DECISION MAKING IN THE TIME OF AN INFLUENZA PANDEMIC
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The 1976 swine flu (H1N1) outbreak sets an interesting backdrop for understanding the aftermath of the 2011 swine flu (H1N1) pandemic. In 1976 President Ford decided that no one would go unprotected. A vaccine was made and a population wide vaccination effort was rolled out. However, no calculations were presented on how many would get sick and how many would be protected by the vaccine. This omission and the ensuing labelling of the vaccination programme as a fiasco would eventually result in the dismissal of the Director of the CDC.

In 2011 a new swine flu pandemic was upon us:” On Saturday, 25 April, upon the advice of the Emergency Committee called under the rules of the International Health Regulations, the Director-General declared this event a Public Health Emergency of International Concern” June 11th WHO raised the level of influenza pandemic alert from phase 5 to phase 6”.

As the Director General for Norway I had the responsibility to lead the health services and its reaction to the developing pandemic. We followed WHO guidelines, treatment with Tamiflu and vaccination.

As it turned out the 2009 flu epidemic was moderate in severity, but this was an important exercise for health authorities, local government and health personnel in the municipalities.

Hindsight is a luxury, particularly so when it comes to dealing with a phase 6 pandemic. However, if government’s response was too extensive or too minuscule will always be the question. Defining parameters in advance can assist decision makers to an extent, but estimates can also fail.

In Norway, debate after the pandemic has in large part been on cases of narcolepsy which have been linked to the vaccine.

When discussing how we should act in the event of a new pandemic we have to consider that the vaccine used during the swine flu pandemic in 2009 might actually be the best option for a new vaccination effort, even though it might be a factor in causing narcolepsy.

The inherent nature of technology and research is progression. Recently, the development of a highly virulent influenza pathogen in labs in Holland and the US created a novel debate. The virus (H1N5) proved highly contagious in the animal protocols. Fear of its accidental release, or release of knowledge that would provide terrorists a deadly bio weapon gave basis for a moratorium on publishing the scientific articles on the work done.

Technology has also challenged the debate on eradication of the smallpox virus. Seeing as it now is possible to synthesize the virus, is it really relevant to dispose of the stocks of variola in the US and Russia?

Reference:
Diagnostic tests use a cutoff point value of a diagnostic variable to distinguish between disease-positive and disease-negative individuals. Diagnostic tests have health care resource costs and health outcome consequences and so are appropriate subjects for economic evaluation. The standard analysis of error in diagnostic tests is based on the receiver-operator characteristic (ROC) curve. By comparing the areas under the two ROC curves clinicians can estimate which one of two tests is more suitable for differentiating healthy from diseased, or any two conditions of interest. However this approach has been criticized since it treats false-positive and false negative outcomes as equally problematic. A more economic approach uses the value of information (VOI) method, based on the consequences of incorrect test results. More recently, ROTS curve analysis, a new method for economic test evaluation, plots the cost and effects of changing test thresholds in a cost-effective space.

Gestational diabetes mellitus (GDM) is the most common medical complication of the pregnancy period. GDM is defined as carbohydrate intolerance of variable severity, with onset or first recognition during pregnancy. In Scotland, there has been controversy over the threshold for screening and diagnosis of GDM, reflecting the lack of international consensus on diagnosis of the condition.

This study illustrates this new technique for economic test evaluation of the ROTS curve to evaluate screening tests of GDM. We show how it can answer three key questions: (1) Is there any test that is worth doing? (2) What is a test’s optimum point in terms of sensitivity and specificity? (3) If more than one test is available, which is best? We emphasise that taking an economic approach to evaluating diagnostic testing necessarily leads to an economic diagnosis of disease since GDM will only be diagnosed if it is cost-effective to provide an intervention to treat the condition.
INFORMATION DISTORTION IN PHYSICIANS’ DIAGNOSTIC JUDGEMENTS
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Background:
Information distortion suggests that people change the evaluation of new information to support an emerging belief. Physicians may do this retrospectively, having made a diagnosis (Kostopoulou et al. 2009). The distortion of information during the diagnostic process has not been measured before. The present study was designed to ascertain and measure the extent to which physicians distort incoming medical information to support an emerging diagnosis.

Design:
Data were collected via an anonymous questionnaire. The experimental group (102 physicians) read 3 patient scenarios, each with 2 competing diagnoses. Physicians first read information that favored one of the 2 diagnoses (the “steer”). They then rated a series of neutral cues that favored neither diagnosis. At each cue presentation, respondents rated the extent to which cue favored either diagnosis and updated the strength of their diagnostic belief. After the neutral cues in the third scenario, respondents rated cues that opposed the initial steer. A control group (36 physicians) rated all the cues in random order and not within scenarios, thus providing unbiased baseline ratings for calculating distortion in the experimental group.

Results:
Distortion was statistically significant (p<0.001) and was driven by the strength of belief in the leading diagnosis. Physicians with over 10 years in practice distorted less than their less experienced counterparts (M=1.04 vs. M=1.78, p<0.05). Having developed an initial diagnostic leaning consistent with the steer, 56% of physicians remained committed to it after receiving the conflicting cues. Distortion had a significant influence on commitment to the steer (OR 1.4, 95% CI: [1.03-1.79] p=0.03).

Limitations:
Physicians did not elicit information themselves, therefore, we cannot estimate the size of distortion in diagnostic tasks involving information search.

Conclusions:
Physicians are not immune to pre-decisional distortion of information, which partly explains their commitment to a diagnosis that may emerge early on in the clinical consultation. The strength of this emerging diagnostic belief, which drives distortion, seems to decline after 10 years in clinical practice.
Purpose:
A 2009 Cochrane review identified several positive outcomes associated with the use of patient decision aids (PDAs). However, theory-based networks of antecedents, mediators and outcomes that illuminate PDA processes and effects are lacking. Using large US adult panel samples, this study provides evidence of specific PDA effects on important pathways between individual difference antecedents, comprehension and attitudinal mediators, and self-confidence outcomes regarding cancer treatment management. Comparison of structural equation models (SEM) for PDA versus non-PDA groups shows in meaningful detail the cognitive and affective processes underlying several patient decision aid effects identified in the Cochrane review.

Methods:
Two online panel samples in the US totaling 935 adults (age 23-81, mean=50; 54% female/46% male) were exposed to a scenario in which they were recently diagnosed with basal cell carcinoma and about to meet with their dermatologist to decide on treatment. The first group (n=522) viewed a PDA with treatment cost/benefit information and values exploration. The second group (n=413) received a standard brochure with general information about the disease. Respondents in the first group evaluated the PDA positively using previously published measures.

Results:
SEM model fit for PDA and non-PDA groups was very strong on all standard indicators. Analysis revealed that PDA exposure reduced the negative path between preferring limited participation in decision making with the physician and cancer comprehension confidence. PDA exposure also reduced the negative path between preferring limited participation and perceived power/control over cancer. For the overall sample, PDA exposure strengthened the positive path from confidence regarding cancer treatment comprehension to attitude toward managing the cancer and from this attitude to perceived power/control over cancer. Last, PDA exposure appeared particularly effective for respondents with higher life satisfaction as the positive path between this construct and perceived power/control over cancer was significant only for individuals in the PDA group.

Conclusions:
This study provides rich detail on several latent constructs and processes through which patient decision aids (PDAs) appear to operate. Depicting this information using theory-based, high fit SEM models enables researchers and practitioners to visualize antecedent, mediator and outcome relationships and thereby better understand the thinking/feeling content and processes that patients experience as result of exposure to a PDA. Such
enhanced understanding is critical to improving shared decision making between health care providers and their patients.

References: (partial)
ASSESSMENT OF COST-EFFECTIVENESS QUADRIVALENT HPV VACCINATION OF GIRLS AND BOYS IN NORWAY USING A DYNAMIC TRANSMISSION MODEL

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Background:
A routine human papillomavirus (HPV) vaccination program has been successfully implemented in Norway in August 2009, and targeted 12-year-old girls, with a quadrivalent (HPV types 6/11/16/18) vaccine. The vaccination coverage rate has reached nearly 80% two years after the program initiation. A previously published health economic evaluation showed a cost-effectiveness ratio for the quadrivalent HPV vaccination program in girls aged 12 years (NOK48,001 or €6,240 per quality-adjusted life year (QALY) gained) below the range accepted as cost-effective in Norway (NOK500,000 or €65,000 per QALY gained). Nonetheless, the burden of HPV-related diseases in males remains substantial, and the indirect protective impact on males through vaccination of girls doesn't avoid the whole HPV burden in the male population.

Objectives: The objective of this study was to assess the epidemiological and economic impact of a boys' quadrivalent vaccination in addition to girls' vaccination in Norway using a dynamic transmission model.

Methods:
A previously published HPV dynamic transmission model for evaluating the impact of quadrivalent HPV vaccination in both genders in the US was adapted to the Norwegian context. The model covered all potential diseases related to specific types of HPV (6/11/16/18) (i.e., cervical cancer, other anogenital cancers - vagina, vulva, anus, and penis -, head & neck cancers, genital warts, and recurrent respiratory papillomatosis). The model was populated with Norwegian-specific data, obtained through a comprehensive literature search when available. The calibration was performed manually to fit Norwegian epidemiological data (incidence and mortality). The base case reference analysis evaluated the addition of quadrivalent HPV vaccination program for 12-year-old boys compared to the quadrivalent HPV vaccination program of 12-year-old girls only, considering vaccination coverage rates of 80% for both genders. The analysis was done from the Norwegian healthcare system perspective.

Results:
Compared with the 12-year-old girls quadrivalent HPV vaccination program only, including 12-year-old boys would be cost-effective (threshold of NOK500,000 or €65,000 per QALY gained) at a price up to NOK815 (or €108) per dose if all expected benefits from quadrivalent HPV vaccine are integrated (i.e., all HPV 6/11/16/18-related diseases) and up to NOK630 (or €83) per dose if only benefits mentioned in the summary of product characteristics of quadrivalent HPV vaccine are considered (i.e., HPV 6/11/16/18-related anogenital cancers and genital warts).

Conclusions:
Vaccinating 12-year-old boys against all potential HPV 6/11/16/18-related diseases provides substantial public health benefits at a cost-effectiveness ratio in accordance with the commonly cited threshold in Norway. This is the first analysis incorporating dynamic transmission modelling to assess cost-effectiveness of gender-neutral quadrivalent HPV vaccination in Norway.
DOES TIME FRAME MATTER? COMMUNICATING AGE-RELATED OR LIFETIME RISKS IN BREAST CANCER RISK COMMUNICATION

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Introduction:
Many women overestimate their risk of breast cancer. Evidence suggests that people fail to adjust their risk perception to account for longer time frames. It has been argued that using narrower time frames (e.g. 10 years) are more appropriate than life time frames. We studied the effects of presenting risk information in age-related 10 years frames in addition to life time risks on the counselees’ understanding and perception of risks and psychological well-being.

Methods:
In a RCT, unaffected women with a breast cancer family history referred to three clinical genetic centers in the Netherlands were recruited. Women received one of two conditions: lifetime risk (i.e. X out of 100 women) (n=63) or life time risks and age-related 10 years risk (n=69). Baseline, 2-week and 6-month follow-up measurements were assessed using questionnaires.

Results:
The addition of age-related risks led to more accurate understanding and lower perceived likelihood of 10 years risks of getting breast cancer but not of life time risks. The addition of age-related risks had no effect on psychological well-being or preventive intentions. Participants evaluated their own risk on breast cancer as more clear when expressed as age-related risks compared to life time risks.

Conclusion:
Our results suggest that this format has an additional value and might thus be added to life time risks of breast cancer.
EFFECTS OF A DECISION AID AND ADDITIONAL DECISIONAL COUNSELING ON CARDIAC RISK REDUCTION BEHAVIOR AND HEALTH OUTCOMES
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Purpose:
To evaluate the effects of a Decision Aid (DA), designed to assist cardiac patients in life style changes, with and without additional individual decisional counseling (DC) on health outcomes and health-related quality of life (HRQoL), mediated by adherence to cardiac risk reduction behavior.

Methods:
In this 3-group RCT with 4 repeated measures over 6 months 363 patients examined for coronary artery disease were randomized into a DA group who received the DA; a DA+DC group who, in addition, received DC; and a usual care control group. Outcomes were: BMI, cholesterol, blood pressure, tobacco use, and HRQoL (primary outcomes), adherence to cardiac risk reduction behavior (intermediate outcome), and knowledge, benefits and barriers of cardiac risk reduction behavior, and health beliefs (mediators).

Results:
There were no significant differences between patients in the DA group who received the DA only and the control group. However, patients who also received the DC had a significant decrease in BMI ($p=.016$), and improved HRQoL in physical role functioning ($p=.02$), general health ($p=.05$), vitality ($p=.02$), role function limitation ($p=.02$) and disease perception ($p=.006$) compared to the control group at six months. The DA+DC group also decreased perceived barriers to cardiac risk reduction behavior ($p=.02$) at two months. There were no significant group differences in adherence to cardiac risk reduction behavior.

Conclusion:
The DA alone did not improve health behaviors or outcomes. However, combining the DA with additional DC resulted in better health outcomes and health-related quality of life.
OUTBREAK ANALYSIS AND MODELLING IN EMERGING EPIDEMICS
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Modelling has become a more prominent tool in planning and response to emerging infectious disease outbreaks. I will start this talk by introducing some basic concepts in epidemic modelling, highlighting the importance of the basic reproduction number, $R_0$, in determining epidemic dynamics. I will then briefly review how statistical, mathematical and computational modelling has been used to analyse the dynamics of past outbreaks. The use of modelling in the last 5 years as an aid to decision making in influenza pandemic preparedness planning will then be discussed. I will then focus on the use of epidemiological analysis and modelling in real-time to aid public health decision making during epidemics. I will begin this section by discussing some of the real-time uses of modelling in responding to past outbreaks, notably BSE/vCJD, the 2001 Foot and Mouth disease epidemic in the UK, and the 2003 SARS epidemic. I will then discuss how analysis and modelling enabled early epidemiological characterisation of the 2009 H1N1 pandemic, while emphasising the difficulty in estimating severity and predicting the trajectory of the 2009 pandemic without good data on underlying infection rates. These challenges will be put into the more general context of real-time outbreak analysis and decision making, when data is ever-changing and incomplete, yet there is a need to draw preliminary conclusions even when underlying uncertainty is large. I will conclude by discussing how recent developments in data capture and analytical methods may affect the response to future emerging infectious disease outbreaks.
VACCINATING NEW PARENTS AGAINST PERTUSSIS TO PROTECT NEW-BORNS: A COST-UTILITY ANALYSIS OF A COCOONING STRATEGY

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Introduction:
Pertussis (whooping cough) is a serious illness in infants less than 6 months old, often resulting in hospitalization. One option to protect new-borns would be to vaccinate new parents (cocooning) in order to reduce transmission to the infant. Our aim was to investigate the cost-effectiveness of a potential cocooning strategy compared to the current situation in the Netherlands.

Methods:
The cost-utility ratio (CUR) for an 8-year program was estimated, assuming no (vaccine-induced) waning immunity. Costs for health care utilization and productivity loss due to illness in infants (parents not able to work) and in parents themselves, as well as impact on health-related quality of life (HRQoL) were included. Data of yearly number of infections in infants was available. Expected number of infections in the age-group of new parents was estimated and adjusted for a probable under-reporting (factor of 25 times reported cases). The estimate of the effectiveness of cocooning vaccination was based on recent results from a household transmission study. Sensitivity analyses were performed for assumptions about waning immunity, HRQoL-weights, factor under-reporting, number of (infant) deaths, life expectancy, and costs for treating infection.

Results and Conclusions:
About 128 pertussis infections yearly and one death have been registered in 2002-2010 in infants. The yearly cost of vaccinating first time mothers would be about €2.3 million and about 7 QALYs could be gained. CUR were €376,000/QALY for vaccinating only the mothers, and €625,000/QALY for vaccinating mothers and fathers. The two most influential parameters in the sensitivity analysis were: (i) the size of under-reporting (100 times number of reported cases, instead of 25), and (ii) assuming that there was one death in an infant yearly (in contrast to 0.1 deaths per year) and that that death could be avoided. The resulting CURs were both around €200,000/QALY. When using the most favourable assumptions for all parameters simultaneous the CUR (€32,000/QALY) could be acceptable compared to (unofficial) thresholds (€20,000-50,000/QALY). Cocooning can reduce the number of infants with pertussis, but the costs for reducing the disease burden are high and the intervention was not likely to achieve the health gain necessary to make it cost-effective.
Efficacy and cost effectiveness of a national hand hygiene program: novel methods and techniques

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Healthcare associated infections represent a significant burden in economic cost and morbidity, and increase the risk of death. One approach to reduce the problem is to improve hand hygiene compliance among hospital staff. Hand Hygiene Australia recently implemented the National Hand Hygiene Initiative, which is based on the WHO recommendations for the 5 moments of hand hygiene. This national program is being evaluated by an NHMRC funded project with two objectives: (1) Has the program been effective in reducing rates of hospital acquired infections after accounting for a range of confounding factors? (2) Has the program been a cost-effective use of scarce healthcare resources? We provide a novel and comprehensive approach to evaluating such a nationwide programme. We are harvesting nine data sets from a range of sources including: attitudinal and behavioural data from 3000 hospital workers, in-depth economic costing data, hospital statistics, and estimates of the willingness to pay for bed days from high level decision makers. Here we focus on a census of all hospital admissions for a five year period, used to estimate the impact of infections on length of stay and mortality. Many studies disregard the time-dependence of healthcare associated infection when estimating any additional length of hospital stay. We specifically account for the timing of infection by using a multi-state model. The extra length of stay due to health care associated SAB infections was 23 days when ignoring time-dependence and only 10.3 days after accounting for the time of infection. The mean hazard ratio of death due to SAB infection was 2.9 (95% CI: 2.4-3.5). The extra length of stay differed with the type of infection, whereas death risks were relatively constant. Ignoring the timing of infection gives estimates that greatly over-estimate its effect on the extra length of hospital stay, which subsequently effect decisions made from cost-effectiveness analyses. Accurate length of stay data are vital for informing a cost effectiveness model and its impact on health care decision making. We also briefly outline the broader methodological approach we have taken in our evaluation of the National Hand Hygiene Initiative.
COST-EFFECTIVENESS ANALYSIS OF UNIVERSAL SCREENING TESTS FOR METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) AT HOSPITAL ADMISSION

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Background:
An estimated 1.7 million health care associated infections resulting in 99,000 deaths occur in the US each year. Methicillin-Resistant Staphylococcus aureus (MRSA) is a drug resistant bacteria and a main pathogen associated with nosocomial infections. Two main screening tests are available for detecting MRSA, rapid PCR and culture-based. While many hospitals screen for MRSA upon admission, there are no set guidelines in the US and the cost-effectiveness of universal hospital screening is unknown.

Objectives:
Compare the cost-effectiveness of universal rapid PCR screening and culture screening to no MRSA screening upon hospital admission.

Methods:
We developed a model of the transmission rates, costs, and incremental cost-effectiveness of universal inpatient screening for MRSA upon hospital admission for both culture and rapid PCR assays and compared them to no hospital MRSA screening. We modeled the efficacy of each screening method as a reduction in the relative risk of MRSA transmission, infection, and death on the basis of the hazards ratios reported in the literature for each scenario. Our target population included all patients admitted to inpatient hospitals in the United States and our main outcome was the number of averted MRSA infections, the cost savings associated with reduced MRSA infections, number of averted MRSA-associated deaths, and quality-adjusted life years. All data are reported per 25,000 patients admitted.

Results:
The reported costs, including screening and isolation include: No screening: $7,967,325; Culture: $3,588,700; and PCR: $1,658,400. The number of MRSA infections in hospitals with no screening is 1,025. Hospitals with culture screening avert 600 infections, 10 deaths, with a cost of $5,981 per infection averted. Hospitals using PCR screening averted 825 infections, 13 deaths, with a $2,010 per infection averted. Comparing PCR vs. culture screening, 225 infections were averted, 3 deaths and the total cost per infection averted was $7,371. Our model was most sensitive to the prevalence of MRSA, sensitivity of both tests, and additional hospitalization cost per bloodstream infection.

Conclusions:
Universal screening for MRSA upon hospital admission is a cost effective option for hospitals to reduce nosocomial infections and their associated costs in the US, and PCR-based screening was superior compared to culture-based MRSA screening.
A DECISION ANALYSIS TO SUPPORT UNIVERSAL SCREENING FOR MRSA COLONIZATION IN A LARGE ACUTE HOSPITAL IN SINGAPORE

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Introduction:
Tan Tock Seng Hospital, an acute hospital with 1300 beds, implemented active surveillance through universal screening of admitting patients and cohorting of MRSA colonized patients to reduce nosocomial transmission. Patients were screened with culture assay with turnaround time of 2 days. During this waiting period, they were in general ward and a transmission source via healthcare workers. Transfers to cohorted ward were incomplete which increased exposure period. To over these, PCR which is costlier was considered. We studied the screening options.

Data:
Local MRSA infected patients stayed 25 days longer, cost $17,680 more and had a 13% higher mortality rate. 7.6% of the admitted patients were community acquired colonizations and an additional 4.3% were hospital acquired colonizations upon discharge. The unit test cost of PCR and culture was $52 and $28.

Method:
The model predicted the transmission considering test sensitivity and specificity on misclassification of the patients, cohorting and transmission. Costs and outcomes were compared with passive surveillance.

Results:
Universal screening with cultures cost $11.5 m annually with the majority of the cost due to excess patient stay ($7.8 m) and testing ($2.9 m). It was $2 m higher than passive surveillance with a potential to save ~15 lives and incremental cost effectiveness ratio (ICER) of ~$140 k per life saved. PCR would cost $11.4 m (ICER ~ $80 k per life saved). Cohorted ward capacity needed to increase from 100 beds to about 140 beds to house the patients.

Discussion:
The increase in the PCR test cost is offset by the savings in inpatient stay cost due to infections reduced. With PCR we reduce the exposure period and infections were estimated to reduce by ~80 per year though the reduction in hospital acquired colonization from 4% to 1%. But the deciding factor that makes it effective is the high MRSA attributed mortality rate of 13%. Sensitivity analysis showed that PCR remained cost effective under a range of conditions.

Conclusion:
Using an infectious disease model, we concluded that using the more expensive PCR was more cost effective than using screening cultures which increased exposure period and hindered complete transfer.
IS IT POSSIBLE TO TRANSFER COST-EFFECTIVENESS RESULTS OF CHILDREN VACCINES BETWEEN COUNTRIES? A LATIN AMERICA AND CARIBBEAN MATRIX ANALYSIS

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Background:
Rotavirus and pneumococcal vaccines are not introduced in all Latin American and Caribbean countries (LAC). With the aim to aid decision-making and assess transferability of results a matrix proposed by the ProVac Initiative of countries based on under-five mortality and income level (World Bank lending groups) was developed (Ucar Matrix) to observe how cost-effectiveness (CE) results grouped.

Methods:
The matrix was first tested with a series of component analyses with Ward’s hierarchical cluster method (16 cluster analyses) to observe the agreement of the conglomerate classifications with Ucar-Matrix. Variables used in the cluster analyses were infant mortality, children mortality, per capita gross national income, per capita health expenditure, GINI index, dependency ratio, DTP vaccine coverage, percentage of private Health Expenditure. A kappa greater than 40% was considered acceptable. Rotavirus and pneumococcal cost-effectiveness models were developed and results were presented for each Ucar-Matrix group.

Results:
Agreement was acceptable for most cluster analysis compared with the Ucar-Matrix. Incremental cost effectiveness ratio (ICER) for LAC countries is USD$493 for pentavalent and USD$876 for monovalent rotavirus vaccine. The countries descriptively appear less heterogeneous in each matrix group with high burden of disease and low per capita income, and more heterogeneous in countries with less burden and more per capita income.

Conclusions:
Despite countries appear to group with similar CE results in each group of the Ucar-Matrix, this matrix may not group countries optimally and data from one country probably cannot be used in another. An appropriate method to test transferability seems to be lacking in current economic literature. Although transferability of results is an experimental issue in CE analysis, this grouping of countries may be useful to explain differences and similarities in CE results/ICER across different countries.
EFFECTIVENESS AND COST-EFFECTIVENESS OF EARLY VACCINATION FOR A HUMAN INFLUENZA A (H5N1) PANDEMIC

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Background: The recent development of laboratory strains of influenza A (H5N1) that may be transmissible between humans has heightened concerns about a potential A (H5N1) pandemic.

Objective: We sought to determine how quickly a vaccination program would need to be implemented to reduce infections, deaths, and healthcare costs in an A (H5N1) pandemic.

Design: We used a model of influenza transmission to estimate the health and economic consequences of an A (H5N1) pandemic in a large metropolitan city.

Target Population: Residents of a U.S. metropolitan city.

Perspective: Societal.

Interventions: Vaccination of 30% of the population at 2, 4, 6, or 9 months.

Outcome Measures: Infections and deaths averted, cost savings.

Results of Base Case Analysis: Assuming a case fatality proportion of 10% and R0 of 2.0, 95,000 deaths would occur in a population of 8 million individuals in 12 months. A vaccine with 56% effectiveness could prevent 44%, 35%, 25% and 9% of deaths if introduced to 30% of the population at 2, 4, 6, or 9 months, respectively. Vaccination would save $20, $51, $71, or $90 million in health care costs for this population at each of these time points.

Results of Sensitivity Analysis: Vaccination at 9 months with increased non-pharmaceutical interventions (e.g., hand hygiene, cough etiquette, social distancing) to 32% of the population would yield a similar reduction in infections and deaths as 25% (assumed base case) non-pharmaceutical interventions with vaccination at 4 months.

Limitations: The model is not designed to evaluate programs targeting specific populations such as children or individuals with comorbidities that may increase the risk of morbidity or mortality from influenza infection.

Conclusions: Our findings highlight the urgency of rapid vaccination in the case of an influenza A (H5N1) pandemic. Early widespread vaccination can significantly reduce morbidity and mortality, as well as healthcare costs. Investment in technology to speed vaccine manufacturing and distribution should be a top priority for policymakers. Maximizing non-pharmaceutical interventions, such as social distancing, can help mitigate a pandemic until a matched vaccine becomes available.
TREATMENT DECISION-MAKING AND COMMUNICATION BETWEEN RADIATION-ONCOLOGISTS AND RECTAL CANCER PATIENTS: A SINGLE-CENTER STUDY
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Introduction:
Given the variation in patient values regarding possible outcomes of treatment, the decision to apply pre-operative radiotherapy (PRT) in patients with rectal cancer should be based both on clinical evidence and patient preferences. This study aimed to examine the communication between radiation-oncologists and patients about (1) treatment options, including benefits and side effects and (2) clinical evidence and patient preferences, all in reference to the decision and/or the decision-making process.

Methods:
Consecutive all first consultations of radiation-oncologists and patients with rectal cancer, eligible for short course (5x5 Gy) radiotherapy, were audio taped. These tapes were transcribed and analyzed concurrently using an adapted version of the ACEPP instrument, parts of the DAS-O instrument, and the OPTION instrument, all relating to aspects of shared decision making and communication of evidence.

Results:
Data collection is still ongoing; currently 30 consultations have been coded and analyzed. In most consultations, no treatment options other than short course radiotherapy - including no adjuvant therapy - are explicitly considered. For radiation-oncologists, research evidence seems to be the main motivation for radiotherapy though this evidence is rarely discussed with patients in the consultation. Patient preferences and patient’s social circumstances are not explicitly incorporated in the final decision. There is great variation in the number of side-effects mentioned, and in how extensively they are being discussed. If probability of these benefits and harms is being mentioned, this mostly happens on a rather basic level by using words without any illustrating numbers or percentages.

Discussion:
Although a treatment suggestion is made by a multidisciplinary team before consultation, a preference-based shared decision should be made during the consultation. This study shows that patient preferences and social circumstances are often not considered in the decision making process regarding PRT in rectal cancer patients. Also, the manner and extent to which clinicians communicate the evidence behind their recommendations for PRT needs to be improved, as a condition for a shared decision.
Background:
Fear of inducing regret makes some clinicians reluctant to increase patient participation in treatment decisions. This study aims to find out whether increased patient participation, by means of a decision aid, affects the likelihood of regret in the context of the treatment choice for prostate cancer.

Methods:
Between 2008 and 2011, 213 patients with localized prostate cancer, were randomized (t1) to a group that discussed the treatment choice with their specialist and a group that, in addition, received a decision aid on the risks and benefits of the treatment options. The treatment options were radical prostatectomy, interstitial or external beam radiotherapy. Regret was measured two weeks after the decision was made (t2), and 6 (t3) and 12 (t4) months after treatment. We used three newly developed regret scales focusing on process regret, option regret and outcome regret, with scores ranging from 1 (no regret) to 5 (strong regret), and the validated Brehaut regret scale (range 0 to 100).

Results:
The decision aid led to an increase in patient involvement in the treatment choice. In the decision aid group less patients indicated that mainly or only the physician had decided on the treatment choice (5%) than in the usual care group (18%, p=0.02). The decision aid did not increase process regret, option regret or outcome regret (see table).

<table>
<thead>
<tr>
<th>Regret scales</th>
<th>Usual Care Mean (sd)</th>
<th>Decision Aid Mean (sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process regret</td>
<td></td>
<td></td>
</tr>
<tr>
<td>at t2 (n=213)</td>
<td>1.81 (.5)</td>
<td>1.84 (.5)</td>
</tr>
<tr>
<td>Option regret</td>
<td></td>
<td></td>
</tr>
<tr>
<td>at t3 (n=204)</td>
<td>1.54 (.6)</td>
<td>1.48 (.5)</td>
</tr>
<tr>
<td>at t4 (n=183)</td>
<td>1.67 (.6)</td>
<td>1.58 (.7)</td>
</tr>
<tr>
<td>Outcome regret</td>
<td></td>
<td></td>
</tr>
<tr>
<td>at t3 (n=207)</td>
<td>2.23 (.9)</td>
<td>2.07 (.8)</td>
</tr>
<tr>
<td>at t4 (n=183)</td>
<td>2.30 (.9)</td>
<td>2.11 (.8)</td>
</tr>
<tr>
<td>Brehaut scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>at t3 (n=207)</td>
<td>16.0 (15.6)</td>
<td>14.3 (14.9)</td>
</tr>
<tr>
<td>at t4 (n=181)</td>
<td>19.5 (17.0)</td>
<td>16.4 (16.7)</td>
</tr>
</tbody>
</table>
Even in patients who experienced a poor outcome, no effect of the decision aid on regret was found (data not shown).

**Conclusion:**
In the treatment choice for prostate cancer, fear of inducing regret with decision aids does not seem warranted. The benefits of using a decision aid do not appear to be counteracted by an increase in any aspect of regret in the year following treatment.
General Practitioners (GPs) often talk about gut feelings and their clinical intuition. But, does intuitive processing ever result in more accurate diagnoses and under what conditions? Unconscious thought theory suggests that for complex tasks, better decisions are made after a period of distraction than after a period of conscious deliberation. This deliberation-without-attention effect (DWA) has been established and studied in consumer psychology but, there are also many failed replications and its theoretical underpinnings are the source of contention. The theory states that the effect should replicate in diagnostic decision-making. We sought to test DWA amongst GPs on real cases experienced in primary care.

Participants were practising GPs and GP trainees. Diagnoses and ratings of concern and confidence were given for three patient cases. Responses were given in one of three conditions: immediate, distracted (completed a 3 minute 2-back memory task before responding) or self-paced conscious deliberation. Information was presented sequentially with each informational cue on screen for 4s only. Diagnoses given were marked against the final diagnosis of the original patient case; correct or incorrect. The sum score of each participant was used to create a combined categorical score: 0, 1 or 2 (no participant achieved 100% accuracy). Data collected from 79 participants to date (34 Female, mean age 40 years SD11.1, mean experience 10.5 years SD11.8) show a significant difference between groups suggesting those in the distracted condition were most accurate (p=.038 Fisher’s exact test). More than half of those participants with the highest score overall were in the distracted condition.

These preliminary results suggest that DWA can be replicated in diagnostic tasks using ecologically valid stimuli. However, more detailed analyses are precluded by sample size at the time of writing. A full dataset and complete analysis will be available for the presentation date.
Misdiagnoses can result from initial hypothesis generation based on physicians’ observations of symptoms. If ambiguous symptoms of a patient activate two or more diagnostic categories, multiple diagnostic hypotheses have to be compared within the reasoning process. But this comparison can be biased due to bounded rationality if physicians stick to their initial hypothesis and neglect alternatives. How to prevent such a confirmation bias? On the one hand explicit highlighting of alternatives may reduce confidence in the initial hypothesis. For example, explicit consideration of alternatives can be instructed. On the other hand, symptoms conflicting with the generated hypothesis can shake confidence in the initial hypothesis and in this way highlight alternative diagnoses implicitly. The present study examines effects of explicit and implicit highlighting on confirmation bias in diagnostic reasoning.

Within three conditions (no, explicit, and implicit highlighting) 119 participants were presented with a chemical accident task, a paradigm of medical diagnostic reasoning with serially perceived symptoms. In order to examine the parallel development of multiple hypotheses, we challenged participants with ambiguous symptom sets. They had to integrate four symptoms with multiple hypothetical causes within a diagnostic process to arrive at a final diagnosis (A or B).

Final diagnoses depended on the highlighting of alternatives. Early symptoms induced a clear and stable confirmation bias towards the initial hypothesis (65% proportion of A-diagnoses; \( p < .001 \)), to the detriment of an equally supported alternative. Explicit highlighting by eliciting ratings of all candidate hypotheses eliminated confirmation bias completely (50% A, 50% B). However, implicit highlighting via inconsistent symptoms was ineffective as reflected in a considerable confirmation bias (60% A; \( p < .01 \)).

Cognitive models of memory processes during diagnostic reasoning account for confirmation bias in deciding between rival hypotheses and can explain the effect of explicit highlighting. Whether the failure of implicit highlighting obtained in a quasi-medical task would generalize to medical experts reasoning about real cases remains to be tested. Yet, explicit highlighting of alternative diagnoses can reduce the bias towards an initial hypothesis in processing series of symptoms in medical practice.
DO DOCTORS AND THEIR PATIENTS MAKE ACCURATE DIAGNOSTIC INFERENCES AND DO VISUAL AIDS HELP?

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²Faculty of Business and Economics, University of Lausanne, Switzerland

Doctors and their patients have difficulties inferring the positive predictive value from information about the prevalence of a disease and the sensitivity and false-alarm rate of a medical test. Previous research has established that communicating such information in a format the human mind is adapted to—namely natural frequencies instead of probabilities—improves such inferences considerably (Hoffrage et al., 2000). In our study, we aimed at investigating to what extent diagnostic inferences can be improved—beyond such format effects—by providing visual aids. Participants were 81 doctors (average age of 49 years, range 40-63 years; 45% males) and 81 patients (average age of 55 years, range 18-82 years; 38% males). We used three tasks: inferring breast cancer from a positive mammogram, colon cancer from a positive hemoccult test, and insulin-dependent diabetes from a genetic test. Half of the participants received the information about prevalence, sensitivity, and false-positive rates of the tests in natural frequencies, while the other half received this information in probabilities. Half of the participants only received numerical information, while the other half additionally received a visual display representing the numerical information. In addition, participants completed a numeracy scale. The three most important findings were: (1) Inferences were better when information was communicated in terms of natural frequencies as compared to probabilities, (2) visual aids were very effective and boosted Bayesian performance even when the information was provided in natural frequencies, and (3) doctors were more accurate in their diagnostic inferences than patients; differences between doctors and patients, however, disappeared when we controlled for participants’ numeracy. These results have important implications for medical practice as they suggest suitable ways to communicate quantitative medical data.
PRIORITIZING RARITY: ARE DOCTORS MORE WILLING TO MAKE HARD CHOICES THAN THE GENERAL PUBLIC?

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Department of Health Management and Health Economics, University of Oslo, Norway

Background:
Preferences for prioritizing treatment of rare versus common diseases elicited from the general public might exhibit a central tendency bias because of a reluctance to make the unpleasant choice of treating one group of patients rather than another. We hypothesized that doctors confronted with the same decision would be willing to set more definitive priorities.

Methods:
We surveyed of a random sample of 551 Norwegian doctors and compared results to a similar survey of the Norwegian population. Respondents chose whether to prioritize treatment of patients with rare versus common diseases and then decided how to allocate funds between the two groups for each of two scenarios: (1) equal costs per person and (2) higher costs for the rare disease. Except for different prevalence, the diseases were described as identical. Respondents were randomized to treatment costs for the rare disease that were either 8 or 25 times higher than treating the common disease (in the costly rare scenario). Outcomes for the allocation exercises were the mean share of funds allocated to the rare disease and the share of respondents dividing funds equally between the two groups. Respondents also indicated which allocation principle health authorities should use in setting priorities.

