Appendix A

Initial Search

a. Medline (1950 - May 2008)

For MeSH terms all subheadings were included.

Number	Search term used	Number of hits
1	nutritional adequacy	493
2	nutritional deficiency	2130
3	nutritional screening	363
4	nutrition assessment (MeSH)	4849
5	nutrition surveys (MeSH)	7368
6	diet surveys (MeSH)	4217
7	malnutrition (MeSH)	2243
8	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7	19554
9	coeliac disease OR celiac disease	12494
10	celiac disease (MeSH)	11535
11	coeliac sprue OR celiac sprue	422
12	gluten-free	2053
13	gluten-free diet	1917
14	gluten enteropathy	134
15	gluten sensitive enteropathy	455
16	gluten intolerance	191
17	gluten allergy	2
18	gluten hypersensitivity	11
19	9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15	12904
	OR 16 OR 17 OR 18	
20	nutrients	20261
21	vitamins (MeSH)	13616
22	micronutrients (MeSH)	1515
23	food (MeSH)	18043
24	iron (MeSH)	59334

25	calcium (MeSH)	208428
26	folic acid (MeSH)	15660
27	B vitamins	861
28	B vitamin complex (MeSH)	3388
29	20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26	331046
	OR 27 OR 28	
30	8 AND 19 AND 29	6

b. EMBASE (1974- May 2008)

For EMTREE terms all subheadings were included.

Number	Search term used	Number of hits
1	nutritional adequacy	239
2	nutritional deficiency	5043
3	nutritional screening	132
4	nutrition assessment (EMTREE)	2991
5	nutrition surveys (EMTREE)	29894
6	diet surveys (EMTREE)	59718
7	malnutrition (EMTREE)	20599
8	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7	110803
9	coeliac disease (EMTREE)	9248
10	celiac disease (EMTREE)	9248
11	coeliac sprue OR celiac sprue	407
12	gluten free	3020
13	gluten free diet (EMTREE)	2307
14	gluten enteropathy	109
15	gluten sensitive enteropathy	1
16	gluten intolerance	153
17	gluten allergy	5
18	gluten hypersensitivity	8
19	9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15	9749

	OR 16 OR 17 OR 18	
20	nutrients	19305
21	vitamins (EMTREE)	11535
22	micronutrients (EMTREE)	10259
23	food (EMTREE)	15818
24	iron (EMTREE)	47993
25	iron absorption (EMTREE)	1718
26	calcium (EMTREE)	13229
27	calcium absorption (EMTREE)	1897
28	folic acid (EMTREE)	21210
29	B vitamins	726
30	vitamin B group (EMTREE)	1829
31	20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26	223991
	OR 27 OR 28 OR 29 OR 30	
32	8 AND 19 AND 31	90

c. The Cochrane Central Register of Controlled Trials (CENTRAL) – Issue 2, 2008

For MeSH terms all subheadings were included.

Number	Search term used	Number of hits
1	nutritional adequacy	69
2	nutritional deficiency	533
3	nutritional screening	106
4	nutrition assessment (MeSH)	368
5	nutrition surveys (MeSH)	166
6	diet surveys (MeSH)	100
7	malnutrition (MeSH)	1026
8	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7	1874
9	coeliac disease OR celiac disease	180
10	celiac disease (MeSH)	134
11	coeliac sprue OR celiac sprue	9
12	gluten free	71

13	gluten free diet	70
14	gluten enteropathy	7
15	gluten sensitive enteropathy	1
16	gluten intolerance	8
17	gluten allergy	3
18	gluten hypersensitivity	6
19	9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15	201
	OR 16 OR 17 OR 18	
20	nutrients	1646
21	vitamins (MeSH)	7855
22	micronutrients (MeSH)	10471
23	food (MeSH)	13156
24	iron (MeSH)	1241
25	calcium (MeSH)	2239
26	folic acid (MeSH)	1446
27	B vitamins	2605
28	vitamin B complex (MeSH)	3275
29	20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26	24220
	OR 27 OR 28	
30	8 AND 19 AND 29	3

d. CINAHL (1982 – May 2008)

For MeSH terms all subheadings were included.

Number	Search term used	Number of hits
1	nutritional adequacy	54
2	nutritional deficiency	72
3	nutritional screening	90
4	nutritional assessment (MH)	5742
5	nutrition surveys	16
6	diet surveys	1
7	malnutrition	2058

8	nutrition disorders (MH)	2936
9	surveys (MH)	39888
10	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	48532
	OR 9	
11	coeliac disease OR celiac disease	785
12	celiac disease (MH)	734
13	coeliac sprue OR celiac sprue	32
14	gluten-free	308
15	diet, gluten-free (MH)	226
16	gluten enteropathy	1
17	gluten sensitive enteropathy	20
18	gluten intolerance	12
19	gluten allergy	1
20	gluten hypersensitivity	0
21	11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17	849
	OR 18 OR 19 OR 20	
22	nutrients	2230
23	vitamins (MH)	2213
24	micronutrients (MH)	557
25	food (MH)	3186
26	iron (MH)	1515
27	calcium (MH)	2843
28	folic acid (MH)	2093
29	B vitamins	163
30	vitamin B complex (MH)	503
31	22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28	13481
	OR 29 OR 30	
32	10 AND 21 AND 31	5

Appendix B

Number of articles appearing in journals

Journals	Reference	Ordered for
		review
Scandinavian Journal of	Tikkakoski <i>et al.</i> (2007)	1
Gastroenterology		
Journal of Human Nutrition and	Thompson et al. (2005)	2
Dietetics	McFarlane <i>et al.</i> (1995)	
American Journal of Clinical Nutrition	Kempainnen <i>et al.</i>	1
	(1998)	
British Journal of Nutrition	Storsrud et al. (2003)	1
International Journal of Clinical	Mitchell and Robinson	1
Practice	(2002)	
Pediatria Oggi Medica e Chirugica	Lucidi <i>et al.</i> (1985)	1
Human Nutrition, Applied Nutrition	Bjorkman <i>et al.</i> (1985)	1
Total		8

Appendix C

Second search including search term 'nutritional status'

a. MEDLINE (1950 - May 2008)

For MeSH terms all subheadings were included.

Number	Search term used	Number of hits
1	nutritional adequacy	308
2	nutritional deficiency	944
3	nutritional screening	156
4	nutrition assessment (MeSH)	4866
5	nutritional status (MeSH)	14911
6	nutrition surveys (MeSH)	7299
7	diet surveys (MeSH)	4194
8	malnutrition (MeSH)	2419
9	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	30837
10	coeliac disease OR celiac disease	12969
11	celiac disease (MeSH)	11628
12	coeliac sprue OR celiac sprue	439
13	gluten-free	2167
14	gluten-free diet	2017
15	gluten enteropathy	134
16	gluten sensitive enteropathy	447
17	gluten intolerance	197
18	gluten allergy	2
19	gluten hypersensitivity	11
20	10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16	13419
	OR 17 OR 18 OR 19	
21	nutrients	21433

22	vitamins (MeSH)	13740
23	micronutrients (MeSH)	1529
24	food (MeSH)	18223
25	iron (MeSH)	59370
26	calcium (MeSH)	207972
27	folic acid (MeSH)	15852
28	B vitamins	942
29	B vitamin complex (MeSH)	3512
30	21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27	332533
	OR 28 OR 29	
31	9 AND 20 AND 30	16

b. EMBASE (1974- May 2008)

For EMTREE terms all subheadings were included.

