The incidence and aetiology of acute pancreatitis across Europe ☆

by

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Short title: Acute pancreatitis across Europe

Key words: Acute pancreatitis, incidence, aetiology, Europe

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Abstract

Background: Acute pancreatitis is increasingly one of the most important acute gastrointestinal conditions throughout much of the world, although incidence and aetiology varies across countries and regions. This study investigated regional and national patterns in the incidence and aetiology of acute pancreatitis, demographic patterns in incidence and trends over time in incidence across Europe.

Methods: A structured review of acute pancreatitis incidence and aetiology from studies of hospitalised patient case series, cohort studies or other population based studies from 1989 to 2015 and a review of trends in incidence from 1970 to 2015 across all 51 European states.

Results: The incidence of acute pancreatitis was reported from 17 countries across Europe and ranged from 4.6 to 100 per 100 000 population. Incidence was usually highest in eastern or northern Europe, although reported rates often varied according to case ascertainment criteria. Of 20 studies that reported on trends in incidence, all but three show percentage increases over time (overall median increase = 3.4% per annum; range = -0.4% to 73%). The highest ratios of gallstone to alcohol aetiologies were identified in southern Europe (Greece, Turkey, Italy and Croatia) with lowest ratios mainly in eastern Europe (Latvia, Finland, Romania, Hungary, Russia and Lithuania).

Conclusions: The incidence of acute pancreatitis varies across Europe. Gallstone is the dominant aetiology in southern Europe and alcohol in eastern Europe with intermediate ratios in northern and western Europe. Acute pancreatitis continues to increase throughout most of Europe.

Introduction

Acute pancreatitis has increasingly become one of the most important acute gastrointestinal disorders throughout much of the world, including Europe, Asia and North America [1-3]. The two main aetiologies of acute pancreatitis, gallstone and alcohol, often account for approximately 60 to 80% of all cases, although this varies across countries and regions. There have been several previous reviews of the incidence or aetiology of acute pancreatitis [1,2,4-7], although they have not focused on Europe [1,2,4-7], or have concentrated on first attacks of acute pancreatitis [2].

In 2013, the main European gastroenterology organisation, United European Gastroenterology, commissioned the authors to review the disease burden of all major gastrointestinal disorders and the organisation and delivery of gastroenterology services across 35 European countries [3]. This study provides a structured review of acute pancreatitis incidence and aetiology across all 51 European states up to December 2015.

The objectives of this review were, first, to establish national and regional patterns in the incidence and aetiology of acute pancreatitis across Europe. Second, to determine demographic patterns in acute pancreatitis incidence. Third, to establish trends over time in incidence, for all cases of acute pancreatitis and also according to aetiology and patient demographics.

Methods

Scope

The coverage of this review was all 51 European countries. The review included studies written in all European languages that covered the 27 year period from January 1st 1989 to December 31st 2015.

The 51 European countries were grouped into the following four regions: northern Europe (Denmark, Finland, Iceland, Ireland, Norway, Sweden and the UK - England, Wales, Scotland and Northern Ireland); western Europe (Austria, Belgium, France, Germany, Liechtenstein, Luxembourg, Monaco, the Netherlands and Switzerland); eastern Europe (Armenia, Azerbaijan, Belarus, Bulgaria, the Czech Republic, Estonia, Georgia, Hungary, Kazakhstan, Latvia, Lithuania, Moldova, Poland, Romania, Russia, Slovakia and the Ukraine) and southern Europe (Albania, Andorra, Bosnia and Herzegovina, Croatia, Cyprus, Greece, Italy, Kosovo, Macedonia, Montenegro, Malta, Portugal, San Marino, Serbia, Slovenia, Spain, Turkey and the Vatican City).

Inclusion and exclusion criteria

For the first two study objectives on acute pancreatitis incidence and aetiology, the review included studies that reported population based incidence or aetiology from hospitalised patient case series, cohort studies or population based epidemiological studies. STROBE guidelines were followed when assessing each of the studies for inclusion in the review. Acute pancreatitis is one of few disorders that almost invariably requires hospitalisation during the acute phase so virtually all evidence on incidence and aetiology is based on inpatient care.

The review excluded studies that focused solely on particular aetiologies or severities of acute pancreatitis, studies of restricted patient demographic groups, studies of less than 30 cases of

acute pancreatitis, and studies of selected patient groups; for example, based on patients with specific co-existing diseases or patients recruited with eligibility criteria for the purposes of randomised controlled trials or case control studies. Although some of the reports incorporated primary care records or data, the review also excluded those that were based entirely on electronic primary care data, as almost all cases of acute pancreatitis are treated through secondary care. The review included studies conducted either wholly or mostly during the 27 year period from 1989 to 2015. For studies that did not specify the study period, we included those published after 1992.

For the third study objective on trends in acute pancreatitis incidence, the review included longitudinal studies based on the same geographical population. It excluded 'repeat' studies on the same location that used differing methodology during separate time periods. For this investigation of trends in incidence, the review period was extended retrospectively from 1989 to include studies with time points that dated back to 1970.

Search criteria

The review was based on PubMed and Embase information sources; World Health Organization reports and publications; grey literature information sources including the System for Information on Grey Literature in Europe (Sigle) and Google Scholar; extensive hand searching of reference lists of papers and reports for further information; and an e-mail survey of 30 United European Gastroenterology national representatives from countries across Europe. The search terms used were "acute pancreatitis" or "pancreatitis" combined with "incidence*", "admission*", "etiology" or "aetiology" and with "Europe" or the 51 individual European countries.

Data extraction

Eligible studies were reviewed for inclusion against the stated criteria. The following data items were extracted using a designed data extraction sheet: country and region, study time period, number of cases, patient age details, population incidence of acute pancreatitis, aetiology and whether the study case definition identified first attacks of acute pancreatitis only, subsequent attacks also or included all hospital admissions for acute pancreatitis. The aetiology of acute pancreatitis was grouped into three categories; gallstone, alcohol and other or idiopathic. The 'other' aetiologies typically include viral infections, trauma, malignancies, cystic fibrosis and complications of chemotherapy or various medications, but usually amount to relatively few cases compared with idiopathic cases. When extracting information from the studies, pairs of investigators/researchers consulted to compare findings and reach consensus. Where consensus was not reached, another investigator was consulted.

Statistical methods

Meta analyses of acute pancreatitis aetiology were based on studies within the same countries and within the same European regions and were weighted by study size. To avoid major under-ascertainment of aetiologies and possible biases, the meta analyses included only studies that determined the two main aetiologies of acute pancreatitis – alcohol or gallstone – in at least 50% of cases. Incidence rates were expressed per 100 000 population. Time trend analysis and mean annual percentage increases or reductions were used to assess changes over time in incidence. Trends were presented graphically, with time points that were spaced at least four years apart. Other statistical methods include Fisher's exact test to compare studies regionally across Europe (east, west, north or south) according to whether they reported a higher alcohol: gallstone or gallstone: alcohol aetiology ratio. Statistical significance was measured at the conventional 5% level.

Results

The numbers of studies and European countries included for the different objectives of the review are as follows: i). national and regional patterns in acute pancreatitis incidence (33 studies across 17 countries) and aetiology (55 studies, 29 countries); ii). demographic patterns in incidence (ten studies, seven countries); iii). trends over time in acute incidence overall (20 studies, 10 countries) and according to aetiology (five studies, five countries) and patient demographics (six studies, five countries). The numbers of studies and countries covered in each objective are summarised for the four regions of Europe in Table 1.

