**Geographical variation in Hepatitis C-related severe liver disease and patient risk factors: A multicentre cross-sectional study**

**Supplementary material**

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**Table S1:** Patient distributions across demographic and social factors for HCV-positive patients recruited from 48 hospital centres across England and Scotland.

|  |  |  |  |
| --- | --- | --- | --- |
| **Factor** | **Level** | **No. (%) of patients: Full data (n=3,829)** | **No. (%) of patients: Reduced data (n=2,851)\*** |
| Age group | <46 years | 1457 (38.05) | 1076 (37.74) |
| 46-59 years | 1754 (45.81) | 1320 (46.3) |
| 60+ years | 617 (16.11) | 455 (15.96) |
| *Missing data* | 1 (0.03) | 0 (0) |
| Sex | Female | 1123 (29.33) | 821(28.8) |
| Male | 2696 (70.41) | 2030 (71.2) |
| *Missing data* | 10 (0.26) | 0 (0) |
| Ethnicity | White | 2935 (76.65) | 2206 (77.38) |
| Asian | 269 (7.03) | 198 (6.94) |
| Black | 67 (1.75) | 49 (1.72) |
| Other | 543 (14.18) | 398 (13.96) |
| *Missing data* | 15 (0.39) | 0 (0) |
| Country of Birth | UK | 2884 (75.32) | 2187 (76.71) |
| Non-UK | 893 (23.32) | 664 (23.29) |
| *Missing data* | 52 (1.36) | 0 (0) |
| Probable infection route | Blood/blood products | 488 (12.74) | 363 (12.73) |
| Injecting drug use | 2358 (61.58) | 1799 (63.1) |
| Other | 356 (9.30) | 270 (9.47) |
| Unknown | 572 (14.94) | 419 (14.7) |
| *Missing data* | 55 (1.44) | 0 (0) |
| History of heavy alcohol consumption | No | 2192 (57.25) | 1657 (58.12) |
| Yes | 1577 (41.19) | 1194 (41.88) |
| *Missing data* | 60 (1.57) | 0 (0) |

\* Dataset used in statistical modelling analyses following the exclusion of patients with missing data.

**Table S2:** Patient distributions across HCV and co-morbidity factors for HCV-positive patients recruited from 48 hospital centres across England and Scotland.

|  |  |  |  |
| --- | --- | --- | --- |
| **Factor** | **Level** | **No. (%) of patients: Full data (n=3,829)** | **No. (%) of patients: Reduced data (n=2,851)\*** |
| Stage of liver disease† | Cirrhosis | 1385 (36.17) | 1042 (36.55) |
| No cirrhosis | 2444 (63.83) | 1809 (63.45) |
| *Missing data* | 0 (0) | 0 (0) |
| Treatment status at enrolment | Untreated | 2730 (71.30) | 1978 (69.38) |
| Non-DAA | 1019 (26.61) | 811 (28.45) |
| DAA | 71 (1.85) | 54 (1.89) |
| Treatment type known | 9 (0.24) | 8 (0.28) |
| *Missing data* | 0 (0) | 0 (0) |
| HCV genotype | 1 | 1978 (51.66) | 1576 (55.28) |
| 3 | 1300 (33.95) | 1033 (36.23) |
| Other¥ | 322 (8.41) | 242 (8.49) |
| *Missing data* | 229 (5.98) |  |
| HIV coinfection | Yes | 174 (4.54) | 137 (4.81) |
| No | 3428 (89.53) | 2714 (95.19) |
| *Missing data* | 227 (5.93) | 0 (0) |
| Body mass index (BMI) | Low (13.12 - 18.49) | 86 (2.25) | 73 (2.56) |
| Normal (18.5 - 25) | 1367 (35.70) | 1145 (40.16) |
| High (25.01 - 29.99) | 1195 (31.21) | 1023 (35.88) |
| Obese (30 - 60.08) | 719 (18.78) | 610 (21.4) |
| *Missing data* | 462 (12.07) | 0 (0) |
| Diabetes | Yes | 387 (10.11) | 296 (10.38) |
| No | 3415 (89.19) | 2555 (89.62) |
| *Missing data* | 27 (0.71) | 0 (0) |

\*Dataset used in statistical modelling analyses following the exclusion of patients with missing data.

