *Moderate* | 26 | 24 | | 23 |
| *Severe* | 2 | 9 | | 7 |
| Degree of villous atrophy, % | | | 0.352 | |
| *Partial* | 37 | 30 | | 33 |
| *Subtotal* | 42 | 38 | | 36 |
| *Total* | 21 | 31 | | 31 |
| Ema/ARA, median ($Q_1$, $Q_3$), titer | 1:200 (1:100, 1:1000) | 1:500 (1:100, 1:1000)[3] | 0.356 | 1:500 (1:100, 1:1000)[4] |
| Haemoglobin, median ($Q_1$, $Q_3$), g/L | 125 (120, 132)[5] | 123 (114, 131) | 0.362 | 127 (118, 134)[6] |

[1]Comparison of patients with and without follow-up. Data available for >80% of patients except in (n): [2]183, [3]116, [4]151, [5]44 and [6]225.
ARA, serum anti-reticulin antibodies; Ema, serum endomysium antibodies; $Q_1$ and $Q_3$, lower and upper quartiles; yr, years.

**Table 2.** Current sociodemographic and lifestyle characteristics, self-reported health, and gluten-free diet in 235 adult coeliac disease patients diagnosed in childhood and divided into those with and without regular follow-up.

| | **Regular adulthood follow-up** | | | |
|---|---|---|---|---|
| | **Yes, n=59** | **No, n=176** | **P-value** | **P-value[a]** |
| Age, median ($Q_1$, $Q_3$), yr | 22.8 (20.2, 28.5) | 29.3 (22.9, 39.5) | **<0.001** | - |
| Time from diagnosis ($Q_1$, $Q_3$), yr | 14.9 (10.7, 19.9) | 20.6 (14.0, 32.3) | **0.001** | 0.578 |
| Working full-time or part-time[1], % | 83 | 78 | 0.543 | - |
| Student, % | 48 | 28 | **0.005** | 0.270 |
| Offspring, % | 35 | 45 | 0.145 | |
| Coeliac disease in the family, % | 48 | 66 | **0.018** | 0.061 |
| Member of coeliac society, % | 62 | 49 | 0.088 | - |
| Smoking, | | | | |
| Current, % | 5 | 16 | **0.042** | 0.114 |
| Quit, % | 6 | 28 | **<0.001** | **0.011** |
| Physical exercise[2], % | 56 | 61 | 0.461 | - |
| Self-reported health, % | | | 0.757 | - |
| *Excellent or good* | 83 | 81 | | |
| *Moderate or poor* | 17 | 19 | | |
| Concerns about health, % | | | 0.371 | - |
| *None or minor* | 86 | 81 | | |
| *Moderate or severe* | 14 | 20 | | |
| Coeliac-related symptoms[3], % | 19 | 25 | 0.320 | - |
| Perception of daily life restrictions[4], % | 55 | 44 | 0.138 | - |
| Adherence to a gluten-free diet, % | | | 0.702 | - |
| *Strict diet* | 83 | 77 | | |
| *Occasional lapses* | 12 | 14 | | |
| *Frequent lapses or non-adherence* | 5 | 9 | | |
| Experience of the gluten-free diet, % | | | 0.155 | - |
| *Easy* | 73 | 81 | | |
| *Somewhat difficult* | 27 | 17 | | |
| *Difficult* | 0 | 2 | | |

Data available for >95% of patients except in (n): [1]186.
[2]At least half an hour, three times a week; [3]self-assessment; [4]caused by coeliac disease.
[a]Adjusted for current age; $Q_1$ and $Q_3$, lower and upper quartiles; yr, years.

**Table 3.** Current symptom and well-being scores in 235 adult coeliac disease patients diagnosed in childhood and divided into those with and without regular follow-up.

| | Regular adulthood follow-up | | P-value |
|---|---|---|---|
| | **Yes, n=59 Median ($Q_1$, $Q_3$)** | **No, n=176 Median ($Q_1$, $Q_3$)** | |
| **GSRS**[1] **(**Gastrointestinal Symptom Rating Scale) | | | |
| Total | 1.9 (1.4, 2.3) | 1.9 (1.5, 2.4) | 0.584 |
| Diarrhoea | 1.3 (1.0, 1.8) | 1.3 (1.0, 2.0) | 0.906 |
| Indigestion | 2.5 (1.8, 3.0) | 2.3 (1.8, 3.3) | 0.901 |
| Constipation | 1.3 (1.0, 2.0) | 1.3 (1.0, 2.3) | 0.530 |
| Pain | 2.0 (1.3, 2.3) | 2.0 (1.3, 2.7) | 0.581 |
| Reflux | 1.0 (1.0, 2.0) | 1.3 (1.0, 2.0) | 0.271 |
| **PGWB**[2] (Psychological General Well-Being) | | | |
| Total | 107 (93, 112) | 105 (93, 114) | 0.955 |
| Anxiety | 24 (19, 26) | 24 (20, 26) | 0.549 |
| Depression | 17 (15, 18) | 17 (15, 18) | 0.874 |
| Positive well-being | 18 (15, 19) | 18 (15, 20) | 0.903 |
| Self-control | 16 (14, 17) | 16 (14, 17) | 0.806 |
| General health | 15 (12, 16) | 14 (11, 16) | 0.526 |
| Vitality | 18 (14, 20) | 17 (15, 19) | 0.727 |