Results:
Doctors’ responses differed significantly from those of the general public. For questions in which the rare disease was more costly to treat, a larger share of doctors (77.4%) than the general public (52.6%) prioritized the common disease group for treatment ($X^2$: $p < 0.001$) while a smaller share (18.2% vs. 42.9%, $X^2$: $p < 0.001$) expressed indifference. When dividing funds between the two patient groups, doctors allocated an average of 27.3% of funds to the rare disease group compared with 41.1% for the general population. Only 14.8% of doctors divided funds equally between the groups compared to 42.0% of the general public. (Mann-Whitney: $p < 0.001$).

Conclusions:
There are significant differences in how doctors and the general population in Norway would prioritize treatment of rare diseases. This information could be useful for policy makers, particularly if the preferences elicited from the general public reflect a reluctance to make difficult choices.
SUBGROUP ANALYSIS WHEN USING THE PROPENSITY SCORE: A MONTE CARLO SIMULATION STUDY

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Objectives:
The use of non-randomized studies, like registry databases, and indirect comparisons has become important. Lack of randomization could lead to confounding or selection bias due to pretreatment differences between patients. To adjust for this bias, the propensity score (PS) method is increasingly applied to estimate treatment effects. However, a treatment effect can vary between different subgroups. It is yet unclear how to perform subgroup analyses when the propensity score method is applied.

Methods:
A Monte Carlo simulation is conducted to test the performance of different PSs in subgroup analyses. The estimation of the PSs differed in: 1) the definition of treatment categories for which the PS was estimated, either univariate on treatment assignment only or multivariate on a combination of the treatment assignment and subgroup variable, and 2) the selected covariates to be included in the PS. The subgroup variable was in- and excluded in the PS. These various PSs were adjusted for in a linear regression model. Simulations were made for 90 different settings varying sample size, correlation between independent variables, correlation between the subgroups with the independent variables, independent variables as categorical variables, skewness and kurtosis in the independent variables and non-linearity on the prediction of the outcome.

Results:
To find accurate treatment effects between subgroups, the PS should be defined multivariate, as the conditional probability of assignment to the treatment and belonging to a subgroup. This multivariate PS should then be added in a regression model, for which additional adjustment on subgroups is not appropriate. The PS with inclusion of variables related to outcome is the most appropriate. In addition, considering the univariate PS, the subgroup variable should not be included in the PS, but only adjusted for in the outcome equation. Small sample sizes gave the least accurate results, as well as a higher correlation between the covariates with the subgroup.

Conclusions:
The results show the feasibility and validity of using the PS in subgroup analyses when analyzing registry databases and indirect comparisons.
Determining the impact of different covariates on health outcomes in longitudinal data is a major research topic in health economics. In practice often a large number of potential covariates is present, making variable selection necessary to obtain efficient inference. However two issues are commonplace, often overlooked by standard methodology and could be addressed better: multicollinearity and time-dependent covariates. We propose penalized generalized estimating equations with Elastic Net or L2-Smoothly Clipped Absolute Deviation penalization to simultaneously select the most important variables and estimate their effects for longitudinal Gaussian data when multicollinearity is present. Variable selection is particularly challenging under multicollinearity due to instability. This problem is avoided by the grouping effect property of the proposed penalty functions, meaning highly correlated variables tend to have similar parameter estimates and therefore to be included or excluded as a group. The grouping effect is a consequence of the convexity of the penalty function, for which we provide conditions on the tuning parameters. The method is able to consistently select and estimate the main effects even when strong correlations are present. In addition the potential pitfall of time-dependent covariates is clarified. The small sample performance is investigated through simulation studies with and without time-dependent covariates. Both asymptotic theory and simulation results reveal the effectiveness of penalization as a data mining tool for longitudinal data, especially when a large number of variables is present. The method is illustrated by mining for the main determinants of life expectancy in Europe.
ASSESSMENT OF THE VALIDITY AND RELIABILITY OF THE WELL-BEING VALUATION METHOD FOR MONETARY VALUATION OF INFORMAL CARE
C.E. Jacobi\textsuperscript{1}, B. van den Berg\textsuperscript{2}, M.E. van den Akker-van Marle\textsuperscript{1}
\textsuperscript{1}Department of Public Health, Leiden University Medical Center, The Netherlands, \textsuperscript{2}Centre for Health Economics, University of York, UK

Introduction:
Economic evaluations from a societal perspective should include the impact of providing informal care on caregivers to prevent suboptimal healthcare decisions. In the last decade, several methods to value informal care have been proposed. The Well-Being Valuation Method, in particular, seems a promising tool for economic evaluations in informal care because in theory captures the total effect of providing informal care on caregivers using only three simple questions.

Aim:
We studied the relationship between well-being and informal care to explore the construct validity of the Well-Being Valuation Method. Furthermore, we studied the reliability of the method by exploring the reproducibility of previous results in a different sample of Dutch informal caregivers.

Methods:
Informal caregivers received a questionnaire including the Well-Being Valuation Method, caregiver and care recipient characteristics and aspects of care. Caregivers were divided into two groups: family caregivers and non-family caregivers. Using univariate and multiple regression analyses, construct validity was studied by examining the relation between well-being and the impact of providing informal care. Monetary valuation of informal care was estimated by performing linear regression analysis.

Results:
In total, 593 respondents were included in our study: 494 family caregivers and 99 non-family caregivers. Family and non-family caregivers’ well-being was statistically significantly different. This difference remained when caregiver and care recipient characteristics were included, but disappeared when also aspects of care were included in the analysis. The monetary valuation in percentage of the weekly household income varied from 14.9\% by increasing the hours of informal care from 9 to 10 hours a week to 2.7\% by going from 49 to 50 hours of care.

Conclusion:
The construct validity of the Well-Being Valuation Method is supported by the results of this study. We showed that caregivers’ well-being reflect the subjective burden as experienced by carers due to caregiving. We also found that the impact of the relationship between caregiver and care recipient on well-being can be explained by differences in care aspects. The reliability of the Well-Being Valuation method is indicated as the monetary valuation outcomes are highly comparable to earlier results.
COST-EFFECTIVENESS ANALYSIS AND BUDGET IMPACT ASSESSMENT: COMBINING THE TWO FOR THE AID OF DECISION MAKERS
M. Paulden, B. Pham
THETA Collaborative, University of Toronto, ON, Canada

Objectives:
Cost-effectiveness analysis has traditionally been seen as a means of satisfying an explicit social objective subject to a fixed budget constraint. As a result, existing methods largely ignore budget impact considerations in health systems where budgets are not fixed, such as the provincial health systems in Canada. In particular, none of the traditional methods of presenting results – such as the cost-effectiveness plane, incremental cost-effectiveness ratios (ICERs), and cost-effectiveness acceptability curves (CEACs) – can be used to summarize the results of a cost-effectiveness analysis and budget impact assessment simultaneously. Our objective was to develop such a method in a way which is useful for decision makers.

Methods:
We present a novel method for combining cost-effectiveness and budget impact considerations into a single analysis. To do this, we disaggregate the incremental costs of the health technology into those costs which fall on the health budget and displace other health activities and those costs which result in an expansion of the health budget. The net health benefit of the technology is then compared directly against the net budget impact.

Results:
Our method clearly reveals the trade-off between the cost-effectiveness and budget impact of the health technology across a range of possible values of the cost-effectiveness threshold.

Conclusions:
Our method aids decision makers by making the trade-off between the cost-effectiveness and budget impact of new health technologies explicit. Our method also allows analysts to provide meaningful information to decision makers on the cost-effectiveness and budget impact of new health technologies.
THE USEFULNESS OF VALUE OF INFORMATION APPROACHES TO CLINICAL TRIAL DESIGN: AN APPLICATION TO ALTERNATIVE TREATMENT STRATEGIES FOR NSTEMI PATIENTS

S. Kent¹, A. Briggs¹, C. Berry²
¹Health Economics and Health Technology Assessment, ²Department of Cardiology, University of Glasgow, Scotland, UK

There exists uncertainty regarding the appropriateness of interventions in individuals with a recent NSTEMI. Diagnosis used to inform subsequent clinical decisions can be performed based on the visual assessment of a coronary angiogram alone or in conjunction with measurement of Fractional Flow Reserve using a pressure wire. Here we construct an economic model that can be used to inform two important questions: 1) Is the routine use of FFR cost-effective, and 2) Is there value in collecting additional research to reduce the uncertainty in this estimate, and, if so, how much evidence should be collected. The economic model suggests that FFR does appear to be cost-effective but there is substantial value in delaying the adoption decision and collecting further information to reduce uncertainties in this estimate. Using frequentist techniques, the optimal sample size should be around 1700 using a clinical outcome and 2400 using an economic outcome. A value of information model is introduced in incremental stages and suggests a wide range of acceptable sample sizes depending on the particular assumptions made. Ignoring opportunity costs and recruitment constraints leads to much larger sample sizes than the frequentist approaches. Introducing recruitment constraints reduces the optimal sample size and incorporating a measure of opportunity costs renders a trial no longer optimal. However, when the relationship between strength of evidence and implementation was modelled, a trial was once again optimal and with a sample considerably less than for either frequentist approach at 1120.
USING EVSI IN ANGER – SOME LESSONS LEARNED

K. Boyd, E. Fenwick, M. Neilson, A. Briggs
HEHTA, Institute of Health and Wellbeing, University of Glasgow, Scotland, UK

Purpose:
To discuss the process of undertaking an EVSI calculation for the design of a clinical trial, and highlight potential pitfalls and common mistakes that could be made, particularly when applying this methodology for the first time. This paper presents the lessons learned from undertaking an EVSI calculation to determine the appropriate sample size for a proposed study of fetal fibronectin (fFN) screening for diagnosing women threatened with pre-term labour.

Methods:
In considering an iterative framework for the process of health technology assessment (1), the expected value of sample information (EVSI) provides an efficient means for designing a trial through considering the value of additional information of a specific nature. Through comparison with the cost of specific research, the EVSI can be used to identify gaps in the evidence base where there are expected net benefits of sampling and further research is worthwhile. The EVSI process has been described by numerous authors (2, 3); while these existing guidelines are comprehensive they are complex and, at various points, are open to (mis)interpretation.

Results:
Potential pitfalls include misinterpretation of the process used to simulate sample data, confusion regarding the various alternative algorithms to use depending on whether the model is linear or non-linear in the parameters of interest and in the complementary parameters, and also potentially misinterpreting what the value of current information represents.

Additionally, computational issues with undertaking the EVSI calculation can arise particularly when deciding upon an appropriate number of iterations to draw from the prior distribution. The time taken to undertake an EVSI calculation may also be a concern when considering the constrained timeframe of any grant submission process.

Conclusions:
The EVSI process has been described by numerous authors; however, existing guidelines are complicated to follow and are open to (mis)interpretation at numerous points. This presentation supports the case for developing a simple guide to EVSI which outlines the process involved at each step and explicitly addresses potential pitfalls. Such a guide could be of considerable help for those new to the methodology or applying it in practice for the first time.

References:
2. Brennan A, Chilcott J, Kharroubi SA, O'Hagan A, Cowan J. A two level Monte Carlo approach to calculating expected value of sample information: How to value a research design. ScHARR Research Paper 2002; School of Health & Related Research, University of Sheffield. Available online at: https://sheffield.ac.uk/content/1/c6/02/96/29/EVSI.doc
INFECTIOUS DISEASE MODELING TO SUPPORT POLICY ASSESSMENTS AND COST-EFFECTIVENESS ANALYSES: TUBERCULOSIS, HIV, AND HEPATITIS C
WORKSHOP

Speakers:
J.D. Goldhaber-Fiebert, Stanford Health Policy, Centers for Health Policy and Primary Care and Outcomes Research, Stanford University, CA, USA
H.H. Thein, Dalla Lana School of Public Health, University of Toronto, ON, Canada
Senior Collaborating Author: A. Bayouni, Department of Medicine and Institute of Health Policy, Management and Evaluation, University of Toronto and St. Michael’s Hospital, Toronto, ON, Canada

Background:
Chronic infectious diseases increasingly threaten global population health. Complex transmission dynamics, long latent periods, social marginalization, and imperfect management and control options present difficult policy challenges. Mathematical modeling can inform related policy decisions, though they necessitate major methodological choices.

Diseases and Policies:
The workshop includes three examples: 1) drug-sensitive (DS) and multi-drug resistant (MDR) TB and the relative value of scaling-up MDR TB treatment or improving DS TB treatment quality in India; 2) The projected health and economic effects of establishing supervised consumption sites – legally sanctioned facilities where people consume illicit drugs under the supervision of trained staff – in Toronto, Canada, focusing on Human Immunodeficiency Virus (HIV) and Hepatitis C virus (HCV) infections; 3) HIV and HCV in populations that differ in terms of individual risk behaviors and spatial access to health services and the role of risk reduction in terms of reduced transmission and improved health outcomes.

Methods:
All models focus on 2+ types of infections and include transmission dynamics. The TB example uses a demographic- and risk-factor stratified microsimulation; the HIV/HCV supervised consumption facility example uses a compartmental model stratified by type of drug use; and the HIV/HCV population example uses an agent-based model linking individual-level behaviors and spatial information. All models employ calibration and empirical data analyses to determine inputs.

Goals:
Examples presented are highly policy relevant. In the case of TB in India, improving DS TB treatment could have a bigger effect on MDR TB than scaling up MDR TB treatment if achieved quickly prior to MDR TB shifting from being a treatment-generated epidemic to primarily a transmitted epidemic. In the case of HIV/HCV and supervised consumption facilities in Toronto, at a threshold of $50,000/QALY, it would be cost-effective to establish three facilities ($41,605/QALY) compared to establishing two facilities. The examples illustrate methodological choices inherent in chronic infectious disease policy modeling.
Collaborating Co-Authors:
a) TB/MDR-TB: Sze-chuan Suen, Eran Bendavid (Stanford); b) HIV/HCV supervised consumption facilities: Eva Enns (Stanford), Greg Zaric (University of Western Ontario), Jennifer Jairam (St. Michael’s Hospital), Carol Strike (University of Toronto), Patricia O’Campo (St. Michael’s Hospital), Susan Shepherd (Toronto Public Health); c) HIV/HCV agent modeling: William Wong, Ahmed Bayoumi, Murray Krahn (University of Toronto), Shamin Kinathil, David Wilson (University of New South Wales)
MEDICAL RISK COMMUNICATION – ACKNOWLEDGING THE HETEROGENEITY OF RISK PERCEPTION
WORKSHOP

Speakers:
J.K. Hammit, Department of Health Policy and Management, Harvard School of Public Health, Center for Risk Analysis, Boston, MA, USA and Toulouse School of Economics (LERNA-INRA), France
J. Nexøe, Odense Risk Group, General Practice, Institute of Public Health, University of Southern Denmark, Odense, Denmark
A. Edwards, Institute of Primary Care and Public Health, Cardiff University School of Medicine, Wales, UK
J.B. Nielsen, Odense Risk Group, General Practice, Institute of Public Health, University of Southern Denmark, Odense, Denmark

Chronic diseases represent a significant burden to society in terms of number of patients and treatment costs. Lifestyle diseases will account for 70% of all chronic diseases by the year 2020, and it has been estimated that 80% of all heart disease, stroke and diabetes, and 40% of all cancers can be prevented or delayed significantly by lifestyle changes and medical interventions. Clinical experience, however, suggests that lack of adherence reduces the efficacy of these preventive interventions significantly.

Preventive interventions depend strongly on self-care, i.e. the ability of an individual to adhere to agreed medical treatment and/or changes in lifestyle. Shared decision making, willingness to take preventive medications, and adherence to treatment all require a thorough understanding by the person at risk and thus an ability of the physician to communicate risks, benefit, potential side effects, costs, and how they interact. Therefore, communication of quantitative risk measures from physician to patient has become increasingly important.

Identifying the potential for welfare gains from disease prevention requires an understanding of what people value when making their own choices, why they value certain outcomes higher than others, and what they perceive as barriers to an intervention.

Managing risk conditions (hypertension, osteoporosis, etc.) is an everyday task of general practice. For shared decision-making between patient and doctor, patients need to have an understanding of the benefits and harms of potential interventions. We aim to provide insight into how doctors can provide patients with risk information and where this fits into shared decision making. We will also examine how these new approaches to communication can integrate with the supportive role that many patients want from their doctors, and discuss examples from clinical experience.

The workshop will present three inputs as background for a discussion on shared decision making and risk communication:

1. Valuing morbidity risks (James Hammit, Harvard School of Public Health, USA)
2. Reasons for accepting or declining medical interventions (Charlotte Gry Harmsen, University of Southern Denmark, Denmark)
3. Shared decision making – clinical experiences (Adrian Edwards, Cardiff University, Wales)
EUFRAT - ESTIMATING THE RISKS FROM OUTBREAKS OF EMERGING INFECTIOUS DISEASES TO BLOOD SAFETY
WORKSHOP
Speakers:
S. Rehmet, European Centre for Disease Prevention and Control, Stockholm, Sweden
M. Carson, European Centre for Disease Prevention and Control, Stockholm, Sweden
W. Oei, Julius Centre for Primary Care and Health Science UMC Utrecht, The Netherlands

Objective:
This workshop will demonstrate the various functions of the novel European Up-Front Risk Assessment Tool (EUFRAT) by allowing participants to use the tool through problem solving and to discuss its application potential.

Topics covered and intended audience:
This workshop covers several public health topics including infectious disease modelling and outbreak decision making. It would be suitable for participants with interests in blood safety, quantitative risk assessment, infectious disease modelling and outbreak preparedness and response.

Description:
Outbreaks of emerging infectious diseases pose a potential threat to blood safety, and require decisions on implementation of protective measures. The browser-based EUFRAT tool provides quantitative, fast and flexible risk estimates for public health decision makers across the five steps of the transfusion chain from the risk of infection in the population to the risk to recipients of blood products. It was developed by the University of Utrecht for the European Centre for Disease Prevention and Control (ECDC) to support decision making for blood safety in outbreak situations. It can be used with any blood-borne infectious disease but contains specific parameters for 18 diseases of outbreak potential in Europe, including West Nile Virus, tick-borne encephalitis, hepatitis A, Q fever and malaria. Users apply population, outbreak and disease-specific data to estimate risk outputs for specific outbreak areas, as well as the associated risks from a traveller returning from an outbreak area. The workshop would let participants apply the tool to data from recent outbreak events of relevance to Europe and discuss the value of such quantified risk assessments.

Audio/visual/material/computer requirements:
The workshop will require the use of laptops and a projector/screen. Handouts will be provided.
WHAT CAN SMDM DO TO GLOBALIZE THE PRINCIPLES AND PRACTICE OF EVIDENCE-INFORMED HEALTH-CARE DECISION-MAKING?

PANEL DISCUSSION

Moderator:

J.L. Mathew, Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, India and Division of Respiratory Medicine, The Hospital for Sick Children, University of Toronto, ON, Canada

Panelists:

M. Krahn, Department of Medicine and Faculty of Pharmacy, University of Toronto, and THETA (Toronto Health Economics and Technology Assessment), Toronto, ON, Canada

J. Van den Ende, Institute of Tropical Medicine, Antwerp, Belgium

Background:

Scientific decision-making practices are one of the key pillars of high quality health-care in institutions and organizations across many European and North American countries. The various tools developed for this include evidence-based health-care, health-technology assessment, decision-analysis systems, etc. In contrast, many other countries and health-care systems lack similar robust processes for decision-making supported by locally relevant scientific information. In such situations, decisions are often made by less rigorous (and sometimes unscientific) methods. This workshop is intended to be a brain-storming session to explore what SMDM can do to facilitate global acceptance and application of the principles and processes of scientific decision-making; with a particular focus on the prevention/control of infections.

Objectives:

To highlight:

1. Principles and practices in decision-making in high-quality health-care systems (using one or more examples related to prevention/control of infections).
2. Decision-making practices in health-care systems that lack rigorous scientific processes, using examples related to prevention/control of infections.
3. SMDM Global Working Group activities to foster robust medical decision-making across the world.
4. Possible options for the way forward.

Intended audience:

SMDM members from all health-care backgrounds with a common interest in globalizing the principles and practice of scientific medical decision-making.

Format:

Interactive presentations and discussions.
Content:
1. Welcome and introductions (10 minutes): All present
2. Principle and practice of decision-making in developed health-care systems (12 minutes): Prof. M. Krahn.
3. How decisions are made in health-care systems lacking scientific processes (12 minutes): Dr. J L Mathew.
5. Discussion on the way forward (45 minutes): All participants
6. Summary and conclusions (4 minutes): Dr. J L Mathew

Expected outcome:
- Sensitization of SMDM members about the gap in decision-making processes between highly developed and less developed health-care systems.
- Creation of interest to share experience and expertise to foster globalization of robust decision-making processes.
- Brain-storming ideas/options to facilitate the above.
- Preparation of an action-plan for SMDM that can be implemented by the Global Health Working Group
HPV-BASED PRIMARY CERVICAL CANCER SCREENING – A BENEFIT ASSESSMENT
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Background/Objectives:
A persistent infection with high-risk types of human papillomavirus (HPV) is the main causal factor for the development of invasive cervical cancer and its precursors. The aim of this systematic benefit assessment performed by the Institute for Quality and Efficiency in Health Care (IQWiG) was to evaluate the beneficial and harmful effects of HPV-based versus cytology-based primary cervical cancer screening.

Methods:
The systematic literature search for randomized controlled trials (RCTs) was conducted in MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials until 01/07/2011. Eligible studies had to compare a strategy including HPV testing alone or in combination with cytology-based testing and a strategy including cytology-based testing alone. Patient relevant outcomes of interest were overall survival, cause-specific mortality, invasive cervical cancer, high-grade cervical intraepithelial neoplasia (CIN3/CIS), screening-related harm, and quality of life. The literature screening was performed by 2 reviewers independently of one another. After an assessment of the risk of bias, the results of the individual studies were evaluated and, if possible, pooled.

Results:
Six RCTs with a total of 235,613 randomized women were included. Screening and work-up strategies, age of included women, and follow-up time varied significantly. Independent on screening strategy, women were already considered for treatment when they were histological diagnosed with CIN2, which may cause overtreatment in a number of cases. Four RCTs, all with a high risk of bias, reported relevant data for a second screening round. In the meta-analyses a reduction in invasive cervical cancer incidence in favour of those women who had formerly undergone an HPV-based screening strategy was observed (RR: 0.22; 95% CI: 0.08 to 0.67; p = 0.007). The number needed to screen to prevent one additional case of cervical cancer was 4800 (2700; 20,800) given a screening interval of 3 to 5 years. However, data on cancer mortality, screening-related harm and quality of life were lacking.

Conclusions:
While available studies provide indications of a benefit of an HPV-based screening strategy, the potential harm from HPV testing in primary cervical cancer screening cannot be assessed due to a lack of data.
COMPARING LONG-TERM COSTS OF INTRODUCING HPV DNA POST-TREATMENT SURVEILLANCE IN NATIONAL CERVICAL CANCER SCREENING IN IRELAND

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Background:
CervicalCheck, The National Cancer Screening Programme of Ireland proposed a new post treatment surveillance policy following colposcopy treatment. The new policy increases the one-time costs of surveillance by incorporating HPV DNA testing but decreases costs by reducing intensity of recalls for women with no detected abnormalities. This joint work by the National Cancer Screening Service and Health Economists projected and compared the 12-year projected costs under the new and conventional surveillance policies.

Methods:
A cost-minimization study using decision analysis was used in which a Markov transition process aggregated testing costs over twelve years. The conventional colposcopy procedure includes laboratory cytology, smear test and speculum exam. The proposed schedule adds an additional HPV DNA laboratory test. While the conventional follow-up recalled women every year for ten years, the proposed schedule recalls women every three years if no abnormalities are found at the six-month and 18 month post-treatment follow up. The model accounted for losses to follow-up or treatment and discounted future costs.

Results:
A steady stream of 8522 patients entered the surveillance algorithms each year for twelve years. Utilizations and costs during that period were aggregated. Aggregated incremental costs of new policy were positive for the first three years but became negative thereafter, generating a cost savings of roughly €20 million in favor of the proposed system over a twelve year period. Results were robust over a range of sensitivity analyses with respect to discount and attrition rates.

Conclusion:
We modeled twelve-year programme costs of two cervical surveillance strategies using a decision-analytic approach and found significant long-term cost savings with the use of the proposed surveillance schedule. Ireland is introducing HPV post-treatment surveillance as part of CervicalCheck in 2012.
Aim:
The main challenge that health care (HC) systems and policy makers face in light of an ageing population is the potential, although difficult to quantify, increase in future HC expenditure. The aim of this research was to analyse, for the first time in Scotland, how HC expenditure projections are influenced through the application of two approaches; the first one only accounting for demographic changes, and the second also implementing a component that accounts for potentially higher HC spending during the time immediately before death (TTD). A comparison of both scenarios provides an estimate of the magnitude of a possible overestimation of future HC costs if remaining TTD is not accounted for, as is often argued in the literature.

Methods:
Future costs for acute inpatient care are estimated for two scenarios: A) the demographic approach and B) the TTD approach. The Scottish Longitudinal Study (SLS) is an anonymised dataset of a representative sample of the Scottish population (5.3%), which draws on data from a series of statistical and administrative sources, and is for the purpose of this study, linked to hospital admissions. Population estimates up until 2031 were obtained for both methods and multiplied separately by cost estimates that were obtained for scenarios A and B.

Results:
Over the next two decades, the growth rate of HC expenditure under the demographic approach was found to be higher than that for HC expenditure under the TTD approach. This was found for all years for which projection was carried out. The gap between both scenarios seemed to widen over time. Projected HC expenditure for acute inpatient care for the year 2028 was overestimated by ~7% when an approach was used that only accounted for the higher proportion of elderly people in a population in the future as compared to an approach that also accounted for the effect that remaining TTD had on costs.

Discussion:
The two approaches of projecting HC expenditure demonstrated that costs did not rise as quickly if factors such as TTD and increasing longevity and also the postponement of diseases into older ages were accounted for. These findings are in line with previous research, although at the lower end of the scale. This might be explained with the selection of the sample and the HC system that had been analysed. It could be argued that there are national differences in the extent of care that is delivered to people close to death. If this was the case this would have an impact on cost estimates that were obtained stratified by TTD and would subsequently have affected the result of HC expenditure projections under a TTD approach. Other factors that might impact on future costs, such as advances in medical technology could not be considered in this analysis, but are expected to be a main contributor to increasing costs over time.
USING ADMINISTRATIVE DATABASES TO ESTIMATE HEALTH CARE COSTS FROM ADVERSE DRUG EFFECTS: THE CASE OF PROSTATE CANCER

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Background:
Adverse events are often estimated suboptimally in cost-effectiveness analyses.

Objectives:
To refine methods to estimate the costs of adverse events using databases.

Methods:
Using the Ontario Cancer Registry and health care administrative databases we selected all prostate cancer patients in Ontario who started >90 days of androgen deprivation therapy (ADT) at age ≥66 in 1995-2005. We identified the following adverse events: myocardial infarction, acute coronary syndrome, congestive heart failure, stroke, deep vein thrombosis/pulmonary embolism, diabetes, fracture/osteoporosis. For each patient, we looked forward from start of ADT (Index date) to December 31, 2007 (or death) and looked back 3 years before Index date. We determined the date of the first event pre-ADT and post-ADT. Each patient’s post-ADT observation time was divided into Phases: ADT (no side effects), ADT_SE (occurrence of side effect), and Final (death and <180 days before). Patients who experienced more than one side effect entered the “Multiple” phase. We estimated mean total costs (hospitalizations, ambulatory care, prescription drugs, radiation, chemotherapy, physician services, home care, long-term care) for each patient in each phase. We divided total costs by the patient’s time in the phase and standardized to a cost per 30 patient-days (2009 Canadian dollars).

Results:
The cohort consisted of 26,809 men; 49% (N=13,093) had ≥1 side effect, and 4,292 patients had time in the Multiple phase. Diabetes was the most frequent (N=4,476) and longest phase (mean = 1,158 days). Congestive heart failure was the shortest at 730 days (N=2,005). The least costly phase was ADT (mean cost per 30 patient-days = $844). Side effect phase costs ranged from $939 per 30 patient-days (Diabetes) to $2,189 (Stroke). The most costly phase was Final ($4,408 per 30 patient-days). With few exceptions, costs increased with comorbidity at Index date, and age at start of the phase. However, the mean cost per 30 patient-days in the Final phase was $4,772 for patients 66-74 years, and $4,319 for patients ≥75, reflecting less intense end-of-life intervention for the oldest patients.

Conclusions:
It is possible and useful to estimate adverse event costs (per 30 days and overall) using administrative data and a phase-based approach.
CORRECTING FOR MULTIPLE FUTURE COHORTS WHEN APPLYING DIFFERENTIAL DISCOUNTING OF COSTS AND HEALTH EFFECTS

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Background:
Differential discounting of costs and health effects can lead to a problem of comparability between cost-effectiveness analyses (CEAs). Interventions modelled with more future recipient cohorts will have more favourable cost-effectiveness estimates than those with fewer cohorts when differential discounting is applied, all else equal. Consequently, it can be misleading to compare the results of CEAs that model different numbers of future cohorts.

Objective:
To show how to make fair comparisons of cost-effectiveness between models with different numbers of future cohorts when differential discounting is applied.

Methods:
We compare the cost-effectiveness estimate of vaccination against human papillomavirus (HPV) infection in the UK from a published CEA featuring 101 recipient cohorts over 101 years to that of a hypothetical intervention with cost-effectiveness equal to the lower bound of the current UK cost-effectiveness threshold range of £20,000 - £30,000 per quality adjusted life year (QALY) gained. Differential discounting rates of 3.5 & 1.5% are applied to costs and health effects respectively. The cost-effectiveness of the hypothetical intervention is considered when implemented with the same number of future cohorts as the HPV model. The cost-effectiveness of the hypothetical intervention implemented over an equal number of future cohorts serves as an adjusted threshold that accounts for the number of future recipient cohorts. An alternative adjustment is also described, whereby rather than adjusting the threshold, we adjust the cost-effectiveness estimate of the intervention itself for the number of future cohorts. This is achieved by dividing the intervention’s cost-effectiveness estimate by the ratio of the adjusted threshold to the current threshold.

Results:
The resulting adjusted cost-effectiveness estimate permits direct comparisons to other interventions and the current threshold. The unadjusted ICER of HPV vaccination is £7,400/ QALY, while adjusting for the number of future cohorts gives an ICER of £13,300/QALY. Although adjusting for the number of future recipient cohorts results in a less favourable ICER, it remains comfortably below the current UK threshold range.

Conclusions:
A simple correction for the number of future recipient cohorts provides a fairer basis for comparison between interventions when differential discounting is used.
Background:
Any approach for handling missing cost data within cost-effectiveness analyses must face a number of challenges. Data with a skewed distribution is a common problem. This is often transformed before imputation. This can result in unlikely values being imputed. Multiple Imputation by Chained Equations (MICE) potentially offers a way of dealing with non-normality of the data using predictive mean matching and imputes only multiples of resource units.

Objective:
To examine how well multiple imputation by chained equations and predictive mean matching perform when faced with the challenges associated with imputing missing cost data.

Methods:
The investigation was carried out on a cost sub-study (115 patients) of a clinical trial (351 patients). This trial compared the effect of chemotherapy to palliative care in treating non-small cell lung cancer. The trial was randomised, prospective and multicentre.
33 patients had missing data. Imputation on incomplete cases was carried out using Multiple Imputation by Chained Equations with predictive mean matching. Five imputations were used. This was performed by Stata’s ICE package. All analyses were carried out in Stata 11, R (2.10.1) and Microsoft Excel 2007. Seven different models were tested.
The investigation took the incremental net-benefit approach. The investigation used cost-effectiveness planes and cost-effectiveness acceptability curves to investigate the cost-effectiveness of chemotherapy compared to palliative care after the imputations had been carried out.

Results:
The cost-effectiveness conclusions showed that chemotherapy was more costly but more effective. The primary model showed that chemotherapy has a higher probability of being the cost-effective treatment option when a decision maker is willing to pay £5000 or more for an extra year of life.
When variables were transformed before imputation, hospice cost values of £42,848 to £1,505,146 were imputed.

Conclusions:
The results showed that transforming variables can result in large and unrealistic imputations. MICE using predictive mean matching does not rely on transformations, and also avoids the issue of negative costs being imputed. Predictive mean matching also offers the advantage of only imputing multiples of resource use. Predictive mean matching is limited to continuous variables and there are questions as to the validity of the logistic regression procedure.
COST-EFFECTIVENESS OF AN AWARENESS CAMPAIGN FOR COLORECTAL CANCER
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Colorectal cancer (CRC) is the third most common cancer in the England. Early detection is associated with improved chances of survival. In England the NHS bowel cancer screening programme obtains uptake rates of between 50 and 60%; however the majority of CRC is detected through symptomatic/chance presentation rather than via screening. A pilot awareness campaign was run in the East and South West of England in early 2011. The campaign aimed to increase awareness of the symptoms associated with CRC and to encourage persons with symptoms to visit their GP. The objective of this study was to estimate the cost-effectiveness of an early awareness campaign for CRC in England.

An existing model of CRC screening in England was updated and refined to allow the cost and effectiveness of an early awareness campaign to be evaluated. The original model consists of two components: the first describes the natural history of CRC by representing the development of adenomas and their progression to CRC, and the second describes the effect of screening and surveillance. Data on the increase in GP appointments/referrals associated with suspected lower GI cancer, colorectal cancer incidence, and screening uptake associated with the pilot campaign was obtained. These data were used to model the impact of the campaign. The analysis captures the direct costs of the campaign, the costs any additional GP consultations/appointments in secondary care resulting from the campaign, and benefits of the campaign in the form of earlier diagnosis and improved screening uptake.

Several interventions were evaluated including: a one-off campaign; an annual awareness campaign; a biennial awareness campaign. The addition of an annual awareness campaign to an existing screening programme has the potential to provide additional benefits via earlier symptomatic presentation and increased uptake at screening. Detailed results will be presented. To fully understand the potential benefits of such campaigns further research into the duration of the impact of a campaign, and the cumulative effect of a repeated campaign is required.
SURGEON VERSUS GENERAL PRACTITIONER ORGANISED FOLLOW-UP AFTER CURATIVE RESECTION FOR COLON CANCER, QUALITY OF LIFE AND COST EFFECTIVENESS. AN INTERIM ANALYSES OF A RANDOMISED CONTROLLED TRIAL


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Background:
Follow-up after curative resection of colon cancer improve overall 5-year survival with 5-10%. National and international most patients are followed in a hospital setting. To clarify controversies regarding follow-up setting and quality of life (QoL), cost-effectiveness (C/E) and serious clinical events (SCE), a randomised controlled trial were initiated.

Interventions:
Follow-up according to national guidelines in surgical outpatient clinics or at the community general practitioner office supported by hospital diagnostic services (chest x-ray, liver ultrasound, colonoscopy).

Participants:
78 GPs, 70 surgeons, 110 patients surgically treated.

Main outcome measures:
Primary outcome measures: C/E and QoL. Secondary outcome measures: SCE, disease free survival, consultation satisfaction and compliance. Data were summarized at 1, 3, 6, 9, 12, 15, 18, 21 and 24-month follow-up cycles and analysed by multivariate methods.

Results:
Fifty-five (50%) patients were randomised to the GP arm, 600 postoperative follow-up cycles were compared. Baseline mean age were 65.4 yrs (± 8.1), 59% were males, 26% were employed, 21% Dukes stage A, 48% Dukes B and 29% Dukes C. Eighty (72%) patients completed 24 months follow-up. There were significant increase in postoperative 1-24 month QoL (p=0.003), but no significant differences between groups: EQ-5D index score; 1 month: GP 0.75 (±0.28) vs. surgeon 0.83 (±0.16), 24 months: GP 0.89 (±0.13) vs. surgeon 0.88 (±0.16), mean difference 1-24 months: 0.013 (±0.016), p =0.4. ERTOC QLQ C-30 Global health score; 1 month: GP 68.4 (±24.5) vs. surgeon 66.4 (±28.7). 24 month: GP 82.2 (±26) vs. surgeon 84.5(±17), mean difference 1-24 months 1.76 (±4.4), p=0.44. The GP group yielded less hospital travels (232 vs. 384), but more overall health care contacts (679 vs. 472). There was similar follow-up compliance (total 468 blood samples, 250 chests x-rays, 187 liver ultrasound, 104 colonoscopies). From a societal perspective 24 month follow-up by GP cost 471 125 $ (1700
$/patient/cycle), surgeon 511 283 $ (1886 $/patient/cycle), total 982 408 $ (1637 $/patient/cycle). There were no differences in serious clinical events, 14 recurrences were detected.