†Patients with cirrhosis diagnosed at any stage during the 31-month study period were assumed to be cirrhotic at enrolment

¥HCV genotypes 2, 4, 5, 6 and mixed genotype infections

**Table S3:** Patient distributions across health authority areas of residence for HCV-positive patients recruited from 48 hospital centres across England and Scotland.

|  |  |  |  |
| --- | --- | --- | --- |
| **Country** | **Regional Health Authorities/Boards** | **No. (%) of patients: Full data (n=3,829)** | **No. (%) of patients: Reduced data (n=2,851)\*** |
| England | East Midlands | 477 (12.46) | 397 (13.92) |
| East of England | 323 (8.44) | 233 (8.17) |
| London | 383 (10.00) | 236 (8.28) |
| North East | 222 (5.80) | 182 (6.38) |
| North West | 284 (7.42) | 214 (7.51) |
| South Central | 258 (6.74) | 196 (6.87) |
| South East Coast | 43 (1.12) | 34 (1.19) |
| South West | 240 (6.27) | 123 (4.31) |
| West Midlands | 275 (7.18) | 225 (7.89) |
| Yorkshire & The Humber | 353 (9.22) | 280 (9.82) |
| All regions of England | 2858 (70.60) | 2120 (74.36) |
| Scotland† | Ayrshire & Arran | 13 (0.34) | 9 (0.32) |
| Borders | 20 (0.52) | 16 (0.56) |
| Fife | 14 (0.37) | 14 (0.49) |
| Forth Valley | 21 (0.55) | 12 (0.42) |
| Grampian | 89 (2.32) | 81 (2.84) |
| Greater Glasgow & Clyde | 523 (13.66) | 363 (12.73) |
| Highland | 14 (0.37) | 6 (0.21) |
| Lanarkshire | 11 (0.29) | 10 (0.35) |
| Lothian | 113 (2.95) | 76 (2.67) |
| Tayside | 153 (4.00) | 144 (5.05) |
| All regions of Scotland | 971 (23.99) | 731 (25.64) |

\*Dataset used in statistical modelling analyses following the exclusion of patients with missing data.

†Patients residing in NHS Shetland and NHS Western Isles were excluded due to small numbers. No patients were recruited from NHS Dumfries & Galloway or NHS Orkney.

**Table S4:** Prevalence (95% confidence intervals) of severe liver disease and treatment by local health authority of residence. Based on 3,829 patients attending HCV-specialist clinics in England and Scotland.

