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Transition from childhood to adulthood in coeliac disease: the Prague consensus report

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ABSTRACT

The process of transition from childhood to adulthood is characterised by physical, mental and psychosocial development. Data on the transition and transfer of care in adolescents/young adults with coeliac disease (CD) are scarce. In this paper, 17 physicians from 10 countries (Sweden, Italy, the USA, Germany, Norway, the Netherlands, Australia, Britain and Denmark) and two representatives from patient organisations (Association of European Coeliac Societies and the US Celiac Disease Foundation) examined the literature on transition from childhood to adulthood in CD. Medline (Ovid) and EMBASE were searched between 1900 and September 2015. Evidence in retrieved reports was evaluated using the Grading of Recommendation Assessment, Development and Evaluation method. The current consensus report aims to help healthcare personnel manage CD in the adolescent and young adult and provide optimal care and transition into adult healthcare for patients with this disease. In adolescence, patients with CD should gradually assume exclusive responsibility for their care, although parental support is still important. Dietary adherence and consequences of non-adherence should be discussed during transition. In most adolescents and young adults, routine small intestinal biopsy is not needed to reconfirm a childhood diagnosis of CD based on European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) or North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) criteria, but a biopsy may be considered where paediatric diagnostic criteria have not been fulfilled, such as, in a patient without biopsy at diagnosis, additional serology (endomysium antibody) has not been performed to confirm 10-fold positivity of tissue transglutaminase antibodies or when a no biopsy strategy has been adopted in an asymptomatic child.

INTRODUCTION

The Child and Adolescent Health Measurement Initiative estimates that one million US children with special health needs make the transition to adult care every year. A large proportion of adolescents/young adults, however, have not been sufficiently prepared for the transfer to adult care.2 3

Coeliac disease (CD)4 is one of the most common chronic disorders in childhood, and children with CD make up an important part of transition healthcare in the Western world. The overall prevalence of CD varies from 0.71% in the USA5 to as high as 2.9% in certain age groups in Sweden.6 Data also suggest that both diagnostic rates7 8 and incidence of undiagnosed and diagnosed CD9 10 are increasing.

Generally, the transition from paediatric to adult care should be a collaborative process involving patients, their parents or caregivers, the physician and the dietician.11 This transition has also been made a top 10 priority by the American Academy of Pediatrics11 with dedicated programmes for patients and professionals (eg, the Bright Future Programme). There are several transition recommendations for chronic disease,12 13 but very few for CD,14 and without comment on CD-specific aspects of different recommendations for diagnostics in childhood15 and adulthood.16 17

In this consensus report, we propose recommendations for the management of CD in adolescents and young adults, and how to facilitate the transition to adult healthcare for patients with CD.

METHODS

Seventeen physicians from 10 countries (Sweden, Israel, Italy, the USA, Germany, Norway, the Netherlands, Australia, Britain and Denmark) and 2 representatives from patient organisations (Association of European Coeliac Societies and the US Celiac Disease Foundation) examined the available literature on the transition from childhood to adulthood CD.

Intent and levels of evidence

We carefully weighed all aspects of the childhood to adulthood transition in relation to CD diagnosis and management. In conjunction with librarians at the Karolinska Institute, Sweden, we searched Medline (Ovid) and EMBASE between 1900 and September 2015 to identify the most relevant information for this review. The following search algorithm was used (“transition of care” or “transition of management” or “continuity of care”) AND (“adolescence” or “pediatrics”) AND (“celiac disease” or “coeliac disease”) and identified 190 references. We also explored the literature on transitional issues in other paediatric fields and additional relevant literature. The working groups developed initial recommendations and rated the quality of evidence and strength according to the Grading of Recommendation Assessment, Development and Evaluation method.

Guidelines

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of evidence for each statement was graded as high, moderate or low (A, B, C).18

Our consensus group consisted of paediatricians (n=8; JFL, IH, SK, MLM, NR, RS, RT, SH), adult gastroenterologists (n=6; CC, SEC, PHRG, KEAL, JAM, DSS), two general practitioners (LA, APH), one histopathologist (MMW) and two representatives from a patient organisation (MGG, TK).

