Assessing the costs and benefits of a pharmacogenetic test to reduce the incidence of adverse events
Fatihah Shabaruddin*, Rachel A Elliott†, Paul Tappenden‡ and Katherine Payne*
Health Services – Economics, University of Manchester†, Department of Pharmacy, University of Malaya, Malaysia‡, School of Pharmacy, University of Nottingham§, UK. XMM, University of Sheffield

Introduction
Pharmacogenetic testing can be used to reduce the incidence of adverse events by stratifying patient populations into different at risk groups. Irinotecan is a chemotherapy drug for advanced colorectal cancer (CRC). The IrMDG regimen is the most frequently prescribed irinotecan-based regimen in the UK. Neutropenia, a key adverse event of irinotecan-based chemotherapy, is associated with infection-related morbidity and mortality, and could be expensive to manage. The UGT1A1 pharmacogenetic test can potentially inform irinotecan dose selection and reduce the incidence of neutropenia-related complications. This study is part of a PhD project funded by the Ministry of Higher Education, Malaysia and the University of Malaya, Kuala Lumpur.

Methods
An economic model was developed to draw together relevant evidence concerning treatment pathways, health outcomes and associated costs (Figure 1) from the NHS perspective over a lifetime horizon. Clinical care pathways were informed by a national survey of NHS CRC consultants (n=44)1. Data from an observational micro-costing study (n=48 patients)2 and a systematic review of the effectiveness and utility literature, elicitation of expert opinion and published literature were used to populate the model. Table 1 presents the data used to populate the model. Deterministic and probabilistic analyses were conducted. Sensitivity analysis of the model parameters and structure were also conducted.

Results
UGT1A1 testing was cost-saving, resulted in fewer episodes of neutropenia and led to a gain of life-years and QALYs compared to current practice. For a cohort of 2,600 NHS patients that are estimated to receive second-line IrMDG chemotherapy per year4,5, the use of the UGT1A1 test compared to standard practice could potentially save £376,687 (equivalent to £44,88 per patient), avoid 195 episodes of grade 3 or 4 neutropaenia (equivalent to 0.04% age per patient), gain 1.67 additional life-years (equivalent to 0.0004% life year per patient) and gain additional £717 QALYs (equivalent to 0.000045 QALY per patient). Cost-effectiveness planes of the probabilistic analysis are presented in Figures 2 and 3. The cost-effectiveness acceptability curve (Figure 4) indicated that the probability that the test is cost-effective at willingness-to-pay thresholds between £20,000 and £30,000 per QALY was above 95%.

Discussion
This is the first economic evaluation of UGT1A1 testing conducted from the UK NHS perspective. Care pathways in the model reflected current NHS patients’ treatment pathways and management strategies. The data used in the economic evaluation were selected to closely reflect NHS clinical pathways, costs and outcomes. The results indicated that UGT1A1 testing was cost-saving, resulting in fewer episodes of grade 3 or 4 neutropaenia and gained more life-years and QALYs. A key driver of cost-effectiveness for the UGT1A1 test was the effect of irinotecan dose reduction on overall survival.

Conclusion
UGT1A1 testing led to lower costs and incidence of irinotecan-related neutropenia and higher life-years and QALYs, conditional on the assumption that irinotecan dose reduction did not adversely affect survival. It is important to appropriately assess interventions that aim to reduce the incidence of adverse events to accurately understand the impact of their use and provide robust evidence to inform NHS decision-making.

Acknowledgments
This study is part of a PhD project funded by the Ministry of Higher Education, Malaysia and the University of Malaya, Kuala Lumpur.

Fatihah.shabaruddin@gmail.com

Key Messages
• The UGT1A1 pharmacogenetic test can potentially inform dose selection of irinotecan-based chemotherapy and reduce the incidence of neutropenia, a key adverse event of irinotecan-based chemotherapy in advanced colorectal cancer patients.
• The results of the economic evaluation indicated that UGT1A1 testing was cost-saving, resulted in fewer episodes of neutropenia and led to a gain of life-years and QALYs compared to current practice.
• These findings were specific to model assumptions and specifications. Sensitivity analysis suggested that the main driver of cost-effectiveness was the effect of irinotecan dose reduction on survival.

References
1 Shabaruddin F, Elliott R, Tappenden P. Understanding chemotherapy treatment pathways and pathways and management strategies. The data used in the economic evaluation were selected to closely reflect NHS clinical pathways, costs and outcomes. The results indicated that UGT1A1 testing was cost-saving, resulting in fewer episodes of grade 3 or 4 neutropaenia and gained more life-years and QALYs. A key driver of cost-effectiveness for the UGT1A1 test was the effect of irinotecan dose reduction on overall survival.

Figure 1: Model structure for the economic evaluation of UGT1A1 testing to reduce the incidence of irinotecan chemotherapy-related grade 3 and 4 neutropaenia.