Socioeconomic Inequalities in Chronic Liver Diseases and Cirrhosis Mortality in European Urban Areas before and after the Onset of the 2008 Economic Recession

Carme Borrell 1,2,3,4,* , Laia Palència 2,3,5,6,7, Lucia Bosakova 6,7, Mercè Gotsens 3,8,9, Joana Morrison 9, Claudia Costa 10, Dagmar Dzurova 11, Patrick Deboosere 12, Michala Lustigova 11, Merc Mari-Dell’Olmo 2,3,13, Sophia Rodopoulou 14 and Paula Santana 10,15

Abstract: Objective: To analyse the trends in chronic liver diseases and cirrhosis mortality, and the associated socioeconomic inequalities, in nine European cities and urban areas before and after the onset of the 2008 financial crisis. Methods: This is an ecological study of trends in three periods of time: two before (2000–2003 and 2004–2008), and one after (2009–2014) the onset of the economic crisis. The units of analysis were the geographical areas of nine cities or urban areas in Europe. We analysed chronic liver diseases and cirrhosis standardised mortality ratios, smoothing them with a hierarchical Bayesian model by each city, area, and sex. An ecological regression model was fitted to analyse the trends in socioeconomic inequalities, and included the socioeconomic deprivation index, the period, and their interaction. Results: In general, chronic liver diseases and cirrhosis mortality rates were higher in men than in women. These rates decreased in all cities during the financial crisis, except among men in Athens (rates increased from 8.50 per 100,000 inhabitants during the second period to 9.42 during the third). Socioeconomic inequalities in chronic liver diseases and cirrhosis mortality were found in six cities/metropolitan areas among men, and in four among women. Finally, in the periods studied, such inequalities did not significantly change. However, among men they increased in Turin and Barcelona and among women, several cities had lower inequalities in the third period. Conclusions: There are geographical socioeconomic inequalities in chronic liver diseases and cirrhosis mortality, mainly among men, that did not change during the 2008 financial crisis. These results should be monitored in the long term.
Keywords: chronic liver diseases; liver cirrhosis; mortality; inequalities; urban areas; financial crisis

1. Introduction
Different studies showed that during the economic recession that started in 2008, some health indicators deteriorate and others remained stable [1–3]. Analyses of the effects of financial crises on inequalities in health and mortality led to heterogeneous results, with inequalities increasing in some countries and remaining stable in others [1,4,5].

Cirrhosis and other chronic liver diseases are a major and preventable cause of death worldwide; the Global Burden of Disease Study 2017 described these diseases as the 13th leading cause of years of life lost globally [6,7]. Variations in cirrhosis mortality between countries reflect differences in risk factors, such as alcohol use and hepatitis B and C infection [8]. Several studies have described inequalities in mortality due to cirrhosis [9–12] and alcohol use [13–15]. However, few studies have analysed trends in liver-related and cirrhosis mortality after the start of the economic recession of 2008 [7,16–18]. Risk factors of cirrhosis mortality may change during economic recessions and influence the trends and socioeconomic inequalities in chronic liver diseases and cirrhosis mortality. For alcohol consumption, there is a contradictory evidence on the impact of economic crises on this consumption and alcohol-related-health problems. Possible mechanisms related to how these crisis affect alcohol consumption have been described as psychological distress, triggered by unemployment and income reductions, that increases alcohol consumption and secondly tighter budget constraints than imply less money spent in alcoholic beverages and reduce consumption [19]. Hepatitis B and C affect vulnerable populations such as for example persons who inject drugs or migrants of low income countries, populations who have suffered the financial crisis [20].

Therefore, the objective of this study was to analyse the trends in chronic liver diseases and cirrhosis mortality, and in socioeconomic inequalities in this mortality, in nine European urban areas before and after the onset of the 2008 financial crisis.

2. Methods
2.1. Design, Units of Analysis, and Study Population
This is an ecological study of trends in three periods of time: two periods before the 2008 economic crisis and one during the crisis (2000–2003, 2004–2008 and 2009–2014). This study is part of the EURO-HEALTHY project (funded by Horizon 2020: http://www.euro-healthy.eu), through which other causes of death have been described [21,22]. The units of analysis were the geographical areas of nine European cities or metropolitan areas (Athens metropolitan area, Barcelona city, Berlin-Brandenburg metropolitan region, Brussels metropolitan area, Lisbon metropolitan area, Greater London, Prague city, Stockholm metropolitan area, and Turin city). The study population consisted of the individual residents in these areas during the three periods mentioned above.

