An editorial perspective on Barbieri and Capri article: Is vaccination good value for money? A review of cost-utility analyses of vaccination strategies in eight European countries

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Vaccine have contributed significantly to reduction of incidence (including eradication) of communicable diseases reducing thus significantly the society burden. Each year, three million lives are saved, through vaccination intervention [1,2] and burden reduction was significant even in Europe [3].

The economic value of vaccine at global level is widely documented and was recently reviewed:

- Vaccine contribution to economic growth is driven by health improvement [4–6]. This is driven by better physical, cognitive, and educational performance [7], and ensures reduction of healthcare resources utilization [8].
- Vaccination is one of the most cost-effective interventions that contribute to healthcare system efficiency [9,10].
- Vaccine contribute to improve productivity gains and subsequently behaviour-related productivity gains such as fertility enhancement and consumption choices for example, and multiple externalities [11, 12].
- Vaccination represent a very low investment offering several short term gain apart from commonly recognisable long-term gains, leading in rapid returns on investments [13-18].

The present article: Is vaccination good value for money? A review of cost-utility analyses of vaccination strategies in eight European countries from Barbieri and Capri represent a valuable piece of information on the economic value of vaccine in a selected sample of European Member States.

A systematic search restricted to English language, of the literature was conducted using the National Health Service Economic Evaluation Database and the PubMed database looking for Cost-utility analyses of any type of vaccination and using vaccine and QALY as research term. The selected countries represent the expected sample where such analysis will likely be perform and published: Belgium, France, Germany, Italy, Spain, Sweden, the Netherlands and the UK.

As expected most identified studies were performed in the Netherlands or UK and the most frequently retrieved vaccines were for Human Papillomavirus (HPV) followed by vaccination against pneumococcal infections. Using a 40 000€/QALY Incremental cost effectiveness ratio (ICER) threshold found that most studies were cost effective however with some obvious heterogeneity.

All varicella and influenza (with one outlier) studies where cost effective while 90% of the studies for HPV, 75% for pneumococcal vaccinations and 30% of rotavirus studies were cost effective.

This research is of very high importance for the various stakeholders involved in vaccination including prescribers, society and general population, decision makers and scientists. It is reassuring that this review confirmed that on a sample

of reference countries using consistently ICER threshold as a pivotal information to support decision making the vast majority of studies are supporting vaccine cost effectiveness profile.

It is however important to highlight some limitations of the study and some discussing points.

The restrictive search to full publications (excluding abstracts), to specific countries and limiting the word search to vaccine and QALY may have contributed to exclude important studies. For example the review on cost effectiveness studies for rotavirus vaccine from Abalea and all [19], with no geographical restriction and a broader term research identified 68 studies of which 53 were published in per review journals. However it is important to stress that finding on a much larger number of studies are consistent with those published by Barbieri and Capri.

The search may have not captured some NITAG report [20] which may have different ICER than those published although most of them led to peer review publications. A comparison of ICER estimates and it's probability to reach a cost effectiveness threshold between NITAG and HTA developed model versus companies developed model may have been enlightening. However the fact that the rotavirus vaccine was found to be the less often cost effective vaccine and the one that face the highest hurdle for reimbursement [21] while other vaccine found to be cost effective and are widely reimbursed across Europe support that the finding are also a fair reflection of policy decision makers appreciation of vaccine value for money and their efficiency.

The price of rotavirus as well as HPV vaccine have been substantially decrease from time of launch in many countries, and achieve lower prices than those published through tenders in many countries too making most of those studies "caduque" and lead to vaccine being further more cost effective as compare to initial publication. Therefore this review under-estimated the actual efficiency of vaccines.

Some vaccine such as flue may have a short term benefit while other may have a longer term expected benefit. Assumptions on the long term extrapolation is a very important point to consider when reviewing vaccine with long term benefit. For long term benefit anticipated vaccine it may have been useful to review the acceptability curve and report the robustness of the finding. Even though it was not done evidence accumulated overtime to support HPV vaccine is a cost effective option [22-23]under a broad range of assumptions and the acceptability curve addresses the uncertainty in a reassuring way.

This publication from Barbieri and Capri represent a highly valuable effort to provide a reliable and compelling picture on cost effectiveness appreciation of vaccine in a critical sample of European Member States. Despite some limitations may be discussed they do not alter the conclusion and the scientific contribution of that article. It allows confirming that vaccines are considered as widely cost effective in the exception of rotavirus. However if rotavirus models were updated today with current rotavirus vaccine price that was eroded from that time or prices achieved in the tenders when available, the ICER may look very different.

Such information is also very important at the time of a hot debate on pharmaceutical prices in the media as it preserves vaccine from this polemic and prevent to fuel the vaccine hesitancy movement [24].

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