



Epidemiology of Coeliac Disease

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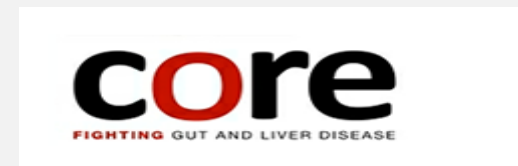
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Introduction

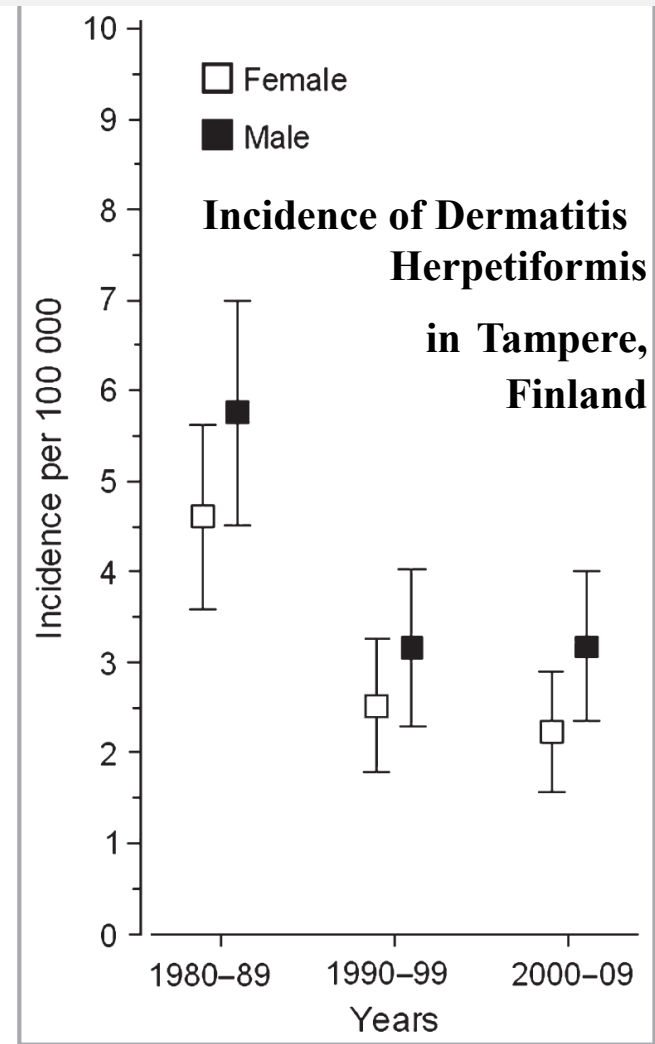
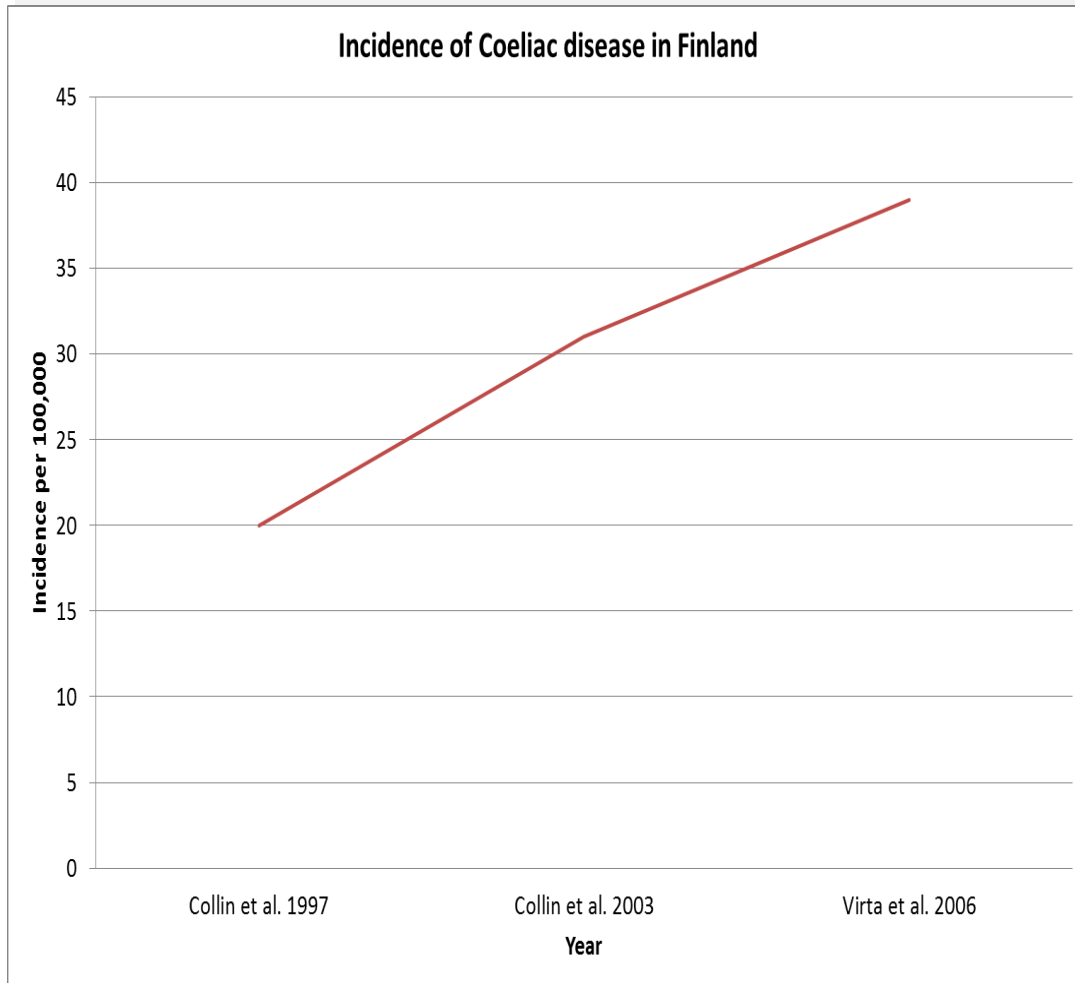
- Prevalence and incidence
 - Maternal and offspring risks
 - Pneumococcal vaccination and pneumonia risk
 - Excess causes of death
-
- 8 publications, incidence paper cited > 32 times



Methods

- THIN
- Clinical Practice Research Datalink
 - HES, GPRD, ONS
- Longitudinal data 1990-2010

Incidence: Finland





Aim

What are the trends and patterns of clinically diagnosed coeliac disease and dermatitis herpetiformis in the UK?