2.2. Data and Measures
The data and measures used were the following:

1. Mortality, corresponding to the number of deaths due to chronic liver diseases and cirrhosis (International Classification of Diseases (ICD)—9: 571; ICD—10: K70 and K74) by area, age group, and sex. Data were obtained from registries provided by local and national statistics institutions. The indicator of chronic liver diseases and cirrhosis mortality used for the analysis was the standardised mortality ratio (SMR), calculated by dividing the observed number of deaths in the study areas by the expected number of deaths (indirect method of age standardization). The latter was calculated considering the age-specific mortality rates in the standard population of the European Union (EU)-28 in the year 2007, and the population of the city/area by age groups. For descriptive purposes, we calculated the crude mortality rate
(MR), and the indirectly standardised mortality rate (ISMR). The latter was calculated by multiplying the SMR in the city/metropolitan area by the crude rate in the standard population.

2. Population, corresponding to the number of inhabitants living in the study areas. Most urban areas had data for the entire period studied or for at least 2 years. These data were stratified by age (5-year groups) and sex and were obtained from census or population registries. The median population of the areas ranged from 271 (Turin) to 193,630 (Berlin) (Table 1).

3. Socioeconomic data, obtained from the census, consisting of several indicators selected to identify the level of deprivation of the areas studied. We built a composite socioeconomic deprivation index using principal component analysis within each city. The variables included in the analysis for 2001 (2002, in the case of Berlin) were the percentages of: unemployed population (≥16 years, economically active population); manual workers (≥16 years); population with primary education as the highest attainment (International Standard Classification of Education 0 and 1, except for London, which was 0, 1, and 2) (25–64 years); and population with university education (25–64 years). The percentage of manual workers was not available for Stockholm and the index was calculated with the other three indicators. The index of deprivation was the first component of the principal component analysis, which was performed separately for each city; therefore, it was possible to show the pattern of deprivation in each setting. The proportion of variance explained by the first component ranged from 0.578 in Lisbon to 0.918 in the Athens metropolitan area. The principal component analysis was performed using the prcomp function of the R statistical software package. The calculation was performed by a singular value decomposition of the data matrix, which is generally the preferred method for numerical accuracy.

2.3. Data Analysis

Due to the excessively variable estimates for the small areas included in this study, we smoothed the SMR and we used the hierarchical Bayesian model proposed by Besag, York and Mollie (BYM) [23]. This model takes two types of random effects into account: spatial and heterogeneous; the former takes into account of the spatial structure of the data, while the latter deals with non-structural (non-spatial) variability. We estimated smoothed SMR (sSMR) for both sexes and periods using the following model:

\[
\begin{align*}
O_i & \sim \text{Poisson}(E_i \theta_i) \\
\log(\theta_i) & \sim \alpha + S_i + H_i
\end{align*}
\]

\[\text{(model 1)}\]

where, for each area \(i\), \(O_i\) is the number of observed cases, \(E_i\) the number of expected cases, \(\theta_i\), the sSMR with respect to the European population, \(S_i\) the spatial effect, and \(H_i\) the heterogeneous effect. Let \(\alpha\) be the intercept of the model. Expected cases were calculated by indirect standardisation, taking the liver cirrhosis mortality rates of the EU-28 in 2007 as reference (using the year approximately in the middle of the period) by age (using 5-year groups).
Table 1. Description of the nine European urban areas: number and type of small areas, period years, and total population (first- p25-, second -p50-, and third -p75- quartiles of the population by small area for men and women).

| Urban Area                        | Short Name | Number of Small Areas | Type of Small Areas | Period Years First Period 2000–2003 | Second Period 2004–2008 | Third Period 2009–2014 | Population (First Year Available) |
|-----------------------------------|------------|-----------------------|---------------------|-------------------------------------|------------------------|------------------------|-----------------------------------|
|                                   |            |                       |                     | Total                               | p25        | p50        | p75        | Total                               | p25       | p50       | p75       |
| Athens metropolitan area          | Athens     | 40                    | municipalities      | 2000–2003                           | 2004–2008   | 2009–2013  | 1,577,172 | 18,565 29,745 35,489 1,710,446 20,136 32,163 39,965 |
| Barcelona city                    | Barcelona  | 1491                  | census tracts       | 2000–2003                           | 2004–2008   | 2009–2013  | 697,563   | 365 457 577  796,497 418 517 648 |
| Berlin-Brandenburg metropolitan region | Berlin    | 30                    | districts           | 2002                                | 2006       | 2011      | 2,927,616 | 66,326 96,176 129,157 3,047,188 68,041 97,454 130,560 |
| Brussels capital region           | Brussels   | 145                   | neighbourhoods      | 2001–2003                           | 2004–2008   | 2009–2011  | 464,364   | 2727 4004 5707  505,673 3058 4288 6172 |
| Lisbon metropolitan area          | Lisbon     | 188                   | parishes            | 2000–2003                           | 2004–2008   | 2009–2012  | 1,275,813 | 2694 5437 8962 1,386,314 2938 5835 9904 |
| Greater London                    | London     | 983                   | census tracts       | 2000–2003                           | 2004–2008   | 2009–2014  | 3,597,120 | 3442 3810 4284 3,725,283 3526 3960 4382 |
| Prague city                       | Prague     | 57                    | districts           | 2001–2003                           | 2004–2008   | 2009–2014  | 549,652   | 1010 2206 15,001 610,466 1024 2100 14,838 |
| Stockholm metropolitan area       | Stockholm  | 1299                  | census tracts       | 2001–2003                           | 2004–2008   | 2009–2011  | 897,487   | 218 560 1050 936,977 232 599 1104 |
| Turin city                        | Turin      | 2678                  | census tracts       | 2000–2003                           | 2004–2008   | 2009–2013  | 425,782   | 88 129 196 465,987 96 142 215 |
Moreover, to analyse the trend in socioeconomic inequalities, we fitted an ecological regression model, which included the socioeconomic deprivation index (through the continuous variable $D$), the period (through two dummy variables, $P_2$ and $P_3$), and their interaction:

