EVALUATING THE CLINICAL EFFECTS AND THE COST-EFFECTIVENESS OF PHYLACTIC CERVICAL CANCER VACCINATION WITHIN AN ORGANISED POPULATION-BASED SCREENING SETTING—CASE FINLAND

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OBJECTIVES: Finland has been a model country for an organised population-based cervical cancer (CC) screening programme. Since its implementation in the 1960’s, both CC incidence and mortality rates have reduced by 80% to annual 130 CC cases and 50–60 CC deaths. Our objective was to test the clinical impact of introducing prophylactic vaccination against human papillomavirus (HPV) within a well functioning organised population-based screening system and to evaluate the cost-effectiveness of vaccination using a cohort based Markov model. METHODS: The model is based upon lifetime Markov processes using Microsoft Excel, modelling the natural history of HPV infection and CC over the lifetime of a one age-cohort of girls. The model simulates the effect of adding vaccination to the current screening programme in terms of number of pre-cancerous lesions, CC cases and CC deaths avoided. Data is collected from literature review, expert opinion and statistics in Finland. All country specific data were reviewed with national experts. Screening coverage was assumed to remain constant over time in the model (2.1 million eligible women and ca. 500,000 annual Pap smears divided into different screening patterns). RESULTS: With 90% vaccination coverage, coinciding with the coverage of the Finnish mass vaccination programme, the model predicts a 66% reduction in CC cases and in CC deaths (from 166 to 56 and from 56 to 19, respectively). Cost-effectiveness was estimated assuming vaccine price of €120/dose, including administration. With the assumed coverage the undiscounted ICER would be less than €7000/QALY. CONCLUSION: Although CC cases and deaths are relatively rare in Finland, it would still be very cost-effective to implement prophylactic cervical cancer vaccination. Additional benefits include avoidance of pre-cancerous lesions, the resource use related to these and their adverse utility effects.

INCORPORATING PROBABILISTIC ATTRIBUTES IN A STATED-CHOICE RISK-BENEFIT SURVEY

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OBJECTIVES: The objective of this study is to elicit preferences for hypothetical risks and benefits of antiretroviral (ART) treatment among treatment-naïve HIV-positive African-Americans using a stated-choice (SC) survey with probabilistic attribute levels. SC surveys often include attributes that describe disease outcomes and treatment features as discrete levels. Rarely do studies describe attributes in probabilistic terms. Understanding and conceptualizing numerical probabilities often is cognitively challenging. Researchers have experimented with various graphical representations to assist respondents in understanding quantitative risks, but there is no general consensus about the most effective approach. METHODS: In a recent study to estimate the willingness of treatment-naïve HIV-positive African-Americans to accept adverse event risks in exchange for improvements in treatment efficacy, four of the five attributes were described as probabilities. We relied on a format that portrays absolute risks using a risk grid in which each square of the grid represents one person. Respondents completed an online survey instrument that included a series of 10 SC tasks. Each hypothetical treatment alternative included different probabilities of virologic failure, hypersensitivity reaction, bone damage, and kidney damage. The fifth attribute described discrete outcomes of bone or kidney damage (degree to which the problem could be treated successfully). We included four questions that tested their understanding of the risk grid format prior to completing the choice questions. RESULTS: In total, 153 respondents completed the survey. The mean (SD) age was 42 (8.6) and there were slightly more males (58%) than females (42%). Seventy-four percent (89%) of respondents answered the first (fourth) risk quiz question correctly indicating a high level of comprehension of risk levels. CONCLUSION: Our risk grid approach, which included both a numerical and graphical representation of absolute risk levels, is an appropriate method for including probabilistic attribute levels in SC surveys.

ADAPTING A HEALTH ECONOMIC MODEL OF THE NATURAL HISTORY OF HPV INFECTION AND CERVICAL CANCER IN A WELL FUNCTIONING POPULATION-BASED SCREENING SYSTEM—A MODEL CALIBRATION TO FINLAND

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OBJECTIVES: The efficiency of the Finnish cervical cancer (CC) screening system is renowned. Consequently, the burden of CC in Finland is amongst the lowest in the world. Our objective was to validate, in this unusual setting, a cohort based Markov model developed for estimating the clinical and health economic impact of adding a prophylactic vaccine against cervical cancer to an existing screening programme. METHODS: An existing Markov model describing the natural history of high-risk HPV infections to CC combined with screening was customized to the Finnish setting. Basic calibration was performed using published data and information on the existing screening programme. One third of total annual pap smears are taken within organized population-based screening. However, the remaining two thirds of total paps (private spontaneous screening) are crucial for the outcomes. In our model, spontaneous screening was extrapolated assuming a similar age-specific distribution to organized screening. The model outcomes of a cohort of 30,000 girls aged 11 years were validated against the age-specific annual number of total pap smears, CC incidence and CC mortality reported over the last 15 years in Finnish statistics. RESULTS: Observed age-specific CC incidences and deaths were closely replicated by the model (correlation coefficients 0.702 and 0.826, respectively). Overall predicted and observed CC incidence and mortality adjusted for world standardized population per 100,000 women coincide (CC 4.2 vs. 4.0; mortality 1.2 vs. 1.2, respectively). The predicted lifetime number of pre-cancerous lesions for the cohort were 14,462 (CIN1) and 1,646 (CIN2-3). The model predicts that vaccination at 90% coverage would reduce CC cases and mortality by 66% (166 to 56 cases; 56 to 19 deaths). CONCLUSION: A Markov model can be used to replicate cancer incidence and mortality in the unique Finnish setting. This model predicts health benefits and cost-effectiveness of a vaccine against cervical cancer in Finland.