Results

Coeliac disease

– N = 9087 Incidence rate = 13.8 / 100,000

Male 9.60 / 100,000

Female 17.93 / 100,000 IRR = 1.85 [1.78,1.94]

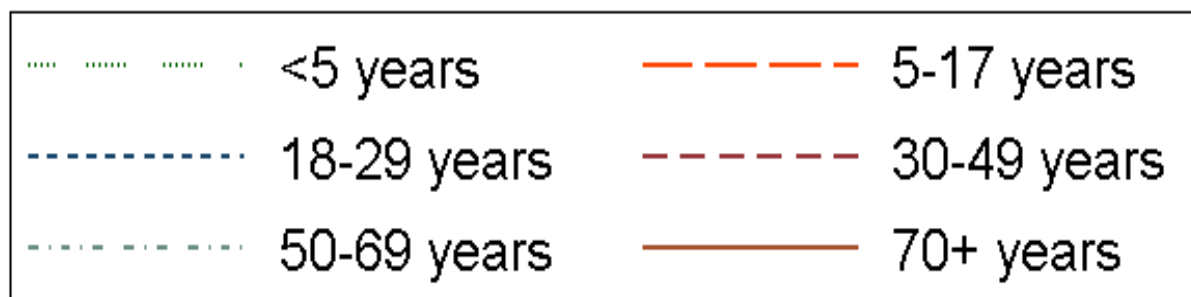
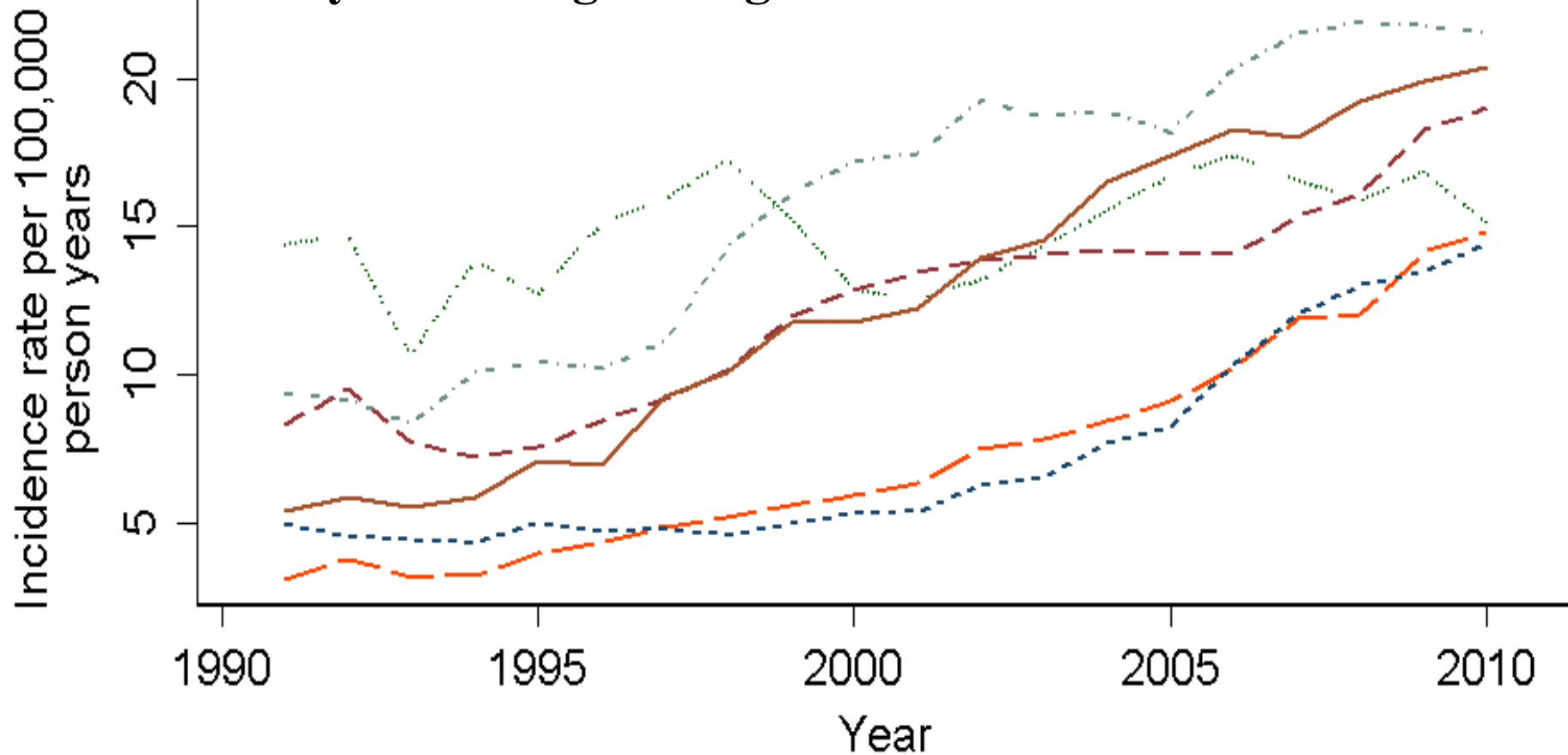
Dermatitis Herpetiformis

