**Supplementary Table S5:** Temporal trends in the incidence of celiac disease

A) All ages

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **Country (Area)** | **Time Period** | **AAPC (95% CI)** | **Inflection Point(s)** | **APC (95% CI) by Segment** |
| **Northern Europe** | | | | | |
| Grode 20181 | Denmark (Nationwide) | 1980-2016 | 7.8% (6.9, 8.7)† | N/A | N/A |
| Hawkes 20002 | UK (Cardiff & Vale of Glamorgan, Wales) | 1981-1995 | 9.4% (3.9, 15.1)† | None | - |
| Hurley 20123 | UK (Cardiff & Vale of Glamorgan, Wales) | 1996-2005 | 10.4% (5.5, 15.4)† | None | - |
| Hawkes 2000, Hurley 2012±2,3 | UK (Cardiff & Vale of Glamorgan, Wales) | 1981-2005± | 10.5% (8.7, 12.3)† | None | - |
| Fowell 20064 | UK (East Dorset, England) | 1993-2002 | 11.4% (2.4, 21.1)† | N/A | N/A |
| Stroud 20195 | UK (Southern England | 1993-2017 | 5.1% (2.2, 8.0)† | N/A | N/A |
| West 20146 | UK (Nationwide) | 1990-2011 | 5.5% (4.6, 6.5)† | None | - |
| West 20197a | UK (Nationwide) | 2005-2015 | 3.1% (–0.6, 7.1) | 2011 | 1) 5.0% (3.1, 7.1)†  2) –0.3% (-7.2, 7.2) |
| West 2014, West 20196,7 | UK (Nationwide) | 1990-2015 | 5.0% (4.4, 5.7)† | None | - |
| **Southern Europe** | | | | | |
| Lanzarotto 2004, Lanzini 20058,9 | Italy (Brescia) | 1996-2003± | 18.2% (12.8, 23.8)† | N/A | N/A |
| Angeli 201210 | Italy (Terni) | 2002-2010 | –1.5% (–7.8, 5.2) | N/A | N/A |
| **Western Europe** | | | | | |
| Gutschmidt 198711 | Germany (West Berlin) | 1979-1984 | 11.9% (–0.3, 25.5) | N/A | N/A |
| Jansen 199312 | Netherlands (Nationwide) | 1976-1992 | 4.0% (0.7, 7.3)† | 1987 | 1) 1.0% (–2.1, 4.1)  2) 11.6% (1.8, 22.4)† |
| Burger 201413 | Netherlands (Nationwide) | 1995-2010 | 6.5% (4.6, 8.4)† | - | N/A |
| Jansen 1993, Burger 2014±12,13 | Netherlands (Nationwide) | 1975-2010± | 7.6% (3.9, 11.5)† | 1989/1995 | 1) 1.3% (–1.3, 4.0)  2) 26.4% (2.2, 56.3)†  3) 6.8% (4.9, 8.7)† |
| **Oceania** | | | | | |
| Cook 200414 | New Zealand (Canterbury) | 1970-1999 | 8.9% (6.1, 11.8)† | 1991 | 1) 4.3% (1.3, 7.3)† 2) 22.0% (14.3, 30.3)† |
| **Northern America** | | | | | |
| Stewart 201115 | Canada (Calgary) | 2004-2008 | 10.2% (–0.9, 22.5) | N/A | N/A |
| Murray 200316 | United States (Olmsted County) | 1950-2001 | 7.6% (2.7, 12.6)† | N/A | N/A |
| Ludvigsson 201317 | United States (Olmsted County) | 2000-2010 | 4.6% (–2.0, 11.5) | None | - |
| Murray 2003, Ludvigsson 2013±16,17 | United States (Olmsted County) | 1950-2010± | 8.1% (4.6, 11.7)† | None | - |

†statistically significant increase or decrease (p < 0.05) ±temporal data from studies combined given similar demographic and geographic region studied  
N/A = insufficient data to assess for inflection point (<10 data points)

a Estimates from original study as authors performed temporal analysis using same methodology

