



Coeliac Disease Detected in Adulthood: Nutritional Consequences of a Decade of Delay

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Abstract

Coeliac disease presenting in adulthood is frequently diagnosed years after symptoms begin, and the nutritional damage accrues in the interval. In a cohort of 500 biopsy-confirmed adults, median latency was 1.2 years in those diagnosed within two years and 5.5 years in those diagnosed later. Delay beyond two years was associated with osteoporosis or low bone density in 40 against 20 per cent, infertility in 20 against 10, and lymphoma in 5 against 1, with adjusted odds ratios of 2.50, 2.25 and 5.20 respectively. The investigators attribute this largely to pre-existing damage present at diagnosis rather than to events occurring after treatment began. Micronutrient deficiency is common at presentation, zinc being the most frequent at 59.4 per cent, alongside iron, vitamin D, copper, vitamin B12 and folate. Recovery on a gluten-free diet is uneven, with zinc improving within weeks and iron deficiency anaemia over six to twelve months.

Keywords: Coeliac disease; Diagnostic delay; Micronutrient deficiency; Bone mineral density; Gluten-free diet

Introduction

Coeliac disease is an immunologically mediated enteropathy caused by permanent intolerance to ingested gluten in genetically susceptible individuals, with reported prevalence approaching 1 in 100 in several populations and 1 in 141 in recent United States data [1,2,3].

The pattern of presentation has changed. The classic syndrome of diarrhoea, weight loss and malabsorption has become less common than subtler presentations such as isolated iron deficiency anaemia, and increasing numbers of patients are diagnosed with non-classical symptoms [1,3,4]. Because those presentations are less suggestive, the diagnosis is often delayed or missed [1,5].

This review examines what accumulates during that delay, how much of the damage is present at the point of diagnosis rather than arising afterwards, and how completely the nutritional consequences resolve once treatment begins.

Objective

This review sets out to establish four things from the published literature. First, how long diagnosis is delayed in adults and what complications are associated with delay. Second, whether those complications represent damage already sustained or outcomes arising after treatment. Third, which nutritional deficiencies are present at diagnosis and at what frequency. And fourth, how far and how quickly they resolve on treatment, since that determines what the delay actually costs.

Literature Review

How long the delay is: A retrospective cohort of 500 biopsy-confirmed adults followed at a tertiary centre between 2015 and 2025, mean age 35.4 plus or minus 12.1 years and 70 per cent female, categorised diagnostic latency as early at two years or less and delayed beyond two years. Median latency was 1.2 years in the early group and 5.5 years in the delayed group (Figure 6) [6].

THE TWO LATENCY GROUPS COMPARED

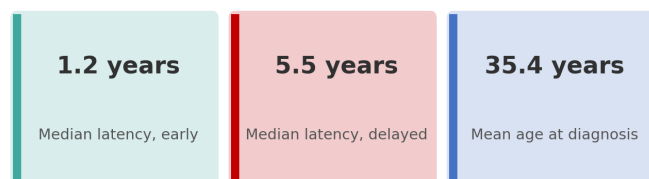


Figure 6: The two latency groups in a cohort of 500 adults [6]

What delay was associated with: Delayed diagnosis was associated with significantly higher prevalence of all three complications examined: osteoporosis or low bone mineral density at 40 against 20 per cent, infertility at 20 against 10 per cent, and lymphoma at 5 against 1 per cent (Figure 1) [6]. Adjusted for age and sex, the odds ratios were 2.50 (95% CI 1.7 to 3.8), 2.25 (1.3 to 3.8) and 5.20 (1.5 to 18.0) respectively (Figure 5) [6].

COMPLICATIONS BY DIAGNOSTIC LATENCY IN 500 ADULTS

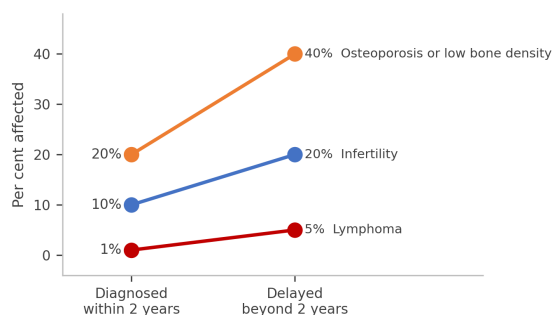


Figure 1: Complications by diagnostic latency in 500 adults [6]