– N = 809 Incidence rate = 1.2 / 100,000

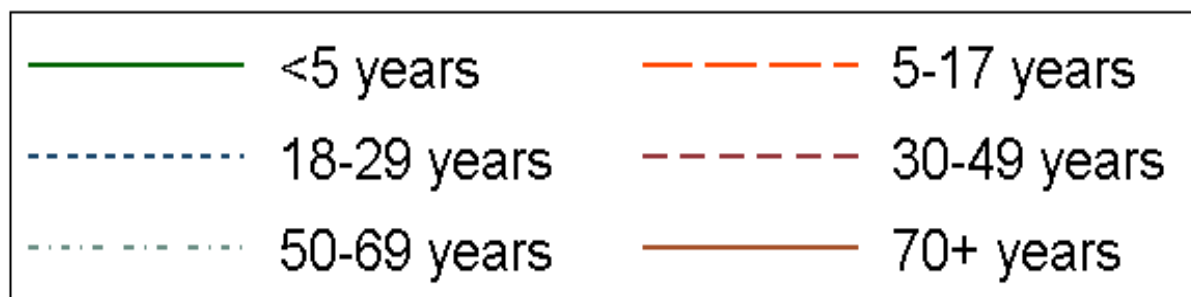
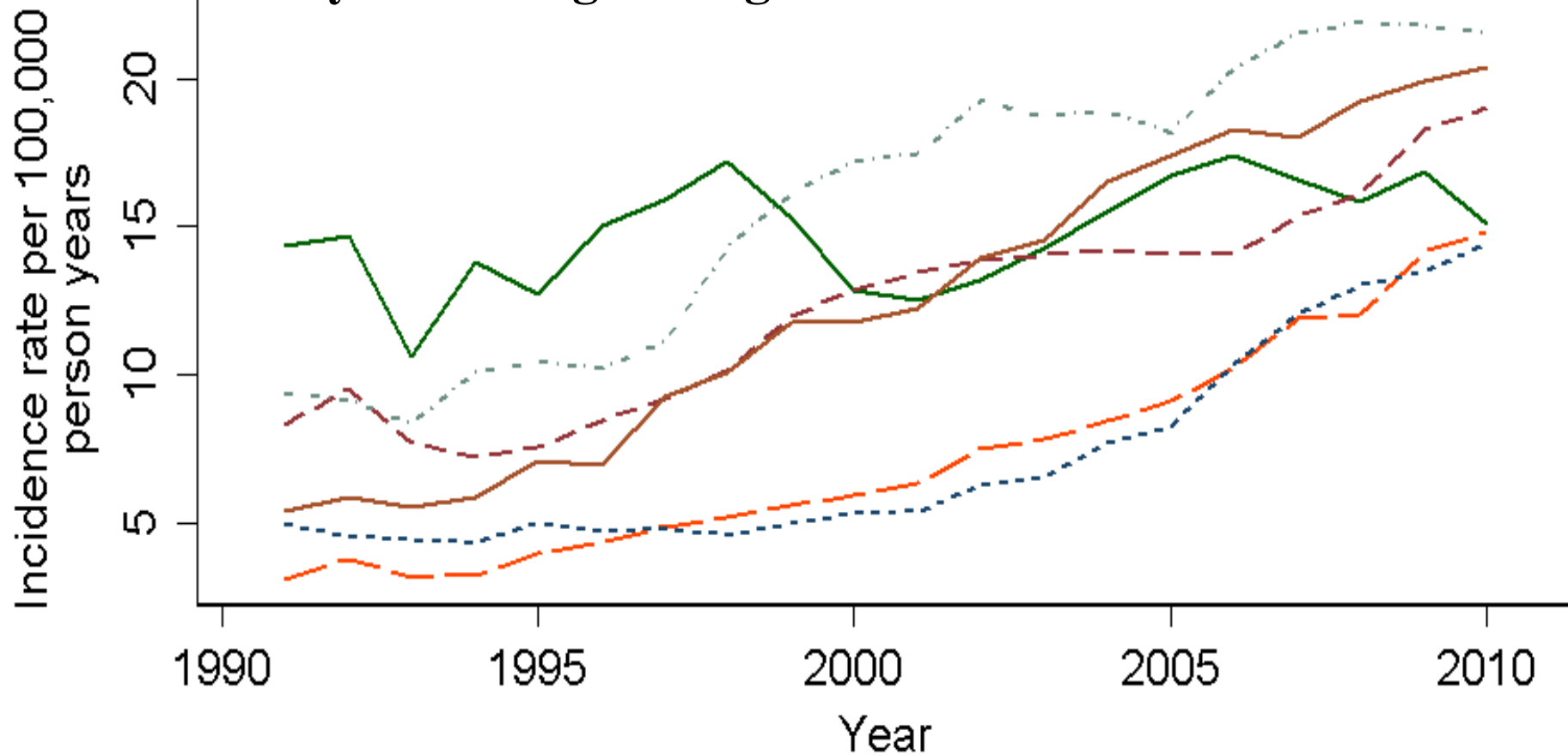
Male 1.21 / 100,000

Female 1.25 / 100,000 IRR = 0.99 [0.87,1.14]

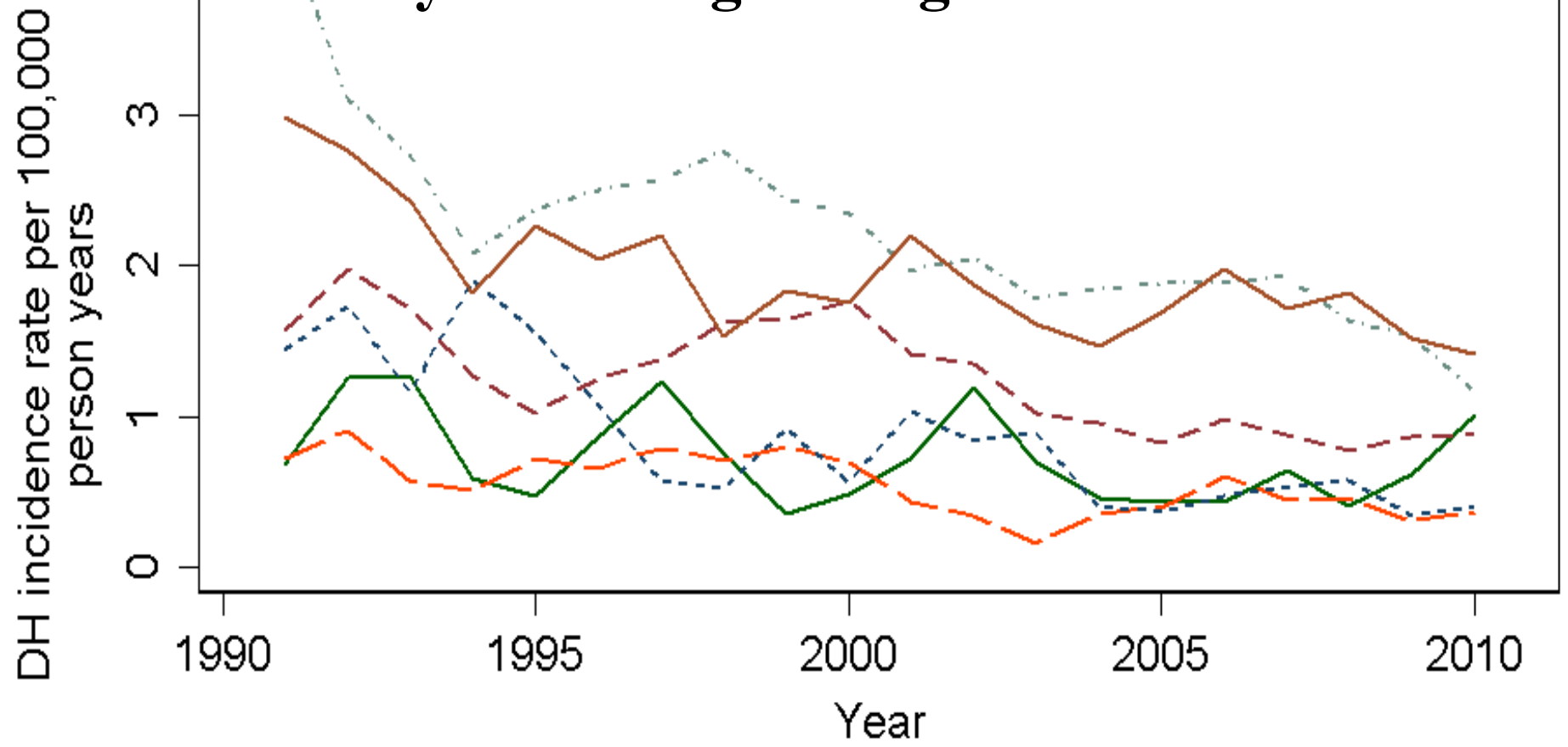
3 year rolling average incidence of coeliac disease



