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Hospitalised incidence and case fatality for upper gastrointestinal bleeding from 1999 to 2007: A record linkage study

by

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Abstract

Background: Upper gastrointestinal (GI) bleeding is the most common emergency managed by gastroenterologists.

Aim: To establish the hospitalised incidence and case fatality for upper gastrointestinal bleeding, and to determine how they are associated with factors including day of admission, hospital size, social deprivation and distance from hospital.

Methods: Systematic record linkage of hospital inpatient and mortality data for 24 421 admissions for upper GI bleeding among 22 299 people in Wales from 1999-2007.

Results: Hospitalised incidence of upper GI bleeding was 134 per 100 000. Case fatality was 10.0%. Incidence was stable from 1999 to 2007; case fatality fell by 3.1% per year (95% CI = 1.3%-4.8%). Incidence was associated significantly with social deprivation. Compared with weekday admissions, case fatality was 13% higher for weekend admissions and 41% higher for admissions on public holidays. There was little variation in case fatality according to social deprivation, hospital size or distance from hospital.

Conclusions: Incidence, but not case fatality, was associated significantly with social deprivation. The higher mortality for weekend and public holiday admissions could not be explained by measures of case mix and may indicate a possible impact of reduced staffing levels and delays to endoscopy at weekends in some hospitals.

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Introduction

Upper gastrointestinal (GI) bleeding is the most common emergency managed by gastroenterologists with approximately 25 000 inpatient admissions annually in the UK.[1] Upper GI bleeding occurs largely among people in older age groups, and has a higher incidence in males than in females.[2-4]

Upper GI bleeding in the UK and in Europe has been caused most frequently by peptic ulcer – particularly duodenal ulcer - followed by other aetiologies including varices, gastritis/erosions, oesophagitis, Mallory-Weiss tear, upper GI malignancies, duodenitis, gastric antral vascular ectasia and portal hypertension.[5-7] Many upper GI bleeds are caused by long term use of non-steroidal anti-inflammatory drugs, especially among older people, although patterns of prescribing have changed over time.[8] Other upper GI bleeding aetiologies are linked to alcohol consumption – such as oesophageal varices, Mallory-Weiss tear and oesophageal malignancies – which are increasing over time in some regions.[6,9] With an ageing population, and with sharp increases in alcohol consumption in the UK in the last 50 years,[10,11] upper GI bleeding is an important disorder.

The incidence of upper GI bleeding varies across the UK, with highest incidence reported in Scotland,[4,12,13] compared with lower rates often reported in southern England.[2,3,14,15] Upper GI bleeding has been associated with high levels of social deprivation in one study of the west of Scotland,[4] although little else has been reported on the relationship between upper GI bleeding and social inequality, particularly on a national scale. Local studies indicate that as the incidence of upper GI bleeding has increased over time, there has been little recent improvement in case fatality, which remains at about 10%.[6,7] There is also current interest in whether prognosis for emergency disorders varies according to the day of admission,[16,17] the size of hospital,[18] and the distance travelled to hospital,[19] although little has been reported about these for upper GI bleeding.

The main objectives of this study were to establish the incidence of hospital admissions for upper GI bleeding in Wales and case fatality at 30 days following admission, and to

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investigate whether case fatality is higher for admissions on weekends and public holidays. Further objectives were to assess trends over time in incidence and case fatality, and whether they are associated with factors including social deprivation, distance from hospital and hospital size.

Our main study hypotheses are that the incidence of upper GI bleed is associated strongly with social deprivation and that case fatality is increased for people who are admitted on weekends and public holidays - rather than on weekdays - and may be lower for people admitted to 'medium' size rather than to small or large hospitals.

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Methods

We used systematic record linkage of hospital inpatient and mortality data from the Patient Episode Database for Wales (PEDW) for 1999-2007. PEDW is a comprehensive administrative database covering inpatient and day case admissions to all NHS hospitals in Wales, incorporating systematic linkage to death certificate data from the Welsh Administrative Registrar,[20] and has been used as the basis of previous published studies.[21-24] The systematic record linkage of inpatient and mortality data enables all repeat hospital admissions to be identified for the same patients, and deaths following discharge from hospital to be included with in-hospital deaths.

We included adult patients who were admitted as an emergency for upper GI bleeding (where upper GI bleeding was recorded as the principal diagnosis on the first episode during the admission). Some upper GI bleeds occur as 'inpatient bleeds' following an admission for another disorder, for surgery or for maternity care. We therefore also included emergency, elective and maternity admissions for all other causes (when recorded as the principal diagnosis on the first episode) but where upper GI bleeding occurred subsequently (when recorded as the principal diagnosis of a subsequent episode during the admission). The International Classification of Diseases, 10th edition (ICD-10) codes used for upper GI bleeding categories are listed in the Appendix.

We included each person's first admission for upper GI bleeding after the start of the study period in April 1st 1999. Subsequent hospitalisations for upper GI bleeding in each patient were also included up to the study end in March 31st 2007, providing they occurred more than 30 days after the preceding admission. We investigated the aetiology/diagnoses for the upper GI bleeds using diagnoses recorded in any of the diagnostic fields during the admission.

Social deprivation scores were assigned anonymously using residential postcodes at the Lower Super Output Areas (LSOA; average population size of each LSOA = ~1500) using the Welsh Index of Multiple Deprivation (WIMD) 2005.[25] The WIMD 2005 is based on seven

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domains of social deprivation including income, housing, employment, environment, health, access to services, and education. The LSOAs were ranked according to their WIMD 2005 score and were categorised into quintiles, with quintile I representing the 20% of least deprived LSOAs and quintile V the 20% of most deprived LSOAs. Hospitals were classified by size based on the number of beds; as small (less than 400 beds), medium (400-599) and large (600+). We compared case fatality for those who were admitted on weekdays (Monday to Friday), weekends (Saturdays and Sundays) and public holidays. We also investigated whether diagnostic endoscopy of the upper gastrointestinal tract had been performed (using the OPCS-4 surgical procedure code G45, when recorded in any procedure field).

Hospitalised incidence rates for upper GI bleeding were calculated using the numbers of hospitalised cases as the numerators and the Welsh adult residential populations as the denominators, expressed per 100 000 population. To standardise incidence rates, we used the direct method and the total Welsh population during the study period as the standard. Case fatality at 30 day follow up was calculated using the numbers of deaths (from all causes) as the numerators and the numbers of hospitalised cases as the denominators, and were expressed as percentages. To standardise case fatality, we used the direct method and the total population of people admitted with upper GI bleeding. When investigating case fatality, we adjusted for major co-morbidities (circulatory diseases, all malignancies except upper GI, liver disease, COPD, diabetes and renal failure) that were recorded in any of the other diagnostic fields during the admission (see notes to Table 3 for ICD-10 codes).

