pelled the questionnaire online. A qualitative analysis of the data, using a combina-
tion of deductive (based on literature) and inductive (based on expert’s opinion),
approaches were performed using NVIVO10 Software. RESULTS: A hierarchical
structure of 100 nodes was designed around 2 main themes: LAIT and chronic graft-
rejection. According to expert interviews, LAIT is a common issue that can have
undesirable health consequences. The main drivers of LAIT were the number of
pills and incidence of adverse events. The main consequences identified by the
experts were antibody mediated graft-rejection and decreased graft survival. CIR
was identified as the second most common cause of graft rejection between 2-3
years post-transplant, behind death with a functioning graft. LAIT could cause up
to 50% of CIR. There is no consensus on treating CIR, but therapies include intrave-
nous immunoglobulins, rituximab and plasmapheresis. Other health resources used
include: at least one diagnostic renal biopsy, 2-fold increase in the cost of health
visits, a higher risk of hospitalization due to complications (infections, heart-failure
and anaemia) and preparation for return to dialysis. Most CIR episodes resulted in
graft rejection and subsequent graft loss (SR). Differences between published and
published meta-analyses with high health-systems costs could be identified, with the
negative effect on the final outcome that otherwise requires long follow-up time. Meta-analysis of
multiple outcomes which takes into account the correlations between them is
particularly suitable for modelling surrogate endpoints. The aim of this study was to
investigate the choice of distributional assumptions when developing meta-
analytic methods for evaluation of surrogate endpoints. METHODS: Two bivariate
meta-analytical models are applied to a case study in chronic myeloid leukaemia when
clearing CML with imatinib. We use two models: 1) the conditional common
response (CCYR) rate at 12 months is a surrogate endpoint. A normal model on
log relative risk scale for both outcomes is applied to evaluate CCYR as a surrogate
endpoint for OS. This model is then extended by relaxing the assumption of nor-
mality in one of the binomial distributions for better fit. RESULTS: The effect on
CCYR was a significant predictor of the effect on OS. Both models gave similar
results for the effect of CCYR on OS. However, the heterogeneity parameter was
larger in the binomial model (2.09-0.92 with 95% CrI, 0.01 to 0.52) compared to normal
case (2.07.0 with 95% CrI, 0.0 to 0.39). CONCLUSIONS: The results of both models
were similar for this case study. However, the choice of distributional assumption
can lead to different estimates of the effect on the final outcome in other disease
areas when the normality assumption is not suitable and consequently this can
impact on HTA decisions.

RESEARCH ON METHODS – Modeling Tools

PRM51 REPLICATION OF A PUBLISHED MARKOV CHRONIC MIGRINE COST-EFFECTIVENESS MODEL FOR PURPOSES OF EARLY PHASE ADAPTATION

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OBJECTIVES: Published cost-effectiveness analysis (CEA) models, especially those
which have been submitted to health technology assessment (HTA) authorities,
are valuable in early phase CEA of interventions in the same or similar disease areas
and documented Markov models can be difficult to repli-
cate. Additionally, differences in disease states, treatment effects, and patient
populations can render a successfully-replicated Markov model non-informative
for early phase investigations. As a basis for future adaptation and expansion, a
published chronic migraine CEA Markov model was replicated in TreeAge Pro
2014 as both a Markov model and as an individual-based state-transition (Monte
Carlo microsimulation [MCM]) model.

METHODS: The published and replicated Markov model results were compared for both base case and sensitivity analyses.
Patient subgroup Markov transition probability (MTP) matrices were implemented
in the MCM, with assumptions regarding unpublished information on post-initial
cycle state transitions. These assumptions involved subgroup treatment effects, patient
decision discontinuation, and treatment stopping rules. The overall patient
population (OPP) MTP matrices generated by the MCM were loaded into the Markov
model to assess the validity of the assumptions. RESULTS: Incremental costs and
quality-adjusted life-years (QALYs) between intervention with onabole-
binumtoxinA and placebo were produced. Differences between published and
replicated Markov model incremental cost and QALY results were small for the base
case (0.0%, -1.1%) and selected sensitivity analyses (maximum differences
of 5.2%, 11.7%). This reflects the assumptions involved with subgroup treatment effects,
patient adherence is considered a preventable but frequent cause of CHR and graft loss.
Treatment simplification and education could improve adherence and burden of
disease for KT patients.