|  |  |  |
| --- | --- | --- |
| **Health authority area** | **% Severe liver disease (95% CI)** | **% Treated pre-enrolment (95% CI)** |
| East Midlands | 37.53 (33.17-42.04) | 36.06 (31.74-40.55) |
| East of England | 45.82 (40.29-51.43) | 37.05 (31.87-42.67) |
| London | 44.65 (39.6-49.78) | 24.54 (20.31-29.17) |
| North East | 28.83 (22.96-35.27) | 36.49 (30.15-43.19) |
| North West | 48.24 (42.3-54.22) | 29.93 (24.66-35.62) |
| South Central | 36.05 (30.18-42.23) | 38.37 (32.41-44.61) |
| South East Coast | 53.49 (37.65-68.82) | 37.21 (22.98-53.27) |
| South West | 37.92 (31.75-44.38) | 29.93 (24.66-35.62) |
| West Midlands | 35.64 (29.98-41.61) | 14.55 (10.60-19.28) |
| Yorkshire and The Humber | 26.91 (22.35-31.86) | 28.33 (23.69-33.34) |
| Ayrshire and Arran | 30.77 (9.09-61.43) | 61.54 (31.58-86.14) |
| Borders | 35 (15.39-59.22) | 20.0 (5.73-43.66) |
| Fife | 7.14 (0.18-33.87) | 21.43 (4.66-50.80) |
| Forth Valley | 14.29 (3.05-36.34) | 52.38 (29.78-74.29) |
| Grampian | 23.6 (15.24-33.78) | 39.33 (29.13-50.25) |
| Greater Glasgow and Clyde | 33.84 (29.79-38.08) | 21.03 (17.62-24.78) |
| Highland | 28.57 (8.39-58.1) | 28.57 (8.39-58.10) |
| Lanarkshire | 45.45 (16.75-76.62) | 45.45 (16.75-76.62) |
| Lothian | 36.28 (27.45-45.86) | 39.82 (30.73-49.46) |
| Tayside | 15.03 (9.77-21.7) | 9.15 (5.09-14.88) |
| **Measure of Geographical Variation (95% CI)†** | 35.45 (27.32-52.32) | 39.52 (30.46-58.33) |

†Coefficient of Variation (CV) with correction for sample size and 95% CI using Normal Approximation method

**Table S5**: Comparing prevalence of severe liver disease among all patients attending HCV specialist services in Scotland with the proportion with severe liver disease among the recruited study population.

|  |  |  |
| --- | --- | --- |
| **NHS board of residence\*\*** | **Scottish HCV Clinical database,** **2012-2014\*\*\*\*** | **HCV Research UK (HCVRUK) study population, 2012-2014** |
| **Diagnosed with severe liver disease, n(%N)\*** | **Total attending HCV specialist services, (N)** | **Rank from high-to-low prevalence** | **Diagnosed with severe liver disease, n(%N)\*** | **Total recruited into HCVRUK over study period, (N)** | **Rank from high-to-low proportions** |
| Greater Glasgow & Clyde | 981 (24.5) | 4,010 (100.0) | 1 | 177 (33.8) | 523 (100) | 4 |
| Lothian\*\*\* | 115 (24.3) | 473 (100.0)  | 2 | 41 (36.3) | 113 (100) | 2 |
| Lanarkshire  | 135 (16.3) | 828 (100.0) | 3 | 5 (45.5) | 11 (100) | 1 |
| Ayrshire & Arran | 105 (14.9) | 706 (100.0) | 4 | 4 (30.8) | 13 (100) | 5 |
| Highland | 45 (13.3) | 339 (100.0) | 5 | 4 (28.6) | 14 (100) | 6 |
| Grampian | 174 (13.2) | 1,319 (100.0) | 6 | 21 (23.6) | 89 (100) | 7 |
| Borders | 6 (11.1) | 54 (100.0)  | 7 | 7 (35.0) | 20 (100) | 3 |
| Tayside | 105 (10.8) | 976 (100.0) | 8 | 23 (15.0) | 153 (100) | 8 |
| Fife | 27 (9.4) | 287 (100.0) | 9 | 1 (7.1) | 14 (100) | 10 |
| Forth Valley | 29 (5.9) | 494 (100.0) | 10 | 3 (14.3) | 21 (100) | 9 |
| Total | 1,722 (18.2) | 9,486 (100.0) | - | 286 (29.5) | 971 (100) | - |

\*Patients attending HCV specialist services with a diagnosis confirmed at any point up to the end of the study period (30th September 2014).

\*\*NHS Shetland and NHS Western Isles were excluded due to small numbers. No patients were recruited from NHS Dumfries & Galloway and NHS Orkney.

\*\*\*Excluding Edinburgh Western General.

\*\*\*\*Source Public Health Scotland.

Colour coding groups together regions with similar ranks across Scottish HCV Clinical Database and HCVRUK, NHS Greater Glasgow & Clyde and Borders anomalies.