$$
O_{it} \sim \text{Poisson}(E_{it}\theta_{it})
$$

$$
\log(\theta_{it}) \sim \alpha + \beta_1 D_i + \beta_2 P_{2i} + \beta_3 P_{3i} + \beta_4 P_2 D_i + \beta_5 P_3 D_i + S_{it} + H_{it}
$$

where, for each area $i$ and period $t$ ($t = 1$ for the first period, $t = 2$ for the second period and $t = 3$ for the third period), $O_{it}$ is the number of observed cases, $E_{it}$ the number of expected cases, $\theta_{it}$ the sSMR with respect to the European population, $D_i$ the deprivation index; $S_{it}$ the spatial effect, and $H_{it}$ the heterogeneous effect. Finally, $P_2$ and $P_3$ took the following values: $P_{jt} = 1$ if $j = t$, and $P_{jt} = 0$ if $j \neq t$. Let $\alpha$ be the intercept of the model and $\beta_1, \beta_2, \beta_3, \beta_4, \beta_5$ the parameters or coefficients associated with the different variables and their interactions. The expected cases were calculated as in the previous model. Changes between periods in the relationship between socioeconomic deprivation index and mortality were evaluated through the interactions included in model 2. Specifically, we studied the change between the first and second period ($\beta_4$) and the second and third period ($\beta_5-\beta_4$).

In the two models (models 1 and 2), an intrinsic conditional autoregressive prior distribution was assigned to the spatial effect, which assumed that the expected value of each area coincided with the mean of the spatial effect of the adjacent areas and had a variance of $\sigma_s^{-2}$, while the heterogeneous effect was represented using independent normal distributions with mean 0 and variance $\sigma_h^{-2}$. A uniform distribution $U(0,\infty)$ was assigned to the standard deviations $\sigma_s$ and $\sigma_h$. A normal vague prior distribution was assigned to the parameters $\alpha, \beta_1, \beta_2, \beta_3, \beta_4,$ and $\beta_5$.

Given that the socioeconomic deprivation index scale is dimensionless and arbitrarily fixed, we calculated the relative risk (RR) for each city/metropolitan area, which compares liver cirrhosis mortality of the 95th percentile value of socioeconomic deprivation (severe deprivation) to its 5th percentile value (low deprivation). RR estimates were obtained based on the mean of their subsequent distribution, along with the corresponding 95% credible intervals (95% CI).

All analyses were performed using the Integrated Nested Laplace Approximation library of the R statistical package.

3. Results

Table 1 shows the characteristics of the nine areas studied. Greater London (7,322,403 inhabitants) is the area with the largest population size, and Turin (891,769 inhabitants) is the smallest. In the majority of areas, the median population (p50) by sex was under 6000, except districts in Berlin (median population of approximately 100,000) and municipalities in Athens (median population of approximately 30,000). Of note, the first period included 4 years (2000–2003), and the second and third period, 5 years (2004–2008 and 2009–2013, respectively) for most cities.

The description of mortality data is presented in Table 2. Chronic liver diseases and cirrhosis mortality rates (crude and age-adjusted) were higher among men than among women in the three periods across all cities. Rates were lower in Athens, Stockholm, and London (and in Lisbon for women only), and higher in Berlin. During the third period, death rates decreased in all settings except in Athens among men, where the ISMR increased from 8.50 per 100,000 inhabitants during the second period to 9.42 during the third.

