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Stakeholder perspectives on European priorities for comprehensive liver cancer control: a conjoint analysis

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Background: As liver cancer incidence and mortality remain high in many parts of Europe, a more comprehensive response is required to reduce the burden. Expert stakeholders should be involved in the design of responses because they have important insights about potentially effective responses and will be affected by policy changes. We aimed to prioritize liver cancer control strategies based on European liver cancer stakeholders’ views of which strategies would have the greatest impact in a comprehensive liver cancer control plan. Methods: One hundred liver cancer clinical, policy and advocacy stakeholders from France, Germany, Italy, Spain and Turkey were surveyed. Respondents completed 12 conjoint choice tasks in which they chose which of two subsets of 11 strategies would have the greatest impact in their country. Results: All strategies were considered likely to have a positive impact (P < 0.01). The highest priority strategy was monitoring of at-risk populations, followed by centres of excellence, clinical education, multidisciplinary management, national guidelines, measuring social burden, public awareness, risk assessment and referral, research infrastructure and access to treatments. Conclusions: Canvassing stakeholder views through a conjoint analysis survey provided a robust quantitative prioritization that can complement traditional qualitative consultation processes. The prioritized strategies provide a logical starting point for decision makers considering developing national plans or collaborative efforts to achieve comprehensive liver cancer control in Europe.

Introduction

Liver cancer is the second most common cause of cancer death among men and the sixth among women worldwide.1 Incidence is relatively high in southern and western Europe,1 and incidence and mortality increased in many European countries over the past 30 years, with a possible plateau or slight decline more recently.2–4 Risk factor profiles are changing, with fluctuations in alcohol...
consumption, reductions in hepatitis B and C and increases in obesity and insulin resistance, making the future public health burden of liver cancer uncertain. There is some recognition that Europe needs to do more to control liver cancer and its risk factors. However, most actions to date by the European Union (EU) and individual jurisdictions have focused on cancer generally or on viral hepatitis rather than adopting a comprehensive approach to liver cancer.\(^6\) With this limited approach, there is a risk that many effective liver cancer control strategies will be overlooked.

Qualitative research has identified a range of clinical management, communication, research and infrastructural strategies addressing antecedents of liver cancer, better care and national and patient-centred connections that could be included in national plans.\(^10\) It is rarely feasible to implement all the known effective strategies, but comprehensive liver cancer control (CLCC) plans could effectively improve population health if they are appropriately prioritized. Some methods for prioritization are based on the concept of technical efficiency, which is concerned with maximizing the output from a given set of inputs.\(^13\) For example, strategies could be compared to identify the alternatives that achieve the greatest reduction in liver cancer mortality in a given health system. In this context, liver cancer experts might provide government decision makers with useful insights as to what could be achieved with particular liver cancer strategies.

An alternative approach would have been to consider which strategies would have been most cost-effective, given scarce resources, as a way to promote the technical efficiency of liver cancer control.\(^14\) This approach would require a great deal of information and/or assumptions to be made on populations at risk, disease progression and, more importantly, the costs and outcomes of each of the strategies to be considered. Furthermore, if such analysis was to be considered as promoting allocative efficiency, the normative values of policy makers and/or citizens of country would need to be assessed. While such methods are feasible for some research questions, although rarely for complex questions regarding allocation problems, like the one that we are addressing, they have been increasingly criticized for being too simplistic and lacking appropriate stakeholder engagement.\(^14\)

The present study addresses the research question of what strategies stakeholders believe should have the highest priority for inclusion in CLCC plans in Europe. It is hypothesized that priorities will be similar to those found in a pilot study in Asia,\(^10\) but that there will be some differences specific to Europe, across the countries studied, and to respondents with different roles. The results will be of interest to analysts and decision makers in the EU and member states looking for the most important strategies to start with when developing CLCC plans.

**Methods**

Our methods were guided by a recent checklist for the application of conjoint analysis.\(^15\) Details are available from the authors on request. Attributes were selected based on rigorous qualitative analysis, described elsewhere.\(^10\) Attributes were presented dichotomously as either present or absent in CLCC plans in our choice tasks. The attributes were tested within a pilot study in Asia.\(^10\) As well as demonstrating the feasibility of stratifying by subgroups of 20 respondents, the pilot identified potential ambiguities in the descriptions of some attributes, which were remedied for the current study.