**Table S6:** Prevalence (95% confidence intervals) of patient demographic and social factors by local health authority of residence. Based on 3,829 patients attending HCV-specialist clinics in England and Scotland.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Health authority area** | **Median age (IQR)** | **% Male (95% CI)** | **% White ethnicity (95% CI)** | **% Born in UK (95% CI)** | **% IDU route (95% CI)** | **% Blood product route (95% CI)** | **% Heavy alcohol user (95% CI)** |
| East Midlands | 50 (IQR=15) | 67.09 (62.67-71.29) | 71.28 (66.99-75.3) | 71.94 (67.66-75.94) | 60.34 (55.77-64.77) | 13.29 (10.37-16.68) | 40.76 (36.29-45.35) |
| East of England | 54 (IQR=13) | 69.57 (64.22-74.55) | 74.14 (68.99-78.85) | 72.5 (67.26-77.32) | 56.88 (51.25-62.37) | 18.75 (14.62-23.47) | 41.25 (35.8-46.86) |
| London | 52 (IQR=14.75) | 69.82 (64.93-74.39) | 45.62 (40.51-50.8) | 44.59 (39.46-49.82) | 42.71 (37.65-47.87) | 13.26 (10.01-17.11) | 34.7 (29.83-39.82) |
| North East | 48 (IQR=18.75) | 71.62 (65.2-77.45) | 81.45 (75.69-86.35) | 80.18 (74.32-85.21) | 56.76 (49.96-63.37) | 16.67 (12.01-22.23) | 42.73 (36.1-49.55) |
| North West | 49 (IQR=11) | 70.11 (64.38-75.4) | 89.01 (84.76-92.41) | 89.82 (85.62-93.13) | 68.79 (63.03-74.16) | 8.87 (5.82-12.81) | 47.87 (41.91-53.88) |
| South Central | 52 (IQR=13) | 72.27 (66.35-77.66) | 76.74 (71.1-81.76) | 73.64 (67.82-78.91) | 62.35 (56.09-68.32) | 13.33 (9.41-18.13) | 40.55 (34.46-46.87) |
| South East Coast | 55 (IQR=13.5) | 72.09 (56.33-84.67) | 72.09 (56.33-84.67) | 69.77 (53.87-82.82) | 59.52 (43.28-74.37) | 26.19 (13.86-42.04) | 35.71 (21.55-51.97) |
| South West | 51 (IQR=13) | 69.17 (62.9-74.95) | 92.05 (87.86-95.15) | 89.12 (84.47-92.77) | 67.36 (61.02-73.27) | 16.32 (11.87-21.63) | 49.79 (43.28-56.31) |
| West Midlands | 49 (IQR=18) | 70.07 (64.27-75.43) | 54.74 (48.64-60.74) | 54.61 (48.48-60.65) | 45.42 (39.41-51.53) | 15.38 (11.32-20.22) | 25.82 (20.75-31.42) |