Incidence of acute pancreatitis across Europe

Table 2 shows population-based incidence rates for acute pancreatitis reported across Europe from 1989 to 2015. Incidence ranged from 4.6 per 100 000 in Tirana, Albania (from 2005 to 2012) [8], to 100 per 100 000 in the Świętokrzyskie Voivodeship province of Poland in 2011 [9]. The only other study from eastern Europe that reported incidence was from Trzebnica, Poland (64 per 100 000 from 2005 to 2010) [10].

Other studies that reported high incidence of >40 per 100,000 were from the north east of England (56.5 per 100 000) [11], Reykjavík, Iceland (46.7) [12], Munich, Germany (42.8) [13], and Alicante, Spain (45.1) [14]. Three other studies in Table 2 with high incidence - national studies from Spain (72.5 per 100 000 in 2011) [15], Scotland (41.9 in 1995) [16], and Finland (73.4 in 1989) [17] – are each based on all admissions for acute pancreatitis, which include re-admissions for the same attacks and thus inflate reported incidence. Some studies in Table 2 reported incidence based on first attack cases of acute pancreatitis, while others included recurrent attacks.

Of ten studies that reported acute pancreatitis incidence according to patient age group (Figure 1a) all show increasing incidence with age. In most studies, incidence increased quite sharply over the youngest adult age groups up to about 40 years, levelled off or fell over middle aged groups from approximately 40 to 60 years, before increasing most sharply across oldest age groups. When restricting this analysis to studies that were based on individual validation of diagnoses as well as exclusion of recurrent attacks of acute pancreatitis [22,44,49], there were more consistent increases in incidence across successive age groups and much lower incidence (<85 per 100 000) in the oldest age groups (Figure 1b).

Three studies reported incidence rates according to patient age group and sex, separately for the two main aetiologies of acute pancreatitis [22,44,46]. They showed peaks in alcoholic acute pancreatitis incidence among both men and women in or around the 35-44 year age group and highest incidence of biliary acute pancreatitis among the oldest study age groups (65+ years in Croatia and 75+ years in Lüneburg County, Germany and across Wales; supplementary figure).

Aetiology of acute pancreatitis across Europe

Table 3 shows the three main aetiologies of acute pancreatitis (alcohol, gallstone and other or idiopathic aetiology) reported from studies across Europe. Of 11 studies from eastern Europe, seven (64%) had a higher ratio of alcohol to gallstone aetiologies [10,24-28,77], which is significantly higher than for two of 16 studies from southern Europe (13%; p=0.012) [8,30], and for three of 21 studies from northern Europe (14%; p=0.013) [29,31], although not significantly different to three of nine studies from western Europe (33%; p=0.37) [28,32]. Studies that reported the highest ratios of gallstone to alcohol acute pancreatitis of more than six to one are solely from southern European Mediterranean countries, Greece [28], Turkey [33], and Italy [34,35], while studies with the lowest ratios of gallstone to alcohol aetiology of

less than 0.5 to one are mainly from eastern European countries, Hungary [28], Latvia [26], and Romania [25], along with Finland [31].

Figure 2 shows a meta analysis of the alcohol: gallstone aetiology ratio for each country, illustrating highest levels of gallstone aetiology all from southern European countries (Greece, Turkey, Italy and Croatia) and highest levels of alcohol aetiology from eastern Europe (Latvia, Romania, Hungary, Russia and Lithuania) and Finland. A meta analysis of aetiology across the four European regions shows the following ratios of alcohol : gallstone : other & idiopathic (as percentages): northern Europe (24:39:37), western Europe (33:39:27), eastern Europe (40:33:26) and southern Europe (20:52:28).

Trends in incidence of acute pancreatitis

Longitudinal trends in incidence of acute pancreatitis since 1970 have been reported from 20 studies (Figure 3a); from northern (13), western (four) and southern (three) Europe. All but three studies, two from Lüneburg County, Germany [18,22], and one from Copenhagen, Denmark [36], show increases over time. The overall median increase was 3.4% per annum (range = -0.4% to 73%). The largest increases in incidence were reported from three of the earliest studies during the 1970s, from Nottingham [39,40], and Bristol, England [41] (Figure 3a). When confining this analysis of trends in incidence to the eight studies that both excluded recurrent attacks of acute pancreatitis and were based on individual validation of diagnoses, increases in incidence over time were sometimes less than in the other studies (Figure 3b).

Trends in incidence according to aetiology

Five studies reported on trends in incidence according to aetiology [18,19,42-44]. A national study from Ireland from 1997 to 2004 reported greater increases in alcohol than biliary acute

pancreatitis from 1997 to 2004 [42], while a study from Malmo, Sweden conversely reported a significant increase for biliary aetiology but a significant reduction for alcohol aetiology from 1985 to 1999 [43]. The other studies, from Lüneburg County, Germany (1987-2006) [18], the North Adriatic region of Croatia (2000-2009) [44], and Bergen, Norway (1996-2006) [19], reported little variation in trends according to main aetiology.

Trends in incidence according to patient demographics

Of the 20 studies that reported on trends in incidence (Figure 3), six reported trends according to patient age group [17,20,21,42,45,46]. Of these six, two reported largest increases among young women aged <35 years, across England from 1998 to 2003 (11% average annual increase) [45], and across Wales from 1999 to 2011 (7.9% increase) [46]. Two other studies reported largest increases among young men; aged 20-29 years across Ireland from 1997 to 2004 [42], and aged 25-44 years across Finland from 1970 to 1989 [17]. The remaining two studies, across Sweden from 1988 to 2003 [20], and North Jutland, Denmark from 1981 to 2000 [21], reported largest increases among people in older age groups of 70+ and 80+ years.

13 studies reported on trends in incidence according to patient demographics. Six identified larger increases among men than women, from Denmark [47], Finland [17], Lüneburg County, Germany [18], Ireland [42], the Oxford region of England [48], and Wales [46]. Six others across England [45], Sweden [20], North Jutland, Denmark [21], Malmo, Sweden [43], the North Adriatic region of Croatia [44], and the Netherlands [49], reported larger increases among women. The remaining study from Bergen, Norway [19], reported similar increases in acute pancreatitis among men and women.

Discussion

This study provides a first review of acute pancreatitis incidence, aetiology and trends in incidence across all 51 European countries.

Incidence of acute pancreatitis across Europe

The incidence of acute pancreatitis varied across Europe with highest incidence (>40 per 100 000 population) usually reported from eastern or northern regions, including studies from Poland, Iceland, Germany, Norway, Spain and the north east of England. High incidence was also reported from Finland, Spain and Scotland, although based on all hospital admissions for acute pancreatitis. Globally, high incidence (>40 per 100 000) has also been reported from countries including Japan (49.4 per 100 000 population) [50], the USA (43.8) [51], and Taiwan (56.9) [52].

Consumption of alcohol across Europe is highest in eastern Europe along with some northern countries including Finland [53,54], which reflects countries with some of the highest incidence of acute pancreatitis across Europe. However, many of the studies with high incidence had gallstone: alcohol aetiology ratios that were roughly equal or moderately higher for gallstone; from Poland (1.22:1 and 0.45) [9,10], Iceland (1.83) [12], Germany (0.94) [13], Spain (2.11) [14], and north east England (1.48) [11]. This suggests that high incidence of acute pancreatitis in many regions is also linked strongly to gallstone disease.

