

**Methods:** A probabilistic model with a Markov-type process was used to depict lifetime risks and costs of pneumococcal disease among a cohort of English adults. Epidemiologic parameters, serotype coverage, costs, vaccine effectiveness and coverage were based on published literature or publicly available data. The National Health Service perspective was adopted, health effects were expressed in quality-adjusted life years (QALYs), and future costs and QALYs were discounted at 3.5 percent.

**Results:** Results suggest that under reasonable assumptions concerning disease burden, vaccine, effectiveness, and vaccine cost, PCV20 implementation of an age- and risk-based strategy targeting all adults aged 65 years or older and younger risk group adults aged 18 to 64 years would reduce a large number of pneumococcal disease hospitalizations and pneumococcal-related deaths compared to currently recommended PPV23.

The incremental cost-effectiveness ratio was well below the current willingness-to-pay range of GBP20,000-GBP30,000 per QALY gained, with PCV20 being cost saving compared with PPV23 in base case and most sensitivity analyses. Probabilistic sensitivity analysis suggests high certainty in recommending PCV20 for vaccination of adults aged 18 to 64 years in risk groups and all aged 65 years or older instead of PPV23.

**Conclusions:** Our findings support replacing PPV23 with PCV20 to directly protect adults against pneumococcal disease, reducing hospitalizations and saving lives in the UK.

## OP79 Gene Expression Profiling In The Diagnosis Of Aggressive Large B Cell Lymphoma: An Early Exploratory Economic Evaluation

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**Introduction:** The addition of gene expression profiles (GEP) to the current clinicopathological diagnosis of aggressive large B cell lymphomas may lead to the reclassification of patients, treatment changes and improved outcomes. A GEP test is in development using TempSeq technology to distinguish Burkitt Lymphoma (BL) and Primary Mediastinal Large B Cell lymphoma (PMBCL) from Diffuse Large B Cell Lymphoma (DLBCL). This study aims to inform developers about the potential impact of the test on costs and health outcomes, and pricing and evidence generation strategies.

**Methods:** Decision models compared current diagnosis with current plus GEP signatures over a lifetime horizon using a UK health and social care perspective. Inputs were taken from the literature and based on assumptions. Threshold estimates were made of the maximum price of the test and impact of incorrect disease classification using a threshold of GBP30,000 (USD37,155) per Quality Adjusted Life year (QALY). One way sensitivity analysis was conducted.

**Results:** At base case values the BL signature delivers incremental QALYs of 0.0249 at an additional cost per patient of GBP508 (USD629). This results in a net monetary benefit (NMB) of GBP239 (USD296). The PMBCL signature delivers 0.0011 QALYs,

a cost saving of GBP202 (USD250) and an NMB of GBP236 (USD292). The maximum threshold price for a combined test to be cost effective is GBP776 (USD961) (base case GBP400 (USD495)). Results are sensitive to cost differences in first line treatments and impact of false diagnoses.

**Conclusions:** A combined test could be cost-effective in a UK context at a price around GBP750 (USD929). The developers can use this estimate to inform return on investment calculations. The number of patients who were reclassified as a result of the addition of GEP in our model was taken from small retrospective studies and the impact of false diagnoses was based on limited evidence. If the developers choose to proceed with the development, these aspects should be incorporated in evidence generation strategies.

## OP80 Diagnostic Molecular Sequencing Of DNA (Exomes And Genomes) Is Not Perfect: Implications For HTA

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**Introduction:** The recent release of powerful next-generation sequencing platforms, which can provide whole exome sequencing (WES) or whole genome sequencing (WGS) in quicker timelines and at reduced costs, has resulted in proposals for these diagnostic testing methods to be routinely integrated into clinical practice in multiple settings. However, the complexities of these diagnostic approaches, and the minimal comparative evidence available on them, creates difficulties in the evaluation of their diagnostic performance. Novel approaches need to be developed to improve the health technology assessment (HTA) of WES and WGS.

**Methods:** Several HTAs on genetic testing and the use of WES or WGS in fetal medicine were reviewed. Information on factors associated with this diagnostic modality that affect typical test accuracy assessment (e.g., sensitivity and specificity) was extracted. The multiple steps required for completing a WES or WGS test, and the potential for the introduction of errors (type I or type II) at each of these steps, were mapped and examples provided. The clinical and economic implications associated with imperfect and uncertain test accuracy were described.

**Results:** Limited data on analytical and clinical validity were identified. WES and WGS are multistep processes and errors were found in sampling, molecular sequencing, bioinformatic filtering, and variant interpretation; therefore, the assumption that WES or WGS is 100 percent sensitive or specific is not reasonable. Although alternative evidence-based estimates are unlikely to be available, the inevitability of such errors, and their implications in terms of comparative effectiveness, safety, and cost effectiveness, should be described in HTAs.

**Conclusions:** While unknown diagnostic accuracy remains an issue with WES and WGS testing, formal sensitivity analysis of test performance characteristics should be conducted as part of HTAs. A checklist has been developed to assist those involved in HTA and