**Conclusions:**
A GP organised follow-up program for patients surgically treated for colon cancer can be performed safely with increased cost-effectiveness and no deterioration in patients QoL. ClinicalTrials.gov identifier NCT00572143
CROSS-VALIDATION BETWEEN A DISCRETE-EVENT SIMULATION MODEL AND A MARKOV MODEL – FOR PERSONALIZED BREAST CANCER TREATMENT STRATEGIES

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Background:
Breast cancer is the most common malignant disease in Western women. In the ONCOTYROL research center, a decision-analytic Breast Cancer Outcomes & Policy (BCOP) model is being developed to evaluate the cost-effectiveness of the new 21-gene assay that supports personalized decisions on adjuvant chemotherapy. Model validation is essential to build confidence in the model results and to influence decision makers. Based on the new ISPOR-SMDM best practice recommendations, the process of model validation will be presented.

Methods:
The 21-gene assay was evaluated by simulating a hypothetical cohort of 50-year-old women over a lifetime time horizon, adopting a societal perspective. Main model outcomes were life-years gained, quality-adjusted life-years (QALYs) gained and costs. The major focus of the presentation is on cross validation, i.e. the comparison of modeling results between the discrete event simulation (DES) BCOP-model and the Markov model of the THETA (Toronto Health Economics and Technology Assessment) Collaborative. Therefore, the BCOP-model has been populated with the Canadian parameters of the THETA-model.

Results:
Cross validation started with comparison of model parameters related to the natural history of the disease (undiscounted life years, number of breast cancer recurrences/deaths). Thereafter, quality of life and cost outcomes were compared. The comparison included point estimates of the outcomes of the probabilistic analysis of the Markov model as well as the probabilistic run with the DES results and combination (ICERs). The absolute differences of expected life years gained for women after surgery ranged from -0.35 to 0.43 years depending on the treatment strategy for specific risk groups. For the probabilistic analysis, confidence intervals as well as distributions of model outcomes were compared.
Discussion:
The cross model validation of the BCOP-model involved several challenges: distinguishing between outcomes differences due to different modeling techniques and modeling errors, definitions for meaningful differences, and utilization of comparison techniques (mean estimates, distributions, multivariate outcomes). One of the major questions addressed by this validation is whether differences led to changes in ranking of effectiveness and whether cost-effectiveness changed.

Conclusion:
Cross model validation is a suitable approach to identify and correct modeling errors and to explain remaining differences of modeling results.
A DECISION-ANALYTIC MODEL FOR ASSESSING THE ADDED VALUE OF TRANSTHORACIC ECHOCARDIOGRAPHY IN MAKING THE DECISION TO PRESCRIBE ORAL ANTICOAGULATION MEDICATION IN PATIENTS WITH NEWLY DIAGNOSED ATRIAL FIBRILLATION

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The decision whether to prescribe oral anticoagulation medication (OACs) in patients with atrial fibrillation (AF) involves balancing competing risks. People with atrial fibrillation have an increased risk of stroke relative to the general population and age and gender matched controls. OACs reduce the risk of stroke, but as a side effect increase the risk of major bleeding events, including severe intracranial haemorrhages that may cause disablement or death. In AF patients with the lowest risk of stroke the risk and consequences of side effects from OACs outweigh the benefits, and so OACs should not be prescribed. In all other AF patients the converse is true and so OACs should be prescribed. Currently clinical prediction rules, such as the CHADS\textsubscript{2} and CHA\textsubscript{2}DS\textsubscript{2}-VASc score, are used to make this clinical decision. These rules use existing patient information, such as age and gender, to assign patients a stroke risk score. Patients with a risk score at or above a certain threshold are recommended OACs. We developed a discrete event simulation (DES) decision-analytic model to assess the clinical consequences of performing a transthoracic echocardiogram (TTE) in all newly diagnosed AF patients in this context. TTE is a relatively simple test that could help to identify a subgroup of patients who, though predicted as low risk using CHADS\textsubscript{2} and CHA\textsubscript{2}DS\textsubscript{2}-VASc scores, are in fact at a substantially higher risk of stroke due to the presence of structural abnormalities within the heart, and so should nonetheless receive OACs. However, with less than perfect specificity, using TTE to help make the decision to prescribe OACs will also lead to more patients who will not benefit from OACs being prescribed it too, increasing the cost of medication for the NHS and the risk of bleeding events for the patient. Our model attempts to determine whether, on balance, using TTE for all newly diagnosed AF patients leads to better clinical outcomes, and if so whether this improvement in outcomes is cost-effective using standard NICE decision thresholds.

We find that using TTE appears cost effective when using the CHADS\textsubscript{2} instrument but not CHA\textsubscript{2}DS\textsubscript{2}-VASc. Our results also appear to depend strongly on which OAC is used, as the choice of OAC affects other key parameters in the model.
SCOTTISH CVD POLICY MODEL: RAPID EVALUATION OF CVD PRIMARY PREVENTION INITIATIVES
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The ultimate aims of prevention are to avoid premature mortality, morbidity and to reduce health inequalities. However, there is a lack of effectiveness and cost effectiveness evidence underpinning alternative interventions. We also lack a single, comprehensive, model that can help clinicians and policymakers make decisions consistently. The overall objective was to create a Scottish CVD Policy Model which can predict quality adjusted life expectancy (QALYs) and total lifetime hospitalisation costs. In application, the model can be used to inform both targeted and population approaches, and for individual and multi-factorial interventions.

Methods:
We had access to the longitudinal dataset used to create the ASSIGN 10-year risk score. This screened over 16,000 asymptomatic individuals for nine CVD risk factors (including deprivation status) who were then linked to all hospitalisations (CVD and non-CVD) and death records. Within a competing risk analysis, we estimated lifetime CVD risk and life expectancy for individual profiles. We then quality adjusted life expectancy predictions, by estimating population norms, the utility impact of non-fatal events, and cost impact from hospitalisations.

We illustrate how the model can be used to inform clinical and policy decision making. First, we assess the implications if patients were prioritised for intervention based upon potential benefit rather than 10-year risk scores. Second, we simulate the impact of reducing salt and trans-fats by 5% across the entire population.

Results:
If clinician’s prioritised individuals for treatment on the basis of potential benefit then there would a switch in prioritisation towards younger patients, females, more deprived groups and smokers. A reduction in salt and trans-fats would result in respective gains across the population of over 141,000 and 368,000 discounted QALYs, with the greatest gains in deprived communities. CVD primary prevention increases hospital costs given prolonged life expectancy, however once costs are also discounted primary prevention becomes cost saving.

Conclusions:
The CVD Policy Model can be used as a clinical tool to prioritise patients, an evaluative tool to assess the impact of (targeted and population-wide) interventions and as a simulation tool to conduct “what-if” analysis to inform the development of new initiatives.
A DECISION ANALYTIC MODELING FRAMEWORK TO PERSONALIZE MAMMOGRAPHY SCREENING

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Introduction:
Breast cancer is the most common non-skin cancer and the second leading cause of cancer-deaths in American women. Although mammography is cost-effective for breast cancer diagnosis, questions remain about whom to screen and how frequently. The possible screening policies are innumerable and difficult to directly assess due to many personal risk factors. Our objective is to develop an analytical modeling framework to personalize mammography-screening policy for a woman's lifetime based on the prior screening history and personal risk characteristics of women.

Methods:
We formulate a finite-horizon Partially Observable Markov Decision Process (POMDP) model that maximizes a woman’s quality-adjusted life-years (QALYs). POMDPs are used to optimize sequential decision making problems in which the information regarding the true disease state is not known with certainty. Instead, the decision maker makes observations (such as screening test results) to estimate the true disease state. We use the University of Wisconsin Breast Cancer Simulation model to estimate the parameters of our POMDP such as transition probabilities and reward functions. Our POMDP model incorporates unobservable disease progression, two methods of detection (self or screen), and mammography accuracy. We solve this POMDP to find the optimal personalized screening policy.

Results:
A woman’s optimal screening policy follows a threshold structure where the optimal decision is to screen if the current breast cancer risk is greater than a certain threshold risk, and not to screen, otherwise. The threshold risk for screening increases with age. Our POMDP model provides individualized fully dynamic screening policies. For example, consider a 40-year-old woman whose insitu and invasive cancer risks are estimated as 0.0016 and 0.0035, respectively. Then, using our base-case utility estimates, we find that the optimal action for this woman is to undergo mammography at age 40. Assuming that the outcome of this and the following mammograms are all negative and no self-detection occurs, this patient should undergo mammography exams at ages 40, 44, 48, 51, 55, 58, 62, 66, and 72. In addition, we find that a woman's prior screening history may significantly influence the estimated risk of breast cancer, and in turn might change the screening recommendations. We further find that our proposed personalized screening schedules outperform the existing guidelines with respect to the total expected QALYs, while significantly decreasing the number of mammograms. For instance, for an average-risk patient, the optimal screening strategy reduces the expected number of mammograms by more
than 20, reduces the number of false-positive mammograms at least by half, and increases the total expected QALYs by 1 month per woman, compared to annual screening between ages 40 and 74.

**Conclusion:**
Unlike many prior studies, our POMDP model considering a woman’s breast cancer risk factors and prior screening history provides optimal screening policies for individual patients.
THE IMPACT OF NARRATIVE REPORTS ABOUT VACCINE ADVERSE EFFECTS ON VACCINATION RISK PERCEPTION: A SIMULATION OF AN ONLINE PATIENT NETWORK

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A growing number of people uses the Internet to obtain health information. A recent trend is the emergence of patient networks, which are comparable to social networks. Such networks typically provide individuals the opportunity to share experiences regarding medications and commonly provide aggregated data (statistics) of such user generated content. However, due to the self-selection of users this type of data might not be representative and is potentially prone to bias.

The goal of this contribution was to quantitatively examine if and how reading narrative reports about vaccine adverse events (VAE) and/or the statistical summary of this information affects vaccination decisions. Previous work suggests that narratives impact risk perceptions and behavioral intentions despite concurrently presented more reliable statistical information [e.g. Betsch C, Ulshöfer C, Renkewitz F, Betsch T. The influence of narrative vs. statistical information on perceiving vaccination risks. Med Decis Making. 2011;31(5):742-753].

In an online study we provided participants with a representative baseline statistic as well as patients’ reports about the occurrence of VAE following immunization against a hypothetical disease. For the latter we adopted the design of a popular patient network (patientslikeme.com) and varied the relative frequency of cases reporting VAE (5, 35 & 85%) as well as the type of information (narratives only, aggregated data only & both) between subjects. Further, we tested if a disclaimer indicating a potential bias (vs. a control disclaimer) would reduce the impact of narrative evidence.

Results indicated that a higher relative frequency of cases reporting VAE decreased the intention to get vaccinated. This relation was mediated by increased risk perception. The type of information moderated the contents’ impact: summary statistics had the smallest impact, while narrative information was more influential and the presence of both types of information had the greatest impact on risk perception. Individuals who received the bias-awareness disclaimer were less influenced by the patient network.

In conclusion, narrative evidence as well as aggregated user data, which are typically provided by online patient networks, can exert considerable influence on vaccination decisions. A disclaimer, indicating the potential bias of such information may reduce that influence.
Consumer-targeted health messages often list "risk factors" that may increase one's likelihood of experiencing a given disease. For example, messages promoting colorectal cancer (CRC) screening often mention that CRC risk is greater among African Americans, smokers, and those with a family history of cancer. Such "risk-factor" statements are intended to help patients better understand disease risks, and to increase vigilance among individuals who are especially vulnerable. However, this study examines whether such statements have an unintended effect: creating a false sense of security among patients who do not possess the listed risk factors. For example, upon hearing that colon-cancer risk is highest among people with a family history of this disease, do patients without any such family history infer that they are "not in the risk group" and forego screening, even though most colon cancers occur among individuals with no family history? To examine this phenomenon, we conducted two experiments.

In the first experiment, young adults were shown risk information concerning a hypothetical disease and vaccination. Participants were randomly assigned to varying information concerning both the disease's absolute incidence within their own demographic group (1%, 20% or no information), and risk-factor statements indicating how disease incidence varied across demographic groups. Results revealed that participants' perceived disease susceptibility and vaccination intentions were not influenced by their own group's absolute incidence rate (1% vs. 20%), but were strongly influenced by comparative "risk-factor" information. Interestingly, subjects were much more likely to be re-assured by favorable risk-factor information (indicating they were at lower risk than other groups) than to be alarmed by unfavorable risk-factor information (indicating they were at higher risk). In fact, there was a significant boomerang effect, in which individuals given reassuring risk-factor information had significantly lower vaccination intentions than control subjects given no risk-factor information. This effect was especially strong among women, and individuals with low prevention orientation. A second experiment involving an actual disease (meningitis) found a similar boomerang effect: giving university students comparative information on meningitis risk factors decreased their intention to get vaccinated.

The presentation will discuss the implications of these findings for risk communication practice and research.
THE EXPECTATION GAP: DO PATIENTS EXPECT TOO MUCH FROM THEIR SURGEONS?

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Background:
Indicators of performance as well as patient-related endpoints are of increasing importance in the field of healthcare evaluation. When subjective performance indicators for trauma surgery outcomes are considered, it is important to gain insights into the process of expectation formation for both patients and surgeons.

Methods:
In total, 201 patients with ankle or pilon fractures were recruited at five clinics in North America and Brazil and followed for a period of twelve months. Expectations were repeatedly measured for both patient and surgeons over a period of six months after surgery by means of a validated 10-items questionnaire to assess expectations with regard to surgery outcome at one year follow-up.

Results:
Surgeons were found to have very stable expectations over time while patients were found to have fluctuating expectation levels with regard to surgical outcome throughout the course of treatment. Before surgery, average patient expectations exceeded surgeon expectations by 5 percentage points. Moreover, average patient expectations were found to rise slightly over time and decrease afterward. Surgeons’ and patients’ expectations did not meet in the first six months following surgery. Factors found to be strongly associated with this patient/surgeon expectation difference post-surgery included fracture location and country. Patient and surgeon expectations were found to diverge considerably if the patient experienced a “pilon” type fracture, with such patients having expectations that exceed that of their surgeons by 10 points on a scale from 0 to 40 (p<0.001). While patients in Brazil and Canada had pre-surgery expectations similar to those held by their surgeons, in the USA, patients’ expectations exceed those of their surgeons by 6 points on average (p<0.001).

Conclusions:
Patients and surgeons can have different expectations in terms of the results that can be achieved after trauma surgery. Measured at the time of trauma surgery, an expectation gap exists which persists over time. Changes to the patient-surgeon communication process may lessen these differences and therefore result in improved overall satisfaction.
SURVIVAL CURVE CONVERGENCES AND CROSSINGS: HOW FREQUENT ARE THEY IN MEDICAL RESEARCH?

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Background:
Survival analysis and similar types of time-to-event analysis are frequently used to study the impact of two or more exposures/interventions on survival. When data from survival analysis are summarized in meta analysis, they are usually based on the number of events at the end of the study. This will bias the estimates of differences in survival unless the relative hazards are relatively constant (the proportional hazards assumption). The aim of this study was to explore this assumption by estimating the frequency of convergences and crossings of survival curves.

Methods:
We reviewed all publications in Annals of Internal Medicine (AIM), British Medical Journal (BMJ), Journal of the American Medical Association (JAMA), New England Journal of Medicine (NEJM) and The Lancet for 2007 and identified studies that included survival graphs. We extracted the following data from included studies: type of disease, type of exposure, type of end-point, sample size and number of events, maximum follow-up time, number and timing of survival curve convergences and crossings, and whether Cox regression and log-rank tests had been performed. Where more than one survival analysis was presented, we analyzed the figure concerning the primary endpoint. If more than two patient groups were presented, we analyzed the two groups with the highest hazard rates.

Results:
Among 175 included studies, 35% had survival curve convergences and 47% crossings. 38% of the crossings occurred later than halfway through the study (40% for convergences). The proportion of crossings by type of disease was 46% for cardiovascular disease, 38% for cancer and 53% for other diseases. Among studies with survival curve crossings, Cox regression was performed in 66% and logrank-test in 70% of the studies. Only 31% of all the studies reported testing for proportional hazards when Cox regression had been employed.

Conclusion:
Survival curve convergences and crossings are common in medical research. Effectiveness estimates based on end of study results will likely be biased unless convergences and crossings are accounted for, and this bias will carry over to meta analyses of individual studies. Researchers frequently employ Cox modeling when the proportional hazard assumption is not met or use log rank tests when other test would be more appropriate.
COST-EFFECTIVENESS AND CLINICAL EFFECTIVENESS OF CATHETER-BASED RENAL DENERVATION FOR RESISTANT HYPERTENSION

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Purpose:
To estimate the long-term clinical and cost-effectiveness of catheter-based renal denervation (RDN) for resistant hypertension.

Methods:
A 34-state Markov model with a one-month cycle length was populated with multivariate equations (Framingham, PROCAM) for risk of cardiovascular events and other sources from the published literature. The base case was a population of 58 year-old patients with a baseline systolic blood pressure (SBP) of 178 mmHg resistant to 3+ drugs, 43% female, 34% diabetic, 16% current smokers without clinical cardiovascular or end-stage renal disease (ESRD). We compared costs and clinical consequences of RDN associated with a 32 mmHg reduction to standard of care alone (SoC). Time horizons computed were ten years or lifetime. The perspective was societal. Discounting was 3% per year. We conducted cross-checks with other cardiovascular models and clinical data as well as structural and other sensitivity analyses.

Results:
RDN substantially reduced event probabilities (ten-year/lifetime relative risks: stroke 0.70/0.83; MI 0.68/0.85; all CHD 0.78/0.90; HF 0.79/0.92; ESRD 0.72/0.81). Median survival was 18.4 (RDN) versus 17.1 years (SoC). The discounted ICER was $3,071/QALY. Findings were relatively insensitive to variations in input parameters except SBP reduction, baseline SBP, and structural changes, e.g., effect duration and repeat procedures. The 95% credible interval for ICER was cost-saving to $31,460/QALY.

Conclusions:
Catheter-based renal denervation is a cost-effective strategy for reducing cardiovascular morbidity and mortality in resistant hypertension.
DEVELOPMENT OF A 'LOAD INDEX MODEL' TO FACILITATE DECISION-MAKING IN CASUALTY EVACUATION PROCESS

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Introduction:
Emergencies are often characterized by massive casualty evacuation to hospitals. Evacuation destinations should be determined based on severity of injuries, duration and means of evacuation, and available hospital resources, in order to avoid overloading a hospital.

Goal:
To develop a tool for comparative measurement of hospitals' emergency congestion levels, to facilitate decision-making regarding casualty evacuation to and between hospitals.

Methods:
Casualty treatment sites, characteristics that affect surge capacity, bottlenecks and their impact were defined through literature review and interview of 20 content experts from the fields of hospital management, Ministry of Health and emergency management. Consequently, a 'load index model' was developed and evaluated through a Delphi process. Consensus was defined as agreement higher than 75%. The relative congestion level of each hospital was determined by calculating its load index value, divided by the highest index value presented among the hospitals. The 'load index model' was tested during a series of simulation exercises in which senior expert teams participated in decision-making regarding casualty evacuation during emergency situations.

Results:
55 out of 100 content experts responded to the Delphi process. Consensus higher than 75% was achieved regarding five elements: Operating Rooms (OR) occupancy in proportion to OR surge capacity; admittance of severe/moderate casualties in trauma departments during the last 24 hours in proportion to number of physicians; number of severe and moderate patients in the surgical departments in proportion to number of physicians in the surgical division; admittance of severe/moderate casualties in trauma departments during the last 24 hours in proportion to intensive care beds; and number of severe/moderate patients hospitalized in the surgical division in proportion to intensive care physicians. Significant variance was found in the simulation exercise among the expert teams' decisions regarding casualty evacuation destinations. The variance decreased following introduction of the data from the 'load index model'.

Conclusions:
In order to facilitate casualty evacuation processes in emergency situations, there is a need for decision-support tools. The developed "load index model" is useful in defining casualty evacuation destinations. Additional tests should be conducted in order to verify sensitivity and efficiency of the model and its implementation.
Introduction:
At the time of the introduction of the two vaccines against human papillomavirus (HPV) types 16 and 18 and types 6, 11, 16 and 18, respectively, focus was primarily on cervical cancer (and precancerous lesions) and genital warts (GW). However, HPV is also attributable to 40%-85% of all cases of anal, penile, vaginal and vulvar cancer (anogenital cancers) and among these cases 74%-93% are attributable to HPV 16 & 18. It has also been demonstrated that 16-28 % of certain head and neck cancers might be attributable to HPV, 86-100% being attributable to HPV 16 or 18.

Some cost-effectiveness studies only include the HPV-vaccines potential protection against anogenital and some head and neck cancers. The objective of this study is to assess the impact of including protection against all HPV-related cancers on the cost-effectiveness of a female vaccination program in a Danish setting.

Methods:
A previously developed model was extended to included non-cervical HPV-related cancers (Olsen & Jepsen, 2010). A strategy of vaccinating 12 years old girls in addition to the screening program was compared to a strategy of screening only. The analysis was performed in two phases: First, simulations in an agent-based transmission model that describes the HPV transmission without and with HPV vaccination, was performed. Second, an analysis of the incremental costs and effects was performed. The results of prevalence estimates of HPV, genital warts, cervical intraepithelial neoplasia, cervical cancer, anogenital cancers and head and neck cancers in the model simulations before and after introduction of HPV vaccination were extrapolated to the Danish population figures. Incremental costs and effects were then estimated. Future costs and effects were discounted at 3%.

Results:
Given a yearly vaccination rate of 85%, the incremental cost effectiveness ratio (ICER) was estimated at 20,265 € per life year gained when only cervical cancers were included, it was valued at 8,093 € per life year gained when genital warts were also considered and at 5,431 € per life year gained when the vaccine’s protection against anogenital cancers were incorporated in the model simulations. If the protection against head and neck cancer was also accounted for, the incremental cost effectiveness ratio was estimated at 3,832 € per life year gained.

Conclusion:
Inclusion of the HPV-vaccines protection against anogenital cancers improves the cost-effectiveness of HPV vaccination in Denmark. In assessment of cost-effectiveness of the HPV-vaccines all protective characteristics of the vaccines should be included in the analyses no to underestimate the value of HPV vaccination.

References:
HIERARCHICAL BAYESIAN MODELS FOR THE SPREAD OF INFECTIOUS DISEASES AS A TOOL FOR MEDICAL DECISION MAKING

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Modeling how infectious diseases spread is of great value for decision makers and the public as it provides a means of short-term predictions on how the diseases will affect local communities, and a statistically sound basis on which to decide upon appropriate measures to be taken. Accurate predictions enable the health service to plan and allocate resources ahead in time.

There has been a large amount of research on modeling how infectious diseases spread, but they are often hindered by computational complexity and poor performance. Recently efficient numerical routines have emerged using Gaussian Markov random fields as a model for geographical structure. By utilizing the Integrated Nested Laplace Approximation for hierarchical Bayesian models high computational speed and improved statistical properties are obtained compared to conventional Markov Chain Monte Carlo methods\textsuperscript{1}.

Data from the microbiology laboratory at the University Hospital of North Norway is a useful proxy for cases of infectious diseases in the region. We used data for 2002–today to model on the municipality level how certain infectious diseases such as Influenza A and Pertussis spread in this sparsely populated area. We show to predict estimates and probability quantiles one period ahead by fitting the model to all previous time points. The prediction results show good fits for these diseases in the most populated municipalities, while very sparsely populated areas provide less coherent results. Nevertheless, the modeling provides valuable insight for providing added value to a real-time disease surveillance system.

Though the current results were obtained using laboratory data, we will integrate the modeling into the Snow agent system (http://snow.cs.uit.no), which will function as a syndromic surveillance system for general practitioners, thus increasing the fidelity of the input data and modeling.

MEASLES IMMUNIZATION IN INDIA: THE USE OF INFECTIOUS DISEASE MODELS TO INFORM POLICY IN A DEVELOPING COUNTRY

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Background:
India has the highest burden of measles amounting to about 80,000 deaths in under-five children annually. Measles immunization was introduced into India’s Universal Immunization Program in the 1980s, providing routinely a single dose of measles-containing vaccine (MCV1). India’s distribution of measles burden is not homogenous, being concentrated in the states/districts with the lowest vaccine coverage. In 2008, India’s Ministry of Health decided that a second dose of measles vaccine (MCV2) be delivered through routine immunization programmes in states with more than 80% MCV1 coverage and through periodic supplemental immunization activities (SIAs) in states with less than 80% MCV1 coverage. The SIAs target 135 million children aged 9 months-10 years in 14 states between 2010 and 2012. However, the long-term impact of SIAs in each state needs to be assessed to inform planning around measles control activities.

Methods:
We use mathematical modeling to assess the impact of the SIAs on the burden of measles at the Indian state/district level. We develop a deterministic compartmental model of measles transmission among children aged 9 months-10 years, which distinctly incorporates MCV1 and MCV2 immunizations, at the district/state levels. We use area- and age-specific data on measles incidence and mortality, coverage of MCV1 and SIA/MCV2, population birth and deaths rates to fit the parameter inputs of the model. The outcomes of interest are measles incidence and mortality, and inter-SIA time period necessary to achieve measles control at the state/district level.

Results:
We identify Indian states/districts for which SIAs can have the greatest impact on reducing measles incidence and mortality. Furthermore, we identify the minimum number of years between SIAs which is expected to lead to consistent measles control at the Indian national/state/district levels.

Conclusions:
Prior routine immunization level (MCV1) and SIA/MCV2 coverage are the main determinants of the impact of SIAs on measles incidence and mortality. The impact is larger and the required time period between two consecutive SIAs shorter when routine coverage of MCV1 is lower. Such a hierarchical (national/state/district) level analysis enables Indian policy makers to make informed decisions about the contextual and timely implementation of SIAs and measles control in India.
VACCINATIONS STRATEGIES ON THE TRANSMISSION OF THE HEPATITIS B VIRUS IN NORWAY: DYNAMIC MODELING APPROACH

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Background:
Within the native Norwegian population, hepatitis B is a horizontally transmitted disease with limited distribution, and an often chronic course. Current hepatitis B virus prevention policies in Norway include screening of pregnant women belonging to risk groups and vaccination of children of parents from high and medium endemic countries. The aim of this study is to evaluate the effectiveness of this hepatitis B virus (HBV) vaccination program in Norway. In addition, the effectiveness of universal vaccination of infants and adolescents has been considered.

Methods:
A dynamic model to estimate future incidence of hepatitis B infection in population was employed. The model has been used previously by Kretzschmar et al. (Epidemiol. Infect. (2002), 128, 229); (Vaccine (2009), 27, 1254-1260). This model describes horizontal, vertical, and sexual transmission of HBV. The population model is structured by sex, age and sexual activity classes. An infected individual goes through a latent stage in which the individual is not yet infectious, then goes on to develop acute infection, after which the individual becomes a carrier or immune. If there is vaccination an individual can move into the vaccinated class. Also, the model incorporates immigration into the population and the age-dependent probability of becoming a carrier after infection with HBV.

Results:
The effects of vaccination on incidence and on the prevalence of the HBV for the various strategies have been modeled. We see that universal vaccination of newborns or adolescents has a strong impact on incidence. The vaccination of immigrant children has a strong impact on the number of new carriers due to the horizontal transmission, but it only reaches full effect on incidence after 20 years. We have seen that catch-up vaccination campaigns move the effects of vaccination forward in time.

Conclusions:
The incidence in the model is higher than the incidence of notified acute infections in Norway. We do know that a large fraction of infections acquired during childhood remain subclinical, therefore they are not diagnosed and not notified. Therefore, notification data does not reflect the amount of infections. Universal vaccination has a great impact in reducing the incidence of hepatitis B; vaccinations of adolescents show an effect almost 9 years earlier and could be more effective. In contrast vaccination of immigrant children shows only a limited benefit.
EFFICIENCY, EQUITY AND AUTONOMY IN VACCINATION POLICY: AN EXPLORATION OF PUBLIC PREFERENCES

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Objectives:
One of the difficult ethical tradeoffs in vaccination policy is the one between claims of efficiency, equity and respect for individual autonomy. Cost-effective vaccination programs may imply selective immunization of population subgroups (e.g. HCW) plus vaccine-uptake stimulating measures (e.g. legal compulsion). From an equity or an autonomy perspective these policies are controversial. Those subgroups that are targeted might consider it discriminative that only they have to carry the burden of vaccination (i.e. adverse effects, or potential stigmatization) or untargeted groups might find selective vaccination an unfair inequality in access to basic medical care. Measures that increase coverage in a vaccine-reluctant population raise autonomy issues. A just vaccination policy therefore requires a careful balance between on the one hand rightful ambitions to maximize public health and on the other hand due limitations in terms of other legitimate social goals like fostering equality among population subgroups or protecting individual liberty. We explored the general public's opinion on these value tradeoffs in c.

Methods:
We executed a survey in a representative sample of the Flemish population (N= 1049) in which we investigated public support for potentially cost-effective vaccination policy options that however imply sacrifices in terms of equality or autonomy. We investigate for three types of disease whether using uptake incentives (legal compulsion, accountability or rewarding) either for the entire population or only for a specific target group (children, HCW, travelers or immigrants) is acceptable when that implies substantial cost-savings or public health benefits. We also added a large list of background questions among which the usual ones but also the EQ-5D, the BMI and a psychological construct that measures the respondents social value orientation.

Results:
We found that (1) equity aspects of vaccination programs are at least equally important as efficiency considerations (2) the use of effective vaccine-uptake incentives is generally well-supported when it applies to the entire population (3) that various measures targeting travelers are well-supported while those targeting immigrants are not. And (4) that one of the most influential variables to predict an individual's attitude to vaccination and preference for vaccination policy is his/her social value orientation.
PUBLIC VOICE IN HEALTH SERVICE INNOVATION INVESTMENT DECISIONS: A DISCRETE CHOICE EXPERIMENT

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Background:
Innovations – new ideas, practices or objects – come in various guises in healthcare. However, in systems where the number of innovations that could be implemented outstrips scarce resources, policy makers need to decide which innovations to invest in. Alongside economic criteria, there is increasing pressure on policy makers to incorporate the views of the public in priority setting and investment decisions. Previous attempts at incorporating public opinion on National Health Service (NHS) resource allocation have often been small scale, inefficient, and limited in scope. We present an approach that seeks to increase the scale and scope of public involvement and increase the efficiency of establishing public preferences by generating research findings that can be ‘reused’ in the future.

Methodology:
Discrete Choice Experiment (DCE), a form of conjoint analysis, was used. We contacted 4000 people by post and email in West Yorkshire, UK in 2011. Within DCE, participants were asked to choose between alternative innovation options that they thought the NHS should invest the most in. Innovations differed in terms of six characteristics: target population, target age group, implementation time, how certain we are that it will work, the potential health benefits, and the cost to the taxpayer. The choice data was then analysed by Latent Class models to address the unobserved heterogeneity in consumers’ preferences. This is the first such study to address consumer heterogeneity in priority-setting context.

Results:
Reassuringly the public preferred innovations that are “scientifically” proven, have clear health benefits, are quick to implement, and are relatively cheap. More intriguingly three distinct groups emerged: type 1 (57%) is relatively more health gain oriented, less sensitive to the cost of innovations, and has the highest willingness to pay (WTP) for innovations targeting people with cancer. Type 2 (25%) disliked spending on ‘unpopular’ conditions (drug addiction or obesity) and preferred to target adults. A smaller group, Type-3 (18%), on the other hand, is more accepting of ‘unpopular’ conditions, and believes that decisions on the prioritisation of innovation options should not be based on the age and the implementation time. We also found some differences in preferences with respect to socio-economic characteristics of the respondents.

Implications:
Discrete choice approaches can help policy makers, those designing innovations, and decision-makers at the NHS make more of the public’s preferences on NHS innovation investment choices.
NO PURE TIME PREFERENCE IN NORWEGIAN SOCIETAL DECISION MAKERS

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It is common in economic evaluation of health care to discount future health benefits at the same rate as future costs. There is increasing agreement in the literature that equal discounting is not a logical necessity and that the appropriate discount rate for health benefits ultimately depends on societal values. We interviewed members of the Health Committee in Parliament, members of the Norwegian Council for Priority Setting in Health Care, employees at the Directorate for Health and the Norwegian Medicine Agency and a sample of students, asking them to express ordinal preferences between preventive programs with equally large and equally certain benefits that differed (only) with respect to when the benefits would occur. Median responses suggested no discrimination against programs with later benefits, i.e. zero discounting on account of time. Choices among fixed response options were supported by informal comments made during the interviews and by responses to a follow up question in terms of willingness-to-pay. The results do not exclude the possibility of discounting on grounds other than time, for instance uncertainty.
VALUING HEALTH AT THE END OF LIFE: AN EMPIRICAL STUDY OF PUBLIC PREFERENCES

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Background:
In 2009, the National Institute for Health and Clinical Excellence (NICE) issued supplementary advice to its Appraisal Committees to be taken into account when appraising life-extending, ‘end of life’ treatments. This indicated that if certain criteria are met, it may be appropriate to recommend the use of such treatments even if their reference case incremental cost-effectiveness ratios exceed the upper end of the range normally considered acceptable. However, the public consultation carried out by NICE revealed concerns that there is little scientific evidence to support the premise that society is prepared to find life-extending treatments that would not meet the cost-effectiveness criteria used for other treatments.

Objective:
This study seeks to examine whether there is public support for giving greater priority to life extending, end of life treatments than to other types of treatment.

Methods:
The survey used six scenarios to address the research question posed, each of which involved asking respondents to choose which of two hypothetical patients they would prefer to treat, assuming that the health service has enough funds to treat one but not both of them. The various scenarios were designed so as to control for age- and time-related preferences, and to examine the trade-off between giving end of life patients a life extension and an improvement in quality of life. The survey was administered using face-to-face interviews.

Results:
Interviews were completed by a sample of 50 members of the general public in England. We found some weak evidence of support for giving priority to the patient with shorter remaining life expectancy, but note that a sizeable minority of respondents expressed the opposite preference. Very few respondents expressed indifference or unwillingness to choose between the two patients.

Discussion:
Whilst the heterogeneous nature of the preference data elicited means that there cannot be described to be a ‘consensus’ set of preferences, the results suggest that the current NICE policy may be insufficient as it does not distinguish between sudden and non-sudden disease progression, and does not involve giving greater weight to quality of life-improving treatments for those at the end of life.
THE PATHOGEN- AND INCIDENCE-BASED DALY APPROACH – A METHOD TO MEASURE THE BURDEN OF INFECTIOUS DISEASES IN EUROPE

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Background:
In 2009, the European Centre for Disease Prevention and Control (ECDC) initiated the ‘Burden of Communicable Diseases in Europe (BCoDE) project which aims to generate evidence-based, robust and comparable disease burden estimates of infectious diseases in Europe.

Methods:
The metric used is the Disability-Adjusted Life Year (DALY), a measure composed of years of life lost due to premature death (YLL) and due to disability (YLD). To better represent burden caused by infectious diseases, a pathogen-based approach was used, which links incidence of infection to sequelae through outcome trees. Health outcomes were included if a causal relationship between infection and outcome exists. WHO life expectancy was used to calculate YLL. For YLD, disability weights are taken from the Global Burden of Disease (GBD) study and alternative sets or proxies. No time discounting or age-weighting was applied. Disease progression parameters are based on literature reviews and expert opinion. Country-specific incidence of infection is preferably based on notification data (average number of cases reported between 2005 and 2007) corrected for underestimation using multiplication factors. The models, implemented in Excel using @Risk, allow for explicit modelling of uncertainty in multiplication factors and conditional transition probabilities via Monte-Carlo simulations.

Results:
Using Salmonella as an illustration, the disease burden in the Netherlands (average from the years 2005-2007) is estimated at 1,209 DALYs per year (723 YLD and 486 YLL), or 7.4 DALYs per 100,000 population per year and 0.03 DALYs per infected case. The sequelae reactive arthritis and
Irritable bowel syndrome account for 54% of the total burden. The young and the elderly show a higher DALYs compared to other age groups.

**Conclusion:**
The current methodology allows for prioritisation and comparison of infectious disease burden and comparison with other health hazards.

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A MEASUREMENT OF PROSPECT THEORY’S PARAMETERS FOR LIFE YEARS
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It is increasingly being acknowledged that expected utility theory (EUT) has substantial empirical deficiencies. Prospect theory (PT) has developed as an important alternative, with more descriptive validity. Several applications of PT have recently been performed in medical decision making, but to date no quantification of PT's full function had been performed in this domain. This paper is the first to do so, by simultaneously measuring the utility function for life duration, probability weighting for both gains and losses, and a loss aversion index. An adaptation of a semi-parametric method introduced for the monetary domain is used for this measurement.