The choice tasks were constructed using a paired-comparison approach, which involved a forced choice comparison of two possible CLCC plans within each choice task. We applied a 2\(^{11}\) main-effects experimental design, identified from the SAS catalogue of designs.\(^16\) This design consists of 12 rows (corresponding with the number of choice tasks necessary to allow orthogonality) and 11 columns representing each of the possible strategies. The design was tested using an online tool that confirmed it was orthogonal and D-optimal, that is, perfect efficiency compared with the optimal design.\(^17\) For each row, a choice task was created such that strategies were placed in the CLCC plan on the left or right if a 1 or \(-1\), respectively, appeared in the column corresponding to that strategy. The result was 12 choice tasks, each containing two plans with between three and eight strategies each. Each strategy appeared once and only once in each choice task, in the plan on the left or on the right but not both. The varied number of strategies across plans may introduce a bias in favour of the plan containing more strategies, but this is unlikely to bias the results because there is no correlation between the number of strategies in a plan and whether a given strategy appears in the plan.

Stakeholder preferences for the content of CLCC plans were elicited by asking each respondent to select which of the two plans they believed would have the greatest impact in their country in each of the 12 tasks. Respondents were not required to justify their choice or detail either the strength of preference or confidence in their answer. An example of the task is shown in figure 1.

Potential respondents were identified in France, Germany, Italy, Spain and Turkey, using methods and a set of inclusion and exclusion criteria designed to ensure respondents would have sufficient experience to be familiar with liver cancer concerns,

![Figure 1 Example of experimental task](image_url)
policy and practices in their countries. The process for identification of potential respondents and inclusion and exclusion criteria are described in detail elsewhere. Purposive sampling was used to recruit an equal number of respondents from each country.

Once identified, potential respondents were sent an e-mail invitation to participate and, if they did not respond within 2 weeks, received a follow-up phone call. Up to four phone calls were attempted before a potential respondent was classified as ‘no response’. Interviewers administered the survey in person or by telephone between September 2010 and April 2011. The survey also collected information on the participants’ roles, specialties and levels of involvement in liver cancer control. Respondents were informed about the potential risks and benefits of the study. Respondents participated voluntarily and without reimbursement. The Johns Hopkins Bloomberg School of Public Health Institutional Review Board determined that the study did not require ethical approval.

Responses were coded as 1 (0) when respondents chose the plan on the left (right). The explanatory variables were the strategies, coded as 1 (−1) if they appeared in the plan on the left (right), thus corresponding to the underlying study design. This coding method meant that negative regression coefficients were possible and indicated that respondents were averse to that strategy. Data were analysed using ordinary least squares (OLS) and Wald tests in Stata 11.2. All analyses used Huber/White/sandwich robust standard errors, which relaxed the assumption of independence to allow for the clustering of observations from each respondent. This method was chosen because OLS does not require the assumption of independence of irrelevant alternatives, the difference between logit and OLS is generally found to be small in conjoint analysis experiments and, given our main-effects design and zero priors on parameters, a linear model can be considered more appropriate.

**Results**

Two hundred and seventy-two potential respondents were identified and 100 completed the survey, giving a completion rate of 37%. Non-response was the main reason for non-participation (n = 96) followed by refusal to participate (n = 43).

From each of the five countries, there were 20 respondents, including 12 working in clinical, five in policy and three in advocacy roles. There were some differences in main field of interest across countries (P = 0.047), with the greatest number of respondents from France, Germany, Italy and Turkey working in hepatocellular carcinoma (HCC), whereas more respondents from Spain worked in hepatitis and transplantation. There were also differences in levels of involvement in liver cancer control (P = 0.001), with most respondents from France and Italy working at national or international levels, and most from Germany, Spain and Turkey working at national or regional/provincial levels.

Figure 2 shows the prioritized strategies in descending order. Coefficients for all strategies were positive and significantly above zero (all P < 0.01), indicating that all were considered likely to have a positive impact. The highest priorities were for monitoring of at-risk populations, centres of excellence, clinical education and multidisciplinary management (all P < 0.001).