Urban/rural residences were measured using five categories, based on 'settlement sizes' of <2500, 2500-9999 up to 100 000 people.[26] Distances from patients' residences to the hospital of admission were calculated using ArcGIS Geographical Information System (GIS) software and were measured in five categories from <3 kilometres (km), 3-9.99 km up to 30+ km. Statistical methods used include multiple logistic regression analysis, Spearman's rank (SR) correlation, the t-test, and the Mann Whitney test.

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Results

From 1999 to 2007 there were 24 421 hospitalisations for upper GI bleeding among 22 299 different adults. 20 724 people were admitted once during the eight year study period, 1239 twice, 221 three times and 115 on four or more separate occasions. Most (21 722; 88.9%) presented with upper GI bleeding, and 2699 (11.1%) occurred as inpatient bleeds. The patients' mean age was 64.1 years (range = 18-108; 95% CI = 63.9-64.4). Women were older (p<0.001) than men (mean 68.5 years vs 60.4 years).

The most common diagnoses for the bleeds were peptic ulcer (5437; 22.3%) – including duodenal ulcer (2661; 10.9%), gastric ulcer (2485, 10.2%) and unspecified peptic ulcer (291; 1.2%) - followed by gastritis & duodenitis (3377; 13.8%), oesophagitis (2459; 10.1%), Mallory-Weiss tear (1485, 6.1%), varices (722; 3.0%) and upper GI malignancies (309; 1.3%).

Incidence of upper GI bleeding

The overall hospitalised incidence rate of upper GI bleeding was 134 per 100 000 population (Table 1). Incidence was significantly higher in men (153 per 100 000) than in women (117) and it increased sharply with age (Table 1) with highest incidence in the oldest age group (85+ years) for both men (864 per 100 000 population) and women (739).

Table 2 and Figure 1 show large geographical variation in the incidence of upper GI bleeding across Wales. Incidence was by far the highest in the local authority with the highest social deprivation, Merthyr Tydfil (268 per 100 000) followed by other local authorities with high levels of deprivation (Table 2). Figure 2a shows a significant association between the incidence of upper GI bleeding and social deprivation. Incidence was 2.0 times higher (95% CI = 1.9-2.1) in the most deprived quintile V (189 per 100 000 population) than in the least deprived quintile I (94).

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Diagnostic endoscopy of the upper GI tract

Diagnostic endoscopy was recorded in 10 594 (43.4%) of the 24 421 admissions. Recorded endoscopy varied from 31.7% to 60.5% across hospitals and was higher (p<0.001) in small (51.5%) than in medium (41.9%) or large (40.6%) hospitals.

1733 (16.4%) of the patients were scoped on the day of admission, 3321 (31.3%) on the following day, 1452 (13.7%) on the second day and 4078 (38.5%) after 3+ days. Recorded endoscopy was significantly lower (p<0.001) for admissions on Fridays (37.1%) and Saturdays (38.8%) than on other days (which varied between 44.3% for Sundays to 47.8% for Tuesdays). Rates of endoscopy on the day of admission were lower (p<0.001) for admissions on Saturdays (8.5%) and Sundays (7.4%) than on weekdays (17.5% to 20.9%). The median time to endoscopy was higher (p<0.001) for admissions on Fridays and Saturdays (both 3 days) and on Sundays (2 days) than for other days of the week (one day).

Case fatality at 30 days following hospital admission

There were 2452 deaths at 30 days, with overall case fatality of 10.0%. Age-specific case fatality increased sharply from <1% among people aged 18-34 years to 21% for people aged 85+ years (Table 3). Overall, age adjusted case fatality was significantly lower among females than among males (odds ratio = 0.89; 95% CI = 0.81-0.97), while age-specific case fatality was higher among males than among females in most age groups.

There was large variation in case fatality across local authorities, ranging from 7.7% to 13.7% (Table 2). Local authorities with lowest case fatality often had the highest incidence. Although case fatality was slightly higher in the most deprived quintiles (IV and V both = 10.5%) than in the most affluent (I = 9.6% and II = 9.4%) this was not significant (Figure 2b).

Age and sex adjusted mortality for weekend admissions was 13% higher than for weekdays (odds ratio = 1.13; 95% CI = 1.02-1.25) while mortality for admissions on public holidays was 41% higher (odds ratio = 1.41; 1.04-1.91; Table 3). After adjusting also for major co-morbidities, the increased mortality for weekend and public holiday admissions was largely

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unaffected (odds ratio = 1.11; 1.00-1.23 and 1.42; 1.05-1.92 respectively). The hospital admission rate was lower on weekends and public holidays (109 and 113 per 100 000 respectively) than during the week (145 per 100 000; Table 3). However, people admitted on weekends and public holidays were slightly but significantly younger (63.4 vs 64.4 years; p=0.020), were discharged slightly sooner (overall median length of stay = 4 days for both; but p=0.022) and had similar levels of co-morbidities recorded compared with patients who were admitted during the week (see notes to Table 3).

Case fatality was slightly lower in medium size hospitals (9.3%) than in small or large hospitals (11.1% and 10.8%) but after adjusting for age and sex, these differences were not significant (Table 3). Patients resident in the most urban locations had slightly higher mortality than those in the most rural locations (odds ratio = 1.14; 95% CI = 1.00-1.31), although after adjusting for social deprivation, this risk was not significant (1.06; 0.91-1.23). There was little variation in case fatality according to distance from hospital (Table 3).

Case fatality varied strongly according to aetiology/diagnoses, with significantly increased age and sex adjusted mortality for upper GI malignancies, varices and duodenal ulcer, and significantly reduced mortality for Mallory Weiss tear, oesophagitis, gastritis & duodenitis, gastric ulcer, other specific diseases of the stomach & duodenum (including gastric antral vascular ectasia) and complications of analgesics, antipyretics and anti-inflammatory drugs (Table 3). Of the major co–morbidities, age and sex adjusted mortality was significantly increased for liver disease (odds ratio = 4.90), renal failure (3.75), non-upper GI malignancies (3.64), circulatory diseases (1.73) and COPD (1.55), but not for diabetes (1.12; Table 3).

Over the study period, out of hours endoscopy services was provided in three study hospitals, which had overall case fatality of 12.2%, 7.7% and 9.2% respectively. Age and sex adjusted case fatality for admissions on weekends and public holidays for these three hospitals was similar to that for all other hospitals (odds ratio=0.98; 95% CI=0.80-1.21; p=0.88). Corresponding mortality for weekday admissions was similar (0.91; 0.82-1.03; p=0.12).

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Trends in the incidence of upper GI bleeding and case fatality

There was no change over time in the incidence of upper GI bleeding over the eight year study period from 1999/2000 to 2006/07 ($p=0.74$; Table 4). However, case fatality fell significantly ($p<0.05$) by 3.1% per year on average (95% CI = 1.3%-4.8%) from 11.4% in 1999/2000 to 8.6% in 2006/07.