I observe a significant amount of loss aversion, comparable in size to estimates in the monetary domain. Furthermore, universal risk aversion is found, which, for gains, can be completely attributed to underweighting of probability ½. That is, the utility function for gained life years becomes close to linear. For losses, however, there is much less probability weighting, and concavity is still substantial even under PT. The latter result contrasts with the common finding in the monetary field of convex utility for losses.

It should be kept in mind that PT was originally proposed to explain choices among lotteries involving small monetary outcomes, and empirical studies reporting convex utility for losses indeed typically used such small amounts. Therefore, it is not at all clear that the use of life years, which are arguably not considered to be small, should also generate convex utility for losses.

Another explanation for concave utility for losses may be that utility of life duration is confounded with time preference; if the latter is positive, i.e., individuals give less weight to the future, it will cause utility of life duration to be more concave, and, hence, may be erroneously interpreted as more risk averse behavior. Surprisingly, though, the degree of implied time preference is higher for losses than for gains; whereas, empirical evidence on time preference often reports the opposite. On the other hand, perhaps people consider the total time frame and discount future years hyperbolically, another established empirical finding.

The results suggest that the classic quality-adjusted life years (QALY) model is indeed not valid if EUT is assumed, justifying the use of non-EUT QALY models. This first attempt to quantify its entire function seems promising, but more research is required to refine estimation methods, and to further investigate the distorting consequences of time preference and the peculiarities found in the loss domain.
RANKING AND TIME TRADE-OFF MAKE RESPONDENTS SENSITIVE TO IMPAIRMENTS OF DIFFERENT EQ-5D DIMENSIONS

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Background:
One suggested method for creating preference-based tariffs for the new five-level EQ-5D is combining time trade-off (TTO) and discrete choice exercises (DCE). Rank values from previous valuation studies can be used as proxies for DCE. This study examined rank and TTO data to determine if the methods differ in sensitivity to the EQ-5D dimensions.

Methods:
We used rank and TTO data for 42 EQ-5D health states from the US and UK EQ-5D(-3L) valuation studies, extracting overall ranks of mean TTO and mean rank values, ranging from 1 (best) to 42 (worst). We identified pairs of health states with reversed overall ranks between TTO and rank data, and regressed overall rank differences (TTO - ranking) on dummy variables representing impairments on EQ-5D dimensions.

Results:
43 (US) and 41 (UK) health state pairs displayed reversed rank order. Both US and UK regression models on rank differences indicated that respondents valued impairments on pain/discomfort and anxiety/depression as relatively worse in TTO than in the ranking task.

Discussion:
Different dimension sensitivity between TTO and ranking suggests that combining TTO and DCE could lead to inconsistent tariffs. Differences could be caused by respondents focusing on the first presented dimensions when ranking states, or could be related to longest endurable time in health states impaired on pain/discomfort or anxiety/depression. Does TTO or ranking/DCE best represent the preferences of the population?
MAKING USE OF QALYS: HOW CONCERNS ABOUT SEVERITY AND EFFECTIVENESS CAN BE MADE EXPLICIT IN HEALTH POLICY DECISIONS

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1Department of Public Health and Primary Health Care, University of Bergen, 2Department of Research and Development, Haukeland University Hospital, Bergen, Norway

There is a lack of understanding on how actual priorities between disease areas, patient groups and medical specialties can be made fairly and cohere to theories of distributive justice. We need a better knowledge of how concerns for the worse off, health gains and cost-effectiveness of interventions can be operationalized and linked to the extensive evidence based literature on particular diseases and interventions.

The objective of our study is to explore how quality-adjusted life year (QALY) data from published health economic evaluations can address concerns for two widely accepted priority setting criteria: (1) the size of the expected health gain and (2) the worse off in terms of health (severity). Five proposed equity concepts are used to quantify severity.

We strategically selected eight disease-intervention pairs based on relevance for priority setting in Norway. For each pair, we primarily searched for published health technology assessments or other studies reporting QALYs as the main outcome measure. We extracted QALY data from each source study. In order to identify the worse off, these data were used to quantify severity according to five equity concepts: 1) absolute shortfall, 2) attainment QALE, 3) lifetime proportional shortfall, 4) prospective health and 5) proportional shortfall.

Preliminary results indicate that it is feasible to quantify severity for the selected patient groups by the use of published QALY data. We show that these quantifications together with the reported QALY gains and ICERs might be instructive in rationing decisions across diverse diseases and interventions by ranking them, since they give explicit credit to crucial concerns such as severity, the expected health gain and cost-effectiveness and elucidate distributional conflicts between them.
HELPING DOCTORS AND PATIENTS MAKE SENSE OF HEALTH STATISTICS

G. Gigerenzer
Center for Adaptive Behavior and Cognition, Max Planck Institute for Human Development, Berlin, Germany

Many people do not understand what health statistics mean or draw wrong conclusions. For instance, many are unaware that higher survival rates with cancer screening do not imply longer life, or that a 25% reduction in the risk of dying from breast cancer through mammography screening in fact means that 1 less death in 1,000 women.

Statistical illiteracy is common to patients and physicians, arises from nontransparent framing of information that isadvertent or inadvertent, and can have serious consequences for health. It should not be attributed to cognitive biases alone, but to the emotional nature of the doctor–patient relationship and conflicts of interest in the healthcare system. The classic doctor–patient relation is based on doctors' paternalism and patients' trust in authority, which make statistical literacy seem redundant, as do the traditional combination of determinism (physicians who seek causes, not chances) and the illusion of certainty (patients who seek certainty when there is none). Information pamphlets, websites, and even medical journals often report evidence in nontransparent forms that suggest big benefits of interventions and small harms. Without understanding the numbers involved, the public is susceptible to emotionally manipulation, which undermines the goals of informed consent and shared decision making.
HOW COMBINING HEALTH TECHNOLOGY ASSESSMENT AND DECISION PSYCHOLOGY CAN ADVANCE PERSONALIZED MEDICINE AND PATIENT CENTERED CARE

WORKSHOP

Speakers:
M.M. Schapira, Department of Medicine, University of Pennsylvania, Philadelphia, PA, USA
S. Braithwaite, Department of Medicine, New York University, NY, USA
A.M. Stiggelbout, Medical Decision Making Unit, Leiden University Medical Center, The Netherlands
O. Kostopoulou, Medical Decision Making and Informatics Research Group, King's College, London, UK
C. Goodman, The Lewin Group, Falls Church, VA, USA
L. Sampietro-Colom, Deputy Director of Innovation, Hospital Clinic Barcelona, Spain

Background:
Health technology assessment (HTA) is a priority across the globe. The focus of HTA is to assess the relative value of alternative options for preventive, diagnostic, and treatment health interventions using a broad array of methods including meta-analysis, clinical trials, and decision modeling. Personalized medicine refers to a clinical approach that is individualized from a behavioral, demographic, psychosocial, economic, environmental, and biologic perspective. In order for the results of HTA to advance goals of personalized medicine and patient centered care, studies must be designed with outcomes that are meaningful to patients and clinicians in the clinical encounter. Further, HTA has often provided summary results across populations without the needed granularity of subgroup analyses to support an individualized approach in the clinical encounter. Questions remain regarding the level of granularity that is desired and useful in the context of clinical decision making. In order to address these issues, efforts are needed to align methods used in HTA to effective strategies in communication and decision making in the clinical encounter. Two fundamental approaches may contribute to this effort. First, research questions and methods should be designed to lead to findings that are meaningful to patients and clinicians in the practice of personalized medicine. Second, insights from decision psychology should be applied to translate findings effectively into patient-centered care.

Questions related to methods in HTA include the following: 1) designing studies to enable and increase the power of subset analysis, 2) development of new methods to detect subgroup response, and 3) choosing primary health outcomes that are directly meaningful for patients. Questions pertaining to the field of decision psychology include: 1) how best to communicate uncertainty in expected outcomes to patients, 2) identifying the degree of differences in outcomes that are meaningful to patients and clinicians, 3) determining the value patients place on various levels of evidence such as from randomized controlled trials, decision models, or expert opinion, 4) how to assist patients in balancing risks and benefits and assess their personal values and preferences, and 5) how costs and cost-effectiveness analyses may influence patient and clinician decision making.
in the context of personalized medicine. A rich literature in the fields of HTA and decision psychology can answer some of these questions while others require future research efforts.

**Objectives:**
The objectives of this workshop are to bring together leaders in the fields of HTA methods and decision psychology to address best practices and directions for future research with regard to translation of HTA methods to support personalized medicine and patient centered care. The outcome of this workshop and subsequent planned collaborations between HTAi and SMDM will be a set of white papers to identify best practices and priorities for future research that can move this field forward.

**Format of Session:**
The session will include an expert panel and discussion between the panel and workshop participants. The expert panel will include international leaders in the fields of HTA and decision psychology. Experts will present key issues relating to the use of HTA in the context of the clinical encounter, both summarizing existing literature and highlighting priorities for future research. Specific topics to be addressed will include the following: 1) key questions in HTA and decision psychology methodology relevant to personalized medicine; 2) clinical applications of personalized medicine; 3) exploring heterogeneity in treatment effects; 4) interactions between HTA groups and the clinical community, 5) challenges for physician cognition and decision making in personalized medicine, and 6) challenges in communicating uncertainty of an evidence base in the clinical setting. Extensive time will be allotted for participant input and interaction.

**Future Plans:**
This workshop will form the foundation of two white papers that will be developed by collaboration between HTAi and SMDM. The white papers will have an international and interdisciplinary perspective with the opportunity for input from both HTAi and SMDM members.

**Program Schedule:**
Introduction and Welcome: Marilyn M. Schapira (10 minutes)
1’st Hour Talks (25 minutes)
Talk #1: Key Questions in HTA Methodology Relevant to Personalized Medicine. Cliff Goodman
Talk #2: Clinical Applications of Personalized Medicine: Applying HTA Results. Scott Braithwaite
Talk #3: Bridging the Clinical and Research Arena. Laura Sampietro-Colom
Panel Discussion (25 minutes)
Coffee Break (30 minutes)
2’nd Hour Talks (25 minutes)
Talk #4: Challenges for Physician Cognition and Decision Making. Olga Kostopoulou
Talk #5: Challenges in Communicating Uncertainty of Evidence in the Clinical Setting. Anne Stiggelbout
Panel Discussion and Closing Comments (25 minutes)
PRINCIPLES FOR THE CONDUCT OF COMPARATIVE EFFECTIVENESS RESEARCH

Moderator:
J.S. Schwartz, Department of Medicine, Perelman School of Medicine and Health Care Management and Economics, Wharton School of Business, University of Pennsylvania, Philadelphia, PA, USA
Panelists:
U. Siebert, Department of Public Health, Medical Decision Making and Health Technology Assessment University for Health Sciences, Medical Informatics and Technology, Hall i.T, Austria,
Panelist TBA

The goal of comparative effectiveness research (CER) is to develop and disseminate evidence on the comparative value of alternative treatments, interventions and strategies to aid healthcare decision makers make more informed choices.

CER funding is already substantial and will continue to grow significantly in the coming years, especially through financial support and organizational direction provided in the U.S. by PCORI and in Europe for research on relative effectiveness. Thus, both the health and economic stakes of CER are high.

CER faces a number of challenges. CER seeks to develop patient-relevant health outcomes in typical patient care settings on representative populations on an extended time horizon. However, decision makers and other stakeholders have multiple, often differing and, at times, conflicting perspectives and objectives and frequently face differing incentives. Thus, CER needs to address a broad range of objectives and perspectives. Performance of rigorous CER also requires creating the right environment for good conduct that transcends responsibilities of an investigator. In contrast to previous initiatives that focused on health technology assessment, outcomes research broadly or methodological practices, our goal was to develop a more general set of principles focusing on the process of conducting CER and the potential for CER to improve health care and health.

To improve the likelihood that CER yields desired results, an international, multi-disciplinary group of clinical investigators and health services researchers used an iterative process to develop 13 principles to guide the conduct of CER.

An initial list of proposed principles was drafted based upon a targeted review of recent CER policy, methods, and related literature. This list was shared informally with a small number of stakeholders and researchers and then carefully reviewed and critiqued by a panel of five independent experts. A revised set of draft principles were reviewed at a one day meeting of seven individuals with expertise in CER policy and/or methods representing five stakeholder sectors (patients, device and pharma manufacturers, clinical medicine, HTA), and via written comments from four individuals representing two additional sectors (insurers, health plans). The final set of principles addressed CER study objectives, stakeholder engagement, study perspectives, relevance to stakeholder needs, bias and transparency, consideration of alternative intervention strategies, relevance
of study outcomes to decision makers, types of data collected and analyzed, assessment methods, heterogeneity of effect, parameter and outcome uncertainty, generalizability of study findings and dissemination, implementation and evaluation of study results.

The 13 principles will be presented briefly, followed by comments and moderated panel discussion by a reactor panel, followed by open questions and discussion.
VACCINES; ARE THEY DIFFERENT FROM DRUGS?
WORKSHOP

Speakers:
J. Roiz, OptumInsight HEOR, Nanterre, France
M. Martin, OptumInsight HEOR, Uxbridge, UK
A. McGuire, Department of Social Policy and LSE Health, London School of Economics, UK

Vaccines have made major contributions to health care. In all developed countries national immunisation schedules ensure the delivery of these valuable medicines. In recent years a number of new vaccines have been launched and implemented in vaccination schedules such as a HPV vaccine, a rotavirus vaccine and a vaccine against herpes zoster. Two new conjugated pneumococcal vaccines and a new meningococcal vaccine were approved in 2009 and 2010. In this workshop we will highlight the issues being faced in the vaccines market and provide examples of these, such as the lack of trust as demonstrated by the reduced uptake of the MMR vaccine, and the free movement of individuals within Europe, while immunisation practices remain local and coverage rates vary substantially between countries. Furthermore we will highlight the differences and similarities between vaccines and drugs. We will discuss best practices for vaccines and argue where deviations from the existing guidelines for the (economic) evaluation of drugs is relevant. This will include matters such as vaccine development and production, licensure, pricing, competition, target population, technology assessment and its requirements and last but not least implications for economic value assessment. We will discuss when infectious disease modelling is appropriate and what should be done about the matter of process utility. Other matters to be addressed will be the perspective of economic analyses.

Audience participation will be via an issues panel-style discussion where members from the audience will be encouraged to argue either the manufacturer or decision maker side thus contributing to the presentation and discussion of proposed changes from established guidelines to better demonstrate the value of vaccines. At the end of the forum a short list of the most urgent matters that need to be addressed for vaccines will be drawn up.
USE OF ECONOMIC EVALUATION FOR DRUG REIMBURSEMENT DECISIONS: COMMON SENSE, NON-SENSE OR JUST WASTE OF MONEY? THE NORWEGIAN EXPERIENCE

PANEL DISCUSSION

Moderator:
B. Robberstad, Faculty of Medicine and Dentistry, University of Bergen, Norway

Panelists:
M. Aaserud, Department of Pharmacoeconomics, Norwegian Medicines Agency, Oslo, Norway
A. Hågå, Department of Public Health, Ministry of Health and Care Service, Oslo, Norway
E. Jørgensen, Biomet Nordic, Oslo, Norway
K. Svanqvist, Department of Pharmacoeconomics, Norwegian Medicines Agency, Oslo, Norway

Background:
The Norwegian Medicines Agency (NoMA) is the decision making body for reimbursement of drugs for outpatients in Norway. Since 2002 the submission of a pharmacoeconomic dossier has been mandatory for reimbursement. The newly updated pharmacoeconomic guidelines together with a set of priority criteria, represent the framework for reimbursement decisions in Norway. Approximately 760 applications for drug reimbursement have been evaluated from 2005-2011. NoMa has granted reimbursement in more than 90% of the applications. The fact that only 10% of all applications have been totally rejected by NoMA may be viewed as a potential challenge to the viability of the reimbursement system because it may indicate that most drugs are reimbursed. In reality, however, it indicates that mandatory use of health economic evaluations improve the quality of the reimbursement process. It is probable that a greater number of reimbursement decisions would be negative if the cost-effectiveness had not been documented. Also, when companies know that cost ineffective drugs will not be reimbursed, they may refrain from applying for drugs that can’t be shown to be cost effective, or apply only for subgroups in which the drug is cost-effective. Consequently, companies have an incentive to apply only patient subgroups, where it is possible to demonstrate cost effectiveness. During the last ten years pharmacoeconomic analysis as a tool for reimbursement decision-making methods have improved and the governmental decision making has improved. The quality of pharmacoeconomic evaluations submitted by industry has improved.

Program:
• 10 minutes: Ten years of experience from an health authority perspective. Kristin Svanqvist, Head of Reimbursement Section, NoMA
• 10 minutes: Experience from a drug company perspective. Eivind Jørgensen, Nordic HCI Director Biomet Nordic
• 40 minutes of panel discussion and interaction with the audience.

To facilitate the discussion we will prepare questions for both the panel and the audience and by using response meters it would be easy to get...
contribution from the audience. There will also be an opportunity for the audience to ask questions and share their experience. Examples of questions could be:

- Has such a system implied that drug and health policy goals/objectives have been met?
- Have the right drugs for the right patients been granted reimbursement?
- Has Norway received value for money for the drugs that have been reimbursed?
- What are the societal costs of the decision making system? Do the benefits of the system outweigh these costs?
In the 1970s, cost-effectiveness analysis (CEA) first appeared in U.S. medical journals as a method to guide priority setting in health care. Over the subsequent 40 years the theoretical foundation has been improved and methods have become much more sophisticated. Despite its growing prominence in the medical literature over the past four decades, and despite the fact that US health care spending continues to grow to what are generally agreed to be unacceptable levels, cost-effectiveness analysis has not gained traction as a practical tool for priority setting in US health care delivery and insurance coverage. On the contrary, use of CEA has been equated by some American politicians as engagement in “death panels.” Despite a widely-cited government-sponsored publication of recommendations on good practices in CEA in the late 1990s (the “Gold Panel”), Medicare does not use CEA to support technology assessment and coverage. Opinion polls indicate that American people are not disposed to have their access to health services limited on account of cost. In Europe, use of cost-effectiveness has been endorsed by governments and health technology assessment (HTA) agencies in several European countries and economic evaluation is part of the framework of EUnetHTA. The UK has probably linked the results of cost-effectiveness analyses more strongly to its decision-making processes than any other country. Several others (among others, Nordic countries and the Netherlands) have also introduced the use of cost-effectiveness analysis, foremost in the area of pharmaceuticals. The use of cost-effectiveness analysis to inform priority setting has been a success in Europe in terms of number of countries, number of health economists involved, and the exponentially increasing number of scientific publications, the situation also has caused concern. Patient groups, not least those representing orphan diseases, fear that they will be denied care on the grounds of cost-effectiveness. Manufacturers of pharmaceuticals and medical devices fear that they will be “denied” market access. Finally, there is an ongoing debate about methodologies, not least in the area of utility measurement. The panel session will present the current situation in Europe and the US and discuss some of the current challenges.
Sound decision making is governed by rational thinking counting on available and the most recent information on any given topic. Decisions are taken with an estimate of the probabilities of future outcomes and the value and desirability of such outcomes.

The decision to destruct the remaining smallpox virus stocks in laboratories, long after we have seen the last case, has been on the table for the World Health Assembly many times.

Smallpox was declared eradicated in 1979. Apart from a laboratory accident in 1978, the last reported natural case was in Somalia in 1977. The variola virus is kept only in two laboratories, Center for Disease Control in USA and State Research Center og Virology and Biotechnology VECTOR in Russia. These laboratories are the only authorised repositories of the variola virus and are subjects to routine inspection by WHO.

Low and middle income countries with little or no medical industries and a high burden of communicable disease are adamant in their call for eradication. Other rich vaccine producing countries want to continue research to develop vaccines and drug regimes that are safe, efficient and able to protect against disease. A complicating factor is the possibility that there might exist unknown stocks of the virus; a potential security risk.

Our paper is proposed to demonstrate how the correct context will change the basis for decision making. We believe that the current debate is missing a point. The risk will be there in any case. The variola virus can be synthesised; making it possible to engineer the virus in a laboratory.

The early discussion has followed the branch of the decision tree that is concerned with the comfort it would be to know that the smallpox threat is gone for ever. The fact that the virus can be rebuilt leads us down another branch: How best to establish global preparation for the possibility of an accident or terrorist attack resulting in the release of the virus.

This is not an issue on decision making solely relevant to that of smallpox. The recent modification of H1N5 into virulent pathogen in laboratories in the Netherlands and the US also brings up a similar dilemma. Sharing of information to develop science is the goal of publication. On the other hand, information might make things easier for those who would like to develop an indiscriminate weapon of terrorism.

Decisions in public health are not solely a function of probabilities and utilities. Moreover decisions are taken in a context of competing interests where the well informed scientific leaders will have an advantage in affecting outcomes on issues relevant to all.
DESCRIBING SEVERITY AS A CRITERION FOR PRIORITY SETTING ALONGSIDE THE COST UTILITY ANALYSIS WORKSHOP

Speakers:
E.B. Torkilseng, Division for Health Economics and Financing, Norwegian Directorate of Health, Oslo, Norway
T. Ottersen, Department of Public Health and Primary Health Care University of Bergen, Bergen, Norway
E.A. Stolk, Institute for Medical Technology Assessment, Erasmus University Rotterdam, The Netherlands

Cost Utility Analysis (CUA) is widely used for priority setting in many health care systems. In CUA health gains are expressed in terms of Quality adjusted life-years (QALYs), making use of the assumptions underlying the conventional QALY-approach.

In Norway the second Lønning-report pointed out three criteria for priority setting in health care: Severity, effectiveness, and cost-effectiveness. Countries such as the Netherlands and Sweden have endorsed similar criteria for priority setting. Severity has been identified as a relevant criterion in several quantitative population preference studies. A number of approaches have been suggested to take account of severity, including equity weighting of the QALY. However, severity is rarely explicitly addressed or quantified alongside a CUA.

The purpose of this workshop is to discuss two alternative approaches to describe severity as a criterion for priority setting.

In this workshop, Trygve Ottersen will discuss how severity can be described in terms of expected lifetime QALYs. This proposal does not refer directly to any concept of QALY-loss or QALY-gap. Moreover, age will be major predictor of severity so specified, and similar approaches have been criticised for favouring the young over the old. Elly Stolk will to some extent depart from both these features and argue in favour of describing severity in terms of relative QALY-loss. This approach has been labelled "proportional shortfall" and is claimed to be an intermediate position between lifetime and future-only specifications of severity.

Einar Torkilseng from the Norwegian Directorate of Health will be the moderator of the session. The audience will be activated by performing a brief survey of the participants experiences from own country and views on different approaches to describe severity.
ABSTRACTS

POSTER PRESENTATIONS
Statistical literacy can be defined as understanding the statistical aspects of and terminology associated with the design, analysis, and conclusions of original research. Statistical literacy training is important for the practice of evidence-based medicine. Most studies that assess statistical literacy have been conducted with limited samples and/or were completed with response rates of 75% or less.

Questions about statistical literacy were included in the obstetrics-gynecology residents’ annual test in 2011 (all residents in the United States are required to complete it each year). Completed surveys were obtained from 4,713 residents (a 95% response rate). Questions were asked about the statistical literacy training they had received during residency and whether their training was adequate, in their opinion. Two statistical knowledge questions were also asked; one about the positive predictive value of a positive mammography, and another about the definition of a p-value. When asked to identify the positive predictive value of a positive mammography screen, only 25.9% chose the correct multiple choice option. When asked whether the p-value is the probability that the null hypothesis is correct, 46.4% said true, 42.3% said false, and 11.3% did not answer. About two-thirds rated their statistical literacy training as adequate, 23.7% rated it as inadequate. Females were more likely to rate their statistical literacy training poorly, with 25.1% of the females indicating inadequate compared with 17.9% of the males (p < .001). Those who answered the positive predictive value question correctly rated their training significantly lower than those who answered it incorrectly (F(6, 4360) = 5.7, p < .001). Fifteen percent said that they had statistical literacy training as part of a course, 50.7% said they had training through journal club, 28.8% said they had informal training, and 11.2% said that they had no training.

Fewer participants answered knowledge questions correctly than previous studies, suggesting that statistical literacy skills among residents may be worse than previous studies indicated. Residents who need training the most may be the least likely to know it. The quality of statistical literacy training deserves further consideration from medical educators.
ATTITUDES TOWARD EUTHANASIA PREDICT TTO VALUES - PROBLEMS USING 'DEATH' AS AN ANCHOR?
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Objective:
Health state values are by convention anchored to ‘perfect health’ and ‘death’. Attitudes toward death may consequently influence the valuations. We used attitudes toward euthanasia (ATE) as a sub-construct for attitudes toward death. We compared the influence on values elicited with time trade-off (TTO), lead-time TTO (LT-TTO) and visual-analogue scale (VAS). The ‘death’ anchor is most explicit in TTO, so we hypothesized that TTO values would be most influenced by ATE.

Methods:
Respondents valued eight EQ-5D health states with VAS, then TTO (n=328) or LT-TTO (n=484). We measured ATE on a scale from -2 to 2, and used multiple linear regressions to predict VAS, TTO and LT-TTO values by ATE, sex, age and education.

Results: A one point increase on the ATE scale predicted a mean TTO value change of -.113 and LT-TTO change of -.072. Demographic variables, but not ATE, predicted VAS values.

Conclusions: TTO appears to measure ATE in addition to preferences for health states. Different ways of incorporating death in the valuation may impact substantially on the resulting values. ‘Death’ is a metaphysically unknown concept, and implications of attitudes toward death should be investigated further to evaluate the appropriateness of using ‘death’ as an anchor.

Figure: TTO values from 218 respondents as a function of attitudes toward euthanasia
COST-EFFECTIVENESS OF ROTAVIRUS VACCINATION IN A MIDDLE INCOME COUNTRY: A DYNAMIC MODELLING APPROACH

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I.S. Kristiansen5

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Objectives:
In the middle income country Kazakhstan, rotavirus infections is a major cause of morbidity and mortality among children. Health authorities consider including rotavirus vaccination in the national childhood vaccination program.

Methods:
We adapted a previously published dynamic compartmental model of rotavirus infection (1). The model was calibrated to available sentinel data of hospitalized rotavirus cases in children < 5 years using a maximum likelihood approach. The model estimates the number of fatalities, hospitalizations, outpatient clinic visits and homecare cases. Based on published cost data (2) and the market price of vaccine ($43 per dose) we estimated the health benefits and cost per year gained from 20 years of vaccination in a societal and health care perspective. We varied the onset of vaccine effect (2-4-6 months) vaccine coverage (20%-100%) using 4 months and 90% in the base case. Uncertainty was further evaluated by means of probabilistic sensitivity analysis.

Results:
In the base case, 20 year of vaccination will entail 1,110 avoided fatalities, 65,000 hospitalizations, 480,000 doctor visits and 2.5 million home care cases with birth cohorts of approximately 300,000 (undiscounted). In the health care perspective, the discounted cost per life year gained was $19,162 which is higher GDP/capita in Kazakhstan ($12,700). This cost was almost uninfluenced by the vaccination rate, but was a linear function of the vaccine price. When including indirect costs of morbidity and mortality, vaccination is cost-saving.

Conclusion:
In a middle income country, rotavirus vaccination results in great impact on morbidity and mortality. The pivotal factors of the cost-effectiveness analysis were the purchasing price of the vaccine and the perspective of the analysis.

Conflict of interest:
This study was funded by the Norwegian Research Council.

References:
ONLINE SHARED DECISION-MAKING AND COLLABORATION TOOLS IN COMMUNITY MENTAL HEALTH: PRELIMINARY RESULTS FROM COMMUNITY-BASED PARTICIPATORY RESEARCH
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As in many other countries, empowering patients to take an active role in managing their health through patient-centered collaborative care are priority health policy goals in Norway. E-health technologies are expected to play key roles in redesigning healthcare along these lines. Among such tools include Interactive Health Communication Applications (IHCA) that build on the principles of shared decision-making. Used by patients, systems can include one or more components such as: support for secure patient and provider communication, self-guided treatments, social support forums, and evidence-based educational material. The potentials of incorporating IHCA-supported shared decision-making into community mental health care are supported by an increasing number of studies.

However, in spite of the growing evidence of the efficacy of IHCA-supported shared decision-making in controlled trials, we know next to nothing about how such tools will translate into community mental health care practices. The fact that it typically takes 14-20 years to implement into practices interventions that have demonstrated efficacy in controlled trials is an international concern that is gaining attention as a research issue in its own right. The rapid turnover of consumer technologies that can support individually tailored IHCA (e.g. smart phones, monitoring devices) compound the mismatch between research results and real world practices.

This paper reports the results of a pre-project that have informed the design of a recently launched study. The study aims to investigate methods for better aligning IHCA adaptation, implementation and evaluation, as well as speedy transfer of knowledge between differing community practices. An urban and a rural community serve as cases. Both the pre-project and the resulting protocol build on community-based participatory research where mental health service users and providers, researchers and IT-experts collaborate as equal partners in practice-research teams. A research-based IHCA-platform called Connect 2.0 served as a point of departure. The pre-project results are reported in conjunction with 3 phases in the main study: 1) IHCA adaptation: 2) Implementation and 3) Evaluation. The findings illustrate how the principles of shared decision-making can be applied to the community level in the form of collaboration between community and researchers.
ECONOMIC EVALUATIONS – IS ONCE ENOUGH: A TAVI CASE STUDY
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Background:
Economic evaluations address two questions: 1) is the technology cost effective compared to alternatives given current information? 2) Is there value in collecting further information? The literature suggests these questions need to be examined and reviewed on an iterative basis as evidence evolves, especially for new technologies. TAVI is a novel technology for severe Aortic Stenosis (AS) with scarce but evolving data. A decision analytical model is built to address these questions for TAVI for operable patients on an iterative basis as the evidence evolves.

Methods:
A probabilistic model of AS was populated and analysed using data from the literature; this was then updated following the release of the first RCT (PARTNER) results. Results identify the cost-effective alternative, generate CEACs and estimate the value for information including population EVPI (pEVPI). A sensitivity analysis is employed to examine the effect of potential improvements in clinical outcomes resulting from intervention and technique development.

Results:
Populating the model with pre-trial data the cost effectiveness analysis demonstrated TAVI was more expensive (£5,472) and more effective (0.08) than AVR. The ICER (£72,412) was outside the range usually considered cost effective. The CEAC demonstrates little uncertainty (12%) surrounding this decision. PEVPI was £501,513 (at £30,000/QALY). Updating the model with PARTNER evidence reveals TAVI is dominated by AVR. The CEAC demonstrates very little uncertainty (0.5%) surrounding the decision and pEVPI was reduced (£16,035 at £30,000/QALY). The sensitivity analysis demonstrated if clinical improvements were realised TAVI would be more expensive and more effective than AVR (ICER = £407,320); decision uncertainty (9%) and pEVPI increase (£499,892 at £30,000/QALY).

Conclusions:
The results indicate TAVI cannot be considered cost effective for operable patients compared to AVR given pre-trial and trial evidence. So decision makers cannot decisively indicate the suitability of TAVI for severe operable AS patients. There is some potential value in collecting further evidence if clinical improvements became a reality, as indicated by EVPI. This evidence may be collected via a trial or registry. However single country trials are expensive, so registries which are cheaper, or cross country trials may be a more efficient use of resources.
HELPING DOCTORS AND THEIR PATIENTS MAKE BETTER DECISIONS ABOUT HEALTH

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Recent research on health literacy and medical decision making has shown that in most cultures doctors and their patients have severe problems grasping a host of numerical concepts that are prerequisites for understanding and communicating health-relevant risk information. However, there is a dearth of published research comparing risk communication in cultures with different health systems. We present the results of three studies conducted in three different countries (US, Germany, and Spain), which converge to demonstrate that problems associated with risk illiteracy are not simply the result of cognitive biases preventing good decision making. Rather, errors occur because ineffective information formats complicate and mislead adaptive decision makers. In particular, we report the effectiveness of visual aids to enhance risk understanding and communication (Study 1), to eliminate biases such as denominator neglect (Study 2) and errors induced by framed messages (Study 3). We conclude that information formats that exploit people’s inherent capacity to recognize relationships in naturally occurring problems (so-called transparent information formats) can dramatically enhance risk comprehension, communication, and recall and foster better decisions about health regardless of culture. We provide some guidelines for transparent communication of health-relevant information.
ESTIMATING THE EXTENT OF THE SEVERELY OBESE POPULATION IN SCOTLAND: AN APPLICATION OF BAYES RULE

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Introduction:
It has been estimated that just over 2\% of the Scottish population has a body mass index (BMI) \( \geq 40 \text{ kg/m}^2 \) but there are no estimates that disaggregate this severely obese population beyond this level. The aim of our research was to estimate the extent of the severely obese population in Scotland according to BMI groupings beyond \( 40 \text{ kg/m}^2 \) (for example, BMI \( \geq 40 \text{ kg/m}^2 \), \( \geq 50 \text{ kg/m}^2 \), \( \geq 60 \text{ kg/m}^2 \) to \( \geq 70 \text{ kg/m}^2 \)).

Methods:
Using secondary cross-sectional data and estimates of disease prevalence associated with varying levels of BMI \( \geq 40 \text{ kg/m}^2 \), we determined the approximate size of the population of the severely obese in Scotland by BMI \( 40 \text{ kg/m}^2 \), \( 50 \text{ kg/m}^2 \), \( 60 \text{ kg/m}^2 \) to \( \geq 70 \text{ kg/m}^2 \). We used the 2008/9 Scottish Health Survey (SHeS) to explore the prevalence of type 2 diabetes (T2DM) associated with BMI \( \geq 40 \text{ kg/m}^2 \) \ldots \( \geq 70 \text{ kg/m}^2 \). We have made the assumption that the SHeS provides an accurate reflection of each BMI grouping. We then established the probability of those with T2DM having a BMI \( \geq 40 \text{ kg/m}^2 \) \ldots \( \geq 70 \text{ kg/m}^2 \) from a national register of people with diagnosed diabetes in Scotland, the Scottish Care Information-Diabetes Collaboration (SCI-DC). Supplementing these conditional probabilities with information concerning the overall prevalence of T2DM in the Scottish population, we used Bayes Rule to estimate the probability of being in each BMI grouping.

Results:
Our estimates suggest that as BMI increases in bands of 10 from \( \geq 40 \text{ kg/m}^2 \) up to \( \geq 70 \text{ kg/m}^2 \), the proportion of the population falling into each BMI grouping falls by a factor of 10 with 2\%, 0.2\% 0.02\% and 0.002\% of the population respectively. In absolute terms, this equates to approximately 100,000; 10,000; 1000 and 100 individuals.

Conclusion:
Our results concur with the literature that just over 2\% of the Scottish population is severely obese. Extrapolating our results to values of BMI above \( 80 \text{ kg/m}^2 \) suggests there are currently few individuals (<100) living in Scotland with BMI at these levels.
APPLICATION OF TRADITIONAL HEALTH ECONOMIC PRINCIPLES FOR TECHNOLOGY FOR AMBIENT ASSISTIVE LIVING (AAL)

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The future challenges of the modern welfare state are well known. A rising proportion of elderly people, together with an increasing number of persons living alone, will put considerable pressure on public services. Technological solutions are said to be the answer to these challenges. But do we know if the technology is efficient in economic terms, i.e., that the benefits outweigh the costs?

Traditional health economic analysis for a certain technology focuses on measuring length of life and quality of life for the patient. Effects are measured in monetary values, and the costs include investments and running expenses. By comparing different technologies with the status quo a recommendation on decisions can be given.

Technology for AAL is used for people who are not necessarily sick, rather they are denoted service-users, or just users. In traditional health economic analysis the effects for non-users are seldom included. Elderly persons or other persons with activity limitations often have relatives, friends or neighbors who are affected by the activity limitation. They may have to spend time taking care of this person, and may be concerned for their health and situation.

SINTEF is undertaking a number of initiatives and projects to test and develop many types of technology for AAL. The question is always: Is this worthwhile? In this project the traditional health economic principles are tested, including an evaluation of some of the benefits for the relatives of the users (non-users). The experience from the economic calculation of several concrete projects will be presented, including a GPS-system for people with dementia and security systems for elderly people in their own homes.
ECONOMIC IMPACT OF THE APPLICATION OF MEDICATION IN FIGHTING INFECTIOUS DISEASES

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Introduction:
Considering that in Germany in 2009 the outbreak of the swine flu and the policy subsequently implemented was estimated by the German Social Health Insurance (GKV) to cost at least EUR 700,000,000, not considering yet the death of people, it is worth thinking about implementing disease spreading simulations in combination with economic data to design efficient health policies.

Background:
Until now, few health policy models (Siebert, 2003) integrate economic factors not yet considering pandemics. In addition, most governmental pandemic plans are static and do not consider geographic or economic data. Therefore, the aim of our work is to show that integrating economic factors in infectious disease spreading models can help based on cost-benefit-considerations to decide the optimal strategy for decision makers on handling pandemic situations.

