Prevalence and management of coeliac disease in people with Down's syndrome.

The aims of this paper are to raise awareness of the increased incidence of coeliac disease in people with Down's syndrome considering how support staff and carers can monitor for signs or symptoms and support early identification through screening. The paper then moves on to discuss treatment for coeliac disease and advice about further monitoring that is required for improved health outcomes.

People with Down's syndrome are more likely to have coeliac disease than the general population. However many people continue to be undiagnosed and therefore the appropriate care to manage this condition is not being recommended leading to additional health complications in this group of people who are now living longer than they were in previous decades. The gold standard approach for managing coeliac disease is currently a gluten free diet, which is often difficult for family, carers and individuals with Down's syndrome to truly adhere to given the number of hidden gluten's in everyday foods.

What is coeliac disease?

Coeliac disease is an autoimmune condition causing an inflamed small intestine and digestive manifestations due to an adverse response to gluten in wheat, barley and rye (Radlovic, 2013). Thus if left untreated not only does the small intestine mucosa show signs of chronic inflammation and loss of structure which are medically described as enteropathy but other complications ensue including malabsorption of essential vitamins, minerals and macronutrients leading to anaemia, reduced bone and fat mass (Bull et al, 2011). These nutritional complications are often more severe in children under one year of age which manifests by low weight and delayed growth spurts in these children (Radlovic, 2013).

Many individuals with coeliac disease are oligosymptomatic meaning that they may only have a few symptoms or mild symptoms of diarrhoea, flatulence, abdominal pain or indigestion and constipation (Radlovic, 2013). Others are symptom free thus making it difficult to ascertain who is appropriate for screening (Costa Gomes et al, 2016). Further indicators that an individual may have coeliac disease and thus should have their serology checked at the registered G.P practice includes fatigue, weight loss, mood changes, skin rashes particularly dermatitis hepetiformis (which typically appears on the elbows, knees and buttocks and presents as extremely itchy with small blisters), neurological changes, pancreatic atrophy, menstrual irregularities and tingling, numbness or swelling in the hands, feet, arms and lower legs (NHS choices, 2016; Venner et al, 2015).

Prevalence of coeliac disease.

Prevalence rates of coeliac disease in the general population have been rising over the last decade which is partly thought to be due to the increased awareness and uptake of screening. Current prevalence rates in the UK are 1-2% which is supported by international studies finding prevalence

ranging from 0.3% to 2.4% with rates in the Middle East and Africa increasing in correlation to the changes in wheat production and preparation (Noori et al, 2016). Research has found an increased incidence of coeliac disease in those with Wilson's disease, diabetes (Admou et al, 2012), hypothyroidism, Williams syndrome (4%; Mihci et al, 2015), Turners syndrome (4%; Dias Mdo et al, 2010) and Down's syndrome (Henderson et al, 2007).

Individuals with Down's syndrome are known to be more likely to have a number of health conditions including cardiovascular disease, lipid metabolic disorders, recurrent infections particularly of the gastrointestinal tract and respiratory system (Adelekan et al, 2012; Roizen et al, 2014; Henderson et al, 2007; Malt et al, 2013). In addition people with Down's syndrome have estimated prevalence rates of 7-50% for thyroid disease, 4% for type 1 diabetes and between 2.5% and 33% for coeliac disease (Malt et al, 2013; Noori et al, 2016). With one UK based study reporting a prevalence of confirmed coeliac disease as 11% in people with Down's syndrome (Henderson et al, 2007). The large divergence in results from 2.5 to 33% prevalence of coeliac disease in people with Down's syndrome is due to a combination of sample selection (including geographical area, recruitment process and size of cohort) and the screening method employed by the researchers with IgA-EMA markers resulting in higher prevalence rates and diagnosis confirmed by biopsy resulting in lower rates of diagnosis (Uibo et al, 2006). Trends across studies from a range of countries have pointed to a consensus of around 6% of individuals with Down's syndrome who have coeliac disease (Szaflarska-Popławskaet al, 2016; Nisihara et al, 2005; Roizen et al, 2014; Goldacre et al, 2004; Nisihara et al, 2005). This may prove to be a conservative estimate given the known under-representation due to atypical and latent coeliac disease (Admou et al, 2012) and diagnostic over shadowing within people who have cognitive impairments.

Despite the increased prevalence of coeliac disease in people with Down's syndrome being undisputed there is currently a dearth of contemporary literature to support mechanistic explanations and best practice for assessment, diagnosis and interventions. Internationally the literature available is sparse but offers some insight and highlights that further research around this topic is much needed.