ADJUSTED ODDS WITH DELAY, AND THE WIDTH OF EACH INTERVAL

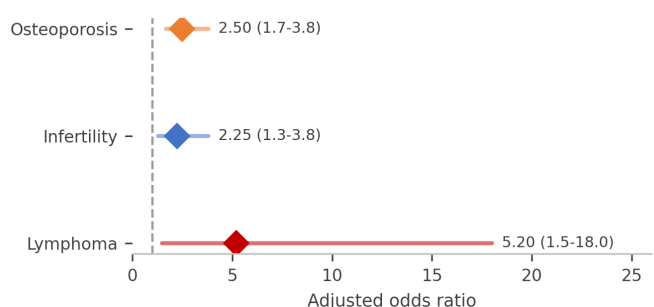


Figure 5: Adjusted odds with delay, and the width of each interval [6]

What the authors concluded about causation: The investigators state that the association largely reflects a substantial burden of pre-existing damage and complications at diagnosis rather than incident outcomes arising after treatment began [6]. That distinction matters for interpretation: the finding argues for

earlier detection rather than indicating that treatment fails.

Table 1: Complications by diagnostic latency, as published [6]

Complication	Early diagnosis	Delayed	Adjusted odds ratio
Osteoporosis or low density	20%	40%	2.50 (1.7 to 3.8)
Infertility	10%	20%	2.25 (1.3 to 3.8)
Lymphoma	1%	5%	5.20 (1.5 to 18.0)

Bone at diagnosis: Disorders of calcium and bone metabolism were the most prevalent complication in a series of adults diagnosed in a rural setting, with 31 per cent osteopenic and 28 per cent osteoporotic (Figure 3) [1]. Approximately 40 per cent of patients with newly diagnosed coeliac disease show low bone mineral density, and fracture risk persists after diagnosis for up to 20 years, though the absolute increase in risk is low [7]. Compliance with a gluten-free diet has been reported to increase bone mineral density in osteopenic patients [1].

BONE STATUS IN AN ADULT SERIES AT DIAGNOSIS

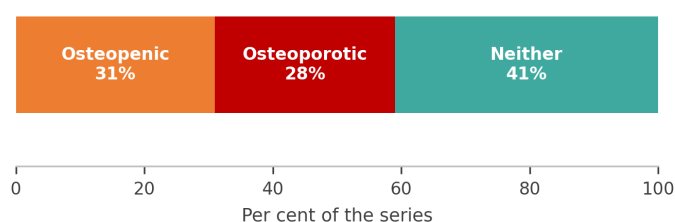


Figure 3: Bone status in an adult series at diagnosis [1]

Micronutrient status at diagnosis: A study of adults at the time of diagnosis found micronutrient deficiencies common, with zinc deficiency observed most frequently at 59.4 per cent, and deficiencies of iron, vitamin D, copper, vitamin B12 and folate also reported (Figure 2). The authors recommend that assessment cover vitamin D, iron, folic acid, vitamin B12, zinc and copper [4]. Deficiencies most commonly described across the wider literature are iron, vitamin D, folate, vitamin B12, vitamin B6 and zinc [8].

Iron as the presenting sign: Iron deficiency has been reported in up to half of newly diagnosed adults and is in itself an indication for screening [8]. The reviewed guidance recommends including serological screening systematically in the evaluation of adults with unexplained iron deficiency anaemia, unexplained gastrointestinal symptoms, or membership of a higher-risk group [1].

Table 2: Nutritional status at diagnosis and reported recovery

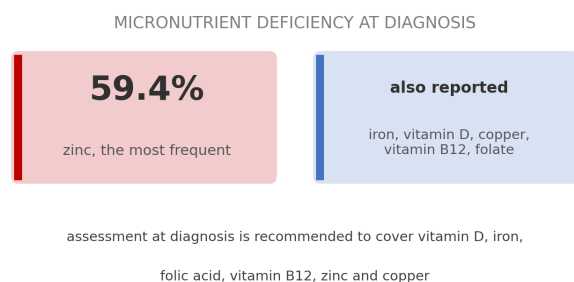


Figure 2: Micronutrient deficiency at diagnosis [4,8]

How quickly deficiencies resolve: A gluten-free diet usually leads to recovery from iron deficiency anaemia within six to twelve months, whereas zinc deficiency improves within weeks (Figure 4) [8]. Some patients with folate or vitamin B12 deficiency develop macrocytic anaemia, which can be difficult to detect where iron deficiency coexists, since the two shift mean cell volume in opposite directions [8,9].