Figures 1 and 2 show the RR of the association between socioeconomic deprivation index and mortality due to chronic liver diseases and cirrhosis, for men and women during the three periods in each city or metropolitan area. Among men, RR was always higher than 1 in all cities, except for Prague, Brussels, and Berlin. The highest RR in the first period was found in Stockholm (RR = 6.24); however, it decreased over time (in the last period, RR = 3.86). Turin’s RR showed an increasing trend, with the highest value observed in
the last period (RR = 4.06). Barcelona had a very similar increasing trend to that of Turin. However, these differences in RR did not have statistical significance.

Table 2. Number of deaths, crude mortality rate (MR), and indirectly standardised mortality rate (ISMR) per 100,000 inhabitants for men and women for each study period.

| Urban Areas | Men First Period (2000–2003) | Second Period (2004–2008) | Third Period (2009–2014) |
|-------------|-------------------------------|---------------------------|--------------------------|
|             | Deaths MR ISMR                | Deaths MR ISMR            | Deaths MR ISMR          |
| Athens      | 489 7.8 8.83                  | 595 7.85 8.5             | 671 9.08 9.42           |
| Barcelona   | 564 19.58 19.66               | 604 15.91 16.36          | 566 14.71 14.88         |
| Berlin      | 999 34.12 35.48               | 913 30.19 30.06          | 771 26.31 24.55         |
| Brussels    | 189 - -                        | 386 - -                  | 207 - -                 |
| Lisbon      | 1178 23.07 25.35              | 1154 17.87 19            | 862 16.25 16.73         |
| London      | 1953 13.5 18.63               | 2369 12.65 17.41         | 2603 10.65 14.45        |
| Prague      | 388 23.42 24.31               | 686 23.81 24.8           | 753 20.68 21.53         |
| Stockholm   | 291 10.73 12.41               | 489 10.38 11.8           | 273 9.41 10.63          |
| Turin       | 377 22.07 20.36               | 496 23.22 21.09          | 417 19.32 17.29         |

| Urban Areas | Women First Period | Second Period | Third Period |
|-------------|-------------------|---------------|--------------|
|             | Deaths MR ISMR    | Deaths MR ISMR| Deaths MR ISMR|
| Athens      | 213 3.13 3.18      | 299 3.62 3.52  | 285 3.52 3.27  |
| Barcelona   | 364 11.18 9.82     | 398 9.45 8.46  | 362 8.51 7.61 |
| Berlin      | 497 16.31 15.25    | 467 14.99 13.69| 422 13.82 12.07|
| Brussels    | 101 - -            | 221 - -       | 121 - -       |
| Lisbon      | 326 5.86 5.77      | 276 3.88 3.72  | 199 3.37 3.15  |
| London      | 968 6.48 8.14      | 1069 5.53 7.06 | 1254 5.01 6.38 |
| Prague      | 215 11.74 10.66    | 386 12.43 11.29| 391 10.14 9.34  |
| Stockholm   | 136 4.81 5.17      | 230 4.72 5.04  | 127 4.27 4.55  |
| Turin       | 331 17.71 14.6     | 360 15.36 12.59| 258 10.86 8.85  |

Note: Crude MR and ISMR are not displayed for Brussels, as population data were interpolated.

Figure 1. Association between socioeconomic deprivation index and liver cirrhosis mortality, relative risk (RR), and 95% credible intervals (CI) for men in nine urban areas. Notes: RR compares liver cirrhosis mortality of the 95th percentile value of socioeconomic deprivation (severe deprivation) to the 5th percentile value (low deprivation). RR$_1$: RR in the first period (2000–2003); RR$_2$: RR in the second period (2004–2008); RR$_3$: RR in the third period (2009–2014).
Figure 2. Association between socioeconomic deprivation index and liver cirrhosis mortality, relative risk (RR), and 95% credible intervals (CI) for women in nine urban areas. Notes: RR compares liver cirrhosis mortality of the 95th percentile value of socioeconomic deprivation (severe deprivation) to the 5th percentile value (low deprivation). RR$_1$: RR in the first period (2000–2003); RR$_2$: RR in the second period (2004–2008); RR$_3$: RR in the third period (2009–2014).

Among women, a positive significant association between deprivation and mortality was identified in Turin, Stockholm, London, and Barcelona. During the third period, the RR only increased in London, although without statistical significance (RR in the second period: 1.74, 95% CI: 1.29–2.29; RR in the third period: 2.09, 95% CI: 1.59–2.71). In the other cities, instead, the RR decreased during this period (Athens, Barcelona, Lisbon, Stockholm, and Turin) although without statistical significance. The decrease in RR in Lisbon was noteworthy (RR in the second period: 1.80, 95% CI: 0.98–3.09; RR in the third period: 0.97, 95% CI: 0.49–1.76).