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Discussion

We found a very strong association between the incidence of upper GI bleeding and social deprivation, with highest incidence among the most deprived groups. Mortality was increased among people who were admitted on weekends and public holidays compared with those admitted during the week. We also found a stable incidence of upper GI bleeding from 1999 to 2007, but a significant reduction over time in mortality.

A major strength of this study is that it is one of the largest investigations of upper GI bleeding, covering more than 24 000 cases in a defined population. It investigated the influence of several factors on upper GI bleed mortality, including week day of admission, size of hospital, distance from hospital and social deprivation. Little has been reported on these factors - particularly on a large scale - so that our findings are quite novel. The study is more than three times larger than the recent national audit of upper GI bleeding across the UK,[7] and six times larger than the major audit in the south east of England and the Midlands during the mid 1990s.[14] Importantly, our study is based on systematic record linkage of abstracts from inpatient records and death certificates, which enables deaths that occur following discharge from hospital to be included with deaths in hospital.

There are several limitations of this study. Firstly, it was restricted to NHS hospitals. However, the private sector is small in Wales and rarely receives acutely ill patients, which would have minimal effect on the study findings. As upper GI bleeding is frequently a symptom of various aetiologies, rather than a defined disorder, it was necessary to use a series of ICD codes. It is possible that we may have missed some upper GI bleeds through the limitations of hospital and ICD coding, and may have included some lower GI bleeds. However, our high incidence of 134 per 100 000 adult population and case fatality of 10% (as expected from the literature) suggests that these discrepancies are small. Our study lacked information on the aetiology/diagnoses for some bleeds, although this can also be quite common in clinical audits and case series. Our administrative inpatient data also lacked detailed information about disease history, pathology, severity of bleeding and treatment, and the recording of diagnostic endoscopy and major co-morbidities was also incomplete.

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Our hospitalised incidence of upper GI bleeding (134 per 100 000) is higher than incidence rates previously reported in most regional or local studies across the UK, although lower than in the west of Scotland study (172 per 100 000).[4] Lower rates of about 50 to 120 per 100 000 have been reported more typically in the UK,[2,3,12,14,15,27] and across Europe,[28,29] during the last 30 years. Factors which may have contributed to our high incidence of upper GI bleeding include high levels of social deprivation and alcohol consumption in some areas of Wales,[30] our criteria of including adults rather than patients of all ages, and a slightly high proportion of mild bleeds: 10% of patients were discharged on the day of admission compared with 7% in the recent UK upper GI bleeding audit.[7]

We found very high risks of upper GI bleeding among elderly people. Among both men and women aged 85+ years, the risk of hospitalisation with upper GI bleeding was almost 1% per year. We found that socioeconomic deprivation was associated strongly with incidence. In the west of Scotland a 2.2 fold increased risk was identified for the most deprived quarter of patients compared with the least deprived quarter.[4] We found a similar 2.0 fold increased risk between the most and least deprived quintiles. Like the Scottish study, we found little association between social deprivation and case fatality.

Our overall case fatality of 10.0% in Wales is about average in the UK. Rates of 6% to 15% have been reported typically in local or regional studies across the UK,[2,4,13-15,31,32-35] although some single centre studies have reported lower case fatality of 3% to 4%.[3,12] We found a stable incidence of upper GI bleeding from 1999 to 2007, but a significant reduction over time in case fatality. Case fatality varied strongly according to the aetiology/diagnoses - with highest mortality for upper GI malignancies and varices and lowest mortality for Mallory Weiss tear – and was affected adversely by major co-morbidities, most importantly liver disease and renal failure.

Case fatality was slightly worse among people resident in the most urban compared with the most rural residences. Although case fatality was slightly lower for medium than for

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small or large hospitals, this was not significant. We also found little evidence that the distance travelled to hospital affected prognosis adversely.

There were large differences in both incidence and case fatality across local authorities. Those with highest incidence of upper GI bleeding often had lowest case fatality. As well as case mix differences, this may indicate lower thresholds for admitting less severe cases and possibly less effective GP out of hours services in some areas. It is known that many patients presenting to general hospitals with low risk upper GI bleeding could be managed safely without hospital admission.[36]

Case fatality was 13% higher for people admitted on weekends and public holidays compared with weekdays. Although admission rates for upper GI bleed were lower on weekends and public holidays than during the week, the increased mortality could not be explained by differences in case mix measures. Compared with patients admitted during the week, patients admitted on weekends and public holidays were significantly younger and had shorter lengths of stay - indicating less severe bleeds - and had similar levels of co-morbidities recorded. These findings are consistent with North American studies that have reported increased mortality for admissions at weekends for acute MI,[37] stroke,[38] peptic ulcer bleeding,[16] upper GI bleeding, [17] abdominal aortic aneurysm,[39] pulmonary embolism,[39] and acute epiglottis.[39] Interestingly, we found that mortality was even more increased (by 41%) for admissions on public holidays.

We found no difference in mortality among patients admitted to hospitals with out of hours endoscopy services on weekends and public holidays, compared with those that had no formal services. This finding is inconclusive, particularly as informal services are provided on an ad hoc basis in most other hospitals.

Possible explanations for the increased mortality at weekends and on public holidays include reduced staffing levels that may lead to less thorough assessment, lack of specialist or senior consultant cover, less application of multidisciplinary team care, poor communication at handover and possible delays to investigation such as endoscopy in some

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hospitals without out of hours services. The efforts of the British Society of Gastroenterology to extend out of hours endoscopy are welcome but further studies are required to understand deficiencies in care at weekends and on public holidays.

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Conflict of interest

None declared

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Table 1 Hospitalised incidence rates for upper GI bleeding according to age group and sex, 1999-2007

		Hospitalised incidence of upper GI bleeding		
		No. of cases	Incidence rate per 100 000	(95% CI)
Age group (years) by sex				
Male	All cases	13 288	153	(150-156)
	18-24	662	63.6	(58.9-68.6)
	25-34	1173	87.1	(82.2-92.2)
	35-44	1494	91.7	(87.1-96.4)
	45-54	1517	101	(96-106)
	55-64	1871	131	(126-138)
	65-74	2499	247	(237-257)
	75-84	2952	488	(471-506)
	85+	1120	864	(815-916)
Female	All cases	11 128	117	(115-119)
	18-24	411	40.1	(36.3-44.2)
	25-34	513	36.4	(33.3-39.7)
	35-44	803	47.0	(43.8-50.3)
	45-54	931	60.0	(56.2-63.9)
	55-64	1097	75.0	(70.6-79.5)
	65-74	1795	159	(152-167)
	75-84	3078	344	(332-356)
	85+	2500	739	(710-768)
All cases		24 421	134	(133-136)