The incidence of gallstone acute pancreatitis was highest in older people and alcohol acute pancreatitis often among young/middle age groups around 35-44 years. However, incidence reported among oldest patient age groups was typically lower in studies that excluded recurrent attacks and were also based on individual validation of diagnoses. This suggests that

the methodology used in different studies partly explains the high incidence reported for oldest patients in some.

Aetiology of acute pancreatitis across Europe

This review shows strong regional patterns in aetiology across Europe. Gallstone is the dominant aetiology in Mediterranean and other southern European countries, including Italy, Greece, Turkey, Spain, Portugal and Croatia, with aetiology ratios for gallstone: alcohol often more than 5:1 and sometimes more than 10:1. Alcohol aetiology is the dominant aetiology in most eastern European studies, while most reports from northern and western Europe show more equal ratios of alcohol to gallstone aetiology.

It was not feasible to provide a satisfactory analysis of alcohol consumption across the European countries in relation to the incidence of alcoholic acute pancreatitis, since pan-European alcohol data are provided at national level, whereas alcohol aetiology incidence data were almost invariably reported from single centre or small regional studies, which are often unrepresentative of the wider countries. Furthermore, there is also a lack of gallstones prevalence data at population level across Europe to enable investigation of a possible relationship with biliary acute pancreatitis. Nonetheless, the strong regional aetiological pattern of acute pancreatitis across Europe almost certainly reflects regional European differences in both alcohol consumption and risk factors for gallstones including thalassaemia, sickle cell disease, obesity and diet. By far the highest European prevalence of thalassaemia, sickle cell disease and other thalassaemia traits is found in the Mediterranean countries of southern Europe [55,56], including Greece, Turkey and Italy, while the highest European incidence of gallstones in recent years has been reported from Greece [57].

A dose response relationship between levels of alcohol consumption and the risk of acute pancreatitis has been established through systematic review and meta analysis [58], although evidence on associations between alcohol consumption and acute pancreatitis incidence at population level is not always consistent [1,2,4,5,13,17,43]. The limited evidence on specific causes of alcoholic acute pancreatitis suggest a causal effect for constituents in spirits but no relationship with wine consumption [59,60]. By far the heaviest consumption of spirits is in parts of eastern Europe and highest wine consumption in Mediterranean countries [53,54], which would further explain the aetiological pattern of acute pancreatitis across Europe.

Trends in incidence of acute pancreatitis

Apart from two studies from Germany [18,22], that were confined to first attacks of acute pancreatitis, and one from Denmark during the late 1970s [36], all other European studies during the last 45 years have documented increases in incidence over time [median increase = 2.9% per annum [range = -0.4% to 73%]. The largest increases were reported from the earliest studies during the 1970s. Other studies dating back further to the 1950s or 1960s similarly reported steep increases in incidence [48,61-64], which would be linked, at least partly, to major diagnostic advances at this time.

Increases in incidence tend to be larger in studies that included recurrent attacks of acute pancreatitis and also in national studies that did not validate diagnoses in individual cases. This suggests that the inclusion of recurrent attacks may contribute to the witnessed increases in incidence in some studies. It is also possible that individual validation of diagnoses in some studies avoids over diagnosing acute pancreatitis which could otherwise inflate increases in incidence over time. The increases in incidence often appear to be greater in large national studies than in smaller localised studies, which are often based around specialist or tertiary centres that receive more referrals of severe and complicated cases. They are also sometimes

located in cities or affluent areas which can be unrepresentative of wider countries, with variation in population risk factors that could also partly explain differential increases in incidence.

Trends in incidence according to aetiology

There is limited and fragmented evidence on trends in acute pancreatitis incidence according to aetiology across Europe, and how they relate to changes in alcohol consumption and gallstone disease. A strong correlation between increasing incidence (overall) and alcohol consumption has been reported from Finland [17]. However, two studies from The Netherlands [38,49], reported increases in incidence (mostly of biliary or idiopathic aetiology) during periods with little or no increase in per capita alcohol consumption.

The overall pattern of increasing incidence throughout much of Europe during the last 45 years, probably reflects increases in alcohol consumption at times in some countries and regions, and a stronger influence of gallstone disease in other regions, while other factors may include changes in diet, medications and lyperlipidaemia. Per capita alcohol consumption increased during the study period in many European countries, especially from the 1970s to the 1990s [53,54]. The very limited evidence on trends in gallstone disease across Europe, mainly from England [65,66], and Greece [67], also shows mostly large increases in incidence over time.

Trends in incidence according to patient demographics

Studies from England and Wales have reported largest increases in acute pancreatitis among young women aged less than 35 years [45,46], and other studies from Ireland and Finland among young men [17,42], which would also be mainly of alcohol aetiology. However, other Scandinavian studies from Denmark and Sweden have reported largest increases in incidence

among oldest age groups, mainly of biliary aetiology [20,21]. There was also no clear pattern across Europe when comparing trends in incidence among men and women.

Strengths and limitations

Strengths of this review include the geographical breadth across 51 European countries. It also sought to address any publication biases by searching grey literature, hand searching reference lists from reports and by conducting an e-mail survey of 30 United European Gastroenterology representatives from countries across Europe. A limitation of the evidence in the review is variation in case inclusion criteria across studies which affects the reported incidence. Many studies were based on validation of diagnoses in individual cases, although for large national studies this would not usually be feasible. In the absence of validated diagnoses, there is potential for over diagnosing cases of acute pancreatitis, for example, as some cases of chronic pancreatitis can present with attacks of acute pancreatitis. Some studies were based on separate cases or attacks of acute pancreatitis, other studies excluded recurrent attacks, while others included all hospital admissions for acute pancreatitis. As subsequent attacks of acute pancreatitis are often of alcoholic rather than gallstone aetiology, inclusion of recurrent attacks can alter the main aetiology distribution. Inclusion of all hospital admissions incorporate readmissions for the same attack and hence inflate reported incidence, although these increases can be less when compared with those through including recurrent with first attacks. Although previous reviews have been confined to studies based on first attacks, as this would eliminate most of the evidence base across Europe, we included all studies, but provided sub analyses and detailed methodological differences throughout.

Further limitations are that incidence rates for gallstone and alcoholic aetiologies were mostly limited to single centre studies, while the proportion of idiopathic cases varies across studies. Although many of the studies included in the review were national studies, some were based on

cities, counties or regions, which may not be representative of the wider countries. There was also a lack of reporting from most eastern European countries and from most of the smallest or most recent European nation states.

Conclusion

The incidence of acute pancreatitis varies quite strongly across Europe, with highest rates reported from eastern and northern Europe. Gallstone is the dominant aetiology in southern Europe, and alcohol in eastern Europe with intermediate ratios of gallstone: alcohol in northern and western Europe. Acute pancreatitis continues to increase throughout most of Europe.

Acknowledgements The study was funded by United European Gastroenterology (UEG) as part of the UEG project "White Book - Survey of Digestive Health across Europe". The authors thank Michael Farthing, the UEG president, the UEG Future Trends Committee and the UEG National Society Representatives across Europe for their helpful advice and help with provision of study data.

Conflict of interest The authors declare that they have no conflict of interest.