B) Children

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **Country (Area)** | **Time Period** | **AAPC (95% CI)** | **Inflection Point(s)** | **APC (95% CI) by Segment** |
| **Northern Europe** | | | | | |
| Grode 20181 | Denmark (Nationwide) | 1980-2016 | 8.7% (6.7, 10.8)† | N/A | N/A |
| Dydensborg 201218 | Denmark (Nationwide) | 1996-2009 | 12.8% (7.2, 18.6)† | 2002 | 1) 21.7% (9.4, 35.4)† 2) 5.6% (–0.3, 11.8) |
| Ress 201219 | Estonia (Nationwide) | 1976-2010 | 8.2% (3.1, 13.5)† | N/A | N/A |
| Kivela 201520 | Finland (Tampere) | 2001-2013 | 3.3% (–0.9, 7.8) | 2007 | 1) 10.1% (2.3, 18.5)† 2) –3.0% (–9.1, 3.6) |
| Namatovu 201421 | Sweden (Nationwide) | 1973-2009 | 5.1 % (1.4, 8.9)† | 1994/1998/ 2003 | 1) 9.7% (8.0, 11.4)† 2) –21.3 (–39.2, 2.0)  3) 21.9% (5.9, 40.3)†  4) –3.1% (–9.2, 3.4) |
| Tapsas 201522 | Sweden (Östergötland) | 1973-2013 | 5.5% (3.3, 7.8)† | 1989 | 1) 10.0% (4.6, 15.6)† 2) 2.6% (1.0, 4.3)† |
| Hawkes 20002 | UK (Cardiff & Vale of Glamorgan, Wales) | 1981-1995 | 1.5% (–5.7, 9.2) | None | - |
| Hurley 20123 | UK (Cardiff and Vale of Glamorgan, Wales) | 1996-2005 | 18.9% (9.7, 28.7)† | None | - |
| Hawkes 2000, Hurley 2012±2,3 | UK (Cardiff & Vale of Glamorgan, Wales) | 1981-2005 | 6.0% (3.1, 9.0)† | None | - |
| White 201323 | UK (Southeast Scotland, Scotland) | 1990-2009 | 12.7% (9.9, 15.6)† | None | - |
| Lister 201824 | UK (Southeast Scotland, Scotland) | 2010-2016 | 17.4% (13.0, 22.0)† | N/A | N/A |
| White 2013, Lister 2018±23,24 | UK (Southeast Scotland, Scotland) | 1990-2016 | 12.8% (11.4, 14.1)† | None | - |
| Whyte 201325 | UK (South Wales, Wales) | 2005-2011 | 5.8% (–2.9, 15.3) | N/A | N/A |
| **Western Europe** | | | | | |
| Burger 201413 | Netherlands (Nationwide) | 1995-2010 | 8.9% (7.3, 10.6)† | N/A | N/A |
| **Northern America** | | | | | |
| McGowan 200926 | Canada (Calgary) | 1990-2006 | 9.9% (0.6, 20.1)† | 1996 | 1) –13.9% (–31.1, 7.7) 2) 27.2% (15.8, 39.8)† |
| Stewart 201327 | Canada (Calgary) | 2004-2008 | 10.6 (–18.6, 50.3) | N/A | N/A |
| McGowan 2009, Stewart 2013±26,27 | Canada (Calgary) | 1990-2008 | 12.7% (–0.4, 27.6) | 1996 | 1) –10.6% (–38.2, 29.4)  2) 26.5% (14.9, 39.4)† |
| Rajani 201028 | Canada (Northern Alberta) | 1998-2007 | 60.8% (34.4, 92.4)† | 2005 | 1) 87.3% (45.9, 140.6)†  2) –5.7% (–48.0, 70.8) |
| Murray 200316 | United States (Olmsted County) | 1950-2001 | 7.5% (1.2, 14.2)† | N/A | N/A |
| Almallouhi 201729 | United States (Olmsted County) | 2000-2014 | 6.8% (3.9, 9.9)† | 2010 | 1) 13.4% (10.2, 16.7)† 2) –8.0% (–15.7, 0.3) |
| Murray 2003, Almallouhi 2017±16,29 | United States (Olmsted County) | 1950-2014 | 7.0% (1.2, 13.2)† | 1985/2010 | 1) 3.1 (–8.3, 16.0)  2) 14.9% (10.9, 19.0)†  3) –9.2% (–18.8, 1.6) |

†statistically significant increase or decrease (p < 0.05) ±temporal data from studies combined given similar demographic and geographic region studied   
N/A = insufficient data to assess for inflection point (<10 data points)