Notes
The ages of five patients were not known

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Table 2 **Hospitalised incidence of upper GI bleeding and case fatality at 30 days, with age of patients, length of hospital stay, and social deprivation levels across local authorities, 1999-2007**

	Hospitalised incidence of upper GI bleeding			30 day follow-up			Patient and local authority characteristics: age, length of stay and social deprivation		
Local authority *	No. of cases	Incidence rate per 100 000 (95% CI)		No. of deaths within 30 days	Case fatality (30 days)	Adjusted mortality odds ratio (95% CI) ‡	Mean age of patients admitted (95% CI)	Median length of hospital stay in days (IQ Range)	Mean social deprivation score in local authority (95% CI)
Blaenau Gwent	827	194	(181-208)	68	8.2%	Ref.	63.7 (62.4-65.0)	5 (2-10)	33.8 (30.2-37.4)
Bridgend	1304	162	(153-171)	112	8.6%	1.08 (0.78-1.49)	62.6 (61.5-63.7)	4 (1-8)	23.2 (20.4-26.0)
Caerphilly	1701	164	(156-172)	165	9.7%	1.28 (0.95-1.73)	61.8 (60.8-62.8)	4 (1-9)	27.0 (24.4-29.6)
Cardiff	2263	119	(114.-124)	190	8.4%	1.05 (0.78-1.41)	62.8 (62.0-63.6)	5 (2-10)	21.3 (18.8-23.8)
Carmarthenshire	1594	145	(138-152)	183	11.5%	1.29 (0.96-1.74)	67.3 (66.4-68.2)	5 (2-12)	22.0 (20.1-23.9)
Ceredigion	676	138	(128-149)	75	11.1%	1.16 (0.81-1.65)	68.8 (67.4-70.2)	5 (2-12)	15.0 (13.2-16.8)
Conwy	849	120	(112-129)	116	13.7%	1.58 (1.14-2.18)	67.0 (65.6-68.4)	4 (2-8)	18.0 (15.4-20.6)
Denbighshire	682	115	(106-124)	67	9.8%	1.09 (0.76-1.57)	65.8 (64.3-67.4)	4 (2-8)	20.4 (16.4-24.4)
Flintshire	895	96.9	(90.7-104)	100	11.2%	1.42 (1.02-1.97)	63.3 (62.0-64.6)	4 (2-9)	15.0 (12.9-17.1)
Gwynedd	772	105	(98.0-113)	70	9.1%	0.98 (0.67-1.40)	66.5 (65.1-67.9)	5 (2-9)	17.3 (15.6-19.0)
Isle of Anglesey	441	103	(93.4-113)	38	8.6%	0.96 (0.63-1.47)	65.5 (63.6-67.4)	5 (2-9)	20.7 (18.1-23.3)
Merthyr Tydfil	917	268	(251-286)	71	7.7%	1.14 (0.80-1.62)	58.7 (57.4-60.0)	3 (0-9)	37.2 (31.7-42.8)
Monmouthshire	726	135	(125-145)	78	10.7%	1.14 (0.80-1.61)	68.3 (66.9-69.7)	5 (2-10)	12.2 (10.7-13.7)
Neath Port Talbot	1083	127	(120-135)	120	11.1%	1.36 (0.98-1.87)	64.1 (62.9-65.3)	5 (2-10)	28.2 (25.2-31.2)
Newport	1267	150	(142-159)	166	13.1%	1.76 (1.30-2.39)	63.1 (62.0-64.2)	4 (2-8)	22.0 (18.9-25.1)
Pembrokeshire	1167	162	(153-172)	114	9.8%	1.12 (0.81-1.55)	65.9 (64.8-67.0)	5 (2-11)	19.4 (17.3-21.5)
Powys	887	109	(102-117)	101	11.4%	1.21 (0.87-1.68)	68.4 (67.2-69.6)	5 (2-9)	14.3 (13.0-15.6)
Rhondda Cynon Taff	1855	130	(124-136)	162	8.7%	1.21 (0.90-1.64)	60.5 (59.6-61.4)	4 (1-9)	29.2 (26.8-31.7)
Swansea	1856	132	(126-138)	189	10.2%	1.24 (0.92-1.67)	64.0 (63.1-64.9)	4 (2-10)	22.6 (19.7-25.5)
Torfaen	905	162	(152-173)	90	9.9%	1.23 (0.88-1.73)	63.7 (62.4-65.0)	5 (2-10)	21.3 (18.6-24.0)
Vale of Glamorgan	1002	136	(128-145)	95	9.5%	1.11 (0.79-1.55)	64.7 (63.4-66.0)	5 (2-9)	15.0 (12.7-17.3)
Wrexham	752	93.3	(86.8-100)	82	10.9%	1.35 (0.95-1.90)	63.5 (62.0-65.0)	4 (2-9)	19.9 (17.0-22.8)
All Wales	24 421	134	(133-136)	2452	10.0%		64.1 (63.9-64.4)	4 (2-9)	21.7 (21.1-22.3)

Notes

* For geographical details of each local authority, see Figure 1.

‡ The mortality odds ratios for local authorities are adjusted for age group and sex. Odds ratios were obtained through multiple logistic regression.

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Table 3 **Case fatality at 30 days and adjusted odds ratios for prognostic and sociodemographic factors following hospital admission for upper GI bleeding, 1999-2007**

		30 day follow-up		
	No. of cases	No. of deaths within 30 days	Unadjusted case fatality (30 days)	Adjusted mortality odds ratio (95% CI) *‡
All cases †	24 421	2452	10.0%	
Age group (years) and sex				
Male – all	13 288	1215	9.1%	
18-24	662	2	0.3%	
25-34	1173	10	0.9%	
35-44	1494	28	1.9%	
45-54	1517	71	4.7%	
55-64	1871	142	7.6%	
65-74	2499	279	11.2%	
75-84	2952	442	15.0%	
85+	1120	241	21.5%	
Female – all	11 128	1237	11.1%	
18-24	411	1	0.2%	
25-34	513	4	0.8%	
35-44	803	25	3.1%	
45-54	931	31	3.3%	
55-64	1097	59	5.4%	
65-74	1795	163	9.1%	
75-84	3078	437	14.2%	
85+	2500	517	20.7%	
Sex				
Male	13 288	1215	9.1%	Ref.
Female	11 128	1237	11.1%	0.89 (0.81-0.97)
Social deprivation				
I (least deprived)	3499	380	10.9%	Ref.
II	4296	434	10.1%	0.96 (0.83-1.12)
III	4933	529	10.7%	1.09 (0.94-1.26)
IV	5462	554	10.1%	1.12 (0.97-1.29)
V (most deprived)	6231	555	8.9%	1.11 (0.97-1.28)
Urban/rural residence				
Under 2,500 people	4497	471	10.5%	Ref.
2,500 - 9,999	3935	376	9.6%	0.98 (0.85-1.13)
10,000 – 24,999	5880	595	10.1%	1.08 (0.95-1.23)
25,000 – 99,999	5355	524	9.8%	1.09 (0.96-1.25)
At least 100,000	4754	486	10.2%	1.14 (1.00-1.31)
Distance from hospital				
Less than 3 km	4133	442	10.7%	Ref.
3 to 9.99 km	8511	792	9.3%	0.88 (0.77-1.01)
10 to 19.99 km	6548	660	10.1%	0.96 (0.84-1.10)
20 to 29.99 km	1846	197	10.7%	0.99 (0.82-1.20)
At least 30 km	2089	222	10.6%	0.98 (0.81-1.17)
Hospital size (beds)				
Small (0-399)	4428	488	11.1%	Ref.
Medium (400-599)	11 658	1084	9.3%	0.97 (0.86-1.09)
Large (600+)	7400	798	10.8%	1.10 (0.97-1.24)
Day of admission ‡				
Weekday	18 285	1792	9.8%	Ref.
Weekend	5686	602	10.6%	1.13 (1.02-1.25)
Public holiday	450	58	12.9%	1.41 (1.04-1.91)