After an initial review of the literature, we formed working groups focusing on different topics (see online supplementary appendix). Each working group worked independently prior to a first draft created by JFL. All data and opinions were discussed among all coauthors to reach consensus. The content of this report was discussed through teleconferencing and at two gastroenterology meetings (Prague, June 2015; Barcelona, October 2015). All authors agreed on the conclusions of the report.

RESULTS
Transfer of responsibility for self-care from the paediatric to the adolescent patient with CD
Paediatric patients with CD are usually seen by their general paediatrician and in a specialised centre by a team comprising a paediatric gastroenterologist, a specialised nurse, a dietician and, if needed, a social worker or psychologist. In children, the delivery of care is fundamentally family-centred, whereas in adulthood, responsibility becomes autonomous and dependent upon the needs of individuals.19

Adolescents typically start to seek independence as part of a structured family environment, but as adults they leave home, learn how to live with others and assume various responsibilities (eg, work and societal and financial commitments).20 The transition process should gradually parallel this evolution of becoming an adult and include an incremental increase in shifting knowledge and decisions to the adolescent patient with CD.15

The actual transfer may also be triggered by non-age-related factors, such as pregnancy, marriage, poor dietary adherence, substance abuse or dropping out from school. While none of these factors may signal maturity, they may draw the family’s attention (and that of the family doctor) to the fact that the adolescent is entering adulthood. The physical, mental and psychosocial development when becoming an adolescent and ultimately an adult is central to transition. This development varies between individuals of the same age, and of note, children with a chronic disease may develop autonomy later than their peers.21

Both the family and the adolescent patient should be at the centre of transition, and the function of the clinician is to balance the parents’ authority and the need for autonomy in the adolescent. Many adolescents/young adults have to work hard to overcome their reliance on their parents. To parents, this means stepping back and allowing their adolescent children to make independent decisions. Both overprotection and insufficient support of the child are undesirable.

In a joint statement,11 three physician organisations suggest that the physician starts a discussion about transition when the adolescent is 12–13 years old, develop a transition plan when the child is 14–15, with the actual transfer taking place at ≥18 years of age. We agree with this timeline, although cultural and social differences as well as individual patient preferences mean variations may occur. Transition is a complex process, and specific aims for transition in adolescents and young adults are listed in Box 1.

Statement: The transition process should gradually parallel evolution of child to adult and include an incremental increase in transferring responsibility for self-care to the adolescent patient with CD. (C)

Recommendation: We recommend to gradually transfer responsibility of medical care to the adolescent patient with CD.

Growth and puberty
Growth impairment is a known consequence of untreated or undertreated CD22 31 though many children with short stature diagnosed with CD in childhood demonstrate good catch-up growth.24 However, catch-up growth may occur more predictably for those with a delayed bone age at diagnosis and where growth velocity acceleration during the first year of treatment for CD is apparent.25 Untreated CD, or CD diagnosed after attainment of adult height, results in shorter adult height than seen in healthy controls, particularly among men.26 27 While the precise pathophysiology may currently be poorly understood, some adolescents and young adults with CD will experience a delay in pubertal development28 and may continue to grow and sexually mature beyond the expected age of pubertal completion.29 This may have implications for emotional maturity, sexual health and menstrual regularity. At the time when transition is anticipated, the paediatric provider should provide data regarding the patient’s history of physical development and should note to the adult provider whether the patient has achieved his or her final adult height. For those patients who have experienced significant pubertal delay where the paediatric provider may be better suited to provide guidance, it may be advisable to coordinate transition to an adult provider at the completion of puberty, particularly where other paediatric specialists such as endocrinologists continue to care for the patient to manage growth failure. A bone age X-ray may be done for cases of observed pubertal delay to inform growth expectations and timing of transition.

Barriers to a successful transition in CD
Several factors inhibit a successful transition; among them is having an adult healthcare provider without experience of the
relevant disease. The paediatric healthcare provider should therefore help the adolescent identify a concerned and capable caregiver for adults. A transition programme can only be successful if organised with the active participation and interest of the adult healthcarers, who may be a gastroenterologist or a general practitioner.