PRM52 RECONSTRUCTION OF INDIVIDUAL PATIENT DATA BASED ON PUBLISHED KAPLAN-MEIER CURVES: CASE OF REGORAFENIB FOR COLORECTAL CANCER

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OBJECTIVES: To conduct pharmacoeconomic analyses, both cost and effective-
ness data are required. Randomized controlled trials (RCTs) are often used as a
source of efficacy data. As RCTs are often of short duration, efficacy data need to
be extrapolated beyond the trial follow-up period to be fit for use in model-based
pharmacoeconomic evaluations. However, RCTs usually report effectiveness data in
terms of Kaplan-Meier (KM) estimates. As a result, researchers need to reconstruc-
t individual patient data (IPD) from published KM curves of trials’ treatment
arms to estimate their long-term effects. This study aims to reconstruct the survival
benefits of regorafenib monotherapy for previously treated metastatic colorectal
cancer (CORRECT), an international, multicentre, randomized, placebo-controlled,
phase 3 trial. METHODS: An algorithm developed by Guoyou and colleagues was
adopted to reconstruct IPD using R statistical package, based on the overall survival
KM curves of the CORRECT trial. The reconstruction of IPD included the following
steps: 1) the KM estimates from published KM curves were used to create a dataset
developmental; 2) creation of a second dataset, and application of the algorithm. The results of
the original trial were compared to the reconstructed data using graphical and quantita-
tive methods, for validation purposes. RESULTS: Based on the IPD reconstruction,
162 and 88 events occurred in the regorafenib and placebo groups respectively. The
median overall survival time in the regorafenib arm was 6.5 months (95% CI 5.83, 8.43) which is about the same as the original trial (6.4 months). In the placebo group,
the median overall survival for the reconstruction data was 5.09 months (95% CI
4.30, 6.81) compared to the trial median survival of 5.0 months. CONCLUSIONS:
The results of this study can be utilized to estimate transition probabilities for
model-based pharmacoeconomic evaluations in the absence of individual patient
data (IPD).

PRM53 CHOICE OF DISTRIBUTIONAL ASSUMPTIONS IN META-ANALYSIS FOR THE EVALUATION OF SURROGATE ENDPOINTS

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OBJECTIVES: In health technology assessment meta-analysis is used to combine
 evidence from a number of studies to inform the decision-making process. When
evaluating new health technologies at early stages of their development, treat-
ment effects on short-term surrogate endpoints may be used to predict the effect
on the final outcome that otherwise requires long follow-up time. Meta-analysis of
multiple outcomes which takes into account the correlations between them is
particularly suitable for modelling surrogate endpoints. The aim of this study was to
investigate the choice of distributional assumptions when developing meta-
analytic methods for evaluation of surrogate endpoints. METHODS: Two bivariate
meta-analytical models are applied to a case study in chronic myeloid leukaemia when
clearing CML with imatinib. We use two models: 1) the conditional common
response (CCYR) rate at 12 months is a surrogate endpoint. A normal model on
log relative risk scale for both outcomes is applied to evaluate CCYR as a surrogate
endpoint for OS. This model is then extended by relaxing the assumption of nor-
mality in one of the binomial distributions for better fit. RESULTS: The effect on
CCYR was a significant predictor of the effect on OS. Both models gave similar
results for the effect of CCYR on OS. However, the heterogeneity parameter was
larger in the binomial model (2.09-0.92 with 95% CrI, 0.01 to 0.52) compared to normal
case (2.07.0 with 95% CrI, 0.0 to 0.39). CONCLUSIONS: The results of both models
were similar for this case study. However, the choice of distributional assumption
can lead to different estimates of the effect on the final outcome in other disease
areas when the normality assumption is not suitable and consequently this can
impact on HTA decisions.