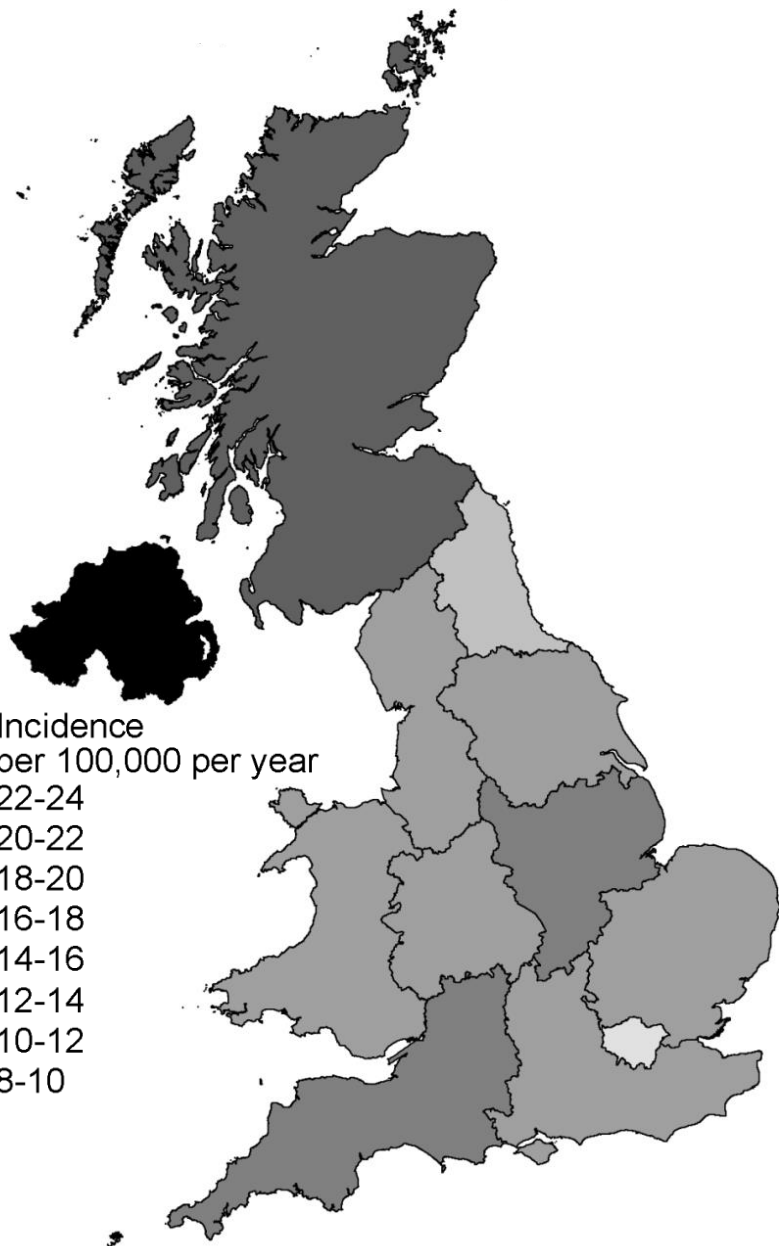
3 year rolling average incidence of coeliac disease