Number	Search term used	Number of hits
1	nutritional adequacy	238
2	nutritional deficiency	5121
3	nutritional screening	136
4	nutrition assessment (EMTREE)	3251
5	nutrition status (EMTREE)	16687
6	nutrition surveys (EMTREE)	30141
7	diet surveys (EMTREE)	60257
8	malnutrition (EMTREE)	20888
9	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	123477
10	coeliac disease (EMTREE)	9413
11	celiac disease (EMTREE)	9413
12	coeliac sprue OR celiac sprue	412
13	gluten free	3085
14	gluten free diet (EMTREE)	2363
15	gluten enteropathy	112

16	gluten sensitive enteropathy	433
17	gluten intolerance	154
18	gluten allergy	5
19	gluten hypersensitivity	10
20	10 OR 11 OR 12 OR 13 OR 14 OR 15 OR	9920
	16 OR 17 OR 18 OR 19	
21	nutrients	19570
22	vitamins (EMTREE)	11608
23	micronutrients (EMTREE)	10338
24	food (EMTREE)	16098
25	iron (EMTREE)	48627
26	iron absorption (EMTREE)	1715
27	calcium (EMTREE)	114616
28	calcium absorption (EMTREE)	1905
29	folic acid (EMTREE)	21282
30	B vitamins	732
31	vitamin B group (EMTREE)	1826
32	21 OR 22 OR 23 OR 24 OR 25 OR 26 OR	226705
	27 OR 28 OR 29 OR 30 OR 31	
33	9 AND 20 AND 32	104

c. The Cochrane Central Register of Controlled Trials (CENTRAL) – Issue 2, 2008

For MeSH terms all subheadings were included.

Number	Search term used	Number of hits
1	nutritional adequacy	69
2	nutritional deficiency	542
3	nutritional screening	107
4	nutritional status (MeSH)	962
5	nutrition assessment (MeSH)	379
6	nutrition surveys (MeSH)	170
7	diet surveys (MeSH)	102

8	malnutrition (MeSH)	1040
9	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	2523
10	coeliac disease OR celiac disease	182
11	celiac disease (MeSH)	136
12	coeliac sprue OR celiac sprue	9
13	gluten free	73
14	gluten free diet	72
15	gluten enteropathy	7
16	gluten sensitive enteropathy	1
17	gluten intolerance	8
18	gluten allergy	3
19	gluten hypersensitivity	6
20	10 OR 11 OR 12 OR 13 OR 14 OR 15 OR	203
	16 OR 17 OR 18 OR 19	
21	nutrients	1648
22	vitamins (MeSH)	7978
23	micronutrients (MeSH)	10634
24	food (MeSH)	13451
25	iron (MeSH)	1256
26	calcium (MeSH)	2259
27	folic acid (MeSH)	1474
28	B vitamins	2609
29	vitamin B complex (MeSH)	3327
30	21 OR 22 OR 23 OR 24 OR 25 OR 26 OR	24599
	27 OR 28 OR 29	
31	9 AND 20 AND 30	5

d. CINAHL (1982 – May 2008)

For MeSH terms all subheadings were included.

Number	Search term used	Number of hits
1	nutritional adequacy	57

2	nutritional deficiency	74
3	nutritional screening	97
4	nutritional status	2768
5	nutritional assessment (MH)	5899
6	nutrition surveys	18
7	diet surveys	1
8	malnutrition	2155
9	nutrition disorders (MH)	3113
10	surveys (MH)	41856
11	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8	52308
	OR 9 OR 10	
12	coeliac disease OR celiac disease	835
13	celiac disease (MH)	783
14	coeliac sprue OR celiac sprue	34
15	gluten-free	334
16	diet, gluten-free (MH)	246
17	gluten enteropathy	1
18	gluten sensitive enteropathy	20
19	gluten intolerance	13
20	gluten allergy	1
21	gluten hypersensitivity	0
22	12 OR 13 OR 14 OR 15 OR 16 OR 17 OR	906
	18 OR 19 OR 20 OR 21	
23	nutrients	2230
24	vitamins (MH)	2213
25	micronutrients (MH)	557
26	food (MH)	3186
27	iron (MH)	1515
28	calcium (MH)	2843
29	folic acid (MH)	2093
30	B vitamins	163
31	vitamin B complex (MH)	503

32	23 OR 24 OR 25 OR 26 OR 27 OR 28 OR	14336
	29 OR 30 OR 31	
33	11 AND 22 AND 32	4

Appendix D

First Authors and key individuals

Dr Robert Anderson Autoimmunity and Transplantation Division, Walter and Eliza Hall, Australia Professor Carlo Catassi – Institute of Clinical Paediatrics, University of Ancona, Italy Professor Paul Ciclitira – The Rayne Institute (KCL), St. Thomas' Hospital, London Professor Pekka Collin – Medical School, University of Tampere, Finland Professor Alessio Fasano – The University of Maryland, Baltimore, US Professor Peter Green – Columbia University, New York, US Professor Claes Hallert – Linköping Universitet, Sweden Professor Anneli Ivarsson – Umeå University, Sweden Dr Knut Lundin – Institute of Immunology, University of Oslo, Norway Professor Marku Makki – Tampere University Hospital, Finland Dr Luisa Mearin – Department of Pediatrics, Leiden University Medical Center and Free University Medical Center, Amsterdam, The Netherlands Professor Chris Mulder – The VU University Medical Center, Amsterdam Dr Carina Venter – The David Hide Asthma and Allergy Research Centre, Isle of Wight

Key institutions/Networks

Allergy and Intolerance Group of the BDA [Isabel Skypala] Association of European Coeliac Societies (AOECS) [Dr Christian Scerri] British Society of Gastroenterology (BSG) [Professor Tom Smith] Chair of the Prolamin Working Group [Professor Martin Stern] Coeliac UK [Health Advisory Council and Health Advisory Associates; Professor Peter Howdle] Gastroenterology Specialist Group of the British Dietetic Association (BDA) [Dr Miranda Lomer] Primary Care Society of Gastroenterology (PCSG) [Dr Richard Stevens] Celiac Disease Foundation, Gluten Intolerance Group, Canadian Celiac Association, The Coeliac Society, Canada [Shelly Case]

Manufacturers

Community Foods General Dietary Ltd. Gluten Free Foods Ltd. Heron Quality Foods Ltd. Innovative Solutions UK Ltd. Juvela Livwell Nutrition Point Ltd. S.D. Parr and Co Ltd. Ultrapharm Ltd. Wellfoods

Appendix E

Papers included in the review

No	Author	Date	Title	Source
1	Collins <i>et al.</i>	1986	Dietary history and nutritional state in treated coeliac patients	Hand search
2	Dickey <i>et al.</i>	2008	Dickey, W. Ward, M., Whittle, C.R., Kelly, M.T., Pentieva, K., Horigan, G., Patton, S. and McNulty, H. (2008) Homocysteine and related B vitamin status in coeliac disease. Effects of gluten exclusion and histological recovery. <i>Scand J</i> <i>Gastro</i> , 43(6), p682-8.	Provided by contact as unpublished [However this study was published before the project was completed, so counted in the final group of papers as a published paper.]
3	Grehn <i>et al.</i>	2001	Dietary habits of Swedish adult coeliac patient treated by a gluten-free diet for 10 years	Hand search
4	Hallert et al.	2002	Evidence of poor vitamin status in coeliac patients on a gluten-free diet for 10 years	Provided by Contact
5	Hopman <i>et al.</i>	2006	Nutritional management of the gluten-free diet in young people with celiac disease in the Netherlands	Provided by contact
6	Kemppainen <i>et</i> al.	1995	Intakes of nutrients and nutritional status in coeliac patients.	Hand search
7	Kinsey and Bannerman	2007	A dietary survey to determine if patients with coeliac disease are meeting current healthy eating guidelines an how their diet compare to that of the British general population	Provided by contact
8	McFarlane et al.	1995	Subclinical nutritional deficiency in treated coeliac disease and nutritional content of the gluten-free diet.	Original search
9	Robins <i>et al.</i>	2008	Leeds Gluten-Free Diet Nutritional Survey: An Assessment of the Nutritional Quality and Health Implications of a Gluten-Free Diet in West Yorkshire	Provided by contact
10	Storsrud et al.	2003	Beneficial effects of oats in the gluten-free diet of adults with special reference to nutrient status, symptoms and subjective experiences.	Original search
11	Thompson et al.	2005	Gluten-free diet survey: are Americans with coeliac disease consuming recommended amounts of fibre, iron, calcium and grain foods?	Original search