| Yorkshire and The Humber | 46 (IQR=16) | 69.69 (64.6-74.44) | 73.3 (68.35-77.85) | 75.28 (70.43-79.7) | 67.06 (61.8-72.01) | 10.20 (7.21-13.91) | 42.53 (37.27-47.91) |
| Ayrshire and Arran | 54 (IQR=7) | 53.85 (25.13-80.78) | 100 (75.29-100) | 100 (75.29-100) | 25 (5.49-57.19) | 41.67 (15.17-72.33) | 30.77 (9.09-61.43) |
| Borders | 46 (IQR=15) | 85 (62.11-96.79) | 90 (68.3-98.77) | 85 (62.11-96.79) | 85 (62.11-96.79) | 10.00 (1.23-31.70) | 60 (36.05-80.88) |
| Fife | 43 (IQR=12.25) | 85.71 (57.19-98.22) | 100 (76.84-100) | 100 (76.84-100) | 71.43 (41.9-91.61) | 7.14 (0.18-33.87) | 50 (23.04-76.96) |
| Forth Valley | 53 (IQR=13) | 52.38 (29.78-74.29) | 100 (83.89-100) | 90.48 (69.62-98.83) | 63.16 (38.36-83.71) | 31.58 (12.58-56.55) | 45 (23.06-68.47) |
| Grampian | 46 (IQR=16) | 78.41 (68.35-86.47) | 87.64 (78.96-93.67) | 86.52 (77.63-92.83) | 74.16 (63.79-82.86) | 11.24 (5.52-19.69) | 51.14 (40.25-61.95) |
| Greater Glasgow and Clyde | 46 (IQR=11) | 74.76 (70.81-78.43) | 93.68 (91.24-95.61) | 93.48 (90.96-95.47) | 75.25 (71.24-78.95) | 8.51 (6.23-11.30) | 47.05 (42.64-51.49) |
| Highland | 54 (IQR=17.75) | 57.14 (28.86-82.34) | 92.86 (66.13-99.82) | 85.71 (57.19-98.22) | 30.77 (9.09-61.43) | 38.46 (13.86-68.42) | 46.15 (19.22-74.87) |
| Lanarkshire | 55 (IQR=12.5) | 54.55 (23.38-83.25) | 81.82 (48.22-97.72) | 81.82 (48.22-97.72) | 36.36 (10.93-69.21) | 54.55 (23.38-83.25) | 27.27 (6.02-60.97) |
| Lothian | 49 (IQR=14) | 70.8 (61.5-78.97) | 88.5 (81.13-93.73) | 87.5 (79.92-92.99) | 72.07 (62.76-80.17) | 7.21 (3.16-13.71) | 47.32 (37.81-56.98) |
| Tayside | 37 (IQR=16) | 71.24 (63.38-78.26) | 92.81 (87.5-96.36) | 93.46 (88.31-96.82) | 87.58 (81.29-92.36) | 3.92 (1.45-8.34) | 41.18 (33.29-49.41) |
| **Measure of Geographical Variation** | 9.33 (7.19-13.77)† | 12.93 (9.96-19.08)† | 17.42 (13.43-25.71)†11.54 (6.44-18.51)‡ | 16.99 (13.10-25.08)† | 27.87 (21.48-41.13)† | 74.99 (57.81-110.69)†36.07 (10.37-57.60)‡ | 19.54 (15.06-28.84)† |

