Adult studies

Bibliographic reference	Ludvigsson, J. F., Nordenskjold, A., Murray, J. A., and Olen, O. A large nationwide population-based case-control study of the association between intussusception and later celiac disease. BMC Gastroenterology 13, 89. 2013.
Study type	Case-control (where CD has been compared against non-CD in a group of patients with intussusception)
quality	**NICE case-control quality checklist** 1. The study addresses an appropriate and clearly focused question? Yes, question clear 2. Cases and controls from comparable populations? Same population of Swedish male conscripts 3. Same exclusion criteria used for both cases and controls? Yes same exclusion criteria applied 4. What was participation rate for each group? Cases: controls: N/A; all blood tested, participation not required from either group 5. Participants and non-participants are compared to establish their similarities or differences? Yes; baseline characteristics the same between groups. 6. Cases are clearly defined and differentiated from controls: cases are defined in terms of seropositivity 7. It is clearly established that controls are not cases? Clear in the fact that cases are seronegative, but without biopy f all 144522 controls cannot be 100% certain that none have CD. For this study purposes, controls are clearly established as non-cases. 8. Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment? Yes, no person was to have had previous suspicion of CD or previous duodenal biopsy 9. Exposure status is measured in a standard, valid, and reliable way? Yes; serological testing for CD was standard 10. Main potential confounders are identified and taken into account in the design and analysis? Only single predictive factor considered other factors nottaken into consideration. As population all same age and gender from same country not likely to have highly differing baseline characteristics. 11. Have confidence intervals been provided? Yes
Aim	Examine the association between coeliac disease and previous intrassuception

Patient characteristics	**Study Population:** Patients with intrassuception, identified via a patient register with reference to international classification of disease codes.
	Control Population: Each patient was matched with up to 5 controls for age, sex, calendar period and country of residence. Controls were identified via a government total population register. Controls must have had no previous duodenal/jejunal biopsy.
	Number of patients in study population: 29096
	Number of patients in control population: 144522
	Number of patients excluded: Not specified
	Median age: Study group: 30 (range 0-90) Control: Not specified, but age matched.
	Males/females: Study group: 18005m/11091f Control group: 54978m/89544f
	Country: Sweden
	Other comments:
Source of funding	Government and charity
Sign/Symptom	Intrassusception
Reference standard	Small intestinal biopsy with villous atrophy (Marsh stage 3)
Results	
Comments	Care has been taken in this study to match case and control subjects on some baseline confounding factors. However, only a single predictive factor was considered, which means there is a high risk of confounding. It is unclear whether the assumptions for logistic regression were met, reducing confidence in the statistical analysis.

Results:

	With Coeliac disease (n=29096)	Control (n=144522)
Previous intrassuception	34 (0.12%)	143 (0.10%)

Conditional Logistic regression:

Unadjusted OR for coeliac disease given previous intrasucception=1.17 (95%CI =0.84-2.05)

Further subgroup analysis was reported for:

Children diagnosed before the age of 2, Intrassuception requiring surgery or radiological intervention, Intrassuception requiring 2 or more healthcare contacts, males and females separately, data divided by age group, data divided by calendar period. No statistically significant effect was found for the predictive effect of intrasucception in any of these subgroups.