The increase in coeliac disease in people with Down's syndrome is not fully understood, with research looking at genomics still identifying the relevant genotype within the general population. Genetic links between Down's syndrome and susceptibility to coeliac disease have been suggested in the literature in relation to the human leukocyte antigens specifically the haplotypes HLA-DQ2 and HLA-DQ8 (Admou et al, 2012; Radlovic, 2013). These antigens aid the immune system by distinguishing between the body's own proteins and proteins that are made by foreign bodies, in coeliac disease the antigens interpret gluten proteins as foreign and send out messages to attack these proteins with surrounding tissues getting caught in the crossfire. Other mechanisms involve chromosome 21 being implicated in the reduced expansion of T cells (a subtype of white blood cells) in the thymus, immature natural killer cells, autoimmune regulatory gene *AIRE* which works to prevent the immune system from attacking its own internal organs (Souto-Rodríguez et al, 2014) and interferon receptors 1 and 2 (Abadie et al, 2011). In addition the increase in prevalence of coeliac disease in those with diabetes and hypothyroidism is undisputed with an increase in both hypothyroidism and type 1 diabetes in individuals who have Down's syndrome (Malt et al, 2013).

<u>Screening for coeliac disease.</u>

Robust guidelines are lacking in relation to screening for coeliac disease in people with Down's syndrome. However, the British Society for Gastroenterology and recent guidance from the National Institute of Clinical Health and Care Excellence advocate for screening for coeliac disease in people with Down's syndrome (Ludvigson et al, 2014; NICE, 2015). Evidence of the increased risks in infancy warrants early screening as advocated for by Bulls committee (2011) who reviewed health supervision in children with Down's syndrome. The pertinence of monitoring coeliac disease in babies with Down's syndrome is due to the links with physical and psychomotor development as well as congenital anomalies (Boskovic et al, 2012; Noori et al, 2016). Further monitoring throughout adult life if symptoms present which indicate signs of even mild gastrointestinal disturbance is also needed. This is corroborated by an increased risk of morbidity and mortality in those with undiagnosed coeliac disease including links to cardiovascular disease, mood disorders, intestinal lymphoma, gastrointestinal cancer, ulcers in the small intestine and infertility (Sharr et al, 2016; Ludvigson, 2012; Radlovic, 2013). The later point is also significant given evidence of the increased risk of emergence of coeliac disease in later life in those individuals who were previously gluten tolerant.

Henderson et al (2007) support the contention that annual health checks for people with a learning disability are ideally suited to screen for history of coeliac disease symptomology and recommend serological assays to be completed in those with markers as well as those with type 1 diabetes, thyroid disease or anaemia. In order to ensure accuracy of blood tests it is important that the person continues to eat a normal healthy diet that contains gluten until the blood test is completed. Following positive serological markers being found biopsy to investigate enteropathy of the small bowel is used to confirm diagnosis. In those refusing to give consent for endoscopy or if consent cannot be given in their best interest then total IgA and anti-tissue transglutaminase antibody (tTG) serological markers and assessment for HLA (DQ2 or DQ8) suffices given the sensitivity and specificity of these analyses when used in combination (Radlovic, 2013).

Treatment of coeliac disease.

Children with Down's syndrome often prefer foods made of simple carbohydrates and have lower intakes of fruit, vegetables and fibre than people who do not have Down's syndrome (Mazurek and Wyka, 2015; Abdallah et al, 2013). Explanations of why individuals can't eat the preferred foods of cake, biscuits, pies, pizza and foods that their peers are eating are often difficult which is exacerbated by a lack of easy read literature on coeliac disease. In addition explanations are needed to explain why the individual is feeling unwell, having bloods taken and what to expect during an endoscopy in which biopsies of the small intestine are taken. In order to support staff and carers with explanations regarding screening a number of easy read leaflets and resources have been produced which can be accessed at easyhealth.org.uk and the learning disabilities public health observatory (iHaL). Community teams, primary and acute care liaison nurses working with people with learning disabilities are also a quality resource to provide easy read information regarding coeliac disease and a gluten free diet.

Currently medicinal treatment for coeliac disease is unavailable and thus the gold standard of treatment remains dietary management through the removal of foods that contain barley, rye or wheat. A gluten free diet has been reported to reduce the increased risk of carcinoma and

lymphoma of untreated coeliac disease as well as potential complications such as osteoporosis and autoimmune disease (Admou et al, 2012).