One inherent barrierimpeding an adolescent’s communication with a health provider is the fear of being judged. Out of the fear of being judged by the adult physician, adolescents may be less likely to ask questions that could reveal a history of non-adherence with medical recommendations. The key here is to establish a regular communication channel between the adolescent/young adult and the adult physician.

The patients’ impression of their provider influences the likelihood of effective communication of health information and patient concerns. Unsurprisingly, conflict with the healthcare provider has a negative impact on adherence to therapeutic regimens.

Cultural distinctions between paediatric and adult providers have been noted, where departure from a child to an adult environment with a greater expectation of patient independence may deter some families. Families of young adults with a variety of chronic conditions report relative decrease in support and availability for advice from their new adult provider. Some patients and parents, therefore, prefer to remain with their paediatrician. Ensuring that no adolescent drops out at transfer of care is crucial.

Statement: The patients’ impression of their provider influences the adherence and communication of health information and patient concerns. (C)

Recommendation: Healthcare providers are advised to consider that their demeanour is likely to influence patient concerns as well as the effectiveness of health information.

The actual transfer of care

There are differences between CD and other chronic diseases. For example, patients do not depend on particular medications with prescriptions and thus visits to a physician are not obligatory. In fact, many patients believe they have mastered the gluten-free diet (GFD) and have minimal contact with healthcare. In addition, non-adherence to diet may not cause symptoms for years, giving a false sense of security. Therefore, adolescents/young adults with CD are at risk of ‘medical’ dropout prior to and during transfer. Meanwhile, adult services expect that their adult patients will be able to care for themselves and be capable of negotiating the hospital clinical system. So, clearly there is a need to bridge the gap between the paediatric and adult services. For adult gastroenterologists, CD is also often perceived as a less serious disease compared with GI cancer or IBD and knowledge may be limited with respect to complications, diet, inheritance, extraintestinal manifestations and how to monitor patients.

The actual transfer can take many forms. In some settings, the paediatric and adult gastroenterologists see the patient at the same visit; in others, paediatric and adult gastroenterologists meet annually to discuss patients in transition. Optimally, joint transition clinics with paediatric and adult service clinicians can be established for information delivery and generating trust in the new physician. Structured transitional models and targeted education are important and in other chronic diseases have been linked to improved care, better health outcome and improved health-related quality of life (QoL). One path to facilitate transition and transfer of care is to create a ‘transition document’, which would allow a smooth transfer of individual medical care data (see online supplementary appendix). Such a transition document should be created by the paediatrician prior to transfer, and at the minimum, contain details of the basis for the coeliac diagnosis and information during follow-up such as serology, anthropometric data, comorbidities and dietary compliance.

Recommendation: We recommend that the actual transfer from paediatric to adult care should be structured and include as the minimum written information on the base of diagnosis, follow-up, anthropometric data, comorbidities and dietary compliance.

Communicating with the adolescent/young adult

Adolescents and young adults may have difficulty communicating with health providers for many reasons. Consequently, providers should be flexible in their communication styles when working with young adult patients. At a face-to-face encounter, it is unclear whether the presence of a parent at the medical visit may be detrimental or supportive to adolescent/young adult communication with the provider. The presence of a parent can be helpful if the adolescent has not been prepared for independent visits.

Traditional medical care for coeliac patients consists of regular physician visits to evaluate their health, including weight and height measurements (in children), dietary adherence and CD-specific serum antibodies. Although important, these measures can be time-consuming. In addition, many patients do not visit their physician for regular CD follow-up.

Young patients may also have difficulty expressing sensitive concerns in person to a provider, but may do so more readily by email. Other types of electronic communication, including videoconferencing, SMS messaging, and online consultations, have also been tested in paediatric groups with some success. Another option can be a self-management e-health coeliac follow-up independent from time and place limitations. Research in other disease areas shows that e-health self-management encourages patients to manage their disease and improve their physical and psychosocial well-being.

Issues that need to be discussed during transition/transfer

Several issues may be discussed during the transition period (box 2). Some adolescents/young adults may question their diagnosis and feel the transition period is a natural point for discussing how the diagnosis was made and whether re-evaluation is appropriate. During transition, patients may also realise that they have a long-term condition that requires monitoring throughout adult life. They may also become aware that CD is linked to increased mortality and comorbidity though the excess risks are generally seen in the first 1–2 years after diagnosis.

