

Pricing of innovative drugs: correlation between incremental cost and survival gain in four countries

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In pharmacoeconomics, ICER (incremental cost-effectiveness ratio) is a recognized parameter that quantifies the cost-effectiveness for the comparison between an innovative drug and the standard of care [McCabe *et al.* 2008]. An extensive literature has been published on how ICERs should be interpreted and how their values ultimately translate into pricing decisions (e.g. value-based pricing). Given that ICER algebraically is the ratio of incremental cost and incremental benefit (i.e. survival gain), we designed a study to assess the correlation between these two parameters in different developed countries. A strong correlation would indicate that drug prices are strictly related to the benefit, while a poor correlation would indicate that prices are unrelated to benefits. To our knowledge, while hundreds of papers have been focused on theoretical and practical implications of ICERs, only a few studies have assessed the above mentioned correlation, and no study at all has performed an international comparison. The present analysis was restricted to anticancer agents and was aimed at carrying out this specific international comparison.

We first performed a literature search in PubMed (www.pubmed.org) and Google Scholar (www.scholar.google.it) covering the period from 1 January 2010 to the present time (the last query was on 17 February 2016). The keywords employed to select eligible papers were the following: survival AND gain AND cost AND (oncology OR 'anticancer drug'). The time interval from 1 January 2010 to present time was selected also to obtain the overall survival (OS) data of those drugs for which this information was unavailable from included studies. Eligible papers were included in our analyses if they met the following criteria for each innovative drug: reporting of clinical indication, standard of care, incremental OS and incremental cost. Papers were included

even though the latter two parameters were not directly presented, but enough information was given to recalculate them. To include as many papers as possible, our search was extended to all citations reported in the references of included articles. We separately examined whether the inclusion criteria were met by individual studies. Differences in this assessment were resolved by consensus. Standard correlation analyses were carried out to generate our results.

Our first extraction of eligible papers from PubMed selected a total of 258 citations. After inspection of the abstract or the full text of these articles, a total of eight studies [Martone *et al.* 2014a, 2014b; Schnipper *et al.* 2015; Ebara *et al.* 2013; Shiroywa *et al.* 2011; Tsuchiya *et al.* 2011; Mouri *et al.* 2013; Österlund *et al.* 2014] were found to satisfy the inclusion criteria; these articles referred to the following four countries: Italy, US, Japan and Scandinavia.

Figure 1 (panels a through d) illustrates the results of our analyses. The values of correlation coefficient showed a substantial association between incremental cost and incremental OS for Scandinavia ($r = 0.767$), Japan ($r = 0.534$) and Italy ($r = 0.432$). In contrast, the US data showed no correlation at all ($r = 0.063$). More details on the data shown in Figure 1 are presented in the supplementary appendix.

The main strength of our study lies in the originality of the design. To the best of the authors' knowledge, this is the first study in which the correlation between incremental cost and incremental OS has been successfully evaluated in a series of different countries. Given that the value-based approach [Young, 2015] is widely recognized to be the most 'modern' solution in this field, it is interesting to note that Scandinavian countries

