national immunization programme. Some lower and middle income countries with fairly strong alignment scores for recently established NITAGs have basic immunisation programmes. This study also found that NITAGs are usually developed following a stepwise maturing process. **CONCLUSIONS:** Our detailed analysis of data from 35 countries suggests that, with the right support, all countries – regardless of their GDP/capita, health expenditures and geographical location – have the potential to establish highly performing NITAGs that are well-aligned with international recommendations. Well-aligned NITAGs are generally instrumental for having strong immunisation programmes. Through awareness of its position in this maturation process, a NITAG can focus on the appropriate next step for development and strengthening.

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DISCONTINUITIES BETWEEN HEALTH TECHNOLOGY ASSESSMENT (HTA) AND HEALTH CARE SERVICE OBJECTIVES OF THE NHS

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OBJECTIVE: Advances in early cancer diagnosis and treatment are enabling patients to live longer with more fulfilling lives. The value assessment in such cases is compelling. Many novel treatments for late-stage cancer also extend life, though prognosis may still be poor. The valuation of such life-extending treatments can be significantly reduced by health care costs associated with managing patients for longer. This study highlights discontinuities between HTA for treatments that extend patients' lives and the NHS's objective to improve cancer patients' survival rates. **METHODS AND RESULTS:** Economic comparison of two treatments with an equivalent QALY gain, one that extends life while the other enhances the quality of life, indicates that to achieve a common cost per QALY outcome the life-extending treatment must be valued lower than the life-enhancing therapy. This anomaly arises primarily because the value assessment for life-extending treatments includes NHS costs of patient management during their extended life in addition to the new treatment costs. For long-term chronic conditions these additional costs may be easily offset; however, for severe, debilitating, or terminal diseases the impact can be significant. Furthermore, for new treatments added in combination to standard care, the greater the cost of existing care the lower the value that may be placed on the new life-extending treatment, to the point that new therapies may be deemed uneconomical even if available at no cost to the NHS. These findings challenge the equitable use of ICERs for HTA including the accounting for health services costs during the extended lifetime of a patient achieved with a new treatment. **CONCLUSION:** Value-based metrics used to appraise new treatments can inadvertently discriminate against life-extending therapies. Use of the ICER in HTA can result in inconsistency with health service objectives e.g. the UK Government's goal to improve 1-year and 5-year survival rates for cancer patients.

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THE ECONOMIC VALUE OF VACCINATION: WHY PREVENTION IS WEALTH

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CONTEXT: Theoretical and empirical evidence has demonstrated that health care is a major driver of economic growth. The European economic crisis has resulted in health care budget cuts conferring consequences for health systems. Preventative programmes, and particularly vaccination, are most vulnerable to short-term cuts because their benefits are not always immediately identifiable. Although its huge public health benefits are recognised, only a minor fraction of the health care budget is allocated to vaccination. It has been suggested that cost-effectiveness analyses, as used in HTA as part of recommendations and reimbursement decisions, may render a too narrow perspective of the overall economic benefits of vaccination. **OBJECTIVES:** The aim of this project is to demonstrate that, in addition to contributing to health care system sustainability, vaccines have importance for wider economic planning. A seven-chapter report was developed to highlight the full economic value of vaccination from different perspectives: macro-economic, health care system, society… Each chapter is illustrated with existing evidence retrieved from peer-reviewed publications. The objective of this report is threefold: 1) to demonstrate the full economic value of vaccination with real life examples; 2) to inform policy-makers on how immunisation contributes to health care systems sustainability and efficiency; 3) to launch a call for action for the consideration of the full economic value of vaccination. **DISCUSSION:** Immunisation programmes require adequate value recognition to ensure quick population access and wide acceptability. Policy-makers should acknowledge that prevention through vaccination involves low levels of investment relative to the substantial incremental benefits it procures. As with other preventative interventions, it is difficult to evaluate the true economic value of vaccines given a number of benefits are intangible and thereby difficult to quantify in pure monetary terms. Taking into account the full economic benefits of vaccination will allow understanding why prevention is the one of the best ways to find efficiency gains.