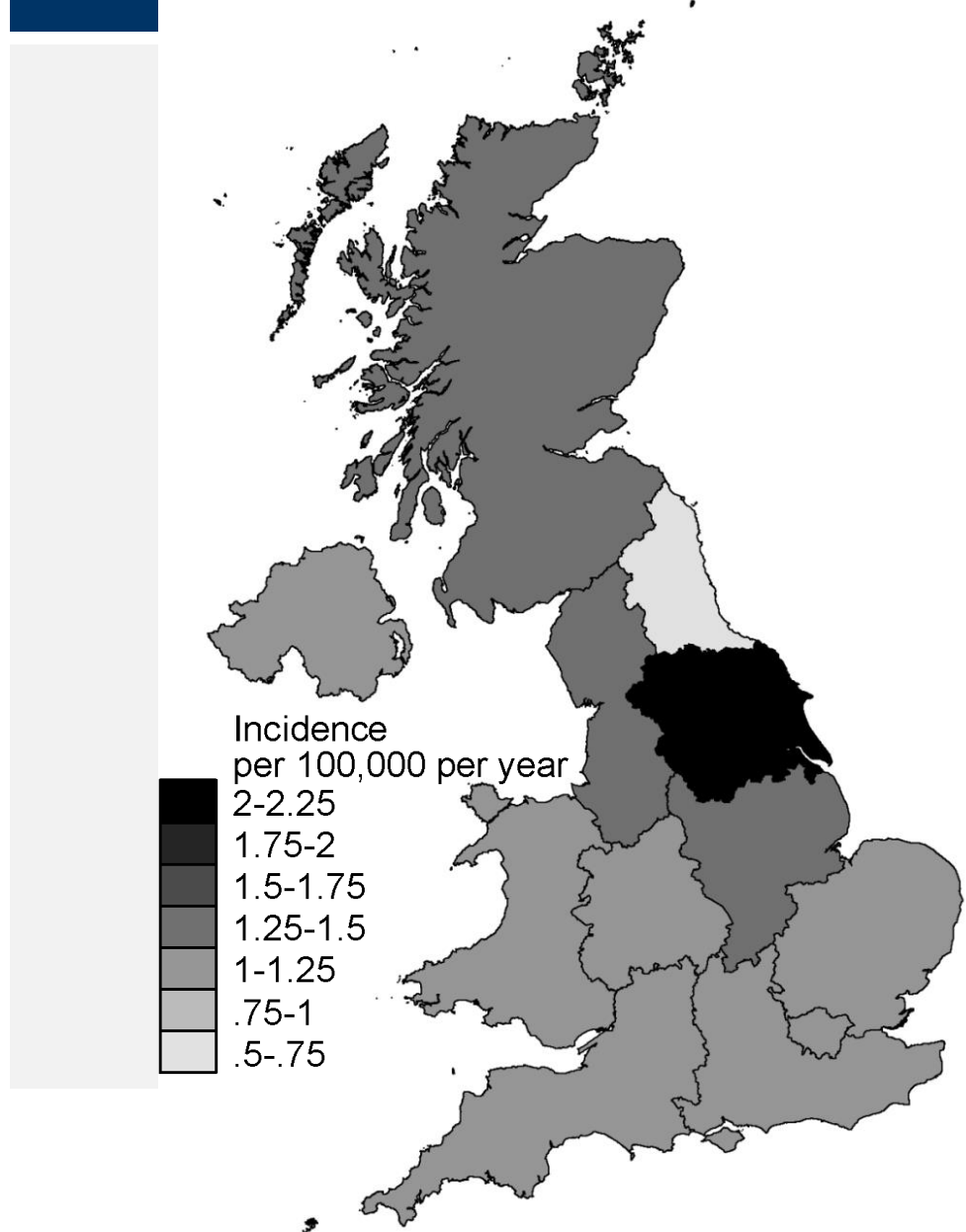
3 year rolling average incidence of DH



Average incidence of Coeliac disease 1990 - 2011

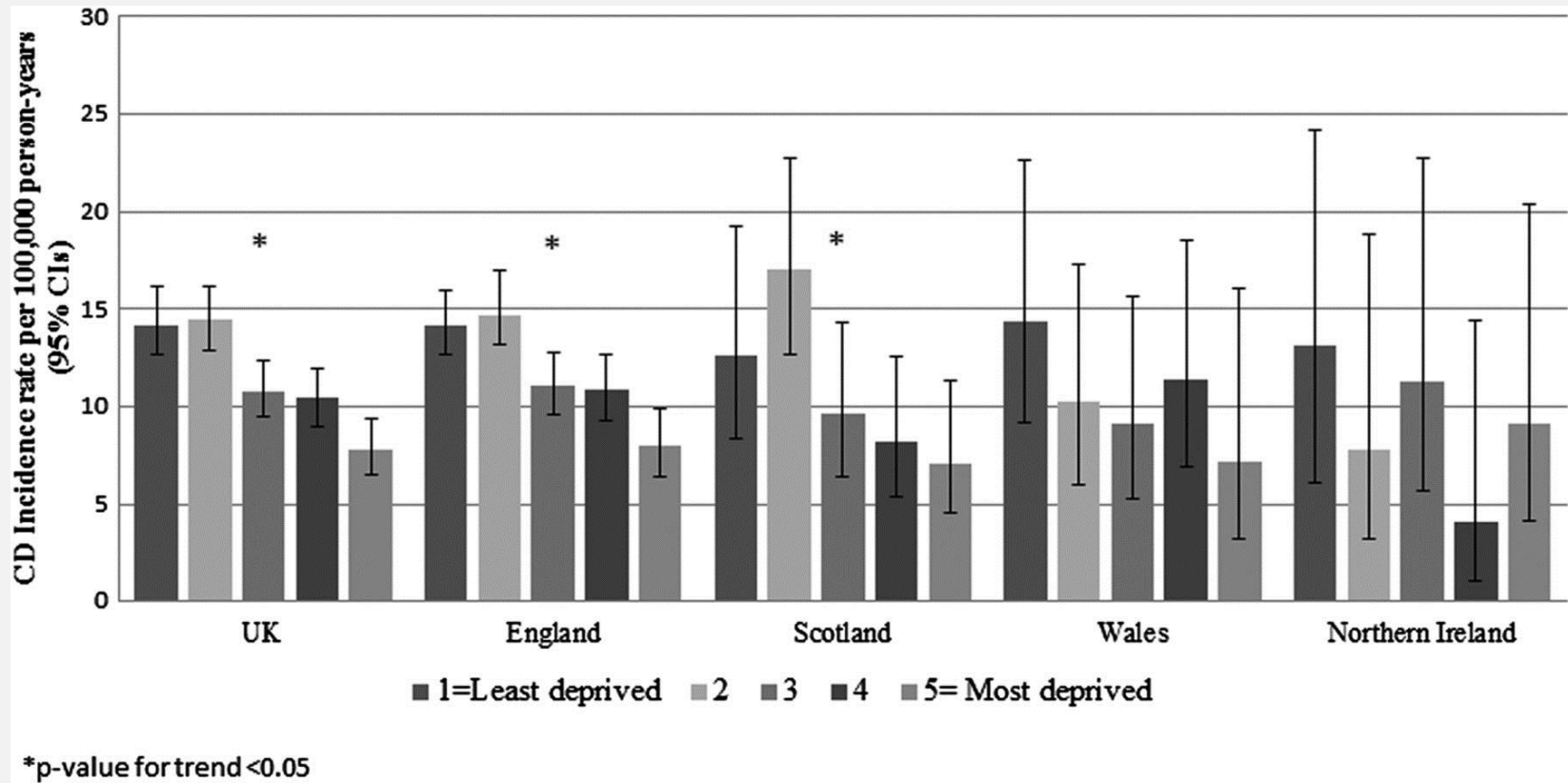


Average incidence of Dermatitis Herpetiformis 1990 - 2011





Coeliac disease incidence across countries of the UK according to socioeconomic group.



Fabiana Zingone et al. Arch Dis Child
doi:10.1136/archdischild-2014-307105





Differences in exposures, genetics, or discrepancies in clinical diagnosis?

Prevalence

- Sero-prevalence
 - 1 - 1.6% across UK
- Coeliac disease prevalence 2011:
 - 0.16 - 0.39%
- Extrapolation:
 - Overall UK prevalence ~ 0.24%
 - ~ 150,000 people with coeliac disease in UK
 - Northern Ireland ~ 0.39%
 - ~ Additional 100,000 people undiagnosed in UK

Summary

- Increasing coeliac diagnosis incidence
- Differing regional patterns of diagnosis
 - Increasing ascertainment or clinical disease?
- Decreasing dermatitis herpetiformis incidence
 - Earlier diagnosis of coeliac - reduced DH?
Salmi et al. Brit. J. Derm. 2011;165(2)354–9.
- Disparities in diagnosis pathways exist



Maternal Risks

Aims

1. Inherited risk
2. Congenital Abnormalities
3. Pregnancy complications



Risks of Coeliac disease in children

- Linkage between mother and children records between 1990 and 2010 in THIN GP dataset
- 708 mothers with Coeliac disease
- Adjusted relative risk 36.7 (95% CI [28.2, 47.7])
- 3.1% more children diagnosed with Coeliac disease

Maternal risks: Congenital Abnormalities



The University of
Nottingham

UNITED KINGDOM · CHINA · MALAYSIA

- 562 332 singleton pregnancies in THIN 1990-2013.
 - 1,880 with Coeliac disease (0.35%)
 - Coeliac disease diagnosed before delivery
 - Diagnosed after delivery (undiagnosed)
- 15,850 children with a major congenital anomaly
- 546,482 children without such conditions.