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Table 3 cont'd

			30 day follow-up			
	No. of cases	(%)	No. of deaths within 30 days	Unadjusted case fatality (30 days)	Adjusted mortality odds ratio (95% CI) *‡	
Main diagnoses/aetiology **						
Mallory Weiss tear	1485	(6.1%)	24	1.6%	0.26	(0.18-0.40)
Oesophagitis	2459	(10.1%)	202	8.2%	0.73	(0.63-0.86)
Varices – oesophageal	656	(2.7%)	107	16.3%	2.69	(2.15-3.56)
Varices – gastric	66	(0.3%)	12	18.2%	3.15	(1.63-6.06)
Ulcer – duodenal	2661	(10.9%)	355	13.3%	1.25	(1.10-1.41)
Ulcer – gastric	2485	(10.2%)	259	10.4%	0.86	(0.75-0.99)
Ulcer – peptic, unspecified	291	(1.2%)	49	16.8%	1.59	(1.16-2.19)
Ulcer – jejunal	34	(0.1%)	4	11.8%	1.03	(0.36-2.99)
Malignancy – oesophageal	112	(0.5%)	40	35.7%	4.40	(2.95-6.56)
Malignancy – gastric/duodenal	197	(0.8%)	48	24.4%	2.24	(1.61-3.14)
Gastritis & duodenitis	3377	(13.8%)	198	5.9%	0.52	(0.44-0.60)
Other specific diseases of stomach & duodenum, including gastric antral vascular ectasia	273	(1.1%)	23	8.4%	0.62	(0.40-0.96)
Complications of analgesics, antipyretics & anti-inflammatory drugs	729	(3.0%)	46	6.3%	0.47	(0.35-0.64)
Major co-morbidities **						
Circulatory diseases	9276	(38.0%)	1439	15.5%	1.73	(1.59-1.89)
Malignancies (all except upper GI))	1147	(4.7%)	351	30.6%	3.64	(3.17-4.17)
Liver disease	1366	(5.6%)	254	18.6%	4.90	(4.15-5.79)
COPD	982	(4.0%)	182	18.5%	1.55	(1.31-1.84)
Diabetes	2565	(10.5%)	328	12.8%	1.12	(0.99-1.27)
Renal failure	812	(3.3%)	271	33.4%	3.75	(3.21-4.39)

Notes:

* The mortality odds ratio for sex is adjusted for age group. The odds ratios for social deprivation, urban/rural residence, distance from hospital, hospital size, day of admission, main diagnoses/aetiology and co-morbidities are adjusted for age group and sex. Odds ratios were obtained through multiple logistic regression.

‡ After adjusting for major co-morbidities (malignancies, circulatory diseases, renal failure, diabetes, COPD and liver disease), the increased mortality for weekend and public holiday admissions was largely unaffected (odds ratio=1.11; 95% CI=1.00-1.23 and 1.42; 1.05-1.92 respectively). The prevalence of co-morbidities across the three patient groups (admitted on weekdays, weekends and public holidays respectively) were as follows: circulatory diseases = 6931 (37.9%), 2162 (38.0%) and 183 (40.7%); respectively; malignancies = 1105 of 18 285 (6.0%), 323 of 5686 (5.7%) and 24 of 450 (5.3%); liver disease = 1003 (5.5%), 341 (6.0%), 22 (4.9%); COPD = 735 (4.0%), 229 (4.0%), 18 (4.0%); diabetes=1921 (10.5%), 599 (10.5%), 45 (10.0%); renal failure = 589 (3.2%), 204 (3.65) and 19 (4.2%). Hence, the prevalence of major co-morbidities was very similar across the three groups of patients.

† For non-variceal bleeds, case fatality was 9.8% overall, based on 23 742 admissions: adjusted case fatality was higher among women than men (OR = 1.11; 95% CI = 1.02-1.22), higher in large than small hospitals (1.11; 1.01-1.30) and highest in the most urban than rural residences (1.16; 1.01-1.34), higher for weekend (1.13; 1.02-1.25), and public holiday (1.48; 1.10-1.98) admissions but it was not associated with distance travelled to hospital

** ICD-10 codes used for the main diagnoses/aetiology were as follows: Mallory Weiss tear (K22.6), oesophagitis (K20, K21.1, K22.1), varices – oesophageal (I85), varices – gastric (I86.4), ulcer – duodenal (K26), ulcer – gastric (K25), ulcer - peptic, unspecified (K27), ulcer – jejunal (K28), malignancy – oesophageal (C15), malignancy – gastric/duodenal (C16, C17.0), gastritis & duodenitis (K29), other specific diseases of stomach & duodenum, including gastric antral vascular ectasia (K31.8), complications of analgesics, antipyretics & anti-inflammatory drugs (Y45). ICD-10 codes used for the co-morbidities were as follows; circulatory diseases (ICD-10 = I00-I99), all malignancies except upper GI (C00-C15, C17.2-C97), liver disease (K70-K77), COPD (J40-J44), diabetes (E10-E14) and renal failure (N17-N19).