Of special importance to the adolescent and young adult with CD is adherence to a GFD. In Europe, adherence to a GFD by children and adolescents varies from 44% to 97%, and accidental transgressions are common. At an early age, a GFD may have been prescriptively provided by carers at home, with some involvement of the school. In adolescence, the responsibility of keeping a GFD must be shared by the child and his or her parents. Adherence to a GFD can be very difficult, particularly as the children face new challenges: peer pressure and the stigma of ‘being different’, school trips and increasing independence from their parents. Adolescence is recognised to be a period when adherence is poor and thus potential risk factors for poor adherence should be recognised. The little (and historic) data that are available reveal that increasing adherence can be maintained by regular follow-up.
Adolescents attending college or university face both the difficulty of an abrupt transition from home to a dining room setting. (C)

Consequences of non-adherence are key components for discussion in a transition setting. (C)

Barriers to adherence and advice to parents are key components for discussion in a transition setting. (C)

Use of biopsy, CD serology and genetic testing in transition to adulthood

While duodenal biopsies have been the reference standard for diagnosis of CD, recently, a selective no biopsy policy has been

Guidelines

Current guidelines for coeliac disease

Recently, several guidelines have appeared for CD diagnosis reflecting the development in diagnosis of CD (eg, better quality of serological tests and the increased awareness of CD). The NASPGHAN guidelines (USA) from 200573 clearly address the questions who to test and how to test using transglutaminase 2 IgA antibody (TG2-IgA) combined with total IgA as a screening tool, followed by referral to a paediatric gastroenterologist and biopsy, with the diagnosis based on a histological analysis. More recently, the ESPGHAN guidelines,13 as well as the British Society for Paediatric Gastroenterology guidelines for the diagnosis of CD,74 advocate TG2-IgA with total IgA (and IgG-based tests in case of IgA deficiency) as a screening tool. Furthermore, based on an evidence report,75 in cases with symptoms and very high TG2-IgA levels (>10× the upper limit of normal (ULN)), which gives a high likelihood for concurrent enteropathy,76 current ESPGHAN guidelines suggest that if carefully selected cases a biopsy avoidance strategy may be employed by undertaking further supportive tests (HLA-DQ2 and DQ8 determination may rule out CD, and the endomysial antibodies (EMAs) test has a high specificity). If these investigations are consistent with the suspicion of CD, the diagnosis may be established without a biopsy after careful discussion with a paediatric gastroenterologist. Conversely, the adult guidelines from Europe16 and the USA17 recommend a diagnosis of CD based on TG2-IgA and with biopsy. The US guidelines17 consider the pre-test probability and recommend in populations with high pre-test probability to use biopsy in conjunction with TG2-IgA. In populations with a lower pre-test probability, the guidelines suggest waiting for the TG2-IgA results before performing a biopsy. The British guidelines in addition use the EMA test for strengthening the suspicion of CD.

There are good reasons to perform an upper endoscopy with biopsies in adults with suspected CD (box 3). However, some of these issues may not apply in children/adolescence. A further complexity of the CD diagnosis is that the histological analysis may show variability between histopathologists,77 and use as the reference standard for the diagnosis of CD has been challenged.78 79 Therefore, it is important, as recommended by all guidelines, to take serology, histology and HLA status into account when there are uncertainties in diagnosis.16

Use of biopsy, CD serology and genetic testing in transition to adulthood

While duodenal biopsies have been the reference standard for diagnosis of CD, recently, a selective no biopsy policy has been

Box 2  Topics that may be discussed during transition in coeliac disease (CD)

Education on the risk of developing complications despite being asymptomatic (there can be a long interval between gluten exposure and the return of symptomatic disease).