Method:
The simulation of what would have happened if the avian flu had had an outbreak in Tyrol is the basis for showing the economic impact of this pandemic (Pfeifer et.al., 2008). Based on six different scenarios including various forms of medication combining amongst others medication and quarantine differences, e.g., in GDP for the region of Tyrol are calculated.

Results:
Results show that with medical treatment compared to no treatment and citizens adapting their social behavior, a reduction in population of approx. 200,000 persons can be avoided, preventing a loss of GDP for the region of EUR 7.1 billion per year. Furthermore, we were able to show that quarantine in combination with medical treatment hardly changes these results, putting into question if this additional costly measure should be taken.
Discussion & Conclusion:
This new conceptual framework for decision makers in health policy could allow them to not only operate more effectively but also more efficiently on fighting infectious diseases. It can give insights on useful combinations of treatments, so that policies can be reflected on a cost-benefit analysis. In the end it should be possible to demonstrate policy makers different possibilities of handling an infectious disease, reflecting on mortality, morbidity as well as on economic factors.
MEASLES SUPPLEMENTAL IMMUNIZATION ACTIVITIES (SIAS) AS A DELIVERY PLATFORM FOR OTHER CHILDHOOD INTERVENTIONS IN INDIA: DEVELOPMENT OF A PLANNING TOOL
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Background:
Between 2010 and 2012, India will deliver a second opportunity for measles-containing vaccine (MCV2) through mass vaccination campaigns (supplemental immunization activities “SIAs”) targeting 135 million children aged 9 months to 10 years. Although their primary purpose is delivery of a specific vaccine, SIAs can also be used to strengthen child health services. At this juncture, Indian states participating in the MCV2 SIAs have not planned to use the SIA platform to deliver other interventions. A more comprehensive SIA design has the potential to increase efficiency and improve health service delivery to the underserved, but these considerations have never been formally assessed in this context.

Objective:
To develop an innovative tool for SIA planning, which gives explicit consideration to the possibility of using measles SIAs as a delivery platform for other child and maternal health interventions.

Methods:
We developed a mathematical model to assess the impact of SIAs on the burden of measles at the Indian state/district level, taking into account dynamic characteristics of measles transmission. We also surveyed the scientific literature to identify interventions that have been offered in conjunction with similar SIAs worldwide. We then adapted the model to consider the impact on disease burden of adding selected interventions singly and in combination to the measles SIA platform. The analysis modelled costs, effects and cost-effectiveness of alternative SIA strategies with a particular emphasis on synergies in costs and effectiveness associated with a common delivery platform.

Results:
Addition of selected interventions to the SIA platform improved the health impact of the SIAs at relatively low marginal cost. A small number of add-on interventions were responsible for the majority of health gains. The value of the add-on interventions differed substantially among states due to variations in epidemiological conditions and in pre-SIA levels of coverage of related interventions. Due to substantial synergies in effects, measles SIAs offering several add-on interventions in combination were particularly beneficial for underserved populations.

Conclusions:
Use of measles SIAs as a platform to deliver additional maternal and child health interventions is a highly effective means to improve population health impact, cost-effectiveness and equity of the SIA strategy.
IMPLEMENTING FUTURE PRICE CHANGES IN COST-EFFECTIVENESS ANALYSIS
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Background and Objective:
Within the proposed new guidelines of economic evaluation of pharmaceuticals in Norway it was suggested that future drug prices of all relevant comparators are to be included in the cost-effectiveness analysis. While this appears a rational and theoretically valid suggestion it raises a number of methodological and practical issues that need to be addressed to ensure a coherent and transparent implementation. The purpose of this work is to outline and discuss some of the methodological and practical challenges in including future price changes in economic evaluation.

Methods:
A stylised example is employed to demonstrate some of the practical and methodological challenges with including future prices in cost-effectiveness analysis. Analysed challenges include the type of pharmaceutical evaluated (e.g. long-term/continuous vs. short terms treatment), the exchangeability of pharmaceuticals after treatment initiation and south-west quadrant issues (switching to cost-effective treatment alternative which are less costly but also less effective).

Results and Discussion:
This analysis demonstrates that there is no one clear way of implementing future drug prices in economic evaluations. How to apply this policy in practice may in addition depend on the type of pharmaceutical being evaluated. Furthermore, the analysis identifies some specific questions that needs to be addressed before a transparent and coherent methodology can be implemented. Should the cost of switching back and forth between treatments be included in the analysis? If so, how and which costs? Are we willing to switch back to a less effective but less costly treatment alternative if it becomes cost-effectiveness after generic competition?

Conclusion:
In principle we agree that knowledge of future prices of drugs should be considered when assessing the cost-effectiveness of pharmaceuticals. However, doing so raises numerous issues that need careful attention before making this a mandatory requirement in cost-effectiveness analysis.
ANALYSING POLICY IMPLICATIONS ON PHARMACEUTICAL RESEARCH AND DEVELOPMENT INCENTIVES
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Background and Objective:
In the light of growing number of treatment options and demographic development, there has understandably been an increased focus on costs and cost containment within the healthcare sector. However, policies aimed at cost containment may have unintended consequences on healthcare provision and ultimately on research and development (R&D) investments within the pharmaceutical sector. The purpose of this work is to analyse how pharmaceutical policies such as international price referencing and generic substitution may influence pharmaceutical R&D incentives. The analysis is based upon and utilises a conceptual framework concerning what constitutes a fair rent on pharmaceuticals.

Method:
The analysis is based on a framework where fair prices are defined such that a pharmaceutical constitutes a net gain to society, which is equivalent to how some define value based pricing. We define a fair rent on pharmaceuticals to be equal to the fair price times the target population times the years left until patent expiry (after marketing authorization), where the target population refers to the population for which the pharmaceutical constitutes a net gain for society. The concept of fair rent is the foundation of the conceptual framework that is used to analyse how different policies effect R&D incentives of the pharmaceutical industry.

Results:
This analysis demonstrates how external price referencing and parallel trade negatively affects fair rent on pharmaceuticals and thus limits incentives for future R&D investments. Hence, employing these policies is to some extend equivalent to substituting health of future generations for short-term cost containment/savings. Furthermore, the importance of generic substitution and implementation of fair priced pharmaceuticals in the beginning of their lifecycle is demonstrated. Failure to ensure that fair priced pharmaceuticals are implemented within their target population will not only be a loss to the pharmaceutical industry but also a net loss to population health. In conclusion this study demonstrates the importance of analysing the long-term consequences of pharmaceutical policies to ensure sustainable R&D incentives within the pharmaceutical sector.
RESOURCE ALLOCATION DECISION MAKING DURING A PANDEMIC: A REPORT ON THE DEVELOPMENT OF A DECISION SUPPORT SYSTEM

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Community-wide disasters and disease outbreaks quickly consume resources and challenge decision makers to increase surge capacity. The 2009 H1N1 pandemic illuminated gaps in healthcare coverage, especially the availability of mental healthcare. While the pandemic was not as severe as predicted, research showed that fear, anxiety, and traumatic stress response was evident in influenza patients and their families throughout Mexico, America and Canada. Unfortunately, at least in the United States, mental health is not well represented in pandemic response plans, nor is there a reserve corps of behavioral health professionals ready to meet surge. In this study, licensed psychologists, social workers and therapists in Kentucky were surveyed to assess their attitudes and willingness to volunteer during a pandemic. More than 75% of respondents indicated an intention to respond, if called upon and if properly trained. Building upon the survey results, a Geographical Information Systems (GIS) map was created to provide decision makers in Kentucky with a visual representation of the local mental health resources available to them. This GIS tool was embedded in a decision support system designed to facilitate resource allocations during a pandemic. This report will show the results of the survey, the GIS map, and the architecture of the decision support system. The overarching goal of this project is to ensure resources, including behavioral health professionals, can be dispersed effectively in the next pandemic or community-wide disaster.
MODELLING THE COST-EFFECTIVENESS OF SCREENING MEN WHO HAVE SEX WITH MEN FOR CHLAMYDIA TRACHOMATIS AT HIV TREATMENT CENTRES
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Introduction:
Men who have sex with men (MSM) are at risk for multiple sexually transmitted infections (STIs). Since STI co-infections in HIV-infected MSM facilitate HIV transmission, finding and treating asymptomatic STIs could potentially decrease the incidence of HIV. HIV infected MSM registered at HIV treatment centres in the Netherlands are routinely screened for some STIs, but not for Chlamydia trachomatis (Ct); the cost of testing present a barrier.

Method:
We assessed the cost-effectiveness of implementing regular anorectal Ct screening. We constructed a dynamic transmission model of HIV and Ct, and investigated how finding and treating Ct infections influences HIV incidence. The model described transmission of these infections in sexual relationships in the Dutch 15- to 69-year old MSM population, stratified according to HIV and Ct status, and risk behaviour (rate of unprotected sexual acts). Parameter values and ranges were based on data from the literature, or on plausible assumptions (expert opinion). The transmission model estimated the yearly number of HIV and Ct infections with and without annual Ct screening, in a 20-year time frame. We performed probabilistic analyses where 1,000 sets of parameter values were drawn. The transmission model was solved numerically with each parameter set. The economic model included costs for screening and costs for treating new Ct and HIV infections, calculating the incremental cost-effectiveness ratio (ICER) of routine screening compared to no routine screening. For HIV, there is a delay between time of infection and entering care, therefore the costs for care were also delayed in the model.

Results:
With four averted HIV infections per year, the ICER was calculated at €115,000/quality-adjusted life year gained (QALY) in the 20-year time frame. Most ICERs from the simulations remained above the threshold value (€20,000-50,000/QALY). The ICER was sensitive to number of averted HIV infections, and averted infections were influenced by the risk behaviour and size of high-risk behaving groups.
RESOLVING THE COORDINATION PROBLEM IN HEALTH CARE: LIMITED RESPONSIBILITY HMO:S

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The fragmentation of health care organizations is a prevailing problem in most countries around the world. The underlying reason for the lack of coordination of health care production is often attributed to the lack of central cost accountability for each individual patient. The rather few health care producers that manages to coordinate health care all the way from primary care to tertiary care are often used as good examples, e.g., Veterans administration, Kaiser Permanente, Intermountain Health Care and The Mayo Clinics.

However, due to large cost variability amongst patients (economic risk), information asymmetries and agency problems, the provision of health care is rarely coordinated. More commonly, the delivery of health care production is reimbursed in a non-coordinated way that creates incentives for sub-optimization and suppresses entrepreneurship among producers.

In this paper we use data from the Medical Expenditure Panel Survey and computer simulations to illustrate that limiting a provider’s cost responsibility for each patient is a much more efficient way of reducing provider risk than to increase the number of patients. Our simulations illustrate that introducing an individual yearly cost-ceiling of 20,000 US-dollars per patient reduces risk as much as increasing the number of patients from 5,000 to 100,000.

The results indicate that it might be possible to create the advantageous opportunities for coordination in managed care organizations, such as those mentioned above, without exposing providers to extensive risk. Reimbursements systems of the type used in Medicare Advantage might thus be slightly adjusted to reduce the barriers of entry (economic risk) and promote the entry of integrated care providers on the market.
EFFECT OF ART ON MALARIA PARASITAEMIA AND CLINICAL EPISODES IN ADULTS IN RURAL UGANDA, 2005-2009: A POPULATION-BASED COHORT STUDY

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Background:
Before the introduction of antiretroviral therapy (ART), HIV infection was associated with an increased frequency of clinical malaria and parasitaemia, particularly with advancing immunosuppression. We have assessed the effect of ART on malaria clinical episodes and parasitaemia.

Methods:
Between 2004-2010, HIV-infected and uninfected study participants in clinical cohort in rural Uganda were followed up quarterly and whenever sick. A blood smear was collected at scheduled visits and whenever participants presented with a fever. Malaria parasites were identified microscopically following a Leishmann stain. Parasite density was determined for all positive smears. HIV serology and CD4 cell counts were measured regularly. The incidence of (i) clinical malaria (parasitaemia concurrent with fever) and (ii) malaria parasitaemia was compared between groups using rate ratios. Random effects Poisson regression models were used to account for repeated events and adjustments were made for covariates.

Results:
Participants follow-up categories were: 228 HIV-uninfected, 327 HIV-infected not yet on ART and 197 HIV-infected on ART. The overall incidence of clinical malaria episodes was 33.2/100 pyrs (95%CI 29.5-37.3) and that of malaria parasitaemia was 61.9/100 pyrs. Compared to the HIV-uninfected, the incidence of malaria clinical episodes was significantly higher among HIV-infected individuals not yet on ART; aRR 1.77 (95%CI 1.37, 2.28) and individuals on ART for less than 2 years; aRR 1.89 (95%CI 1.47, 2.42), but there was no significant difference when compared to that among individuals on ART for more than 2 years; aRR 0.63 (95%CI 0.45, 0.89). The incidence of malaria clinical episodes decreased with increasing age (p trend <0.001) and increasing CD4 cell counts (p trend<0.001). Similar associations and trends were seen for the incidence of malaria parasitaemia, according to HIV/ART status. The malaria strains identified were Plasmodium falciparum (93.6%) followed by Plasmodium malarie (6.3%) and Plasmodium ovale (0.1%).

Conclusion:
HIV is a risk factor for both malaria clinical episodes and parasitaemia. Sustained treatment with ART reduces malaria clinical episodes and parasitemia among HIV-infected individuals.
ECONOMIC ANALYSIS OF HARMONIC SCALPEL IN GASTRECTOMY

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Objective:
To compare cost-effectiveness of harmonic scalpel and conventional methods in open gastrectomy in Korea.

Methods:
The analysis was conducted from the public payer perspective in one-surgery time horizon. Harmonic scalpel in open access was compared to the standard procedure (open gastrectomy). A systematic data review was performed in order to assess effectiveness of harmonic knife and standard gastrectomy. Cost-related data were collected by interviews with surgeons from Korea. The final result of the analysis is incremental cost-effectiveness ratio, where the effectiveness was measured in the aspects of: surgery duration, hospitalization time, intraoperative blood loss and number of postoperative complications. One-way sensitivity analyses were performed for the key input parameters.

Results:
Gastrectomy with harmonic scalpel is connected with shorter length of surgery (215 min vs 243 min), smaller intraoperative blood loss (0.65 units vs 1.37 units), shorter length of postoperative hospitalization (9.3 days vs 12.5 days) and smaller number of postoperative complications (0.17 vs 0.35). The differences are statistically significant for each end point above.

Cost of one gastrectomy with harmonic scalpel from the public payer perspective is 5.1 M? while the cost of one conventional gastrectomy is 4.8 M?. The difference in cost is not statistically significant (0.3 M?; CI95% -0.3; 1.0 M?).

Incremental cost-effectiveness ratio equals: 11 k? per surgery minute saved, 432 k? per blood unit transfused saved, 98 k? per hospitalization day saved and 1.8 M? per postoperative complication avoided.

These results do not take into account all differences in costs between procedures. The use of harmonic scalpel could lead to savings in other fields. Some of potential savings were shown in sensitivity analysis.

Conclusion:
Open gastrectomy with harmonic scalpel is connected to shorter time of surgery and hospitalization length when compared to the conventional gastrectomy with open access. Gastrectomy with harmonic scalpel causes smaller number of postoperative complications and requires smaller amounts of transfused blood. Harmonic scalpel use in gastrectomy is more expensive than the conventional open gastrectomy. The differences in effectiveness are statistically significant and difference in costs are not. For this reason open gastrectomy with harmonic scalpel can be considered as a dominant intervention.
THE MULTIDIMENSIONAL ANALYSIS OF COGNITIVE AND EMOTIONAL RESPONSES TO SCENIC LANDSCAPES WITH THE AIM OF IMPROVING THE CONTROL OF BEHAVIOUR BY MEANS OF THE VISUAL ENVIRONMENT

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Background and Aims:
The visual environment influences on emotional condition and behavior of the observer. Our investigation was the necessary stage of development of the Information System for forecasting of emotional and behavioral responses to visual environment. This information system will improve methods for the prevention and correction of emotional distress, and control of the observer behavior by means of the visual environment. Fuzzy logic and linear programming algorithms are used in the decision-making module for this Information System.

Methods:
Using multidimensional scaling, we investigated the general and individual differences of perception of natural and anthropogenous landscapes (slides) and also associating with them words denoting emotions and various forms of human-being behavior. Qualitative interpretation of properties of multidimentional landscapes-words spaces was given in terms of B.F. Skinner's Concept. The stimulus-response connections were investigated on the ratio of landscapes to words in psychological spaces.

Results:
Associations between different landscapes and forms of human activity (labor, education, vocation activities, etc.) have been specified. Landscapes differ on degree of comfort, habitualness, anthropogenous intervention. In psychological spaces they have formed several groups: (1) urban work environment; (2) vacation places; (3) places for playing sports; (4) points of interests; (5) unusual environment. Landscapes differ on such characteristics of emotional tone as: “pleasant - unpleasant”, “sleep - tension”, “attention - rejection”. Positive reinforcements decreasing frustration are accompanied by a reduction of "attention - rejection" dimension of psychological space and by displacement of points representing landscapes and words in a direction to "attention" pole.

Conclusion:
Changing properties of visual environment it is possible to modify a behavior and emotional reactions of the observer. Specially setted environment can be used in the personified medicine (psychotherapy) and personality focused pedagogic. On the ratio of landscapes to words in multidimentional psychological spaces it is possible to specify the most significant properties of landscapes. Individual differences of the associations between the certain landscapes and words depend on value which observer attributes to the separate properties, or to the combinations of several properties, or a landscape as a whole.
COST-EFFECTIVENESS ANALYSIS OF SCREENING STRATEGIES TO PREDICT PROTECTION AGAINST TETANUS WITH CONDITIONAL POST-EXPOSURE PROPHYLAXIS IN ADULT PATIENTS SEEKING EMERGENCY CARE FOR A WOUND

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In France, tetanus has nearly been eradicated as the result of the mandatory childhood immunization program started in the early fifties, and a booster immunization recommended every 10 years in all adults. While very high level of protection against tetanus progressively reaches cohorts 60 years and older, continuing post-exposure prophylaxis in all adults seeking emergency care for a wound may be scrutinized at a time of limited resources.

We performed a model-based cost-effectiveness analysis of 4 screening strategies to predict patient’s protection against tetanus with conditional post-exposure prophylaxis in unprotected patients: medical interview relying on the history of tetanus immunizations (STANDARD, ALL); systematic use of Quick Diagnostic Test® of higher sensitivity (69% vs. 62%) and specificity (98% vs. 79%) than medical interview (QDT, ALL); reserving post-exposure prophylaxis to patients aged 60+, with either QDT (QDT, 60+) or no screening but systematic post-exposure prophylaxis (BOOST, 60+). We relied on published literature to estimate probabilities, and costs were measured from a societal perspective. We simulated the number of tetanus cases, life-years gained, and costs for all 1,200,000 French adults seeking emergency care for a wound in 2010.

The number of tetanus cases was: 1.69 (STANDARD, ALL), 1.01 (QDT, ALL), 1.09 (QDT, 60+), and 0.10 (BOOST, 60+). As compared to standard practice incurring a total cost of 78.2 m€ (STANDARD, ALL), systematic use of QDT was more expensive at 80.1 m€ (QDT, ALL). In contrast, targeting post-exposure prophylaxis to patients 60+ was cheaper at 67.3 m€ (QDT, 60+) and 71.8 m€ (SYST, 60+). Accordingly, (QDT, 60+) provided the best value for money; (SYST, 60+) had an ICER of 1.5 m€ per LY gained as compared to (QDT, 60+); and continuing post-exposure prophylaxis was dominated. Results were robust in sensitivity analyses. At an implausible QDT sensitivity of 100%, (QDT, ALL) would save 7.3 m€ as compared to (STANDARD, ALL), but still cost 4.3 m€ more than (QDT, 60+) for 0.16 LY gained.

In conclusion, while QDT is more accurate than medical interview to predict patient’s protection against tetanus, reserving post-exposure prophylaxis to patients 60+ may provide the best value for money.
NON-HEALTHCARE COSTS ASSOCIATED WITH STROKE – A REVIEW OF THE LITERATURE

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Objective:
Several jurisdictions around the world require a societal perspective in the economic evaluation of treatment strategies. For treatment strategies in the cardiovascular field this implies that non-healthcare costs associated with stroke need to be included in the analysis. The objective of this work was to systematically review and compile the literature on costs of home care, nursing home, productivity loss and informal care in patients with stroke.

Methods:
We searched MEDLINE and EMBASE until April 2012 using relevant cardiovascular and cost keywords using Boolean logic. Abstracts and full text articles were reviewed for relevance to the following eligibility criteria: population of interest; (Stroke patients in Western Europe countries, North America or Australia); study design of interest (cost studies); outcomes of interest (mean annual cost per patient). Mean annual costs per patient, adjusted to 2010 price level, were then summarized and reported in Euros (EUR).

Results:
The search yielded 87 citations of which 12 studies fulfilled the inclusion criteria for this review. In patients with stroke, mean annual home care costs were reported in 8 studies and ranged from EUR156 to 5,902; mean annual nursing home costs were reported in 9 studies and ranged from EUR696 to EUR25,883; mean annual costs of productivity loss were reported in 3 studies and ranged from EUR935 to EUR28,633; and mean annual costs of informal care were reported in 8 studies and ranged from EUR608 to EUR25,846. The reported non-healthcare costs varied extensively between the identified studies, mainly due to different methods applied and heterogeneity in investigated study populations. This variation may contribute to an additional layer of uncertainty in economic evaluation of treatment strategies in stroke with a societal perspective.

Conclusion:
The literature review suggests high non-healthcare costs due to stroke. The reported mean costs vary extensively between the studies, and the choice of which source to apply may have implications for the economic evaluation of treatment strategies in stroke with a societal perspective.
COST-EFFECTIVENESS OF PNEUMOCOCCAL VACCINE IN LATIN AMERICAN AND CARIBBEAN COUNTRIES TO SUPPORT DECISION-MAKING AND TRANSFERABILITY OF RESULTS

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Background:
Cost-effectiveness models have been developed for pneumococcal conjugate vaccine assessment in Latin American and Caribbean (LAC) countries. A generalized model—the ProVac Initiative’s TRIVAC model—has been used in 8 countries. Generalized models such as TRIVAC require country support for parameter development. We undertook this set of analyses to exemplify parameter development at country level for estimation of pneumococcal conjugate vaccine cost-effectiveness in LAC countries.

Methods:
A proportional mortality decision-tree excel-based model was adapted from a previously published model to estimate cost-effectiveness of pneumococcal vaccine in LAC. Results are based on the 2004 cohort of under-five children for each country. Vaccine efficacy of overall under-five deaths was estimated for each country based on randomized controlled trial data. Costs were abstracted from WHO-CHOICE. Burden of disease parameters were taken from World Bank and Pan American Health Organization published estimates. A discount rate of 3% and third payer perspective were taken.

Results:
Of 35 LAC countries, 30 had data to perform cost-effectiveness analyses: Argentina ($7,216), Bahamas ($2,996), Barbados ($6,168), Belize ($1,537), Bolivia ($191), Brazil ($978), Chile ($7,677), Colombia ($1,931), Costa Rica ($6,488), Cuba ($16,207), Dominican Republic ($1,142), Ecuador ($1,031), El Salvador ($1,667), Grenada ($3,598), Guatemala ($532), Guyana ($335), Haiti ($93), Honduras ($618), Jamaica ($699), Mexico ($1,658), Nicaragua ($631), Panama ($1,564), Paraguay ($1,078), Peru ($721), Saint Lucia ($3,503), Saint Vincent and the Grenadines ($1,454), Suriname ($946), Trinidad and Tobago ($557), Uruguay ($3,537), and Venezuela ($1,415). Overall cost per life-year gained would be USD$915. Willingness-to-pay (per capita Gross Domestic Product) in LAC would be USD$8,096 in 2004.

Conclusions:
These results may be used as guide for the introduction of the 10 and 13-valent pneumococcal vaccine in LAC. Despite model limitations and parameter uncertainty the results suggest the introduction of the pneumococcal vaccine is cost-effective. These base-results, along with other models and results, may provide support in low and middle income countries who need evidence to support vaccine introduction decisions.
Background:
Delivering information on medication risk in the most appropriate format is important to support individuals in their treatment decisions.

Aims:
To determine what kind of information patients prefer when being explained side effects from medication and whether preferences are correlated to demographic characteristics.

Methods:
A cohort of patients having experienced pain in the previous 12 months was recruited from Primary Care to take part in a discrete choice experiment in form of a postal survey. The probability of suffering serious side effects from a non-steroidal anti-inflammatory drug (NSAID) was expressed in different ways: verbally (captured in words), numerically (captured in numbers) and visually (captured in icons, graphs or colours). Sets of risk information were presented in both high and low risk scenarios, and patients were asked to select the most appropriate information of each pair. Presuming that respondents choose the information that would provide them with the highest benefit and assuming a linear utility function, patient utility of risk information was analysed via regression techniques. The inclusion of interaction terms into the regression model aimed to determine the impact of patient characteristics on preferences.

Results:
36 out of 2000 patients (32%) completed the postal survey. The risk level clearly determined patients’ preferences for risk information. In the low risk scenario, numeric risk presentation achieved the highest utility (number needed to harm, p<0.05), whereas verbal statements scored lowest. In the high risk scenario, overall utility was less evident. Income, education and household size had a statistically significant impact on the choice of information, which was not the case for age and gender.

Conclusion:
Preferences for risk information are both associated with patient characteristics and the level of risk presented. This emphasises the necessity to offer patients a wide spectrum of risk information. Whether the results of this study are transferable to adverse effects of other medication will need to be established further.
OFFERING PATIENTS CHOICES: A PILOT STUDY OF INTERACTIONS IN A NEUROLOGY CLINIC

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Background:
Offering patients choice about treatment options is part of the evidence based guidance for high-quality care; and there is evidence that shared decision making brings a range of physical and psychological benefits to patients (Crawford et al., 2002). However, observational studies have found low levels of patient participation in decision making (Ford et al., 2006; Stevenson et al., 2001) and a study of treatment decisions in epilepsy found that the decision making process was perceived to be clinician dominated (McCorry et al., 2009).

Methods:
In this pilot study, we explore consultations in one outpatient neurology clinic in the UK using the qualitative method of conversation analysis. This method involves using audio- and video-recordings of naturally occurring interactions, to enable direct observation of real-life consultations and detailed analysis of communication strategies and their consequences.

Results:
We show that in all of the recorded consultations, the clinician offered some form of choice to patients - in eight cases the clinician proposed a course of action (to be accepted or rejected by the patient) and in five the clinician offered a “menu” of options. However, our analysis shows that although explicitly listing a “menu” of options appears to be an approach that offers more choice than proposing a single course of action for acceptance or rejection, the way in which a “menu” of options was offered showed substantial variability. In this presentation we suggest that using the “machinery” of providing a menu does not, in itself, ensure that the patient is offered a fully open choice. Rather, the choices offered may vary in openness, depending on how the individual options are presented; it is possible to use the “machinery” of a menu-based approach in such a way that the outcome is akin to a recommendation for a particular option. Conversely, the absence of explicit choice doesn’t mean the neurologist hasn’t taken the patient’s preferences into account.

Conclusions:
We conclude that future research, which involves close linguistic and interactional analyses of larger number of consultations, may shed light on why doctors feel they are offering choices, but patients report that the decision was clinician dominated. It may be that, having used a menu based approach, doctors perceive themselves to have offered the patient “choice,” whereas the patient may - sometimes quite correctly - perceive the way in which the doctor produces the options as constraining.
References:
ESTIMATION OF QUALITY-ADJUSTED SURVIVAL OF MILD OBSTRUCTIVE SLEEP APNOEA PATIENTS WITH SIX QUALITY OF LIFE (QOL) ASSESSMENTS: COMPARISON BETWEEN TRAPEZOID RULE, CROSS-SECTIONAL AND MIXED MODEL ESTIMATES


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Background:
In randomized clinical trials (RCT), quality-adjusted life-years (QALY) are commonly estimated as area under curves without explicit heterogeneity consideration. A RCT comparing outcomes in patients with mild obstructive sleep apnoea receiving lifestyle intervention with very low calorie diet (VLCD) or without VLCD (conventional) was performed in Kuopio University Hospital, Kuopio, Finland.

Objective and methods:
To compare QALYs in the VLCD and conventional groups (N=77) using four approaches.

Methods:
First, QALYs were estimated based on the EQ-5D measurements (UK tariff) at 0, 3, 6, 12, 18 and 24 months using trapezoid rule. Second, the patient-level QoL measurement time variability was taken into account. Third, cross-sectional population-averaged generalized estimation equations (GEE) were built. Fourth, individual-specific effect models with random slopes (mixed models) were done. For the comparison, analytical time-frame was adjusted to two years and discounting was ignored.

Results:
Trapezoid-based QALYs were 1.845 (1.848) for VLCD and 1.818 (1.819) for conventional group when ignoring (taking into account) the QoL measurement time differences. When heterogeneity and QoL measurement time variability at cross-sectional (individual level) were accounted for, QALYs were 1.811 (1.791) for VLCD and 1.774 (1.760) for conventional group.

Conclusions:
Quality-adjusted survival estimates can be impacted by between-group and between-individual heterogeneity even in the RCT setting. Mixed models can capture more heterogeneity in comparison to QALY estimation based on cross-sectional or trapezium rules.

*References:
COMPARISON OF EQ-5D- AND 15D-BASED QUALITY-ADJUSTED LIFE-YEARS (QALY) IN PATIENTS WITH MILD OBSTRUCTIVE SLEEP APNOEA USING MIXED MODELLING: MEASUREMENT TOOL AND TARIFF MATTER

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Background:
Various generic quality of life (QoL) tools can be used to estimate quality-adjusted survival as QALYs. However, only few QoL tool comparisons have included individual-specific time-dependent modelling or different country-specific preferences (tariff values).

Objective and methods:
To compare QALYs based on EQ-5D and 15D.

Methods:
A randomized controlled trial (RCT*) with six EQ-5D and 15D measurements in patients with mild obstructive sleep apnoea (N=77) was performed in Kuopio University Hospital, Kuopio, Finland. In the RCT, lifestyle intervention with very low calorie diet (VLCD) was compared to lifestyle intervention without VLCD (conventional). Individual-specific time-dependent (QoL, body mass index) mixed models with patient-level covariates (gender, intervention) and random slopes (measurements) were done to assess the QALYs based on EQ-5D (Finnish or UK tariff) and Finnish 15D. For the comparison, time-frame was adjusted to two years and discounting was ignored.

Results:
15D- and EQ-5D-based (Finnish tariff) QALYs were correspondent (1.776 and 1.777 for VLCD, and 1.721 and 1.738 for conventional, respectively). EQ-5D based QALYs with UK tariff (1.791 for VLCD and 1.760 for conventional) differed significantly (p<0.01) from both Finnish values. The QALY difference between the groups was insignificant based on EQ-5D with UK tariff and significant based on both Finnish results (15D p<0.01, EQ-5D p<0.05).

Conclusions:
The scale and significance of QALY estimates were impacted by tariff values and QoL tool. EQ-5D with UK tariff can significantly underestimate QALYs in the Finnish setting.

*References:
QUALITATIVE ANALYSIS OF AMOUNT AND NATURE OF INTERVIEWER HELP ANSWERING THE TTO
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Objectives:
The TTO is seen as one of the most important direct utility measurements in cost-utility analyses. Although obtaining utilities with TTO is challenging and interviewer help seems required, the use of web-based TTO measurements without interviewer help is increasing. Studies obtaining web-based TTO utilities, however, report up to 42% drop-outs and 49% illogical responses. The aim of this study was to get insight into the importance of the interviewer help with the aim of improving internet-based elicitation. We examined the amount and nature of interviewer help in face-to-face interviews.

Method:
A random selection from available audio-taped interviews among students and public (45), patients (127), partners of patients (70) and public (65) were transcribed and coded. All respondents rated six EQ-5D health states on a TTO. Patients also rated their own health, partners rated their partners’ health, and the public rated a detailed health description. The sample of students and public started with an example TTO. Two independent raters experienced in utility assessment double-coded the transcripts. Judges used a priori and inductive coding, discrepancies were resolved through discussion and review of the transcripts. Transcribing and coding continued until saturation was reached.

Results:
In total 91 interviews were coded, 22 of students and public, 24 of patients, 22 of partners, and 22 of the public. Codings were grouped into three categories: ‘TTO is not correctly understood’, e.g., participant wonders if the health state remains constant over time (N=69, 76%); ‘Negative reactions towards the TTO’, e.g., the TTO is not asking realistic questions (N=39, 43%); and ‘EQ-5D health state description is unclear’, e.g., uncertainty about what is meant by ‘other complaints’ (N = 50, 55%). Post hoc chi-square test showed that most help was reported among patients and least help among students (chi-square (3) = 22, p < 0.001).

Conclusions:
Overall 86% of the participants needed interviewer help at least once when rating health states on a TTO. Help such as from an interviewer seems necessary especially when health state utilities are retrieved from patients. Internet-based elicitation needs improvement by incorporating help as from an interviewer
SIMULATING PHARMACOKINETICS USING COMPARTMENT MODELS TO ASSESS THE BEST TIME FOR FOLLOW-UP MEDICATION WITH INFLIXIMAB

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Purpose:
Treatment of inflammatory bowel disease with the intravenously administered biologic infliximab is highly efficacious, but expensive. Application is currently performed according to a standardized regimen irrespective of the individual pharmacokinetic profile of a patient. Ideally, timing of administration could be adapted to the actual serum concentration of the drug which should not fall below a certain threshold level. Thus, calculating the optimal time for the next infusion may further improve the outcome of the treatment.

Methods:
A clearance model for infliximab already exists. We aimed to adapt and extend this model by use of a multi-dimensional optimization strategy and inclusion of further patient characteristics. The model consists of a central and a peripheral compartment. The fluid kinetics are determined by the amount of infliximab in the two compartments, infusion strategy, exchange transports and elimination process. The flows are weighted by additional parameters like weight, sex, baseline albumin and ATI status of the patient. The applicability of the standard model was analysed for 100 patients with Crohn’s disease. Afterwards, we performed parameter identification to optimize the model for a specific test sample. Due to the lack of enough measure points the corresponding equations for parameter identification for single patients are underdetermined, that is why multi-dimensional optimization algorithms have to be used.

Results:
Optimizing the model with data from many patients leads to a significantly reduction of variance of calculated to actual concentration of the substance in the bloodstream without increasing overestimation of the real concentration, which is good provided that declining under a threshold makes the treatment less likely efficacious.

Conclusion:
Dynamic compartment models can be used to simulate blood kinetics in humans. Simulating elimination of infliximab in human blood helps deciding when the next dose should be administered and therefore may lead to more beneficial outcomes both safety- and efficacy-wise.
THE ECONOMIC BURDEN OF PREMATURITY IN THE UNITED KINGDOM AND CANADA


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Background:
Preterm birth, before the completion of 37 weeks gestation (wGA), is a risk factor for morbidity and mortality among infants worldwide, and imposes considerable burden on health, education and social services, and on families and caregivers. Morbidity and mortality resulting from preterm birth is highest among early (<28 wGA) and moderate (28-32 wGA) preterm infants, relative to late preterm infants (33-36 wGA). However, substantial societal burden is associated with late prematurity due to the larger number of late preterm infants. The aim in this study was to characterize burden of premature birth until age ten, including resource utilization, direct medical costs, parental out-of-pocket costs, education costs, and mortality.

Methods:
Study objectives were addressed using two complementary methods: an economic decision model for the UK, and analysis of an administrative, population-based database in Québec, Canada. The decision model consisted of linking of epidemiological parameters describing mortality and disability trajectories over the first two years of life with a Markov model projecting transitions over time and across health states defined by level of physical and mental disability. For the Québec administrative analysis, summary statistics describing mortality and resource utilization until age ten were calculated directly using empirical data.

Results:
Within the UK decision model, ten-year costs-per-infant were highest for early preterms at £108,560, compared to £65,130 per late preterm infants. However, total societal costs were more than six-fold higher for late preterms due to the larger population size. In the Québec analysis of 8,474 preterms born during 1996-1997, similar trends were observed, with greater resource utilization consistently observed in early and moderate preterms. In particular, average intensive-care hospital days in Quebec ranged from 1.3 days for late preterms to 19.7 days for early preterms. Mortality was consistently highest early in life, and substantially higher for early preterms.