Ref = reference category

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Table 4 **Trends in hospitalised incidence, case fatality and length of stay for upper GI bleeding, 1999-2007**

	Hospitalised incidence of upper GI bleeding			30 day follow-up			Length of hospital stay	
Year	No. of cases	Incidence rate per 100 000 (95% CI)		No. of deaths	Case fatality (95% CI)		Median (IQ range)	
1999/2000	2866	132	(126-135)	324	11.4%	(10.2%-12.7%)	4	(4-9)
2000/2001	3186	144	(139-149)	317	10.4%	(9.3%-11.5%)	4	(4-8)
2001/2002	3041	136	(131-141)	316	10.6%	(9.4%-11.7%)	4	(4-10)
2002/2003	2912	129	(124-134)	313	10.6%	(9.4%-11.8%)	5	(5-9)
2003/2004	3064	135	(130-139)	334	10.8%	(9.6%-11.9%)	5	(5-10)
2004/2005	3204	139	(135-144)	281	8.8%	(7.8%-9.8%)	4	(2-9)
2005/2006	3166	136	(131-141)	305	9.5%	(8.4%-10.6%)	5	(5-10)
2006/2007	2982	127	(122-131)	262	8.6%	(7.5%-9.6%)	4	(2-9)
All years	**24 421**	**134**	**(133-136)**	**2452**	**10.0%**	**(9.7%-10.4%)**	**4**	**(2-9)**

Notes
Hospitalised incidence and case fatality rates are standardised for age group and sex.
There was no significant change over time in the incidence of upper GI bleeding, but a 3.1% (95% CI = 1.3%-4.8%) average annual reduction over time in case fatality. Correspondingly, for non-variceal bleeds, there was no change in incidence but a 3.4% (1.5%-5.2%) average annual reduction in case fatality.

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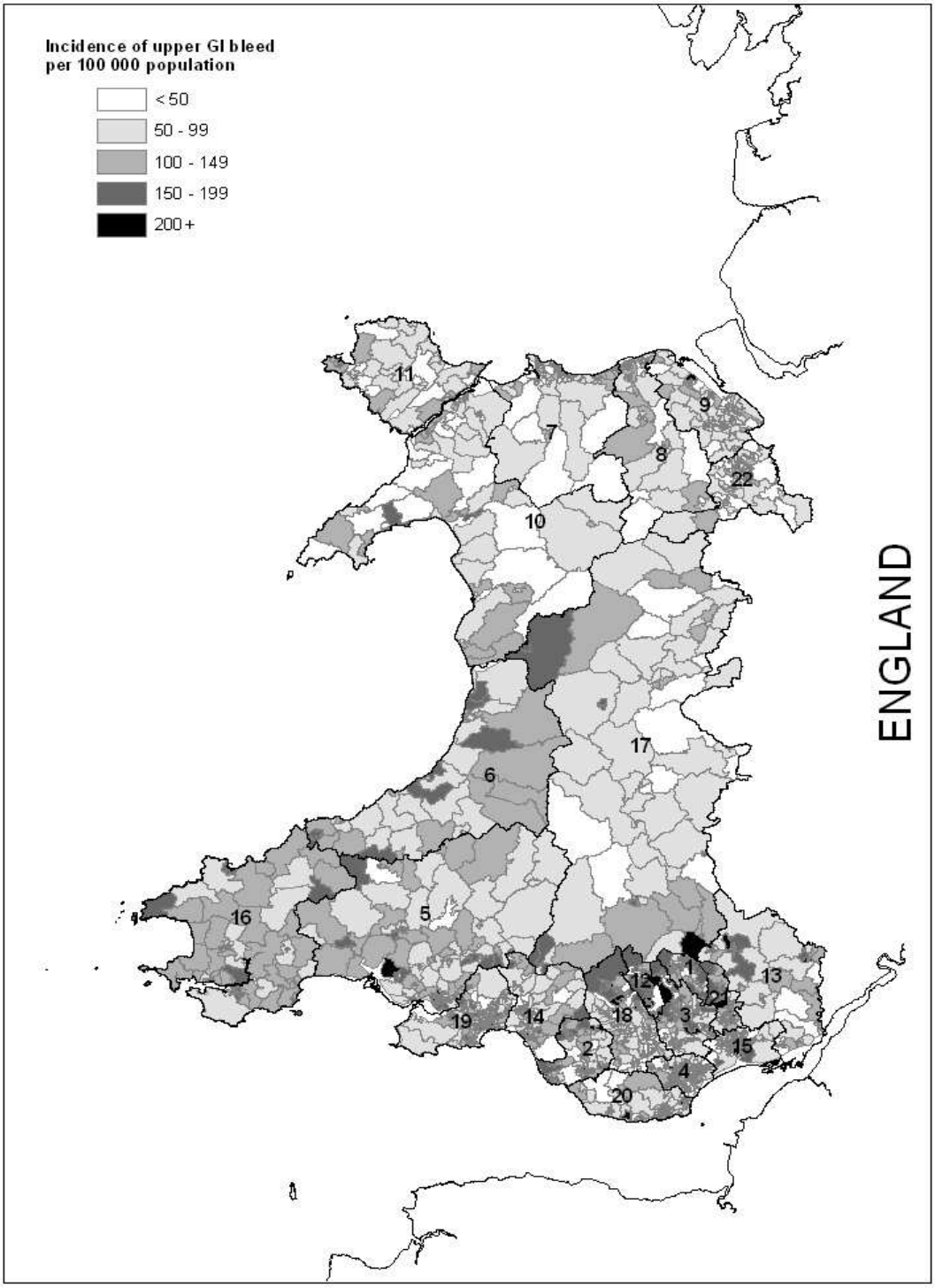
Figure 1 Hospitalised incidence of upper GI bleeding across Wales