Appendix F

Excluded papers

No	Author	Date	Title	Reason	Sourced
1	Alliet <i>et al.</i>	2008	Dietary habits in children with coeliac disease.	Not enough information available.	Provided by contact
2	Bardella et al.	2000	Body Composition and dietary intakes in adult celiac disease patients consuming a strict gluten-free diet.	No analysis of nutrients.	Hand search
3	Benson et al.	1964	Adult coeliac disease with emphasis on response to the gluten-free diet.	No diet History taken.	Hand search
4	Bjorkman et al.	1985	Changes in food consumption and its nutritional quality when on a gluten-free diet for dermatitis Herpetiformis.	No reference value given. Only compared against individual values before and after diagnosis.	Original search
5	Bode et al.	1991	Body composition and calcium metabolism in adult treated coeliac disease.	Not clear diet histories taken. No clear ref/ control.	Hand search
6	Dahele et al.	2001	Vitamin B12 deficiency in untreated celiac disease.	No clear diet history (also participants only on GF diet from 2 months).	Hand search
7	Dissanayake et al.	1974	Jejunal mucosal recovery in coeliac disease in relation to the degree of adherence to a gluten-free diet.	No dietary analysis. Supplements reported in diet history but unclear if included in analysis.	Hand search
8	Haapalahti et al.	2005	Nutritional status in adolescents and young adults with screen detected coeliac disease.	No clear diet history. No info re how long on GF diet.	Hand search
9	Hakala- Lahinen <i>et al.</i>	2001	Celiakipatienters konsumtion avsamt deras naringsintage och matutgifter (Consumption of foods, nutrient intake and food by patients with coeliac disease).	Diagnosis not clear.	Hand search
10	Hjelt and Krasilnikoff	1990	The impact of gluten on haematological status, dietary intakes of haemopoietic nutrients and vitamin B12 and folic acid absorption in children with coeliac disease.	Not clear that diet histories have been taken.	Hand search
11	Holdoway, A.	2008	Untitled.	Not enough information provided.	Provided by contact
12	Janatuinen et	1995	A comparison of diet with and without oats	Unrelated. Focused on diet history not on	Hand search

	al.		in adults with coeliac disease.	NA of GF diet.	
13	Kemppainen et al.	1998	Nutritional status of newly diagnosed celiac disease patients before and after the institution of a celiac disease diet association with the grade of mucosal villous atrophy.	No clear analysis of diet histories. No mention of supplementation and if included in analysis.	Original search
14	Kluge et al.	1982	Follow up of treated coeliac disease: clinical and morphological study.	Not clear that diet history taken and analysed.	Hand search
15	Lovik, A.	2008	Untitled.	Not enough information available.	Provided by contact
16	Lucidi et al.	1985	Behaviour of some nutritional indexes in 156 celiac patients.	No diet history taken.	Original search
17	Macdonald et al.	1964	Studies of coeliac sprue. IV. The response of the whole length of the small bowel to a gluten-free diet.	No diet history taken.	Hand search
18	Mariana et al.	1998	The gluten-free diet. A nutritional risk factor for adolescents with celiac disease?	Does not clarify how long people have been on GF diet.	Hand search
19	Mitchell and Robinson	2002	Monitoring dietary compliance in coeliac disease using red cell distribution width.	No information regarding diet histories.	Original search
20	Rea <i>et al.</i>	1996	Restoration of body composition in celiac children after one year of gluten-free diet.	No information re if supp excluded for analysis. No analysis of diet history.	Hand search
21	Sabry et al.	1992	Nutrient intakes of a group of adults on a gluten-free diet.	No information on how participants diagnosed.	Hand search
22	Sategna- Guidetti <i>et al.</i>	2000	The effects of 1 year gluten withdrawal on bone mass bone metabolism and nutritional status in newly diagnosed adult coeliac patients.	No diet history taken.	Hand search
23	Stern	2008	Current Therapy.	Review.	Provided by contact
24	Tikkakoski <i>et al.</i>	2007	Undiagnosed coeliac disease and nutritional deficiencies in adults screened in primary health care.	No clear diet history or analysis. No time specified for participants following gluten-free diet.	Original search

Appendix G

Collation of data extraction forms

Data Extraction Form

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details				
Data extractor (initials):	Emma	Date of extraction:	22/07/2008	
Part 2: Study details				
Study design: RCT/Cohor	t/ Case-control /case s	eries (circle as appropriat	te)	
Country of study/study location	on: Royal Victoria	a Hospital, Belfast		
Date of study: 1986				
Authors: Collins, B.J., Bell, P.M., Thompson, J.M., Fee, D.B, Willson, E.A., Love, A.H.G.				
Title: Dietary history and nutriti	ional state in treated co	peliac patients		
ource (Journal - vol/pages): J Royal Soc of Med, 79, p206-209				

Language: English

Contact address/e-mail of author: Not current. Unable to make contact. Dr PM Bell. Department of Medicine, Queens University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast, BT12 6BJ

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO INDIVIDUAL DATA
A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met
B. Moderate risk of bias	Plausible bias that raises some doubts about the results	One or more of the criteria partly met
C. High risk of bias	Plausible bias that seriously weakens confidence in the results	One or more of the criteria not met

	PARTICIPANTS	CONTROLS
How was sample obtained?	Attendees of Royal Victoria Hospital, Belfast contacted by letter	Recommended Daily Allowance (1979)
Response rate	30%	n/a
Total number of participants	18	n/a
Age (mean+/-SD) Range	44 years (18-59years range)	n/a
Sex males females	9 9	n/a
Method of diagnosis of CD	Small bowel biopsy and serology	n/a
Time since diagnosis	Not stated	n/a
Duration on gluten- free diet	17month- 15years	n/a
What intervention was used (if any)?	n/a	n/a
Assessment method (type and length of dietary assessment)	 dietetic assessment using computer analysis (energy, protein, CHO, fat, iron, calcium, vitamins B1, B2) dietitian assessed grade and extent of gluten avoidance type and length not stated 	n/a
Outcome/s measured (specify)	<i>Dietary Assessment</i> Energy, Pro, CHO, Fat, Fe, Ca, Vit B1, Vit B2, Vit C, Grade/extent gluten avoidance	n/a

	Height, Weight, AMC, AC, TS	
	Blood review, Ca, Albumin, Urea, Liver enzymes, Glu, Se, Folic acid, B12, Serum copper, Magnesium, Zinc	
	Jejunal biopsy- Crosby capsule	
Inclusion criteria	Not stated	n/a
Exclusion criteria	Not stated	n/a
Other confounding factors (please list)	 smoking, alcohol intake not discussed special diets (lactose-free, weight-loss) – vegan/vegetarian diets not highlighted 8 (44%) participants taking gluten taking gluten regularly possible concomitant conditions 	n/a
Possible cause of bias	 sample taken from groups regularly attending gastroenterology clinic in Belfast no comparison with a control group low response rate unclear if vitamins/supplements included in dietary analysis [unable to make author contact] risk of underreporting 	n/a
Primary outcomes	most (65%) consumed a diet that met or exceeded RDA's	n/a
Secondary outcomes	undiagnosed concomitant conditions, PVA, SVA, restrictive diets associated with inadequate diet	n/a
Baseline results	Only 17 completed the diet history: -11 (65%) consumed diet that met or exceeded RDA's. - of the 6 (35%) that did not: - 2 were deliberately restricting - 1 was lactose-free All those who had low RDA's had PVA (1 had inaccurate biopsy so VA unknown)	n/a
Other information (please specify)		n/a

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):EmmaDate of extraction:22/07/2008

Part 2: Study details

Study design: RCT/Cohort/**Case-control**/case series (circle as appropriate)

Country of study/study location: Belfast

Date of study: 2008

Authors: Dickey, W. Ward, M., Whittle, C.R., Kelly, M.T., Pentieva, K., Horigan, G., Patton, S., McNulty, H

Title: Homocysteine and related B vitamin status in coeliac disease. Effects of gluten exclusion and histological recovery

Source (Journal - vol/pages): Scand J Gastro, 43(6), p682-8.