Conclusion:
UK and Canadian analyses of the burden of premature birth indicated similar trends. Resource utilization by individual infants was greatest for early preterms, while total utilization for the entire population was greatest for late preterms. Interventions to delay and prevent preterm birth have the potential to prevent morbidity, mortality, and societal economic burden.
EFFECTIVENESS OF THE HOSPITAL ACQUIRED INFECTION CONTROL PROGRAM IN INTENSIVE CARE UNITS

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Aim:
Nosocomial, or hospital-acquired, infections are the most common complications affecting hospitalized patients. Many studies performed to estimate increased hospital stay and related costs attributable. In recent years many programs has been developed to control hospital-acquired infections in Iran. The aim of this study is to assess the effectiveness of these programs, which established in Intensive Care Units (ICUs) in a hospital in 2011.

Method:
An outcome research was used to assess the effectiveness of the Hospital Infection Control Program in two ICUs of an acute hospital in Tehran. Two checklists and one questionnaire were developed to collect data about structure (staff training, hospital facilities and budget…), process (performance of personnel, guidelines and rules…) and outcomes of the program (the hospital infection rate). Three researchers observed staff performances of two ICUs and assessed (patient profiles and other documents about guidelines, costs…) for three months.

Results:
During three months, performances of 31 personnel (physicians, nurses, and assistants) in ICUs were observed three times (by three different observers) and all documents for infection control programs were assessed. Findings showed that there were significant differences between cost of infection control programs (p=0.01), hospital facilities (p=0.04), staff performance (p=0.03) and the hospital infection rate (p<0.05).

Conclusion:
This study revealed that the worth of infection control program which established in the hospital succeed to reduced the rate of infection among patients in ICUs.

Key words:
Hospital acquired infection; Intensive Care Unit; Program effectiveness
ADVERSE LIFESTYLE EFFECTS OF COLORECTAL CANCER SCREENING. DOES THE INCIDENCE OF SELECTED LIFESTYLE-RELATED CoMORBIDITIES CHANGE DEPENDING UPON A SCREENING OUTCOME?

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Cost-effectiveness analyses of health care interventions are now demanded as a fundamental piece of information for governmental decisions. One possible consequence of screening is the risk of participant’s misinterpretation of the screening result, specifically the Health Certificate Effect (HCE). The HCE implies that a screening participant’s lifestyle behavior is affected by the findings (test results) at the screening. One argument is that participants with a negative finding could have a negative change in lifestyle. Such a change in lifestyle is likely to affect the risk of lifestyle-related diseases and the need for health care services. The study aim is to examine whether a screening result could change the amount of health care services used in five different lifestyle related diseases.

The data contained information about 100,000 individuals from the NORCCAP screening (RCT from 1999 to 2001). The individuals were divided in groups according to screening status: Control group, non-participants, excluded, participants with colorectal cancer, participants with a positive test (not cancer) and participants with a negative test. The screening information were merge with information from 1998 to 2004 on treatment and diagnosis from Norwegian Patient Register, time and cause of death and socio demographic variables from Statistics Norway. Five lifestyle-related disease groups were identified (diabetes mellitus, hypertension and secondary hypertension, chronic obstructive pulmonary disease, angina pectoris, acute myocardial infarction). Risk adjustments were included by looking at the need for lifestyle-related health care services before the screening. A logistic panel regression model was used to study the effect of health care usage according to screening outcome in each of the lifestyle-related disease.

Preliminary findings indicate that screening results appear to change the incidence of lifestyle related diseases, for instance screening participants who had a negative test result had an increased probability of requiring outpatient care for complications relating to Diabetes Mellitus and Hypertension. However not all the results could be explained by the Health Certificate Effect.

Attention must be paid to the effects of screening on screening outcomes when evaluating a mass-screening program. This study has demonstrated that screening results can change the risk of requiring care for other lifestyle-related diseases.
COST-EFFECTIVENESS OF ADHERENCE INTERVENTIONS FOR ANTIRETROVIRAL THERAPY IN HIV-INFECTED PATIENTS – A SYSTEMATIC REVIEW
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Background:
Adherence is one of the main factors for a successful therapy. It is especially a crucial aspect with respect to the highly active antiretroviral therapy (HAART) for HIV. However, many HIV-infected patients adhere less due to their oftentimes difficult living conditions. Several studies have shown that adherence interventions have the potential to save costs. Nevertheless, the impact of adherence on cost-effectiveness is often misjudged.

The objective of this systematic review was to evaluate the cost-effectiveness of adherence interventions for HAART in HIV-infected patients.

Methods:
A systematic search for comparative health economic studies was conducted in the following databases: EMBASE, MEDLINE, NHS Economic Evaluation Database, CINAHL and EconLit. The identified publications were selected by two reviewers independently according to predefined inclusion and exclusion criteria. Further, these were evaluated by using the instrument for assessing economic studies provided by the Ludwig Boltzmann Institute (LBI) in Austria and finally extracted, analyzed and summarized.

Results:
The search resulted in a total of 959 hits. After reviewing the abstracts and full-texts four relevant studies were identified involving cost-effectiveness-analyses. A critical aspect to be considered was particularly the poor transparency of the cost data. Different educational programmes were compared as well as the Directly Observed Therapy (DOT), an intervention in which the pharmaceutical treatment is dispensed in the presence of a health care professional, compared with standard care.

In three cost-effectiveness-analyses the costs per QALY in the baseline scenario were each under 15,000$ (US). The sensitivity analyses with a presumed maximum threshold of 50,000$/QALY show a predominantly cost-effective result. In one study that examined DOT the costs add up to over 150,000$/QALY.

Conclusion:
The quality of the included studies is deficient and only a few of the possible adherence interventions are regarded. Thus, the cost-effectiveness of adherence interventions in general cannot be finally judged. Further, a conclusion cannot be made regarding which factors might contribute to the cost-effectiveness. Moreover, modelling should be conducted based on high-quality and transparent data and further adherence interventions need to be taken into account.
IMPROVING VALUATION SAMPLING OF EUROQOL EQ-5D HEALTH STATES

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Background:
The valuation exercise leading to the UK EQ-5D time trade-off (TTO) social tariff of health states, employed a sampling scheme involving 43 health states using data gathered from a sample of the general UK population. Dolan (1997) described issues considered when selecting these states as follows: “In choosing the states both for use in the study itself and for each respondent, the most important consideration was that they should be spread widely over the valuation space so as to include as many combinations of levels across the five dimensions as possible. This was subject to the constraint that the states were likely to be considered plausible by respondents.” Dolan did not suggest explicit criteria for assessing the adequacy of health state subsets for determining weightings, either for the coverage of the valuation space, or for plausibility.

Aims:
In applying the MVH paradigm in several non-UK settings, the originally selected 43 states were modified or reduced for practicality and local convenience, but was not reassessed against clearly defined objectives and measurable criteria. The aim of this study is to define such objectives and criteria, and illustrate how they may be applied to identify more relevant and efficient sampling schemes.

Method:
Three quantifiable criteria were identified: plausibility/relevance of states, full and balanced severity coverage, maximising direct valuation of 'adjacent' states. Four sampling schemes from valuation studies in seven countries were compared using these criteria.

Findings:
Schemes showed performance differences; the Danish study used the largest number of health states and gave better performance. An alternative pattern of states was developed which showed superior performance on all measures.

Implications for future valuation studies:
Future valuation exercises framed in this way may offer benefits in terms of greater precision, avoidance of bias in favour of less severe states, and a higher proportion of research observations valued directly rather than through extrapolation modelling.

Reference:
Dolan P. 1997 Modeling valuations for EuroQol health states. Medical Care 35: 1095-1108
INTENTION TO SCREEN USING PRIMARY HUMAN PAPILLOMAVIRUS (HPV) TESTING: A RANDOMIZED SURVEY OF NORWEGIAN WOMEN

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Background:
Several countries are considering replacing cytology (Pap smear) with human papillomavirus (HPV) testing for primary screening of cervical cancer. Whether explicitly testing for a sexually transmitted infection (STI) will impact screening adherence is not known. We hypothesized that inviting women to HPV testing may influence a woman’s intent to participate in screening and follow-up testing due to stigma, anxiety or underestimation of personal risk of STIs.

Methods:
We used a web-based questionnaire to randomize a representative sample of Norwegian women to one of three invitation letters according to conventional practice (i.e., triennial Pap smear screening) or one of two versions of an invitation to HPV testing with varying degrees of information about HPV infections. Study endpoints included intention to participate in the initial screening test (measured as binary response and on a Likert scale), anxiety level, correct interpretation of a positive test and whether women intend to follow-up on a positive result. The study was powered to detect a 4% difference in proportions (≈1090 in each group). Differences between groups were tested using chi-squared and nonparametric Kruskal-Wallis.

Results:
The survey sample consisted of 3540 women and was representative of the Norwegian population with respect to age, civil status and geographic location, although educated women were slightly overrepresented. No significant difference across invitation letters was found in women’s intent to participate in screening (range 91.8-92.3%), their anxiety level (p=0.184) or inclination to follow-up on an abnormal result (97.1-97.6%). When intention to participate was measured on a Likert scale, intent to participate in the HPV program was only marginally lower, albeit significant (p=0.008). After being told to imagine they had a positive result, only 36-40 % of respondents in the HPV invitations understood that they likely had an STI, 3% were certain of STI positivity.

Conclusion:
Results indicated that there may be only a small impact on stated intent to participate in screening using HPV testing. Results were not affected by the level of information provided on the HPV screening invitation. However, women lacked the proper interpretation of their HPV-test result which may impact willingness to participate and level of anxiety.
SYSTEMATIC REVIEW OF HEALTH PROGRAMS FOR ELDERLY PEOPLE
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Introduction:
The 2000 IBGE Census estimates that the elderly population in Brazil represents a contingent of nearly 15 million people, representing 8.6\% of the population. These seniors are concentrated in large cities. The elderly over 75 years was the stratum of the population with the highest growth and increased 49.3\% over the past 10 years.

Objective:
Search and evaluate studies of efficacy and effectiveness of health interventions program for elderly people.

Methods:
We performed a systematic review on Medline, The Cochrane Library and Lilacs. Two reviewers selected the articles by titles, abstracts, full text.

Search strategy:

Results:
The search returned 833 titles. We selected 386 abstracts and 373 full texts. 72studies had the interventions described and 15 were included in the metanalysis. Most of the studies were excluded because they were only descriptive. Most of the interventions focus on active aging and physical activity and the prevention/ promotion activity. The studies that were included on the metanalysis analyzed more frequent 3 outcomes: mortality, elective hospitalization and anti-Pneumococcal vaccination. There was no significant impact on mortality. There was no significant impact on elective hospitalization. Was observed a higher pneumococcal vaccination uptake in the group that received HRA-O program, being greater adherence in women than in men.

Conclusion:
The group that received the HRA-O program showed a higher pneumococcal vaccination uptake. Health public programs didn’t impact in elderly mortality. The outcome hospitalization should be better studied because of the heterogeneity of studies and differences between the intervention and control groups. Studies on effectiveness of the programs require more complex designs. The field of aging needs more studies with adequate methodology.
FROM DOCUMENTATION TO EVIDENCE-BASED MEDICINE. HOW OVER 50 YEARS OF COLLECTING PATIENT INFORMATION BY THE AO HAS IMPACTED ON THE WORLDWIDE TREATMENT OF FRACTURES
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"Our effort to document our patient case studies was the start for evidence based medicine"

Maurice E. Müller
SICOT Surgeon of the Century and an AO Founding Father

Introduction:
The Arbeitsgemeinschaft für Osteosynthesefragen (AO) was founded in 1958 in Biel, Switzerland, by a group of 13 young surgeons who wanted to investigate the possibilities of internal fixation for the treatment of fractures, an area they felt was neglected. The wide-ranging consequences of that initial meeting are enjoyed by millions of patients around the world who are still treated according to the (lightly modified) AO Principles of Fracture Fixation and with AO-developed implants and techniques.

Role of documentation:
The AO Documentation Center, founded 1959, played a critical role in collecting the necessary evidence to overcome widespread doubt and resistance among the surgical community. Around 1,000 cases were recorded during the 1st year of operation alone. Despite some incomplete documentation, the data collected proved to be very useful. For example, from 1980-1983 alone, AO documentation helped to answer >300 complex questions and was the basis for >40 publications or dissertations. Today, over 200,000 cases and approximately 1.2 million documented radiographs are housed in the AO Center. It is this unique repository of collected cases which provided the basis in the 1980s for the Müller AO Classification—Long Bone Fractures, a system known and used as standard by surgeons around the world.

Move toward clinical investigation:
However, by the 1990s it was realized that the concept of documentation no longer met contemporary standards and that a reorganization of AO clinical study activities was necessary. AO Clinical Investigation and Documentation (AOCID) was founded in 1999 to conduct studies to proactively answer clinical questions.

Collecting evidence at the AO today:
AOCID is currently involved in approximately 50 multicenter, international studies of every type of study design. AOCID has worked with almost 300 different clinics scattered around the globe. In 2011, the >20 peer-reviewed publications, 55 presentations at scientific conferences, and the >400 citations of AOCID work in peer-reviewed publications are testimony to the modern realization of a vision that is over 50 years old.
THE VALIDITY OF HEALTH CARE QUALITY INDICATORS FOR PATIENT DECISION MAKING

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Introduction:
Information on hospital performance is presented as hospital rankings for patient decision making in many countries in Europe and the US these days. However, there are concerns about the validity of currently used performance indicators and the quality of the databases used to calculate these indicators. Registration differences, such as including different patient populations and using different definitions can cause huge differences in outcome of interest. And consequences can be large, for example when used for patient decision making. In this study we investigate the data quality and construct validity of two indicator sets used for quality measurement in the Netherlands.

Methods:
We investigated three national databases (one including administrative hospital data on patient level (A), one including administrative hospital aggregated on a hospital level (B), and one including data on patient experience on patient level (C)) from which indicator sets on hip/knee replacement and breast cancer treatment are calculated. Data were available for the years 2008 and 2009. In a first step the denominators of matching hospitals were compared between the two administrative datasets (A and B). In a second step the hospital scores of an indicator available in both one administrative database (B) and the patients experience data (C), were compared.

Results:
The data base filling improved in all three dataset in database A and B from 2008 to 2009, seen back by the number of the number of delivering hospitals, the number of registered patients and the number of hospitals possible to match (for breast cancer 32 hospitals in 2008 to 41 hospitals in 2009, for hip replacement from 40 hospitals to 50 hospitals and for knee replacement from 36 hospitals to 53 hospitals). However, when looking at the data quality by comparing the denominators between databases A and B, no improvement in agreement of denominators can be observed from 2008 to 2009 (Breast cancer denominator difference 2008: 1747, 2009:2327, hip replacement 2008: 23, 2009:732, Knee replacement 2008: 1285, 2009:1523). Database C, the patient experience database, was poorly filled. When comparing database B and C, which included two identical breast cancer indicators, correlations were low to modest; (% of patients experiencing left over tissue after breast cancer operation, correlation coefficient 0.474, p=0.000) (% of patients being operated within 4 weeks after test result, correlation coefficient 0.183, p=0.124).

Discussion:
Two main conclusions can be drawn from our data. The data filling improved from 2008 to 2009. However, the data must be regarded with caution when aiming to calculate quality indicators and further use that information for decision making since the data quality did not improve. We can therefore not conclude that construct validity of those indicators is sufficient to inform patients. Further work need to be undertaken to investigate data quality and identify sources of disagreement.
HEALTH RELATED QUALITY OF LIFE IN PEOPLE WITH DIABETES IN SCOTLAND: A FEASIBILITY STUDY
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Background:
Quality of life data in people with diabetes allows research into the predictors of patient health status, and the cost-effectiveness of treatment and preventative strategies. Our aim was to assess the feasibility of routinely collecting EQ-5D data in people with diabetes.

Methods:
Machine-readable EQ-5D questionnaires were developed and printed. Over the course of 11 sessions between 3rd November 2011 to 24th December 2011, patients in the Diabetes Centre, New Stobhill Hospital, Glasgow were asked to complete EQ-5D questionnaire. Reasons for refusal were recorded. A further 10 questionnaires were issued to a primary care practice (Gardner Street, Glasgow). The EQ-5Q score was calculated for completed questionnaires.

Results:
In the secondary care clinical setting, 252 patients were asked to complete an EQ-5D questionnaire while waiting for their appointment. While the nurses were present, a total of 55 patients did not attend for their appointments. Of those asked, 221 (88%) completed their questionnaires, 19 (7%) returned incomplete questionnaires and 14 (5%) refused to answer. Main reasons for refusal were inability to read the print due to poor eyesight or inability to read English. Only 8 completed questionnaires were returned from primary care. For the completed questionnaires, the average score was 0.59 (sd 0.36) for males and 0.54 (sd 0.39) for females.

Discussion:
In secondary care, the research nurses found that the majority of patients were happy to complete the questionnaire, with only 1 or 2 minutes required to complete it. Those unable to read the form had the question read out, but some felt that the questions were too personal to answer in front of other patients. Due to lack of responses it may not be feasible to collect EQ-5D in primary care. However, collection of EQ-5D information is feasible within diabetes clinics in Scotland. The use of multiple language questionnaires and perhaps questionnaires on electronic formats may aid in the collection of quality of life data.
CAN IDI AND NRI BE TRUSTED?

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IDI and NRI are statistics proposed as measures of the incremental prognostic impact that a new biomarker will have when added to an existing prediction model for a binary outcome. Both measures are intuitively plausible. We shall argue, however, that their popularity is undeserved. If IDI or NRI is used to measure prognostic power, a given prediction rule can be “improved” simply by making its predictions more extreme: the largest increase in IDI and NRI is obtained when predicted risks above the prevalence (average risk) are increased to 100% and predicted risks below are replaced with 0%.

The implications are not pleasant. When IDI or NRI are used to optimize decision making, good performance can be faked:
- A cheater can beat the best probabilistic model.
- Spurious results may arise when risks, instead of being well calibrated, are overconfident, exaggerating the probability of the probable and the improbability of the improbable.
- Simply by exploiting knowledge of the assessment measure a poor prognostician can outperform a good prognostician.

We illustrate the magnitude of this bias for a breast cancer model which predicts response to chemotherapy based on five markers. For example, the IDI of a new model which introduced an additional (real) measurement was 0.019, whereas an artificial new model which enforces 100% or 0% predictions as just described achieves an IDI of 0.19.

Instead we recommend the use of proper scoring rules (PSRs). The main property of a PSR is this:
- Good performance cannot be faked.
- It pays for a diagnostician or prognostician to strive to fully use the data at hand and to honestly report his assessment.
- A poor prognostician cannot, by exploiting his knowledge of the scoring machinery, outperform a better one.

Ideally, clinical innovations should be rated in human utility terms. New information sources, in particular, should be valued in terms of the clinical benefit that is expected to accrue from optimal use of the enlarged body of information (Value-of-Information statistics). Such statistics, in fact, are PSRs. Being fakable, IDI is not a PSR, so there exists no decision scenario – not even an artificial one – that has IDI as its utility criterion.
ASSESSMENT OF CHRONIC MYELOID LEUKEMIA PATIENT QUALITY OF LIFE USING THE EQ-5D – A PILOT STUDY IN INNSBRUCK, AUSTRIA

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Background:
Chronic Myeloid Leukemia (CML) is a progressive, largely fatal cancer. However, due to new medications such as imatinib, patients’ life expectancy has dramatically increased (Garcia-Manero, 2003, Deininger, 2008). Therefore, the assessment of patients’ quality of life (QoL) and patient preferences becomes an increasingly important issue for the lifelong treatment of CML. QoL may, for example, depend on different treatment strategies and national practice patterns. Few studies have investigated CML patients’ QoL. The aim of our study is to assess the QoL of, and derive utility values for, CML registry patients in Innsbruck, Austria.

Methods:
Patients with CML are currently completing the Euro Quality of Life-5 Dimensions (EQ-5D) descriptive system and EQ visual analogue scale (EQ-VAS) on a tablet PC. The survey will be administered once per patient. Inclusion criteria for the study include: a prior diagnosis of CML, fluency in the German language, age between 18 and 80 years and an expected survival time of at least three months. The analysis will include descriptive statistics of the sample population and derivation of a utility value for each patient. In addition, we will conduct subgroup evaluations for different stages of the disease and different treatment strategies.

Results:
Data collection started in November 2011 and will end in early April 2012. Results will be available in late April 2012. Utility values derived from the EQ-5D will serve as indicators for patients’ QoL. These utility values can be used, for example, to calculate quality-adjusted life years (QALYs), which are commonly used in health economic evaluations, such as cost-utility analyses. It is expected that the patients’ QoL differ depending on the treatment strategy as well as on the stage of the disease. Our results will
then be compared to studies evaluating QoL in other national health care contexts.

**Outlook:**
It is important for clinicians and health policy decision makers to not only consider mortality reduction of different treatment strategies but also consider the patients’ QoL and patient preferences in a standardized and systematic way to optimize patient care.
CAN THE MASS SCREENING OF HELICOBACTER PYLORI INFECTION BE ACCEPTABLE SOCIO-ECONOMICALLY FOR THE PREVENTION OF GASTRIC CANCER?

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Background:
The gastric cancer is one of most common cancers in Japan. Helicobacter pylori infection is associated with gastric cancer, and high prevalence of H. pylori infection is observed among middle-aged Japanese. For this reason, H. pylori eradication treatment might reduce the risk for gastric cancer. It is necessary to evaluate the H. pylori eradication strategy from the economical viewpoint, in addition to the clinical viewpoint whether mortality of gastric cancer would be improved.

Methods:
Using vital statistics of Ministry of Health, Labor and Welfare, patient survey, basic survey on wage structure, point list of payment for medical services and so on, we conducted the cost benefit analysis. The cost is the expense of mass screening and eradication treatment. The benefit is the sum of treatment fee for gastric cancer associated with H. pylori infection, the monetary value of the time and activities lost due to disease and the future loss of earnings caused by premature death.

Results:
Assuming that the youth from 16 to 39 years old is set as the target of screening and that the screening rate and the rate of eradication treatment are 30% and 60% respectively, the cost amounted to €740 million. On the other hand, the benefit is €699 million (treatment fee: €82 million, loss of economic productivity: €617 million). Therefore, the cost benefit ratio of the H. pylori screening is considered to be about one.

Conclusions:
When the screening rate and the rate of eradication treatment are low, the program requires little cost, but it lasts for a long time. When these are high, the cost comes to an enormous total of money, but the program will end over a short period of time.
THE SIGNET PROGRAMME: A MODEL CAPACITY AND CAPABILITY BUILDING INITIATIVE FOR EVIDENCE-INFORMED HEALTH-CARE DECISION-MAKING

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**Background:**
There is great need to practice contextually relevant, evidence-based health-care in Indian health-care systems. Indian researchers have gradually developed skills in producing high quality evidence through systematic reviews. However this capacity did not readily translate to practice because of inability of end-users (as opposed to producers) to appraise and apply the results of systematic reviews. The SIGNET Programme addresses this by training users of evidence (policy-makers, clinicians, nursing personnel, and hospital administrators) to understand and apply the products of research evidence.

**Process:**
The SIGNET Programme is a training-of-trainers initiative to build institutional capacity and capability in evidence-based health-care management through a cascading flow of knowledge and skills transfer. Its key elements include (i)Learning-by-doing approach, (ii)Focus on local context, (iii)Efficient utilization of time and resources, and (iv)Partnership relationship between participating stakeholders.

**Outcomes:**
Sixteen training workshops (480 personnel) and 12 short-term implementation projects have been completed to build and demonstrate individual capacity and institutional capability in evidence-based decision-making. A significant outcome is the acceptance of evidence-based decision-making processes in the participating institutions. Other institution-specific outcomes include initiation of evidence-based (i) health-technology procurement process in one hospital, (ii)strategies to reduce hospital acquired infection, and (iii)systems to streamline pharmacy services. The experiences to date suggest that SIGNET is a highly cost-efficient model that can be implemented in other health-care systems as well.

**Conclusion:**
The SIGNET Programme is a successful model to enhance evidence-based decision-making in the Indian health-care context and can be readily implemented in other resource-limited settings as well.
Background:
Since cancer is a major cause of death with an increasing incidence, new agents are being developed that are targeted at certain disease mechanisms. In combination with predictive markers that indicate the presence of a specific mechanism, targeted therapies often produce an increased treatment success and less adverse events. There are several ways to design trials to evaluate these test-treatment combinations (i.e. companion diagnostics).

Research Question:
A systematic review was performed to identify and characterize randomized controlled trial (RCT) subtypes that can be applied to validate test-treatment strategies in phase III clinical cancer trials. Also, these study designs were assessed for their ability to provide valid results.

Methods:
A systematic literature search of the databases MEDLINE, EMBASE and The Cochrane Library was performed (up to June 2011). A standardized extraction form was used to extract the following data for each identified RCT subtype: questions the design can answer; ethical considerations; influence of marker prevalence, test and treatment properties; internal validity; external validity; and precision

Results:
After literature search and explicit screening process, 22 methodological papers were included. From these, four different prospective RCT subtypes were identified (Enrichment Design, Biomarker-Stratified Design, and two Marker-based Strategy Designs) as well as a retrospective approach. The identified RCT subtypes differed in their research objective, prerequisites concerning test and treatment characteristics, generalizability, feasibility according to ethical demands, and required sample size. Additionally, various design-specific sources of bias and analysis strategies were explored.

Conclusions:
This review provides a detailed overview and assessment of existing RCT subtypes to evaluate test-treatment strategies in oncology. Thereby, it can be used as a basis for further application in terms of evidence-based research in the field of companion diagnostics. Furthermore, these findings provide valuable input for methodological research in terms of trial design and will serve as an input to an HTA framework on personalized cancer medicine.
PREDICTORS OF ANTIRETROVIRAL TREATMENT ASSOCIATED TUBERCULOSIS IN ETHIOPIA: A NESTED CASE CONTROL STUDY

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Background:
Little is known about the predictors of antiretroviral treatment (ART) associated tuberculosis (TB) in developing nations. The objective of this study was to determine predictors of ART associated TB in adults with HIV infection at Jimma University Hospital, Ethiopia.

Methods:
A nested case control study was conducted in October, 2009. The study population consisted of adults with HIV infection (> 14 years) who developed active TB in the first six months of ART initiation and controls that did not develop active TB. Data were collected using a structured and pre-tested questionnaire. Cox proportions hazards analysis was done to determine predictors of ART associated TB.

Results:
A total of 357 patients (119 cases and 238 controls) participated in the study. After six months of follow up, cumulative incidence of ART associated TB was 5.2% (123/2,355). Forty (33.6%) cases were lost to follow up after they developed ART associated TB and 11(9.2%) died. Fifty one (21.4%) controls interrupted ART and 11(4.6%) died. CD4 lymphocyte count increase > 0.5/µl/day [AHR=19.80, 95%CI: 9.52: 41.12, P<0.001], a base-line CD4 lymphocyte count <200 cells/µL [AHR=9.59, 95%CI: 2.36: 39.04, P=0.002], WHO clinical stage 3 or 4 [AHR=3.04, 95%CI: 1.62: 5.69, P<0.001], night sweats during ART initiation [AHR=1.53, 95%CI: 1.06: 2.21, P<0.001] and high ART adherence [AHR=1.30, 95%CI: 1.13: 1.50, P<0.001] were independent predictors of ART associated TB.

Conclusions:
HIV infected adults with a low CD4 lymphocyte count, night sweats for more than two weeks, or in WHO clinical stage 3 or 4 at ART initiation should be cautiously followed for the development of ART associated TB. Good ART adherence and a good immunological response during ART was associated with ART associated TB probably because of an immune reconstitution inflammatory syndrome unmasking the TB.
ECONOMIC ASPECTS OF INTRODUCING FIRST TRIMESTER ULTRASOUND SCREENING IN PREGNANCY
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Background:
As part of prenatal care, a publicly financed routine ultrasound scan is currently offered to all pregnant women in the second trimester. An additional scan in the first trimester has the potential to better detect cases of monochorionic twins, congenital heart defects and Down syndrome. Whether or not the current recommendation should be expanded to include an early scan is currently a heated debate in Norway.

Objectives:
To assess the cost-effectiveness and cost consequences of expanding the screening programme to include a first trimester ultrasound.

Methods:
Based on discussions with clinicians, two options were considered realistic to add on to the current recommendation: ultrasound in the first trimester with nuchal translucency (NT) or combined NT and blood sample. We developed a decision tree that followed pregnancies until a diagnosis was confirmed. Costs were collected from national tariffs and diagnostic accuracy from the systematic review part of this HTA.

Results:
The alternative that maximises the number of detected cases, the first trimester combined test, is likely to be the most cost-effective strategy assuming a willingness to pay per detected case of more than € 51 000. This strategy is likely to double the running costs associated with ultrasound and foetal diagnostics compared to the current recommendation.

Discussion: The actual utilization of ultrasound and foetal diagnostic procedures does however seem to be higher than the levels estimated in the strategies in the model. It is therefore not evident that an expanded public programme will lead to an increase in the running costs associated with ultrasound and foetal diagnostics in Norwegian obstetric care. Implications for the health system/professionals/patients/society: The decision of whether or not to implement early ultrasound rests heavily on other factors besides economics. However, if such a decision is made, our results may contribute to identifying the most efficient strategy.
HOW DOES CONTEXTUAL INFORMATION AFFECT OUR UNDERSTANDING OF NUMERICAL PROBABILITIES?
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Numerical probabilities representing health risks are constantly communicated to the general public. These probabilities are often embedded in contextual information in the form of a narrative or news broadcast. One recent study, using a terrorism forecast scenario, suggests that people will perceive a risk as greater when probability information is communicated along with narrative evidence [1]. However, whether this effect applies in more commonly encountered risk judgment contexts is not known. In this study, we hypothesized that the presence of contextual information in the form of a televised newscast would increase perceived risk of vaccine side effects.

We presented 75 student volunteers (59 females, $M_{age} = 22.6$) with information about the side effects of the swine flu vaccine taken by approximately half the Norwegian population in 2009 and subsequently assessed their perceived risk of side effects. The participants were randomly assigned to one of three conditions varying on how the health information and risk was communicated: 1) Probability Only: a brief written "fact box" with a numerical probability. 2) Probability and Newscast: the same "fact box" along with a televised newscast on the relative overall increase in side effects from 2008 to 2009 caused by the swine flu vaccine. 3) Newscast Only.

Results show substantially increased perceived risk in the Probability and newscast condition and in the Newscast only condition, compared to the Probability only condition. These results indicate that when a newscast is presented along with numerical probability information, people perceive the risk as greater than when the numerical probability is presented alone. Furthermore, perceived risk is almost as high when the news report and the probability both are presented as when the news report is presented alone. In other words, numerical probabilities do not seem to provide an effective anchor for perceived risk when contextual information is present.

Reference:
PREDICTORS OF MEDICAL AND NEUROLOGICAL OUTCOMES IN HOSPITAL ADMITTED STROKE PATIENTS IN ADDIS ABABA, ETHIOPIA

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Background and purpose:
Preventable medical and neurologic complications of acute stroke adversely impact outcome. However there is scarcity of data about predictors of those outcomes. The current study aims to identify determinant factors for the development of medical and neurologic complications among stroke patients.

Method:
The study is done in 71 patients of acute stroke (except SAH) admitted to three hospitals in Addis Ababa from June 2008 – March 2009. The patients were prospectively followed until their discharge or death to look for the nature and frequency of neuro-medical complication. Basic demographic date, stroke related medical information, preexisting medical conditions, admission laboratory and imaging abnormalities were recorded. All events were documented for each patient clinical outcomes using predefined medical complication data collection format. Both descriptive and analytic statistical tests were performed. Statistical analysis was limited to the ten medical conditions which already are assumed to be common. Multivariate logistic regression analysis was used to determine determining complications.

Results:
Various complications were detected in 51 patients (71.8%). Most common complication was aspiration pneumonia 24(33.8%). Miscellaneous complications were reported in 17(25%) patients. Severe neurologic deficit measured by Glasgow coma scale and old age (p< 0.05) were significantly associated with both developments of complications after stroke and mortality related to stroke in admitted patients.

Conclusion:
Glasgow coma scale measurement at admission is important predictor of complications and death following stroke. Being aware of the types of common complications and associated risk factors helps the clinical team involved in the care of stroke patients to make preparations and plans for the best possible care also to take preventive measures that will save lives with best possible use of meager resources available.
MEASURING QALY GAINS IN PRACTICE: A REVIEW OF 323 CEA/CUA PUBLISHED IN 2010

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Based on a review of all cost-effectiveness analyses (CEA) and cost-utility analyses (CUA) published in the year 2010 which had measured health outcomes in terms of quality adjusted life years (QALYs) gained, this paper reveals some important methodological patterns in the current use of QALYs. The key inclusion criteria in the review process were that papers should be published in peer-reviewed English language journals and report from an applied study. Studies are categorized into i) journal type in which they are published (clinical, general health and medicine, health economics), ii) main diagnostic group, and iii) country of origin. Three separate issues are explored: 1) Which generic descriptive systems and valuation methodologies are used?; 2) What are the magnitudes of the incremental QALY gains?, and; 3) What are the health prospects without the new treatment (i.e. the size of QALY in the comparators)? Reporting of both descriptive systems and valuation methodology was generally poor. About half of the studies which reported descriptive system had applied EQ-5D. Only about half the studies reported both QALY in the comparator group and incremental QALY gain. The median reported incremental QALY gain was about 0.1. The median discounted QALY in the comparator arm was about 5 QALYs. The average age in the patient groups was 52 years. The general conclusion from this comprehensive review of recent published studies is that the assumptions and methods underlying the QALY calculations is not reported in a sufficiently transparent way. There are systematic differences between the three different journal types with regards to quality of the reporting.
ADVANCING THE METHODS OF COST-EFFECTIVENESS ANALYSIS: WHY IT’S TIME TO MOVE ON FROM ICERS AND THRESHOLDS

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Objectives:
Cost-effectiveness analysis of health technologies typically involves the calculation of incremental cost-effectiveness ratios (ICERs). In some jurisdictions, decision makers compare these ICERs to an explicit cost-effectiveness “threshold” as part of their deliberations. The use of a threshold remains controversial and there is disagreement over what such a threshold, if adopted, should represent. Furthermore, there are many issues and limitations with the interpretation of ICERs. This paper argues that the needs of decision makers and patients would be better served by abandoning ICERs and thresholds altogether and adopting instead a decision framework based upon a modified notion of “net benefit”.

Methods and Results:
Using recent Ontario-based cost-effectiveness analyses as examples, we demonstrate that the traditional interpretation of ICERs can be misleading. We also demonstrate why comparing ICERs to an explicit threshold cannot satisfy the needs of decision makers or patients – regardless of the threshold used – except under very specific circumstances. We then show how the traditional “net benefit” approach to decision making may be modified to incorporate concerns for efficiency, equity, societal and ethical values, and patient preferences.

Conclusions:
Abandoning ICERs and thresholds and adopting a decision framework based upon a modified notion of “net benefit” would not only address many of the issues with ICERs and thresholds but would be easier for decision makers to interpret. It would also allow decision makers who adopt multiple decision making criteria (such as concerns for efficiency, equity, societal and ethical values, and patient preferences) to make explicit trade offs between these criteria.
PATIENTS' SELF-REPORTED
ADHERENCE VS. PSYCHIATRISTS' IMPRESSIONS
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Adherence to prescribed psychiatric medications is frequently assessed
through subjective measures as patients' self-report or psychiatrists' report.
This study examined the agreement among measures of adherence to
prescribed medications among 90 consecutive psychiatric outpatients with
affective disorders attended at a Mental Health Care Unit from the Canary
Islands Health Service.

Method:
Participants were assessed during a visit to their Mental Health Care Unit.
Adherence was assessed by using two subjective measures: Morisky
Medication-Taking Adherence Scale (MMAS) and psychiatrists’
impressions report of adherence based on the clinical state of the patient).
Clinical and socio-demographic variables were evaluated for association
with compliance using multivariate logistic regression analysis.

Results:
The 90 psychiatric outpatients who participated in the study had a mean age
of 56.2±12 years (range, 30–76) and 74% were female. Concerning
educational level the 14.4% had no formal education, 48.9% had completed
primary studies, 18.9% had completed secondary studies and 17.8% had a
university degree. The mean number of psychotropic drugs used was
3.2±1.3 (range 1–7; 6.7% under monotherapy, 24.4% received two drugs,
36.7% received three, and 32.2% received four or more drugs). 27.7% of
patients had a bipolar disorder, 17.8% had a depressive episode, 22.2% a
recurrent depressive disorder, and 32.2% had dysthymia. Psychiatrists
considered 82.2% of the sample to be compliant, but only 58.9% of
psychiatric outpatients with affective disorder considered themselves
compliant. 52.2% of patients were considered compliant by both psychiatrist
and patient whereas 11.1% were considered non-compliant by both
psychiatrist and patient resulting in a Kappa concordance coefficient κ=-
0.055 (tip error=0.031; sig.=0.055)). Psychiatrist-rated adherence was lower
in patients with bipolar disorder and in those with more drugs prescribed.
Patient-rated compliance did not registered significant associations with
socio-demographic or clinical variables considered.