Maintaining a gluten free diet is complicated by ingredients lists often using names of the derivatives of foods which contain the prolamins that can trigger gastrointestinal reactions. This includes semolina, durum, spelt, cous cous, farro, farina, malt, brewers yeast and hops in beer, ales and lagers (see Table 1 for suggested dietary changes and refer to the coeliac organisation website at https://www.coeliac.org.uk/gluten-free-diet-and-lifestyle/ for a more in-depth review of potentially harmful foods). In addition many foods contain hidden gluten such as yoghurts, salad dressings, soups, gravy, crisps and meats that are seasoned with malt vinegar, soy sauce or thickened with wheat starch. A final word of caution revolves around the confusion caused by labelling on products such as the term "wheat-free" indicating that the product may contain other sources of gluten such as rye or barley. This can in part explain the results from Galeazzi et al's study (2014) which reported that 37% of children diagnosed with coeliac disease and on a gluten free diet for over 6 months still had traces of gluten in their stools.

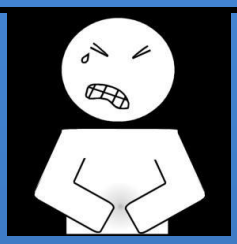
Food labels indicating the product is gluten free must meet the Food Advisory Committees standards of having less than 20 parts per million of gluten (as of 2014), which is deemed adequate for the majority of individuals with coeliac disease. If symptoms persist then a dietician should be consulted in order to discuss potential hidden glutens in the diet, cross contamination from other food sources and treatment for refractory coeliac disease.

Table 1: Common foods that contain gluten and alternative foods.

Foods that contain gluten	Alternative options.
Breads, pasta, noodles.	Gluten free bread, rice, potato, quinoa, millet or buckwheat.
Pastry, cakes and biscuits.	Fruit and vegetable crudités. Chocolate bars that do not contain biscuit pieces, sweets.
Cereal and Breakfasts	Oats, puffed rice or cornflakes that are not processed in factories that manufacture cereals containing gluten. Scrambled eggs and toast made from gluten free bread.
Pre-pared breaded / coated / battered foods.	Processed foods that state gluten free on packaging or meat, fish and seafood without added coatings. Homemade potato wedges and
Vegetarian meet free substitutes.	Vegetables, beans, legumes and nuts.

Exercise to complete: Making your own food board to encourage good food choices.

Encourage the individual to think about some of the foods that they like but are unable to eat on the gluten free diet. Place pictures of these foods in the left column then discuss any symptoms that they have after eating these foods which can be matched to the picture above the food.

	
	 
Add more pictures here	..and here

Ask the individual to choose pictures of alternative foods that can be eaten instead of the food that will make them unwell. Place these pictures in column 2.

The collage can be laminated to make a place mat or stuck on the fridge so that others can see it and offer options that the person likes and has chosen as an alternative

<u>Further monitoring and conclusions.</u>

Regular monitoring of symptomology and nutritional status is required for those with a diagnosis of coeliac disease. This is particularly pertinent if the individual is deficient in micronutrients caused by malabsorption from the gluten sensitivity and can often be easily corrected with supplementation. Lactose intolerance has been found to have an increased risk ratio to coeliac disease (Chiu et al, 2016) thus reducing milk based products if the individual has lactose intolerance will also aid absorption of essential vitamins and minerals. Monitoring should consider if the individual has unintentionally lost weight, are often tired, look pale or have other signs of anaemia (Bhat et al, 2013). In addition annual health checks are a prime opportunity for the GP to review if additional blood test and a DEXA scan of the individuals bone density are required. The GP should also consider

other long term complications and the need for specialist referrals to dieticians or specialised consultants (NICE, 2015).

Individuals who support people with Down's syndrome from primary and acute care doctors to staff and family members should be aware of and consider the additional health complications such as coeliac disease which are highly prevalent in people with Down's syndrome. In order to enhance their health through the life stages via supporting them to adequately manage their diet if found to have coeliac disease or nutritional deficiencies. Dietary modifications can not only reduce the symptomology of coeliac disease which can be painful for the person but also decrease the risk of other comorbid health complications associated with untreated enteropathy.

Implications for practice.

- *Raising awareness of the symptoms of coeliac disease in order to monitor for health concerns.*
- *Use easy to read or alternative resources for people with a learning disability to explain coeliac disease and gluten free diets. Which are free to download from easy health organization and improving health and lives or from local learning disability community teams.*
- *Regular screening for coeliac disease should be completed annually as part of the annual health review with the individuals GPs.*
- *Encourage a gluten free diet to manage coeliac disease. Offer the individual alternative options that they enjoy eating and encourage them to make good food choices.*
- *Raise awareness of hidden glutens in food which may cause adverse reactions.*
- *Review symptoms, anemia, bone density, weight loss and micronutrient deficiencies at least annually as part of health check with the registered G.P. or before this date if concerns have been raised.*

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