Additional regression models tested whether there were differences in strategies’ level of priority across countries, roles, main area and level of involvement in liver cancer. Spearman rank correlation coefficients indicated the order of priorities was similar between Italy and Germany (P < 0.001), between Italy and France (P = 0.002) and between respondents who worked mainly in HCC and those working mainly in transplantation (P = 0.015), whereas the priorities of all other pairs of subgroups had low rank order correlations. There were some differences across countries in how the strategies were ranked, particularly for Turkey, as shown in table 1. Based on standard deviations (SD) of ranks, there was most disagreement on the priority of measuring social burden (SD = 3.97), which ranged from a ranking of 1 for Turkey to 10 for Germany and Spain, and national guidelines (SD = 3.58), which was ranked 1 for Germany and 9 for Spain and Turkey. However, Wald tests for individual strategies indicated no significant differences across countries in level of priority for 10 of the strategies. There was a significant difference for national guidelines (P = 0.048), driven by respondents from Germany giving this strategy significantly higher priority than those from Spain (P = 0.034) and Turkey (P = 0.009), and by respondents from Italy also giving it a higher priority than those from Turkey (P = 0.050).

There were significant differences by role for just one strategy, monitoring of at-risk populations (P = 0.039), with respondents working in advocacy roles prioritizing this strategy significantly lower than those working in clinical (P = 0.024) or policy (P = 0.017) roles. There was only one strategy, transplantation infrastructure, for which the level of priority differed significantly across areas of involvement (P = 0.014). Respondents who were mainly involved in hepatitis prioritized this strategy significantly lower than those who were mainly involved in metastatic liver cancer (P = 0.005) or transplantation (P = 0.021).

There were significant differences by level of involvement for four strategies: monitoring of at-risk populations (P < 0.001), access to treatments (P < 0.001), centres of excellence (P = 0.045) and measuring social burden (P < 0.001). Compared with each other group, respondents working at the local/municipality level gave a lower (actually negative at P < 0.001) priority to measuring social burden (all P < 0.001) and a higher priority to monitoring at-risk populations (all P < 0.001). For access to treatments, respondents working at the international level gave a lower and negative (P < 0.001) priority than respondents working at local/municipality (P < 0.001) or regional/provincial (P = 0.018) levels. Finally, respondents working at a national level had a lower priority for centres of excellence than those working at an international level (P = 0.009).

**Discussion**

The significant public health burden of liver cancer in Europe has been recognized, but no country has yet attempted to address this issue in a comprehensive manner. In this study, we found that liver cancer stakeholders from five countries in Europe considered all 11 strategies under evaluation to be likely to have an impact in their countries, and identified which strategies were considered to have the highest priority. We now relate these findings to previous research in the field, including exploring some possible reasons for the observed differences across countries, outline some strengths and limitations of the study and discuss implications and next steps for decision makers.

There are a few possible reasons for the differences observed across countries. Turkey had different priorities compared with the other countries, possibly reflecting differences in existing infrastructure. Turkey’s high priority for measuring social burden may reflect concerns that registries are still developing, such that accurate cancer incidence estimates were available for Turkey only recently, but a more relevant reason may be that the cancer burden and profile of Turkey is different to that in other countries. Almost two-thirds of the cancers in Turkey are tobacco-related, and control and awareness programmes are directed to tobacco control programmes, instead of liver cancer. This suggests why respondents from Turkey may have considered centres of excellence to be a relatively low priority.

National guidelines were considered the highest priority in Germany and third in Italy, but as low as ninth for Spain and Turkey. European countries may follow guidelines published by the European Society for Medical Oncology, the European Association for the Study of the Liver or other international
bodies, or may use their own guidelines. German, French and Spanish guidelines for HCC diagnosis and treatment have been published, as have diagnostic guidelines for Italy. The level of priority for this strategy may reflect differences across countries in the strength and diffusion of existing national recommendations, satisfaction with existing guidelines or opinions as to whether national guidelines are necessary, given the existence of European guidelines. After data collection for this survey had been completed, a review of

