no missed studies in 6 reviews and 1 in each of 2 reviews (0.3 and 1.5% eligible studies). Estimated human FN rates were 0.11 - 0.94%. These NLPs achieved consensus exclusion for a median of 26% of records (range 3-57%). Descriptive assessment of NLP FNs suggested no or little impact on the reviews' results/conclusions. ***Conclusions:*** In these reviews, NB/SVM classifiers, running independently, incorrectly excluded fewer records than individual human reviewers. Even in this conservative scenario, these tools decreased workload to identify relevant literature. This adds to the growing body of evidence to help review teams considering such tools. Additional research spanning review topics and types will inform the use of this continually evolving technology.

Cost-Effectiveness Studies

CC1
RE-EVALUATION OF THE COST-EFFECTIVENESS OF CASCADE SCREENING AND TREATMENT STRATEGIES FOR ADULTS WITH FAMILIAL HYPERCHOLESTEROLEMIA IN THE UNITED STATES

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Objectives: Familial hypercholesterolemia (FH) is a genetic disorder that leads to premature cardiovascular disease if untreated. Although it was previously thought that cascade genetic screening for FH is not cost-effective in the US, the cost of genetic testing has decreased substantially while PCSK9 inhibitors, a novel new lipid-lowering treatment, have been approved for use in FH. This study aimed to re-examine whether cascade genetic screening or cascade lipid screening is cost-effective for first-degree relatives of adults diagnosed with heterozygous FH in the US, compared to no cascade screening, and whether follow-on treatment with statins plus PCSK9 inhibitors (PCSK9i) is cost-effective, compared to high-intensity standard-of-care treatment with statins plus ezetimibe (HI-SOC). ***Methods:*** A decision tree was used to evaluate disease detection with the three screening strategies, while a lifetime Markov model was used to evaluate disease progression in one-year cycles until death. We report the incremental cost-effectiveness ratios (ICER) in terms of costs and quality-adjusted life years (QALYs) between six screening and treatment strategies, considering the US societal perspective. ***Results:*** At a willingness-to-pay threshold of $150,000/QALY, cascade genetic screening, whether paired with HI-SOC or PCSK9i, is the most cost-effective screening strategy, dominating all other alternatives assessed. Compared to cascade genetic screening with HI-SOC, cascade genetic screening with PCSK9i is cost-effective with an ICER of $56,034/QALY. Results were robust in one-way and probabilistic sensitivity analyses. Baseline cholesterol levels, treatment-adjusted cholesterol levels, and diagnostic test sensitivities had the greatest impact on ICERs. ***Conclusions:*** This study is the first to incorporate lower genetic testing costs, newly available information on diagnostic test accuracy, effects of novel treatments, disease prognosis, and increased cardiovascular risk in this population. The results support cascade genetic screening for FH with subsequent HI-SOC or PCSK9i treatment as an evidence-based intervention that dominates alternative strategies and provides good value relative to costs.

CC2
COST-EFFECTIVENESS ANALYSIS OF NEWBORN SCREENING AND TREATMENT FOR SPINAL MUSCULAR ATROPHY

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Objectives: Spinal muscular atrophy (SMA), a rare pediatric disorder, was recommended for national screening in the U.S in 2018. However, the high cost of the only available drug treatment (nusinersen) and a potential future gene therapy (onasemnogene abeparvovec) raises the question of whether newborn screening for SMA will be economically favorable. The objective is to evaluate the cost-effectiveness of newborn screening and treatment of SMA in the U.S. ***Methods:*** We compared the costs and health outcomes of newborn screening (NBS) and clinical identification (CI) from a healthcare sector perspective. Treatments included standard care, drug (nusinersen, estimated $750,000, first year; $375,000, annually/patient), or gene therapy (onasemnogene abeparvovec, estimated $2,000,000/patient, one-time cost). Four strategies were compared: NBS/drug (future practice), NBS/gene therapy (future practice), CI/drug (current practice), CI/standard care (former practice). We developed a state-transition model to simulate the costs and health outcomes of a hypothetical cohort of 4,000,000 newborns over a lifetime. State-transition probabilities, costs, and health utilities were derived from published literature. Primary outcomes included costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs). Costs and QALYs were discounted at 3%. ***Results:*** NBS strategies had higher costs and QALYs than CI strategies (NBS/drug: $843, 30.2440 QALYs; NBS/gene therapy: $454, 30.2442 QALYs; CI/drug: $178, 30.2428 QALYs; CI/standard care: $13, 30.2427 QALYs). When compared with CI/standard care, CI/drug had an ICER of $2,694,167/QALY. When compared to CI/drug, NBS/gene therapy had an ICER of $187,650/QALY. NBS/drug was dominated by NBS/gene therapy due to higher costs and slightly lower QALYs. However, when compared with CI/drug, NBS/drug had an ICER of $515,555/QALY. ***Conclusions:*** When compared to clinical identification with drug, newborn screening with drug or gene therapy yield cost-effectiveness results that are unlikely to be considered favorable. Future research should explore under what conditions receiving these new treatments would maximize patient benefit yet be considered more economically favorable.

