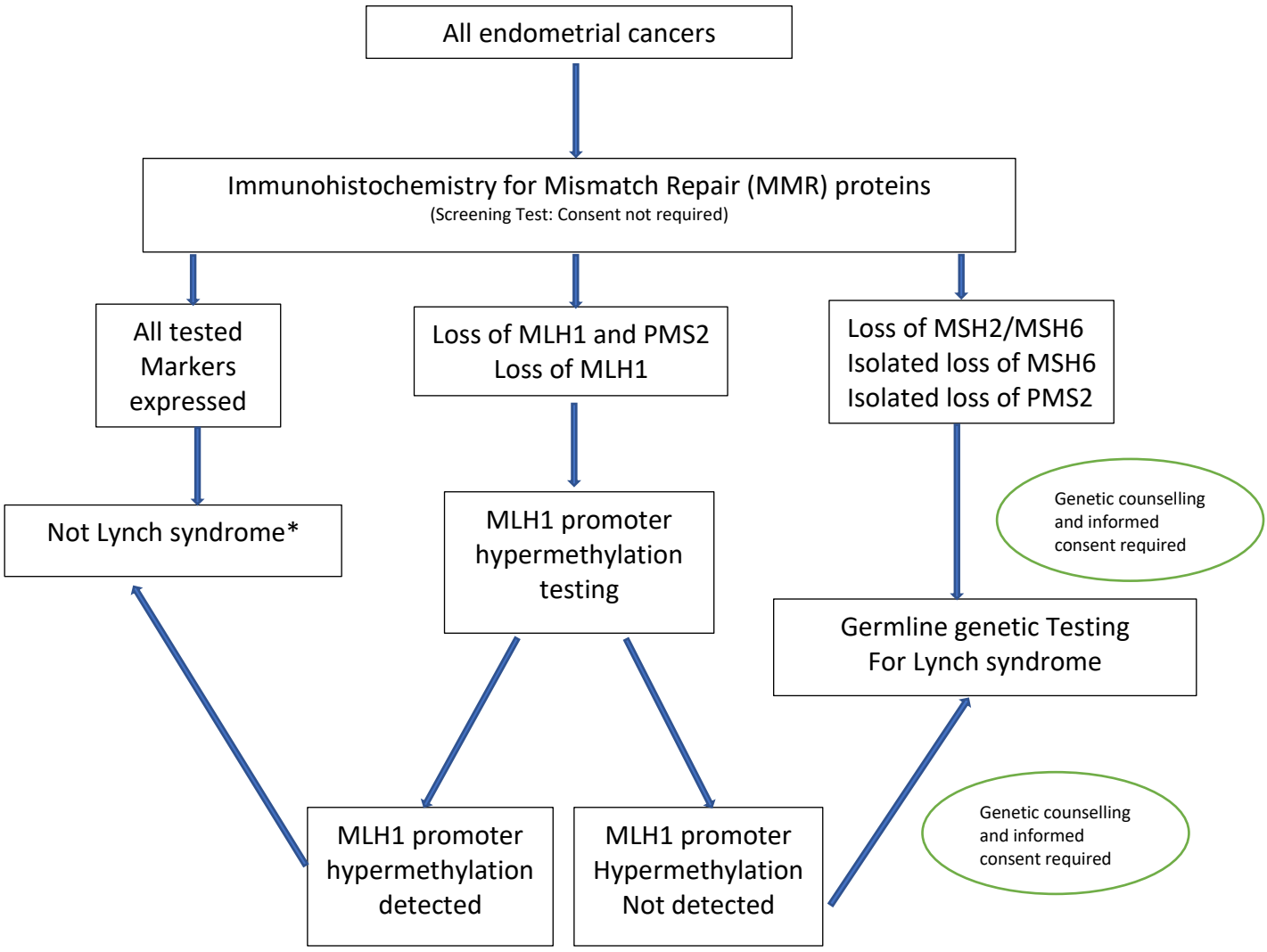
NICE diagnostics guidance DG42: Testing strategies for Lynch syndrome in people with endometrial cancer

On 28th October 2020, the National Institute of Health and Care Excellence (NICE) published the above document stating that testing for Lynch syndrome should be offered when a person is diagnosed with endometrial cancer. Testing is done on tumour tissue by immunohistochemistry, then MLH1 promoter hypermethylation if needed. If the results show that Lynch syndrome is likely, further tests are offered to confirm this. This is a flow chart of the proposed pathway followed by a recap of the terminology (endorsed by NICE in DG42).



MMR result	*Recommended report*	*NICE guideline based action*
Normal, MLH1, PMS2, MSH2 and MSH6 tested **Or** **Normal, only MSH6 and PMS2 tested**	**MMR IHC Normal:** The tumour cells show normal nuclear staining for MLH1, PMS2, MSH2 and MSH6. Conclusion: There is no immunohistochemical evidence of a mismatch repair deficiency or Lynch syndrome.*	**No action***
Abnormal, MSH6 loss	**MMR IHC Abnormal, MSH6 loss:** The tumour cells show loss of expression of the mismatch repair protein MSH6 (with normal nuclear staining for MLH1, MSH2 and PMS2). Conclusion: This mismatch repair deficiency is associated with Lynch and related syndromes.	**Referral for Germline genetic testing for Lynch syndrome**
Abnormal, PMS2 loss	**MMR IHC Abnormal, PMS2 loss:** The tumour cells show loss of expression of the mismatch repair protein PMS2 (with normal nuclear staining for MLH1, MSH2 and MSH6). Conclusion: This mismatch repair deficiency is associated with Lynch and related syndromes.	**Referral for Germline genetic testing for Lynch syndrome**

Abnormal, MSH2 and MSH6 loss	**MMR IHC Abnormal, MSH2 loss:** The tumour cells show loss of expression of the mismatch repair proteins MSH2 and MSH6 (with normal nuclear staining for MLH1 and PMS2). Conclusion: This mismatch repair deficiency is associated with Lynch and related syndromes.	**Referral for Germline genetic testing for Lynch syndrome**
Abnormal, MLH1 and PMS2 loss **Or** **MLH1 loss**	**MMR IHC Abnormal, MLH1 and PMS2 loss MLH1 loss** The tumour cells show loss of expression of the mismatch repair proteins MLH1 and PMS2 (with normal nuclear staining for MSH2 and MSH6). Conclusion: This mismatch repair deficiency requires MLH1 promoter hypermethylation testing	**MLH1 promoter hypermethylation testing** **If MLH1 promoter hypermethylation not detected, referral for germline genetic testing for Lynch syndrome** **If MLH1 promoter hypermethylation detected, no germline testing needed***

* Despite this result, if there is a strong family/clinical history suggestive of Lynch and related syndromes; referral to Clinical Genetics services should be considered.

Link to NICE DG42 https://www.nice.org.uk/guidance/dg42

Link to BAGP guidance document https://www.thebagp.org/resources/?wpdmc=bagp-guidance-documents