BACKGROUND: Strategies for screening colorectal cancers (CRC) for possible Lynch syndrome (LS) are evolving rapidly. The costs and optimal strategy are unclear.

AIMS: To compare the diagnostic results and costs from two LS screening strategies: Targeted Screening (TS) and Universal Screening (US) of tumors for mismatch repair (MMR) abnormalities.

METHODS: In 2010-2011, we employed TS (age<60 and/or meeting Bethesda criteria for LS). From 2012, we screened all CRC. Immunohistochemistry (IHC) for the four MMR proteins was done in all cases. Microsatellite instability, BRAF mutation, MLH1 methylation testing, and/or germline DNA testing was done in selected cases. We modeled the diagnostic costs of detecting LS, and the downstream costs of preventing CRC by colonoscopy screening, using a system dynamics model, built in the Anylogic program.

RESULTS: Using TS, 51/175 (29%) incident CRCs were screened; 15 (29%) showed abnormal loss of >1 MMR protein. Germ line MMR gene mutations were found in 4 cases and were suspected but not demonstrated in 11 cases. Using US, 194 CRCs were screened; 13 (6.7%) of CRCs had abnormal IHC suspicious for LS. MMR mutations were found in only 2/9 cases abnormal for IHC. Cost to identify the LS probands was ~$8,339/LS case diagnosed for targeted screening (four mutation carriers/18 months) and ~$32,708/LS case diagnosed for universal screening (two mutation carriers/24 months).

CONCLUSIONS: Real-world results were more complicated than anticipated, including atypical IHC results and incomplete follow-up. Economic analysis suggests that TS is less costly than US, but it will miss some cases of mildly penetrant LS. Changes in testing costs could change the optimal algorithm.