Language: English

Contact address/e-mail of author: wildickey@aol.com

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

Summary (Fredse dok one)		
RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO INDIVIDUAL DATA
A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met
B. Moderate risk of	Plausible bias that raises some	One or more of the
bias	doubts about the results	criteria partly met
C. High risk of bias	Plausible bias that seriously weakens	One or more of the
	confidence in the results	criteria not met

	PARTICIPANTS	CONTROLS
How was sample obtained?	Recruited when attending initial or follow up biopsy at CD specialized clinic	Healthy participants of ongoing B vitamin studies from University of Ulster database [previous studies]
Response rate	100	200
Total number of participants	100	200
Age (mean+/-SD) Range	54.7 (12.4sd)	55.0 (11.7sd)
Sex males females	29 (29%) 71 (71%)	58 (29%) 142 (71%)
Method of diagnosis of CD	Positive serum EMA and duodenal biopsy showing VA with intraepithelial lymphocytosis	No gi symptoms and no history of gi disease
Time since diagnosis	Groups 1.Untreated n=70 0 2. Persistent VA n=24 >12 months 3. Recovered n=41 >12 months	n/a
Duration on gluten- free diet	Groups 1.Untreated n=70 0 2. Persistent VA n=24 >12 months 3. Recovered n=41 >12 months	n/a
What intervention was used (if any)?	n/a	n/a
Assessment method (type and length of dietary assessment)	4 day dietary assessment. WISP v3 used to calculate mean energy/B vits	4 day dietary assessment. WISP v3 used to calculate mean energy/B vits
Outcome/s measured (specify)	Wt, ht, BMI Energy B vitamin intake	Wt, ht, BMI Energy B vitamin intake
	Serology, homocysteine, red cell folate, b21, p5p (vit b6), riboflavin	Serology, homocysteine, red cell folate, b21, p5p, riboflavin
Inclusion criteria	Not stated	Not stated

Exclusion criteria	 hepatic disease, CVD, renal disease, haematological disorders, supps containing B vits or drugs known to interfere with the metabolism of folate or related B vitamins patients taking supplements 	 History of GI disease GI symptoms Hepatic disease, CVD, renal disease, haematological disorders, supps containing B vits or drugs known to interfere with the metabolism of folate or related B vitamins
Other confounding factors (please list)	 smoking, alcohol, PA not stated FH risk of CHD hypercholesterolaemia not stated 	
Possible cause of bias	 using controls that are willing to be in a study may cause bias individuals may be following a special or restricted diet, not stated ?weekend day including in diet history risk of underreporting 	Not been ascertained that controls have do not have undiagnosed CD
Primary outcomes	Homocysteine and folate low in those not following GF diet. B6 and riboflavin not effected. Homocsyteine and folate normal in those with no VA and on GF diet.	
Secondary outcomes	B6 and B12 levels considerably higher in in recovered patients than in controls	
Baseline results	 untreated CD had significantly raised homocysteine levels and correspondingly reduced folate. results normal in those with no VA intermediate values in those with some VA lower B12 in those with VA treated and untreated CD (not sig) B6 and riboflavin not compromised in any group dietary intakes of folate, vit B12, vit B6 no different between any groups/controls all patient groups had higher riboflavin intakes compared with controls (p<0.05 for two patient groups with VA and p<0.01 for recovered VA) 	
Other information (please specify)		

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):EmmaDate of extraction:23/07/2008

Part 2: Study details

Study design: RCT/Cohort/**Case-control**/case series (circle as appropriate)

Country of study/study location: Sweden

Date of study: 2001 [nb study performed 1996-97)

Authors: Grehn, S., Fridell, K., Lilliecreutz, M. and Hallert, C.

Title: Dietary habits of Swedish adult coeliac patient treated by a gluten-free diet for 10 years

Source (Journal - vol/pages): *Scan J* Nutri, 45, 178-182

Language: English

Contact address/e-mail of author: Claes.Hallert@lio.se

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO INDIVIDUAL DATA
A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met
B. Moderate risk of bias	Plausible bias that raises some doubts about the results	One or more of the criteria partly met

C. High risk of bias	Plausible bias that seriously weakens	One or more of the
	confidence in the results	criteria not met

	DADTICIDANTS	
	PARTICIPANTS	CONTROLS
How was sample	From 6 gastro departments in SW	Swedish NS
obtained?	Sweden 1984-88	Nordic nutritional
		requirements
Response rate	65	
Total number of	49	498 (SNS)
participants		
Age (mean+/-SD) Range	45-66years	45-64 years
Sex males	17	250
females	32	248
of CD	Jejunal biopsy	n/a
Time since	?	n/a
alagitoolo		
Duration on gluten-	8-12 years	n/a
free diet		
What intervention	n/a	n/a
was used (if any)?		
Assessment method	4 day food record including 1 holiday	- based on 7 day food record
(type and length of		including 1 holiday
dietary assessment)		[acknowledged by authors] as
		also used
Outcome/s	Compliance – histologically tested	For NS
measured		Energy, and relative
(specify)	Serology	contributions pro, fat, CHO
	Hb, alb, ca, alp, sn, ferritin, chol, trigs	same for cases and controls
	Energy and relative contributions pro	Vit F selenium low compared
	fat, CHO same for cases and controls	to cases
	Fibre (p<0.000), folate (ns in women,	
	<0.01 in men), vit B12 (<0.000 in	
	women, <0.05 in men), niacin (<0.05 in	
	women, ns for men), ca (<0.05 in	

	women, ns in men), phos (<0.001 in women, <0.05 in men), zn (<0.001 in women, ns in men)– lower in cases	
	Vit E, thiamine, vit c – higher in cases	
	Fat% higher cases CHO % lower cases	
	The following are not stated as to whether significant or not Fibre n=49(100%) cases failed to meet RDI Folate n=48 (98%) Vit C n=16 (33%) Vit D n=26 (53%) Vit B6 n= 2 (4%) Calcium n= 19 (39%) Zinc n=15 (31%)	
	41% of adults had raised homocysteine levels	
Inclusion criteria	Not stated	Not stated
Exclusion criteria	VA Concurrent dermatitis herpetiformis	Not stated
Other confounding factors (please list)	- alcohol, smoking, PA	
Possible cause of bias	 not clear if supplementation included as part of the analysis Selection process for participants unclear 1/3 of CD patients not working or on disability pension risk of underreporting limited to Swedish population where dietary habits may differ to UK 	-? Data out of date (1989)
Primary outcomes	Intakes of nutrients lower in some men and women with coeliac disease. Mean serology not lower in adults with coeliac disease	
Secondary outcomes	Vit E, selenium tended to be low in controls compared to cases	
Baseline results	Mean serology results showed no nutritional deficiencies. Patients with	

	coeliac disease following a gluten-free diet showed some lower intakes of fibre, vit B12, niacin, ca, phos, zinc although few statistically significant.	
Other information		
(please specify)		

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):EmmaDate of extraction:23/07/2008

Part 2: Study details

Study design: RCT/Cohort/**Case-control**/case series (circle as appropriate)

Country of study/study location: Sweden

Date of study: 2002 (data taken from cohort 1984-88)

Authors: Hallert, C., Grant, C., Grehn, S., Granno, C, Hulton, S., Midhagen, G., Strom, M., Svensson, H. and Vladimarsson.