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Table 1 **A summary of the numbers of studies and countries regionally across Europe that are covered for each of the review objectives**

Study objective	Number of studies (and number of countries) covered			
	Northern Europe	Western Europe	Eastern Europe	Southern Europe
1a). National and regional patterns in acute pancreatitis incidence	20 (9)	5 (2)	3 (2)	5 (4)
1b). National and regional patterns in the aetiology of acute pancreatitis	19 (8)	10 (5)	11 (7)	15 (9)
2). Demographic patterns in acute pancreatitis incidence	6 (4)	2 (2)	1 (1)	1 (1)
3a). Trends over time in acute pancreatitis incidence	13 (5)	4 (2)		3 (3)
3b). Trends over time in acute pancreatitis incidence according to aetiology	3 (3)	1 (1)		1 (1)
3c). Trends over time in acute pancreatitis incidence according to patient demographics	6 (6)			

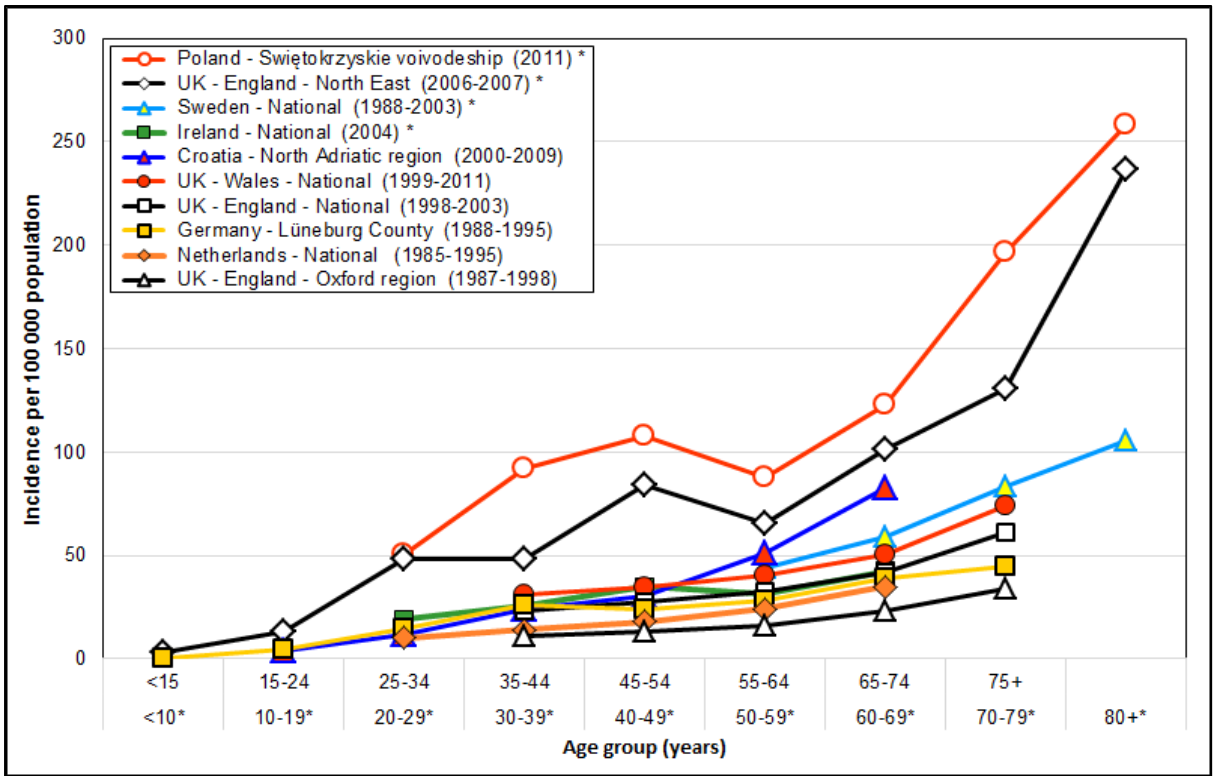
Table 2 Incidence rates for acute pancreatitis across Europe: studies ordered chronologically

Country	Region	Study Period	No. of Cases	Patient age range (Mean, SD)	Incidence per 100 000 population	Authors & reference
Poland	Świętokrzyskie Voivodeship province	2011	1044	20-90 [50] *	100	Gluszek SS and Koziel DD, 2012 [9]
Spain	National	2011	29 459 **	18+ [63.2] *	72.5	Méndez-Bailón M et al, 2015 [15]
UK – Wales	National	2011	1094	All (57.7, 19.2) §	35.8	Roberts SE et al, 2013 [46]
Iceland	Reykjavik	2010-11	134 †	All [57, 42-71] *	46.7	Vidarsdottir H et al, 2013 [12]
Albania	Tirana	2005-12	964 †	All (54.4, 16.9)	5.6	Kurti F et al, 2015 [8]
Germany	Munich	2008	188 †	All (55.5)	42.8	Phillip V et al, 2011 [13]
Poland	Trzebnica	2005-10	298 †	17-91 (50.5)	64.4	Bogdan D et al, 2012 [10]
UK – England	NE England	2006-07	963 †	All 57 [41-74] *	56.5	Ellis MP et al, 2009 [11]
Czech Republic	Olomouc	2006-07	170 †	5-91 (56.5)	17.0	Vinklerova I at al, 2010 [68]
Spain	National	2006	24 970 **	18+ [63.2] *	68.1	Méndez-Bailón et al, 2015 [15]
UK – Wales	National	2005	885	All (57.7, 19.2) §	30.1	Roberts SE et al, 2013 [46]
Germany	Lüneburg County	2002-06	175 †‡	All, ns	13	Lankisch PG et al, 2009 [18]
Croatia	North Adriatic region	2000-09	922 †‡	All (61, 15)	30.2	Stimac D et al, 2013 [44]
Ireland	National	2004	959	All (51.1, 19.9) §	23.6	O'Farrell A, 2007 [42]
Netherlands	National	2004	3120	All, ns	19.2	Spanier BW et al, 2008 [38]
Italy	Veneto region	2000-07	11 685	All [61.6,41.3-81.9] *	30.6	Saia M and Pietrobon F, 2009 [37]
Norway	Bergen	1996-06	567 †‡	7-98 [58] *	14.6	Omdal T et al, 2011 [19]
UK – England	National	1998-03	55 215	All (51.1, 19.9) §	22.4	Roberts SE et al, 2008 [45]
Sweden	National	1998-03	17 699 ‡	All [60, 45-74] *	33.1	Sandzen B et al, 2009 [20]
Spain	National	2001	22 148 **	18+ [63.2] *	67.0	Méndez-Bailón et al, 2015 [15]
UK – Wales	National	1999	789	All (57.7, 19.2) §	27.6	Roberts SE et al, 2013 [46]
Denmark	North Jutland	2000	2350 ‡	All, ns	24	Floyd A et al, 2002 [21]
UK – England	National	1999-00	11 373	All, ns	20.7	Tinto A et al, 2002 [69]
Germany	Lüneburg County	1997-01	172 †‡	All, ns	14	Lankisch PG et al, 2009 [18]
Iceland	Reykjavík	1998-99	67 †	19-85 [61]	32.3	Birgisson H et al, 2002 [70]
Sweden	Malmo	1999	ns †‡	All (59.4, 17.9) §	37	Lindkvist B et al, 2004 [43]
Ireland	National	1997	622	All (51.1, 19.9) §	17.5	O'Farrell A et al, 2007 [42]
Denmark	Copenhagen	1995-98	155 †‡	All (48)	33.5	Lund H et al. 2006 [29]
Sweden	National	1993-97	14 126 ‡	All [60, 45-74] *	32.0	Sandzen B et al, 2009 [20]
UK – Scotland	National	1995	ns **	All [54]	41.9	McKay CJ et al, 1999 [16]
Netherlands	National	1995	19 327 ‡	All (56.3)	15.9	Eland IA et al, 2000 [49]
UK – England	Wessex region	1994-95	186 †‡	15-98 [54] *	15.2	Toh SK et al, 2000 [71]
Germany	Lüneburg County	1992-96	142 †‡	All (55.3)	12	Lankisch PG et al, 2009 [18]
UK – England	Oxford region	1987-98	2979	All (56.3, 19.2) §	9.8	Goldacre MG and Roberts SE, 2004 [48]
Norway	Buskerud County	1992	93 †	21-96 [64] *	42	Halvorsen FA and Ritland S et al, 1996 [72]
Germany	Lüneburg County	1988-95	228 †‡	All, (55.3)	19.7	Lankisch PG et al, 2002 [22]
Denmark	National	1992	ns	All [43] * §	35.4	Worning H et al, 1994 [47]
Netherlands	National	1992	1785	All, (55.3)	11.8	Spanier BW et al, 2008 [38]
Spain	Alicante	1991	473 †	All [59, 42-76] *	45.1	Mínguez M et al, 1995 [14]
Sweden	National	1987-91	11 590 ‡	All [60, 45-74] *	27.0	Sandzen B et al, 2009 [20]
Norway	Bergen	1986-95	978 **	16-97 [64] *	30.6	Gislason H et al, 2004 [73]
UK – England	National	1989-90	7602	All, ns	14.5	Tinto A et al, 2002 [69]
Sweden	Malmo	1985-94	883 †**	All, ns	38.2	Appelros S and Borgstrom A, 1999 [23]
Sweden	Malmo	1985-94	547 †‡	All, ns	23.4	Appelros S and Borgstrom A, 1999 [23]
Finland	National	1989	2389 **	All, ns	73.4	Jaakkola M and Nordback I, 1993 [17]