4. Discussion

This study found that mortality rates of chronic liver diseases and cirrhosis mortality decreased in all cities during the financial crisis period, except among men in Athens. Mortality rates in men were higher than those in women. Moreover, socioeconomic inequalities in liver cirrhosis mortality were found in 6 cities/metropolitan areas among men, and in 4 among women. Although changes in inequalities were not statistically significant among men, these increased in Turin and Barcelona. Among women, several cities had lower RR in the third period.

Previous studies on the long-term trends in cirrhosis mortality showed it decreased in the last four decades in the majority of countries in Western Europe, except for the UK, Ireland, and Finland [8,24–27]. This decline was mainly due to a decrease in alcohol consumption and an improvement in alcohol quality. Indeed, in EU member states, around 60–80% of deaths from liver disease are due to excessive alcohol consumption [2–4]. However, some countries in Eastern Europe had higher rates of cirrhosis-related mortality. Such mortality mainly increased during the 1980s and early 1990s as a result of the dissolution of the Union of Soviet Socialist Republics and the use of low-quality alcohol;
more recently, rates decreased in the majority of these countries [25,26]. In Central Europe, cirrhosis-related mortality rates were high with a stable trend [8]. In our analysis, the only city where the rates did not decrease was Athens, where the financial crisis was particularly impactful. On this note, an increase in cirrhosis mortality and alcohol consumption in the Greek population aged 15–49 has been presented by the Global Burden of Diseases project (Greece) [28]. Bosque-Prous et al. carried out a study in 2006–2013 on alcohol consumption among adults aged 50–64 and found the prevalence of hazardous drinking decreased and abstention from alcohol consumption increased in the majority of European countries, except for the Czech Republic, where the opposite trends were observed among men [29]. However, the review carried out by Dom et al. [30] found mixed results, mainly related to a general decrease in alcohol consumption and an increase in harmful use within specific vulnerable social subgroups. As described above a systematic review found that, during economic crises, increased psychological distress and tighter budget constraints due to income reductions are the main behavioural mechanisms behind alcohol consumption and alcohol-related health problems. The former was found to lead to higher and more frequent alcohol consumption, and to a higher prevalence of drinking problems to cope with the distress; the latter can lead instead to lower alcohol consumption [19].

Although in Europe alcohol is the main contributor to chronic liver disease and cirrhosis mortality, other causes include hepatitis B or C infection and non-alcohol fatty liver disease, associated to obesity and type 2 diabetes. Pimpim reported that in this century viral hepatitis mortality increased in most Northern European countries, Hungary, Italy, Croatia and Portugal, but remained stable or decreased in others [26]. Ireland et al. observed a stable trend in mortality among individuals diagnosed with hepatitis C in England [31].

The fact that in our study chronic liver diseases and cirrhosis mortality was observed to be higher among men than women might be due to the higher alcohol consumption among men. Of note, a study of Bosque-Prous et al. [32] found that European countries with higher gender equality presented lower gender differences in hazardous drinking, mainly due to higher consumption among women. Due to this, the authors recommended policies aimed at improving gender equality to be accompanied by specific alcohol control policies.

We found socioeconomic inequalities in chronic liver diseases and cirrhosis mortality in men in the majority of cities, and in four cities among women. These inequalities are related to the different factors associated with chronic liver diseases and cirrhosis, namely alcohol consumption, and hepatitis B and C. It is important to take into account that deprived areas have a higher proportion of vulnerable populations, such as drug users and marginalised groups, who can be at a greater risk of contracting hepatitis B and C [20], and exhibit higher alcohol consumption [33]. However, some reviews that have analysed area-level factors on alcohol use [33–35] did not find clear evidence that area-level disadvantage is associated with increased alcohol use. Previous studies have shown also socioeconomic inequalities in cirrhosis mortality in urban areas of European cities [15,36]. Moreover, studies that have analysed socioeconomic inequalities in alcohol-attributable mortality have found it is higher in lower socioeconomic groups in the majority of countries, and is similar in men and women [14,33,37,38]. Ford et al. described the increase of hepatitis C mortality in New York, from 2006 to 2014, and the highest rates occurred in neighbourhoods comprising socioeconomically disadvantaged groups [39].