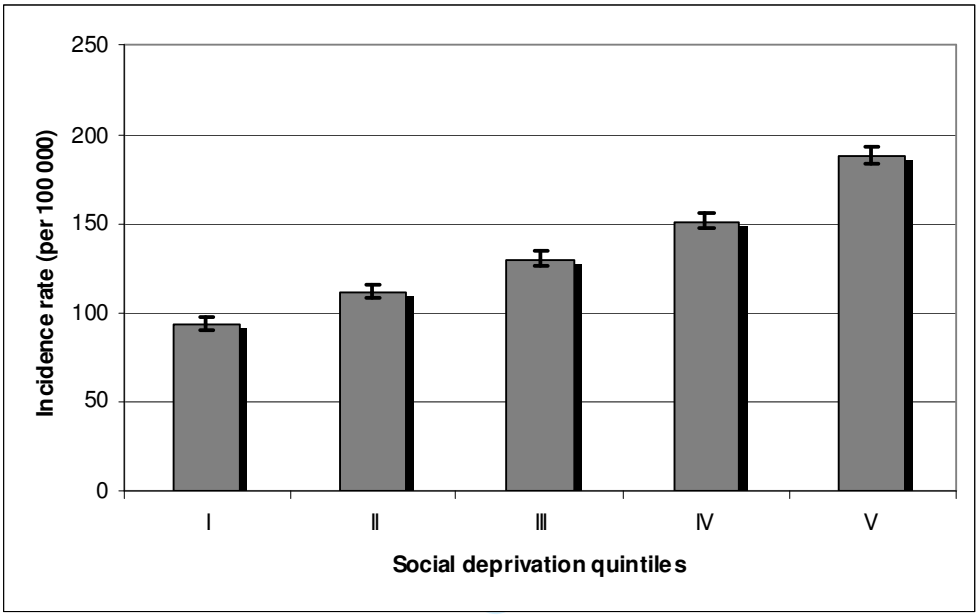


Notes

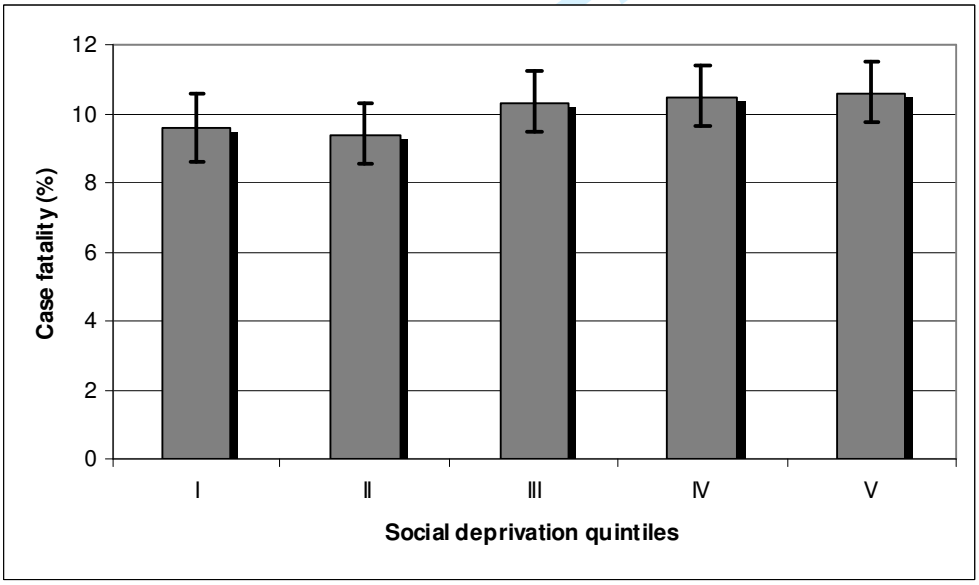
For comparison with Table 2, the key to the health authority numbering in this map is as follows: 1 = Blaenau Gwent; 2 = Bridgend; 3 = Caerphilly; 4 = Cardiff; 5 = Carmarthenshire; 6 = Ceredigion; 7 = Conwy; 8 = Denbighshire; 9 = Flintshire; 10 = Gwynedd; 11 = Isle of Anglesey; 12 = Merthyr Tydfil; 13 = Monmouthshire; 14 = Neath Port Talbot; 15 = Newport; 16 = Pembrokeshire; 17 = Powys; 18 = Rhondda Cynon Taff; 19 = Swansea; 20 = Torfaen; 21 = The Vale of Glamorgan; 22 = Wrexham.

Figure 2 **Hospitalised incidence and case fatality for upper GI bleeding according to social deprivation, 1999-2007**

a). Hospitalised incidence



b). Case fatality



Notes

I = least deprived social deprivation quintile, V = most deprived

Vertical bars represent 95% confidence intervals

Incidence and case fatality rates are standardised for age group and sex

The relative risk of an upper GI bleed for quintile V vs quintile I was 2.0 for non-variceal upper GI bleeds and for upper GI bleeds overall

Appendix 1 ICD-10 codes used for upper GI bleeding

K22.6	Gastro-oesophageal laceration-haemorrhage syndrome (Mallory-Weiss Syndrome)
K22.8	Other specified diseases of oesophagus: Haemorrhage of oesophagus NOS
K25.0	Gastric ulcer - Acute with haemorrhage
K25.2	Gastric ulcer - Acute with both haemorrhage and perforation
K25.4	Gastric ulcer - Chronic or unspecified with haemorrhage
K25.6	Gastric ulcer - Chronic or unspecified with both haemorrhage and perforation
K26.0	Duodenal ulcer - Acute with haemorrhage
K26.2	Duodenal ulcer - Acute with both haemorrhage and perforation
K26.4	Duodenal ulcer - Chronic or unspecified with haemorrhage
K26.6	Duodenal ulcer - Chronic or unspecified with both haemorrhage and perforation
K27.0	Peptic ulcer, unspecified - Acute with haemorrhage
K27.2	Peptic ulcer, unspecified - Acute with both haemorrhage and perforation
K27.4	Peptic ulcer, unspecified - Chronic or unspecified with haemorrhage
K27.6	Peptic ulcer, unspecified - Chronic or unspecified with both haemorrhage and perforation
K28.0	Gastrojejunal ulcer – Acute with haemorrhage
K28.2	Gastrojejunal ulcer – Acute with both haemorrhage and perforation
K28.4	Gastrojejunal ulcer – Chronic or unspecified with haemorrhage
K28.6	Gastrojejunal ulcer – Chronic or unspecified with both haemorrhage and perforation
K29.0	Acute haemorrhagic gastritis
I85.0	Oesophageal varices with bleeding
K92.0	Haematemesis
K92.1	Melaena
K92.2	Gastrointestinal haemorrhage, unspecified, unless present with a secondary or subsidiary diagnosis of lower gastrointestinal disease (C17.1-C21, K50-K52, K55-K57 or K60-K63)

For Peer Review

References

1. Palmer KR. Haematemesis and melaena. *Postgrad Med J* 2003; 31: 19-24.

2. Katschinski BD, Logan RFA, Davies J, Langman MJS. Audit of mortality in upper gastrointestinal bleeding. *Postgrad Med J* 1989; 65: 913-7.

3. Holman RA, Davis M, Gough KR, Gartell P, Britton DC, Smith RB. Value of a centralised approach in the management of haematemesis and melaena: experience in a district general hospital. *Gut* 1990; 31: 504-8.

4. Blatchford O, Davidson L, Murray W, Blatchford M, Pell J. Acute upper gastrointestinal haemorrhage in west of Scotland: case ascertainment study. BMJ 1997; 315(7107): 510-4.

5. Vreeburg EM, Snel P, deBruijne JW, Bartelsman JF, Rauws EAJ, Tytgat GNJ. Acute upper gastrointestinal bleeding in the Amsterdam area: incidence, diagnosis and clinical outcome. *Am J Gastroenterol* 1997; 92: 236-42.

6. Williams JG, Roberts SE, Ali MF, Cheung WY, Cohen DR, Demery G, *et al*. Gastroenterology services in the UK. The burden of disease, and the organisation and delivery of services for gastrointestinal and liver disorders: a review of the evidence. *Gut* 2007; 56 Suppl 1: 1-113.

7. Hearnshaw SA, Logan RF, Lowe D, Travis SP, Murphy MF, Palmer KR. Use of endoscopy for management of acute upper gastrointestinal bleeding in the UK: results of a nationwide audit. *Gut* 2010; 59: 1022-9.