A preventive care plan to increase adolescent/young adult health, even for factors not directly related to CD,122 such as education about smoking,123 alcohol and drug abuse,124 and the importance of physical exercise.125 Dietary education that is aimed to avoid deficiencies and to control weight.126

Medical monitoring with laboratory tests and healthcare visits according to the management of all chronic conditions.11

 Allocating time and space to discuss with experts about psychological aspects as CD may influence self-image and self-esteem12 and interfere with school, education and work.127 128

Sexuality and fertility. Dietary adherence is especially important before conception and during pregnancy as women with untreated CD are more likely to suffer an adverse pregnancy outcome.67 68 Several large studies have, however, shown that lifetime fertility is similar in individuals with and without CD.129–131

The gluten-free diet (see text).

Box 3  Reasons for performing a biopsy in the young adult with a new (suspected) diagnosis of coeliac disease

Antibodies do not have a 100% positive predictive value.132–134

Patients with either irritable bowel syndrome or Crohn’s disease of the small bowel can be pseudo-improved by adhering to a gluten-free diet.135

Baseline histology can allow assessment of severity (degree of villous atrophy).62 66 87

Many patients need an upper endoscopy anyway because they have anaemia or other significant symptoms.136

An upper endoscopy is more easily tolerated by adults and does not typically require general anaesthesia.137
proposed for some children. In comparison, the policy adopted by gastroenterologists who care for adult patients uniformly requires a biopsy for diagnosis and frequently a follow-up biopsy to document healing for management and prognostic information. The no biopsy policy was adopted by ESPGHAN, but it is not widely accepted in the USA or Australia. This difference between paediatric and adult gastroenterologists may present a topic for discussion in the transition from paediatric to adult care. Both parties will be interested in the quality of the diagnosis of CD to attain the best quality of care. All diagnostic test results must be available to the accepting physician. Of importance to recognise is that the respective guidelines may not have been followed by the physician who made the initial CD diagnosis. The main themes are as follows:

1. Patient diagnosed according to the ‘old’ 1990 ESPGHAN criteria. Review of the results of serology testing and the biopsy result will lead to an acceptable diagnosis, allowing the managing physician to continue the care of the patient.
2. Patient diagnosed according to the ‘new’ 2012 ESPGHAN criteria. Review of the symptoms, results of serology, HLA status and response to GFD. For levels of TG2-IgA <10× ULN, biopsy data must be available.

Different scenarios may be envisaged:

1. The child was symptomatic at diagnosis with malabsorption and the diagnosis based on a TG2-IgA >10× ULN, appropriate HLA, positive EMA on a second blood draw and a good response to a GFD. This diagnosis appears to be of high quality that should prompt continuing management with a strict GFD.
2. The child was asymptomatic with, for example, type 1 diabetes mellitus (T1DM) and TG2-IgA >10× ULN, appropriate HLA and no biopsy. A single positive rTG IgA test may have been obtained without a second blood draw, confirming a positive rTG or EMA. In this setting, it is necessary to consider whether there may be a temporary coeliac autoimmunity as has been seen in children and adults.

Table 1 Histology in children and adults with suspected coeliac disease (CD)

| Children | Adults |
|----------|--------|
| Is a biopsy necessary for diagnosis? | Recommendation for biopsy—all guidelines emphasise the combined use of biopsy and serological analyses for diagnosis. However, in low-resource countries, a positive TG2 with symptom improvement on a GFD may be considered sufficient for diagnosis. At least four, including bulb biopsy. |
| How many biopsies? And where from? | Adherence to submitting ≥4 specimens is low in the USA. Adherence yields a doubling of the diagnostic rate of CD. |
| Adherence to guidelines for biopsy? | Normal architecture with increased IELs is considered non-specific in paediatric guidelines. Normal architecture with ≥25 IELs/100 enterocytes has been validated as a cut-off point in adults. |
| Intraepithelial lymphocytes/100 enterocytes. What is the cut-off count? | |

GFD, gluten-free diet; IEL, intraepithelial lymphocyte; TG2, transglutaminase 2.

The serological diagnosis of CD is dependent on the quality of the assay employed. For TG2-IgA, the majority of the tests are based on ELISA and eminently suited for assay quality control measures. EMA testing is based on immune fluorescence and with an operator-dependent read-out with possibilities for variability. Yet, EMA testing is the assay with the highest specificity. As stated in the ESPGHAN diagnostic guideline, to rely on serology, the tests have to be subject to continuous participation in control measures (such as the National External Quality Assurance Scheme (NEQUAS) initiative in Europe). In non-European countries, significant laboratory variability may occur and whether these cut-offs are valid in countries such as the USA are yet to be confirmed. A diagnosis made according to the ESPGHAN guidelines outside of Europe should be considered in the context of this potential uncertainty.