Title: Evidence of poor vitamin status in coeliac patients on a gluten-free diet for 10 years.

Source (Journal - vol/pages): APT, 16, p1333-1339

Language: English

Contact address/e-mail of author: Claes.Hallert@lio.se

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO
		INDIVIDUAL DATA

A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met
B. Moderate risk of bias	Plausible bias that raises some doubts about the results	One or more of the criteria partly met
C. High risk of bias	Plausible bias that seriously weakens confidence in the results	One or more of the criteria not met

	PARTICIPANTS	CONTROLS
How was sample obtained?	From 6 gastro departments in SW Sweden 1984-88	Swedish NS Nordic nutritional requirements
Response rate	47	?
Total number of participants	30	500 (SNS)
Age (mean+/-SD) Range	45-64 years (mean 55 years	45-64 years
Sex males females	12 18	250 250
Method of diagnosis of CD	Jejunal biopsy	n/a
Time since diagnosis	?	n/a
Duration on gluten- free diet	8-12 years	n/a
What intervention was used (if any)?	n/a	n/a
Assessment method (type and length of dietary assessment)	4 day food record including 1 holiday	- based on 7 day food record including 1 holiday as Swedish NS, although NNR also used
Outcome/s measured (specify)	Compliance – histologically and EMA tested serology folate (3 low), p5p (8 low), b12 (3 low p5p and folate), Not stated if this is significant. intakes	For NS Energy, and relative contributions pro, fat, CHO same for cases and controls

	folate lower in cases (p<0.05) and lower than recs in both groups vit B6 similar in controls and cases vit B12 (p<0.001) lower in coeliac group, but higher than recs in both groups Ht. wt. smoking, meds, PA	
Inclusion criteria	Not stated	Not stated
Exclusion criteria	VA – ALTHOUGH HISTOLOGY SHOWED 5 PTS WITH BORDERLINE HISTOLOGY	Not stated
Other confounding factors (please list)	 Smoking, medications and PA assessed as possible CF 	
Possible cause of bias	 concomitant conditions include thyroid (n=4), depression (n=3), seizures (n=2) risk of underreporting, group underestimated their EAR by 25% limited to Swedish population where dietary habits may differ to UK ? Technique assessing folate, B6 and B12 via homocysteine consistency between plasma levels and dietary intakes poor r<0.18 author bias inconsistency regarding folate supplementation with individuals. Poor vitamin status in 56% of coeliac pts including 6 on folate suppthese individuals were not include? 	
Primary outcomes	Authors suggest that the results show people adhering to GF diet prone to develop nutri def. Notably folate def. However controls also low in folate.	
Secondary outcomes	No levels were lower than the recommended! Authors gloss over this.	
Baseline results	No nutritional deficiencies other than folate, which controls also have	
Other information (please specify)		

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):EmmaDate of extraction:23/07/2008

Part 2: Study details

Study design: RCT/Cohort/**Case-control**/case series (circle as appropriate)

Country of study/study location: Netherlands

Date of study: 2006

Authors: Hopman, E.G.D, Le Cessie, S., von Blomberg, M.E., and M.L. Mearin

Title: Nutritional management of the gluten-free diet in young people with celiac disease in the Netherlands.

Source (Journal - vol/pages): J of Ped Gastro Nutr,43, p102-108.

Language: English

Contact address/e-mail of author: <u>G.D.Hopman@lumc.nl;</u> M.L.Mearin_Manrique@lumc.nl; <u>cessie@lumc.nl</u> [Professor Saskia le Cessie]

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO INDIVIDUAL DATA
A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met
B. Moderate risk of	Plausible bias that raises some	One or more of the
bias	doubts about the results	criteria partly met
C. High risk of bias	Plausible bias that seriously weakens	One or more of the
	confidence in the results	criteria not met

	PARTICIPANTS	CONTROLS
How was sample obtained?	395 members of Dutch coeliac society invited to take part	DRDA ARDA General Dutch population
Response rate	219	
Total number of participants	111	
Age (mean+/-SD) Range	Group split into two: Group 1: 12-16 years (n=80) Group 2 17-25 years (n=52)	
Sex males females	Group 1 Group 2 43% (34) 26% (14) 57% (46) 74% (38)	
Method of diagnosis of CD	Small intestinal biopsy	
Time since diagnosis	?	
Duration on gluten- free diet	Group 1: 8.5years median (+/-3.9) Group 2: 11.2years median (+-8.2)	
What intervention was used (if any)?	n/a	
Assessment method (type and length of dietary assessment)	3 day food diary (2 weekdays, 1 weekend) 34 item questionnaire Becel 5 computerised analysis tool	
Outcome/s measured (specify)	Ht, wt Energy, Macronutrient intake	

	SFA, vitamins B2, B2, B6, iron, ca, fibre, IgA, TTG, EMA	
Inclusion criteria	Not stated	
Exclusion criteria	Not stated	
Other confounding factors (please list)	Medications	
Possible cause of bias	 -not all participants completely adhered to gluten-free diet, although most willing participants appeared to be more compliant -participant split up by age, total sample not included -use of just adolescents makes it difficult to compare with the rest of the population -sample from Dutch Coeliac Society may provide conscientious individual with higher level skills (acknowledged by authors) -ht and wt self-reported and lower than clinical measurements taken later -parental intervention with food diaries -authors acknowledge responders younger than non-responders and had higher BMI -8% had associated disease -22% use vitamin or mineral supplement ? if included in analysis age groups do not add up to total n 	Categories of ARDA not similar to those of DRDA
Primary outcomes	Iron (p<0.05), fibre (<0.05)) lower than ARDA, DRDA SFA (0.05) higher than DRDA Ca – in pts <19 lower (P<0.05) than ARDA B vits reached or exceeded the RDA Self reported compliance as for serology antibodies (17%v15% for each group)	
Secondary outcomes	N/a	

Baseline results	Nutritional intake of young people similar to the GDP in Netherlands (higher SFA, lower fibre, iron) and good compliance with GF diet	
Other information		
(please specify)		

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):	Emma	Date of extraction:	26/07/2008
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Part 2: Study details

Study design: RCT/Cohort/**Case-control**/case series (circle as appropriate)

Country of study/study location: Kuopio, Finland

Date of study: 1995 (patients recruited 1988-1990)

Authors: Kemppainen, T., Uusitupa, M., Janatuinen, E., Jarvinen, R., Julkunen, R. And Pikkarainen, P.

Title: .Intakes of nutrients and nutritional status in coeliac patients.

Source (Journal - vol/pages): Scand J of Gastroetnerol, 30(6), 575-579.

Language: English

Contact address/e-mail of author: <u>Tarja.Kemppainen@uku.fi</u>; matti.uusitupa@uku.fi

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

Summary (Please tick one)

RISK OF BIAS	INTERPRETATION	
		INDIVIDUAL DATA
A. Low risk of bias	Plausible bias unlikely to alter the	All of the criteria met
	interpretation of the results	
B. Moderate risk of	Plausible bias that raises some	One or more of the
bias	doubts about the results	criteria partly met
C. High risk of bias	Plausible bias that seriously weakens	One or more of the
	confidence in the results	criteria not met

	PARTICIPANTS	CONTROLS
How was sample obtained?	Recruited from an intervention study on coeliac patients 1988-1991 (Janatuinen <i>et al.</i> , 1993) diagnosed at Kuopio hospital in last 10 years	Recruited from two population based surveys in Kuopio area.
	1988-1990 for newly diagnosed	Control group of men from pilot study of OP and atherosclerosis prevention survey of 1990. Women from case-control on breast ca and nutria factors
Response rate	154	Not stated
-		
Total number of	92	77
participants	52 in remission [3 of these excluded	
	from analysis, 1 due to pregnancy, 2	
	due to grossily underestimated records],	
	analysis due to incomplete food record	
Age (mean+/-SD)	Remission Untreated	
Range	Men $16\pm 12(21-64)$ $17\pm 12(21-65)$	M_{0} 52+0 (51-53)
	Women 45+-11 (19-72) 44+-11 (19-72)	Women 53+-13 (26-70)
	Remission Untreated	
Sex males	33% (17) 27% (11)	52% (40)
females	67% (35) 73% (29)	48% (37)
Method of diagnosis of CD	Biopsy	n/a
Time since diagnosis	Not stated	n/a