Maternal risks: Congenital Abnormalities



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- Compared to women without CD, women with CD had lower BMI
- Were less likely to smoke
- Had higher prevalence of diabetes
- Pregnant women with diagnosed CD were older than those with undiagnosed CD but otherwise had similar maternal characteristics.

Table 4. Absolute risks and adjusted odds ratios of major congenital anomalies in children of mothers with undiagnosed and diagnosed coeliac disease

	Diagnosed CD				Undiagnosed CD			
	<i>n</i> = 909				<i>n</i> = 971			
	<i>n</i>	<i>n</i> /10 000	aOR*	95% CI	<i>n</i>	<i>n</i> /10 000	aOR*	95% CI
Major congenital anomalies overall	21	231	0.80	0.52–1.24	34	350	1.14	0.79–1.64
Heart	7	77	0.89	0.42–1.87	8	82	0.95	0.48–1.91
Limb	7	77	1.44	0.69–3.04	9	93	1.53	0.79–2.94
Genital system	1	11	0.26	0.04–1.83	7	72	1.66	0.79–3.50
Urinary system	4	44	1.60	0.60–4.29	2	21	0.74	0.18–2.98
Chromosomal	2	22	1.06	0.26–4.24	0	–	–	–
Orofacial cleft	2	22	1.67	0.42–6.67	1	10	0.70	0.10–5.01
Nervous system	0	–	–	–	5	51	2.98	1.06–8.33
Neural tube defects**	0	–	–	–	1	10	4.16	0.59–29.45
Musculoskeletal system	1	11	0.89	0.13–6.38	1	10	0.62	0.09–4.41
Digestive system	0	–	–	–	0	–	–	–
Eye	0	–	–	–	0	–	–	–
Other malformations***	0	–	–	–	3	31	2.50	0.58–10.73
Respiratory system	0	–	–	–	0	–	–	–
Ear, face, and neck	0	–	–	–	0	–	–	–
Abdominal wall	0	–	–	–	0	–	–	–

Comparison group includes children of women without CD; empty cells indicated insufficient numbers.

*Odds ratio adjusted for maternal age, body mass index, smoking, socio-economic status, periconceptional folic acid supplementation, type-1 diabetes, rheumatoid arthritis, and thyroid disorders.

**Including anencephalus, encephalocele, and spina bifida.

***E.g. asplenia, situs inversus, and skin disorders.

Maternal risks: Pregnancy complications



- 276,399 women 15-44 years in CPRD-HES 1997 to 2012
 - 363,930 singleton pregnancies resulting in a live or a stillbirth
- 892 pregnancies with CD (0.25%)
 - 62% (n=551) were diagnosed before childbirth (diagnosed CD)
 - 38% (n=341) were diagnosed after childbirth (undiagnosed CD)
- 363,038 pregnancies without CD

Table 2: Relative risks of pregnancy complication and adverse birth outcome among women with **diagnosed CD and without CD.**

Variables	Absolute excess risk (%)	Adjusted OR (95% CI)
Pregnancy complication		
Postpartum haemorrhage	3.5	1.34 (1.04-1.72)
Preeclampsia/eclampsia	0.2	1.16 (0.65-2.05)
Antepartum haemorrhage	1.1	1.28 (0.89-1.83)
<i>Mode of delivery</i>		
Assisted	3.3	1.34 (1.05-1.71)
Elective caesarean	1.3	1.10 (0.81-1.40)
Emergency caesarean	2.5	1.26 (0.98-1.64)
Birth outcomes		
Stillbirth	0.3	1.70 (0.63-4.54)
<i>Length of gestation</i>		
Pre-term	1.1	1.14 (0.83-1.60)
<i>Birth weight</i>		
Underweight < 2500 grams	0.8	1.15 (0.76-1.74)

Pregnancy Complications and Adverse Birth Outcomes Among Women With Celiac Disease: A Population-Based Study From England Alyshah Abdul Sultan, Laila J Tata, Kate M Fleming, Colin J Crooks, Jonas F Ludvigsson, Nafeesa N Dhalwani, Lu Ban and Joe West. *Am J Gastroenterol* 2014; 109:1653–1661; doi:10.1038/ajg.2014.196; published online 5 August 2014

Table 2: Relative risks of pregnancy complication and adverse birth outcome among women with **undiagnosed CD and without CD.**

Variables	Absolute excess risk (%)	Adjusted OR (95%CI)
Pregnancy complication		
Postpartum haemorrhage ³	-1.2	0.94 (0.63-1.40)
Preeclampsia/eclampsia ³	0.6	1.25 (0.59-2.76)
Antepartum haemorrhage	0.3	1.14 (0.70-1.84)
<i>Mode of delivery</i>		
Assisted	0.2	1.02 (0.73-1.41)
Elective caesarean	3.7	1.39 (0.94-2.05)
Emergency caesarean	0.5	1.00 (0.71-1.42)
Birth outcomes		
Stillbirth	0.2	1.42 (0.35-5.64)
<i>Length of gestation</i>		
Pre-term	1.1	1.24 (0.82-1.87)
<i>Birth weight</i>		
Underweight < 2500 grams	1.1	1.36 (0.83-2.24)