The histological evaluation may also be indeterminate and transition into adult care could be a convenient time for re-evaluation, even when the initial diagnosis is definitive. Table 1 is an overview of differences in the use of histology for diagnostic purposes in children and adults.

Persistent mucosal lesions are common in adults with CD, despite normalisation of serologies. Concomitant with these lesions are augmented risks of morbidity such as lymphoma and certain fractures. Whereas these risks may be lower in children, refractory CD and consequently enteropathy associated t-cell lymphoma (EATL) is extremely rare in subjects with CD diagnosed in and treated since childhood, adolescents and young adults with CD may have greater difficulty with dietary adherence, whether accidental or intentional. Early identification of such risks may thwart future adverse outcomes and identify those in need of greater surveillance.

Also important is the procedure adopted for transitional follow-up. If the existing diagnostic guidelines have not been met and the diagnosis needs re-evaluation, a new diagnostic approach should be instituted. Serology and histology may be part of this approach. However, undertaking duodenal biopsies while on a GFD may be uninformative, except for ruling out differential diagnosis and to confirm mucosal healing. After transition, care will be determined dependent upon the results of nutritional, serological, genetic and dietary assessment. There are four indications for performing a biopsy before or after transition to adult care in some settings with a gluten challenge:
1. if the existing guidelines have not been met;
2. the adolescent has ceased a GFD because he or she doubts the diagnosis;
3. the patient or the physician requires documentation of healing;
4. the presence of symptoms suggests active CD or another diagnosis.

The potential contribution of genetics in ruling out CD in suspect or insufficiently diagnosed cases is important. CD is strongly associated with the HLA-DQ2 and HLA-DQ8 genotypes. While HLA-DQ2 or DQ8 occurs in >99% of people with CD, it is found in ~30% of the general population, and therefore, a positive genetic test does not confirm a CD diagnosis.

Statement: In adolescents and young adults, biopsy to reconfirm a childhood diagnosis of CD may be considered when the 10-fold positive tissue transglutaminase antibody result has not been confirmed by positive EMA in a second serology at the time of diagnosis or when the ESPGHAN diagnostic criteria have not been met in a child without duodenal biopsies. Biopsies may also be relevant when the adolescent has ceased a GFD because he or she doubts the diagnosis; the patient or the physician requires documentation of healing; and the presence of symptoms suggests active CD. (C)

Recommendation: We recommend that in adolescents and young adults, routine small intestinal biopsy is not required to reconfirm a childhood diagnosis of CD when the diagnosis has been made according to ESPGHAN or NASPGHAN criteria.

Statement: HLA testing can be used to rule out CD in unclear cases. (B)

Recommendation: We recommend testing for HLA-DQ2 and HLA-DQ8 genotypes in unclear cases.

The gluten challenge
A gluten challenge after transfer to adult care is normally not needed if diagnostic criteria have been followed, including children diagnosed younger than 2 years of age. A gluten challenge is indicated when the primary diagnosis of CD was not performed according to standards and guidelines. A second circumstance when a gluten challenge is applicable is when the patient requests proof of the diagnosis, even though the initial diagnosis was performed according to the current standards.

There are no well-established rules in a gluten challenge. The clinical tolerability and the time to relapse vary between patients, but traditionally a 3 months’ challenge with moderate to high amounts of gluten has been advocated, keeping in mind that an enteropathy may occur after an extended period of time. Before gluten challenge, serology for CD-specific autoantibodies should be performed (duodenal biopsies should preferentially be obtained as well). An increase in CD-specific serum autoantibodies follows histological change. Therefore, if the patient remains asymptomatic, the biopsies should be performed when serology is positive.