Figure 2 Priority liver cancer control strategies for five countries

<table>
<thead>
<tr>
<th>Strategy</th>
<th>France</th>
<th>Germany</th>
<th>Italy</th>
<th>Spain</th>
<th>Turkey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring of at-risk populations</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Centers of excellence</td>
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<td>0.017</td>
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<td>&lt;0.001</td>
<td>0.023</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multidisciplinary management</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.004</td>
<td>0.059</td>
</tr>
<tr>
<td>National guidelines</td>
<td>0.022</td>
<td>&lt;0.001</td>
<td>0.001</td>
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<td>0.059</td>
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<tr>
<td>Public awareness</td>
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<td>0.023</td>
<td>0.001</td>
<td>0.102</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Measuring social burden</td>
<td>0.032</td>
<td>0.136</td>
<td>0.001</td>
<td>0.047</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Risk assessment and referral</td>
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<td>0.012</td>
<td>0.001</td>
<td>0.025</td>
<td>0.001</td>
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<tr>
<td>Research infrastructure</td>
<td>0.138</td>
<td>0.007</td>
<td>0.002</td>
<td>0.005</td>
<td>0.677</td>
</tr>
<tr>
<td>Access to treatments</td>
<td>0.691</td>
<td>0.113</td>
<td>0.221</td>
<td>0.002</td>
<td>0.359</td>
</tr>
<tr>
<td>Transplantation infrastructure</td>
<td>0.104</td>
<td>0.237</td>
<td>0.250</td>
<td>0.252</td>
<td>0.090</td>
</tr>
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</table>
HCC clinical practice guidelines published in English and German between 2001 and 2009 concluded that most guidelines contained serious problems, with the exception of the Italian guideline and three North American guidelines. Given these findings, our results may underestimate the current priority for national guidelines.

The higher priority for centres of excellence in Spain and Italy may reflect concerns about access to timely treatment. Given the fast progression of HCC, a delay of a few months between diagnosis and treatment can mean that the recommended treatment is no longer the best strategy. Centres of excellence may provide better treatment options, with rapid decision making and multidisciplinary teams that can ensure the patient does not lose critical time getting treatment. In this way, centres of excellence may be considered the next step in improving care if there is already reasonable funding for treatment, which has been identified as more of a concern in Turkey than the other countries.

The priorities are similar to those found in our previous research with 80 stakeholders from four countries in Asia. As shown in figure 3, the biggest difference in priority between the two samples was for centres of excellence, which was the second highest priority for the European respondents but only sixth for the Asian respondents. As in Turkey, centres of excellence may be of less interest in Asia than in Europe because funding for treatment is a more immediate need in these countries.

A strength of this study is that it remedied a concern from the pilot study that the respondents were too homogeneous to produce reliable and generalizable results. Some heterogeneity among respondents was thus expected in the present study, given the subjective nature of the conjoint tasks, differences in health systems and disease aetiology across countries, and differences in perspectives or interests according to respondents’ roles and specialties. We did find evidence of heterogeneity by level of involvement in liver cancer for four strategies, which appear to reflect the different perspectives of those respondents. People working at local/municipal level may have more interest in patient access and monitoring and less interest in statistics if they have more direct involvement with patients and less involvement with policy. In contrast, people working at the international level may be more interested in centres of excellence if they have more awareness of the achievements of centres of excellence overseas or in their own countries. However, for 10 of the 11 strategies, we found no evidence of heterogeneity by country, respondent role or area of involvement in liver cancer. This suggests our results are relatively robust and that they may also be relevant to European countries that were not included in the survey.

There are three significant limitations with this study. Firstly, there may be unobserved heterogeneity that was not associated with country or observed respondent characteristics that we were able to analyse. A mixed logit regression model could identify such heterogeneity, but this type of model is unstable with only 100 respondents, and it was not possible to recruit 1000 liver cancer experts to ensure stability. Secondly, despite using results from

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Total</th>
<th>France</th>
<th>Germany</th>
<th>Italy</th>
<th>Spain</th>
<th>Turkey</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring of at-risk populations</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>0.71</td>
</tr>
<tr>
<td>Centres of excellence</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>2.49</td>
</tr>
<tr>
<td>Clinical education</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>4</td>
<td>1.30</td>
</tr>
<tr>
<td>Multidisciplinary management</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>0.55</td>
</tr>
<tr>
<td>National guidelines</td>
<td>5</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>9</td>
<td>9</td>
<td>3.58</td>
</tr>
<tr>
<td>Public awareness</td>
<td>6</td>
<td>10</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>3</td>
<td>2.59</td>
</tr>
<tr>
<td>Measuring social burden</td>
<td>7</td>
<td>4</td>
<td>10</td>
<td>10</td>
<td>8</td>
<td>10</td>
<td>3.97</td>
</tr>
<tr>
<td>Risk assessment and referral</td>
<td>8</td>
<td>9</td>
<td>8</td>
<td>9</td>
<td>7</td>
<td>6</td>
<td>1.30</td>
</tr>
<tr>
<td>Research infrastructure</td>
<td>9</td>
<td>7</td>
<td>7</td>
<td>6</td>
<td>6</td>
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<td>Access to treatments</td>
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<td>1.64</td>
</tr>
</tbody>
</table>
qualitative interviews to identify the strategies,\textsuperscript{10} there may yet be important strategies that were not included, although we tried to mitigate this possibility by working with a research council of international experts. Thirdly, the method does not provide all the information necessary for decision-making. Stakeholder engagement is a critical input to policy development, but data on etiology and existing services should also be considered before implementation.