Conclusion:
Psychiatric medication adherence is an important multidetermined public
health issue where multimodal approach is likely to be most effective.
It is universally recognized that medical education is providing the learner with knowledge, attitudes and skills in order to practice medicine and healthcare in the most competent manner. Development of cognitive skills - problem analyzing/solving and decision making seem to be of particular importance. Uncertainty is almost always present in clinical medicine, incl. pediatrics, and thus complicates further the process of making appropriate decisions. Notwithstanding importance of medical decision making (MDM) skills, in pre-service training they are given insufficient consideration. During the recent years we have been teaching MDM-related topics during the course of Child and Adolescent Medicine at the Tbilisi State Medical University, Georgia. Aim of presented work is sharing of our experience. Child & Adolescent Medicine is taught in the VI year. Duration of the course is 25 days during which in addition to classes five interactive lectures are delivered. Two of them are dedicated to the general issues of diagnostics and treatment. First of all principles of MDM process are tackled. Fuzzy logic approach and necessity of permanent weighing of probabilities are considered too. In order to reduce the risk of human errors the purposefulness of decision support systems (guidelines, algorithms, expert systems) is emphasized. The original approach how to choose adequate guidelines is presented (Pagava K et al. 2010). The particular attention is focused on the diagnostics of rare diseases, first of all by revealing of atypical clinical picture and course of presumptive “common diseases” (Acampora G, Kiseliova T, Pagava K, Vitiello A, 2011). In treatment the advantage of coherence over correspondence reasoning (Wigton RS, Tape TG, 2010) is underlined. During the classes preference is given to case studies (ranging from simple common cases to sophisticated and sometimes unclear ones). All stages of management are discussed one after another with all necessary details. Methodology of role playing is also used. For students’ summative assessment the proportion of tests on MDM has been essentially increased. Having no other evidence besides experts’ (colleagues and team members) suggestions we suppose that emphasizing MDM skills acquisition in pre-service training will contribute to improvement of the future professional activity of learners.
EVALUATING THE COST-EFFECTIVENESS OF ADJUVANT CHEMOTHERAPY GUIDED USING ONCOTYPEDX AND IHC4 IN THE UK

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Gene expression profiling (GEP) and expanded immunohistochemistry (IHC) tests aim to improve decision-making relating to adjuvant chemotherapy for women with early breast cancer (EBC) at intermediate or high risk of recurrence following primary surgery.

A probabilistic model was developed to evaluate the cost effectiveness of adjuvant chemotherapy treatment guided using the OncotypeDx and IHC4 tests compared with current clinical practice in England and Wales using clinico-pathological parameters. Analysis was undertaken for women with oestrogen receptor positive (ER+), lymph node negative (LN−), and HER2−EBC from a NHS perspective.

In the comparator arm of the economic model cancer registry data was used to inform the proportion of patients receiving chemotherapy under current practice. In the intervention arm (new test in addition to current practice) patients were classified into different risk categories based on the result of the new test. The likelihood of receiving chemotherapy was dependent on this classification. The natural history of breast cancer was then simulated using a state transition Markov model, taking into account the reduction in the risk of recurrence associated with chemotherapy. Patients were able to move between five possible health states - recurrence free, distant recurrence, local recurrence, long term adverse events (LTAE) and death (from breast cancer, adverse events or other causes). The model used UK specific data where possible. The model used a lifetime horizon and costs and benefits were discounted at 3.5% per annum. The uncertainty was captured in univariate sensitivity analysis and probabilistic sensitivity analysis (PSA).

The economic analysis suggested that treatment guided using IHC4 has the most potential to be cost-effective at a threshold of £20,000 per QALY gained; however the evidence base to support IHC4 needs further research to confirm the analytical validity of the test and to clarify the cost of the test in clinical practice. OncotypeDX has a more robust evidence base, but further evidence on the impact on decision making in the UK and the predictive ability of the test in an ER+, LN−, HER− population receiving current treatment regimens is needed to confirm whether or not it constitutes a cost-effective option in the UK.
EMPIRICAL EVIDENCE OF UTILIZATION AND PRACTICE OF SELF-PAY SERVICES IN THE GERMAN AMBULATORY HEALTH CARE SETTING. RESULTS OF A HTA

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Introduction:
The German Institute for Medical Documentation and Information commissioned this health technology assessment about individual health services (IGeL). These are medical self-pay services that are not under the liability of the German statutory health insurance. We investigated empirical data on offers, utilization, practice, acceptance, influence on patient-doctor relationship and economic significance of these services in the ambulatory health care, as well as related ethical, social and legal aspects.

Methods:
We performed a systematic literature search and internet search for original studies and publications about ethical, social and legal aspects of IGeL. Two independent authors screened the references according to defined criteria and in- or excluded them from the information synthesis. We assessed study quality with checklists and presented the results in summary tables.

Results:
Of 1344 references, we screened 571 full text articles and included 64. 31 of them were publications of original studies on IGeL and 33 were publications on ethical, social and legal issues. Between 19 and 53 % of insured persons received IGeL offers by their physician of which three-quarters were actually realized. 10 to 19 % of patients actively asked for such services. The most frequent IGeL was intraocular tension measurement and accounted for up to 40 % of the offered services. It was followed by ultrasound examinations with up to 25 % of offers. Cancer screening and blood or laboratory tests represent great parts of the patients’ requests. The ethical, social and legal aspects discussed in this context concern competent patient decision, commercialization of medicine, information requirements, evidence of patient benefit, role and relationship of physician and patient, relation of self-pay services to the statutory health insurance system, social inequality and formal requirements on self-pay service provision.

Discussion:
Since they are relatively wide spread in the ambulatory health care of the statutory health insurance, the provision of IGeL should be more transparent with respect to quality and quantity of services. Independent, evidence-based information should be available for the patient. Generally, self-pay services need to be considered in the context of the political design of the health care system.
THE CONTRIBUTION OF HTA TO THE TRANSLATIONAL RESEARCH PROCESS

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Background:
Translational Research comprises activities aimed at the generation of biomedical knowledge, its transfer into clinical practice, and the take-up of research questions in biomedical research. It is described as a non-unidirectional process with mutual interchange between different development stages. We investigated the role of HTA in the generation and translation of evidence in a case study of cancer genomics within the multinational ELSAGEN research collaboration on ethical, legal, socio-cultural and economic aspects of genomics and related sciences. Our aim was to look at HTA methods in this field and at real life experiences of players in TR with HTA. Here, we present how HTA is integrated in the TR process from the view of involved parties.

Methods:
We performed a literature search and qualitative expert interviews to build a concept that captures the characteristics of interactions with different TR players. Four basic/clinical researchers, 3 HTA experts, 1 industry representative and 1 decision maker were purposively recruited for interviews with respect to their involvement in TR and professional background.

Results:
Traditionally, HTA is applied on a ‘societal level’, where it addresses public and clinical decision-makers and provides information primarily about population health benefit, cost-effectiveness, ethical, legal and social aspects. Our analysis indicates that feed-back of HTA results regarding evidence gaps into the research agenda could be strengthened. But HTA can also be performed on a ‘project level’ to contribute in early phases of development by evaluating premature technologies and giving information to manufacturers, clinicians and, to a less extent, (basic) researchers, e.g., about the potential (cost-) effectiveness, long-term consequences or public health impact of an intervention. HTA also provides input for study design, evidence gaps to be filled, and characteristics of a technology that need to be modified.

Conclusion:
HTA is regarded not only as a tool to promote successful TR, but also as an additional actor that influences the translation of a technology in different stages. However, in practice, exchange between some stakeholders is limited and could be expanded.
THE POTENTIAL ROLE OF "FOCUSED OPERATION MANAGEMENT" IN THE EMERGENCY DEPARTMENT

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Objectives:
Emergency Department (ED) overcrowding (OC) is plaguing EDs worldwide with grave implications on patient and caregiver comfort and quality of care. Alleviating this problem tops agendas of governmental and professional agencies. Many contributing factors have been cited and many approaches have been tried, without widespread success. Focused Operations Management (FM) integrates novel managerial theories and practical tools {such as the Theory of Constraints (TOC) and the Pareto principle and the Just-in-Time/LEAN together with the complete kit concept} into a systematic approach. This approach helps managers to analyze complex operational systems, find bottlenecks and root causes and finally, chart routes to improved throughput and quality. This approach has proved effective in the industry and service sectors, radically improving performance at little additional cost. The FM approach has never been implemented in the ED and could considerably enhance its operations management. As a first research phase interviews with key stakeholders were performed.

Methods:
ED operations literature search was performed to identify major ED operational challenges, metrics and alleviating measures. Semi-structured interviews with ED head nurses, ED managers, hospital administrators and Ministry of Health administrators were conducted. The interviews centered on validation of major challenges identified in the literature search and assessing potential utility of FM tools.

Results:
The major challenges we identified included ED boarding, prolonged length of stay, unjustified ED utilization and slow access to specialist consults, lab tests and imaging studies. Of the FM tools presented to specialists, those assessed to be most promising were "the complete kit” concept and TOC methods to identify and alleviate bottlenecks and to reduce “work in progress”.

In the semi-structured interviews major differences were found in the ranking of the five major ED operational challenges between hospital administrators and ED directors. While ED directors and head nurse ranked as first ED overcrowding due to patient boarding it was not ranked at all among the five major challenges by hospital administrators.

Conclusions:
Implementation of novel FM strategies has enhanced operations and performance in many industries and services. The ED is in dire need and a good candidate for the use of these tools. The first step is quantifying and measuring the proportional contribution of various factors and agreeing on a common language among stakeholders regarding the major ED operational challenges.
QUALITY OF LIFE MEASUREMENTS: A THREE STAGE DELPHI CONSENSUS PROCEDURE TO DETERMINE ESSENTIAL DOMAINS THAT CONSTITUTE QUALITY OF LIFE

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\textbf{Background:}
Allocation of inevitably limited financial resources for health-care requires judgments about the cost-effectiveness of interventions. Health-related quality of life (QoL) measures, like the EQ-5D and SF-6D are commonly used to assess the effectiveness of interventions. However, health interventions are likely to affect QoL in a broader sense than is quantifiable with these existing measures. That is, these measures mainly focus on physical health and not that much on psychological or social aspects (e.g., Dolan, 2009; Ware, 1995). To better judge the effectiveness of health interventions, measures need to go beyond the traditional health-related QoL measures. The question is ‘What are the essential domains of QoL?’

\textbf{Methods:}
We have conducted a three-stage Delphi consensus procedure to identify essential domains of QoL. Five stakeholder groups (i.e., patients, relatives of patients, physicians, general population and scientists) were asked, on three consecutive occasions, what they perceive as the most important domains of QoL (N=153). The results of a literature review formed the basis of the Delphi procedure; a total 40 different domains of QoL were identified and part of round 1. In the first round participants could also provide suggestions for additional domains. In round 3 participants were also asked to identify their top five of most important domains of QoL.

\textbf{Results:}
A total of 49 domains of QoL were judged; these domains covered physical, mental and social aspects. The five groups of participants differ substantially in the domains they perceive as essential. However, there is also consensus about a subset of domains. That is, all participants rate self-esteem, social contacts and independence as essential. A key outcome is that mental and social domains are perceived as more essential than physical domains across stakeholders groups.

\textbf{Discussion:}
Our Delphi consensus procedure identifies the diverse spectrum of potential domains that constitute people’s complete state of QoL - with strong emphases on social and mental domains. The traditionally used economic health-related QoL measures focus almost exclusively on physical health. The Delphi procedure shows that traditionally used measures may need to include additional or different domains to capture aspects of QoL that are essential to people.
POTENTIAL IMPACT OF QUADRIVALENT VERSUS MONOVALENT MENINGOCOCCAL VACCINE POLICIES IN CANADA: A MODEL-BASED ANALYSIS

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Poster to be presented by: O. Topachevskyi, GlaxoSmithKline Biologicals, Wavre, Belgium

Objectives:
Neisseria meningitidis (Nm) is a leading cause of bacterial meningitis and bacteremia worldwide. While infection (carriage) is common throughout a person’s life history, invasive meningococcal disease (IMD) is rare and is disproportionately observed in infants and adolescents. Advisory committees in Canada and the United States have recently approved updated recommendations for the use of quadrivalent meningococcal conjugate vaccines (against serogroups A, C, W-135, and Y) in adolescents and individuals at persistent high risk of IMD. Our objective was to model optimally effective meningococcal vaccination policies in Canada.

Methods:
We formulated a dynamic stochastic compartmental model of Nm transmission within an age-structured population. On account of its stochastic nature, the model reproduced population-level IMD outbreaks. We assumed partial cross-immunity amongst two aggregated categories of co-circulating serogroups: “AWY” containing A, W-135, and Y; and “Other” containing B, C, and ungroupable types. Model parameters were calibrated using a probabilistic method: out of 25000 Monte Carlo realizations of potential input parameter sets, only those sets yielding carriage or IMD case notifications within empirical ranges based on age-stratified Canadian data from 1997 to 2006 were accepted and used to generate results. The impact of infant and adolescent vaccine programmes, comparing C- versus ACWY vaccines, on prevalence of Nm carriage and IMD incidence was examined. Vaccine efficacy against “AWY” and “Other” infection was weighted by proportion of IMD in those groupings attributable to vaccine-included serogroups, giving 42% for C vaccine and 58% for ACWY vaccine.

Results:
Though both mono- and quadrivalent vaccines are projected to impact Nm carriage prevalence and IMD incidence, routine infant immunization (at 12 months) and adolescent boosting (at 12 years) with a quadrivalent vaccine (for coverage rates of 90% and 80%, respectively) is estimated to have the largest impact on total IMD incidence (from all serogroups): a 63% reduction over 20 years, versus a 30% reduction for the same schedule and coverage with the monovalent vaccine.

Conclusions:
Our results suggest that implementing a quadrivalent vaccine programme that routinely immunizes infants at 12 months and boosts adolescents at 12 years would provide the best reduction in the morbidity of this infection.
FACTORS LIMITING THE REGISTRATION OF ALCOHOLIC PATIENTS TO THE WAITING LIST FOR LIVER TRANSPLANTATION: THE ROLE OF HOSPITAL PHYSICIANS
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Purposes:
In the context of scarcity of resources, questions arose on the indications the most beneficial for patients among the indications for liver transplantation (LT). In France, the number of patients with alcoholic cirrhosis registered on the National Waiting List (NWL) is lower than that of others. Alcoholic cirrhosis has been identified as an indication of LT as well as cirrhoses of other origins given certain conditions. Patients with alcoholic liver disease when transplanted had been found to have similar or better outcomes than those with other liver diseases. The objective of this study was to determine among characteristics of inpatients, hospital physician opinion and settings, the factors associated with the patient being considered as a potential candidate to LT.

Methods:
An observational study of the consecutive inpatients with liver cirrhosis of whatever origin included in a multi-centre cohort constituted in mostly non teaching hospital from February 2003 to May 2008, monitored every six months for 24 months and using structured questionnaires. Potential candidates for LT in the opinion of the hospital physicians was defined as potential candidates to LT. Patients were considered as alcoholic when the consumption was more than 30g/j for a man and of 20g/j for a woman.

Results:
Four hundred and three inpatients were included. Their average age was 58.2 years (standard deviation: 10.9), 71.0% were men, 85.0% had alcoholic cirrhosis, 39.5% a Child-Pugh score class C and 21.0% were considered as potential candidates to LT. There were no significant differences between potential candidates and the others according to sex, duration of alcohol consumption, and between alcoholic and non alcoholic patients. The factors independently associated with being a potential candidate for LT were: physician empathy (Odds Ratio [OR] = 12.0; 95% CI: 4.1-35.2), treatment observance (OR = 8.4; 95% CI: 1.7-40.2), Languedoc-Roussillon area (OR=7.4 ; 95% CI: 2.0-29.3), Child-Pugh score class B (OR = 2.7; 95% CI:1.1-6.6), non or low frequency alcohol consumption (OR = 2.4; 95% CI: 1.1-5.3) and patient age (OR = 2.4; 95% CI: 1.1-5.0).

Conclusion:
Alcohol does not directly link to selection of potential candidatures to LT. However, the hospital physician’s opinion on the patient and of his or her involvement in managing his or her illness seems to be important.
BARRIERS FOR COMPLIANCE AMONG CHRONICALLY ILL PATIENTS TO AN ESSENTIAL TREATMENT: THE CASE MODEL OF COUMADIN FOR PATIENTS IN NEED OF ANTI COAGULATION THERAPY

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Scientific Background:
Non-compliance for essential medication among chronic patients causes co-morbidity, lowers the quality-of-life, and is costly to the healthcare system.

Objectives:
To examine the factors of non-adherence for chronic essential medication: Coumadin a case model - for anti-coagulation therapy.

Methodology:
A cross sectional research among all patients (11,196), insured by the Clalit Health Care Services Southern-Region, aged 30+, who required Coumadin treatment during a ten year period (2000-2009). The data was collected from: (A) computerized databases (retrospective study) and (B) Telephone interview among a sample of patients (n=676). Three components of non-compliance were analyzed: (1) Less than 8 INR tests per year. (2) Average INR values. (3) Less than 4 Coumadin prescriptions purchased per-year. These components were weighted into a binary index to measure compliance.

Findings:
The patient population included 47% Men with an average age of 72. The participation rate of the telephone survey was 40%.
A compliance rate of 50% and 20% were found for each non-compliant component and for the weighted index respectively. Non-compliance to Coumadin treatment based on computerized databases was found to be related to: (1) Increased age (P<0.05), (2) Long duration of treatment (P<0.05), (3) Higher utilization of health services i.e number of physician visits, total days of hospitalization, total hospital admissions (P<0.05) and (5) Lower income (welfare allowance) (P=0.06).
Additional categorical variables for non-compliance, from the telephone survey are significant (P<0.05) and have an influence on the binary compliance index: language and place of birth, morbidity, disabilities and frustration resulting from treatment, timing of drug consumption, and access to INR results.

Conclusions:
This is the first study in Israel seeking to define barriers for chronic patients’ compliance using long term essential medication. The low rate of non-compliance for an essential drug such as Coumadin provides evidence to an iceberg phenomenon that is hazardous to patients requiring chronic essential medication. Understanding these barriers allows decision makers to suggest change in policies and the construction of intervention programs which empower the patient and medical staff to improve patients' compliance.
REPRESENTING PARAMETER UNCERTAINTY IN DECISION MODELS: CHARACTERIZATION OF PROBABILITY DISTRIBUTIONS
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Background:
It is recommended to construct decision models for economic evaluation as probabilistic models. In practice, this means putting probability distributions on all variables where parameter uncertainty is an issue. Several researchers, mainly at beginner or intermediate level, have difficulties in assigning these distributions due to a lack of clear guidance.

Objective:
We aim to inform beginners and intermediate decision analysts about choosing distributions for probabilistic decision models.

Methods:
We have reviewed several sources in the search for guidance on how to choose and parameterize distributions. Even though our objective is to inform researchers in the field of health economic evaluations, we have searched for literature outside the field of health, to supplement the, somewhat sparse, literature.
Based on literature and our own experience, we have categorized the different types of variables that are needed for a decision model and give clear guidance on what type(s) of distributions that are recommended for each type. We also demonstrate why the suggested distribution types are recommended and give some guidance in how to incorporate these into decision models.

Discussion:
Even though we give clear guidance on types of distributions, we accommodate further suggestions.
ELICITING PREFERENCES FOR PRIORITIZING RARE DISEASES: DO RESPONDENTS REACT TO OPPORTUNITY COSTS OR FRAMING ISSUES?

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**Purpose:**
To test the extent to which preferences for prioritizing rare versus common disease treatments are consistent with the predictions of economic theory or sensitive to alternate framings.

**Methods:**
We surveyed a random sample of 2,767 Norwegians aged 40-67. Respondents allocated a given amount of resources between two patient groups (rare versus common disease). Diseases descriptions were identical in terms of severity and expected treatment benefits, but the rare disease was more costly to treat. The allocation decision was accomplished by moving a pointer along a horizontal bar marked with different combinations of numbers of rare and common disease patients. Respondents were randomized to 8 survey versions, in which either the cost of treating the rare disease, the mechanism for making the allocation decision, or the amount or type of other information provided were varied, allowing us to test for price effects and four different framing effects. Outcome measures in each case were the mean share of funds devoted to treating rare disease patients and the percent of respondents recommending an equal division of resources between rare and common disease patients.

**Results:**
Framing had a significant effect on outcomes in most cases. Particularly important was the finding of a visual central tendency bias associated with using the horizontal bar for the allocation decision; 40% of respondents divided resources equally using the horizontal bar compared to 13% using the alternate selection mechanism. Outcome variables were also sensitive to “naming,” and to an extra task of selecting the allocation principle respondents felt should be applied to setting priorities. Evidence of rational economic price responses was less clear. The share of resources allocated to the rare disease declined as the price of the rare disease increased, as economic theory predicts, but the extent of the change was minimal, which can be interpreted as “scope insensitivity.”

**Conclusions:**
Preferences elicited using person trade-off techniques are sensitive to a variety of framing effects. The small response to price changes may be indication of scope insensitivity, calling into question the degree to which results reflect rational economic responses.
DUAL PROCESSING MODEL OF MEDICAL DECISION-MAKING

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Dual processing theory of human cognition postulates that reasoning and decision-making is a function of both intuitive, experiential, affective (system I) as well as analytical, deliberative (system II) brain processing. To date no formal model of medical decision-making based on dual processing theory has been developed. Here we describe such a model as applied to common clinical situation: whether treatment should be administered to the patient who may or may not have a disease.

Because affect plays a key role in how outcomes are felt and processed and regret is a key emotion that plays a role in assessing the values of outcomes, our model assumes that valuation by system I is influenced by regret, while system II processes are dominated by using rational, analytical deliberations according to the postulates of expected utility theory. We first demonstrate that our decision-making is a function of how system I and system II process information on benefits and harms of health interventions. We then formulate our model using the threshold concept to show how it can be used in decision-making at bedside as well as provide explanation for the widespread variation in clinical practice. Specifically, we show that our action -whether we should treat at higher or lower probability than the thresholds obtained via usage of system II – depends on the extent of involvement of system I in decision-making and whether the ratio of benefit and harms under system I and II is negative or positive fraction. Under some conditions, the threshold based on dual cognitive processing may dramatically drop below the expected utility threshold derived by system II. This can explain the overtreatment that dominates the contemporary practice. The opposite can also occur such as in the situations when empirical evidence is considered not reliable, or when cognitive processes of decision-makers are biased through the distorted recent experience: the action threshold will increase in comparison with the one based on the system II expected utility threshold. Consequently, the decision-maker will require higher diagnostic certainty before she acts.

In summary, we describe the first dual processing model of medical decision-making, which has potential to enrich the current medical decision-making field dominated by expected utility theory.
THE BURDEN OF ENDOSCOPE REPROCESSING – EFFECTS ON STAFF HEALTH OUTCOMES, STAFF TIME, AND COSTS

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Purpose:
Evidence suggests that current endoscope reprocessing methods may cause health problems for staff, including: respiratory symptoms, eye and skin irritation (from chemicals), and muscular-skeletal problems (from brushing and cleaning large numbers of endoscopes). The review presented here provides a summary of recently published literature on the impact of device reprocessing on staff health, staff time, and the resultant impact on associated costs.

Methods:
A literature review was conducted by Via Research in PubMed using the search term ((Endoscope OR endoscopy) AND (Reprocessing OR Cleaning OR Disinfection OR Biofilms)). Articles published between Jan 1, 2007 and March 7, 2012 that investigated the adverse effects of endoscope reprocessing on staff were selected for analysis. Reference lists of key papers were also searched for relevant literature.

Results:
In total, eight studies of interest were identified. One study was conducted in the US, a second in Canada and a third in Japan, while the five remaining studies were conducted in Europe.

Three studies used surveys to examine the link between job conditions related to disinfection, and health problems in reprocessing staff. One of these studies compared manual and automatic disinfection methods, and found that median ortho-phthalaldehyde exposure concentrations were twice as high for workers using manual disinfection compared to automatic disinfection. Of the 80 workers involved in disinfection in this study, many reported health issues that they attributed to disinfection procedures: 10\% reported issues with skin, 9\% with eyes and 16\% reported respiratory problems. A second study conducted a pre-post assessment of five endoscope reprocessing sites (2 sites changed from manual cleaning plus an Automated Endoscope Reprocessor (AER) to an Endoscope Cleaner and Reprocessor (ECR), 2 sites went from old ECR to new ECR, and one site used Manual High Level Disinfection (MHLD) at both times). Considering MHLD vs. ECR, levels of staff health problems were notably higher in the MHLD group. This study also recorded high physical discomfort associated with reprocessing, and stress associated with reprocessing load and time.

A further study investigated the time and cost savings of using an ECR, compared to manual cleaning with AER. Time savings ranged from 12.5 minutes for each colonoscope, to 5.7 minutes per bronchoscope, and 6.3 minutes per gastroscope, and resulted in notable cost savings for the healthcare facility.

Conclusions:
The studies included in this analysis highlight the burden of reprocessing methods on staff in terms of health outcomes, reprocessing time, and the resultant impact on costs. Some of the studies identified discussed the use of automated reprocessing and cleaning, and the potential benefits these processes could have for the healthcare professionals that use them.
SHOULD WE INCLUDE DIRECT PATIENT COMPLIANCE MANAGEMENT IN HYPERTENSION PHARMACOLOGICAL TREATMENT PROGRAMS? A SYSTEMATIC REVIEW

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Background:
Whether interventions designed to correct patients’ attitude to antihypertensive medication can improve hypertension management outcomes is unclear. Direct patient compliance management (which can include measurement, feedback and counselling) may be considered and used as an active component of hypertension treatment programs. This novel approach is known as compliance measurement-guided (medication) management (CMGM). We conducted a systematic review to determine the effectiveness of CMGM programs in essential hypertension.

Methods:
Data sources included MEDLINE, EMBASE, CENTRAL, hypertension meetings abstracts, and bibliographies of identified articles. Randomized controlled trials (RCT) and observational studies (OS) were included in the review and assessed by 2 reviewers independently. Quality assessment was performed with the Cochrane risk of bias tool and evaluated in a four-point continuum. A narrative data synthesis was performed due to significant heterogeneity among studies.

Results:
13 studies (8 RCT, 5 OS) involving 2150 hypertensives were included. Five trials of CMGM with electronic devices as a sole intervention suggested a decrease in blood pressure (BP), but the result may have been due to bias. Short-term BP improvement under CMGM in complex interventions was revealed in 4 studies of low-to-moderate quality. In 4 integrated care studies of higher quality the impact of CMGM component was not possible to distil due to potential confounding by medication regimens. Regular feedback to the treating physician seems to be an essential component of CMGM and may be effectively mediated by a nurse or a pharmacist and via telecommunication.

Conclusions:
No definitive evidence for the effectiveness of CMGM as a health technology was found due to non-optimal study designs and methodological quality. Future research should follow accepted quality standards as well as current guidelines for the treatment of hypertension, include specific groups of patients with compliance problems, and consider clinical, economic, patient-reported and organizational outcomes.
COMPARISON OF METHODS TO ESTIMATE HEALTH STATE UTILITIES USING QUALITY OF LIFE DATA

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Background:
In an era of health care cost containment, cost-effectiveness analyses (CEA) are increasingly needed to inform decisions about care. Cancer clinical trials in the US often collect quality of life (QOL) data using the FACT instruments, but only rarely include utility instruments for CEA. Two algorithms (Cheung and Dobrez) have been developed using the FACT to map QOL to a utility value. It is unknown how they compare when applied to a gynecologic cancer population, information which is necessary if CEA are to use FACT data in their estimation of the quality-adjusted effectiveness of treatments in this population.

Methods:
GOG-0152 was a 550-patient randomized phase III trial comparing interval cytoreduction versus no interval cytoreduction and GOG-0172 was a 415-patient randomized phase III trial comparing intravenous (IV) cisplatin plus IV paclitaxel versus intraperitoneal cisplatin plus IV paclitaxel among women with advanced ovarian cancer. QOL data were collected at four time points in each study. The Cheung and Dobrez mapping algorithms were each applied to these data. The agreement between measures was assessed by the concordance correlation coefficient ($\rho_{CCC}$) and paired t-tests were used to compare means between the estimated utility values.

Results:
Results using the Cheung score were highly continuous, while the Dobrez score was not; there are only 48 possible values of the Dobrez score. Agreement between estimation algorithms ranged from 0.722 to 0.813 at the various time points in the study. However, there were statistically significant ($p<0.001$) differences between the two scores at all time points in both protocols: mean scores were slightly higher with Dobrez than with Cheung (differences in means ranged from 0.018 [0.863-0.845] to 0.054 [0.785-0.731]).

Conclusions:
If CEA incorporate mapping algorithms to obtain utility estimates in the absence of prospectively collected utility data in the setting of ovarian cancer, investigators should take into account the variability and differences in estimates depending on the algorithm selected. Interpretations of CEA have the potential to vary given the significant difference between these two algorithms. Future work is needed to assess if these algorithms obtain estimates that are comparable to values obtained by standard utility instruments in this population.
DEVELOPMENT OF A PUBLICLY ACCESSIBLE MEDICAL RISK INFORMATION SYSTEM AND EVALUATION TOOL

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Introduction:
In the age of an evolving communications landscape it is crucial for public information providers to have an appropriate evaluation tool which can measure user’s search strategies, gathered opinions, and by using formal tests, the knowledge extracted after searching.

Purpose:
We aimed at developing an evidence-based, online medical information tool (OMIT) and accompanying evaluation instrument (proof-of-principle study). Infections with human papillomaviruses (HPV) served as an example. The developed OMIT was primarily evaluated in terms of functionality, the amount of knowledge gained and exposure time to the OMIT. Designed for medical laypersons, the OMIT took into account recent findings in the field of psychology of perception [1, 2]. The presented medical information was evidence-based, with references for every statement and subdivided in up to three information levels. Users could determine the level of information displayed.

Methods:
Participants (N=44) were students (20 women, 24 men, on average 24 years old). Survey instruments were self-administered online interviews = CAWI (Computer Assisted Web-Interviewing) before and after online exposition to the OMIT. Participants exposure time and use of the OMIT was analyzed electronically.

Main Results:
The participants’ higher knowledge after intervention was statistically significant (mode of transmission: 50% vs. 89%, p<0.0005; genital warts as possible consequences: 39% vs. 98%, p<0.0001; cervical cancer as possible consequence: 41% vs. 100%, p<0.0001; vaccination as preventive measure: 48 % vs. 95 %, p<0.0001; best time to get vaccinated: 48% vs. 93%, p<0.0001). Average exposure time to the OMIT was 4 minutes 8 seconds, average exposure time to the basic information 3 minutes 20 seconds. 30 participants (57%) out of 53 accessed at least one page with additional information. No participant accessed all additional pages.

Conclusion:
Even actively interested participants had relatively little knowledge beforehand. Nevertheless, with only a short intervention, knowledge about HPV infections could be increased significantly. In the future it is planned to develop and evaluate interactive computer kiosk modules aiming to inform laypersons on particular medical issues.

References:
PATIENT PARTICIPATION IN TREATMENT DECISION MAKING: A QUALITATIVE STUDY AMONG PATIENTS WITH STAGE I NON-SMALL CELL LUNG CANCER

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Introduction:
In the field of oncology, patient participation in treatment decision making has been promoted as standard element of care. For stage I non-small cell lung cancer (NSCLC), there are currently two treatment options available, namely surgical resection and stereotactic ablative radiotherapy (SABR). Some patients are in now a position to choose between these options. To be able to facilitate patient participation in this decision, we need to get insight into how the decision making process currently occurs and what role both patients and physicians have. In this study, we investigated patients experiences, perceptions and preferences regarding this decision making process.

Methods:
Interviews with patients who had made a decision in the past between SABR and surgery (N=11) were conducted. The Patient Perception Scale was used to assess and explore patients’ perceptions of who actually made the decision. Interviews were audio-taped, transcribed literally and coded. We conducted qualitative analysis to assess main themes describing the current decision process, as well as the preferences and experiences of patients.

Results:
Data analysis resulted in the identification of six themes. Most patients wanted to be involved in the decision making process to some extent. They often searched for information themselves, particularly on the Internet, and had their own preferences about treatment options. Although physicians usually respected patients own preferences if expressed, they did not always offer a choice and seemed to provide quite firm advises as to treatment. While patients perceived to have had a crucial role in the decision, the preferences of physicians seemed to be more decisive.

Conclusions:
Although patients wanted to be involved in the decision process and also participated to some extent, physicians clearly directed the decision from an early stage in the process. In striving towards a more shared decision making approach, physicians could give more detailed information about both options and should elicit patients’ preferences regarding their participation in treatment decision making. Taking this into account, a well-considered choice can be made.
Context Knowledge concerning sensitivity and specificity of medical imaging tests is indispensable for choosing the appropriate imaging technique and interpreting imaging results. The extensive number of publications hampers radiologists and clinicians in their effort to keep their knowledge up-to-date.

Objective (1) Provide a systematic review of meta-analyses concerning the sensitivities and specificities of MRI, CT, ultrasound, conventional radiography, PET, SPECT, and scintigraphy for a range of clinical indications. (2) Launch a Wikipedia page with an overview of the results. (3) Initiate a collective effort among clinicians and radiologists to keep the review up-to-date.

Data Sources A Pubmed search was performed to identify all meta-analyses published up until December 2011, analyzing the sensitivity and specificity of the 7 imaging modalities.

Study Selection Studies were excluded if (a) the aim of the study was not to investigate the sensitivity and specificity of the imaging modality, (b) no specific imaging indication was investigated, (c) the journal in which the article was published was not assigned an impact factor in the JCR Science Edition 2010, (d) sensitivity and specificity were not reported, (e) the full-text meta-analysis could not be retrieved despite our efforts to contact the author.

Data Extraction Two independent reviewers extracted year of publication, journal, imaging modality, clinical indication, imaging protocol, study quality assessment, number of original studies, number of patients, subgroup analyses, sensitivity, and specificity.

Results The search retrieved 368 publications. After excluding studies based on the exclusion criteria, we included 55 MRI, 81 CT, 85 ultrasound, 15 conventional radiography, 43 PET, 12 SPECT, and 21 scintigraphy studies. An exponential increase in number of meta-analyses was found over time. The overview is available on Wikipedia.

Conclusions We are initiating a collective effort to provide up-to-date information on diagnostic performance of imaging tests in an accessible web-based system.
THE CONCEPT OF THE SYSTEM OF RATIONAL CHOICE OF MEDICAL EQUIPMENT BY AN EXAMPLE OF MRIS

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The 2010 WHO report suggests as a solution to a part of the described problems, creation of systems for management of medical equipment. Thus, creation of a system for rational selection of medical equipment becomes one of key prerequisites for building a clear system for resources control in health care.

The purpose of the study is to develop a theoretical and methodological foundation for a universal system of rational choice of medical equipment using MRIs as an example.

The Analytic Hierarchy Processes by T.L. Salty approach was determined to be the best Multi-Criteria Analysis method for solving problems in medical equipment choice. The Delphi method was used for compiling expert opinions. A method was developed to determine the qualifications for the expert team (quality and quantity). This method utilized the degree of participation in problem solving, level of professionalism, statistical methods, and completeness of the expert’s replies for determining the quality of the expert’s opinion. To determine a sufficient quantity of experts, the Kendall's coefficient of concordance method was used.

The system of rational choice of medical equipment was created. This system can be applied for any type of medical equipment or devices in any type of medical facility. Kladno Regional Hospital (Czech Republic) is currently implementing our system while buying MR-imagers.

Use of our system will help to minimize financial expenses in global system in public health, help to fix mistakes in management system of healthcare, help to optimise control system of technical resources and improving the actual quality of medical care.
APPLICATION OF REAL WORLD DATA TO INFORM A DECISION-ANALYTIC MODEL IN BREAST CANCER IN AUSTRIA AND THE U.S

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Background:
Decision-analytic models are applied to transfer differences in geographic epidemiology, health care standards and practice patterns. In the research centre ONCOTYROL a decision-analytic Breast Cancer Outcomes & Policy (BCOP) microsimulation model is being developed to evaluate cost-effectiveness of the 21-gene recurrence score (RS) assay in Austria. This genetic test quantifies the likelihood of breast cancer recurrence and predicts the benefit of adjuvant chemotherapy. The goal is to adapt the model to a United States (US) context and to use real world data collected from the Huntsman Cancer Institute in Salt Lake City, Utah. We aim to study the impact of real world data and country-specific settings on cost-effectiveness results.

Methods:
The BCOP-model simulates a hypothetical cohort of 50-year-old women over a lifetime time horizon adopting a societal perspective. Main model outcome parameters are life-years gained, quality-adjusted life-years (QALYs) gained and costs. Input data are synthesised from international clinical trials and Austrian based costs. The model is transferred to a US setting using data from breast cancer patients treated at the Huntsman Cancer Institute via a comprehensive electronic data warehouse linked to the Utah Population Database containing genealogy, linked to discharge diagnoses, state cancer registry, and death certificate information.