Non-coeliac gluten sensitivity in children
Non-coeliac gluten sensitivity (NCGS) is a differential diagnosis to consider in patients with symptoms of CD, but TG2-IgA and EMA are negative and the histology is normal or near normal (only lymphocytic duodenosis is accepted). The genotypes HLA-DQ2/DQ8 may or may not be present. The distinction between wheat allergies with negative IgE antibodies may be difficult. In children, circumstantial evidence suggests that a proportion of children suspected of CD, but with the characteristics mentioned above, may have NCGS.

However, to our knowledge, no study of blinded, placebo-controlled food challenges has been performed in children with gastroenterological symptoms of NCGS. The prevalence of NCGS in children is still unclear, and further studies are needed.

Statement: There is as yet no reliable prevalence data on NCGS in children. (C)

Recommendation: We recommend that the diagnosis of NCGS in children/adolescents is not made on a regular basis, but awaits further documentation.

Follow-up
Follow-up of patients with CD is advocated to ensure dietary adherence, prevent or detect complications or associated conditions including autoimmune thyroid disease, and promote optimal health. Data, though limited, suggest continued follow-up improves dietary adherence, whereas lack of regular follow-up seems to be a particular problem for the phase of transition between paediatric and adult care. Based on expert opinion, all paediatric patients should be seen at 3–6-month intervals for the first year after diagnosis. Once symptoms have resolved and serological tests for CD have normalised, an annual follow-up visit is recommended.

CD is associated with fracture risk, predominantly before treatment or in the setting of non-adherence to GFD. Bone mineral density is frequently depressed in both children and adults with CD at the time of diagnosis, and deficits have been shown to correlate with degree of histological severity. The vast majority of children recover from bone mineral density abnormalities following appropriate therapy. Thus, dual-energy X-ray absorptiometry should only be considered for young adults at high risk (eg, known history of low-energy bone fractures, dietary non-adherence, established persistent villous atrophy or low body mass index (<20 kg/m²)).

A subset of patients with CD suffer from other diseases of autoimmune pathogenesis such as T1DM and thyroid disease. CD is more often seen in patients with Down’s syndrome. Some of these patients may present specific problems in the transition phase and guidelines have been published on transition in T1DM and Down’s syndrome. As far as CD is concerned, in patients with T1DM, the GFD may represent a special challenge as diet is already an issue in patients with T1DM.

Dermatitis herpetiformis is a pruritic skin condition strongly linked to CD. Adolescents and young adults with dermatitis herpetiformis should be aware that medical treatment with dapsone will remedy itch but will have no influence on small intestinal inflammation. Hence, a strict GFD is crucial for this group of patients.

Primary care involvement
In many countries, adolescents leaving paediatric care are often cared for by a general practitioner rather than by an adult gastroenterologist. Primary care physicians (PCPs) are then also responsible for the healthcare during and after transition. In adults, PCPs may take a major role in care, dependent upon management care programmes and the availability of skilled personnel and local practice.

Some adolescent/young adult patients are also referred to primary care when they are considered healthy after diagnostic work-up information and initial follow-up in secondary care (either with a paediatrician or an adult gastroenterologist). Primary care may also be a suitable care provider if adequate
resources in terms of personnel skills and laboratory facilities are sufficient for long-term follow-up. In settings where the PCP has access to upper endoscopies with biopsies, the adolescent/young adult be solely cared for by the PCR provided that relevant skills, a dietician with expertise is available, and that the care results in good self-reported health and normalised laboratory data. Whenever the patient’s follow-up is in primary care, a management plan should be followed.\cite{15,16} When seeing an adolescent/young adult with CD, the PCP also has to consider an increased risk for other autoimmune diseases.\cite{30,108,113}

**Statement:** The PCP is often the care provider who is closest to the adult patient with CD. (C)

**Recommendation:** Primary care may be a suitable care provider if adequate personnel skills and laboratory facilities are sufficient for long-term follow-up, and this may depend on local practice.

### Economic issues

The cost of gluten-free products is often substantially higher than that of gluten-containing products.\cite{116-118} Different economic models are used to compensate patients with CD, with tax deduction used in parts of Europe (eg, Germany) and North America,\cite{119} and prescriptions for GFD in many European countries. Prescriptions may, however, only apply to children and in, for example, Austria, Estonia, Finland, Hungary, Spain and Ukraine, adults with CD receive no government support for extra costs (personal communication, T Koltai, 17 February 2016). While in Italy there are no requirements for the quality of food prescribed, the coeliac society in the UK restricts the prescribed list to essential products, excluding gluten-free foods considered ‘unhealthy’ such as gluten-free snacks and desserts. In those countries where prescription and rebates on GFD are restricted to children, becoming an adult will incur extra costs of GFD, potentially having a negative impact on dietary adherence.