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Summary

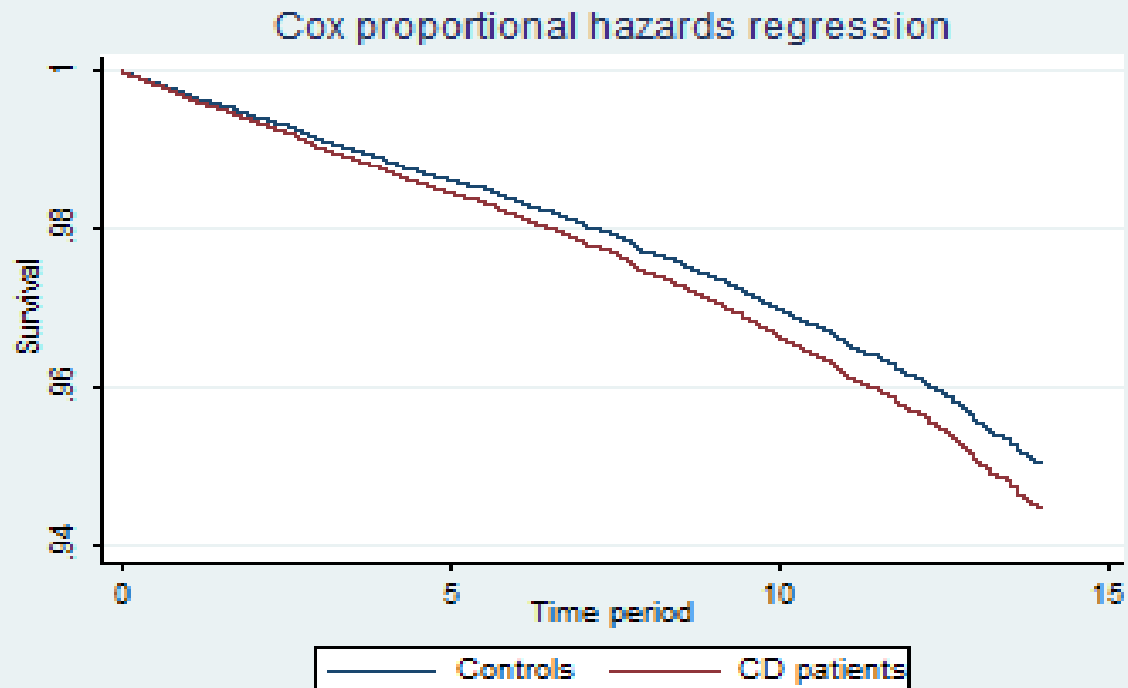
- Most pregnancies with CD are not complicated by an adverse event or congenital abnormality
- Small increased risk of assisted delivery and postpartum bleeding in diagnosed Coeliac disease
- Overall our results are reassuring to both women and practitioners

Risk of pneumonia

- CPRD – HES linked cohort
- 1997-2011
- Coeliac patients with 10 age frequency matched controls
- Vaccination status
 - 37% Coeliac disease patients vaccinated

Pneumonia rates

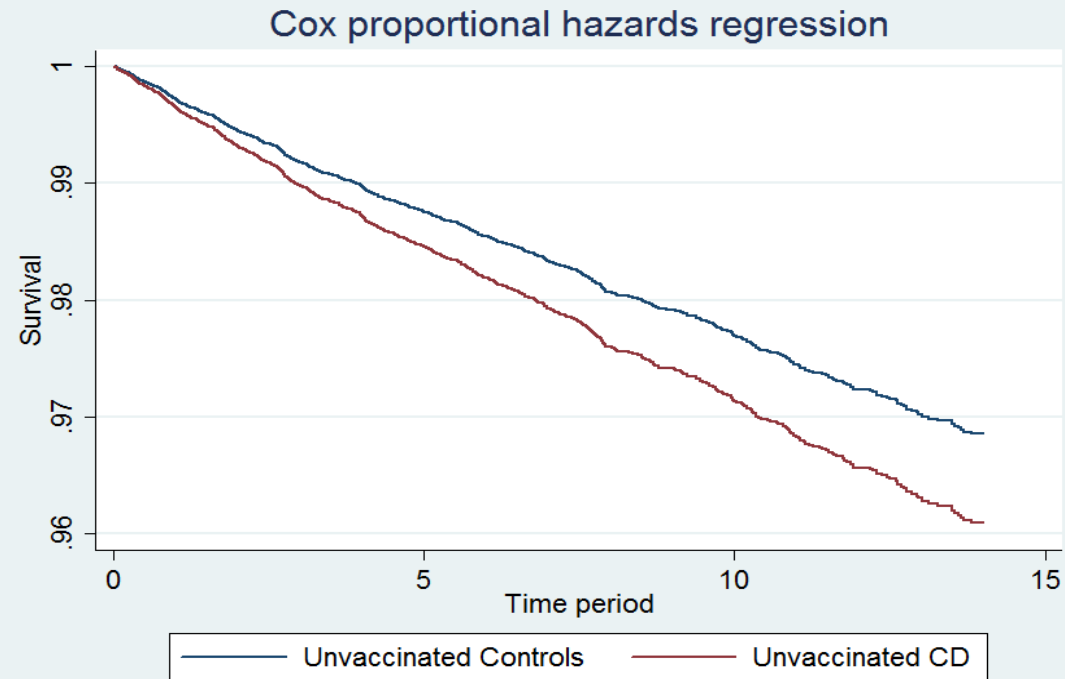
- 3.12 /1000 person years in controls
- 3.42 /1000 person years in coeliac patients
- HR 1.07,
95% CI 0.91-1.24