HOW TO IMPROVE THE EXTERNAL VALIDITY AND EXTEND THE EXPIRATION DATE OF ECONOMIC EVALUATIONS

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OBJECTIVES: Due to changes in population, health care system and methodological factors the external validity of economic...
In our study, we investigated the major factors affecting the “expiration date” of economic evaluations using conjugate meningococcal vaccination strategies as a case example. METHODS: In March 2007, we conducted a systematic literature review of journal articles, based on a comprehensive key-word based search in generic (PUBMED, EMBASE) and specialized electronic databases (HEED, NHS EED), accompanied by manual searches of specific journals. The applied methodology in the identified studies was compared and matched to the respective national guidelines for economic evaluation. The current external validity of the study results and possible adjustments for its improvement were examined.

RESULTS: A total of six published economic evaluations of conjugate meningococcal vaccination strategies were found. Overall, they showed that the investigated vaccination strategies were cost-effective, especially the ones targeting children at approximately age 1. Adherence of the evaluations to the respective guidelines was high except for the discount rate. The latter was however directly related to the recent change in Dutch and UK recommendations. Sensitivity analysis was available for many factors, inclusive the discount rate allowing the estimation of the impact of those recent changes. Similarly, the effect of new findings about the vaccination protection duration and herd immunity could also be estimated for those evaluations that included those factors in their sensitivity analysis. These were however scarce. CONCLUSION: An extensive sensitivity analysis for all important factors that might change over time can extend the expiration date of economic evaluations. Ultimately, user-friendly and highly flexible models available on the internet might be the best way to transfer study results over time.

INFECTION—Patient Reported Outcomes

A CROSS-SECTIONAL VALIDATION OF THE MINI-HIV QUESTIONNAIRE

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OBJECTIVES: The purpose of this study was to validate cross-sectionally the MINI-HIV questionnaire in HIV patients treated with saquinavir in Spanish hospitals. METHODS: Cross-sectional observational post-launch and multicentre study. HIV Patients over 18 years, who were under HAART with Saquinavir. One visit was carried out. Socio-demographic and clinical variables (symptoms, time since HIV diagnosis, CDC stage, CD4 and viral load), treatment adherence (GEEMA questionnaire), a question about general health status and the specific QoL questionnaire Mini-HIV (0 = better QoL; 100 = worse QoL) were collected. RESULTS: A total of 948 patients were included. Mean age (SD) was 42 (8.62) years. Mean (SD) time since diagnosis was 11.3 (5.6). A total of 36.1% were in Stage C of CDC. Mean score (SD) obtained in Mini-HIV was of 30.2 (17.8). A total of 64.9% had bad QoL (cut of point under 22 score). Correlation between Mini-HIV score and CD4 was low (0.134) although it was significant (p < 0.01). In patients with detectable viral load mean (SD) of MINI-HIV score was lower than in patients with undetectable viral load (32.9 (18.1) vs. 28.8 (17.5); p < 0.01). QoL was worse in patients who presented symptoms in the last two weeks or that presented other concomitant disease (p < 0.01). The more frequent symptoms were weakness, anxiety, insomnia and depression. There was no difference in MINI-HIV score according to the form of administration (BID vs OD); internal consistency of MINI-HIV was of 0.914 (higher than 0.7 theoretical). General health status was ‘very good’ in 42.3% of the patients. MINI-HIV scores were related to the general health status question (p < 0.01). Non adherent patients obtained higher scores (worse QoL) than adherent patients (p < 0.01). CONCLUSION: The results of this study show that Mini-HIV has good psychometrical properties and can be a good tool for monitoring treatment effectiveness and health states of HIV patients.

DEVELOPMENT AND PSYCHOMETRIC VALIDATION OF THE VACCINEES’ PERCEPTION OF INJECTION (VAPI) QUESTIONNAIRE TO ASSESS SUBJECTS’ ACCEPTANCE OF INFLUENZA VACCINATION

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OBJECTIVES: To develop and validate a self-administered questionnaire assessing subjects’ perception and experience with injection, and their acceptance of injection site reactions (ISR) including pain following influenza vaccination. METHODS: Following a literature review, the VAPI questionnaire was simultaneously developed in US English, German and French, based on interviews of subjects (n = 33) vaccinated intramuscularly (IM) or subcutaneously (ID) with an influenza vaccine. Items were generated from subjects’ verbatim, comprehension tested with elderly and adult vaccines (n = 23); then a linguistic validation was done. The initial, 44 item-version of the questionnaire was administered 21 days after vaccination to subjects from Belgium, France, Spain, the UK, Germany and Italy who were participating in clinical trials comparing ID versus IM influenza vaccination. Scale construction and item reduction were conducted using principal component and multitrait analyses with 549 English subjects. Psychometric validation of the final questionnaire was performed per country (n = 5,543) and included: 1) construct validity by item convergent and discriminant validity; 2) internal consistency reliability by Cronbach’s alpha and 3) clinical validity by describing the scores according to ISR severity. RESULTS: After item reduction, the final questionnaire comprised 4 multi-item dimensions (“bother”; “arm movement”; “sleep”; “acceptability”) grouping 16 items plus 5 individual items (anxiety before vaccination; bother by pain during vaccination; satisfaction with the injection system; anxiety of being vaccinated next year; willingness to be vaccinated again). Item convergent and discriminant validity was confirmed for all scales in most countries. Multi-item dimension internal consistency reliability was good to excellent for all countries (Cronbach’s alpha ranging from 0.73 to 0.94), except for the “sleep” dimension in Italy (0.68). Dimension scores demonstrated good clinical validity: greater severity of ISR was associated with higher scores. CONCLUSION: The self-administered VAPI questionnaire is valid and reliable. Therefore, it is a promising tool for the assessment of the acceptance of a vaccine injection system.