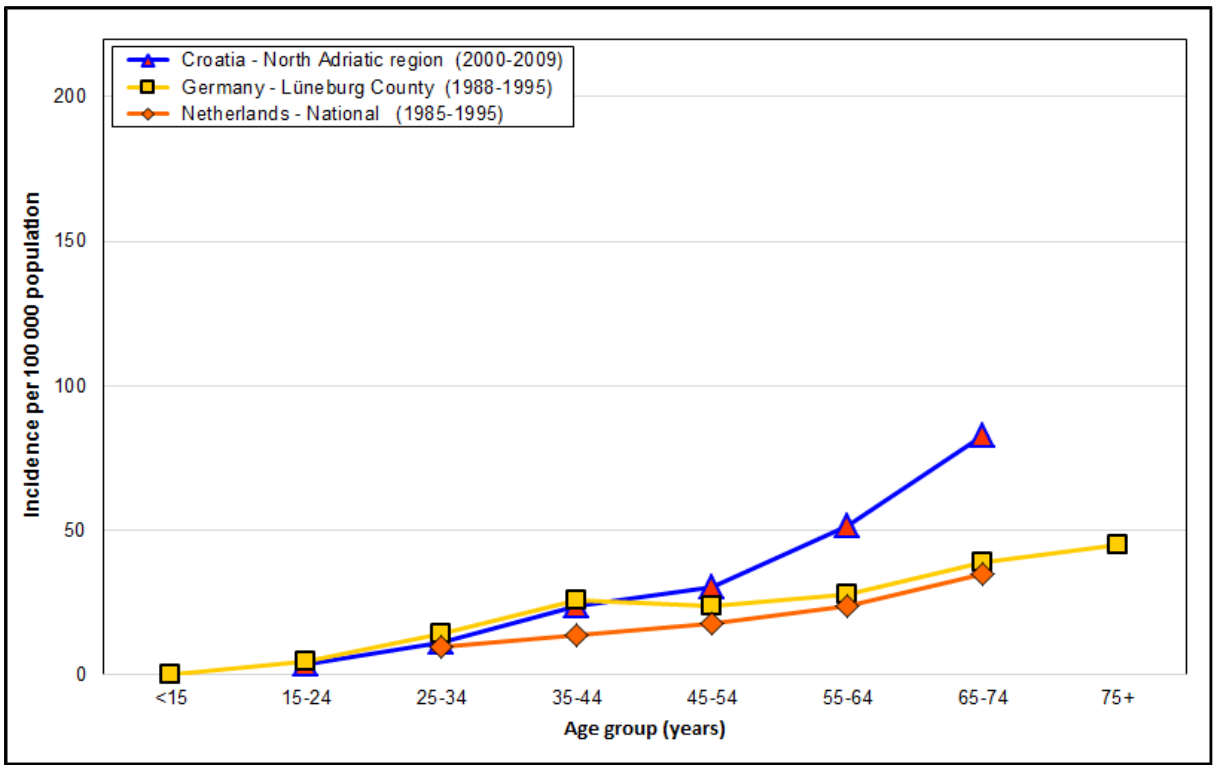
Notes

* Median (and Interquartile range) rather than mean age and SD reported
† Denotes studies based on individual diagnostic case validation
‡ Denotes studies that excluded recurrent attacks of acute pancreatitis
** Denotes studies that included all hospital admissions for acute pancreatitis, including re-admissions for the same attack
§ Refers to the entire study rather than the year(s) cited
ns not specified

Figure 1a **Age specific incidence rates for acute pancreatitis reported from studies across Europe**



1b) **Age specific incidence rates for acute pancreatitis reported from studies across Europe that were based on individual validation of cases and excluded recurrent attacks**



Notes
Details and references for these studies are provided in Table 2

Table 3 The main aetiologies of acute pancreatitis (expressed as percentages) across Europe: studies ordered chronologically