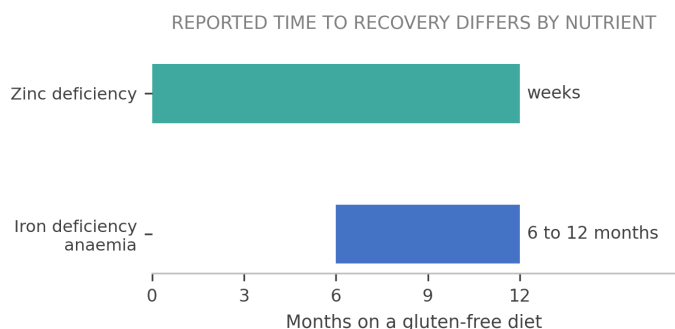


Figure 4: Reported time to recovery differs by nutrient [8]

Nutrient	Reported at diagnosis	Recovery on treatment
Zinc	59.4%, most frequent	Within weeks [4,8]
Iron	Up to half of adults	Six to twelve months [8]
Vitamin D	Reported	Not specified here [4]
Vitamin B12 and folate	Reported	Not specified here [4,8]
Copper	Reported	Not specified here [4]

Undiagnosed disease in the community: Screening of 1,900 adults aged 18 to 64 in primary care found 22, or 1 per cent, reporting a previous diagnosis, and identified further cases serologically, with folate, iron and transferrin receptor assessed in both groups [10]. In an older Australian community cohort of 2,122 participants aged 55 to 85, the prevalence of at-risk serology defined by both antibody and genotype positivity was 5 per cent, and 3.4 per cent met criteria for osteoporosis at baseline [7].

What the guidelines specify: National and international guidance on diagnosis and management of adult coeliac disease has been issued by several societies [12,13,14], and the condition has been

reviewed comprehensively [29,30]. Global prevalence has been estimated by systematic review and meta-analysis [31]. Claims database analysis has examined delay specifically among patients already carrying high-risk screening conditions [15].

What delay costs beyond the complications counted: Delay has been related to reduced health-related quality of life [16,18] and to incremental use of health care services and medicines in a prospective nationwide study [18]. Population survey has compared quality of life before and after diagnosis [17]. These outcomes accrue during the same interval as the nutritional damage and are less often quantified [16,18].

Bone in more detail: Osteoporosis prevalence and its association with vitamin D deficiency have been examined directly in this population [19], bone and coeliac disease reviewed as a topic [20], and recovery of bone mineral density assessed by systematic review [21]. Haematological manifestations have likewise been described [22], with anaemia in coeliac disease found to be multifactorial in origin rather than attributable to iron alone [23].

Deficiency before and after treatment: Vitamin and mineral deficiencies are highly prevalent in newly diagnosed patients [24], and appropriate supplementation has been considered separately [25]. The gluten-free diet itself carries nutritional inadequacies, described both in recently diagnosed and long-term patients [26,27,28], so treatment does not automatically restore adequacy across every nutrient [26,28].

Malignancy risk in context: Small intestinal histopathology has been related to mortality risk [32] and to lymphoproliferative malignancy [33], and meta-analysis has examined all-cause mortality, any malignancy and lymphoid malignancy together [34]. Those analyses provide the background against which the lymphoma figure in the latency cohort should be read [6,34].

Table 3: What is and is not established about delayed diagnosis in adults

Question	What the evidence supports
Is diagnosis delayed?	Median 5.5 years in the delayed group [6]
Does delay associate with harm?	Yes, for three complications [6]
Did the harm follow treatment?	Largely present at diagnosis [6]
Is deficiency common?	Zinc 59.4%, iron up to half [4,8]
Does treatment restore status?	Unevenly; the diet has its own gaps [8,26]

Method

Search strategy: PubMed and the archives of the major gastroenterology, clinical nutrition and general medical journals were searched for studies of coeliac disease diagnosed in adulthood. Search terms combined coeliac disease and celiac disease with diagnostic delay, adult diagnosis, micronutrient deficiency, bone mineral density and gluten-free diet. Reference lists of the diagnostic latency cohort [6] and the management review [8] were screened by hand for primary sources.

Eligibility: Studies were included if they reported diagnostic delay, nutritional status at diagnosis, or complications in adults with coeliac disease. Screening studies in unselected populations are included where they bear on the size of the undiagnosed group and are identified as such.