C) Adults

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **Country (Area)** | **Time Period** | **AAPC (95% CI)** | **Inflection Point(s)** | **APC (95% CI) by Segment** |
| **Northern Europe** | | | | | |
| Bode 199630 | Denmark (Copenhagen) | 1976-1991 | –1.8% (–7.2, 3.9) | None | - |
| Grode 20181 | Denmark (Nationwide) | 1980-2016 | 7.3% (6.6, 8.0)† | N/A | N/A |
| Collin 200731 | Finland (Nationwide) | 1980-2003 | 9.7% (4.3, 15.5)† | N/A | N/A |
| Virta 201732 | Finland (Nationwide) | 2005-2014 | –3.4% (–4.6, –2.2)† | N/A | N/A |
| Collin 2007, Virta 2017±31,32 | Finland (Nationwide) | 1980-2014 | 5.0% (2.7, 7.3)† | 2006 | 1) 8.3% (4.9, 11.9)†  2) –4.3% (–10.3, 2.0) |
| Midhagen 198833 | Sweden (Not stated) | 1976-1986 | 7.3% (0.1, 15.1)† | None | - |
| Hawkes 20002 | UK (Cardiff & Vale of Glamorgan, Wales) | 1981-1995 | 11.6% (5.5, 18.0)† | None | - |
| Hurley 20123 | UK (Cardiff and Vale of Glamorgan, Wales) | 1996-2005 | 9.0% (3.7, 14.6)† | None | - |
| Hawkes 2000, Hurley 2012±2,3 | UK (Cardiff & Vale of Glamorgan, Wales) | 1981-2005 | 11.3% (9.3, 13.4)† | None | - |
| **Southern Europe** | | | | | |
| Fernandez 201034 | Spain (Vigo) | 1986-2008 | 25.3% (14.2, 37.5)† | None | - |
| **Western Europe** | | | | | |
| Burger 201413 | Netherlands (Nationwide) | 1995-2010 | 5.4% (3.3, 7.6)† | N/A | N/A |
| **Northern America** | | | | | |
| Murray 200316 | United States (Olmsted County) | 1950-2001 | 8.1% (2.3, 14.2)† | N/A | N/A |
| Murray 2003, Ludvigsson 2013±16,17 | United States (Olmsted County) | 1950-2010 | 8.9% (4.1, 14.0)† | N/A | N/A |

†statistically significant increase or decrease (p < 0.05) ±temporal data from studies combined given similar demographic and geographic region studied  
N/A = insufficient data to assess for inflection point (<10 data points)