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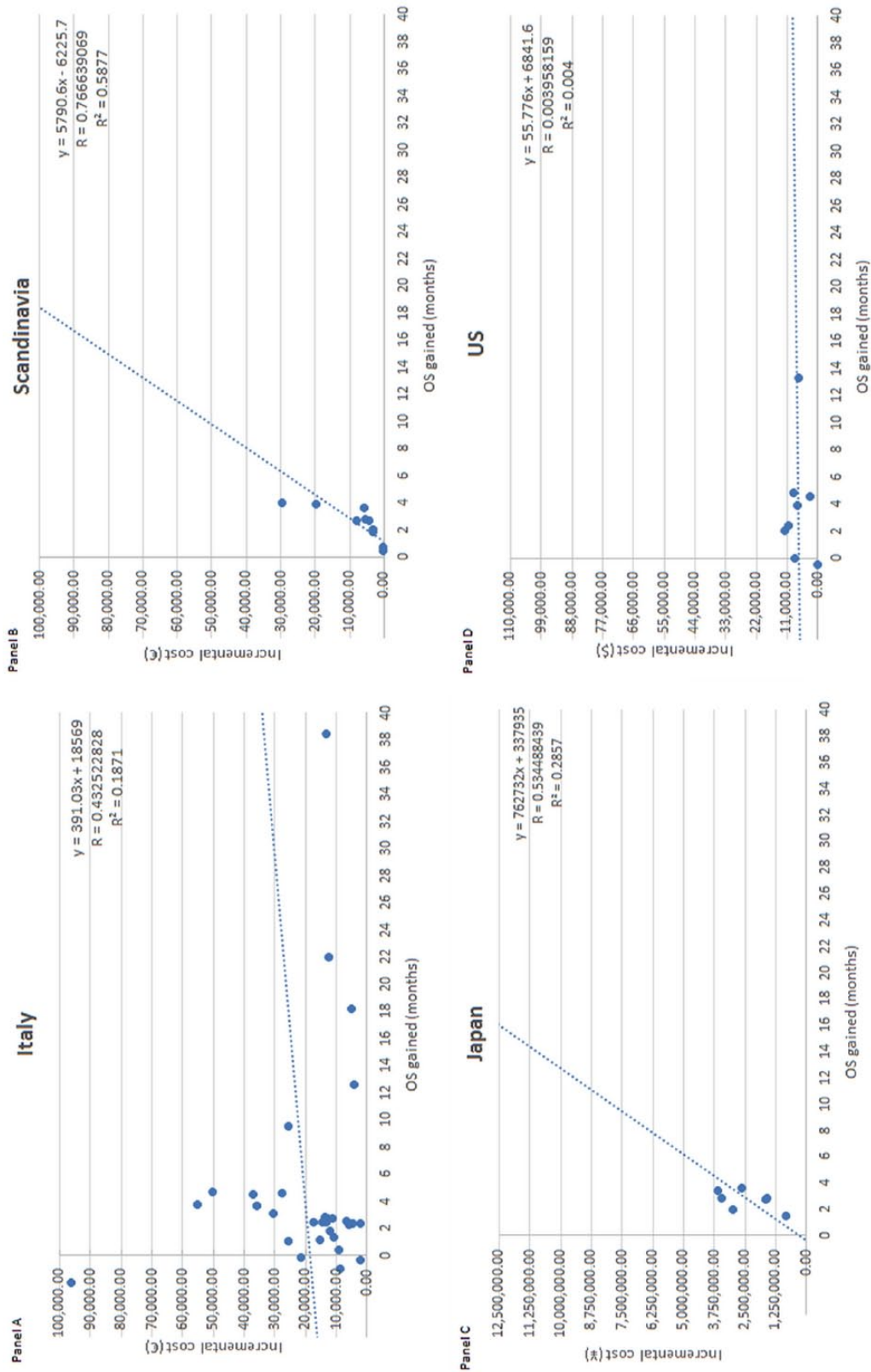


Figure 1. Correlation between incremental cost and incremental overall survival for different series of anticancer drugs evaluated in four countries. Panel a, Italy; panel b, Scandinavia; panel c, Japan; panel d, US. Each graph shows the correlation coefficient r , the determination coefficient r^2 , and the equation of the regression line. The regression line is shown as a dotted line. When currencies were other than euro, the values of Y max were set to represent approximately the equivalent of €100,000, according to current exchange rates. OS, overall survival.

[Vogler *et al.* 2015] and, to a lesser extent, Japan [Takayama and Narukawa, 2015] and Italy [Martone *et al.* 2014a] routinely employ the value-based approach for pricing new anticancer agents, whereas the US does not [Conti and Rosenthal, 2016]. Our results are perfectly in line with these different strategies adopted by these four countries. In particular, in the US a lively debate is ongoing on how drugs should be priced, mainly because the results obtained thus far based on the current approach are largely thought to be unsatisfactory [Conti and Rosenthal, 2016].

Our study had several limitations. Firstly, the anti-cancer drugs evaluated in these four countries were not the same; this likely explains why the slopes of the regression differed across Scandinavia, Japan, and Italy. Another consequence of this different selection of the agents examined is that our analyses evaluated more the overall pricing strategies adopted in these countries than the decisions made on individual drugs. Hence, we cannot exclude that further analyses based on a longer list of included agents (which is presently unfeasible due to the lack of sufficient literature) could give quite different results. Secondly, the *y-versus-x* data pairs for Japan were only a few, and this could have affected the results we found for this specific country.

In conclusion, on the one hand our study had the merit to evaluate the correlation between incremental cost and incremental OS in four countries. On the other, it represents the first study thus far conducted in this specific area.

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Conflict of interest statement

The author(s) declared that there is no conflict of interest.

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