NICE National Institute for Health and Care Excellence

Testing strategies for Lynch syndrome in people with endometrial cancer

Diagnostics Assessment Report (DAR) - Comments

Stakeholder	Comment no.	Page no.	Section no.	Comment	EAG Response
University of Exeter	1	53	3.3.2.2	Please clarify whether cohorts with different MMR genes affected are being modelled separately or if their risks are being aggregated into an "average" Lynch syndrome case. I believe from inspecting the model that the genes are modelled separately.	The risks are modelled separately
University of Exeter	2	53	3.3.2.2	Please confirm what age probands are assumed to be in the base case. They will generally be younger than unselected endometrial cancer patients (and this will depend on which MMR gene is affected) but there will be a broad range of ages. If results are calculated by averaging across a number of ages these should be weighted appropriately (not uniformly). If the outputs from an "average aged" proband are being used, it should be demonstrated that outputs are linear with respect to age, otherwise this will be a biased estimate of the average outputs over age.	We have calculated long-term outcomes for a range of proband ages, but our base case results use the long-outcomes predicted for women aged 49. We chose this as 'typical' for the population, as we were not aware of robust data on the distribution of ages likely to be found on testing. This is a limitation of the analysis, but we would be happy to conduct sensitivity analysis on this assumption over a plausible range, as we have the results already to do this. These results suggest that this parameter has minimal impact on cost-effectiveness.
University of Exeter	3	54	3.3.2.2	It is stated "We do not model outcomes for those without Lynch, on the assumption that they experience no long term costs and benefits from Lynch testing." However, if individuals are being recommended to undergo cancer surveillance in line with those recommended for those diagnosed with Lynch syndrome (FP accepting), then they will incur costs of surveillance (probably for minimal benefit). Omitting these costs biases in favour of testing for Lynch syndrome.	We assume that germline testing is 100% accurate and that there are therefore no FP accepting. Even if there were, numbers are likely to be negligible.
University of Exeter	4	56	3.3.2.2	CRC stage IV has ***dis***utility of 0.178 rather than utility.	We have assumed a utility rather than a disutility, which would lead us to overestimate the benefits of surveillance. However, we note other comments received suggesting that the

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					utilities we assume are likely to over-estimate quality of life in those with cancer, so that the disutility of 0.178 is itself likely to be an underestimate. In any case, the impact of this parameter is minimal, as survival in stage IV is low, and QALY gains in the model are driven by mortality.
University of Exeter	5	56	3.3.2.2	Endometrial cancer survival may be improved with Lynch syndrome versus unselected endometrial cancer patients. See for example Dominguez-Valentin et al. 2020 for the most recent survival estimates from the PLSD, and see Shikama et al. 2016 for a case series of consecutive patients. Note that women with Lynch syndrome who develop endometrial cancer are likely to be younger and less obese than women without Lynch syndrome who develop endometrial cancer.	We accept this is possible, but were unable to incorporate it in the current version of the model.
University of Exeter	6	229	6.4.2	Please confirm whether costs of lifetime surveillance are incorporated for false positive diagnoses (i.e., those with positive tumour test results who decline genetic testing and are assumed to have Lynch syndrome).	These costs are included.
Institute of Biomedical Science				Thank you for the opportunity to comment on the DAR for testing strategies for Lynch syndrome in people with endometrial cancer. The documents have been reviewed by our specialist advisory panel with no comments made.	