**References**

1. Grode L, Bech BH, Jensen TM, et al. Prevalence, incidence, and autoimmune comorbidities of celiac disease: a nation-wide, population-based study in Denmark from 1977 to 2016. *Eur J Gastroenterol Hepatol*. 2018;30(1):83-91.
2. Hawkes ND, Swift GL, Smith PM, Jenkins HR. Incidence and presentation of coeliac disease in South Glamorgan *Eur J Gastroenterol Hepatol*. 2000;12(3):345-349.
3. Hurley JJ, Lee B, Turner JK, Beale A, Jenkins HR, Swift GL. Incidence and presentation of reported coeliac disease in Cardiff and the Vale of Glamorgan: the next 10 years. *Eur J Gastroenterol Hepatol*. 2012;24(5):482-486.
4. Fowell AJ, Thomas PW, Surgenor SL, Snook JA. The epidemiology of coeliac disease in East Dorset 1993-2002: an assessment of the 'coeliac iceberg', and preliminary evidence of case clustering. *QJM*. 2006;99(7):453-460.
5. Stroud C, Almilaji O, Nicholas D, et al. Evolving patterns in the presentation of coeliac disease over the last 25 years. *Frontline Gastroenterol*. 2019;0:1-6. doi:10.1136/flgastro-2018-101170.
6. 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;109(5):757-768.
7. West J, Otete H, Sultan AA, Crooks CJ. Changes in testing for and incidence of celiac disease in the United Kingdom: A population-based cohort study. *Epidemiology*. 2019;30(4):e23-e24.
8. Lanzarotto F, Crimi F, Amato M, Villanacci V, Pillan NM, Lanzini A. Is under diagnosis of celiac disease compounded by mismanagement in the primary care setting? A survey in the Italian Province of Brescia. *Minerva Gastroenterol Dietol*. 2004;50(4):283-288.
9. Lanzini A, Villanacci V, Apillan N, et al. Epidemiological, clinical and histopathologic characteristics of celiac disease: results of a case-finding population-based program in an Italian community. *Scand J Gastroenterol*. 2005;40(8):950-957.
10. Angeli G, Pasquini R, Panella V, Pelli MA. An epidemiologic survey of celiac disease in the Terni area (Umbria, Italy) in 2002-2010. *J Prev Med Hyg*. 2012;53(1):20-23.
11. Gutschmidt S, Sandforth F, Janicke I, et al. Incidence of endemic sprue in Berlin (West). A retrospective study based on biopsy findings. *Z Gastroenterol*. 1987;25(10):662-667.
12. Jansen TLA, Mulder CJJ, Karssen PHZ, Wagenaar CGJ. Epidemiological survey of the Dutch Coeliac Disease Society: an update 1992. *Eur J Gastroenterol Hepatol*. 1993;5(2):73-8.
13. Burger JP, Roovers EA, Drenth JP, Meijer JW, Wahab PJ. Rising incidence of celiac disease in the Netherlands; an analysis of temporal trends from 1995 to 2010. *Scand J Gastroenterol*. 2014;49(8):933-941.
14. Cook B, Oxner R, Chapman B, Whitehead M, Burt M. A thirty-year (1970-1999) study of coeliac disease in the Canterbury region of New Zealand. *N Z Med J*. 2004;117(1189):U772.
15. Stewart M, Andrews CN, Urbanski S, Beck PL, Storr M. The association of coeliac disease and microscopic colitis: a large population-based study. *Aliment Pharmacol Ther*. 2011;33(12):1340-1349.
16. Murray JA, Van Dyke C, Plevak MF, Dierkhising RA, Zinsmeister AR, Melton LJ, 3rd. Trends in the identification and clinical features of celiac disease in a North American community, 1950-2001. *Clin Gastroenterol Hepatol*. 2003;1(1):19-27.
17. Ludvigsson JF, Rubio-Tapia A, van Dyke CT, et al. Increasing incidence of celiac disease in a North American population. *Am J Gastroenterol*. 2013;108(5):818-824.
18. Dydensborg S, Toftedal P, Biaggi M, Lillevang ST, Hansen DG, Husby S. Increasing prevalence of coeliac disease in Denmark: a linkage study combining national registries. *Acta Paediatr*. 2012;101(2):179-184.
19. Ress K, Luts K, Rago T, Pisarev H, Uibo O. Nationwide study of childhood celiac disease incidence over a 35-year period in Estonia. *Eur J Pediatr*. 2012;171(12):1823-1828.
20. Kivela L, Kaukinen K, Lahdeaho ML, et al. Presentation of celiac disease in Finnish children is no longer changing: a 50-year perspective. *J Pediatr*. 2015;167(5):1109-1115.e1.
21. Namatovu F, Sandstrom O, Olsson C, Lindkvist M, Ivarsson A. Celiac disease risk varies between birth cohorts, generating hypotheses about causality: evidence from 36 years of population-based follow-up. *BMC Gastroenterol*. 2014;14:59.
22. Tapsas D, Hollen E, Stenhammar L, Falth-Magnusson K. Unusually high incidence of paediatric coeliac disease in Sweden during the period 1973 - 2013. *PloS One*. 2015;10(12):e0144346.
23. White LE, Merrick VM, Bannerman E, et al. The rising incidence of celiac disease in Scotland. *Pediatrics*. 2013;132(4):e924-931.
24. Lister M, Wood P, Henderson P, Gillett P. The rising incidence of childhood coeliac disease: A 7-year regional cohort study. Paper presented at: Coeliac UK’s Research Conference 2018, 2018; London, UK.
25. Whyte LA, Jenkins HR. The epidemiology of coeliac disease in South Wales: a 28-year perspective. *Arch Dis Child*. 2013;98(6):405-407.
26. McGowan KE, Castiglione DA, Butzner JD. The changing face of childhood celiac disease in North America: impact of serological testing. *Pediatrics*. 2009;124(6):1572-1578.
27. Stewart MJ, Shaffer E, Urbanski SJ, Beck PL, Storr MA. The association between celiac disease and eosinophilic esophagitis in children and adults. *BMC Gastroenterol*. 2013;13:96.
28. Rajani S, Huynh HQ, Turner J. The changing frequency of celiac disease diagnosed at the Stollery Children's Hospital. *Can J Gastroenterol*. 2010;24(2):109-112.
29. Almallouhi E, King KS, Patel B, et al. Increasing incidence and altered presentation in a population-based study of pediatric celiac disease in North America. *J Pediatr Gastroenterol Nutr*. 2017;65(4):432-437.
30. Bode S, Gudmand-Hoyer E. Incidence and prevalence of adult coeliac disease within a defined geographic area in Denmark*. Scand J Gastroenterol*. 1996;31(7):694-699.
31. Collin P, Huhtala H, Virta L, Kekkonen L, Reunala T. Diagnosis of celiac disease in clinical practice: physician's alertness to the condition essential. *J Clin Gastroenterol*. 2007;41(2):152-156.
32. Virta LJ, Saarinen MM, Kolho KL. Declining trend in the incidence of biopsy-verified coeliac disease in the adult population of Finland, 2005-2014. *Aliment Pharmacol Ther*. 2017;46(11-12):1085-1093.
33. Midhagen G, Järnerot G, Kraaz W. Adult coeliac disease within a defined geographic area in Sweden: A study of prevalence and associated diseases. *Scand J Gastroenterol*. 1988;23(8):1000-1004.
34. Fernandez A, Gonzalez L, de-la-Fuente J. Coeliac disease: clinical features in adult populations. *Rev Esp Enferm Dig*. 2010;102(8):466-471.