Duration on gluten- free diet	>12 months	n/a
What intervention was used (if any)?	n/a	n/a
Assessment method (type and length of dietary assessment)	4 day food diary (Thu – Sun) Nutricia computer programme analysis	
Outcome/s measured (specify)	Anthropometric, bw, ht, BMI, MAC, MAMC, Biochemical – Hb, pro, alb, iron, ferr, vit B12, ca, mg, folic acid	
Inclusion criteria	 Remission group In remission Diagnosed with CD Aged over 18 years Normal or almost normal villous architecture Gluten-free diet for at least 12 Months Untreated group VA or PVA no reason for secondary CA 	Not stated
Exclusion criteria	Remission refusal to participate CD not in remission Other serious disease Diagnosis not well defined Untreated group refusal to participate other serious disease 	Not stated
Other confounding factors (please list)	- PA, medications, smoking	
Possible cause of bias	 respondents who choose to be in a study likely to be more motivated and compliant ? why American RDA's have been used 	
Primary outcomes	Fibre intake –pts in remission lower than other coeliac group Fat intake- pts in remission higher than other coeliac group	

	(other than use of cereals higher in untreated group p<0.001 no other significant differences)	
	In untreated – Energy, CHO In remission – Energy , CHO, fat - higher than in controls	
	In remission – Fibre - lower than in controls	
	Mean daily intakes of nutrients in both coeliac groups and controls met RDA. (although individuals had low levels of B vits, fe, ca, vit D, E, A below 75% of RDA in all groups)	
	Higher levels of untreated patients had serum nutria levels below ref values. This was lower for those in remission. Low in untreated v remission:	
	Ferritin 30% v 8% (p<0.01) Iron 38% v17% HB 30% v7% B12 8% v3% (p<0.01) Folate 35% v 4% (p<0.001)	
Secondary	None stated	
outcomes		
Baseline results	Nutritional status of patients with coeliac disease in remission is normal	
Other information		
(please specify)		

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details Data extractor (initials): Emma Date of extraction: 31/07/2008 Part 2: Study details Study design: RCT/Cohort/**Case-control**/case series (circle as appropriate) Country of study/study location: Manchester, England Date of study: 2007 Kinsey, L., Burden, S.T. and Bannerman, E. Authors: **Title:** A dietary survey to determine if patients with coeliac disease are meeting current healthy eating guidelines an how their diet compare to that of the British general population. Source (Journal - vol/pages): Euro J Clin Nutri, 1-10. Language: English Contact address/e-mail of author: laurakinsey@aintree.nhs.uk; e.bannerman@qmu.ac.uk

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO INDIVIDUAL DATA
A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met
B. Moderate risk of	Plausible bias that raises some	One or more of the
bias	doubts about the results	criteria partly met
C. High risk of bias	Plausible bias that seriously weakens confidence in the results	One or more of the criteria not met

Summary (Please tick one)

	PARTICIPANTS	CONTROLS
How was sample obtained?	All patients diagnosed attending adult coeliac clinic at Manchester Royal Infirmary	NDNS and DRV's
Response rate	49% (106 invited to participated)	
Total number of participants	48	4710
Age (mean+/-SD) Range	58.6years (+-17 years)	4-18 years (1711) 19-64 years (1724) >65 years (1275)
Sex males females	12 (12%)makes 47 does not add up 35 (75%)	
Method of diagnosis of CD	Not stated	
Time since diagnosis	8.9 years (+-11.2years)??	
Duration on gluten- free diet	Not stated	
What intervention was used (if any)?	n/a	
Assessment method (type and length of dietary assessment)	3 day unweighed food diary, 2 weekdays, 1 weekend Questionnaire - 4 individuals took supplements, but these	7 day weighed diaries 4 day weighed (>65years)

	were not included in the food analysis	
Outcome/s measured (specify) Inclusion criteria	Energy Fat, protein, CHO, NSP, ca, folate, vit B12, vit D Not stated	
Exclusion criteria	Not stated	
Other confounding factors (please list)	PA, smoking, medicationsOther serious condition	
Possible cause of bias	 potential underestimation difference in food diaries between cases and controls non respondents, mean 10 years younger and on diet for longer (2.8years mean) 	
Primary outcomes	Energy – (p<0.05) 83% (n=40)sig below the EAR Pro – in excess of RNI (96% exceeded DRV) CHO – 49% of E (p<0.05) sig more above DRV (n=34), below DRV (n=14) FAT – 31% of E(p<0.05) sig lower than DRV NSP (p<0.05) sig proportion lower than recommended (98% n=47) Mean intake of Vit B12 was above RNI Mean Iron intake higher than RNI in 16- 64yrs (lower in >64years) Ca – 95% (n=45) (p<0.05) Intake below Energy, CHO as energy was comparable with the intakes of the general population People with CD obtained more energy from fat, pro (P<0.05). No sig difference for iron, folate (general pop also higher) Ca higher in coeliac group than general population (not stat sig). No have below LRNI greater than general pop In aged 16-64yrs, vit D lower in coeliac group than general population (P<0.05) in males NSP below rec, but same as general pop	
Secondary		

outcomes		
Baseline results	 People with CD produce less than rec amounts for energy, NSP, vit D, and Ca and consume excess Pro. Energy, NSP, as for general pop. General pop also have higher pro Sig differences in pro (19-64yrs) Fat (females 19-64years, males >65yrs) vit D (males 19-64yrs, >65yrs vit B12) folate (females 19-64yrs) food sources as E 	
Other information	2 clarity regarding statistical	
(please specify)	significance	

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):	Emma	Date of extraction:	26/07/2008
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Part 2: Study details

Study design: RCT/Cohort/**Case-control**/case series (circle as appropriate)

Country of study/study location: Bath, UK

Date of study: 1995 (patients recruited 1988-1990)

Authors: McFarlane, X.A., Marsham, J., Reeves, D., Bhalla, A.K., Robertson, A.F.

Title: Subclinical nutritional deficiency in treated coeliac disease and nutritional content of the gluten-free diet

Source (Journal - vol/pages): J Hum Nutri Diet, 8, p231-237

Language: English

Contact address/e-mail of author: <u>Ashok.bhalla@rnhrd.nhs.uk</u>; duncan.robertson@ruhbath.swest.nhs.uk

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO INDIVIDUAL DATA	
A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met	
B. Moderate risk of bias	Plausible bias that raises some doubts about the results	One or more of the criteria partly met	
C. High risk of bias	Plausible bias that seriously weakens confidence in the results	One or more of the criteria not met	