Our study found that, during the 2008 economic crises, changes in the trends of socioeconomic inequalities in chronic liver diseases and cirrhosis mortality did not have statistical significance. Nevertheless, an increase was observed among men in Barcelona and Turin in the third period. Other studies analysing the trends in inequalities in cirrhosis mortality before the economic recession found different results: no increase for Barcelona [9] and an increase in Australia [12] The authors suggest that the increase in socioeconomic inequalities in Australia was due to the increased harmful alcohol consumption among lower socioeconomic groups, which might be attributed to a relative increased affordability of alcohol over time. Crombie and Precious described a reversal in the social class gradient
of cirrhosis mortality during the 20th century (from advantaged classes to disadvantaged ones). These findings indicate a major change in risk factor distributions across social classes, possibly explained by differential changes in alcohol consumption [40]. The study by Mackenback et al. [14] found a rise in inequality in alcohol-related mortality through the years (1980–2009) in several countries in Eastern Europe (Hungary, Lithuania, and Estonia) and Northern Europe (Finland and Denmark). These findings can be explained by a rapid rise in alcohol-related mortality in lower socioeconomic groups. These trends should be monitored in the near future to observe their progress.

Strengths and Limitations

This study reported, for the first time, chronic liver diseases and cirrhosis mortality and socioeconomic inequalities in 9 cities/metropolitan areas of Europe before and during the financial crisis. It is worth mentioning that vital statistics are a good source of information to study cirrhosis mortality in Europe [8] This study has some limitations. First, data used for socioeconomic indicators were dated from 2001, and the deprivation of areas could have changed over time; however, the rank of areas by socioeconomic deprivation has probably remained unchanged. Second, the number of areas included per city varied considerably, which may have affected the robustness of estimates (small number of deaths); we addressed this by using Bayesian methods to smooth the SMR of small areas. Third, the size of the small areas differed between the urban areas studied: smaller areas are more homogeneous and the possibility of observing stronger effects is higher, which may partly explain some of the higher RRs for Barcelona, Stockholm and Turin mainly among men.

5. Conclusions

This study shows a decrease in chronic liver diseases and cirrhosis mortality in men and women in European urban areas (except among men in Athens); the existence of geographical socioeconomic inequalities in this mortality; and the lack of significant change in these inequalities over time, after the onset of the financial crisis of 2008. However, these results should be monitored in the long term in order to study future changes.

Our findings hint at implementing policies to decrease risk factors for chronic liver diseases and cirrhosis, mainly among vulnerable populations. For alcohol consumption, we suggest policies such as: tax increase, the establishment of a minimum price for alcohol [24], marketing restrictions, and screening and behavioural interventions. Additionally, vaccination for hepatitis B for all population groups and the implementation of harm reduction programs for drug users should be prioritized [26].