The cost of healthcare in the transitional period between adolescence and adulthood will vary according to the country of residence. Indeed, in some countries one in three young adults has unmet health needs because of cost.\cite{120} Special issues arise in the USA with its hybrid healthcare system. Poor children may be covered by Medicaid or Children’s Health Insurance Program. In the USA, the Patient Protection and Affordable Care Act (2010) included a provision for a child to remain under his or her parents’ insurance plan until age 26. This act also prevented denial of coverage based on the presence of a chronic condition. However, the parents’ insurance may be inadequate to make the needed care affordable.

### DISCUSSION

Seventeen physicians and two representatives from CD patient organisations wrote this consensus report after reviewing the literature on the transition of CD care from childhood to adulthood.

The strengths of our paper lie in the systematic literature search and the involvement of patient organisation representatives. However, we acknowledge several weaknesses, including a low level of evidence, and we are not aware of any randomised trials on transition in CD. Despite the lack of CD-specific evidence, we have tried to make statements and recommendations, sometimes based on inference from data in other chronic diseases and sometimes on our own pooled clinical experience. We have listed several recommendations of care adding to more general recommendations of diagnostics and management in CD.\cite{15-17} Still, we understand that countries, and thereby the conditions for care of delivery, differ. We also recognise that resource limitations will hinder some providers from offering joint clinics and follow-up as suggested.

We believe that we offer a working approach to adolescents and young adults who were once diagnosed without a small intestinal biopsy\cite{15,16} and now enter adult healthcare where biopsy is still generally recommended to diagnose the condition.\cite{16,17} That said, we recognise that there is international variation of practice based on social practice and that individual patient preferences may also influence the transition process.

We recommend that the diagnosis be re-evaluated only when made outside current ESPGHAN or NASPGHAN recommendations or when the patient questions his/her diagnosis. That does not mean that a paediatric CD diagnosis is more erroneous than a diagnosis made by an adult gastroenterologist.

The implementation of a systematic transition policy in CD has been limited by a lack of clinical guidelines based on outcome-related research and clear and consistent definitions.\cite{3} In the absence of solid evidence, different models of transition will be likely developed locally. We still do not know if a standardised protocol-driven transition process is superior to a process that varies both nationally and internally. These differences will contribute to the differences that exist between the different healthcare systems. Models of transition\cite{12} will eventually need to be evaluated in randomised controlled trials with clear patient outcome measures. It is crucial to know to what extent a well-structured and planned transition will influence adherence to a GFD, which in CD is imperative for restoration of health and well-being. This aspect will depend on the prevalence and quality of complications, as well as on health-related QoL.\cite{37,121} Socio-economic effectiveness and outcomes of care of the different models should also be carefully evaluated. Further studies are needed to identify and remove barriers\cite{20} to transition.

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Competing interests PHRG: scientific advisory board of Alvine Pharmaceuticals and ImmusanT. JAM: consultant for Alba Pharmaceuticals, Alvine Therapeutics, Flamentera, 2GPharma Boeringer-Ingelheim and ImmusanT. KEAL: ImmusanT, Regeneron and Alvine Pharmaceuticals. DSS: has received an educational grant from Coeliac UK, Biocad, Simtomax and Dr Schär (a gluten-free food manufacturer) to undertake an investigator-led research study on CD and/or gluten sensitivity. IH: Alvote Scientific Advisory Group Member, RS: consultant to Bioline. SK: Received funding for a CD-related research projects from Nestle, R-Biopham, Schär, Phadia-ThermoFisher, Eurospital, Euroimmun, Inova. NR: clinical advisory board for ImmusanT. SH: educational grant from Thermo-Fisher, advisory board for Simtomax.

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Transition from childhood to adulthood in coeliac disease: the Prague consensus report

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