8. Thompson PW, Tee L, McBride J, Quincey D, Strat Liddiard G. Long-term

For Peer Review

NSAID use in primary care: changes over a decade and NICE risk factors for gastrointestinal adverse events. *Rheumatology (Oxford)* 2005; 44: 1308-10.

9. Fleming KM, Aithal GP, Solaymani-Dodaran M, Card TR, West J. Incidence and prevalence of cirrhosis in the United Kingdom, 1992-2001: a general population-based study. *J Hepatol* 2008; 49: 732-8.

10. Johnson CD, Hosking S. National statistics for diet, alcohol consumption, and chronic pancreatitis in England and Wales, 1960-88. *Gut* 1991; 32: 1401-5.

11. Pincock S. Binge drinking on rise in UK and elsewhere. Government report shows increases in alcohol consumption, cirrhosis, and premature deaths. *Lancet* 2003; 362(9390): 1126-7.

12. Masson J, Bramley PN, Herd K, McKnight GM, Park K, Brunt PW, *et al*. Upper gastrointestinal bleeding in an open-access dedicated unit. *J R Coll Physicians Lond* 1996; 30: 436-42.

13. Johnston SJ, Jones PF, Kyle J, Needham CD. Epidemiology and course of gastrointestinal haemorrhage in North-east Scotland. *BMJ* 1973: 655-60.

14. Rockall TA, Logan RFA, Devlin HB, Northfield TC. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. *BMJ* 1995; 311(6999): 222-6.

15. Berry AR, Collin J, Frostick SP, Dudley NE, Morris PJ. Upper gastrointestinal haemorrhage in Oxford. A prospective study. *J R Coll Surg Edinb* 1984; 29: 134-8.

For Peer Review

16. Ananthakrishnan AN, McGinley EL, Saeian K. Outcomes of weekend admissions for upper gastrointestinal hemorrhage: a nationwide analysis. *Clin Gastroenterol Hepatol* 2009; 7: 296-302.

17. Shaheen AA, Kaplan GG, Myers RP. Weekend versus weekday admission and mortality from gastrointestinal hemorrhage caused by peptic ulcer disease. *Clin Gastroenterol Hepatol* 2009; 7: 303-10.

18. Coyne JS, Richards MT, Short R, Shultz K, Singh SG. Hospital cost and efficiency: do hospital size and ownership type really matter? *J Healthc Manag* 2009; 54: 163-74.

19. Nicholl J, West J, Goodacre S, Turner J. The relationship between distance to hospital and patient mortality in emergencies: an observational study. *Emerg Med J* 2007; 24: 665-8.

20. Welsh Assembly Government. *NHS Administrative Register*. Cardiff: Welsh Assembly Government, 2006.

21. Lyons RA, Jones SJ, Deacon T, Heaven M. Socioeconomic variation in injury in children and older people: a population based study. *Inj Prev* 2003; 9: 33-7.

22. Polinder S, Meerding WJ, Lyons RA, Haagsma JA, Toet H, Petridou ET, *et al*. International variation in clinical injury incidence: exploring the performance of indicators based on health care, anatomical and outcome criteria. *Accid Anal Prev* 2008; 40: 182-91.

23. Lyons RA, Ward H, Brunt H, Macey S, Thoreau R, Bodger OG, et al. Using multiple datasets to understand trends in serious road traffic casualties.

For Peer Review

Accid Anal Prev 2008; 40: 1406-10.

24 Button LA Roberts SE, Goldacre MJ, Akbari A, Williams JG. Hospitalised prevalence and 5 year mortality for IBD: record linkage study. *World J Gastroenterol* 2010; 16: 431-8.

25. Welsh Assembly Government. *Welsh Index of Multiple Deprivation (WIMD) 2005*. Cardiff: Welsh Assembly Government, 2005.

26. Welsh Assembly Government. *A statistical focus on rural Wales: 2008 Edition*. Statistics for Wales. Cardiff: Welsh Assembly Government, 2008.

27. Madden MV, Griffith GH. Management of upper gastrointestinal bleeding in a district general hospital. *J R Coll Physicians Lond* 1985; 20: 213-5.

28. Longstreth GF. Epidemiology of hospitalization for acute upper gastrointestinal haemorrhage: a population-based study. *Am J Gastroenterol* 1995; 90: 206-10.

29. van Leerdam ME, Vreeburg EM, Rauws EA, Geraedts AA, Tijssen JG, Reitsma JB, *et al*. Acute upper GI bleeding: did anything change? Time trend analysis of incidence and outcome of acute upper GI bleeding between 1993/1994 and 2000. *Am J Gastroenterol* 2003; 98: 1494-9.

30. National Public Health Service for Wales. *Alcohol and health in Wales: a major public health issue.* Cardiff: National Public Health Service for Wales, 2006.

31. Schiller KF, Truelove SC, Williams DG. Haematemesis and melaena, with special reference to factors influencing the outcome. *BMJ* 1970; 2(700): 7-14.

For Peer Review

32. Sanders DS, Perry MJ, Jones SG, McFarlane E, Johnson AG, Gleeson DC, *et al*. Effectiveness of an upper-gastrointestinal haemorrhage unit: a prospective analysis of 900 concecutive cases using the Rockall score as a method of risk standardisation. *Eur J Gastroenterol Hepatol* 2004; 16: 487-94.

33. Mayberry JF, Penny WJ, Counsell BR, Rhodes J. Mortality in acute upper gastrointestinal haemorrhage: a six-year survey from the University Hospital of Wales. *Postgrad Med J* 1981; 57: 627-32.

34. Sanderson JD, Taylor RF, Pugh S, Vicary FR. Sepcialized gastrointestinal units for the management of upper gastrointestinal haemorrhage. *Postgrad Med J* 1990; 66: 654-6.

35. Clements D, Aslan S, Foster D, Stamatakis J, Wilkins WE, Morris JS. Acute upper gastrointestinal haemorrhage in a district general hospital: audit of an agreed management policy. *J R Coll Physicians Lond* 1991; 25: 27-30.

36. Stanley AJ, Ashley D, Dalton HR, Mowat C, Gaya DR, Thompson E, *et al*. Outpatient management of patients with low-risk upper-gastrointestinal haemorrhage: multicentre validation and prospective evaluation. *Lancet* 2009; 373(9657): 42-7.

37. Kostis WJ, Demissie K, Marcella SW, Shao YH, Wilson AC, Moreyra AE. Weekend versus weekday admission and mortality from myocardial infarction. *N Engl J Med* 2007; 356: 1099-109.

38. Saposnik G, Baibergenova A, Bayer N, Hachinski V. Weekends: a dangerous time for having a stroke? *Stroke* 2007; 38: 1211-5.

For Peer Review

39. Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001; 345: 663-8.

For Peer Review