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References
1. Parmar, D.; Stavropoulou, C.; Ioannidis, J.P.A. Health outcomes during the 2008 financial crisis in Europe: Systematic literature review. BMJ 2016, 354, i4586. [CrossRef]
2. Stuckler, D.; Basu, S.; Suhrcke, M.; Coutts, A.; McKee, M. Effects of the 2008 recession on health: A first look at European data. Lancet 2011, 378, 128–125. [CrossRef]
3. Bacigalupo, A.; Shahidi, F.; Sulkowska, U.; Manczuk, M.; Rehm, J.; Boffetta, P.; Lowenfels, A.B.; La Vecchia, C. Liver Cirrhosis Mortality in Europe, with Special Attention to Central and Eastern Europe. Eur. J. Public Health 2010, 16, 193–201. [CrossRef] [PubMed]
4. Karanikolos, M.; Heino, P.; McKee, M.; Stuckler, D.; Legido-Quigley, H. Effects of the Global Financial Crisis on Health in High-Income Oecd Countries. Int. J. Health Serv. 2016, 46, 208–240. [CrossRef]
5. Bacigalupo, A.; Escolar-Pujolar, A. The impact of economic crises on social inequalities in health: What do we know so far? Int. J. Equity Health 2014, 13, 52. [CrossRef]
6. A Roth, G.; Abate, D.; Abate, K.H.; Ayub, S.M.; Abbafati, C.; Abbasi, N.; Abbastabar, H.; Abd-Allah, F.; Abdela, J.; Abdelalim, A.; et al. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018, 392, 1736–1788. [CrossRef]
7. Li, W.; Kemos, P.; Saliccioli, J.D.; Marshall, D.C.; Shalhoub, J.; Alazawi, W. Socioeconomic Factors Associated With Liver-Related Mortality From 1985 to 2015 in 36 Developed Countries. Clin. Gastroenterol. Hepatol. 2020. [CrossRef] [PubMed]
8. Mokdad, A.; Lopez, A.D.; Shahraz, S.; Lozano, R.; Stanaway, J.; Murray, C.J.L.; Naghavi, M. Liver cirrhosis mortality in 187 countries between 1980 and 2010: A systematic analysis. BMC Med. 2014, 12, 1–24. [CrossRef]
9. Dalmay-Bueno, A.; García-Alités, A.; Mari-Dell’Olmo, M.; Pérez, K.; Espelt, A.; Kunst, A.E.; Borrell, C. Trends in socioeconomic inequalities in cirrhosis mortality in an urban area of Southern Europe: A multilevel approach. J. Epidemiol. Community Health 2009, 64, 720–727. [CrossRef] [PubMed]
10. Aguilar, I.; Feja, C.; Compès, M.L.; Rabanaque, M.J.; Esteban, M.; Alcalá, T.; Martos, M.C. Desigualdades y mortalidad por cirrosis en varones (Zaragoza, 1996-2003). Gac. Sanit. 2011, 25, 139–145. [CrossRef]
11. Icaza, G.; Núñez, L.; Ordaz, N.; Verdugo, C.; Caglieri, S.; Castillo-Carniglia, A. Asociación entre variables demográficas y socioeconomicas y mortalidad por cirrosis y otras enfermedades del hígado. Rev. Méd. Chil 2017, 145, 1412–1420. [CrossRef]
12. Najman, J.M.; Williams, G.; Room, R. Increasing socioeconomic inequalities in male cirrhosis of the liver mortality: Australia 1981-2002. Drug Alcohol Rev. 2007, 26, 273–278. [CrossRef] [PubMed]
13. Mackenbach, J.P.; Kuhlánová, I.; Menvielle, G.; Bopp, M.; Borrell, C.; Costa, G.; Deboosere, P.; Esnaola, S.; Kalediene, R.; Kovacs, K.; et al. Trends in inequalities in premature mortality: A study of 3.2 million deaths in 13 European countries. J. Epidemiol. Community Health 2014, 69, 207–217. [CrossRef] [PubMed]
14. Mackenbach, J.P.; Kuhlánová, I.; Bopp, M.; Borrell, C.; Deboosere, P.; Kovács, K.; Looman, C.W.N.; Leinsalu, M.; Mäkelä, P.; Martikainen, P.; et al. Inequalities in Alcohol-Related Mortality in 17 European Countries: A Retrospective Analysis of Mortality Registers. PLoS Med. 2015, 12, e1001909. [CrossRef]
15. Santana, P.; Costa, C.; Mari-Dell’Olmo, M.; Gotsens, M.; Borrell, C. Mortality, material deprivation and urbanization: Exploring the social patterns of a metropolitan area. Int. J. Equity Health 2015, 14, 1–13. [CrossRef] [PubMed]
16. Tapper, E.B.; Parikh, N.D. Mortality due to cirrhosis and liver cancer in the United States, 1999-2016: Observational study. BMJ 2018, 362, k2817. [CrossRef]
17. Zou, B.; Yeo, Y.H.; Jeong, D.; Park, H.; Sheen, E.; Lee, D.H.; Henry, L.; Garcia, G.; Ingelsson, E.; Cheung, R.; et al. A Nationwide Study of Inpatient Admissions, Mortality, and Costs for Patients with Cirrhosis from 2005 to 2015 in the USA. Dig. Dis. Sci. 2019, 65, 1520–1528. [CrossRef] [PubMed]
18. Trias-Llimós, S.; Bijsma, M.J.; Jansen, F. The role of birth cohorts in long-term trends in liver cirrhosis mortality across eight European countries. Addiction 2016, 112, 250–258. [CrossRef]
19. de Goeij, M.C.; Suhrcke, M.; Toffolotti, V.; van de Mheen, D.; Schoenmakers, T.M.; Kunst, A.E. How economic crises affect alcohol consumption and alcohol-related health problems: A realist systematic review. Soc. Sci. Med. 2015, 131, 131–146. [CrossRef]
20. World Health Organization. Global Hepatitis Report; World Health Organization: Geneva, Switzerland, 2017.