					Main aetiology (% of cases)				
Country	City / Region	Study period	No. of Cases	Mean patient age	Alcohol	Gallstone	Other & idiopathic	Ratio (gallstone: alcohol)	Authors & reference
Poland	Świętokrzyskie Voivodeship	2011	1044 †	53 *	27%	33%	40%	1.22	Gluszek S & Koziel D, 2012 [9]
Slovenia	Gradec, Zagreb	2010-12	139 †	56.5	39%	39%	22%	1.00	Vujasinovic et al, 2014 [74]
Iceland	Reykjavik	2010-11	134 †	57 *	23%	42%	35%	1.83	Vidarsdottir H et al, 2013 [12]
Serbia	Belgrade	2009-10	51 †	62	21%	55%	34%	2.55	Bezmarevic M et al, 2012 [75]
Albania	Tirana	2005-12	964 †	54.4	40%	38%	22%	0.95	Kurti F et al, 2015 [8]
Poland	Trzebnica	2005-10	298 †	50.5	49%	27%	24%	0.55	Bogdan J et al, 2012 [10]
Germany	Munich	2008	188 †	55.5	37%	35%	28%	0.94	Phillip V et al, 2011 [13]
UK - England	NE England	2006-07	963 †	57 *	29%	43%	28%	1.48	Ellis MP et al, 2009 [11]
Czech Republic	Olomouc	2006-07	170 †	57	31%	53%	16%	1.71	Vinklerova I at al, 2010 [68]
Slovenia	Gradec, Zagreb	2006-07	111 †	52	24%	21%	55%	0.85	Vujasinovic M et al, 2015 [74]
Lithuania	Kaunas	2005-07	108 †	54.1	43%	25%	32%	1.70	Dambrauskas Z et al, 2010 [24]
Denmark	Copenhagen	2005	32 †	ns	28%	44%	28%	1.57	Nøjgaard C et al, 2010 [76]
Romania	Bucharest	2004-05	62 †	49	58%	23%	19%	0.39	Diculescu M et al, 2005 [25]
Croatia	N Adriatic region	2000-09	922 †‡	61	19%	61%	20%	3.13	Stimac D et al, 2013 [44]
UK - Wales	National	1999-11	10 589	57.7	22%	37%	41%	1.68	Roberts SE et al, 2013 [46]
Hungary	Szeged	2004	124 †	59.8	14%	44%	42%	3.18	Takács T et al, 2008 [77]
Turkey	İzmir	ns	68 †	51	4%	65%	31%	11.3	Kasap E et al, 2009 [78]
Netherlands	North, 18 centres	2003	166 †‡	50	18%	43%	39%	2.37	Spanier BW et al, 2010 [79]
Norway	Bergen	1996-06	567 †‡	58	10%	50%	40%	5.15	Omdal T et al, 2011 [19]
Finland	Tampere	ns	233 †	48	56%	21%	23%	0.38	Khan J et al, 2013 [31]
Latvia	Riga	1999-06	274 †	47	54%	19%	27%	0.35	Pupelis G et al, 2008 [26]
UK - Scotland	Edinburgh	2000-04	759 †	57 *	33%	47%	20%	1.44	Mofidi R et al, 2007 [80]
Belgium	Brussels	2001-02	39 †	47	28%	49%	13%	1.75	Arvanitakis M et al, 2004 [81]
Turkey	Isparta	ns	61 †	49.7	8%	44%	48%	5.40	Cüre E et al, 2007 [82]
Russia	Nizhny Novgorod	ns	167 †	53	55%	32%	13%	0.59	Petrov MS et al, 2007 [27]
Italy	Ferrara	1998-02	549	65	9%	52%	39%	5.99	Gallerani M et al, 2004 [83]
Italy	37 centres	1996-00	1005 †	59.6	9%	60%	31%	7.06	Cavallini G et al, 2004 [34]
Turkey	Samsun	1998-02	199 †	55	7%	53%	40%	7.53	Kaya E et al, 2007 [33]
France	Paris	1999	88 †	58.5	38%	41%	21%	1.09	Karsenti D et al, 2002 [84]
Iceland	Reykjavík	1998-99	67 †	61	32%	42%	26%	1.31	Birgisson H et al, 2002 [70]
Poland	Warsaw	1989-07	533 †	ns	36%	48%	16%	1.33	Sieklucki J & Krzesniak N, 2009 [85]
Croatia	Zabok	1996-99	57 †	47	51%	49%	0%	0.97	Huis M et al, 2001 [30]
Denmark	Copenhagen	1995-98	155 †‡	48	45%	32%	23%	0.72	Lund H et al, 2006 [29]
Hungary	Szeged	1996	126 †	50.7	45%	29%	26%	0.63	Takács T et al, 2008 [77]
France	Nice	1994-95	121 †	ns	31%	43%	26%	1.37	Maes B et al, 1999 [86]
UK - England	Wessex region	1994-95	186 †	54 *	20%	33%	47%	1.63	Toh SK et al, 2000 [71]
Denmark	Copenhagen	1994	55 †	ns	49%	29%	22%	0.59	Nøjgaard C et al, 2010 [76]
Norway	Buskerud	1992	93 †	64 *	15%	51%	34%	3.36	Halvorsen FA & Ritland S, 1996 [72]
Austria	Graz	1992-94	91 †	55	41%	40%	19%	0.98	Kaufmann P et al, 1996 [32]
UK - England	Somerset	1991-95	210 †‡	67 *	11%	56%	32%	4.92	Norton SA et al, 2001 [87]
Sweden	Malmo	1985-99	929 †‡	59.4	25%	42%	33%	1.72	Lindkvist B et al, 2004 [43]
Germany	Ulm, Lüneburg	1990-94	232 †	ns	38%	35%	27%	0.92	Gullo L et al, 2002 [28]
Greece	Thessaloniki	1990-94	84 †	ns	6%	71%	23%	11.9	Gullo L et al, 2002 [28]
Hungary	Gyor, Szeged	1990-94	483 †	ns	61%	24%	13%	0.40	Gullo L et al, 2002 [28]
Italy	Bologna	1990-94	204 †	ns	13%	60%	27%	4.56	Gullo L et al, 2002 [28]
France	Paris	1990-94	65 †	ns	39%	25%	26%	0.64	Gullo L et al, 2002 [28]
Sweden	Malmo	1986-94	547 †‡	ns	32%	38%	30%	1.23	Appelros S & Borgstrom A, 1999 [23]
UK - Scotland	Glasgow	1989-93	279 †	53.3 *	35%	42%	24%	1.20	de Beaux AC et al, 1995 [88]
Spain	Alicante	1991	473 †	59 *	20%	52%	28%	2.11	Minguez M et al, 1995 [14]
UK - England	NW Thames	1988-92	631 †	53	29%	30%	41%	1.02	Mann DV et al, 1994 [89]
Germany	Lüneburg County	1988-95	228 †‡	55.3	32%	40%	28%	1.25	Lankisch PG et al, 2002 [22]
Norway	Bergen	1986-95	978 **	64 *	19%	49%	32%	2.51	Gislason H et al, 2004 [73]
France	Nice	1986-94	57 †	59.2	25%	51%	24%	2.07	Benchimol D et al, 1996 [90]
Portugal	Coimbra	1988-91	91 †	59	24%	59%	17%	2.45	Milheiro A et al, 1995 [91]

Notes

* Median rather than mean patient age reported

† Denotes studies based on individual diagnostic case validation

‡ Denotes studies that excluded recurrent attacks of acute pancreatitis

** Denotes studies that included all hospital admissions for acute pancreatitis, including re-admissions for the same attack

ns not specified

Figure 2 **A meta analysis of the main aetiologies of acute pancreatitis across Europe, based on 55 studies: countries ordered according to the ratio of alcohol to gallstone aetiology**