	PARTICIPANTS	CONTROLS
How was sample obtained?	Not stated	Not stated
Response rate	Not stated	Not stated
Total number of participants	54	54
Age (mean+/-SD) Range	50.1years (range 27-69 years)	Age matched
Sex males females	10 44	10 44
Method of diagnosis of CD	Biopsy	n/a
Time since diagnosis	Not stated	n/a
Duration on gluten- free diet	Median time on the gluten-free diet 5.5years (0.5-40 years)	n/a
What intervention was used (if any)?	n/a	n/a
Assessment method (type and length of dietary assessment)	10 day weighed diet history Microdiet assessed	
Outcome/s measured (specify)	Anthropometric measurements Weight Height BMI - Measured at 0 and 12 months TSF MAC AMC Blood investigations - Hb - Mean corpuscular volume - Red cell folate - 25 hydroxyvitaminD Compliance assessed through self	Anthropometric measurements Weight Height BMI - Measured at 0 and 12 months TSF MAC AMC Blood investigations - Hb - Mean corpuscular volume - Red cell folate

	assessment	- 25 hydroxyvitaminD
		Compliance assessed
	Not stated	through self assessment
Inclusion criteria	Not stated	Not stated
Exclusion criteria	Not stated	Not stated
Other confounding	- PA	
factors (please list)	 Medications, alcohol, smoking Weight loss/specialized diets supplements 	
Possible cause of bias	- However more participants were below 5 th percentile for wt, BMI than general	
	pop.	
	- not assessed as statistically significant	
	- EMA/TTgA not used to assess	
	adherence to diet	
	- Not all followed a strict gluten free diet -42 (78%)	
	Intake less than 1/12 – 8 (15%)	
	Intake at least 1/12 – 4(7%)	
Primary outcomes	Low MAC and MAC and normal TSF	
	hb, MCV, red cell folate and 25 hvdroxyvitamin D all in normal range	
	For those on the gluten-free diet for >12	
	months significant increase in weight for males $(n>0.02)$ but not females	
	40 patients reported sig reduced bread	
	since on GF diet.4 (7%) used no bread.	
	Low intakes of:	
	Ca 6(11%)	
	Fe 18 (33%)	
	Vit B6 6 (11)	
	$\begin{array}{c} V \parallel D \mid Z \\ \hline \\ C \mid C \mid C \\ C \mid C \mid C \\ C \mid C \mid$	
	Other deficiencies include Energy Ma	
	Zn, Copper, retinol, vit D, vit C	
	Not stated if significant	
	No correlation between compliance with	
	the GFD and any of the nutritional or	

	anthropometric parameters measured	
Secondary outcomes	n/a	
Baseline results	A third (33%) of patients reportedly had low intakes of iron and folic acid (35%). Not all participants met RNI's however, unclear if this is significant. Blood results were normal	
Other information		
(please specily)		

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):EmmaDate of extraction:31/07/2008

Part 2: Study details

Study design: RCT/**Cohort/**Case-control/case series (circle as appropriate)

Country of study/study location: Gothenburg, Sweden

Date of study: 2003 (recruited participants 1996-7)

Authors: Storsrud, S., Hulthen, L.R. and Lenner, R.A.

Title: Beneficial effects of oats in the gluten-free diet of adults with special reference to nutrient status, symptoms and subjective experiences.

Source (Journal - vol/pages): Brit J Nutr, 90, 101-107

Language: English

Contact address/e-mail of author: <u>stine.storsrud@nutrition.gu.se</u>

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO INDIVIDUAL DATA
A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met
B. Moderate risk of bias	Plausible bias that raises some doubts about the results	One or more of the criteria partly met
C. High risk of bias	Plausible bias that seriously weakens confidence in the results	One or more of the criteria not met

	PARTICIPANTS	CONTROLS
How was sample obtained?	GI clinic at Sahlfrenska Uni Hospital in Gothenburg, Sweden	Nordic Nutritional recommendations NNR
Response rate	20	n/a
Total number of participants	 18 (15 after 6 months) 1 women withdrew after one month 1 man after 6 mths due to abdo symptoms 1 man withdrew after 6 mths 1 women withdrew after 6 mths for non medical reasons 1 women withdrew due to lack of co- operation on dietary survey 	n/a
Age (mean+/-SD) Range	41 years at baseline (22-71years)	n/a
Sex males females	6 after 6 months 7 prior to 6 months 9 11	n/a
Method of diagnosis of CD	Duodenal biopsy	n/a
Time since diagnosis	2-25 years	n/a
Duration on gluten- free diet	2-25 years	n/a
What intervention was used (if any)?	Oats included in diet (100g/d).	n/a
Assessment method (type and length of dietary assessment)	 4 day consecutive food diary, 1 weekend day 24 hour recall -symptoms assessed by dietitian and questionnaire monthly 	n/a
Outcome/s measured (specify)	 nutritional supplements assessed but not included in final analysis Diet hx Symptoms Serology 	n/a

		· · · · · · · · · · · · · · · · · · ·
	EMA, antigliadin – negative, so good adherence except in 1 pt, this was –ive at 24 months	
	Hb, ferritin, vit B12, Zn, folate, alb, alk phos	
	BMI, wt, ht	
Inclusion criteria	-adults over 18 years -established diagnosis of coeliac disease - normal or almost normal duodenal mucosa after GF diet initiated -on GF diet for at least 12 months	n/a
Exclusion criteria	 not eating strict GF diet other serious medical conditions 	n/a
Other confounding factors (please list)	- PA, smoking, medications	n/a
Possible cause of bias	 participants followed up for such an extended period of time are likely to follow a strict gf well balanced diet small sample size oats looked at in diet, which may effect what we are looking at in terms of nutritional adequacy large amounts of oats are a little unrealistic 	n/a
Primary outcomes	Mean intake of Fe, Fibre, phytate (increased on diet with oats (P<0.001) and thiamine and zinc (p,0.02) Trend towards lower fat, higher CHO when oats included. Sucrose same.	n/a
Secondary outcomes	Fe absorption decreased when oats in diet. Bioavailability of iron reduced as phytate increased (P,0.001)	n/a
Baseline results	Inclusion of oats increased intake of Fe, fibre, phytate, thiamine and zinc. However, already meeting reference values and had nutritionally well balanced and complete diet	n/a
Other information		
(please specify)		

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):EmmaDate of extraction:31/07/2008

Part 2: Study details

Study design: RCT/Cohort/**Case-control**/case series (circle as appropriate)

Country of study/study location: United States of America

Date of study: 2005 (recruited 2002)

Authors: Thompson, T., Dennis, M., Higgins, L.A., Lee, A.R., Sharrett, M.K.

Title: Gluten-free diet survey: are Americans with coeliac disease consuming recommended amounts of fibre, iron, calcium and grain foods?

Source (Journal - vol/pages): J Hum Nutr Diet, 18, p 163-169

Language: English

Contact address/e-mail of author: tricia_s_thompson@hotmail.com

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO INDIVIDUAL DATA
A. Low risk of bias	Plausible bias unlikely to alter the interpretation of the results	All of the criteria met
B. Moderate risk of bias	Plausible bias that raises some doubts about the results	One or more of the criteria partly met
C. High risk of bias	Plausible bias that seriously weakens confidence in the results	One or more of the criteria not met

	PARTICIPANTS	CONTROLS
How was sample obtained?	Recruited 2002 Coeliac disease support newsletters, national and regional in US	Controls: AMDR (Instittute of medicine 2002), ADA (2002), DRI (Food and Nutri Board, 2001), US dept agriculture, dept of Health and human services – pyramid NHANES also used in discussion to compare Fe
Response rate	57	
Total number of participants	47	
Age (mean+/-SD) Range	21-73 (mean 51years)	
Sex males females	8 (17%) 39 (83%)	
Method of diagnosis of CD	Small intestinal biopsy	
Time since diagnosis	0.33-23 years	
Duration on gluten- free diet	0.33-23 years	
What intervention was used (if any)?	n/a	
Assessment method (type and length of dietary assessment)	3 day unweighed estimated food diary -No holiday included although most people included one weekend day -supplement usage was assessed but not included in final analysis. - adherence was assessed by participants	
Outcome/s measured (specify)	Wt, Ht, BMI Kcal CHO Fibre Iron Ca	