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THE COST-EFFECTIVENESS THRESHOLD FOR ORPHAN DESIGNATIONS IN POLAND BASED ON REIMBURSEMENT DECISIONS

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The aim of this study was to identify the cost-effectiveness threshold for an orphan designations in Poland. According to criteria specified by the European Medicines Agency (EMA) a medicine must meet a strict criteria to qualify for orphan designation, such as: treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating; disease prevalence level in the European Union (EU) of no more than 5 cases in 10,000 patients is necessary; no satisfactory method of disease diagnosis, prevention, treatment or if such method exists, the drug must deliver significant benefits to patients. In Poland, orphan drugs undergo full pharmacoeconomic evaluations and coverage decision processes similar to any other innovative medicines. One of the important element of reimbursement recommendations is cost-effectiveness information. Currently in Poland there is no specific formal threshold for orphan designations, there is only a general cost-effectiveness threshold that equals 3 x GDP per capita for ICUR/QALY (for CUA) or ICER/LYG (for CEA), which in 2014 is approximately € 26 800. We extracted data on orphan drugs from our database of medical technologies assessments from 2009 to March 2014. Data on the cost-effectiveness (QALY / LYG) were put together with the decision of reimbursement. On the basis of these data the threshold of cost effectiveness in Poland for orphan designations was determined and summarized with the cost-effectiveness thresholds current for a given time interval. Determination of the threshold of cost effectiveness for orphan designations, that would be different (higher) than the generally accepted cost-effectiveness threshold (due to high price of orphan drugs to provide value for money is unlikely), is particularly important from an ethical point of view, because of substantial therapeutic meaning of these drugs and/or absence of other treatment options of proven benefit for the disease.

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CONFLICT OF INTEREST IN HTA RECOMMENDATIONS AND CASE LAW IN FRANCE

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OBJECTIVES: The slow reaction of French authorities to the "Mediator saga" in France led to investigations that questioned the way conflicts of interest are reported. This policy research reviewed the Loi Bertrand, known as French Sunshine Act, and reported case law from the French Council of State (COS) related to conflict of interest in HTA recommendations. **METHODS:** Literature review and analysis of recent laws and decrees were conducted to understand French policy in the field of conflict of interest. A review of COS' decisions related to conflicts of interest among members of HAS commissions was performed. **RESULTS:** France implemented the Loi Bertrand in May 2013 with the aim of specifying the scope of disclosure obligations. It affects most of the agreements concluded between health care professionals and companies and covers a vast range of health products. Six cases examined by the COS were analyzed, most of them related to removal of products from refundable list. Four cases led to suspension or invalidation of decisions based on HAS recommendations due to conflicts of interest. In the two other cases the HAS provided the declarations of interest when required by the COS and the COS considered the conflicts of interest as irrelevant for the decision. It appears that the COS based its decisions on two main criteria: the acknowledgement of negative conflict of interest (link with competitors) and the unavailability of declarations of conflict of interest, which have to be provided by latest when required by legal authorities. **CONCLUSIONS:** The strengthening of the regulation on declarations of interest might lead to more transparency but also more cases ruled by the COS.

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MEASURING AND OBSERVING POSITIVE AND NEGATIVE EXTERNALITIES CAUSED BY VACCINES: DO WE HAVE THE RIGHT ASSESSMENT APPROACH AVAILABLE?

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OBJECTIVES: Vaccination not only results in direct protection to those being vaccinated, it also has the potential of inducing indirect protection among unvaccinated individuals (=herd protection or positive externality). However, negative unintended consequences or externalities may also result from vaccination programmes (e.g. rebound effects). It is our purpose to present how and when these positive and negative externalities can be observed and measured. **METHODS:** We first identify under what conditions herd protection is most likely to occur. We then explore how negative rebound effects can also be manifested. Detailed illustrations of both positive and negative effects are presented for different infections in relation to mass vaccination programmes. Lastly, we discuss methods for observing and measuring these externalities. **RESULTS:** Optimal herd protection is likely to be observed when the vaccine has a high quality-induced immunity, substantial effect on the force of infection, and appropriate vaccine coverage and distribution. Example: HPV vaccination of 12-16 year old girls resulted in a 50% decrease of anogenital warts in 15-19 year aged adolescents in Denmark observed over a 4-year period. Rebound effects may potentially occur due to vaccine-related age shifting, decreased natural immunity, serotype replacement, low-medium coverage and non-homogeneous vaccine distribution. Example: increased herpes zoster incidence in elderly post-varicella vaccine introduction. Those externalities can be captured through observational studies using real-life data, or may be estimated using dynamic transmission modelling techniques. **CONCLUSIONS:** Limitations are inherent in those studies and involve substantial ambiguity in the process of observing and quantifying the indirect effects, making accurate evaluation troublesome. However the nature of these outcomes could be critical for achieving good economic value when decision- makers are evaluating a novel vaccine for introduction into a particular region or people group. More investigation is needed to identify and develop successful assessment methodologies for precisely analysing these outcomes.

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MARKET ACCESS AND REIMBURSEMENT: THE INCREASING ROLE OF REAL-WORLD EVIDENCE

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Randomised controlled trials (RCTs) have historically been considered the primary source of evidence to support market access and reimbursement. However, real-world data (RWD) are increasingly being considered by industry and payers. The objectives of this research were to review the current perception of RWD across Europe and to assess how RWD can support market access and reimbursement. A review of the literature, guidelines from European health technology assessment (HTA) agencies