Proceedings of the 2018 Winter Simulation Conference
M. Rabe, A.A. Juan, N. Mustafee, A. Skoogh, S. Jain, and B. Johansson, eds.

SIMULATING THE COST-EFFECTIVENESS OF STRATEGIES TO REDUCE THE PROBABILITY OF SURGICALLY-TRANSMITTED CREUTZFELDT-JAKOB DISEASE

Matt Stevenson

The University of Sheffield
30 Regent Street
Sheffield, S1 4DA, ENGLAND

Jeremy Oakley

The University of Sheffield
Hounsfield Road
Sheffield, S3 7RH, ENGLAND

Stephen E. Chick

INSEAD
Boulevard de Constance
77300 Fontainebleau FRANCE

Lesley Uttley
Christopher Carroll

The University of Sheffield
30 Regent Street
Sheffield, S1 4DA, ENGLAND

ABSTRACT

Creutzfeldt-Jakob disease (CJD) is a fatal disease caused by prions. Prions on surgical instruments are not completely deactivated and subsequent patients may become infected resulting in surgically transmitted CJD (stCJD). Work was undertaken to assess the cost-effectiveness of strategies to reduce the probability of stCJD. Strategies evaluated included: no changes; ensuring that instruments were kept moist; prohibiting instrument migration between sets; and employing single-use instruments. A stochastic mathematical model was constructed with key model parameters populated via elicitation. The model was calibrated to match the possible number of observed stCJD cases between 2005 and 2018, noting that stCJD cases could be misdiagnosed. Results indicated that keeping instruments moist reduced the number of stCJD cases and saved money. Further measures (prohibiting set migration, or single-use instruments) reduced the risk of stCJD cases, compared with keeping instrument moist, but at considerable cost and poor value for money.

1 INTRODUCTION

Prions are abnormal infectious proteins which are not completely deactivated by conventional hospital cleansing techniques. Therefore, subsequent patients may be infected by surgical instruments, resulting in a surgically-transmitted CJD (stCJD) case. Work undertaken previously by the authors was used to inform guidance by the National Institute for Health and Care Excellence (NICE 2006). Having observed more data, we were asked by NICE to revisit the modelling and to estimate the cost-effectiveness of strategies to reduce the probability of stCJD. Strategies evaluated included: doing nothing; ensuring that instruments were kept moist; prohibiting instrument migration between sets; and employing single-use instruments. NICE validated the model structure and helped inform model parameters.

2 METHODS

The model reported in Stevenson et al. (2009) was amended to consider views from experts on the NICE committee. Key changes included the possibility that stCJD cases could be misdiagnosed as a different neurodegenerative disease, and that all patients were susceptible to infection.

The mathematical model was a mixed model, with discrete event simulation modeling the usage, management, and potential mixing of surgical instruments, and with continuous differential equation

models to represent population dynamics of individuals which may be carriers of prions and may need to undergo high risk surgical procedures. Thus, there were two main sources of randomness in the model: stochastic simulations modeled the numbers of stCJD cases given a set of input parameters; Monte Carlo simulations to represent unknown disease transmission, natural history of infection, and other relevant parameters were done to perform a so-called probabilistic sensitivity analysis.

Data from systematic literature reviews that could inform the model were limited and thus elicitation was used to populate key parameters including: efficacy of decontamination; incubation period associated with stCJD; and possibility of misdiagnosis. A key difference is that in contrast to the earlier work we had data from multiple years on which to calibrate the model. Zero stCJD cases have been observed since 2005, although there may have been potentially 15 identified sporadic CJD cases that may have been stCJD. Approximate Bayesian Computation ("ABC"; see, e.g., Sunnåker et al. 2013) was used to obtain samples from the posterior distribution of the model parameters, and hence obtain calibrated model predictions, by running the model forward over the posterior samples. Due to the computational expense of running the model and implementing ABC, various heuristics were used to accelerate the algorithm.

3 RESULTS

Compared with no change (O1), keeping instruments moist (O2) reduced the risk of stCJD cases, increased quality-adjusted life years (QALYs) and saved money. Further measures of prohibiting set migration (O3), or using single-use instruments (O4) reduced the estimated risk of stCJD cases compared with O2 but at a considerable cost which represented poor value for money with cost per QALY values in excess of £1.5 million; markedly higher than NICE's published thresholds. For O2 it was expected that there would be fewer than 0.09 stCJD cases caused by infection between 2019 and 2023, with a maximum number of 1.74 stCJD cases. Corresponding values were: 0.43/4.26 for O1; 0.05/0.51 for O3; and 0.00/0.00 for O4. QALY losses were: 4.01 (SE 0.53) for O1; 0.87 (SE 0.15) for O2; 0.46 (SE 0.07) for O3; and 0.00 (SE 0.00) for O4. All results are presented in terms of a surgical unit (1/27 of England).

4 CONCLUSIONS

Ensuring that instruments are kept moist appears to be clinically effective, highly cost-effective and with a small number of simulated stCJD cases. None of the strategies evaluated to further reduce the probability of stCJD cases appear cost-effective.

ACKNOWLEDGMENTS

This report was commissioned by the NIHR HTA Programme as project number 17/48/01.

REFERENCES

NICE. 2006. "Patient safety and reduction of risk of transmission of Creutzfeldt-Jakob (CJD) via interventional procedures. National Institute for Health and Care Excellence". https://www.nice.org.uk/Guidance/IPG196. Accessed 7th March 2018.

Stevenson, M.D., J.E. Oakley, S.E. Chick, and K. Chalkidou. 2009. "The Cost-Effectiveness Of Surgical Instrument Management Policies To Reduce the Risk Of Vcjd Transmission To Humans". *Journal of the Operational Research Society* 60(4):506 - 518.

Sunnåker, M., A.G.Busetto, E. Numminen, J. Corander, M. Foll, and C. Dessimoz. 2013. "Approximate Bayesian computation". PLOS Computational Biology". 9(1):e1002803. doi.org/10.1371/journal.pcbi.1002803.