Data extraction and handling: Population, the definition of delay applied, the measure of nutritional status and the reported figure were extracted as published. Where an association between delay and complication is reported, the authors' own statement about whether the damage preceded or followed diagnosis is reported alongside it, because that determines what the association implies for practice. This review reports published findings and does not constitute dietary, supplementation or screening guidance for any individual, which are matters for the treating clinician. No pooling or re-analysis was performed. Figures 1 to 6 and Tables 1 to 3 reproduce published values only. This is a narrative synthesis of published literature and was not registered as a systematic review.

Concluding Remarks

The central result is a gradient across latency: 20 against 40 per cent for low bone density, 10 against 20 for infertility, 1 against 5 for lymphoma, with the delayed group having waited a median of 5.5 years against 1.2 [6]. Read alone, that reads as damage accruing while the diagnosis is missed, which is the reading the title of this review assumes.

The investigators are more careful than that, and their caution should be carried forward. They attribute the association largely to pre-existing damage and complications present at diagnosis rather than to incident outcomes after treatment [6]. The practical difference is substantial. It means the case is for earlier detection rather than for more intensive treatment of those found late, and it means the complication figures describe a state on arrival rather than a trajectory under care.

The lymphoma figure needs its interval stated whenever it is quoted. An adjusted odds ratio of 5.20 is arresting; the confidence interval runs from 1.5 to 18.0, and the underlying counts are 5 per cent against 1 per cent [6]. The association is real in direction and very imprecisely estimated in magnitude, and a reader given only the point estimate would form a firmer impression than the data support.

On nutrition specifically, the finding that reframes the clinical task is that zinc deficiency was the most frequent at diagnosis, at 59.4 per cent, ahead of iron [4]. Iron is what prompts most of the screening, being present in up to half of newly diagnosed adults and an indication for testing in its own right [8]. A deficiency more common than the one that triggered the investigation is easy to leave unmeasured, which is why the recommendation to assess a defined panel rather than a single analyte matters [4].

The recovery data complicate the phrase in the title in a useful direction. Zinc deficiency improves within weeks and iron deficiency anaemia within six to twelve months on a gluten-free diet [8]. Much of the nutritional consequence of a long delay is therefore reversible on a timescale of months. What is less reversible is the bone: around 40 per cent of newly diagnosed patients have low bone density, and fracture risk persists for up to two decades after diagnosis even though the absolute increase is low [7].

A detection point follows from how the presentation has shifted. Diagnoses are increasingly made in patients without the classic syndrome, and in older adults the features that might prompt investigation, including low bone density and calcium or vitamin D deficiency, are unremarkable enough at that age that further investigation is often not considered [3,11]. The subtler the presentation becomes, the more the diagnosis depends on serological testing being applied to unexplained findings rather than on clinical suspicion [1,5].

Three limitations belong with these conclusions. The latency cohort is retrospective, from a single tertiary centre, and defines delay from patient-reported symptom onset, which is subject to recall [6]. Prevalence of deficiency at diagnosis varies with which analytes are measured and which thresholds applied, so figures from different series are not directly comparable [4,8]. And several of the series describing presentation patterns are older, predating the current serological testing that has itself changed who is diagnosed and when [1,5].

There is a second nutritional problem that begins at diagnosis rather than ending there. The gluten-free diet itself carries inadequacies, described in both recently diagnosed and long-term patients [26,27,28]. A patient whose zinc and iron recover on treatment may drift into different shortfalls on the diet that treats them, which means monitoring has a role after diagnosis and not only at it [25,28].

The malignancy question deserves the wider context the specialist literature supplies. Small intestinal histopathology has been related to mortality and to lymphoproliferative malignancy in large cohorts, and meta-analysis has examined all-cause mortality, any malignancy and lymphoid malignancy together [32,33,34]. Against that background, a fivefold odds ratio from 500 patients with five events in one arm is a signal consistent with a known association rather than a new finding on its own

[6,34].

What would strengthen the case for earlier detection is different evidence from more of the same. The latency cohort establishes that late-diagnosed patients arrive with more damage [6]. It does not establish that a screening programme would find them earlier, nor at what cost, and claims database work suggests delay persists even among patients already carrying recognised high-risk conditions [15]. That last finding is the more actionable one, since it concerns patients already in contact with services [15].

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Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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