†Coefficient of Variation (CV) with correction for sample size and 95% CI using Normal Approximation method. Asymptotic test of equivalence of CV p<0.001

‡Coefficient of Quartile Variation (CQV) and 95% CI using Normal Approximation method; applied to variables with visually highly skewed distributions and supported by Shapiro-Wilk test of normality (p-value <0.05).

**Table S7:** Prevalence (95% confidence intervals) of patients HCV-related and comorbidity factors by local health authority of residence. Based on 3,829 patients attending HCV-specialist clinics in England and Scotland.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Health authority area** | **% Diabetic (95% CI)** | **% Obese (95% CI)** | **% HCV-genotype 1 (95% CI)** | **% HCV-genotype 3 (95% CI)** | **% HIV positive** **(95% CI)** |
| East Midlands | 11.11 (8.43-14.28) | 28.15 (24.01-32.59) | 53.2 (48.49-57.87) | 37.53 (33.05-42.17) | 5.02 (3.21-7.44) |
| East of England | 13.93 (10.35-18.19) | 21.27 (16.88-26.21) | 68.77 (63.35-73.83) | 24.29 (19.67-29.4) | 2 (0.65-4.61) |
| London | 12.57 (9.41-16.31) | 17.79 (13.62-22.61) | 52.63 (47.19-58.03) | 32.46 (27.52-37.7) | 10.86 (7.84-14.55) |
| North East | 9.91 (6.32-14.62) | 22.16 (16.53-28.67) | 58.57 (51.59-65.31) | 34.29 (27.89-41.13) | 2.73 (1.01-5.84) |
| North West | 10.71 (7.35-14.94) | 26.54 (21.27-32.35) | 47.29 (41.06-53.57) | 46.12 (39.92-52.42) | 1.47 (0.4-3.71) |
| South Central | 9.73 (6.39-14.02) | 20.85 (15.58-26.96) | 59.2 (52.83-65.35) | 28 (22.53-34.01) | 2.75 (1.11-5.57) |
| South East Coast | 11.63 (3.89-25.08) | 15.38 (5.86-30.53) | 58.97 (42.1-74.43) | 38.46 (23.36-55.38) | 4.76 (0.58-16.16) |
| South West | 12.5 (8.59-17.36) | 19.31 (13.23-26.69) | 55.75 (49.02-62.34) | 31.86 (25.84-38.36) | 1.41 (0.29-4.06) |
| West Midlands | 15.3 (11.21-20.18) | 22.3 (17.47-27.76) | 45.87 (39.47-52.37) | 43.8 (37.45-50.3) | 4.04 (2.04-7.12) |
| Yorkshire and The Humber | 10.51 (7.51-14.2) | 22.44 (17.93-27.48) | 53.24 (47.78-58.64) | 39.71 (34.47-45.12) | 2.93 (1.42-5.33) |
| Ayrshire and Arran | 0 (0-24.71) | 10 (0.25-44.5) | 76.92 (46.19-94.96) | 15.38 (1.92-45.45) | 8.33 (0.21-38.48) |
| Borders | 10 (1.23-31.7) | 21.05 (6.05-45.57) | 57.89 (33.5-79.75) | 42.11 (20.25-66.5) | 27.78 (9.69-53.48) |
| Fife | 0 (0-23.16) | 7.14 (0.18-33.87) | 71.43 (41.9-91.61) | 28.57 (8.39-58.1) | 7.14 (0.18-33.87) |
| Forth Valley | 9.52 (1.17-30.38) | 5.88 (0.15-28.69) | 80.95 (58.09-94.55) | 14.29 (3.05-36.34) | 0 (0-17.65) |
| Grampian | 4.55 (1.25-11.23) | 12.64 (6.48-21.5) | 67.86 (56.78-77.64) | 25 (16.19-35.64) | 2.25 (0.27-7.88) |
| Greater Glasgow and Clyde | 5.78 (3.93-8.15) | 21.52 (17.85-25.56) | 53.11 (48.62-57.56) | 39.48 (35.16-43.92) | 3.68 (2.2-5.76) |
| Highland | 7.69 (0.19-36.03) | 0 (0-33.63) | 53.85 (25.13-80.78) | 30.77 (9.09-61.43) | 7.14 (0.18-33.87) |
| Lanarkshire | 9.09 (0.23-41.28) | 30 (6.67-65.25) | 54.55 (23.38-83.25) | 36.36 (10.93-69.21) | 0 (0-28.49) |
| Lothian | 6.6 (2.7-13.13) | 13.59 (7.63-21.75) | 65.05 (55.02-74.18) | 25.24 (17.2-34.76) | 33 (23.92-43.12) |
| Tayside | 2.61 (0.72-6.56) | 13.25 (8.28-19.71) | 37.67 (29.79-46.06) | 57.53 (49.09-65.67) | 1.96 (0.41-5.62) |
| **Measure of Geographical Variation** | 47.68 (36.75-70.37)† | 44.07 (33.97-65.04)† | 17.80 (13.72-26.27)† | 31.0 (23.89-45.75)† | 146.09 (112.61-215.62)†55.56 (30.06-83.05)‡ |

†Coefficient of variation (CV) with correction for sample size and 95% CI using Normal Approximation method. Asymptotic test of equivalence of CV p<0.001

‡Coefficient of Quartile Variation (CQV) and 95% CI using Normal Approximation method; applied to variables with visually highly skewed distributions and supported by Shapiro-Wilk test of normality (p-value <0.05).