CC4
COST-EFFECTIVENESS ANALYSIS OF THE STEPPED EXERCISE PROGRAM FOR PATIENTS WITH KNEE OSTEOARTHRITIS (STEP-KOA) TRIAL

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Objectives: To evaluate the cost-effectiveness of the STepped Exercise Program for patients with Knee OsteoArthritis (STEP-KOA). ***Methods:*** The randomized control trial included 230 intervention and 115 control patients at two Veterans Affairs (VA) medical centers. A decision tree was used to simulate outcomes for cohorts of patients receiving Arthritis Education (control) or STEP-KOA (intervention), which consisted of an internet-based exercise training program (Step 1), phone counseling (Step 2), and physical therapy (Step 3) according to patient needs. Of the 60% (n=138) progressing to Step 2, 59% (n=81) progressed to Step 3. A VA-owned tablet with data was provided to 15% (n=35) of STEP-KOA participants. Micro-costing was used to derive costs from the VA perspective using invoices and VA labor rates. Quality-of-life (QOL) was measured using EQ-5D-5L US utility weights and differential change between arms estimated using site- and sex-adjusted linear mixed models. Incremental cost-effectiveness ratios (ICER) were calculated as the difference in costs divided by the difference in quality adjusted life years (QALY) between arms at 9 months. A Monte Carlo probabilistic sensitivity analysis (PSA) with 1000 simulations was used to generate a cost-effectiveness acceptability curve. ***Results:*** The trial found differential improvement in utility weights of 0.04 (95% confidence interval (CI) 0.003, 0.080; p=0.03) for STEP-KOA versus control at 9 months. In the base case, STEP-KOA resulted in an incremental gain of 0.03 QALYs and an incremental cost of $287 per patient for an ICER of $9,138. One-way sensitivity analyses found the largest sources of variation in the ICER were the impact on QOL and the proportion needing a VA-owned tablet. The PSA found a 99% probability of cost-effectiveness at $50,000 willingness-to-pay per QALY. ***Conclusions:*** STEP-KOA improves QOL by reducing KOA pain and has a high probability of cost-effectiveness. Resources needed to implement the program will decline as ownership of mobile health devices increases.

Comparative Effectiveness Studies & Methods

CE1
METHODOLOGICAL CHALLENGES WITH CONDUCTING NETWORK META-ANALYSES ASSESSING LONG-TERM COMPARATIVE EFFICACY IN PSORIASIS: A CRITIQUE OF ASSUMPTIONS UNDERPINNING RECENT INDIRECT TREATMENT COMPARISONS

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Objectives: In network meta-analysis (NMA) of psoriasis trials, cross-over after an initial placebo-controlled period limits the connectivity of long-term evidence networks. We illustrate the challenges with conducting NMAs assessing efficacy beyond cross-over in psoriasis by critically appraising the assumptions underpinning recent long-term NMAs. ***Methods:*** We compared three recent NMA studies (Armstrong et al. 2019, Sawyer et al. 2018, and Diels et al. 2017) assessing long-term (beyond 16 to 24 weeks) comparative efficacy in psoriasis and investigated how the three studies derived comparative efficacy estimates in the absence of a connected network. While