Pneumonia

HR 0.88 (0.70 to 1.10) in vaccinated

HR 1.28 (1.02 to 1.60) in unvaccinated





Pneumonia

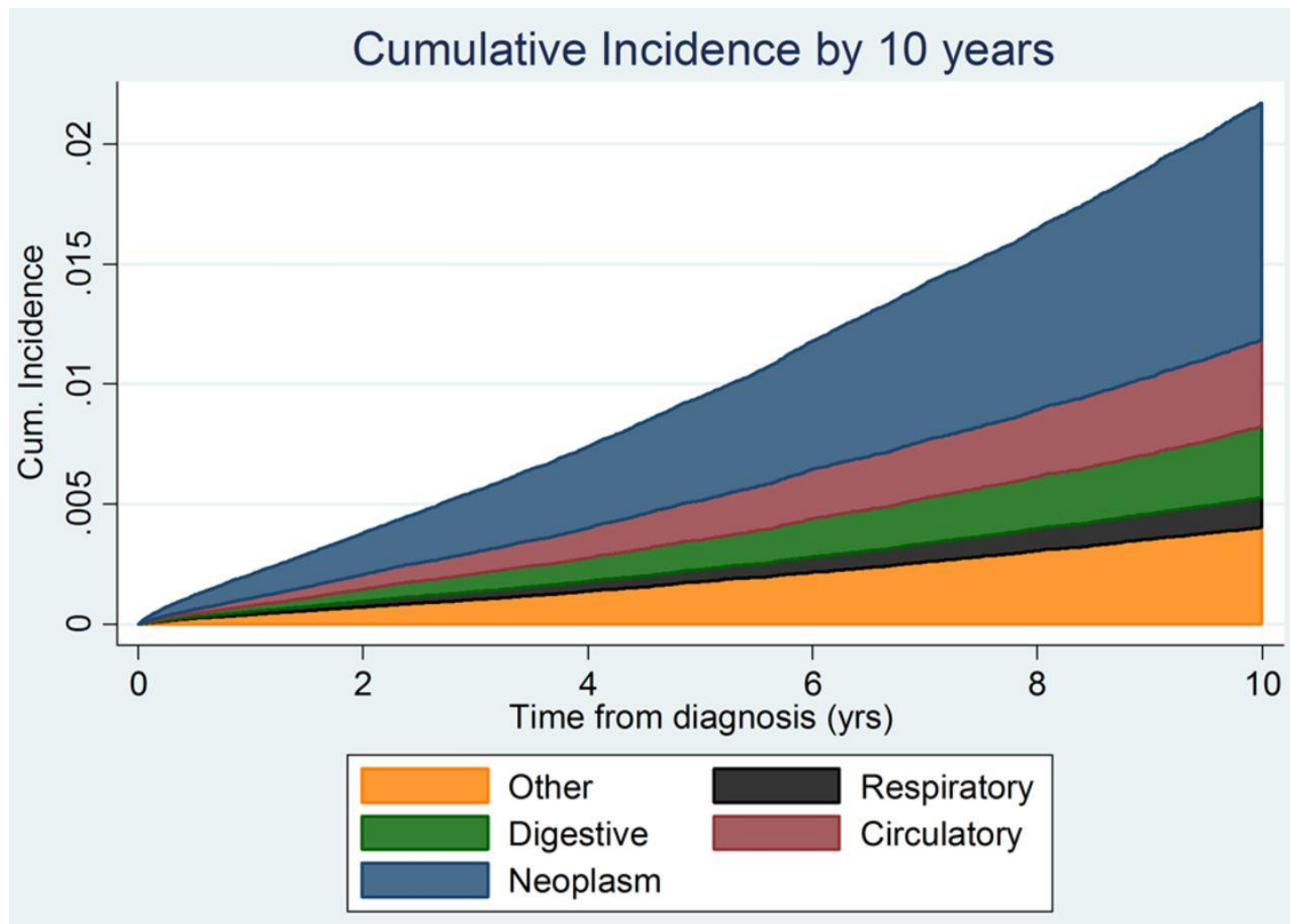
- Under 65 years, male, normal BMI, least deprived
- Increased risk persisted for 5 years of follow up



ONS linked data for death certificates

- Cumulative incidence adjusted for competing risks
- Compared to frequency matched controls on age

Cumulative incidence by time after diagnosis, adjusting for competing events, age and sex.



Alyshah Abdul Sultan et al. Gut 2015;64:1220-1226

Table 4 Cumulative incidence function by 10 years of diagnosis adjusted for competing risk, age, socioeconomic status and gender

Cause of death	With CD	Without CD	Excess	95% CI*	
Cardiovascular	0.32	0.41	-0.08	-0.13	-0.04
Ischemic heart disease	0.15	0.26	-0.05	-0.10	-0.00
Respiratory	0.11	0.10	0.00	-0.02	0.03
Respiratory infection	0.16	0.20	-0.04	-0.09	0.01
Neoplasm	1.24	1.21	0.04	-0.10	0.18
Non-Hodgkin's lymphoma	0.21	0.06	0.15	0.03	0.27
Digestive	0.24	0.16	0.07	-0.01	0.16
Others	0.27	0.29	-0.02	-0.07	0.04
Not coded	0.27	0.25	0.02	-0.07	0.10

* Bootstrap 50 iterations.
CD, coeliac disease.

Alyshah Abdul Sultan et al. *Gut* 2015;64:1220-1226



Summary

- Variations in incidence of diagnosed disease
- Reassuringly no significant adverse effects on congenital abnormalities, pregnancy complications, fertility in diagnosed Coeliac disease
- Vaccinated patients have no increased risk of pneumonia

Future work

- Current Coeliac UK grant to update incidence and prevalence
- Health care utilisation study and preferred models of follow up

1. *Fabiana Zingone, Joe West, Colin Crooks, Kate M. Fleming, Timothy R. Card, Carolina Ciacci, Laila J. Tata. Socioeconomic variation in the incidence of childhood coeliac disease in the United Kingdom. Archives of diseases in childhood 2015 doi: 10.1136/archdischild-2014-307105
2. *Alyshah Abdul Sultan, Colin Crooks, Tim Card, Laila Tata, Kate M Fleming, Joe West. Causes of death in people with coeliac disease in England compared to the general population: A competing risk analysis. Gut 2014 Oct 24 doi:10.1136/gutjnl-2014-308285
3. *Lu Ban, Joe West, Alyshah Abdul Sultan, Nafeesa N Dhalwani, Jonas F Ludvigsson, Laila J Tata. Limited risks of major congenital anomalies in children of mothers with coeliac disease: A population-based cohort study. British Journal of Obstetrics and Gynaecology 2014 Oct 7 doi:10.1111/1471-0528.13102
4. *Canavan C, Card T, West J. The Incidence of Other Gastroenterological Disease following Diagnosis of Irritable Bowel Syndrome in the UK: A Cohort Study. PLoSOne. 2014 Sep 19;9(9):e106478. doi: 10.1371/journal.pone.0106478. eCollection 2014. PubMed PMID: 25238408.
5. *Dhalwani NN, West J, Sultan AA, Ban L, Tata LJ. Women with Celiac Disease Present with Fertility Problems No More often than Women in the General Population. Gastroenterology. 2014 Aug 22. pii: S0016-5085(14)01036-1. doi:10.1053/j.gastro.2014.08.025. [Epub ahead of print] PubMed PMID: 25157666.
6. *Abdul Sultan A, Tata LJ, Fleming KM, Crooks CJ, Ludvigsson JF, Dhalwani NN, Ban L, West J. Pregnancy Complications and Adverse Birth Outcomes Among Women With Celiac Disease: A Population-Based Study From England. Am J Gastroenterol. 2014 Aug 5. doi: 10.1038/ajg.2014.196. [Epub ahead of print] PubMed PMID:25091060.
7. *West J, Fleming KM, Tata LJ, Card TR, Crooks CJ. Incidence and prevalence of celiac disease and dermatitis herpetiformis in the UK over two decades: population-based study. Am J Gastroenterol. 2014 May;109(5):757-68. doi:10.1038/ajg.2014.55. Epub 2014 Mar 25. PubMed PMID: 24667576; PubMed Central PMCID: PMC4012300.
8. Risk of Community-Acquired Pneumonia Among Patients with Coeliac Disease Compared to the General Population: a Cohort Study. Currently under revision with AP&T



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