Higher scores indicate either [1]more severe symptoms or [2] better quality of life.
Data available for ≥90% of patients in each variable.
$Q_1$ and $Q_3$, lower and upper quartiles.

**Table 4.** Co-morbidities in 235 adult coeliac disease patients diagnosed in childhood and divided into those with and without regular follow-up.

| | Regular adulthood follow-up | | P-value |
|---|---|---|---|
| | Yes, n=59 % | No, n=176 % | |
| **Coeliac disease-related conditions** | | | |
| Type 1 diabetes | 19 | 4 | **0.001**[6] |
| Hypo/hyperthyroidism | 14 | 9 | 0.265 |
| **Other diseases** | | | |
| Allergy[1] | 39 | 43 | 0.587 |
| Asthma | 16 | 10 | 0.229 |
| Cancer[2] | 4 | 1 | 0.257 |
| Depression | 7 | 15 | 0.132 |
| Dermatologic disease[3] | 18 | 15 | 0.612 |
| Eating disorder | 4 | 4 | 1.000 |
| Gastrointestinal disease[4] | 5 | 7 | 1.000 |
| Hypertension | 7 | 4 | 0.472 |
| Osteoporosis | 4 | 1 | 0.257 |
| Rheumatic disease[5] | 4 | 4 | 1.000 |
| Fracture(s) | 23 | 25 | 0.755 |
| Miscarriage(s) | 5 | 12 | 0.248 |

[1]E.g., pollen, food, or medicines; [2]e.g., cancer of central nervous system, breast cancer, or Hodgkin's lymphoma; [3]e.g., atopic eczema, acne, or psoriasis; [4]e.g., ulcerative colitis, Crohn's disease, gastric ulcer, or irritable bowel syndrome; [5]e.g., rheumatoid arthritis, fibromyalgia, or Still's disease.
[6]P-value=0.001 when the groups were adjusted for current age.
Data available for ≥95% of patients in each variable.

**Table 5.** Subgroup analysis of 59 regularly followed-up adult coeliac disease patients diagnosed in childhood with personal visits to a doctor/nurse and other contact with healthcare.

| | **Personal follow-up visits** | | |
|---|---|---|---|
| | **Yes, n=22** | **No, n=37** | **P-value** |
| Women, % | 68 | 68 | 0.961 |
| Age, median ($Q_1$, $Q_3$), yr | 24.4 (19.7, 29.8) | 22.1 (20.2, 29.7) | 0.649 |
| Time from diagnosis ($Q_1$, $Q_3$), yr | 15.0 (9.8, 21.1) | 14.9 (11.6, 19.6) | 0.888 |
| Coeliac disease in the family, % | 46 | 50 | 0.737 |
| Member of coeliac society, % | 64 | 61 | 0.847 |
| **Comorbidities/complications** | | | |
| Type 1 diabetes, % | 32 | 11 | 0.081 |
| Hypo/hyperthyroidism, % | 19 | 11 | 0.443 |
| Depression, % | 15 | 3 | 0.125 |
| Osteoporosis, % | 10 | 0 | 0.119 |
| Fractures, % | 40 | 14 | **0.044** |
| Miscarriage(s), % | 5 | 3 | 1.000 |
| Cancer, % | 0 | 5 | 0.536 |
| Self-reported health, % | | | 0.729 |
| *Excellent or good* | 86 | 81 | |
| *Moderate or poor* | 14 | 19 | |
| Concerns about health, % | | | 0.462 |
| *None or minor* | 82 | 89 | |
| *Moderate or severe* | 18 | 11 | |
| Coeliac-related symptoms[1], % | 32 | 11 | 0.081 |
| Perception of daily life restrictions[2], % | 67 | 49 | 0.185 |
| Adherence to a gluten-free diet, % | | | 0.080 |
| *Strict diet* | 73 | 89 | |
| *Occasional lapses* | 14 | 11 | |
| *Frequent lapses or non-adherence* | 14 | 0 | |
| Experience of the gluten-free diet, % | | | **0.015** |
| *Easy* | 55 | 84 | |
| *Somewhat difficult* | 46 | 16 | |
| *Difficult* | 0 | 0 | |

[1]Self-assessment; [2]caused by coeliac disease. Data available for >95% of patients.