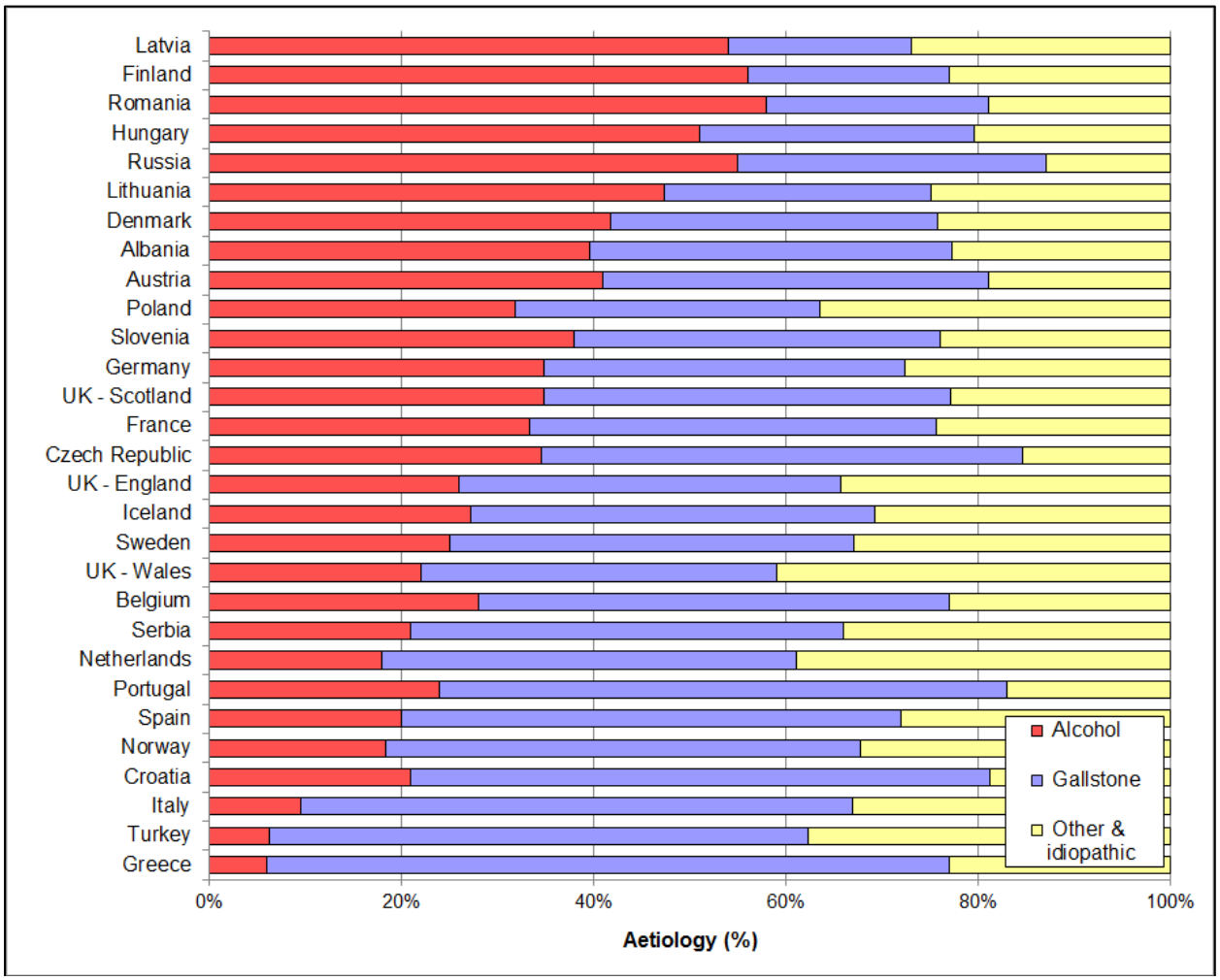


Figure 3a **Trends over time in the incidence of acute pancreatitis across Europe, based on longitudinal studies**

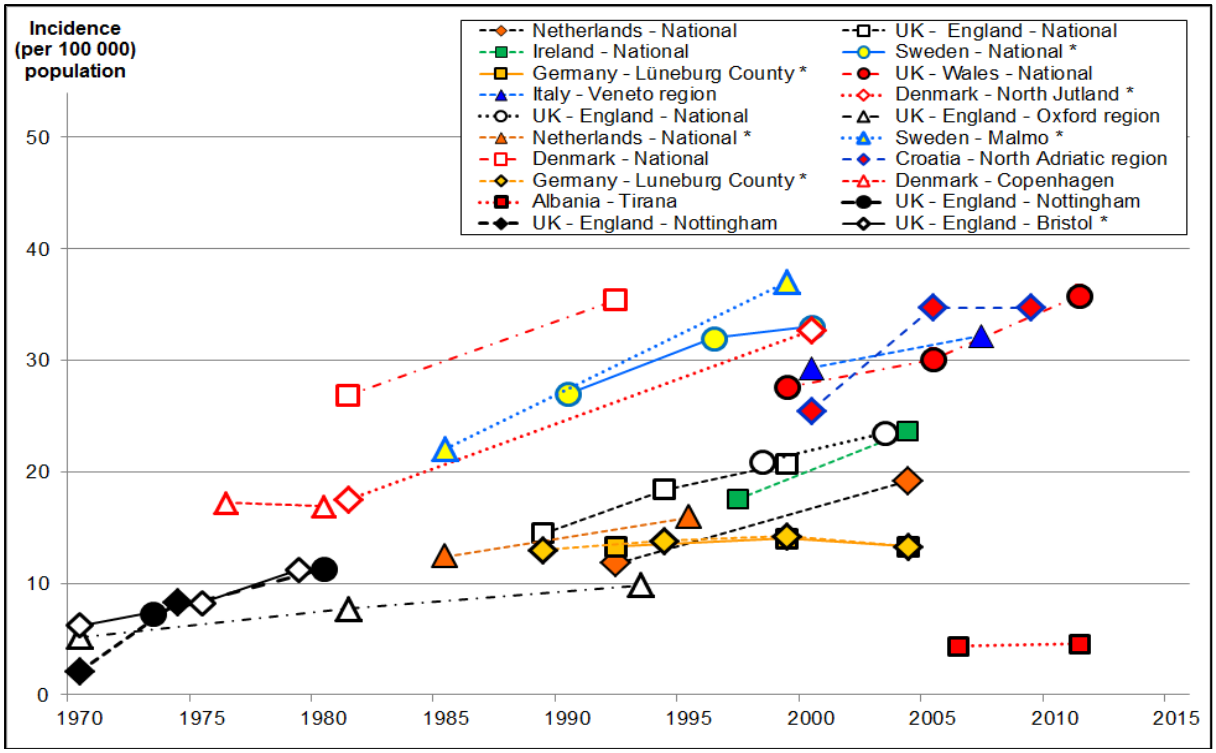
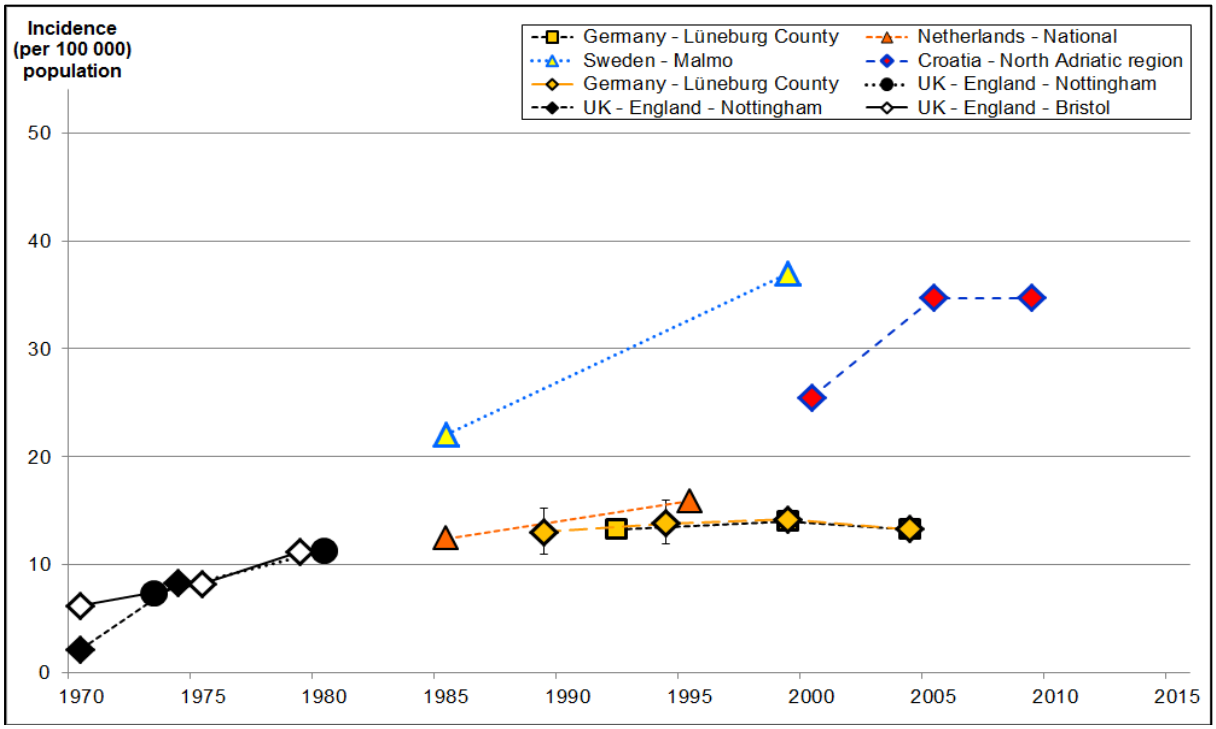