21. Andersen, L.L.; Jensen, P.H.; Sundstrup, E. Barriers and opportunities for prolonging working life across different occupational groups: The SeniorWorkingLife study. Eur. J. Public Health 2019, 30, 241–246. [CrossRef]
22. Lillie, P.J.; Samson, A.; Li, A.; Adams, K.; Capstick, R.; Barlow, G.D.; Easm, N.; Hamilton, E.; Moss, P.J.; Evans, A.; et al. Novel coronavirus disease (Covid-19): The first two patients in the UK with person to person transmission. J. Infect. 2020, 80, 578–606. [CrossRef] [PubMed]
23. Besag, J.; York, J. Bayesian image restoration, with two applications in spatial statistics. Ann. Inst. Stat. Math. 1991, 43, 1–20. [CrossRef]
24. Sheron, N. Alcohol and liver disease in Europe – Simple measures have the potential to prevent tens of thousands of premature deaths. J. Hepatol. 2015, 64, 957–967. [CrossRef]
25. Zatoroski, W.A.; Sulkowska, U.; Mančzuk, M.; Rehm, J.; Boffetta, P.; Lowenfels, A.B.; La Vecchia, C. Liver Cirrhosis Mortality in Europe, with Special Attention to Central and Eastern Europe. Eur. Addict. Res. 2010, 16, 193–201. [CrossRef] [PubMed]
26. Pimpin, L.; Cortez-Pinto, H.; Negro, F.; Corbould, E.; Lazarus, J.; Webber, L.; Sheron, N. Burden of liver disease in Europe: Epidemiology and analysis of risk factors to identify prevention policies. *J. Hepatol.* 2018, 69, 718–735. [CrossRef] [PubMed]
27. Ascione, A.; Fontanella, L.; Imparato, M.; Rinaldi, L.; De Luca, M. Mortality from cirrhosis and hepatocellular carcinoma in Western Europe over the last 40 years. *Liver Int.* 2017, 37, 1193–1201. [CrossRef]
28. Tyrovolas, S.; Kassebaum, N.J.; Stengachis, A.; Abraha, H.N.; Alla, F.; Androudi, S.; Car, M.; Chrepa, V.; Fullman, N.; Fürst, T.; et al. The burden of disease in Greece, health loss, risk factors, and health financing, 2000–16: An analysis of the Global Burden of Disease Study 2016. *Lancet Public Health* 2018, 3, e395–e406. [CrossRef]
29. Bosque-Prous, M.; Kunst, A.E.; Brugal, M.T.; Espelt, A. Changes in alcohol consumption in the 50–64-year-old European economically active population during an economic crisis. *Eur. J. Public Health* 2017, 27, 711–716. [CrossRef]
30. Dom, G.; Samochowiec, J.; Evans-Lacko, S.; Wahlbeck, K.; Van Hal, G.; McDaid, D. The Impact of the 2008 Economic Crisis on Substance Use Patterns in the Countries of the European Union. *Int. J. Environ. Res. Public Health* 2016, 13, 122. [CrossRef]
31. Ireland, G.; Mandal, S.; Hickman, M.; Ramsay, M.E.; Harris, R.; Simmons, R. Mortality rates among individuals diagnosed with hepatitis C virus (HCV); an observational cohort study, England, 2008 to 2016. *Eurosurveillance* 2019, 24, 1800695. [CrossRef] [PubMed]
32. Bosque-Prous, M.; Espelt, A.; Borrell, C.; Bartroli, M.; Guitart, A.M.; Villalbi, J.; Brugal, M.T. Gender differences in hazardous drinking among middle-aged in Europe: The role of social context and women’s empowerment. *Eur. J. Public Health* 2015, 25, 698–705. [CrossRef] [PubMed]
33. Collins, S.E. Associations Between Socioeconomic Factors and Alcohol Outcomes. *Alcohol Res. Curr. Rev.* 2016, 38, 83–94.
34. Bryden, A.; Roberts, B.; Petticrew, M.; McKee, M. A systematic review of the influence of community level social factors on alcohol use. *Heal. Place* 2013, 21, 70–85. [CrossRef]
35. Karriker-Jaffe, K.J. Areas of disadvantage: A systematic review of effects of area-level socioeconomic status on substance use outcomes. *Drug Alcohol Rev.* 2011, 30, 84–95. [CrossRef] [PubMed]
36. Mari-Dell’Olmo, M.; Gotsens, M.; Palencia, L.; Burstström, B.; Corman, D.; Costa, C.; Deboosere, P.; Diez, E.; Domínguez-Berjón, M.E.; Dzurova, D.; et al. Socioeconomic inequalities in cause-specific mortality in 15 European cities. *J. Epidemiol. Commun. Health* 2015, 69, 432–441. [CrossRef]
37. Probst, C.; Roerecke, M.; Behrendt, S.; Rehm, J. Socioeconomic differences in alcohol-attributable mortality compared with all-cause mortality: A systematic review and meta-analysis. *Int. J. Epidemiol.* 2014, 43, 1314–1327. [CrossRef]
38. Probst, C.; Roerecke, M.; Behrendt, S.; Rehm, J. Gender differences in socioeconomic inequality of alcohol-attributable mortality: A systematic review and meta-analysis. *Drug Alcohol Rev.* 2014, 34, 267–277. [CrossRef]
39. Ford, M.M.; Desai, P.S.; Maduro, G.; Laraque, F. Neighborhood Inequalities in Hepatitis C Mortality: Spatial and Temporal Patterns and Associated Factors. *J. Hered.* 2017, 94, 746–755. [CrossRef]
40. Crombie, I.K.; Precious, E. Changes in the Social Class Gradient of Cirrhosis Mortality in England and Wales across the 20th Century. *Alcohol Alcohol.* 2010, 46, 80–82. [CrossRef] [PubMed]