Bibliographic reference	Mollazadegan, K. and Ludvigsson, J. F. Coeliac disease does not affect visual acuity: a study of young men in the Swedish national conscripts register. 20100126. Scandinavian Journal of Gastroenterology 44(11), 1304-1309. 2009.
Study type	Case-control (people with and without coeliac disease were compared)
quality	**NICE case-control quality checklist** 1. The study addresses an appropriate and clearly focused question? Yes, question clear 2. Cases and controls from comparable populations? Same population of Swedish male conscripts 3. Same exclusion criteria used for both cases and controls? Yes same exclusion criteria applied 4. What was participation rate for each group? Cases: controls: N/A; all blood tested, participation not required from either group 5. Participants and non-participants are compared to establish their similarities or differences? Yes; baseline characteristics the same between groups. 6. Cases are clearly defined and differentiated from controls: cases are defined in terms of seropositivity 7. It is clearly established that controls are not cases? Clear in the fact that cases are seronegative, but without biopsy of all controls cannot be 100% certain that none have CD. For this study purposes, controls are clearly established as non-cases. 8. Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment? Yes, no person was to have had previous suspicion of CD or previous duodenal biopsy 9. Exposure status is measured in a standard, valid, and reliable way? Yes; serological testing for CD was standard 10. Main potential confounders are identified and taken into account in the design and analysis? Only single predictive factor considered other factors not taken into consideration. As population all same age and gender from same country not likely to have highly differing baseline characteristics. 11. Have confidence intervals been provided? Yes
Aim	Examine the association between visual acuity and subsequent diagnosis of coeliac disease (also examined the association between visual acuity and coeliac disease that had already been diagnosed, but this element does not meet the inclusion criteria for this review).
Patient characteristics	**Study Population:** Men identified through the Swedish national inpatients register as having coeliac disease which led to an inpatient stay before or after conscription. In order to be eligible, visual acuity data had to be also available from the national conscripts register before 2000. Before 2000 most Swedish men were conscripted (80%-98% between 1996 and 2000). **Control Population:** Each patient was matched with up to 5 controls for age, sex, calendar period and country of residence.

	Controls were identified via a government total population register. **Number of patients in study population:** 69 with coeliac disease undiagnosed at the time of visual acuity testing (additional 996 with coeliac disease diagnosed before conscription – data not reported in this review) **Number of patients in control population:** 6850 **Number of patients excluded:** study participants: 210 control participants: 543 (either were born outside of Sweden, coeliac diagnosis status or visual acuity data was not available). **Mean age:** Study group: 18.9 (sd 0.5) Control group: 18.7 (sd 0.6) **Males/females:** All male **Country:** Sweden **Other comments:** Only data for participants who were diagnosed with coeliac disease after the visual acuity data was gather are eligible for this review are reported below.
Source of funding	Government and charity
Sign/Symptom	Visual acuity
Reference standard	Inpatient stay related to coeliac disease as defined by international classification of disease codes (ICD-7: 286.00; ICD-8:269.00, 269.98, ICD-9: 579A; ICD-10: K90.0)
Results	<table><tr><td></td><td>Coeliac disease (n=69)</td><td>Control (n=6850)</td></tr><tr><td>Impaired visual acuity (snellen fraction < 9)</td><td>25 (36.2%)</td><td>2418 (35.3%)</td></tr></table> Adjusted logistic regression (adjusted for socioeconomic index, calander period, and presence/absence of diabetes mellitus): OR=1.04 (95% CI 0.9-1.19) (No significant relation between visual acuity and coeliac disease)
Comments	Case and control participants were matched for baseline characteristics, which controls some confounding factors. However, only a single predictive factor was considered, which means there is a high risk of confounding. Participants were identified from a conscription register which may have biased the sample to less severe cases.

Bibliographic reference	Olen, O., Montgomery, S. M., Marcus, C., Ekbom, A., and Ludvigsson, J. F. Coeliac disease and body mass index: a study of two Swedish general population-based registers. 20100308. Scandinavian Journal of Gastroenterology 44(10), 1198-1206. 2009.
Aim	To examine the relation between body mass index (BMI) and in patient diagnosis of coeliac disease.
quality	**NICE case-control quality checklist** 1. The study addresses an appropriate and clearly focused question? Yes, question clear 2. Cases and controls from comparable populations? Same population of Swedish male conscripts 3. Same exclusion criteria used for both cases and controls? Yes same exclusion criteria applied 4. What was participation rate for each group? Cases: controls: N/A; all blood tested, participation not required from either group 5. Participants and non-participants are compared to establish their similarities or differences? Yes; baseline characteristics the same between groups. 6. Cases are clearly defined and differentiated from controls: cases are defined in terms of seropositivity 7. It is clearly established that controls are not cases? Clear in the fact that cases are seronegative, but without biopsy of all controls cannot be 100% certain that none have CD. For this study purposes, controls are clearly established as non-cases. 8. Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment? Yes, no person was to have had previous suspicion of CD or previous duodenal biopsy 9. Exposure status is measured in a standard, valid, and reliable way? Yes; serological testing for CD was standard 10. Main potential confounders are identified and taken into account in the design and analysis? Only single predictive factor considered other factors not taken into consideration. As population all same age and gender from same country not likely to have highly differing baseline characteristics. 11. Have confidence intervals been provided? Yes
Study type	**PART 1** Cohort study **PART 2** Case-control study
Patient characteristics	**The study is split into two parts:** **PART 1** **Study Population:** Pregnant females identified from the Swedish medical birth register, aged 18-50, with data available on pre-pregnancy weight (restricted to women with weight 30-200 Kg), height (restricted to women with height 130-200 cm), nationality, pariety, civil status and smoking status.