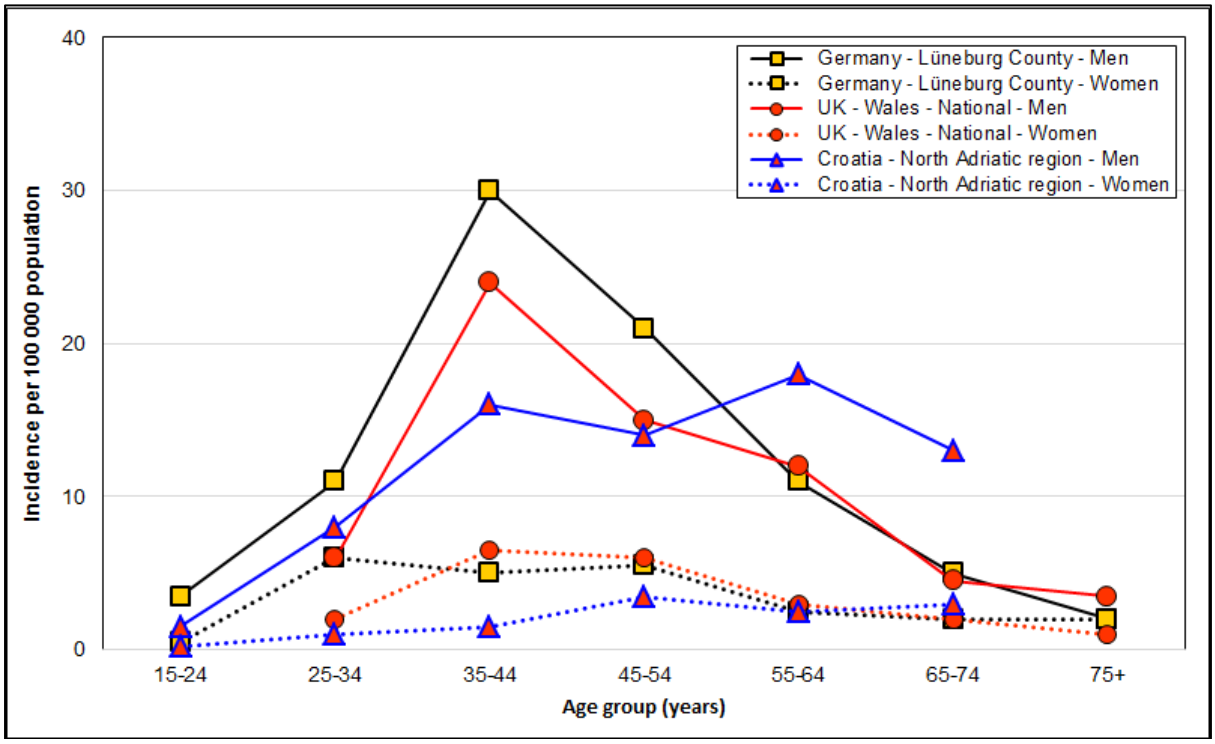
Figure 3b **Trends over time in the incidence of acute pancreatitis across Europe, based on longitudinal studies with individual validation of cases and exclusion of recurrent attacks of acute pancreatitis**



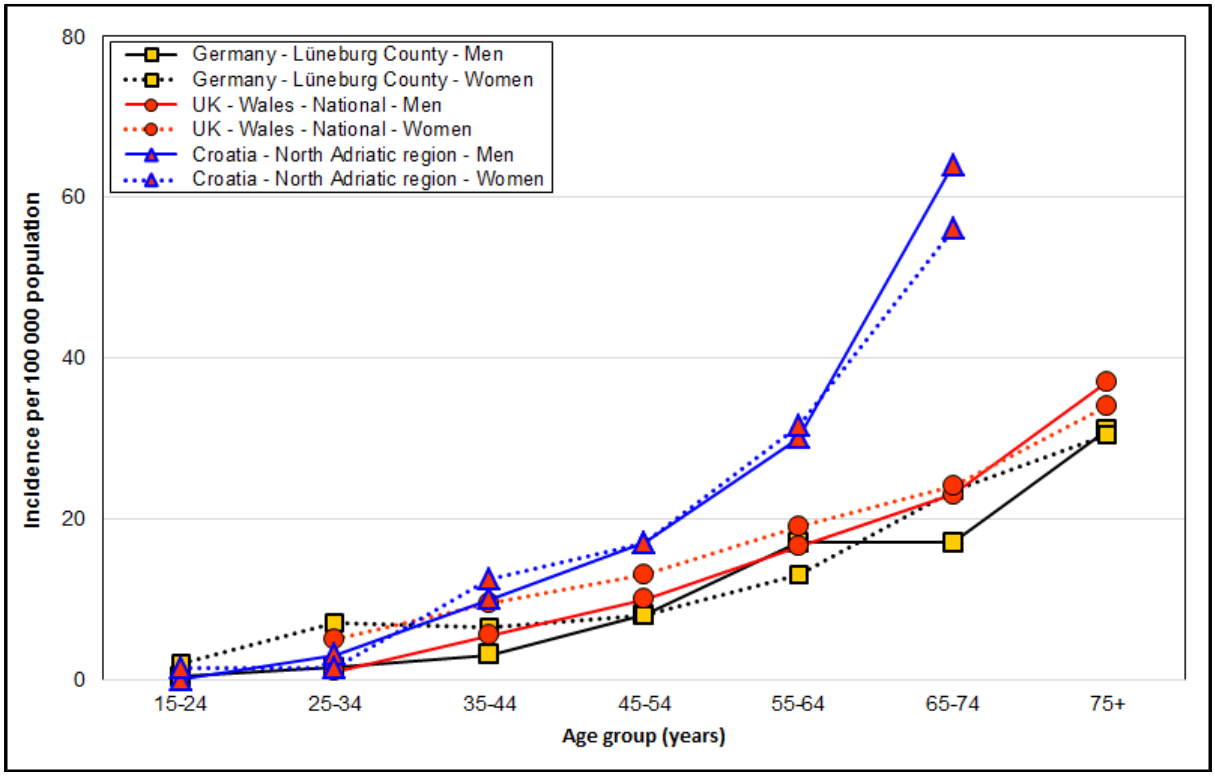
Notes
This graph excludes studies that included all hospital admissions for acute pancreatitis, which includes re-admissions for the same attack that can vary over time and inflate incidence
Details and references for the studies in this graph are included in Table 2 or are as follows: UK – England – Nottingham [39,40], UK – England – Bristol [41] and Denmark – Copenhagen [36]

Supplementary figure **Age specific incidence of the main aetiologies of acute pancreatitis reported from studies across Europe**

a). Alcohol aetiology



b). Gallstone aetiology



Notes
Details and references for these studies are provided in Table 2