The cost-effectiveness of genetic testing strategies to diagnose lynch syndrome in incident colorectal cancer patients in Singapore

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ABSTRACT

Introduction: Universal genetic testing in colorectal cancer (CRC) patients coupled with cascade testing among family members has been proposed as a public health strategy to reduce LS-related cancer burden in a cost-effective manner. However, it has never been validated in Singapore's context. Therefore, the current study aims to investigate whether universal genetic testing plus cascade testing is cost-effective to detect and manage LS in incident CRC patients and their first-degree relatives (FDRs). **Materials and Methods:** This model-based economic evaluation adopted a healthcare system perspective to compare universal genetic testing with universal tumor-based testing strategies (standard of care) and no testing. A decision tree along with Markov models was constructed to simulate the lifetimes of CRC patients and their FDRs (siblings and children), estimating the outcomes of the diagnostic strategies, LS-associated cancer surveillance, and/or prophylactic surgery. We assumed that probands develop up to two cancers and the second cancer can be either CRC, gastric or endometrial cancer. We also assumed 30% acceptance of genetic testing in the FDRs and 80% compliance with LS-specific surveillance programs in the simulated population. Costs and quality-adjusted life years (QALYs) were calculated for each strategy and discounted at 3% annually. Costs were in SGD, May 2024. **Results:** In the base-case analysis with ~4 FDRs per patient, immunohistochemistry-guided GT strategy was the most cost-effective strategy with an incremental cost-effectiveness ratio (ICER) of 32,307/QALY. Universal GT is the most effective strategy, detecting 99.5% of LS cases and yielding the highest QALYs, but requires a higher WTP to be cost-effective. **Conclusion:** In Singapore, universal genetic testing is likely cost-effective for LS screening in incident CRC patients compared to no testing, but not compared to IHC-guided GT. This finding has significant policy implications, supporting the consideration of universal genetic testing as a routine strategy and subsidy allocation.

Keywords: Cost-utility analysis, genetic testing, Lynch syndrome, Colorectal cancer, economic evaluation