	Number of patients in study population: 788,710 **Number of patients excluded:** 1218763 (data not available or did not meet height/weight criteria above**)** **Age:**18-50 **Males/females:** all female **PART 2** **Study Population:** Men identified through the Swedish national inpatients register as having coeliac disease which led to an inpatient stay before or after conscription. In order to be eligible, data on weight (restricted to men with weight 30-200 Kg) and height (restricted to men with height 130-200 cm) had to be also available from the national conscripts register before 2000. Before 2000 most Swedish men were conscripted (80%-98% between 1996 and 2000). **Data are reported for men diagnosed with coeliac disease before and after weight measurement – only the data for men diagnosed after weight measurement are eligible for the review and are reported below.** **Control Population:** Each patient was matched with up to 5 controls for age, sex, calendar period and country of residence. Controls were identified via a government total population register. **Number of patients in study population:** 70 (1047 men with existing coeliac disease at the time of weight measurement were also included but not reported here) **Number of patients in control population:** 6887 **Number of patients excluded:** 1218763 (data not available or did not meet height/weight criteria above**)** **Age:**18-50 **Males/females:** all male **Country:** Sweden **Other comments:**
Source of funding	Government and charity
Sign/Symptom	Body mass index
Reference standard	Inpatient stay related to coeliac disease as defined by international classification of disease codes (ICD-7: 286.00; ICD-8:269.00, 269.98, ICD-9: 579A; ICD-10: K90.0)
Results	**PART 1**

	With coeliac disease (n=174)	Without coeliac disease (n=787986)
BMI<18	29 (16.7%)	41100 (5.2%)
BMI 18-24.9	129 (74.1%)	574195 (72.9.%)
BMI >=25	16 (9.2 %)	172691 (21.9%)

Regression adjusted for age parity, smoking, calendar period and civil status for predictive value of BMI<18 for coeliac disease: Adjusted HR =2.5 (95% CI 1.7-4.9)

PART 2

	With coeliac disease (n=70)	Without coeliac disease (n=6887)
BMI<18	10 (9.8%)	446 (6.5%)
BMI 18-24.9	50 (71.4%)	5449 (79.1%)
BMI >=25	10 (14.3 %)	992 (14.4%)

Regression adjusted for calendar period and socioeconomic group for predictive value of BMI<18 for coeliac disease: Adjusted OR =2.2 (95% CI 1.0-4.8)

Comments	**PART 1:**
	The study population was limited to women who were pregnant – this may limit the generalizability of these findings to coeliac disease patients as a whole, and may introduce bias because the control participants were recruited from a general population register (not required to be pregnant). Coeliac disease was only identified if associated with an inpatient stay, potentially misidentifying some individuals with coeliac disease. **PART 2:** Case and control participants were matched for some baseline characteristics, limiting the impact of some confounding factors. However, only single sign/symptom was investigated, so there is still a high risk of confounding. Also the way that the populations were selected may mean that it does not reflect coeliac patients as a whole. For example, an inpatient stay was required for individuals to be identified as having coeliac disease, which may have biased the sample to more severe cases of coeliac disease. Conversely, participants were identified from a conscription register which may have biased the sample to less severe cases.