Results:
The BCOP-model is currently populated with Austrian input data. In the database of the Huntsman Cancer Institute there were 3109 breast cancer patients, with the majority (42%) in stage I and age between 46 and 64 years. A text search identified information about the 21-gene RS assay in up to 150 cases. Data will be used to assess the benefits of chemotherapy based on genetic and other prognostic markers and to retrieve model input parameters. Austrian model results will be transferred using routine-
effectiveness of the 21-gene RS assay, respective practice of the provision of adjuvant chemotherapy, costs etc. and cost-effectiveness results will be compared.

**Discussion:**
The presentation highlights challenges of the model transfer focusing on real world data application for personalized decision making. The major question is whether cost-effectiveness of the genetic test changes in a routine care setting. This information will support future evidence development and reimbursement decisions.
MAPPING FROM THE PARKINSON’S DISEASE QUESTIONNAIRE PDQ-39 AND PDQ-8 ONTO THE GENERIC EUROQOL (EQ-5D)

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Background:
In the UK Quality Adjusted Life Years (QALYs) as measured by the EQ-5D are widely used in decision making and enable comparison of research within and across disease areas. For decision making purposes related to Parkinson’s disease it is important to develop algorithms that enable the estimation of EQ-5D utilities when only condition specific measures of health are available. This article develops algorithms that map onto the EQ-5D from responses to the Parkinson’s Disease Questionnaire (PDQ), a widely used measure of quality of life in people with Parkinson’s.

Methods:
We use ordinary least squares (OLS) and multinomial logistic (MNL) regression models to estimate EQ-5D utility values using domain scores from the PDQ-39 and question level responses from PDQ-8. Estimation is performed using a large clinical trial, PD_MED, and validated on data from a separate trial, PD_SURG. Models are compared at the group level according to the magnitude of their predicted to actual mean EQ-5D tariff difference and at the individual level using mean absolute and root mean squared errors.

Results:
MNL models performed marginally better than OLS. In the external validation sample, PDQ-39 models performed marginally better at the individual level but worse at the group level than PDQ-8 models. Performance was worst at extreme utilities, in particular, low levels of utility.

Conclusions:
The choice of algorithm depends on the instruments available and the context of the study, including the appropriate country-specific tariff valuations. These algorithms can potentially be used extensively in economic evaluations of treatments and interventions related to Parkinson’s where PDQ data have been collected. The aim of such methodological developments is to facilitate increased economic comparability across Parkinson’s research as well as other disease areas. Each algorithm is subject to uncertainty and this should be reflected in its application.
PATIENTS’ PREFERENCES AND DEMAND FOR OBSTRUCTIVE SLEEP APNEA SYNDROME TREATMENT: A DISCRETE CHOICE EXPERIMENT

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Rationale:
Obstructive sleep apnea syndrome (OSAS) affects 4 percent of middle-aged men and 2 percent of middle-aged women. Despite high level of effectiveness, continuous positive airway pressure (CPAP) has rates of initial acceptance and compliance somewhat low. Oral appliances (OAs) can be an alternative in case of CPAP failure or also as a first line treatment in mild to moderate OSAS. To improve patient engagement in their treatment physicians are advised to take into account patient preferences and to share the therapeutic decision. Our objectives were 1/ to determine patients’ preferences for OSAS treatment-related attributes, and 2/ to predict patients’ demand for both CPAP and OAs.

Methods:
We used a discrete choice experiment approach (DCE) in which patients were requested to choose among hypothetical OSAS treatment options. We used 5 attributes (effectiveness, severity of side effects, time to wait between the initiation of treatment and its benefits, negative impact on daily life, out-of-pocket payment) to describe the treatment options. Between September 2010 and June 2011, 140 newly diagnosed patients were recruited consecutively in a sleep unit in a hospital in Paris. Each patient performed 8 choice tasks between “treatment A”, “treatment B” that had different combinations of attribute levels and “no treatment”, that is a no improvement at no financial cost option. The responses were analyzed with a nested logit model to estimate the preferences of patients for the various attributes of the OSAS treatment options. According to the estimated preferences and the actual attributes’ levels for CPAP and OA, we predicted the demanding probabilities for CPAP and OA.

Results:
The model used 2,904 observations to estimate parameters. All the coefficients were significant, and of the expected sign: effectiveness (1.06), side effects (0.63), time to wait (0.41), impact on daily life (1.58) and out-of-pocket payment (-0.004). “Negative impact on daily life” accounts for 58.6% of the model fitting, and “effectiveness” for 25.9%. The demanding probabilities for CPAP and OA were 68.2% and 25% respectively (for a 20% out-of-pocket payment).

Conclusions:
When patients faced choice among several treatment options for OSAS, the “rate of effectiveness” and “negative impact on daily life” appeared to be important determinants for the choice.
COST-OF-ILLNESS AND DALY OF THIRTEEN FOOD-RELATED PATHOGENS IN 2010 IN THE NETHERLANDS – RANKING CHANGES ACCORDING TO CRITERIA USED

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Background:
Since 2008, RIVM regularly publishes estimates of the incidence, burden and costs of food-related pathogens. Using trend information from epidemiological, surveillance and demographic information incidence cases, DALYs and costs were estimated for the year 2010. The following pathogens are considered: norovirus; rotavirus; Cryptosporidium spp.; Giardia spp.; Bacillus cereus toxin, Clostridium perfringens toxin, Staphylococcus aureus toxin infections, Campylobacter spp.; Shiga toxin producing Echerichia coli O157, non typhoid Salmonella spp. hepatitis-A virus, hepatitis-E virus and Listeria monocytogenes.

Methods:
To better represent the burden caused by infectious diseases a pathogen based approach was used, which links incidence of infections to their sequelae through outcome trees. DALY (Disability-Adjusted Life Year) is the metric used to measure loss of health-related quality of life: years of life lost due to premature death (YLL) and years lived with disability (YLD). Monetary costs-of-illness (COI) include direct healthcare costs (DHC); direct non-health care costs (DNHC) and indirect non-health care costs (INHC). WHO standard life expectancy and Dutch disability weights were used. No age-weighting is applied. Costs and effects are presented both discounted and undiscounted. The model, implemented in Analytica® allows explicit modeling of uncertainty via Monte-Carlo simulations.

Results:
The disease and cost burden of these pathogens was estimated at 11,300 DALYs and at € 376 million in 2010. DHC accounted for approximately 20% and INHC for 80% of the total costs. At the population level, norovirus, rotavirus and Staphylococcus aureus toxin resulted in the most community-acquired cases, whereas norovirus, rotavirus, Salmonella spp. and Campylobacter spp. resulted in the most fatal cases. Expressed in DALYS, Campylobacter spp., rotavirus and norovirus had the highest disease burden at population level. The same ranking was found when considering only DHC. When considering total costs, norovirus, Staphylococcus aureus toxin and Campylobacter spp. had the highest costs at population level. At the case level Listeria monocytogenes and hepatitis-E virus caused the highest burden for both disease and costs.

Conclusion:
The current study shows that the burden and costs of enteric disease in an industrialized nation are considerable, and provides evidence for prioritizing interventions.
EVALUATION OF THE STANFORD CENTER ON ADVANCING DECISION MAKING IN AGING (CADMA)

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Background:
Authorized by Congress in 1993 and named for former House Select Committee on Aging Chair Edward R. Roybal, the centers are designed to move promising social and behavioral basic research findings out of the laboratory and into programs, practices, and policies that will improve the lives of older people and the capacity of society to adapt to societal aging. CADMA is one of 14 Roybal centers funded by the National Institutes on Aging.

Specific Aims:
CADMA aims are: 1. To investigate the roles that age-related changes in emotion and cognition play in decision making, especially those surrounding cognitively complex (e.g., health care plan choice) and emotionally-charged (e.g., decisions about end-of-life care) topics. 2. To learn how decision making processes influence day-to-day decisions, such as choices regarding exercise and diet, that influence health and functional status of the elderly. 3. To develop and evaluate support tools or information useful to such tools that could be provided at or near the time of when people face difficult life decisions.

Methods:
We conduct annual evaluations of the productivity of the program in terms of publication and follow on grants, and develop short summaries of each project's approach and findings.

Results:
CADMA has funded on average 3 new seed pilots per year since its inception, totaling 23 pilot projects since 2004, with 20 completed to date. The funded pilot projects have resulted in 14 publications and 1 book. Five pilot projects have continued on to proposals funded by NIH or other sponsors and 43% of projects relate to health care decision making. Currently 70% of the projects relate to Specific Aim #1, 17% to Aim #2 and 13% to Aim #3. Three health-related projects were completed in the past year. One project explored mechanisms to randomize the quantity/duration of exercise to people and the use of behavioral economic devices in increasing longer-term exercise and exercise habits. The research showed that randomized nudges on exercise contract duration, strongly shifts a large portion of individuals into different exercise commitment contracts without changing their likelihood of signing the contract, the frequency of exercise they contract for, or the financial penalties they choose for failing to live up to the contract. The results also showed that older adults tend to select longer contracts on average adjusting for other major individual and contract features—this may have implications in terms of their self-knowledge about how hard it is to form habits and also in terms of their personal rates of discount/time preference. Another project evaluated the immediate and delayed affective and cognitive consequences of receiving results of comprehensive genetic testing. Findings indicate that participants
reported more anxiety after receiving genetic- (vs. population-) based risk estimates of disease. Similarly, participants showed greater physiological reactivity (i.e., skin conductance) after receiving genetic- (vs. population) based risk estimates. In addition, participants sought more information about how to prevent diseases that they are at high risk for when the risk estimate was based on genetics, rather than only their gender and ethnicity (i.e., population-based). These effects were similar for young and middle-aged adults.

**Conclusions:**
The program is well established and is producing novel research at the interface of economics, psychology and medicine to advance decision making for aging adults.
A common problem in survival analysis is the issue of how to cope with censored data. 'Right-censoring' is a particular type of censoring in which an individual's survival time is only known to exceed some value (for example, when a patient drops out of a study before its end-date). Right-censoring has the effect of biasing the survival estimator, and as a result any estimators that make use of the survival estimator are also biased. One such estimator is that of the mean total utility over a sample of individuals, where utility is a measure of an individual's quality of life, with zero representing death and one representing perfect health. In our investigation, we make use of the mean total utility estimator to measure the effects of censoring on a sample of individuals. Survival data are typically analysed in the order in which they were observed, with time advancing in the natural 'wall-clock' reference frame. An alternative approach involves analysing survival data 'backwards' (in the time-from-death reference frame), where each individual's time of death is aligned at some common reference point and then all subsequent calculations are performed starting from the time of death. We design a simulation study that allows us to investigate whether or not, by changing the temporal reference frame, we can reduce the bias associated with the mean total utility estimator in the presence of censoring. We generate a population of 1,000,000 individuals, each with an associated survival time, censoring time and time-varying utility profile, and then employ a bootstrap resampling method to obtain the required performance measures for each approach. Survival times are generated by drawing from an arbitrary Gompertz distribution, whilst censoring times are derived from a uniform random generator. Time-varying utility profiles are assumed to be a function of survival time, and we assume that both inter-patient and intra-patient noise within each utility profile is normally distributed. Our preliminary results suggest that, in the presence of censoring, the bias associated with the mean total utility estimator is reduced by roughly a factor of two when the data are analysed in the 'backwards' reference frame.
ESTIMATING THE TRANSFUSION TRANSMISSION RISKS OF Q FEVER IN THE NETHERLANDS

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Background:
The Q fever outbreak in the Netherlands prompted the public health authorities to take measures including ad hoc temporary screening of blood donations for C. burnetii. Risk assessments may allow transfusion regulators to decide when and where the screening should be targeted and when it may be stopped. The EUFRAT model was developed to support decision making for blood safety during infectious disease outbreaks.

Aims:
To assess the transfusion transmission risks of Q fever during the outbreak in the Netherlands.

Methods:
Q fever notified cases from selected high risk areas during period of 1 June 2009 until 31 January 2010 were extracted. Transfusion infection risks were assessed: 1) the prevalence of infection amongst donors, 2) the risk of collecting infected donations, 3) components, 4) end products, and 5) the risk of transmitting the infection to recipients. The prevalence estimated using the EUFRAT model was compared with the results of an independent donation screening study. The EUFRAT model, which involves detailed blood processing procedure, uses the prevalence to estimate number of infected donations and the subsequent risks for transfusion recipients. The model also estimates daily and cumulative risks during the outbreak.

Results:
We estimated a prevalence of Q fever infection amongst donors of 484.93 (95%CI, 296.35-794.30) per 100,000. In blood donation screening three out of 1004 (=393.70 per 100,000) serum samples tested positive for C. burnetii DNA by PCR and by IFA for presence of IgG phase II; this is in the same order of magnitude with EUFRAT result and therefore provides some validation for our model. The EUFRAT estimates lead to 3.26 (95%CI, 0.67-11.52) infected donations, 9.78 (95%CI, 2.31-31.83) infected components (step 3), 5.74 (95%CI, 2.31-31.83) infected end products (step 4), and 0.23 (95%CI, 0.23-0.32) chronic infections in recipients (step 5).

Conclusion:
We quantified the transfusion transmission risks of Q fever during an outbreak using the EUFRAT model. The model can support decision making about when and where additional safety measures should be targeted during a Q fever outbreak.

Acknowledgment:
The study has been funded by the European Centre for Disease Prevention and Control and Sanquin Blood Supply Foundation.
WHAT GOES ON IN HOSPITALS?
IDENTIFICATION, CLASSIFICATION AND DISTRIBUTION OF CLINICAL DECISIONS IN HOSPITAL ENCOUNTERS

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Purpose:
Doctors apply medical knowledge continuously, working with everything from evaluating small bits of information to handling complex clinical situations. Previous research has focused on difficult decisions that patients should be involved in. As a result the medical literature provides no tool adequate for identifying and categorizing the wide array of decisions actually made in clinical encounters. To understand decision-making processes and the potentials and limits of shared decision making, we aimed to identify all statements that convey clinical decisions in patient-physician consultations.

Method:
Building on previous work by Braddock et al1 and Elwyn2 et al, we developed the tool DICTUM (The Decision Identification and Classification Typology for Use in Medicine) through a content-driven iterative process informed by the experiences and perspectives of four doctors. The material comprised videotapes with 71 doctors from eight specialties in authentic clinical situations in a Norwegian general hospital.

Result:
In internal medicine consultations we found an average of 16 (range 5-26) statements made by the doctor reflecting clinically relevant decisions. These decisions could be categorized in ten dimensions with varying implications for the patient. Many were rather simple statements nevertheless representing clinical judgment, while others were conclusions based on complex analyses of data and context. On average doctors repeated statements reflecting decisions 4 (0-10) times per encounter.

The most frequent decisions concerned drugs (22%) and defining the problem (24%). Decisions about evaluation of tests (13%), advice and precaution (13%), further information gathering (9%) and control and referral (9%) were also frequent. Less commonly, decisions concerned legally related issues (4%), non-pharmaceutical interventions (3%) and treatment goals (1%). Deferments were rare (1%).

Conclusion:
Doctors convey numerous decisions of varying nature, content and consequence during clinical encounters. The amount and variety of decisions and potential implications are likely to be challenging for patients to follow, remember and respond to. This could entail passivity in patients and reduce doctors’ willingness and ability to actively encourage patient involvement and shared decision-making.

References:
A SYSTEMATIC REVIEW ABOUT WEB BASED PATIENT DECISION AIDS

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Introduction:
Patient decision aids (PtDAs) have traditionally been paper-based but recently they have begun to be developed as interactive web based applications of health communication. The aim of this work was to conduct a systematic review to identify and create an inventory of PtDAs available on the Web for users of the health system who are facing treatment or screening decisions, in order to improve their decision making and health outcomes.

Methods:
Studies were identified via Medline, Pre-Medline, CINAHL, Embase, PsycINFO, Cochrane Library, and CRD databases (from 2000 to 2011). Reference lists of relevant articles were examined for further eligible studies. We included primary studies (quantitative and qualitative methods) with Web based PtDAs, excluding decision aids with CD format or informatics programs. Two investigators independently extracted data on the PtDAs: title, health condition, aim (treatment or screening decisions), options included, developer, acceptability and usefulness perceived by patients, and decision-making process measures.

Results:
A total of 7545 references were considered after the elimination of duplicates. We selected 208 for detailed assessment, and finally 11 studies met all inclusion criteria. Regarding the aim of the Web based PtDAs identified, 5 are for patients facing treatment decisions and 6 for screening decisions. Four studies are about prostate cancer and the other studies are about breast cancer, colorectal cancer, depression, neurological rehabilitation, intracranial aneurysm, genetic vulnerability, and attention deficit hyperactivity disorder. The main outcomes of the included studies are acceptability (7/11), knowledge (6/11), decisional conflict (5/11), and satisfaction (3/11). The PtDAs evaluated show a good acceptability and have a positive effect on users as they acquire more knowledge, they feel more supported, which can affect their behaviour and clinical outcomes.

Discussion:
On the Web there are many health information resources, but few are focused on shared decision-making (SDM) and PtDAs, which appears to be useful for individuals facing preference-sensitive decisions. The incorporation of online format and advanced visual features may facilitate participant involvement and disseminating information easily, making Web based PtDAs a potential strategy to promote SDM.
ACCEPTABILITY OF A WEB-BASED DECISION AID FOR PATIENTS WITH DEPRESSION

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Introduction:
Previous research suggests that many patients with depression feel ambivalent about make a decision of a treatment for depression. Patient decision aids (PtDAs) are tools that help patients weigh up the advantages and disadvantages of different treatment options and reach more informed decisions. This study aimed to develop and assess a Web-based PtDAs for patients with depression who have to make decisions about their health.

Method:
A two-phase process was employed. Phase 1: To development a Web-based PtDAs for patients with depression taking into account the quality criteria IPDAS - International Patient Decision Aid Standards, as well as the iterative process proposed by Elwyn et al. (2010) for the development of a Web-based PtDAs. It was developed by a multidisciplinary team of researchers, healthcare professionals, patients, programmers and graphic designers. Phase 2: To evaluate the acceptability of the Web-based PtDAs. Patients who had have depression were recruited. Socio-demographic selection criteria such as age, education, and participation in support groups were established. Semi-structured interviews with patients were conducted to explore the acceptability of the Web-based PtDAs (quantity, clarity and usefulness of the information displayed), and issues regarding to the perceived Web aesthetics, usability, visual appeal.

Results:
Phase 1: The Web-based PtDAs presented general information about depression and the treatment options, a qualitative and quantitative description of the health-related benefits and harms of each option, the decision under consideration and the importance of personal values and preferences in determining the best treatment, and a value clarification exercise. Phase 2: Web-based PtDAs has been evaluated positively by patients, whom consider it a useful resource that provides valid and reliable information, encouraging active participation in the process of making decisions about their health. Patients would recommend their use in clinical practice.

Conclusions:
Results of this acceptability study suggest that a Web-based PtDAs could be useful to encourage more active participation of patients with depression in decisions related to their health and choice of treatments.
Vaccination is the most efficient and cost-effective method to prevent influenza. No WHO/CDC recommendations have ever considered the effect of previous individual illness in determining future vaccination policy for that individual. By using contact network epidemiology simulations, we show that in contrast to standard epidemiological strategy, immunizing those who have been infected in a previous season, especially before the peak of the disease, can substantially reduce infection rates for a wide range of influenza viruses when considering cross reactivity levels between influenza strains.
Empirical evidence indicates strong public support for the sharing of health resources even in the absence of the attributes commonly associated with equity (age, social class, ethnicity, disease severity or location). This poses a challenge for measurement. If government is to secure quantitative advice concerning the equity-efficiency trade-off then methods are needed which allow the expression of preferences for sharing per se in addition to other preferences.

This presentation reports the results of a representative population survey of 532 Australians which tested a technique for achieving this. The survey did not include any of the attributes usually associated with equity but was designed to quantify the respective importance of life expectancy, outcome egalitarianism, and resource sharing in respondent’s decision making and to observe the changing importance of cost per life year (efficiency) as the other attributes varied. Analysis of over 13,000 discrete choices indicated that sharing, not cost per life year, dominated decision making. Results are of significance because they indicate the irreducible lower limit to the willingness to trade off efficiency for equity in the context of life extending programs.
SYSTEMATIC REVIEW OF MICROSIMULATION IN COST-EFFECTIVENESS ANALYSIS OF BIOLOGICS IN RHEUMATOID ARTHRITIS

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Background:
A number of economic evaluations, comparing both the costs and consequences of biologic therapies for the treatment of rheumatoid arthritis (RA), have been published.

Objective:
To assess the structural and methodological aspects of published cost effectiveness models associated with the use of biologic therapies in rheumatoid arthritis with a focus on the simulation level (i.e., cohort vs. microsimulation).

Methods:
A systematic literature search was performed using the databases (Pre) MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews and Health Technology Assessment, and NHS EED (Economic Evaluation Database) from the literature published from January 1996 to January 2012. To be included, studies had to evaluate the cost effectiveness of a biologic (or a treatment sequence involving biologic therapy) for the management of RA. Each model was assessed by 3 evaluators.

Results:
A total of 38 studies were identified, the majority of which included cost-utility models (n=33) that used cost per quality-adjusted life-year gained as the primary outcome. All of the models used societal and/or healthcare provider/payer perspectives. Modeling approaches employed across the studies included decision trees (n=5), Markov/state transition models (n=24), discrete event simulations (n=7) and other statistical models (n=2) with time horizons ranging from 6 months (n=2) to lifetime (n=20). 27 of the 38 models were analyzed on a patient level. Of these 27 microsimulation models, 16 were state transition models, 7 were discrete event simulations, 3 were decision trees, and 1 was a purely statistical model. Of the 20 analyses with a lifetime horizon, 18 were performed as a patient level simulation.

Conclusion:
Microsimulation is preferred over cohort simulation in cost-effectiveness analysis of biologic treatments in rheumatoid arthritis, especially if long time horizons are considered. This can be explained by the multitude of treatment pathways and the dependency of these pathways on individual patient characteristics, disease severity, response levels and duration of response.
RAPID ASSESSMENT OF THE CLINICAL EFFECTIVENESS OF VAGINAL ULTRASOUND SCREENING FOR OVARIAN CANCER OFFERED AS SELF-PAY SERVICE

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Introduction:
In the context of a health technology assessment (HTA) about self-pay services commissioned by the German Institute for Medical Documentation and Information, the evidence on screening for ovarian carcinoma using vaginal ultrasound (VUS) was investigated as an example for medical services not covered by the German statutory health insurance.

Methods:
We performed a systematic rapid assessment of VUS screening. First, we searched for HTA reports and systematic reviews and then for randomized controlled trials (RCT) that were published after the research-period of the latest review/HTA report. We included studies with asymptomatic adult women who underwent screening for ovarian cancer with VUS alone or in combination and a comparison group with no screening. Endpoints were cancer related mortality, morbidity, health related quality of life and harm due to the screening. Two independent authors reviewed the references according to predefined criteria and in- or excluded them in the information synthesis. Study quality was assessed with checklists and results were summarized in evidence tables.

Results:
Out of 1381 references, we included one HTA report and seven publications of three RCTs. To the date of our report, no mortality data were available from the HTA report or from the original studies. One study detected more stage I and II tumors in the screening group compared to the control group (67% and 44%, respectively; p=0.2285). Due to the small number of cases, the difference was not statistically significant. The data on diagnostics show that screening induces in a high extent of over diagnosis associated with invasive procedures. The positive predictive value ranges from 0.75 % to 2.8 %. For each detected invasive carcinoma, between 30 and 35 surgeries were performed in the screening trials.

Discussion:
The benefit of VUS screening for the early-detection of ovarian cancer cannot be judged without patient-relevant outcomes as mortality and quality of life. However, the potential harm caused by unnecessary surgeries is evident. The transferability of the study results to VUS as self-pay service is limited since these are – other than the study populations- also offered to pre-menopausal women in whom even more false-positive results are expected.
NATIONAL SURVEILLANCE OF EMERGENCY DEPARTMENT DIAGNOSES – IMPLICATIONS FOR DECISION MAKERS AND HEALTH SERVICES PLANNING

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Introduction:
The knowledge accumulated in the Emergency Department (ED) regarding the health needs of the patients attending, echoes the health of the population and the availability of health services in the surrounding community. This information is therefore valuable to policy setters and public health systems managers. Surveying ED utilization continuously can support educated planning and decision making. In Israel, a form for recording ED diagnoses has been used nationally since 2002. The current study aimed to examine the completeness and quality of coding in order to evaluate the usefulness of the database as a basis for health care planning.

Methods:
Both qualitative and quantitative methods were used. The qualitative assessment aimed at identifying medical conditions and procedures that are useful for portraying health needs. The codes associated with these conditions were retrieved retrospectively from archived patient records at four hospitals.

Results:
An expert group produced queries that could serve as a basis for decision making among health policy setters. These were requested from the information branch of the MOH for the period of 2008-2009, the most recent data-set available nationally. Data extracted from the ED data repository enabled profiling the visitors and visits by the various diagnoses. Comparison of written and coded diagnoses was carried out in 17,761 records. Large variance was found between the hospitals in regard to the proportion of records coded in the ED. Complete mismatch between coding and diagnosis in the record was rare and occurred in a few cases only. Where coded, a complete match was consistently higher among patients that were hospitalized. No differences were found in the quality of coding between various shifts, yet differences existed between weekdays.

Discussion and Recommendations:
The analysis of patient diagnosis enables the delineation of patients’ profiles to assist caregivers, health authorities and decision makers in planning and providing optimal care. Based on our findings we recommend (1) To continue encouraging diagnosis coding in the ED while acting for the improvement of completeness and quality of coding. (2) To involve senior officials in the healthcare system in submitting queries to promote evidence-based decisions among health care planners in Israel.
DO EXISTING COST-EFFECTIVENESS THRESHOLDS ADEQUATELY SUPPORT DECISION-MAKING FOR PCM?
A REVIEW OF INTERNATIONAL PRACTICE

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Background:
Incremental cost-effectiveness ratios (ICERs) in health technology assessments (HTA) are compared to explicit or implicit cost-effectiveness thresholds in reimbursement decisions. Technologies in oncology are strong cost drivers; but there is hope that personalized cancer medicine (PCM) provides a new framework in treatment decisions, raising the question of whether thresholds should also differ in PCM. The purpose of this project was to identify ICER thresholds (representing willingness-to-pay [WTP]) worldwide and to compare them to each country’s estimated ability-to-pay (ATP). In addition, we sought to identify whether there are special thresholds or rules in oncology and PCM.

Methods:
We chose 12 HTA agencies from 10 countries in four continents: AHRQ/USA, BIQG-GOEG/Austria, CADTH/Canada, DAHTA@DIMD/Germany, DECIT-CGATS/Brazil, HAS/France, HITAP/Thailand, IQWiG/Germany, LBI-HTA/Austria, MSAC/Australia, NICE/United Kingdom, and SBU/Sweden. We interpreted ICER thresholds as proxy for society’s WTP. ATP was approximated by (1) the gross domestic product per capita (GDPPC), (2) 3-times GDPPC, and (3) the World Bank Income Level. We collected data on each country’s WTP and ATP from methodological guidelines, economic analyses, health economists’ expert publications, and statistical sources (e.g., Organisation for Economic Co-operation and Development [OECD]). We used Spearman rank correlation and graphical inspection to compare WTP and ATP.
Results:
Of the 10 countries, we identified only two countries with explicit ICER thresholds (NICE, HITAP) and six countries with implicit ones; no thresholds could be identified for Germany and Austria. WTP was associated with ATP, especially if a priori GDPPC thresholds are chosen. Most of the thresholds identified were general and unspecific to personalized medicine or cancer. Only NICE particularly allows cancer-specific ICER thresholds. Other agencies address specific PCM or cancer-related guidance without any link to ICER thresholds.

Conclusions:
Cost-effectiveness is only one of many criteria in health care decision making; and it is rarely explicit and transparent. ICER thresholds correlate with reasonable criteria such as the wealth of a country. Further work in the fast evolving field of personalized medicine and high-cost interventions could help inform the multitude of criteria used to evaluate new technologies, identify best practices and suggest innovative ways for more informed decision making.
ADMINISTRATION COSTS OF INTRAVENOUS BIOLOGIC
DRUGS FOR RHEUMATOID ARTHRITIS: DISCREPANCY
BETWEEN LIST COST PRICES AND PUBLISHED COSTS

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Background:
In Finland the intravenous drugs are financed by municipalities who are
responsible for organizing health care services for their residents. The
services are organised in a non-profit setting and therefore the price lists of
health service providers can be used to estimate the costs of infusible drugs
for the Finnish public payer.

Objectives:
To estimate the drug-specific administration cost of biologic intravenous
rheumatoid arthritis (RA) drugs in adult population and to compare the
obtained costs to cost estimates used in published literature.

Methods:
Cost price data for biologic intravenous RA drugs was systematically
collected from the year 2011 Finnish price lists. Further adjustments for
drug brand, dose, and hospital type were done using regression methods
(ordinary least squares with and without logarithmic transformation, and
generalized linear modelling) in order to improve the comparability between
drugs.
A rapid literature review was performed to obtain administration cost
estimates used in publications. The published costs were converted to
Finnish values using base-year purchasing power parities and indexing to
year 2011.

Results:
82 out of 176 cost price observations reported the drug brand and dose
correspondent to the average RA patient weight and RA indication
(infliximab 3mg/kg, rituximab 0.5–1g, abatacept 750mg, tocilizumab
8mg/kg), and were included. The average administration costs/infusion for
infliximab, rituximab, abatacept, and tocilizumab were €355.91; €561.21;
€334.00; and €293.96, respectively. The regression-adjusted mean
administration costs were €289.12/infusion (95%CI €222.61–375.48) for
infliximab and €542.28/infusion (95%CI €307.23–957.09) for rituximab.
A disparity was observed. The estimated average administration costs were
1.8–3.3-fold higher than the previously published average administration
costs (n=17) for RA. Many published studies ignored differences in
administration times and assumed that the administration cost would equal
an outpatient visit cost.

Conclusions:
The administration costs of intravenous RA drugs vary between drugs, and
more effort should be used to find realistic estimates for health economic
evaluations.
Decision making in child protection is coming under increasing public scrutiny but there is limited robust research, theorising or modelling on this topic. Some key decisions in this field might be conceptualised as judging the information about a child and family situation in relation to a threshold. Examples are whether or not a referral warrants a full investigation; whether or not a child’s name should be put on, or taken off, the Child Protection Register (or equivalent); whether or not a child is considered to be at risk of significant harm; and whether or not a child should be taken into state care.

Six databases (ASSIA, Medline, PsycInfo Social Care Online, Social Services Abstracts and SSCI) were searched to identify studies reporting threshold decisions relevant to any category of child abuse and neglect using advanced search techniques adapted from those used for Cochrane Collaboration systematic reviews (Taylor et al, 2007). The inclusion criteria were that the papers must report empirical research; be published from 1995 in English; focus on decision making by child protection social workers; and address the creation, use or interpretation of a threshold against which a child and family circumstances must be judged. Hand searching of references within articles was undertaken to identify additional material.

The two reviewers independently appraised each possible article for relevance and discussed any disagreements to reach consensus on the application of the inclusion criteria. Data is now being extracted from relevant articles and synthesized.

This poster will:

1. outline the process of identifying relevant studies;
2. identify theoretical approaches to decision making used in the studies; and
3. synthesize findings in relation to decision models used.

References:
THE IMPACT OF AFFECTIVE AND COGNITIVE EVALUATIONS ON PREGNANT WOMEN’S DECISION ABOUT PRENATAL SCREENING

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Background:
Affect influences decision making by affective evaluations during decision making (Slovic et al 2002) or anticipating emotional reactions to consequences of decisions (Mellers et al 1999), and may have a greater impact on risk-taking behavior than cognitive evaluations. The aim of the present study is to establish the effects of cognitive and affective evaluations as well as anticipated emotions on pregnant women’s decisions about prenatal screening for Down syndrome, a complex and emotional decision.

Methods:
1650 women attending one of 44 midwifery and gynecology practices in the Netherlands were asked to fill out postal questionnaires before and after the prenatal screening offer. Measures included cognitive variables (perceived probability and perceived severity of getting a child with Down syndrome), affective variables (child-related anxiety, emotions related to decision making) and a measure of anticipating emotions (“I imagined how I would feel if I take / do not take the test”).

Results:
Logistic regression analysis on women’s decision to have a screening test showed that pregnant women’s decisions are mainly determined by perceived severity of having a child with Down syndrome, emotions related to making the decision and the anticipation of emotions as a consequence of not taking the test. Perceived probability of having a child with Down syndrome as well as anticipated emotions of taking the test did not affect women’s decisions.

Conclusion:
The decision about prenatal screening is mainly determined by emotions during decision making as well as the anticipated emotions as a consequence of not doing the test.
REDUCING THE EFFECT OF MALARIA IN PREGNANCY ON LOW BIRTH WEIGHT AND INFANT MORTALITY: A DECISION ANALYSIS MODEL ON THE POTENTIAL ROLE OF RAPID DIAGNOSIS TESTS

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Background:
The spread of resistance to sulfadoxine-pyrimethamine across sub-Saharan Africa is compromising the effectiveness of intermittent preventive treatment of malaria in pregnancy. Investigations on alternatives drugs for intermittent preventive treatment or alternatives strategies for the prevention of malaria in pregnancy are therefore important. Intermittent screening with a rapid diagnostic test followed by treatment if positive was presented as an alternative strategy. We reviewed papers reporting on the use of rapid diagnosis tests (RDT) in pregnancy and we carried out an analysis using decision tree models to examine the potential gain of using RDT during pregnancy in term of reduction of low birth weight (LBW) and infant mortality.

Methods and findings:
We searched studies reporting on the use of RDTs in pregnancy until 2010 and reported in English in electronic databases, MEDLINE and Web of science using several combinations of key words. A published modeling framework was used to develop a decision-tree for introducing the screening of pregnant women with RDT as a new diagnostic tool to detect falciparum infection during pregnancy. This model was used to estimate the potential benefit of RDT when compared to the current situation, in terms of reduced LBW and infant death. Introducing a RDT with 90% sensitivity and 95% specificity at an access level of 50%, about 432,000 LBW and 25,000 subsequent infant’s deaths would be averted, mounting to 50,000 averted infant deaths (range: 24.210 to 64.560), if all at risk pregnant women were given access to it.

Conclusion:
Intermittent screening and treatment using RDTs could reduce the burden of malaria infection during pregnancy, the risk of LBW and the associated infant mortality. Field studies on the effectiveness of this strategy should be carried out to confirm such predictions, possibly in areas of differing endemicity and SP resistance.
DEVELOPING AND BENCHMARKING POLICY SOLUTIONS FOR MEDICINES ADHERENCE INTERVENTIONS FOR EUROPE

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Objective:
Patient nonadherence to prescribed medication is common and widespread. Despite much research to understand the causes, consequences and solutions to medication nonadherence, clear research-based evidence of how to reduce non-adherence remains elusive. This paper describes two related studies conducted as part of the FP7 European Commission funded Ascertaining Barriers to Compliance (ABC) project. We sought to develop consensus-based policy solutions to address medicines adherence and benchmark current implementation activity for those policy solutions.

Methods:
Delphi study:
A four round Delphi study was conducted. The panel comprised 49 participants from 14 countries and were representatives of a range of stakeholder groups. Participants engaged in the study remotely, anonymously and electronically. Participants were initially invited to respond to open questions about the causes, consequences and solutions to medication nonadherence. Subsequent rounds refined responses, and sought ratings of the relative importance, operational and political feasibility of each potential solution to medication nonadherence. Feedback of individual and group responses was provided to participants after each round. A consensus meeting was held upon completion of the Delphi study to discuss and further refine the proposed policy solutions.

National self-assessment study:
An online survey and semi-structured follow-up telephone interview were conducted based on policy solutions resulting from the consensus study. National medicines leads within the Ministries of Health for the 27 European Union member states were invited to participate. Participants rated the extent and appropriateness of implementation of each policy solution in their country.

Principal Findings:
43 separate policy solutions to medication non-adherence were agreed by the Panel. 25 policy solutions were prioritised based on composite scores for importance, operational and political feasibility. Prioritised policy solutions focused on interventions for patients, training for healthcare professionals, and actions to support partnership between patients and healthcare professionals. Few solutions concerned actions by governments, healthcare payers, or interventions at the system level.

Implementation varied across nations. Some European nations had not identified medication adherence as a priority and tended to be concerned with developing more general clinical governance arrangements. Some European nations had much more systematic, co-ordinated approaches to implementing policy solutions to address medication nonadherence.