	Grain food group	
Inclusion criteria	 >20years not pregnant or breastfeeding resident of the US CD diagnosed using intestinal biopsy Strict adherence to a gluten-free diet 	
Exclusion criteria	- not included if food diary unusable	
Other confounding factors (please list)	 PA, smoking, alcohol Medications Other disease/conditions 	
Possible cause of bias	 height and weight was self-reported Potential underestimation gluten-free diet is assessed by participant no TGA/EMA used to assess compliance to GF diet Use of ADA and DRI increases opportunity for 'results' B vitamins assessed – reason given that most manufacturers do not analyse their specialized GF products. No attempt to make judgements based on gluten-containing foods 1 participant had been on GF for only 4 months large focus on the results for females and unclear why this is acknowledge potential bias from self reported food diary, small sample size, diets may differ between regions in US CHO – 89% within normal range [45- 65% total kcal] 	
	recommended intake ADA Iron- 53% met or exceeded recommended DRI Ca-36% met or exceeded DRI Grain food group – 28% consumed at least minimum daily servings of grain food (6) recommended by food guide pyramid.	
Secondary outcomes		

Baseline results	54% of females had low intakes of fibre (12% males)	
	56% females had low intakes of iron (0% males)	
	69% females had low intakes of calcium (37% males)	
	79% females did not meet servings of grain foods advised (37% males)	
Other information	Data was not assessed for statistical	
(please specify)	significance	

Systematic review on the nutritional adequacy of a typical gluten-free diet with particular reference to iron, calcium, folate and B vitamins

Part 1: Extraction details

Data extractor (initials):EmmaDate of extraction:8/8/08

Part 2: Study details

Study design: RCT/Cohort/Case-control/case series (circle as appropriate)

Country of study/study location: Leeds, United Kingdom

Date of study: 2008

Authors: Robins, G.G., Wild, D. and Howdle, P.D.

Title: Leeds Gluten-Free Diet Nutritional Survey: An Assessment of the Nutritional Quality and Health Implications of a Gluten-Free Diet in West Yorkshire

Source (Journal - vol/pages): unpublished

Language: English

Contact address/e-mail of author: <u>gerryrobins@hotmail.com;</u> gerry.robins@york.nhs.uk

Part 3: Quality assessment

To be independently assessed by at least two reviewers using checklists recommended by the Scottish Intercollegiate Guidelines Network. There are different checklists for appraising different studies.

RISK OF BIAS	INTERPRETATION	RELATIONSHIP TO		
		INDIVIDUAL DATA		
A. Low risk of bias	Plausible bias unlikely to alter the	All of the criteria met		
	interpretation of the results			
B. Moderate risk of	Plausible bias that raises some	One or more of the		
bias	doubts about the results	criteria partly met		
C. High risk of bias	Plausible bias that seriously weakens	One or more of the		
	confidence in the results	criteria not met		

	PARTICIPANTS	CONTROLS
How was sample obtained?	All patients attending weekly specialist gastro clinic in Leeds asked to attend	NDNS 19-64 years
Response rate	113	
Total number of participants	70 (62%)	
Age (mean+/-SD) Range	54.3years (range 21-79 years)	
Sex males females	19 (27%) 51 (73%)	
Method of diagnosis of CD	Duodenal biopsy	
Time since diagnosis	?	
Duration on gluten-free diet	>6 months	
What intervention was used (if any)?	n/a	
Assessment method (type and length of dietary assessment)	5 day validated food diary Microdiet	
Outcome/s measured (specify)		
Inclusion criteria	 histologically confirmed CD GFD at least 6 months over 18 years 	
Exclusion criteria	 A modified diet for any other reason (e.g. diabetes) 'Obvious' non compliance to GFD 	
Other confounding factors (please list)	-PA -medications -other medical conditions - smoking, alcohol	
Possible cause of bias	 self-reported any assessment via serology to assess compliance to GF diet 	

Primary outcomes	Women 33% Energy obtained from fats, 48% from CHO (inc 14% from NMES), 16% from protein Males 35% fats, 46% from CHO (15% NMES), and 14% protein (not sig) Women 1870kcal Men 2505kcal P<0.001 Women 240g per day NMES accounts for 20g of this (1 g fibre) p<0.0001 30% extra kcal Males 310g	compared to female 34% from fats, 49% from CHO (12% from NMES), 17% from protein women 1618kcal men 2259kcal 202g per day		
	NMES intake was 16.9g p=0.01 higher 26% extra kcal Fibre (1.1g slightly lower)	males 266g		
	Intakes compared to RNI (no stats presented) % men meeting RNI: 95% folate, 68% 700mg Ca, 11% 1500mg Ca, 71% iron % women meeting RNI: 78% folate, 67% 700 mg Ca, 2% 1500mg Ca, those aged 18-54 11% met iron RNI, and for those 55-74, 76% met 8.7mg target			
Secondary outcomes				
Baseline results	Female CD pts on a strict GFD have significantly higher energy intake % of this accounted for by simple sugars. Males also have sig more NMES			
Other information (please specify)				

Appendix H

Data Extraction Summary

Author	Date	Risk of	Sample	Age range	Duration of GF	Assessment		Assessment		nent	Baseline results
		bias	size	(yrs)	diet	D	S	В			
Collins <i>et al.</i>	1986	High	18	18-59 Mean 44	17 mth to 15 yrs	Y ? type/ length	Y	Y	11 (65%) had diet that met or exceeded RDA's. Of 6 (6 not, 2 were restricting, 1 was lactose free. All those with had PVA (1 biopsy inaccurate so VA unknown).		
Dickey <i>et al.</i>	2008	Moderate	100	54.7	>12mths	Y 4 d	Y	Y	Dietary intake folate, vitB12, vitB6 not statistically differe groups and control. Intake of riboflavin higher in pt group Untreated CD had high HC levels and low folate. Norma VA.		
Grehn <i>et al.</i>	2001	Moderate	49	45-66	8-12 years	Y 4 d	Y	Y	Serology markers no difference in those with CD cf cont Compared to recommended requirements, men had sign lower intake folate,		
Hallert <i>et al.</i>	2002	High	30	45-64 Mean 55	8-12 years	Y 4 d	Y	Y	All participants low dietary folate compared to controls a recommended requirements. Poor correlation betwee intakes and plasma levels		
Hopman <i>et</i> <i>al.</i>	2006	Moderate	111	12-25	Median G1 8.5yrs G2 11.2yrs	Y 3 d	Y	N	Nutritional intake of young people similar to GDP in Netl and good compliance with GF diet. All had higher SFA, iron.		
Kemppaine n <i>et al.</i>	1995	Moderate	92	19-65	>12 months	Y 4 d	Ν	N	Nutritional status, as assessed by blood nutrient levels with CD in remission were within normal ranges.		
Kinsey et al.	2007	Moderate	48	Mean 58.6 (+-17 yrs)	UNCLEAR	Y 3 d	N	N	People with CD produce less than rec amounts for E, N: and Ca and consume excess protein. E, NSP and high for general pop.		
McFarlane <i>et al.</i>	1995	High	54	27-69 Mean 50.1	Median 5.5yrs (0.5-40yrs)	Y 10 d W'd	Y	N	Reported intake 33% low iron, 35% low folic acid. Not a participants met RNI's, unclear if significant. All serolog measurements normal		
Robins <i>et al.</i>	2008	Moderate	70	Mean54.3 21-79	>6 months	Y 5 d	Y	Ν	Females with CD have sig higher energy intake. % of the accounted by NMES. Males also have higher NMES.		
Storsrud et al.	2003	Moderate	18	Mean 41 22-71	2-25 years	Y 4d/ 24hr	Y	N	Inclusion of oats increased intake of iron, fibre, phytate, zinc.		
Thompson et al.	2005	High	47	Mean 47 21-73	4 months-23 years	Y 3 d	Ν	N	Individuals low in grain foods (poss B vits) and calcium. also low in fibre and iron. No statistical analysis		

S – Serological assessment **B** – Duodenal biopsy

KeyD – Dietary assessmentRDA: Recommended Daily AmountHC HomocysteineGDP: General Dutch PopulationNMES: Non Milk Extrinsic SugarSFA: Saturated Fat