We have presented a robust quantitative prioritization of strategies based on the views of key stakeholders in five European countries. Their highest priority strategy was monitoring of at-risk populations, followed by centres of excellence, clinical education, multidisciplinary management, national guidelines, measuring social burden, public awareness, risk assessment and referral, research infrastructure, access to treatments and transplantation infrastructure. In addition, there were relatively few differences in priorities across countries or other stakeholder characteristics, suggesting priorities are robust and potentially generalizable to other countries in the region. Armed with systematic evidence on stakeholders’ priorities, decision makers now have a logical starting point for developing national or sub-national plans, or initiating cross-national collaborative efforts. The next steps for decision makers are to consider the existing level of services and strategies in their jurisdictions, to assess the level of resources required to implement the priority strategies and to identify factors that could act as barriers or facilitators to implementation. Implementation of CLCC plans composed of high-priority strategies could have a significant impact in reducing the public health burden of this common and lethal disease in Europe.

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**Conflicts of interest:** None declared.

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**Key points**

- Liver cancer stakeholders in five European countries consider the strategy most likely to have an impact in CLCC plans to be monitoring of at-risk populations, followed by centres of excellence, clinical education, multidisciplinary management, national guidelines, measuring social burden, public awareness, risk assessment and referral, research infrastructure, access to treatments and transplantation infrastructure.
- Priorities were relatively consistent across countries and stakeholder roles.
- The results suggest which strategies analysts and decision makers should focus on in efforts to control liver cancer, and imply that international collaborations could be beneficial.

**References**


Introduction

The chief objective of any collection of indicators of health for a number of countries will be to highlight and interpret differences found between countries, with the ultimate aim of suggesting possible causes associated with risk factors or health care. Current applications of international comparisons of health and health care are published on the websites of EUROSTAT and WHO and in the European Community Atlas of Avoidable Death. In addition, a wide range of commercially available databases and programs can be found on the Internet.

In the perinatal field, each country collects data used to derive indicators through civil registration, hospital discharge systems or specialist registers. The indicators include mothers’ and children’s health, clinical practices and maternal risk factors. Thus, in the European Union, all countries produce sufficient data to construct at least 10 core indicators, to describe their situation. Comparison of these indicators across countries is an essential tool for defining national policy priorities, or generating hypotheses on factors that might explain differences such as risk factors or health policies. To achieve this aim, it is essential to display data in a way that is cumulative and voluminous to digest.

To achieve this aim, it is essential to display data in a way that is useful. The implied rank order is largely a result of heterogeneous population sizes. Distinctions between geographically adjacent regions are not visible. Methods: Regional data are plotted in a geographical map shaded in terms of percentiles of the indicator value. Degree of departure is determined relative to control limits of a corresponding funnel plot. Five methods for displaying outcome and degree of departure from a reference level are proposed for four indicators selected from the 2004 European Perinatal Health Report. Results: Spread of indicator values was generally largest for small population sizes, with results for large populations lying mostly close to respective European medians. The high neonatal mortality rate for Poland (4.9 per 1000); high low-birthweight rates for England and Wales (7.8%), Germany (7.3%) and Estonia (4.5%); and high caesarean section rates for Italy (37.8%), Poland (26.3%), Portugal (33.1%) and Germany (27.3%) were statistically significant exceptions to this pattern. Estonia also showed an extreme result for maternal mortality (29.6 per 100 000). Conclusion: Extreme deviations from EU reference levels are either correlated with small population sizes or may be interpreted in terms of differing medical practices, as in the case of caesarean section rate. EURO-PERISTAT has now decided to use 5-year averages for maternal mortality to reduce the variance in outcome. Use of two colours in three intensities and solid fill versus crosshatching is best suited to display rate and significance of difference.